Understanding the outpatient medication use and spending of cognitively impaired older adults under changing Medicare Part D policy

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Abstract

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Background

Between 2011 and 2020, the Affordable Care Act progressively closed the Medicare Part D coverage gap, reducing coinsurance from 100% to 25% to alleviate financial burdens and improve prescription drug access. Individuals with cognitive impairment face particularly high drug costs and are at greater risk for medication discontinuation. Furthermore, adherence is essential in this population for managing their disease and comorbidities to reduce their healthcare use and expenditures. We evaluated the effect of reduced coinsurance on out-of-pocket (OOP) costs and medication use for beneficiaries with cognitive impairment, as well as the association between medication adherence and inpatient (IP) and emergency department (ED) related healthcare costs and visits.

Methods

The study sample was Health and Retirement Study respondents with cognitive impairment, linked to Medicare claims (2006-2018). Aim 1 evaluated the causal effect of coverage gap closure on Part D OOP spending using a difference-in-differences (DID) event study approach. Aim 2 assessed the causal effect of coverage gap closure on medication use with a DID analysis. For these two aims, we estimated the change in the outcome for non-low-income subsidy (LIS) respondents, as compared to LIS respondents, who were not subject to the coverage gap. Aim 3 examined the association between adherence to AD medication and IP and ED utilization and costs using two-part models.

Results

Closure of the coverage gap resulted in a significant reduction in annual OOP spending (2011 vs. 2010: -$134; 95% CI: -174 to -94; $p<0.001$) in beneficiaries with cognitive impairment and in an increase in the probability of AD medication use in those with ADRD (4.3 percentage points [ppts]; 95% CI: 1.2-7.4; $p=0.017$). In terms of healthcare resource utilization and cost, adherence to AD drugs was associated with significant reductions in the probability of incurring IP (-2.4 ppts; 95% CI: -4.3 to -0.55 ppts; $p=0.011$) and ED healthcare costs (-6.4 ppts; 95% CI: -9.8 to -2.9 ppts; $p<0.001$), and of having an IP hospitalization (-2.3 ppts; 95% CI: -4.26 to -0.40 ppts; $p=0.018$) or ED visit (-6.4 ppts; 95% CI: -10.1 to -2.8 ppts; $p<0.001$). However, adherence was not significantly associated with the amount of IP costs incurred conditioning on incurring any costs or the number of hospitalizations conditioning on having any hospitalizations. In contrast,

adherence resulted in a 19.3 ppt reduction in total non-zero ED costs (95% CI: -30.2 to -6.7 ppts; $p<0.01$) and a 15.9 ppt reduction in the number of ED visits (95% CI: -22.7 to -8.2 ppts; $p<0.01$).

Conclusion

In this sample of cognitively impaired Medicare beneficiaries, we found that closure of the Medicare Part D coverage gap successfully reduced OOP spending and increased medication use. Furthermore, medication adherence was associated with a significant reduction in the probability of healthcare resource utilization and cost. This research lays a foundation for the study of other chronic conditions and of the effects of the OOP spending caps that will be implemented by the Inflation Reduction Act.

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To my wife, Veronica, your unwavering support and belief in me got me to the finish line.

INTRODUCTION

Health insurance policies in the United States are continually evolving, adapting to the shifting landscape of healthcare needs, rising costs, and demographic changes. As healthcare spending escalates and the population ages, it is increasingly important to understand the impacts of these policy changes on access to care, financial burden, and health outcomes, particularly for vulnerable populations.

Medicare, a health insurance program in the U.S. for people aged 65 years or older and younger people with disabilities, launched its Part D prescription drug benefit in 2006. Under the original design, beneficiaries whose total drug spend exceeded an initial coverage limit entered a coverage gap where they became responsible for 100% of drug costs until their out-of-pocket (OOP) spending reached the threshold amount that qualified them for catastrophic coverage.[1] The motivation to launch the Medicare Part D prescription drug benefit in 2006 was to reduce financial barriers to facilitate the use of drugs that would not have been used in the absence of coverage.[2] The benefit was a success, and studies of the overall effect of Part D have found that the policy resulted in an increase in prescription drug use and a decrease in OOP spending.[3,4] Despite this progress, the Part D coverage gap maintained a financial barrier due to its 100% coinsurance rate. Previous studies found that the coverage gap was associated with lower medication use and adherence; whereas others saw no change for essential drugs.[5–7]

