Exploratory Research in Clinical and Social Pharmacy 13 (2024) 100420

Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop

Effects of Medicare Part D medication therapy management on racial/ethnic disparities in adherence to antidementia medications among patients with Alzheimer's disease and related dementias: An observational study

Xiaobei Dong [a,1], Chi Chun Steve Tsang [a], Jim Y. Wan [b], Marie A. Chisholm-Burns [a,2], Christopher K. Finch [a], Jack W. Tsao [c,3], Jamie A. Browning [a], Joseph Garuccio [a], Rose Zeng [a], Junling Wang [a,*]

[a] Department of Clinical Pharmacy and Translational Science, University of Tennessee Health Science Center College of Pharmacy, 881 Madison Avenue, Memphis, TN 38163, USA
[b] Department of Preventive Medicine, University of Tennessee Health Science Center College of Medicine, 66 North Pauline St, Memphis, TN 38163, USA
[c] Department of Neurology, University of Tennessee Health Science Center College of Medicine, 855 Monroe Avenue, Memphis, TN 38163, USA

ARTICLE INFO

Keywords:
Health care policy
Health disparities
Health services use

ABSTRACT

Background: Evidence is sparse on the effects of Medicare medication therapy management (MTM) on racial/ethnic disparities in medication adherence among patients with Alzheimer's disease and related dementias.
Objectives: This study examined the Medicare MTM program's effects on racial/ethnic disparities in the adherence to antidementia medications among patients with Alzheimer's disease and related dementias.
Methods: This is a retrospective analysis of 100% of 2010–2017 Medicare Parts A, B, and D data linked to Area Health Resources Files. The study outcome was nonadherence to antidementia medications, and intervention was defined as new MTM enrollment in 2017. Propensity score matching was conducted to create intervention and comparison groups with comparable characteristics. A difference-in-differences model was employed with logistic regression, including interaction terms of dummy variables for the intervention group and racial/ethnic minorities.
Results: Unadjusted comparisons revealed that Black, Hispanic, and Asian/Pacific Islander patients were more likely to be nonadherent than non-Hispanic White (White) patients in 2016. Differences in odds of nonadherence between Black and White patients among the intervention group were lower in 2017 than in 2016 by 27% (odds ratios [OR]: 0.73, 95% confidence interval [CI]: 0.65–0.82). A similar lowering was seen between Hispanic and White patients by 26% (OR: 0.74, 95% CI: 0.63–0.87). MTM enrollment was associated with reduced disparities in nonadherence for Black-White patients of 33% (OR: 0.67, 95% CI: 0.57–0.78) and Hispanic-White patients of 19% (OR: 0.81, 95% CI: 0.67–0.99).
Discussion: The Medicare MTM program was associated with lower disparities in adherence to antidementia medications between Black and White patients, and between Hispanic and White patients in the population with Alzheimer's disease and related dementias.

Abbreviations: AD, Alzheimer's disease; ADRD, Alzheimer's disease and related dementias; AHRF, Area Health Resources Files; Asian, Asian/Pacific Islander; CI, Confidence interval; CMS, Centers for Medicare and Medicaid Services; DID, Difference-in-Differences; FDA, Food and Drug Administration; HSPA, Health Professional Shortage Area; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; MSA, Metropolitan statistical area; MTM, Medication Therapy Management; OR, Odds ratio; PDC, Proportion of days covered; PQA, Pharmacy Quality Alliance; White, Non-Hispanic White..

* Corresponding author.
E-mail addresses: xdong16@uthsc.edu (X. Dong), ctsang@uthsc.edu (C.C.S. Tsang), jwan@uthsc.edu (J.Y. Wan), mchisho3@uthsc.edu (M.A. Chisholm-Burns), cfinch@uthsc.edu (C.K. Finch), jtsao@uthsc.edu (J.W. Tsao), jwiggi10@uthsc.edu (J.A. Browning), jgarucci@uthsc.edu (J. Garuccio), rzeng3@uthsc.edu (R. Zeng), jwang26@uthsc.edu (J. Wang).
[1] Present: Assistant Professor, Joseph J. Zilber College of Public Health, University of Wisconsin-Milwaukee. E-mail address: dong7@uwm.edu.
[2] Present: J.S. Reinschmidt Endowed Professor and Executive Vice President and Provost, Oregon Health and Science University. E-mail address: chishmar@ohsu.edu.
[3] Present: Professor, Department of Neurology, Grossman School of Medicine, New York University. E-mail address: jack.tsao@nyulangone.org.

https://doi.org/10.1016/j.rcsop.2024.100420
Received 12 April 2023; Received in revised form 18 August 2023; Accepted 8 February 2024
Available online 10 February 2024

Conclusions: Expanding the MTM program may particularly benefit racial/ethnic minorities in Alzheimer's disease and related dementia care.

Introduction

Alzheimer's disease and related dementias (ADRD) is an umbrella term encompassing Alzheimer's disease (AD) and other forms of dementia, including frontotemporal degeneration, Lewy body dementia, vascular contributions to cognitive impairment and dementia, and mixed etiology dementias.[1] More than six million older Americans aged ≥65 years are estimated to have ADRD in 2021, accounting for 11% of the U.S. population in this age group.[2] This estimate is projected to increase to nearly 14 million by 2060, marking more than a twofold increase in less than four decades.[2]

ADRD are devastating conditions whose burden on patients and society manifests in multiple aspects. Pharmacologically, no treatment cures or slows the progression of ADRD. Thus far, the U.S. Food and Drug Administration (FDA) has approved six medications, five of which (i.e., donepezil, galantamine, rivastigmine, memantine, and memantine combined with donepezil) are antidementia medications and merely intended to mitigate cognitive symptoms.[2] Aducanumab, a medication that received accelerated FDA approval in June 2021, is the only treatment option touted to delay the progression of AD.[3] While it is still too early to fully evaluate the effects of aducanumab, evidence on the other five medications is mixed.[4,5] In particular, previous studies revealed minor enhancements in cognitive functioning among individuals with mild dementia who took antidementia medications.[4,5] These medications act to decelerate but do not reverse cognitive decline, leading to limited effects on the recovery of patients' behavioral symptoms.[4,5] Nonetheless, due to their prospects of improving patients' quality of life, the medications have been included in recommended treatment guidelines and are widely prescribed to patients with ADRD.[5,6]

The availability of these antidementia medications, however, does not equate to effective utilization of them. Medication nonadherence is common among older patients with ADRD due to memory loss and cognitive impairment.[7] The proportion of patients nonadherent to oral antidementia medications ranges from 33%[8,9] to over 40%.[10] Aside from pharmacological and medication management challenges, ADRD care is costly for both individuals and society. The estimated cost of care in 2021 totaled $355 billion, with the largest share (51%) covered by Medicare.[2] Older Medicare beneficiaries with ADRD incur out-of-pocket expenses that are more than four times higher than those without ADRD.[2]

