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Racial and Ethnic Differences in Initiation and Discontinuation of Antidementia Drugs by Medicare Beneficiaries

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Abstract

BACKGROUND/OBJECTIVES—Clinical practice guidelines support using acetylcholinesterase inhibitors (AChEIs) and memantine to treat dementia, but conflicting evidence of effectiveness and frequent side effects limit use in practice. We examined racial/ethnic differences in initiation and time to discontinuation of antidementia medication in Medicare beneficiaries.

DESIGN—Retrospective cohort study.

SETTING—Secondary analysis of 2009/2010 enrollment, claims, and Part D prescription data for a 10% national sample of U.S. Medicare fee-for-service enrollees.

PARTICIPANTS—Beneficiaries aged 65+ with Alzheimer's Disease or Related Disorder (ADRD) prior to 2009 and no fills for antidementia medications in the first half of 2009 (n=84,043).

MEASUREMENTS—Initiation was defined as having ≥1 fill for antidementia medication in the second half of 2009, and discontinuation as a gap in coverage of ≥30 days during one year after initiation. Covariate selection was guided by the Andersen Behavioral Model.

RESULTS—Overall, 3,481 (4.1%) of previous non-users initiated antidementia medication in the second half of 2009. Of those initiating one drug class (AChEIs or memantine), 9% later added the other class and 2% switched classes. Among initiators, 23% discontinued within one month and 62% discontinued within one year. Hispanic beneficiaries were more likely than White beneficiaries to initiate (adjusted odds ratio [OR]=1.25, 95% CI=1.10-1.41). Black and White beneficiaries did not differ in likelihood of initiation. Hispanic and Black beneficiaries discontinued at a faster rate than White beneficiaries (adjusted hazard ratio [HR]=1.56, 95% CI=1.34-1.82 and HR=1.25, 95% CI=1.08-1.44, respectively).

CONCLUSION—Relative to White beneficiaries, initiation of antidementia medications was no different in Black beneficiaries and more likely in Hispanic beneficiaries. However, Black and Hispanic beneficiaries discontinued at a faster rate. More research into reasons explaining these differences is needed.

Keywords

Dementia; health disparities; anti-dementia medications; Medicare; medication discontinuation

INTRODUCTION

The economic and emotional toll of Alzheimer's disease and related dementias (ADRD) on older adults and their families is substantial.[1] In addition, as cognitive impairment

progresses, dementia patients and their families face a number of difficult decisions about medical care. One decision is whether and when to use antidementia medications, including acetylcholinesterase inhibitors (AChEIs; donepezil, galantamine, rivastigmine, and tacrine) and a N-Methyl-D-aspartate (NMDA) receptor antagonist (memantine).[2] These agents are approved for the symptoms of Alzheimer's Disease and are often used off-label for non-Alzheimer's dementia.[3] Data from randomized trials have shown short-term benefits in cognitive, functional, and behavioral outcomes with these medications.[2,4,5] Persistent use for three years after initiation slows rates of cognitive and functional decline,[6] although does not reverse its course.[7] Although professional organizations recommend antidementia medications for mild to moderate dementia,[8-10] use has been controversial due to lack of convincing evidence in real-world populations that they improve outcomes that are meaningful to patients and caregivers, e.g. quality of life.[11-13] Additionally, as many as one in three patients stop using AChEIs due to adverse effects (nausea, vomiting, diarrhea, dizziness, confusion),[6,14,15] and guidelines regarding optimal timing of initiation and discontinuation are inconsistent.[16-18] This likely contributes to considerable variation in when and how these medications are used.

It is well-established that racial/ethnic minority groups often have lower access to healthcare and medications compared to White patients.[19-21] However, few studies have examined racial and ethnic differences in antidementia medication use, with mixed findings.[22-28] These studies were limited by use of older data, enrollment of small numbers of patients from geographically select areas, or enrollment of patients affiliated with Alzheimer's specialty centers which may provide higher-quality dementia care. There are only a few studies examining racial/ethnic differences in treatment duration or discontinuation with antidementia medication,[27,28] and none in the U.S. Medicare Part D population. Given guidelines supporting the use of these drugs and evidence suggesting benefits of persistent use of these medications, it is important to examine whether racial/ethnic differences exist with regard to their initiation and discontinuation, and underlying reasons driving any differences that are observed.

We used Medicare claims and enrollment data to examine patterns of and racial/ethnic differences in antidementia medication initiation and discontinuation, in a national sample of Medicare fee-for-service (FFS) beneficiaries aged 65+ with ADRD.