Medication use is related to healthcare spending, as good adherence is associated with improved health outcomes and lower health care resource utilization.[8–12] While not all medications are expected to have direct health effects that influence healthcare resource use, good adherence may

help symptom management and serve as a proxy for better management of comorbidities, thereby leading to potential effects on healthcare costs and utilization. To diminish the financial burden on beneficiaries and improve medication adherence, the Affordable Care Act (ACA) included a provision to gradually eliminate the Medicare Part D prescription drug coverage gap between 2011 and 2020 by reducing beneficiary contribution from 100% to 25%.[13] Evidence from previous studies suggested that filling the coverage gap decreased patient OOP spending and increased medication utilization.[13,14] However, little attention has been given to chronic conditions in the Medicare population, which result in considerable OOP spending and medication use, including the impact on medication adherence.

Cognitive impairment, including Alzheimer's disease and related dementias (ADRD), is among the most common chronic conditions for Medicare beneficiaries and a growing public health issue.[15,16] People with these conditions may require long-term health care and services, including management of chronic conditions and medications, and assistance with personal care.[17] In a patient population where financial and healthcare decision-making are often impaired, changes in benefits and coverage may be more challenging to track.[18,19] Furthermore, these patients often have multiple comorbid conditions and higher medication use. Therefore, it is important to understand the burden they experience due to Part D, as they are particularly vulnerable to the consequences of the design.[20]

The effects of the Part D coverage gap closure are of interest to patients, providers, and policy makers. It is critical to understand trends in spending and medication use, and the impact to personal budgets.[21] Addressing these evidence gaps will serve as further foundation for

considering changes to prescription drug coverage and cost, which is timely as new ADRD medications arrive on the market and in the context of the Inflation Reduction Act (IRA), which will have profound effects on OOP spending.[21]

The objective of this dissertation was to evaluate the effects of Medicare Part D coverage gap closure on OOP spending and medication use for individuals with cognitive impairment, including ADRD and other memory-related disorders. The following three aims addressed this objective. First, we evaluated the causal effect of coverage gap closure on Part D OOP spending using a difference-in-differences (DID) event study approach. Second, we assessed the causal effect of coverage gap closure on medication use with a DID analysis. Finally, we examined the association between medication adherence and inpatient and emergency department utilization and costs using two-part models.

1. THE EFFECTS OF CLOSING THE MEDICARE PART D COVERAGE GAP ON OUT-OF-POCKET SPENDING FOR COGNITIVELY IMPAIRED OLDER ADULTS

ABSTRACT

Background

The Affordable Care Act gradually eliminated the Medicare Part D coverage gap between 2011-2020 by reducing coinsurance from 100% to 25% to reduce the burden of prescription drug costs. Cognitively impaired individuals incur 70% greater healthcare costs, 40% higher drug-specific spending, and double the risk of entering the coverage gap compared to individuals without these conditions. We evaluated the effects of reduced coinsurance on out-of-pocket (OOP) costs for beneficiaries with cognitive impairment.

Methods

The study sample was Health and Retirement Study respondents with cognitive impairment, linked to Medicare claims (2006-2018). The outcome of interest was annual OOP drug spending. Using a difference-in-differences event study approach, we estimated the annual differential change in OOP spending for non-low-income subsidy (LIS) respondents, as compared to LIS respondents, who were not subject to the coverage gap.

Results

A total of 1923 non-LIS and 1329 LIS individuals with cognitive impairment were identified (63.6% female, mean age 73.9 years). Closure of the coverage gap immediately resulted in a significant reduction in annual OOP spending (2011 vs. 2010: -$134; 95% CI: -174 to -94;

p<0.001). The reduction was larger for older patients (age 85+: -$149, 95% CI: -231 to -67, p<0.001; age 75-84: -$147, 95% CI: -211 to -82, p<0.001; age 65-74: -$79, 95% CI: -158 to 0.42, p=0.051).