To control costs and improve therapeutic outcomes for patients with challenging diseases such as ADRD, the Centers for Medicare and Medicaid Services (CMS) has since required Medicare Part D sponsors to provide medication therapy management (MTM) services to eligible Medicare beneficiaries.[11] Medicare Part D is Medicare's outpatient prescription drug benefit, offered through either a Medicare managed care (Medicare Advantage) plan or a stand-alone prescription drug plan. Mostly provided by pharmacists, MTM services typically include medication reviews and follow-up action plans.[12] Each Part D sponsor establishes its own MTM eligibility criteria using the CMS guidelines, which mandate that sponsors target beneficiaries with multiple chronic conditions, take multiple Part D medications, and are likely to incur high medication expenditures.[12] In addition, the guidelines require sponsors to choose from a list of core chronic conditions, including AD, when determining the specific conditions to target in their MTM eligibility criteria.[12]

Evidence on the positive effects of Medicare MTM on medication adherence has thus far been limited. A CMS-commissioned evaluation reported a positive effect on MTM enrollees with diabetes, congestive heart failure, and chronic obstructive pulmonary disease.[13] Among more recent studies, Peasah and colleagues noted that a more robust MTM intervention led to increased anticoagulant adherence among Medicare beneficiaries.[14] Another study focusing on AD patients found that comprehensive medication review, a required component of the Medicare MTM program, had reduced nonadherence to medications for diabetes, hypertension, and hyperlipidemia.[15] These findings were consistent with results from the broader literature on non-Medicare MTM services that generally noted a positive effect of such services on adherence, although the evidence is far from conclusive due to heterogeneity in methodology and sample size across studies.[16,17]

In the MTM literature, few studies have examined the effects of MTM on medication utilization by racial/ethnic minorities. This is primarily due to the lack of these patient characteristics in publicly available data.[16,18] Several studies reported racial/ethnic disparities in the use of antidementia medications among ADRD patients, such as finding minorities less likely to be treated with antidementia medications than non-Hispanic Whites (Whites).[19] Minorities also used fewer antidementia medications[6,20,21] and discontinued the medications faster.[22] We bridge the gap in MTM and ADRD research by examining the effects of the Medicare MTM program on racial/ethnic disparities in adherence to antidementia medications among older beneficiaries with ADRD.

Methods

Data Source

We conducted a retrospective study using 100% of 2010–2017 Medicare Parts A/B/D administrative data linked to the Master Beneficiary Summary File and Area Health Resources Files (AHRF).[23,24] Medicare administrative data and Master Beneficiary Summary File provided information on diagnosis records, medication fills, MTM enrollment, and beneficiary demographic characteristics.[23] The AHRF provided county-level data on the socioeconomic and health service characteristics of the beneficiaries' county of residence.[24] All Medicare data, including Part A/B/D records and Master Beneficiary Summary File, were accessed through the CMS Virtual Research Data Center (VRDC). The AHRF data were uploaded to the VRDC by the research team.

Study Sample

We identified our study sample based on the following inclusion criteria for beneficiaries: (1) had an ADRD diagnosis; (2) were at least 65 years of age at the beginning of 2016 and alive at the end of 2017; (3) maintained continuous Parts A, B, and D coverage; and (4) had at least two prescription claims for antidementia medications and >60 days of supply in each of the two years.[25] Patients with ADRD diagnoses were identified using data from 2010 to 2016 based on the International Classification of Diseases, Ninth and Tenth Revisions of Clinical Modification (ICD-9-CM and ICD-10-CM) codes specified in the algorithm for ADRD in CMS Chronic Conditions Warehouse.[26]

Based on the technical specifications of the Pharmacy Quality Alliance (PQA), we included donepezil, galantamine, rivastigmine, and memantine as antidementia medications.[25] Established by CMS in 2006, PQA is a non-governmental, nonprofit organization that develops and maintains medication performance measures, some of which have been adopted by CMS in its Star Ratings program for Parts C and D health insurance plans.[27] Race/ethnicity in our study sample was categorized into five groups based on the Research Triangle Institute Race Code:

White, Black, Hispanic, Asian/Pacific Islander (Asian), and Other. The Other category encompassed American Indians, Alaska Natives, unknown, and other races/ethnicities to gain a sufficient sample size.[23]

Study Groups Construction

To facilitate a difference-in-differences (DID) analysis, we constructed an intervention group and a comparison group. The intervention group consisted of new MTM enrollees in 2017. The comparison group included MTM non-enrollees who satisfied the CMS guidelines for MTM eligibility but were not enrolled in MTM during the study period. Note that MTM enrollees in 2016 were not included in the analysis.

For the years studied, the CMS guidelines required plans to target beneficiaries who met the following criteria: (1) had at least two to three chronic conditions; (2) were prescribed at least two to eight covered medications; and (3) were likely to incur at least an annual medication expense of $3507 in 2016 and $3919 in 2017.[28,29] Because most plan sponsors adopted three chronic conditions and eight covered medications in their MTM eligibility criteria,[30,31] we used these two values in conjunction with the annual medication spending requirement to identify beneficiaries in the comparison group. Given that data on the exact chronic conditions targeted by individual MTM programs were unavailable, a beneficiary's number of chronic conditions was determined based on the 25 prevalent chronic diseases in MTM programs.[32]

To reduce the imbalance in beneficiary baseline characteristics between intervention and comparison groups, we matched MTM non-enrollees to enrollees in a 1:1 ratio based on a propensity score that predicted the likelihood of a beneficiary's MTM enrollment. We employed a nearest neighborhood algorithm without replacement for the matching because the algorithm created the most balanced groups compared with alternative algorithms.[33]

Outcome Measure

The outcome measured was nonadherence to antidementia medications. A binary outcome variable was constructed based on the proportion of days covered (PDC), calculated as the total number of days that a beneficiary was covered by at least one antidementia medication over the total number of days in the measurement period. For the comparison group in both years and the intervention group in 2016, the measurement period began from the earliest date of an antidementia medication fill through the end of the year. For the intervention group in 2017, the period started on the first prescription fill date after the MTM enrollment date. Beneficiaries were classified as nonadherent if their PDC was <80% and adherent otherwise ($1 = PDC < 0.80$; $0 = PDC \geq 0.80$) in the main analysis. A PDC threshold of 0.80 was selected due to its strong association with hospitalizations, health care costs, and clinical outcomes among patients with chronic conditions.[34–37] Furthermore, 0.80 as an adherence threshold is widely accepted based on recent studies on antidementia medications[38,39] and the Medicare Part D Star Ratings program.[40] In a sensitivity analysis, PDC thresholds of 0.70 and 0.90 were analyzed to determine the effects of varying adherence thresholds.

Covariates

The conceptual framework for this study was Gelberg-Andersen's Behavioral Model for Vulnerable Populations, and medication utilization patterns was considered a function of predisposing, enabling, and need factors.[41] Predisposing factors influence a beneficiary's inclination to seek medications. Enabling factors facilitate or hinder the use and access of medications. Need factors signify a beneficiary's need for medication. We used the following covariates for this study: the predisposing variables included age, sex, race/ethnicity, the proportion of married-couple families, the proportion of people with at least high school education, per capita income, and the proportion of people without health insurance. The enabling variables included dummy variables for metropolitan statistical area (MSA), Health Professional Shortage Area (HPSA), and census regions. The need variable was a CMS risk adjustment summary score. A higher score indicated greater expected health care utilization. Among the covariates, age, sex, race/ethnicity, and risk adjustment summary score were beneficiary-level, while all other covariates were measured at the community level based on a beneficiary's county of residence. The grouping of the covariates was based on the definition of the categories in the conceptual framework and the nature of the covariates.