METHODS

Setting and Data

The University of Pittsburgh Institutional Review Board (IRB) deemed this study to be exempt from the requirement of IRB review and approval. This retrospective cohort study used 2009-2010 Medicare enrollment, Part A and B medical claims, and Part D prescription drug event (PDE) data for a 10% national sample of FFS beneficiaries (randomly selected on the basis of two digits within their Medicare Claim Account Number) with continuous 2009 enrollment in Medicare Parts A, B, and D (which offer coverage for hospital care, outpatient services, and prescription drugs, respectively). Medical claims (inpatient, skilled nursing, outpatient, home health, hospice, carrier, durable medical equipment) include diagnosis and procedure codes, physician identifiers, and date, place and type of service. The Master

Beneficiary Summary File (MBSF) includes data on demographics, enrollment in different benefits, date of death, and date of first diagnosis for 21 chronic conditions. PDEs capture all prescriptions filled through Part D, including national drug code (NDC), and date and days' supply dispensed. We also linked patients' county of residence to county-level data on healthcare resource availability in the Area Health Resources File (AHRF).[29]

Sample

From these data (n=1,478,852), we identified beneficiaries aged ≥65 years (n=1,121,187, 76%) with a diagnosis of ADRD (n=158,074, 14%) prior to 01/01/2009, as per the MBSF.[30] The MBSF ADRD algorithm contains only minor differences from a claims-based algorithm that has shown good sensitivity (0.85) and specificity (0.89) for identifying dementia as a broad set of conditions when compared to a gold-standard clinical dementia assessment.[31,32] Due to lack of medication data for Medicare Part A-covered skilled nursing facility (SNF) and hospital stays (which are not covered by Part D), we limited the sample to patients who spent <30 days in a hospital or SNF during 2009 (n=136,037, 86%). A "wash-out" period consisting of the first six months of 2009 was also implemented; patients were included if they did not fill prescriptions for AChEIs or memantine during this time (n=88,164, 65%). Finally, we used the MBSF RTI Race Code to limit the sample to non-Hispanic White, Black, and Hispanic beneficiaries. We excluded beneficiaries coded as American Indian/ Alaskan Native (n=417), Asian/Pacific Islander (n=3,034), "Other" (n=523), or missing (n=147) due to small numbers and/or lower accuracy of the RTI Race Code in correctly identifying these races/ethnicities.[33] Thus, 84,043 beneficiaries served as the primary sample for initiation analyses.

For sensitivity analyses limited to patients specifically diagnosed with Alzheimer's Disease (AD), we identified the subset of the full ADRD sample who had at least one inpatient, skilled nursing, home health, outpatient, or carrier claim with an ICD-9 diagnosis code of 331.0 specifically for AD (n=31,013, 36.9%). This code has been shown to have excellent specificity (0.95) but lower sensitivity (0.64) for identifying patients with AD.[32]

For discontinuation analyses, we further limited this sample to those identified as initiators of antidementia medication in the second half of 2009 (July-December; ADRD sample n=3,481; AD subsample n=1,787 [51.3%]), to ensure availability of 12 months of follow-up (until 12/31/2010) to identify discontinuation. Each patient was followed from date of drug initiation until discontinuation (defined below) or censoring. Patients were censored upon death (n=90, 2.6%), discontinuation of Medicare Parts A, B, or D coverage (n=46, 1.3%), enrollment in Medicare Advantage (n=18, 0.5%), accumulating ≥30 days in a SNF or hospital (n=175, 5.0%), or reaching end of follow-up (365 days post- initiation; n=1,067, 30.7%).

Measures

Antidementia Drug Initiation—Beneficiaries were identified as initiating antidementia medications if they had ≥1 dispensing for an NDC corresponding to an AChEI or memantine[34] in PDE files between 7/1/2009-12/31/2009. The specific drug class (AChEI or NMDA receptor antagonist/memantine) initiated was captured, along with subsequent

medication changes occurring after initiation and prior to discontinuation (defined below) or censoring. Patients who initiated an AChEI and then later filled a prescription for memantine were classified as having switched medications if they never filled another AChEI prescription after the memantine prescription; otherwise, they were classified as having added memantine if additional AChEI prescriptions were subsequently filled. A similar process was used to identify patients who initiated memantine and later switched to or added an AChEI.

Antidementia Drug Discontinuation—The primary outcome variable for the discontinuation analysis was number of days between the date of the first fill for antidementia medication until the first gap in antidementia drug availability of ≥30 days,[35] within one year after initiation. To identify gaps, we used dispensing date and days' supply to determine the date on which each antidementia fill would be expected to be exhausted (i.e., the fill end date). If there was no fill for an antidementia medication by 30 days after this end date, patients were assigned a discontinuation date of the first day of the gap. Calculation of gaps occurred at the drug class level (e.g., separately for AChEIs vs. memantine). Patients initiating both classes on the same date or adding or switching to the other class were only counted as having discontinued if there was a 30-day gap in both classes.