Conclusion

In beneficiaries with cognitive impairment, closure of the Medicare Part D coverage gap resulted in a significant reduction in OOP spending, indicating the policy's success in higher spending and vulnerable populations.

1.1. Background

Medicare launched its Part D prescription drug benefit in 2006 with the goal of increasing the affordability of and access to medications by reducing financial barriers and facilitating the use of drugs that would not have been used in the absence of coverage.[2] The benefit was a success, as studies on the overall effect of Part D have found that the policy resulted in a 5.9-12.8% increase in prescription drug use and a 13.1-15.6% decrease in out-of-pocket (OOP) spending.[3,4] Established through Part D in partnership with state Medicaid programs, the low-income subsidy (LIS) helps beneficiaries with limited income by assisting with the premiums and cost-sharing associated with the Part D benefit. Beneficiaries receiving the LIS have never been subject to Part D coinsurance.[14]

Despite this progress, the benefit design of Part D included substantial cost sharing for non-LIS beneficiaries. Under the original design, non-LIS beneficiaries whose total drug spending exceeded an initial coverage limit entered a "coverage gap" where they became responsible for

100% of drug costs until their OOP spending reached a threshold, after which they paid 5% coinsurance in the "catastrophic coverage" phase.[1] In 2006, the initial coverage limit was $750 and the catastrophic phase began at $3600, meaning that beneficiaries were responsible for $2850 during the coverage gap.[22] To diminish the burden of this cost sharing on beneficiaries, the Affordable Care Act (ACA) included a provision to gradually eliminate the Medicare Part D prescription drug coverage gap between 2011 and 2020 by reducing beneficiary coinsurance rate in this phase from 100% to 25%.[13] Since the closing of the coverage gap began in 2011, several studies have examined health and economic consequences, and shown that closing the coverage gap decreased patient OOP spending.[13,14,23–27] However, little attention has been given to the subpopulation of Medicare beneficiaries with chronic conditions, who incur considerable OOP spending.[28]

Cognitive impairment, including Alzheimer's disease and related dementias (ADRD), affects up to 36% of US adults over 65,[29] making them among the most common chronic conditions for Medicare beneficiaries. Alzheimer's disease alone is expected to affect 13.8 million older Americans by 2060,[30] making it an important public health issue.[15,16] The closing of the coverage gap is especially important for people with cognitive impairment because their financial and healthcare decision-making are often impaired, and they typically have multiple comorbid conditions leading to higher medication use. Therefore, changes in benefits and coverage may be more challenging to track, making them particularly vulnerable to the cost burden of the Part D design.[18–20] Studies of older adults with cognitive impairment or ADRD have found that overall OOP costs are 1.7 times greater, that drug-specific spending is 40% higher, and that risk of entering the coverage gap is doubled compared to individuals without these conditions.[20,31–34]

Furthermore, research has demonstrated that the financial burden of ADRD also leads to medication non-adherence, which has important consequences for patient outcomes.[6,35,36] Closing the coverage gap could have meaningful financial and disease management benefits to enrollees with cognitive impairment, yet no prior studies have been reported on these topics.

The effects of the Part D coverage gap closure are of interest to patients, providers, and policy makers. It is critical to understand trends in spending and the impact to personal budgets, especially as policies continue to change, such as with the Inflation Reduction Act (IRA), which will lead to lower drug costs and capped OOP spending.[21] The objective of this study was to evaluate the effects of Medicare Part D coverage gap closure on OOP costs for individuals with cognitive impairment, including ADRD and other memory-related disorders.