Empirical Approach and Statistical Analysis

We first conducted descriptive analyses concerning the baseline characteristics and study outcomes of the intervention and comparison groups. We then analyzed the effects of MTM on racial/ethnic disparities in three steps by estimating a different multivariable logistic regression model at each step.

First, we included in our model a dummy for each racial/ethnic minority, with Whites being the reference group, to determine whether racial/ethnic disparities in nonadherence to antidementia medications existed in the baseline year for both intervention and comparison groups. If the odds ratio (OR) of a minority dummy was significantly greater than one, this would indicate that the minority group was more likely than Whites to be nonadherent.

Next, we incorporated interaction terms between dummy variables for the year 2017 and racial/ethnic minorities to examine changes in racial/ethnic disparities over time. If the OR of the interaction term for a minority group was significantly lower than one, this would indicate that the disparities between Whites and the minority group decreased in 2017.

Finally, we used a DID approach by incorporating three-way interaction terms of dummy variables for MTM enrollment, the year 2017, and racial/ethnic minorities to compare the changes in racial/ethnic disparities between the intervention and comparison groups. If the OR of the three-way interaction term for a minority group was significantly lower than one, this would indicate that the difference in the odds of Nonadherence between Whites and the minority group in the intervention group was reduced by a greater magnitude over time than the comparison group. This would demonstrate that MTM enrollment was associated with reduced racial/ethnic disparities concerning medication nonadherence. Employing a pre-post DID design combined with propensity score matching is a common approach to address the potential effects of extraneous factors.[42–44]

In all regression models, standard errors were clustered at the county level to account for potential within-county correlation. Statistical significance was determined at a two-sided alpha value of 0.05. All analyses were conducted with SAS Enterprise Guide 7.1 at the CMS VRDC. All important data analysis codes can be found on the study website (https://mtmstarvalue.uthsc.edu/codes/). The Institutional Review Board at the University of Tennessee Health Science Center US approved the study (approval number: #20–07197-XM).

Results

Descriptive statistics for the baseline beneficiary characteristics are reported in Table 1. After propensity score matching, the final study sample consisted of 56,426 Medicare beneficiaries, with the intervention and comparison groups each accounting for 50% of the study population (Fig. 1). There were 72.2% Whites, 11.7% Blacks, 10.8% Hispanics, 4.0% Asians, and 1.4% Other in the study sample. All characteristics were balanced and were not significantly different across the two study groups ($P > 0.05$). Fig. 2 indicates that there are non-overlap regions for the propensity scores of the two study groups. Individuals in those areas were excluded from the study sample after the propensity score matching.

Table 1
Baseline characteristics of study population in 2016 by intervention status.

Characteristics	Intervention Group (n = 28,213, 50%)		Comparison Group (n = 28,213, 50%)	
	Number	%	Number	%
Predisposing Factors				
Age, mean (SD)	80.71 (7.02)		80.68 (7.24)	
Male	9262	32.83	9262	32.83
Race/Ethnicity				
Non-Hispanic Whites	20,355	72.15	20,355	72.15
Blacks	3302	11.70	3302	11.70
Hispanics	3043	10.79	3043	10.79
Asians/Pacific Islanders	1119	3.97	1119	3.97
Other	394	1.40	394	1.40
Proportion of Married-Couple Families, mean (SD)[a]	0.72 (0.07)		0.72 (0.07)	
Proportion of Education ≥ High School, mean (SD)[a]	0.86 (0.06)		0.86 (0.06)	
Per Capita Income (in $1000), mean (SD)[a]	47.53 (15.84)		47.75 (15.60)	
Proportion of No Insurance, mean (SD)[a]	0.11(0.05)		0.11(0.05)	
Enabling Factors				
Metropolitan Statistical Area[a]	22,426	79.49	22,426	79.49
Health Professional Shortage Area[a]	25,677	91.01	25,677	91.01
Census Regions[a]				
Northeast	5803	20.57	5842	20.71
Midwest	6364	22.56	6418	22.75
South	12,089	42.85	12,010	42.57
West	3957	14.03	3943	13.98
Need Factor				
Risk Adjustment Summary Score, mean (SD)	2.41 (1.37)		2.42 (1.22)	

All characteristics were not statistically different between the intervention and comparison groups ($P > 0.05$).
SD, standard deviation.
[a] Indicates a county-level characteristic.

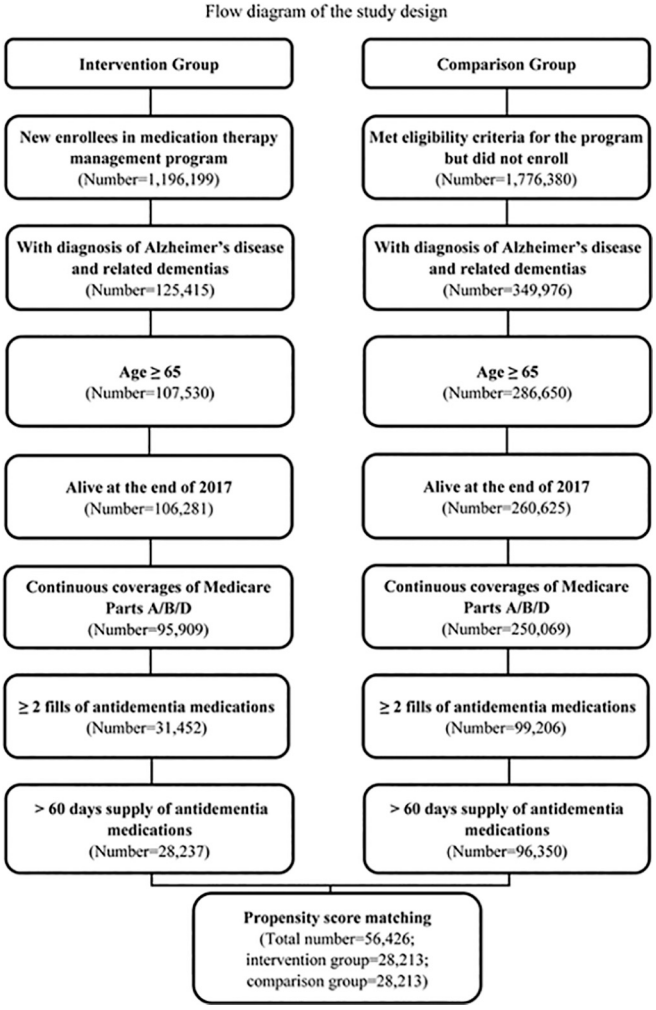

Fig. 1. Flow diagram of the study design.
The diagram illustrates the sample selection process to create patient cohorts for the analysis.