Race/Ethnicity—As described above, we used the RTI Race Code to characterize race/ethnicity as Non-Hispanic White, Non-Hispanic Black, or Hispanic.[33]

Covariates—Covariate selection was guided by the Andersen Behavioral Model of health service use.[36] Predisposing factors included sex and age (65-69, 70-74, 75-79, 80+ years). Enabling variables are factors that facilitate patient access to health services. Thus, we created a three-category variable indicating whether beneficiaries were 1) dually enrolled in both Medicare and Medicaid, 2) recipients of the low-income subsidy (LIS) for Part D benefits but not Medicaid, or 3) neither enrolled in Medicaid or the LIS. This variable serves as both a proxy for income as well as the degree of cost-sharing for Part D prescriptions, because Medicare beneficiaries with Medicaid or the LIS are eligible for reduced Part D premiums, deductibles, and copays. The AHRF was used to characterize participants' county of residence with regard to health care accessibility: whether it is a full or partial primary care shortage area; number of federally qualified health centers (FQHCs) (0, 1, or 2+); and rurality using U.S. Department of Agriculture Urban Influence Codes (large metropolitan, small metropolitan, micropolitan, non-core rural).[37] Finally, because providers of different specialties may differ in propensity for prescribing antidementia medications, we captured number of outpatient encounters with primary care providers, neurologists, and geriatricians.[38,39] Medical need variables included comorbidity using the Charlson index[40] applied to 2009 medical claims (categorized as 0, 1, 2, 3, 4, 5+ because of high skewness); Alzheimer's versus non-Alzheimer's dementia; duration since the patient's first Medicare claim for ADRD (0.5 to <1 year, 1 to <2 years, 2 to <5 years, 5+ years); and number of hospital admissions during the washout period.

Analytic Approach

Analyses were conducted with SAS v9.4 (SAS, Inc., Cary, NC) and Stata v14 (StataCorp LP, College Station, TX). We described predisposing, enabling, and medical need variables for the sample and used chi-square tests to compare across race/ethnicity groups. We calculated the proportion of baseline non-users who initiated any antidementia medication in the second half of 2009. We examined proportions initiating AChEIs vs. memantine vs. both classes of medications, and proportions subsequently switching to or adding the other class. We used logistic regression to examine unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between race/ethnicity and initiation of antidementia medication.

We used a Kaplan-Meier survival curve to illustrate the time (in days) from initiation until discontinuation by racial/ethnic group, and a log-rank test to compare differences across groups. We estimated Cox proportional hazards models to identify unadjusted and adjusted associations of race/ethnicity with time to discontinuation.

We ran two sensitivity analyses. First, to examine whether patterns of initiation and discontinuation across racial/ethnic groups were different for patients diagnosed specifically with Alzheimer's versus non-Alzheimer's dementia, we re-ran all analyses for the Alzheimer's subsample. Second, we re-ran all discontinuation models using a more conservative definition of discontinuation used in some prior studies,[41,42] requiring a gap in antidementia drug availability of ≥60 days instead of ≥30 days.

Very few (0.6%) patients had missing values for any variables; all multivariable analyses were conducted using listwise deletion.

RESULTS

Sample Characteristics

Of the 84,043 ADRD patients who were baseline non-users of antidementia medications (Table 1), 79.5% were White, 11.6% Black, and 8.9% Hispanic. A majority were female (71.8%) and ≥80 years old (60.0%); 41.4% were dually eligible for Medicaid and 12.6% received the Part D LIS. Almost 37% (n=31,013) had a claim for Alzheimer's Disease, and the majority had their first Medicare ADRD claim ≥2 years prior to the study period. Chi-square tests revealed significant differences ($p<.0001$) in all characteristics by race/ethnicity. Compared to White beneficiaries, Black and Hispanic beneficiaries were younger and more likely to be dually eligible for Medicaid, live in a large metropolitan area and counties with FQHCs, and have Alzheimer's ($p<.0001$). Differences shown in Table 1 for characteristics of Black versus Hispanic patients were all statistically significant ($p<.0001$), except dementia type and baseline hospital admissions.

Patterns of initiation, switching, and discontinuation

Among non-users of antidementia medication in the first half of 2009, 4.1% (n=3,481) initiated antidementia medication in the second half of 2009. As shown in Table 2, 68.7% of new users initiated AChEIs, 26.5% initiated memantine, and 4.9% initiated both classes

simultaneously. Of 2,390 patients initiating AChEIs, 9.3% subsequently added memantine and 2.3% switched to memantine. Of 921 patients initiating memantine, 11.7% subsequently added AChEIs and 1.9% switched to AChEIs. Sixty percent of initiators subsequently discontinued use of all antidementia medications during follow-up.