1.2. Materials & Methods

1.2.1. Data Sources

We used the Health and Retirement Study (HRS) linked to Medicare claims from 2006 to 2018.[37] The HRS has been fielded since 1992 and surveys more than 30,000 people aged 50 and older every two years. Of the Medicare data files, we used the beneficiary summary files, fee-for-service inpatient and outpatient files, and Part D event files. To obtain zip code level income data, we used the Agency for Healthcare Research and Quality (AHRQ) Social Determinants of Health data (2011-2020).[38]

1.2.2. Sample Selection

Our analytic sample included person-waves in which the respondent had a diagnosis of either ADRD, senile dementia, MCI, memory loss, other types of dementia, or cognitive deficit. These conditions were identified using Medicare claims Chronic Conditions Warehouse variables, International Classification of Disease codes 9th (ICD-9) and 10th (ICD-10) versions and the HRS Langa-Weir Classification of Cognitive Function (Appendix A1. 1).[39,40] We required continuous Medicare enrollment for at least one year before initiation of coverage gap closure (January 1, 2011) and one year after closure initiation, and at least one non-zero dollar Part D claim (Appendix A1. 2). The control group was comprised of person-waves for individuals either deemed eligible for or enrolled in the LIS, as these beneficiaries were never subject to the coverage gap.

1.2.3. Measures

Individuals were considered exposed to the policy if they experienced the effects of Part D coverage gap closure, as defined by not receiving LIS. Initiation of coverage gap closure occurred in 2011, with coinsurance rates dropping from 100% to 50% (93%) for branded (generic) drugs (Table 1.1).

Table 1.1. Coinsurance* rates in the Medicare Part D coverage gap over time.

	2006-2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Branded	100%	50%	50%	47.5%	47.5%	45%	45%	40%	35%	30%	25%
Generic	100%	93%	86%	79%	72%	65%	58%	51%	44%	37%	25%

*The proportion of the medication cost borne by the beneficiary.

OOP spending, the outcome of interest, was based on Part D event claims and was defined as the total prescription drug spending per year. All costs were inflation-adjusted to 2018 US dollars

(USD) using the medical care component of the Consumer Price Index from the US Bureau of Labor and Statistics.[41]

In addition to year and individual fixed effects, the following time-varying covariates were included in the model: a categorical count (0, 1, 2, 3+) of high-priority chronic conditions defined by CMS, and median income by zip code.[42] Median income by zip code from 2011 to 2018 was directly available from AHRQ. Median income was imputed for prior years (2006 to 2010) by deflating AHRQ income values using the US Bureau of Labor and Statistics Employment Cost Index.[43] Income values were inflation adjusted to 2018 USD.

1.2.4. Study Design & Analysis

Using a difference-in-differences (DID) event study approach with an ordinary least squares regression, we estimated the change in beneficiary-level OOP spending between the non-LIS and LIS groups in each year from 2006 to 2018 compared to 2010 as the baseline period. This analysis is represented by the following regression model (Equation 1.1):

$$Y_{it} = \beta_0 + \alpha_i + \sum_t \beta_1 Year_t + \sum_t \beta_2 nonLIS_i + \sum_t \beta_3 nonLIS_i \cdot Year_t + \beta_4 X'_{it} + \epsilon_{it}, \qquad (1.1)$$

where Y_{it} represents the outcome, OOP spending, for beneficiary i in year t; α_i is a set of dummy variables for individual fixed effects; $Year_t$ is a set of year indicator variables for year fixed effects; $nonLIS_i$ is an indicator variable for assignment of beneficiary i to the non-LIS ($nonLIS_i$ =1) or LIS group ($nonLIS_i$ =0) based on receipt of the LIS; X'_{it} is a set of time-varying covariates; and ε_{it} is the error term. The β_3 coefficients are the effects of coverage gap closure in

each year on OOP spending relative to the reference year (2010), one year prior to the policy implementation, between the treatment and control groups. Standard errors were clustered at the state level.

To examine heterogeneity in the effects of coverage gap closure, we performed subgroup analyses according to age (65-74, 75-84, 85+ years) and sex, as defined by the Medicare beneficiary summary file. The statistical analyses were performed using R Studio, version 4.3.2 (RStudio, PBC, Boston, MA, US).