The percentages of nonadherent beneficiaries by race/ethnicity and study year for both study groups are illustrated in Fig. 3. In the baseline year 2016, Whites had lower percentages of nonadherence to antidementia medications than Blacks, Asians, Hispanics, and Other in both the comparison group ($P < 0.001$ for all races/ethnicities) and the intervention group ($P < 0.001$, $P < 0.001$, $P < 0.001$, $P = 0.0148$ respectively). Specifically, within the intervention group, the difference was 8.6 percentage points (22.4% − 13.8%) between Blacks and Whites, 7.3 (21.1% − 13.8%) between Hispanics and Whites, 3.2 (17.0% − 13.8%) between Asians and Whites, and 4.2 (18.0% − 13.8%) between Other and Whites. Similarly, for the comparison group, the difference was 4.1 percentage points (13.8% − 9.7%) between Blacks and Whites, 6.8 (16.5% − 9.7%) between Hispanics and Whites, 6.4 (16.1% − 9.7%) between Asians and Whites, and 5.0 (14.7% − 9.7%) between Other and Whites. By comparison, the intervention group experienced smaller differences between Whites and two racial/ethnic minorities in 2017 ($P < 0.001$): the difference was 3.7 percentage points (18.5% − 14.8%) between Blacks and Whites and 2.9 (17.7% − 14.8%) between Hispanics and Whites. The comparison group did not see any significant changes concerning racial/ethnic differences in nonadherence across time.

Table 2 first presents the multivariable regression results concerning racial/ethnic disparities in medication nonadherence for both intervention and comparison groups. In 2016, racial/ethnic disparities were found in nonadherence to antidementia medications for both study groups. After adjusting for beneficiary characteristics, racial/ethnic minorities, except for Other in the intervention group, were found to have significantly higher odds of being nonadherent than Whites. Specifically for the intervention group in 2016, the adjusted ORs for Blacks, Hispanics, and Asians were respectively 1.64 (95% confidence interval [CI]: 1.47–1.82), 1.53 (95% CI: 1.35–1.73), and 1.36 (95% CI: 1.16–1.59). Regarding the comparison group, the adjusted ORs for Blacks, Hispanics, Asians, and Other were respectively 1.20 (95% CI: 1.07–1.35), 1.52 (95% CI: 1.29–1.80), 1.74 (95% CI: 1.45–2.09), and 1.45 (95% CI: 1.14–1.84).

Across the two study years, disparities were only reduced for Blacks and Hispanics in the intervention group (Table 2): the ORs of the interaction terms show that differences in the odds of medication nonadherence were significantly lowered by 27% (OR: 0.73, 95% CI: 0.65–0.82) between Blacks and Whites and by 26% (OR: 0.74, 95% CI: 0.63–0.87) between Hispanics-Whites. By comparison, no significant reduction in the differences for Asians-Whites and Other-Whites was observed in the intervention group. Similarly, the disparities between Whites and racial/ethnic minorities in the comparison group were not significantly different across time.

Table 3 exhibits the regression results of the unadjusted and multivariable DID logistic models. The results indicate that MTM enrollment was associated with significantly lower racial/ethnic disparities in the likelihood of Nonadherence for Blacks and Hispanics. In the unadjusted analysis, ORs of the three-way interaction terms of MTM enrollment, the year 2017, and racial/ethnic minority dummies show that differences in the odds of medication nonadherence for Blacks-Whites and for Hispanics-Whites in the intervention group were respectively reduced over time by 35% (OR: 0.65, 95% CI: 0.56–0.76) and 19% (OR: 0.81, 95% CI: 0.67–0.97) more than the comparison group. The reduction in

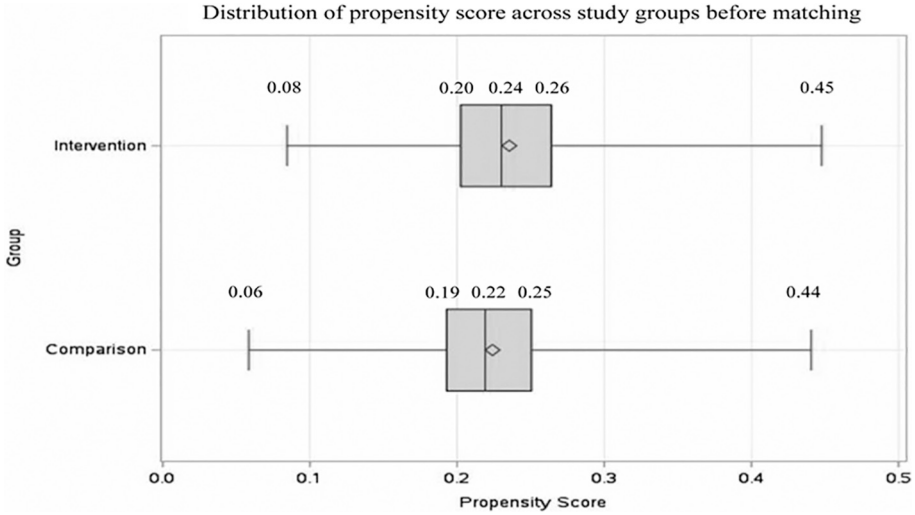

Fig. 2. Distribution of propensity score across study groups before matching.
Each box and whisker plot displays the mean (diamond), quartiles (vertical lines), and minimum and maximum propensity scores for individuals in a study group. Individuals in the non-overlap region of the distributions were excluded from the final study sample after propensity score matching.

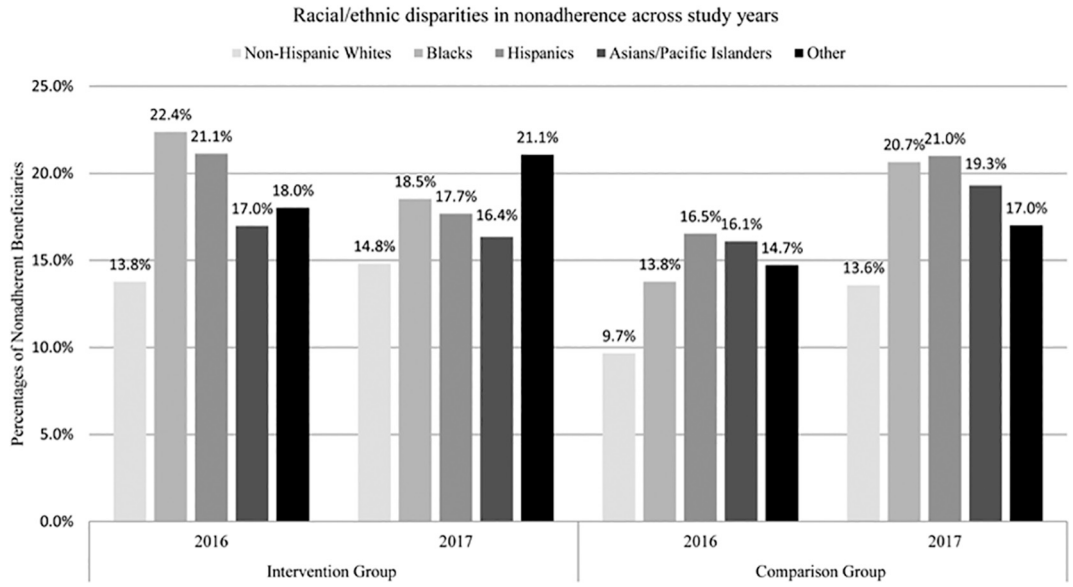

Fig. 3. Racial/ethnic disparities in nonadherence across study years.
The differences in percentages of nonadherence between non-Hispanic Whites (Whites) and each racial/ethnic minority were significant among both groups in 2016 ($P < 0.05$). With the exception of Asians/Pacific Islanders in the intervention group and Other in the comparison group, the differences in nonadherent percentages between Whites and racial/ethnic minority pairs were significant among both groups in 2017 ($P < 0.05$). The differences in percentages of nonadherence across years were only significant for Blacks-Whites and Hispanics-Whites in the intervention group ($P < 0.05$).