Initiation analyses

As shown in Table 3, 4.1% of White patients initiated antidementia medications, compared to 3.8% of Black patients and 4.9% of Hispanic patients. Odds of initiation among Hispanic patients were significantly higher versus White patients in unadjusted (OR=1.19, 95% CI=1.06, 1.33) and fully adjusted analyses (OR=1.25, 95% CI=1.10, 1.41). There were no significant differences in unadjusted or adjusted odds of initiation in Black versus White patients. Other factors independently associated with greater odds of initiation included older age, Alzheimer's diagnosis, greater co-morbidity, more primary care visits, and having seen a neurologist or geriatrician in the baseline period. Patients receiving Medicaid or the LIS, living in a primary care shortage area, living in a county with ≥2 FQHCs, living in a small metropolitan county, with longer duration since first ADRD claim, and having ≥2 baseline hospital admissions had lower odds of initiation.

Discontinuation Analysis

Kaplan-Meier analyses revealed that 23.2% of initiators with ADRD discontinued use at 30 days and 62.4% within one year. The rate of discontinuation varied significantly by race/ethnicity ($p<.001$ for log-rank test), with 60.5% of Whites discontinuing by one year, versus 64.1% of Black patients and 75.1% of Hispanic patients (Figure 1).

In the unadjusted proportional hazards model (Table 4), Hispanic patients demonstrated faster discontinuation versus White patients (HR=1.45, 95% CI=1.27-1.65). There was no difference in discontinuation rate for Black versus White patients (HR=1.11, 95% CI=0.97-1.28). After adjustment, both minority groups exhibited faster discontinuation compared to White patients (Table 4). In addition, having primary care visits during baseline predicted faster discontinuation, while female sex, receipt of Medicaid or LIS, and small metropolitan county of residence predicted slower discontinuation.

Sensitivity Analyses—A total of 5.7% (n=1,787) of the Alzheimer's subsample initiated antidementia medication, compared to 4.1% of all ADRD patients. However, the results of all other analyses were substantively similar for the Alzheimer's subsample, including overall rates of discontinuation, racial/ethnic differences in initiation and discontinuation, and other significant predictors of initiation and discontinuation (results available from author). When a 60-day gap was used to identify discontinuation, 18.1% of initiators with ADRD discontinued at 30 days and 52.6% within one year. However, the observed racial/ethnic differences and other predictors of discontinuation remained substantively unchanged (results available upon request).

DISCUSSION

In this national sample of 84,043 Medicare beneficiaries with dementia, we observed racial/ethnic differences in patterns of initiation and discontinuation of antidementia medications. Compared to White beneficiaries, Hispanic beneficiaries were more likely to initiate antidementia medications, although they also discontinued them at a faster rate. In addition, although we observed no difference between Black and White beneficiaries in initiation, Black patients also discontinued medications at a faster rate. These results were robust when limiting to patients specifically diagnosed with Alzheimer's (for which antidementia medications are specifically indicated), and when a more conservative 60-day (rather than 30-day) gap in medication supply was used to identify discontinuation. Our multivariate analyses also showed that these racial/ethnic differences could not be explained by differences in predisposing, enabling, or medical need factors assessed in this study.

This study provides updated national U.S. data on patterns of antidementia medication use in Medicare Part D fee-for-service enrollees with dementia. In developing our sample, we found that 35% of Medicare beneficiaries with dementia were taking antidementia medication over the six-month wash-out period, and an additional 4% of remaining non-users initiated them in the following six months. This annual prevalence estimate is higher than the previously-reported estimate of just 26% of MCBS respondents during the pre-Part D era.[23] These results are consistent with data showing that implementation of the Medicare Part D policy increased use of antidementia medications in Medicare Advantage beneficiaries.[43] We also found that almost a quarter of new users discontinued by one month and 63% discontinued by one year, although one-month and one-year discontinuation rates were reduced to 18% and 53%, respectively, when the more conservative 60-day gap was used to identify discontinuation. These observed rates of discontinuation within one year are consistent with ranges reported in recent studies conducted in Europe, Canada, and state Medicaid programs.[41,42,44,45]

Our study adds in several ways to the limited and conflicting existing data on racial/ethnic differences in use of antidementia medications by examining more recent patterns of antidementia medication initiation and discontinuation in a larger, national, and more generalizable dataset. We found that Hispanic beneficiaries were more likely to initiate medications than White beneficiaries, but also subsequently discontinued them at a faster rate. In contrast, no difference in likelihood of initiation was seen for Black compared to White beneficiaries, but Blacks discontinued at a faster rate. These findings are somewhat in contrast to the MCBS prevalence study conducted in the pre-Part D era, which found higher annual prevalence of use among Whites compared to Hispanic and Black beneficiaries,[23] but are consistent with findings from a prior study of users of the Veterans Affairs healthcare system,[28] where access to medications is generally greater. Our findings may reflect an overall effect of Medicare Part D on reducing disparities in access to medications between Hispanic and White patients that has been reported for other medications.[46]