1.3. Results

1.3.1. Study Sample

A total of 3252 individuals, accounting for 29,841 person-year observations over the study period, were included in the analysis (Appendix A1. 2). There were 1923 and 1329 individuals in the non-LIS and LIS arms, respectively. The mean age of all individuals was 73.9 years (standard deviation [SD], 8.92), 63.6% were female, 51.2% had three or more chronic conditions, the average median income by zip code was $45,800 (SD, 17,900), and 55.6% had a diagnosis of ADRD (Table 1.2). Descriptive statistics demonstrated differences between the two arms. The LIS group had a larger proportion of females and individuals under age 65 years, and more chronic conditions compared to the non-LIS arm (Table 1.2). See Appendix A1. 3 for sample sizes by year and subgroup.

Table 1.2. Sample characteristics.

	LIS	non-LIS	Overall
N	1329	1923	3252
Age			
Mean (SD)	71.4 (10.4)	75.0 (7.27)	73.9 (8.92)
Median [Min, Max]	71.0 [34.0, 105]	75.0 [51.0, 97.0]	74.0 [34.0, 105]
Age Group			
<65	262 (19.7%)	49 (2.5%)	311 (9.6%)
65-74	578 (43.5%)	847 (44.0%)	1425 (43.8%)
75-84	349 (26.3%)	787 (40.9%)	1136 (34.9%)
85+	140 (10.5%)	240 (12.5%)	380 (11.7%)
Sex			
Male	366 (27.5%)	818 (42.5%)	1184 (36.4%)
Female	963 (72.5%)	1105 (57.5%)	2068 (63.6%)
Chronic Conditions			
0	224 (16.9%)	695 (36.1%)	919 (28.3%)
1	135 (10.2%)	201 (10.5%)	336 (10.3%)
2	151 (11.4%)	181 (9.4%)	332 (10.2%)
3+	819 (61.6%)	846 (44.0%)	1665 (51.2%)
Income Quintiles by Zip			
1st	23 (1.7%)	31 (1.6%)	54 (1.7%)
2nd	516 (38.8%)	736 (38.3%)	1252 (38.5%)
3rd	556 (41.8%)	826 (43.0%)	1382 (42.5%)
4th	215 (16.2%)	296 (15.4%)	511 (15.7%)
5th	17 (1.3%)	30 (1.6%)	47 (1.4%)
Missing	2 (0.2%)	4 (0.2%)	6 (0.2%)
Hospice			
Yes	6 (0.5%)	0 (0%)	6 (0.2%)

Diagnosis			
ADRD	710 (53.4%)	1097 (57.0%)	1807 (55.6%)
Dementia, other	110 (8.3%)	73 (3.8%)	183 (5.6%)
MCI	495 (37.2%)	722 (37.5%)	1217 (37.4%)
Other	14 (1.1%)	31 (1.6%)	45 (1.4%)

Notes: Characteristics of individuals in the study sample (2006-2018). Individuals had a diagnosis of either ADRD, senile dementia, MCI, memory loss, other types of dementia (unspecified dementia without behavioral disturbance, corticobasal degeneration, other specified senile psychotic conditions, unspecified senile psychotic conditions), or cognitive deficit, or were classified as cognitive impairment with or without dementia according to the Langa-Weir algorithm. We required continuous enrollment for the entire year, enrollment in at least one year before and one year after initiation of coverage gap closure, and at least one non-zero Part D claim. The control group was person-waves for individuals either deemed eligible for or enrolled in the LIS.
LIS: Low-income subsidy.

1.3.2. Overall Effect

The effect of coverage gap closure on annual OOP spending is represented by the estimated β_3 coefficients from Equation (1.1). The fully adjusted model showed a significant decrease in OOP spending in the first year after initiation of coverage gap closure, which is maintained until the end of the study period (Figure 1.1). The donut hole closure resulted in an average decrease in OOP spending of $134 (95% CI: -174 to -94; $p<0.001$) in 2011 compared to 2010 among cognitively impaired Medicare beneficiaries, with further decrease in later years, though the estimates become noisier towards the end of the study period as the sample size gets smaller (Figure 1.1 and Appendix A1. 3). The parallel trends assumption is validated, demonstrated by non-significant changes in OOP from 2006 to 2009.