racial/ethnic disparities remained robust after adjusting for beneficiary characteristics: disparities among intervention group were reduced by 33% (OR: 0.67, 95% CI: 0.57–0.78) between Blacks-Whites and by 19% (OR: 0.81, 95% CI: 0.67–0.99) between Hispanics-Whites. In the sensitivity analysis, there was still a significant reduction in Black-White disparities, but the reductions in disparities between Hispanic and White patients were not significant.

Several beneficiary and community characteristics exhibited significant relationships with medication nonadherence (Table 3). Age (OR: 0.986, 95% CI: 0.983–0.989), being male (OR: 0.93, 95% CI: 0.89–0.96), the proportion of married-couple families in the community (OR: 0.37, 95% CI: 0.24–0.57), and living in an HPSA (OR: 0.91, 95% CI: 0.85–0.98) were associated with lower likelihood of medication nonadherence. However, per capita income in the community (OR: 1.002, 95% CI: 1.001–1.004), the proportion of people in the community without health insurance (OR: 3.32, 95% CI: 1.67–6.60), and risk adjustment summary score (OR: 1.22, 95% CI: 1.21–1.24) were associated with a higher likelihood of medication nonadherence.

Discussion

Our adjusted comparisons in the baseline year indicated that Blacks, Hispanics, and Asians were more likely to be nonadherent than Whites. The findings were consistent with results from the broader ADRD literature that used less restrictive outcome measures to examine racial/ethnic disparities in antidementia medication utilization.[6,19–21] For example, a recent study analyzed a 20% random sample of Medicare claims for outcomes of different adherence thresholds that ranged up to

Table 2
Racial/ethnic disparity patterns in nonadherence to antidementia medications by intervention status.

Characteristics	Intervention Group		Intervention Group		Comparison Group		Comparison Group	
	Year 2016		Year 2016 & 2017		Year 2016		Year 2016 & 2017	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Predisposing Factors								
Race/Ethnicity								
Blacks	1.64	1.47–1.82	1.64	1.48–1.81	1.2	1.07–1.35	1.21	1.08–1.35
Hispanics	1.53	1.35–1.73	1.55	1.38–1.74	1.52	1.29–1.80	1.58	1.36–1.83
Asians/Pacific Islanders	1.36	1.16–1.59	1.34	1.16–1.55	1.74	1.45–2.09	1.77	1.49–2.11
Other	1.27	0.97–1.65	1.27	0.98–1.65	1.45	1.14–1.84	1.48	1.17–1.87
Year 2017			1.052	0.995–1.111			1.43	1.35–1.53
Year 2017 × Race/Ethnicity								
Blacks			0.73	0.65–0.82			1.1	0.97–1.24
Hispanics			0.74	0.63–0.87			0.91	0.80–1.03
Asians/Pacific Islanders			0.88	0.74–1.05			0.85	0.68–1.06
Other			1.12	0.77–1.62			0.79	0.57–1.09
Age	0.986	0.981–0.990	0.986	0.983–0.990	0.981	0.976–0.987	0.986	0.982–0.990
Male	0.97	0.90–1.04	0.945	0.895–0.998	0.95	0.88–1.04	0.9	0.85–0.96
Proportion of Married-couple Families[a]	0.47	0.27–0.82	0.44	0.28–0.70	0.39	0.17–0.87	0.3	0.16–0.56
Proportion of Education ≥ High School[a]	1.14	0.49–2.68	1.14	0.59–2.23	0.81	0.28–2.37	1.1	0.48–2.53
Per Capita Income (in $1000)[a]	1.002	1.001–1.004	1.002	1.001–1.003	1.0029	0.9998–1.0060	1.0025	1.0004–1.0045
Proportion of No Insurance[a]	5.72	1.94–16.88	3.76	1.70–8.30	2.9	0.74–11.38	2.85	1.06–7.65
Enabling Factors								
Metropolitan Statistical Area[a]	0.916	0.838–1.003	0.96	0.90–1.02	1.02	0.91–1.14	0.99	0.91–1.07
Health Professional Shortage Area[a]	0.97	0.86–1.08	0.91	0.84–0.99	0.98	0.86–1.12	0.91	0.83–1.01
Census Regions[a]								
Midwest	0.997	0.891–1.116	0.96	0.88–1.05	0.93	0.78–1.11	0.99	0.87–1.12
South	1.06	0.93–1.20	1.04	0.95–1.15	1.14	0.95–1.36	1.132	0.999–1.283
West	0.98	0.87–1.10	0.97	0.88–1.06	1.08	0.92–1.27	1.09	0.97–1.22
Need Factor								
Risk Adjustment Summary Score	1.21	1.19–1.23	1.2	1.19–1.22	1.25	1.22–1.29	1.25	1.22–1.27

Reference groups: non-Hispanic Whites, year 2016, female, non-metropolitan statistical area, non-health professional shortage area, and Northeast region.
OR, odds ratio; CI, confidence interval.
[a] Indicates a county-level characteristic.

270 possession days and two claims in a year. The results showed that Hispanics were less likely to use antidementia medications at higher thresholds, while Blacks and Asians were less likely to use the medications at all thresholds than Whites.[6]

Our adjusted comparisons across the two study years indicated that the Black-White and Hispanic-White differences were significantly reduced in the second year for the intervention group. In contrast, the gaps between Asians and Whites in the intervention group and between all minorities and Whites in the comparison group did not significantly change over time. The DID analysis further showed that the Black-White and Hispanic-White disparities in the intervention group decreased more over time than the comparison group, although the decrease in Hispanic-White disparities was not significant in the sensitivity analysis. The findings, therefore, provided evidence that the Medicare MTM program was associated with reduced disparities in antidementia medication nonadherence for older Black and Hispanic patients with ADRD.

Our multivariable analyses revealed that several patient and community characteristics deserve more attention in ADRD-specific interventions. For instance, nonadherence was positively associated with living in a community with a higher uninsured rate and having a higher risk adjustment summary score. The community-level uninsured rate may be a proxy for the affluence of the area and the level of health care access. As noted earlier, the risk adjustment summary score is a proxy for health status. Health care access and disease burden are both well-documented determinants of adherence.[45,46] Considering that the patients in the study population had access to healthcare due to Medicare enrollment, the observed association for community-level uninsured rate suggests that individuals residing in less affluent communities may still have more access issues than their counterparts from more affluent neighborhoods. Our results, therefore, may highlight the essential role of health care access in reducing medication nonadherence and the importance of timely screening and interventions.