The observed racial/ethnic differences in discontinuation persisted after controlling for all other independent variables in multivariate analyses, suggesting that they are not driven by racial/ethnic differences in these predisposing, enabling, or medical need factors and are

likely due to other, unmeasured factors. Specifically, our results suggest that the faster discontinuation observed among minorities is not likely cost-related. Minorities were more likely to be dually enrolled in Medicaid or receive the LIS, which reduces beneficiary cost burden, and the observed differences in discontinuation persisted after controlling for Medicaid and LIS enrollment. Faster discontinuation rates among minority groups could also not be explained by racial/ethnic differences in age, comorbidity, or diagnosis with Alzheimer's versus another type of dementia (i.e., off-label prescribing for non-Alzheimer's dementia). Finally, geographical availability of healthcare resources or access to healthcare providers of various specialties did not explain observed racial/ethnic differences, although we cannot rule out the role of differential access to higher-quality vs. lower-quality care.

Experiences of side effects or adverse drug events.[47] perceived decline in cognitive/functional status, and worsening behavioral symptoms[47] have been linked in prior studies to discontinuation of antidementia medication. As we did not have data on these factors, it is possible that they contribute to faster discontinuation in minority groups. In addition, we did not examine initiation and discontinuation for different types of AChEIs, which may have different rates of adherence and tolerability.[45]

Differential knowledge, attitudes, and beliefs about dementia and antidementia medication across racial/ethnic groups, as well as provider and health care system factors, may also contribute to disparities in discontinuation. Prior research has shown that Black and Hispanic individuals are more likely to view memory loss as a normal part of aging, and tend to be less knowledgeable about dementia, compared to White individuals.[48] Although minorities with good access to care and few financial barriers may be willing to try antidementia medications when presented this option, their less medicalized view of dementia may contribute to lower persistence with these medications, especially if they experience side effects or perceive low effectiveness. Lack of effective provider education and communication about these issues, low cultural competency among providers, and lower trust in providers by minority patients[48] may also contribute.

Our study has several limitations. We relied on ICD-9 codes to identify dementia patients, which have some error. We likely missed identifying some patients as specifically having Alzheimer's versus another type of dementia, as the 331.0 ICD-9 code has lower sensitivity (64%) for identifying Alzheimer's, compared to the sensitivity of the set of ADRD codes for identifying dementia (85%). However, the algorithms we used have demonstrated good sensitivity and specificity for identifying dementia as a broad set of conditions and high specificity (95%) for Alzheimer's Disease,[32] and the proportion of our full ADRD sample with Alzheimer's tracks closely with data reported by the Medicare Chronic Conditions Warehouse.[49] Because of small numbers and lower accuracy in identifying Asian and Alaskan Native/American Indian beneficiaries, we were unable to examine differences in initiation or discontinuation for these groups. We lacked measures of dementia severity and symptoms, and could not examine these as contributors to racial differences. Although we are able to construct a proxy for dementia duration using the date of the first ADRD claim, this may not accurately reflect duration for more recently enrolled Medicare beneficiaries or those experiencing delays in diagnosis. In addition, our measures of medication initiation and discontinuation reflect prescription refills rather than actual medication ingestion.

Finally, although our results are generalizable to the large population of U.S. Medicare FFS beneficiaries with ADRD, their generalizability to other populations is unknown.

CONCLUSION

This large national study of Medicare beneficiaries confirms less recent studies in smaller, select samples or conducted outside of the U.S. showing short treatment duration for antidementia medications, and may be reflective of low perceived effectiveness and high frequency of side effects experienced by patients and their caregivers. It also suggests that racial/ethnic minority groups discontinue these medications more quickly than White patients, for reasons that may be unrelated to medication cost or access to care. Future studies should investigate the role of knowledge and beliefs about antidementia medication, the patient/caregiver-provider relationship, and provider and system factors as possible contributors to differences in duration of antidementia medication use.