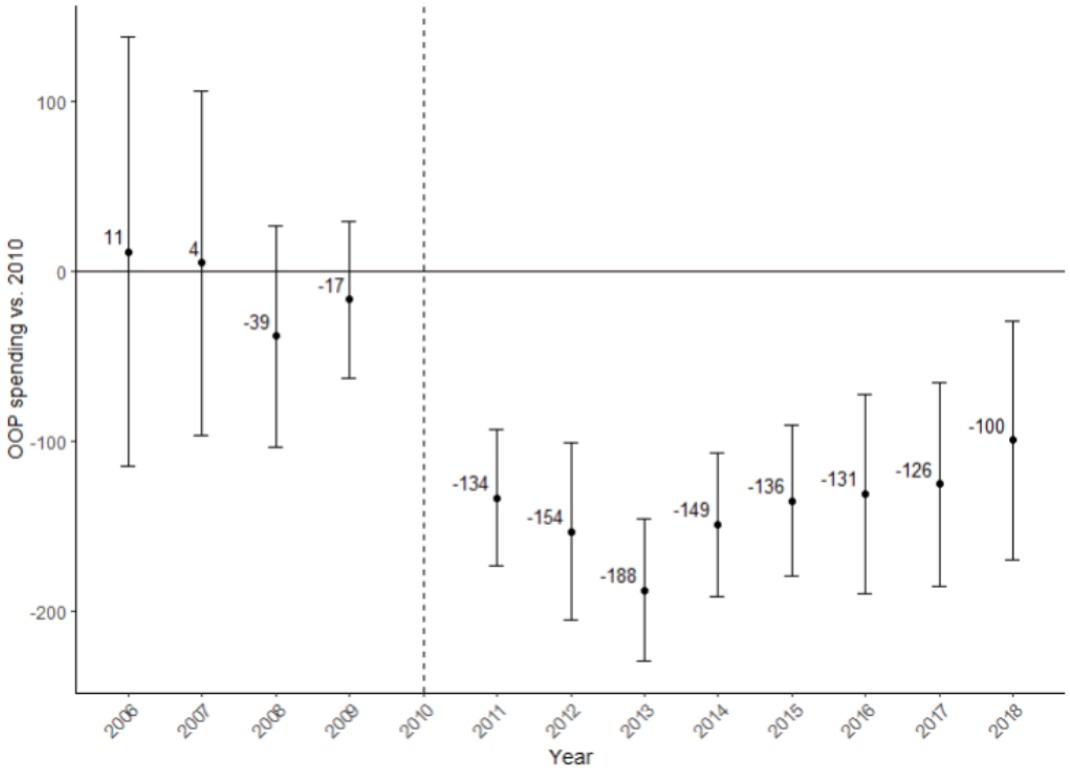

Figure 1.1. Effects of coverage gap closure on OOP spending compared to 2010.

This figure reports the coefficients on nonLIS*Year using Equation (1.1), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.

Figure 1.2 depicts the predicted values for OOP spending over time from the fully adjusted model. The non-LIS group experiences a consistent decline in OOP spending after enactment of the ACA, whereas OOP spending in the LIS group remains quite stable (Figure 1.2).