Several other covariates that were also significantly associated with nonadherence included age, male, living in an HPSA, and the per capita income level in a community. Being older and being male both had a negative association with nonadherence, which was consistent with the findings of previous studies. Researchers noted that older age was associated with a reduced risk of nonadherence and that female patients were more likely to be nonadherent than male patients.[45,47,48] The gender difference in nonadherence was speculated to stem from women's caring nature that placed others' health care needs ahead of the women's own.[47,48] Nonadherence was negatively associated with living in an HPSA, likely because patients in these areas again had issues with health care access. The counterintuitive positive relationship between per capita income in the community and nonadherence warrants further investigation in the future.

Another community characteristic associated with lower nonadherence is living in a community with a higher proportion of married-couple families, which may be a proxy for a higher level of social support.[49] For ADRD patients, the main social support sources may come from caregivers and health care providers. Caregivers play a pivotal role in antidementia medication adherence due to the caregivers' high level of involvement in ADRD patients' medication management. A recent Lancet report stressed the need to incorporate family caregivers into ADRD interventions.[50] Taking care of an ADRD patient is stressful due to the patient's psychiatric and behavioral symptoms.[51] For family caregivers, the stress is compounded by the fact that they not only lack the necessary skills to deal with the patient's psychiatric and behavioral problems, but also have to juggle their own work and family

Table 3
The effects of MTM on racial/ethnic disparities in nonadherence to antidementia medications.

Characteristics	Unadjusted		Adjusted	
	OR	95% CI	OR	95% CI
Predisposing Factors				
Race/Ethnicity				
Blacks	1.49	1.34–1.66	1.24	1.11–1.38
Hispanics	1.85	1.54–2.22	1.6	1.38–1.86
Asians/Pacific Islanders	1.79	1.51–2.13	1.82	1.54–2.15
Other	1.61	1.27–2.05	1.5	1.18–1.90
MTM	1.49	1.40–1.60	1.48	1.38–1.58
Year 2017	1.47	1.38–1.56	1.44	1.35–1.53
MTM × Year 2017	0.74	0.68–0.81	0.73	0.67–0.79
MTM × Race/Ethnicity				
Blacks	1.21	1.05–1.38	1.3	1.13–1.49
Hispanics	0.91	0.72–1.14	0.96	0.78–1.17
Asians/Pacific Islanders	0.71	0.56–0.91	0.72	0.57–0.91
Other	0.85	0.62–1.18	0.84	0.60–1.17
Year 2017 × Race/Ethnicity				
Blacks	1.11	0.98–1.25	1.1	0.97–1.24
Hispanics	0.91	0.81–1.04	0.91	0.80–1.03
Asians/Pacific Islanders	0.85	0.68–1.06	0.85	0.68–1.06
Other	0.81	0.59–1.11	0.79	0.57–1.09
MTM × Year 2017 × Race/Ethnicity				
Blacks	0.65	0.56–0.76	0.67	0.57–0.78
Hispanics	0.81	0.67–0.97	0.81	0.67–0.99
Asians/Pacific Islanders	1.03	0.74–1.44	1.04	0.75–1.44
Other	1.38	0.89–2.13	1.41	0.90–2.20
Age			0.986	0.983–0.989
Male			0.93	0.89–0.96
Proportion of Married-Couple Families[a]			0.37	0.24–0.57
Proportion of Education ≥ High School[a]			1.13	0.63–2.04
Per Capita Income (in $1000)[a]			1.002	1.001–1.004
Proportion of No Insurance[a]			3.32	1.67–6.60
Enabling Factors				
Metropolitan Statistical Area[a]			0.97	0.92–1.03
Health Professional Shortage Area[a]			0.91	0.85–0.98
Census Regions[a]				
Midwest			0.97	0.89–1.06
South			1.08	0.99–1.19
West			1.02	0.94–1.11
Need Factor				
Risk Adjustment Summary Score			1.22	1.21–1.24

Reference groups: non-Hispanic Whites, MTM non-enrollees, year 2016, female, non-metropolitan statistical area, non-health professional shortage area, and Northeast region.

CI, confidence interval; OR, odds ratio; MTM, medication therapy management.

[a] Indicates a county-level characteristic.

responsibilities outside of the caring schedule.[52] Caregiver education focusing on communication, behavioral, and stress management skills is therefore essential in ADRD medication management.[52–56]

Currently, there are no adequate standard procedures for the Medicare MTM services except that Part D plans are required to use a CMS-developed standardized form in comprehensive medication reviews.[29] It is largely at the plans' discretion how the services are provided. CMS may consider incorporating caregiver and provider education in the MTM program requirements, particularly for challenging diseases such as ADRD. Given the disease's long-term nature, equipping caregivers and frontline providers with the necessary knowledge and skills not only improves the quality of MTM services but also is a more sustainable and cost-effective approach for ADRD care. In addition, existing literature suggested that racial/ethnic disparities in antidementia medication use might be due to cultural beliefs of dementia being fateful as a result of God's will among racial/ethnic minorities.[21,22] Consequently, enhancing the cultural competency of frontline MTM service providers, including pharmacists, is crucial for promoting medication adherence among diverse racial/ethnic populations affected by ADRD.

To our knowledge, this study is the first to examine the effects of the Medicare MTM program on racial/ethnic disparities in adherence to antidementia medications. It bridged the gap in the existing MTM and ADRD literature by providing initial evidence of the Medicare MTM effects on reducing racial/ethnic disparities in adherence for older Black and Hispanic ADRD patients relative to their White counterparts. Methodologically, the study applied rigorous methods by studying a 100% Medicare population and using a DID design that incorporates propensity score-matched groups.

The present study examined racial/ethnic disparities in adherence to antidementia medications, and it is noteworthy that the effects of these medications are limited. Considering the higher risk of polypharmacy among the study population, a future study is needed to take a more nuanced approach to evaluate the effects of MTM on more comprehensive measures of medication utilization. Further, the longer-term impact of MTM services was not examined in this study, and the authors did not distinguish between MTM enrollment with CMR receipt versus MTM enrollment with other program components. Future studies are warranted to examine the long-term effects of CMR and other parts of the MTM program.