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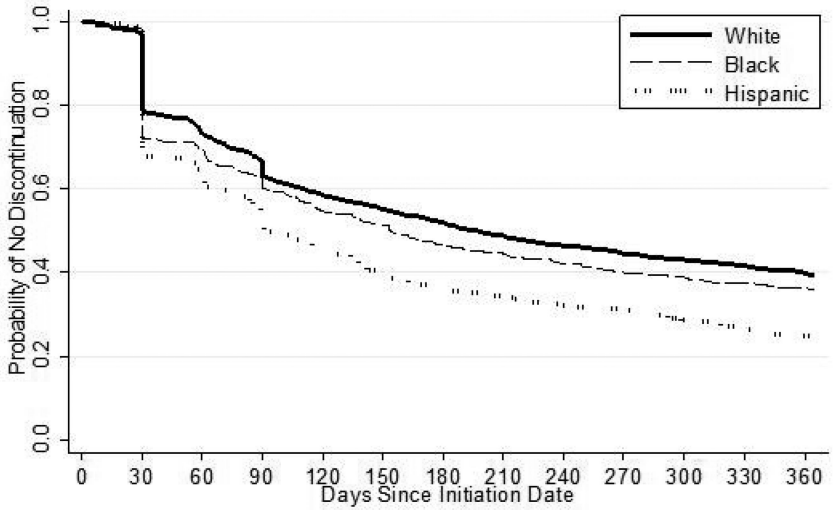

Figure 1.

Kaplan-Meier plot of time to antidementia medication discontinuation, by beneficiary race/ethnicity.

Table 1

Characteristics of Fee-for-Service Medicare Beneficiaries with Alzheimer's Disease or a Related Disorder (ADRD) Not Using Antidementia Medications in the First Half of 2009, Overall and by Race/Ethnicity.

	All Patients N=84,043 (100%) n (%)	White N=66,806 (79.5%) n (%)	Black N=9,781 (11.6%) n (%)	Hispanic N=7,456 (8.9%) n (%)	p-value[a]
Sex					<.0001
Male	23717 (28.2)	18567 (27.8)	2676 (27.4)	2474 (33.2)	
Female	60326 (71.8)	48239 (72.2)	7105 (72.6)	4982 (66.8)	
Age at 07/01/2009					<.0001
65-69 years	6837 (8.1)	4999 (7.5)	1103 (11.3)	735 (9.9)	
70-74 years	11669 (13.9)	8622 (12.9)	1643 (16.8)	1404 (18.8)	
75-79 years	15097 (18.0)	11593 (17.4)	1812 (18.5)	1692 (22.7)	
80+ years	50440 (60.0)	41592 (62.3)	5223 (53.4)	3625 (48.6)	
Part D low-income subsidy or Dually eligible for Medicaid ever in baseline					<.0001
No Medicaid or low-income subsidy	38664 (46.0)	35719 (53.5)	1660 (17.0)	1285 (17.2)	
Low-income subsidy but no Medicaid	10624 (12.6)	8719 (13.1)	1360 (13.9)	545 (7.3)	
Medicaid	34755 (41.4)	22368 (33.5)	6761 (69.1)	5626 (75.5)	
Primary care shortage area					<.0001
Not a shortage area	35093 (41.8)	26311 (39.4)	4815 (49.2)	3967 (53.2)	
Partial shortage area	36263 (43.1)	29334 (43.9)	3969 (40.6)	2960 (39.7)	
Full shortage area	12589 (15.0)	11105 (16.6)	972 (9.9)	512 (6.9)	
Missing		56 (0.1)	25 (0.3)	17 (0.2)	
Federally qualified health centers in county					<.0001
0 centers	20085 (23.9)	18002 (26.9)	1437 (14.7)	646 (8.7)	
1 center	13178 (15.7)	11291 (16.9)	1374 (14.0)	513 (6.9)	
2 or more centers	50682 (60.3)	37457 (56.1)	6945 (71.0)	6280 (84.2)	
Missing	98 (0.1)	56 (0.1)	25 (0.3)	17 (0.2)	
Area of residence					<.0001
Large metro	37946 (45.2)	27778 (41.6)	5712 (58.4)	4456 (59.8)	
Small metro	25147 (29.9)	20856 (31.2)	2323 (23.8)	1968 (26.4)	
Micropolitan	11322 (13.5)	9946 (14.9)	960 (9.8)	416 (5.6)	
Non-core rural	9139 (10.9)	8170 (12.2)	760 (7.8)	209 (2.8)	
Missing	504 (0.6)	56 (0.1)	26 (0.3)	407 (5.5)	
Visits to primary care in baseline					<.0001
0 visits	40849 (48.6)	32278 (48.3)	5480 (56.0)	3091 (41.5)	
1 visit	11399 (13.6)	9345 (14.0)	1173 (12.0)	881 (11.8)	
2 visits	10752 (12.8)	8655 (13.0)	1162 (11.9)	935 (12.5)	
3 or more visits	21043 (25.0)	16528 (24.7)	1966 (20.1)	2549 (34.2)	
Any visits to neurologist in baseline					<.0001
No	77467 (92.2)	61230 (91.7)	9344 (95.5)	6893 (92.4)	
Yes	6576 (7.8)	5576 (8.3)	437 (4.5)	563 (7.6)	