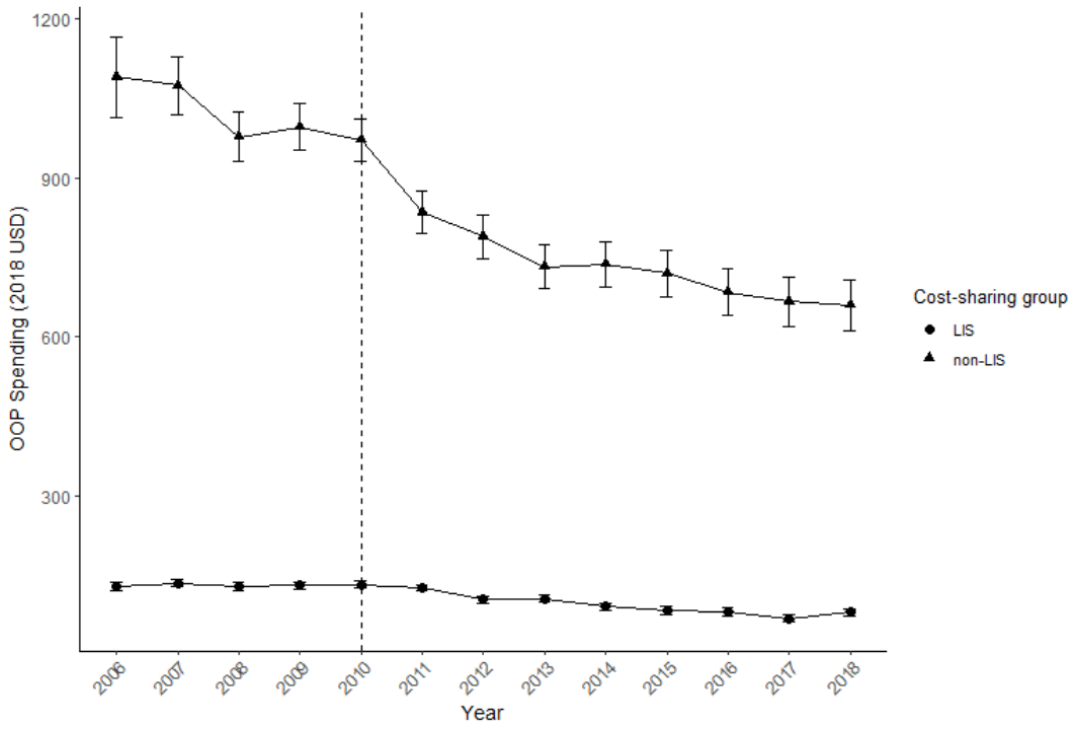

Figure 1.2. OOP spending over time based on predicted values from the fully adjusted model.

1.3.3. Subgroup Analyses

1.3.3.1. Age

Similar to the results of the overall sample, the fully adjusted models for age subgroups (65-74, 75-84, 85 and over) show an immediate decrease in OOP spending the first year after the ACA is implemented (Figure 1.3, Panels A, B, C). For example, for individuals aged 75-84 years, the impact of donut hole closure was an average decrease in OOP spending of $147 (95% CI: -211 to -82; $p<0.001$) in 2011 (Figure 1.3, Panel B). However, not all of the post-period changes in OOP spending were statistically significant, likely due to small subgroup sample sizes. The policy had a more prominent impact among the older subgroups, with individuals aged 85 years or older experiencing more consistent and statistically significant decreases in OOP spending for most

years during the post period. As with the full sample analyses, the parallel trends assumption is validated.

1.3.3.2. Sex

As with the results of the overall sample, the fully adjusted models for sex subgroups (female, male) show an immediate decrease in OOP spending the first year after the ACA is implemented (Figure 1.3, Panels D and E). For example, for females, the impact of donut hole closure was an average decrease in OOP spending of $140 (95% CI: -188 to -91; $p<0.001$) in 2011 (Figure 1.3, Panel E). For the male subgroup, the parallel trends assumption was violated and therefore the post-period changes in OOP spending were not interpretable. Conversely, the assumption held in the female subgroup and all post-period changes were statistically significant, except for 2018, again likely due to small sample size.