The nature of the data and study design warrants a discussion of limitations. First, county-level proxies were used for patient characteristics such as income and education because such variables are unavailable in Medicare claims and Master Beneficiary Summary Files. While this is a widely used strategy, due to their aggregated nature, the proxies only approximated the individual characteristics. Second, the widely accepted PDC measure computed the proportion of days covered by medication fills, not whether a patient took the medications in prescribed doses. Further, some miscalculations may result, such as double counting, when patients are dispensed multiple prescriptions for similar or identical medications within a short time of one another due to lost medicines or medication switches owing to side effects. In essence, PDC was only a proxy for adherence. Third, the comparison group was identified by a patient's predicted probability of MTM enrollment. The prediction model did not differentiate what conditions and medications a patient had, which probably varied in the actual MTM eligibility criteria of different plans. Therefore, the predicted probability may not reflect the actual likelihood of MTM enrollment. However, because information on individual plans' eligibility criteria was not available, using the threshold values most frequently used (i.e., three conditions and eight covered drugs) was the best possible option in the propensity score matching. Fourth, using Research Triangle Institute Race Code is associated with limitations, such as not differentiating non-Hispanic Black and Hispanic Black patients. Fifth, to improve data completeness, this study imposed certain inclusion criteria, such as the beneficiaries alive at the end of the year, continuous Medicare coverage, and a minimum of two prescription fills with a minimum of a 60-day supply. While this practice may introduce survival bias, since the inclusion of such patients may lead to an underestimate of the effects of MTM, while this study made positive findings, such bias may not threaten the validity of the study conclusion. Sixth, the misalignment of index dates between the intervention and comparison groups may introduce immortal time bias. This may also lead to downward estimates of the treatment effect because the follow-up for the intervention groups was started later (after MTM enrollment), and patients' adherence can decrease over time. Again, thanks to the positive findings of this study, such immortal time bias may not be a major concern. Future studies might consider including exposure to dementia medications in a time-varying fashion for patients in the comparison group. Finally, due to the unavailability of Parts A and B claims, this study could not include patients from the Medicare Advantage plans.

Conclusions

The Medicare MTM program was associated with reduced racial/ethnic disparities in adherence to antidementia medications between older Blacks and Whites, as well as between older Hispanics and Whites.

No effect of the program was detected on the disparities between Asians and Whites. Our results suggested that a lower level of health care access and a heavier disease burden may lead to higher nonadherence, whereas a higher level of social support may reduce nonadherence. Incorporating caregiver and provider education in the MTM program may facilitate more effective and sustainable service delivery. Future research is warranted to investigate the specific areas of training related to Medicare MTM services that caregivers and frontline providers may need so that the MTM program's benefits may be optimized.

Authors' contributions

Xiaobei Dong, Chi Chun Steve Tsang, Jamie A. Browning, Joseph Garuccio, and Rose Zeng: concept and design, analysis and interpretation of data, and writing (original draft and editing). Jim Y. Wan, Marie A. Chisholm-Burns, Christopher K. Finch, and Jack W. Tsao: funding acquisition, concept and design, analysis and interpretation of data, and writing (original draft and editing). Junling Wang: funding acquisition, concept and design, analysis and interpretation of data, writing (original draft and editing), and project administration. All authors read and approved the final manuscript.

Funding

Research reported in this publication was supported by the National Institute on Aging of the National Institutes of Health under Awards Number R01AG040146. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Declaration of competing interest

The authors list the following conflicts of interest: Xiaobei Dong, Chi Chun Steve Tsang, Jim Y. Wan, Christopher K. Finch, Jack W. Tsao, Jamie A. Browning, Joseph Garuccio, Rose Zeng: None; Marie A. Chisholm-Burns: Received funding from Carlos and Marguerite Mason Trust; Junling Wang: Received funding from AbbVie, Curo, Bristol Myers Squibb, Pfizer, and Pharmaceutical Research and Manufacturers of America (PhRMA), and serves on the Health Outcomes Research Advisor Committee of the PhRMA Foundation.

Acknowledgements

The authors would like to acknowledge the following individuals for assistance with the formatting of the final manuscript: Lorraine Todor, Oluwasefunmi Agbanigo, Hannah Foster, all PharmD students, and Yongbo Sim, a postdoctoral scholar, at the University of Tennessee Health Science Center College of Pharmacy.

References

1.. National Institute of Neurological Disorders and Stroke. Focus on Alzheimer's disease and related dementias. https://www.ninds.nih.gov/current-research/focus-disorders/focus-alzheimers-disease-and-related-dementias.
2.. 2021 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2021;17(3):327–406.
3.. Food and Drug Administration. Food and Drug Administration FDA grants accelerated approval for Alzheimer's drug. https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug; 2021.
4. Fowler NR, Chen YF, Thurton CA, Men A, Rodriguez EG, Donohue JM. The impact of Medicare prescription drug coverage on the use of antidementia drugs. *BMC Geriatr*. 2013;13(37).
5. Koller D, Hua T, Bynum JP. Treatment patterns with antidementia drugs in the United States: Medicare cohort study. *J Am Geriatr Soc*. 2016;64(8):1540–1548.
6. Barthold D, Joyce G, Ferido P, et al. Pharmaceutical treatment for Alzheimer's disease and related dementias: utilization and disparities. *J Alzheimers Dis*. 2020;76(2):579–589.
7.. Smith D, Lovell J, Weller C, et al. A systematic review of medication non-adherence in persons with dementia or cognitive impairment. *PloS One*. 2017;12(2), e0170651.
8. Schwalbe O, Scheerans C, Freiberg I, Schmidt-Pokrzywniak A, Stang A, Kloft C. Compliance assessment of ambulatory Alzheimer patients to aid therapeutic decisions by healthcare professionals. *BMC Health Serv Res*. 2010;10(232).
9. Zhang P, Chen L, Gu W, Xu Z, Gao Y, Li Y. In vitro and in vivo evaluation of donepezil-sustained release microparticles for the treatment of Alzheimer's disease. *Biomaterials*. 2007;28(10):1882–1888.
10. Borah B, Sacco P, Zarotsky V. Predictors of adherence among Alzheimer's disease patients receiving oral therapy. *Curr Med Res Opin*. 2010;26(8):1957–1965.
11. Centers for Medicare & Medicaid Services. Medicare program; contract year 2015 policy and technical changes to the Medicare Advantage and the Medicare Prescription Drug Benefit programs. Final Rule. *Fed Regist*. 2014;79(100):29843–29968.
12.. Centers for Medicare & Medicaid Services. Medication therapy management. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/MTM. Updated Jan 2023 (accessed 10 April 2023).
13. Perlroth D., Marrufo G., Montesinos A., et al. Medication therapy management in chronically ill populations: final report (accessed 10 April, 2023). https://www.cms.gov/priorities/innovation/files/reports/mtm_final_report.pdf.
14. Peasah SK, Hammonds T, Liu Y, Campbell V, Manolis C, Good CB. Economic assessment of changes to an existing medication therapy management program of a large regional health plan. *J Manag Care Spec Pharm*. 2021;27(2):147–156.
15. Dong X, Tsang CCS, Zhao S, et al. Effects of the Medicare Part D comprehensive medication review on medication adherence among patients with Alzheimer's disease. *Curr Med Res Opin*. 2021;37(9):1581–1588.
16. Ai AL, Carretta H, Beitsch LM, Watson L, Munn J, Mehriary S. Medication therapy management programs: promises and pitfalls. *J Manag Care Spec Pharm*. 2014;20(12):1162–1182.
17. Viswanathan M, Kahwati LC, Golin CE, et al. Medication therapy management interventions in outpatient settings: a systematic review and meta-analysis. *JAMA Intern Med*. 2015;175(1):76–87.
18. Pestka DL, Zillich AJ, Coe AB, et al. Nationwide estimates of medication therapy management delivery under the Medicare prescription drug benefit. *J Am Pharm Assoc*. 2020;60(3):456–461.
19. Gruber-Baldini AL, Stuart B, Zuckerman IH, Simoni-Wastila L, Miller R. Treatment of dementia in community-dwelling and institutionalized Medicare beneficiaries. *J Am Geriatr Soc*. 2007;55(10):1508–1516.
20. Mehta KM, Yin M, Resendez C, Yaffe K. Ethnic differences in acetylcholinesterase inhibitor use for Alzheimer disease. *Neurology*. 2005;65(1):159–162.
21. Zuckerman IH, Ryder PT, Simoni-Wastila L, et al. Racial and ethnic disparities in the treatment of dementia among Medicare beneficiaries. *J Gerontol B Psychol Sci Soc Sci*. 2008;63(5):S328–S333.
22. Thorpe CT, Fowler NR, Harrigan K, et al. Racial and ethnic differences in initiation and discontinuation of antidementia drugs by Medicare beneficiaries. *J Am Geriatr Soc*. 2016;64(9):1806–1814.
23.. Research Data Assistance Center. Data file search. https://www.resdac.org/cms-data?tid_1%5B%5D=1; 2023 (accessed 10 April 2023).
24.. Health Resources & Services Administration. Area health resources files. https://data.hrsa.gov/topics/health-workforce/ahrf; 2022 (accessed 10 April 2023).
25.. Pharmacy Quality Alliance. *Technical specifications for PQA-endorsed measures*. 2018.
26.. Chronic Conditions Data Warehouse. Condition categories. https://www2.ccwdata.org/web/guest/condition-categories; 2023 (accessed 10 April 2023).
27.. Pharmacy Quality Alliance. About PQA. https://www.pqaalliance.org/our-story; 2022 (accessed 10 April 2023).
28.. Centers for Medicare & Medicaid Services. CY 2016 medication therapy management program guidance and submission instructions. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Memo-Contract-Year-2016-Medication-Therapy-Management-MTM-Program-Submission-v-040715.pdf; 2015 (accessed 10 April 2023).
29.. Centers for Medicare & Medicaid Services. CY 2017 medication therapy management program guidance and submission instructions. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Memo-Contract-Year-2017-Medication-Therapy-Management-MTM-Program-Submission-v-040816.pdf; 2016 (accessed 10 April 2023).
30.. Centers for Medicare & Medicaid Services. 2016 Medicare Part D medication therapy management (MTM) programs: Fact sheet. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/CY2016-MTM-Fact-Sheet.pdf; 2016 (accessed 10 April 2023).
31.. Centers for Medicare & Medicaid Services. 2017 Medicare Part D medication therapy management (MTM) programs: Fact sheet. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/CY2017-MTM-Fact-sheet.pdf; 2017 (accessed 10 April 2023).
32. Daniel GW, Malone DC. Characteristics of older adults who meet the annual prescription drug expenditure threshold for Medicare medication therapy management programs. *J Manag Care Pharm*. 2007;13(2):142–154.
33. Austin PC. A comparison of 12 algorithms for matching on the propensity score. *Stat Med*. 2014;33(6):1057–1069.
34. Karve S, Cleves MA, Helm M, Hudson TJ, West DS, Martin BC. Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. *Curr Med Res Opin*. 2009;25(9):2303–2310.
35. Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy*. 2014;7:35–44.
36. Baumgartner PC, Haynes RB, Hersberger KE, Arnet I. A systematic review of medication adherence thresholds dependent of clinical outcomes. *Front Pharmacol*. 2018;9:1290.
37. El-Saifi N, Moyle W, Jones C, Tuffaha H. Medication adherence in older patients with dementia: a systematic literature review. *J Pharm Pract*. 2018;31(3):322–334.