	All Patients N=84,043 (100%) n (%)	White N=66,806 (79.5%) n (%)	Black N=9,781 (11.6%) n (%)	Hispanic N=7,456 (8.9%) n (%)	p-value[a]
Any visits to geriatrician in baseline					<.0001
No	83179 (99.0)	66158 (99.0)	9640 (98.6)	7381 (99.0)	
Yes	864 (1.0)	648 (1.0)	141 (1.4)	75 (1.0)	
Dementia Type					<.0001
Non-Alzheimer's[c]	53030 (63.1)	42729 (64.0)	5847 (59.8)	4454 (59.7)	
Alzheimer's[d]	31013 (36.9)	24077 (36.0)	3934 (40.2)	3002 (40.3)	
Duration at 07/01/2009 since dementia diagnosis					<.0001
0.5 to <1 year	7772 (9.2)	6289 (9.4)	807 (8.3)	676 (9.1)	
1 to <2 years	14706 (17.5)	11839 (17.7)	1566 (16.0)	1301 (17.4)	
2 to <5 years	31764 (37.8)	25329 (37.9)	3491 (35.7)	2944 (39.5)	
5+ years	29801 (35.5)	23349 (35.0)	3917 (40.0)	2535 (34.0)	
Charlson score in 2009					<.0001
0	8338 (9.9)	6587 (9.9)	908 (9.3)	843 (11.3)	
1	9852 (11.7)	7893 (11.8)	1004 (10.3)	955 (12.8)	
2	11842 (14.1)	9664 (14.5)	1184 (12.1)	994 (13.3)	
3	13332 (15.9)	10866 (16.3)	1427 (14.6)	1039 (13.9)	
4	11951 (14.2)	9706 (14.5)	1322 (13.5)	923 (12.4)	
5 or more	28728 (34.2)	22090 (33.1)	3936 (40.2)	2702 (36.2)	
Hospital admissions in baseline					<.0001
None	73916 (88.0)	59103 (88.5)	8405 (85.9)	6408 (85.9)	
1	7943 (9.5)	6127 (9.2)	1021 (10.4)	795 (10.7)	
2 or more	2184 (2.6)	1576 (2.4)	355 (3.6)	253 (3.4)	

[a] Chi-square test for differences between initiators and non-initiators.

Table 2

Patterns of initiation, switching, and discontinuation of antidementia medications in previous non-users.

	Initiation N=3,481, 100% n (%)	**Discontinuation N=2,085, 59.9% n (%)**
Initiated AChEI	2390 (68.7)	1438 (60.2)
Single drug, consistently on AChEI only	2112 (88.4%)	1373 (65.0)
Switched from AChEI to memantine	56 (2.3%)	25 (44.6)
Added memantine	222 (9.3%)	40 (18.0)
Initiated memantine	921 (26.5)	548 (59.5)
Single drug, consistently on memantine only	796 (86.4%)	501 (62.9)
Switched from memantine to AChEI	17 (1.9)	11 (64.7)
Added AChEI	108 (11.7)	36 (33.3)
Initiated both AChEI and memantine at the same date	170 (4.9)	99 (58.2)

Table 3

Unadjusted and adjusted associations of patient race/ethnicity and other socio-demographic, clinical, and provider factors with initiation of antidementia medication in the second half of 2009 among baseline non-users.

	N (%) Initiating Medication N=84,043	Unadjusted OR (95% CI) N=84,043	Adjusted OR (95% CI) N=83,554[a]
Race and ethnicity			
White	2,744 (4.1%)	1.00	1.00
Black	375 (3.8%)	0.93 (0.83, 1.04)	1.03 (0.92,1.16)
Hispanic	362 (4.9%)	1.19 (1.06, 1.33)**	1.25 (1.10,1.41)***
Sex			
Male			1.00
Female			1.03 (0.95,1.11)
Age, n (%)			
65-69 years			1.00
70-74 years			1.32 (1.11,1.56)**
75-79 years			1.59 (1.35,1.87)***
80+ years			1.57 (1.35,1.82)***
Part D low-income subsidy or Dually eligible for Medicaid ever in baseline			
No Medicaid or low-income subsidy			1.00
Low-income subsidy but no Medicaid			0.80 (0.71,0.90)***
Medicaid			0.86 (0.79,0.94)***
Primary care shortage area			
Not a shortage area			1.00
Partial shortage area			0.92 (0.85,0.99)*
Full shortage area			0.87 (0.77,0.98)*
Federally qualified health centers in county			
0 centers			1.00
1 center			0.95 (0.85,1.07)
2 or more centers			0.89 (0.80,0.99)*
Rural/urban area of residence			
Large metro			1.00
Small metro			0.92 (0.84,0.99)*
Micropolitan			0.95 (0.84,1.06)
Non-core rural			0.96 (0.84,1.09)
Visits to primary care in baseline			
0 visits			1.00

	N (%) Initiating Medication N=84,043	Unadjusted OR (95% CI) N=84,043	Adjusted OR (95% CI) N=83,554[a]
1 visit			1.44 (1.30,1.61)***
2 visits			1.36 (1.22,1.52)***
3 or more visits			1.42 (1.29,1.55)***
Any visits to neurologist in baseline			
No			1.00
Yes			1.69 (1.52,1.87)***
Any visits to geriatrician in baseline			
No			1.00
Yes			1.34 (1.01,1.79)*
Alzheimer's disease			
No			1.00
Yes			2.15 (2.00,2.31)***
Duration since first Medicare claim for ADRD			
Less than 1 year			1.00
Less than 2 years			0.95 (0.84,1.07)
2 to 5 years			0.67 (0.60,0.75)***
More than 5 years			0.45 (0.40,0.51)***
Charlson co-morbidity score			
0			1.00
1			1.27 (1.08,1.50)**
2			1.28 (1.10,1.51)**
3			1.31 (1.12,1.53)***
4			1.39 (1.19,1.63)***
5 or more			1.56 (1.35,1.80)***
Hospital admissions in baseline			
None			1.00
1			0.93 (0.83,1.04)
2 or more			0.75 (0.59,0.94)*

[a] 489 (0.6%) of patients were removed from the full sample of 84,043 for imitation analysis due to missing data.

* p<.05

** p<.01

*** p≤.001

Table 4

Unadjusted and adjusted associations of patient race/ethnicity and other socio-demographic, clinical, and provider factors with time to medication discontinuation, among those initiating antidementia medications in the second half of 2009.

	Unadjusted HR (95% CI) N=3,481	Adjusted HR (95% CI) N=3458[a]
Race and ethnicity		
White	1.00	1.00
Black	1.11 (0.97, 1.28)	1.25 (1.08,1.44)**
Hispanic	1.45 (1.27, 1.65)***	1.56 (1.34,1.82)***
Initiation drug type		
AChEI		1.00
Memantine		0.97 (0.88,1.07)
Both prescribed at the same date		0.93 (0.76,1.15)
Sex		
Male		1.00
Female		0.86 (0.78,0.95)**
Age, n (%)		
65-69 years		1.00
70-74 years		1.14 (0.91,1.42)
75-79 years		1.11 (0.90,1.37)
80+ years		1.08 (0.89,1.31)
Part D low-income subsidy or Dually eligible for Medicaid ever in baseline		
No Medicaid or low-income subsidy		1.00
Low-income subsidy but no Medicaid		0.77 (0.66,0.90)***
Medicaid		0.77 (0.69,0.86)***
Primary care shortage area		
Not a shortage area		1.00
Partial shortage area		0.96 (0.87,1.05)
Full shortage area		1.03 (0.88,1.19)
Federally qualified health centers in county		
0 centers		1.00
1 center		1.04 (0.89,1.21)
2 or more centers		1.11 (0.97,1.27)
Rural/urban area of residence		
Large metro		1.00
Small metro		0.91 (0.81,1.01)
Micropolitan		0.97 (0.84,1.13)
Non-core rural		0.99 (0.84,1.18)
Visits to primary care in baseline		
0 visits		1.00

	Unadjusted HR (95% CI) N=3,481	Adjusted HR (95% CI) N=3458[a]
1 visit		1.14 (1.00,1.31)*
2 visits		1.22 (1.06,1.39)**
3 or more visits		1.26 (1.13,1.40)***
Any visits to neurologist in baseline		
No		1.00
Yes		1.01 (0.89,1.14)
Any visits to geriatrician in baseline		
No		1.00
Yes		1.26 (0.90,1.77)
Alzheimer's disease		
No		1.00
Yes		1.04 (0.95,1.13)
Duration since first Medicare claim for ADRD		
Less than 1 year		1.00
Less than 2 years		0.94 (0.81,1.09)
2 to 5 years		0.95 (0.82,1.09)
More than 5 years		1.00 (0.86,1.16)
Charlson co-morbidity score		
0		1.00
1		1.00 (0.81,1.23)
2		1.11 (0.91,1.35)
3		1.00 (0.82,1.22)
4		0.93 (0.76,1.14)
5 or more		1.00 (0.84,1.20)
Hospital admissions in baseline		
None		1.00
1		0.93 (0.80,1.07)
2 or more		0.99 (0.75,1.31)

[a] 23 (0.7%) patients were removed from the full sample of 3,481 for discontinuation analysis due to missing data

* p<.05

** p<.01

*** p≤.001