38. Xiong S, Wu J, Li M, Lu K. Association between satisfaction with quality of care and ANTI-Dementia medication adherence among elderly adults with Alzheimer's disease and related dementias. *Value Health*. 2021;24:S93.
39. Olchanski N, Daly AT, Zhu Y, et al. Alzheimer's disease medication use and adherence patterns by race and ethnicity. *Alzheimers Dement*. 2023;19(4):1184–1193.
40. Centers for Medicare & Medicaid Services. Medicare 2022 Part C & D Star Ratings technical notes. Updated October 2022 (accessed 17 June 2023) https://www.cms.gov/files/document/2022-star-ratings-technical-notes-oct-4-2022.pdf.
41. Gelberg L, Andersen RM, Leake BD. The behavioral model for vulnerable populations: application to medical care use and outcomes for homeless people. *Health Serv Res*. 2000;34(6):1273–1302.
42. Godard-Sebillotte C, Karunananthan S, Vedel I. Difference-in-differences analysis and the propensity score to estimate the impact of non-randomized primary care interventions. *Fam Pract*. 2019;36(2):247–251.
43. Robins JM, Hernán MA, Brumback B. Marginal structural models and causal inference in epidemiology. *Epidemiology*. 2000;11:550–560.
44. Dimick JB, Ryan AM. Methods for evaluating changes in health care policy: the difference-in-differences approach. *JAMA*. 2014;312:2401–2402.
45. Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. *J Gen Intern Med*. 2007;22(6):864–871.
46. Hughes CM. Medication non-adherence in the elderly: how big is the problem. *Drugs Aging*. 2004;21(12):793–811.
47. Puskas CM, Forrest JI, Parashar S, et al. Women and vulnerability to HAART non-adherence: a literature review of treatment adherence by gender from 2000 to 2011. *Curr HIV/AIDS Rep*. 2011;8(4):277–287.
48. Vimalananda VG, Miller DR, Hofer TP, Holleman RG, Klamerus ML, Kerr EA. Accounting for clinical action reduces estimates of gender disparities in lipid management for diabetic veterans. *J Gen Intern Med*. 2013;28(suppl 2):S529–S535.
49. Oxman TE, Berkman LF, Kasl S, Freeman DH, Barrett J. Social support and depressive symptoms in the elderly. *Am J Epidemiol*. 1992;135(4):356–368.
50. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*. 2020;396(10248):413–446.
51. Pasqualetti G, Tognini S, Calsolaro V, Polini A, Monzani F. Potential drug-drug interactions in Alzheimer patients with behavioral symptoms. *Clin Interv Aging*. 2015;10:1457–1466.
52. Boada M, Arranz FJ. Transdermal is better than oral: observational research of the satisfaction of caregivers of patients with Alzheimer's disease treated with rivastigmine. *Dement Geriatr Cogn Disord*. 2013;35(1–2):23–33.
53. Brady R, Weinman J. Adherence to cholinesterase inhibitors in Alzheimer's disease: a review. *Dement Geriatr Cogn Disord*. 2013;35(5–6):351–363.
54. Callahan CM, Boustani MA, Unverzagt FW, et al. Effectiveness of collaborative care for older adults with Alzheimer disease in primary care: a randomized controlled trial. *JAMA*. 2006;295(18):2148–2157.
55. Deudon A, Maubourguet N, Gervais X, et al. Non-pharmacological management of behavioural symptoms in nursing homes. *Int J Geriatr Psychiatry*. 2009;24(12):1386–1395.
56. Nguyen K, Hoffman H, Chakkamparambil B, Grossberg GT. Evaluation of rivastigmine in Alzheimer's disease. *Neurodegener Dis Manag*. 2021;11(1):35–48.