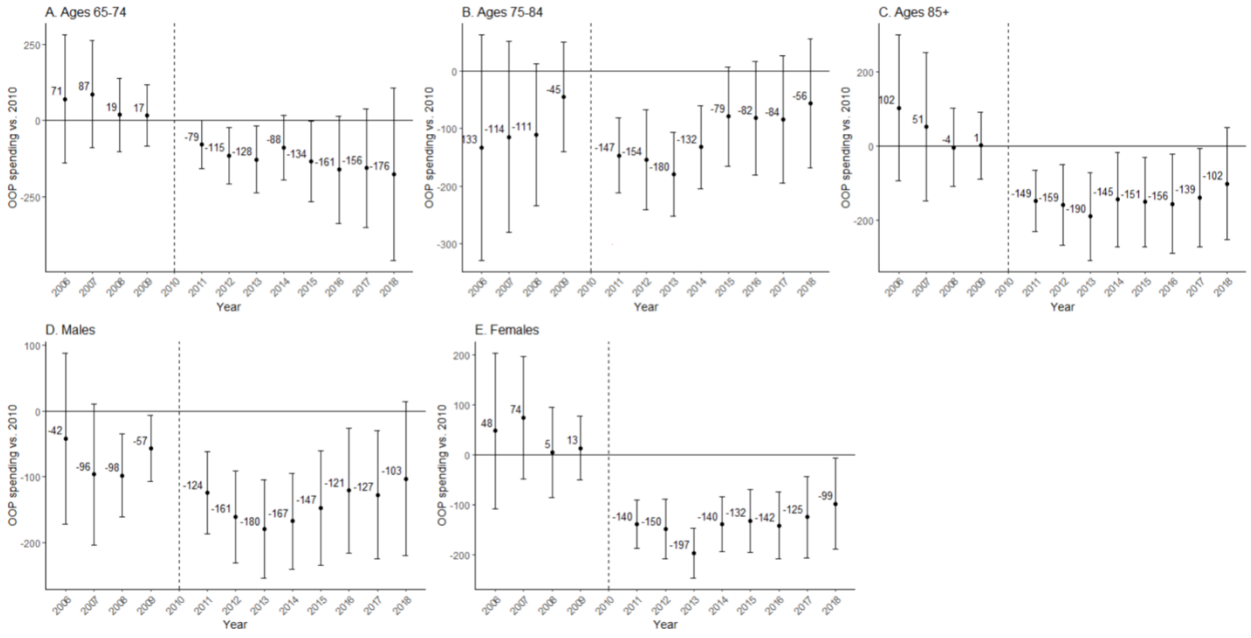

Figure 1.3. Age and sex subgroup effects of coverage gap closure on OOP spending compared to 2010.

This figure reports the coefficients on nonLIS*Year using Equation (1.1), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.

1.4. Discussion

We conducted a quasi-experimental study with a differences-in-differences event study approach to evaluate the effect of Medicare Part D coverage gap closure from 2011-2018 on OOP spending in cognitively impaired beneficiaries. We found that closure of the Medicare Part D coverage gap resulted in a significant reduction in OOP spending in Medicare beneficiaries with cognitive impairment. This result remained consistent across age subgroups (65-74, 75-84, 85+ years) and among females in our sample.

From a policy perspective, our findings of decreased OOP spending suggest that affordable medication initiatives, such as the IRA, can be successful in reducing the patient cost burden for vulnerable subpopulations. Reduced OOP spending is likely to improve medication adherence and disease management. Studies show that increased insurance coverage in the Part D coverage gap led to higher medication adherence and use among the general Medicare population and those with chronic conditions, such as diabetes and heart disease. [7,14,44] Nonadherence to medications for chronic conditions could have consequences for morbidity, mortality, and healthcare costs.[44–46] Better management of comorbidities, such as diabetes, heart failure, and hypertension, can allow healthier aging for vulnerable older adults with cognitive impairment.[17]

To our knowledge, this is the first analysis of the impact of Part D coverage gap closure in people with cognitive impairment. Our results show that these beneficiaries are affected by the policy as we observe a reduction in their OOP spending, indicating that it successfully increased the affordability of their medication. This reduction is especially meaningful in light of previous literature showing that patients with dementia face a considerable economic burden due to their prescription medications, which stems from their diagnosis and the fact that they often have multiple chronic conditions.[33,47] This mechanism is supported by earlier literature, including a study by Liu *et al.*, which focused on beneficiaries with mental health disorders, including Alzheimer's disease, and found similar results, with more substantial decreases in spending due to the greater number of medications used compared to the general Medicare population.[13] According to the Alzheimer's Association, 73% of people with ADRD also have hypertension, 38% have heart disease, and 37% have diabetes, which are all conditions that require chronic

medication.[48] Furthermore, polypharmacy is an important issue in patients with dementia. In fact, compared to individuals without dementia, they are more likely to be on 5 or more, or 10 or more repeat prescriptions.[47] This level of OOP spending is such that patients with dementia had an extreme high risk of entering the coverage gap compared to individuals with other conditions. One study found that 39.5% of dementia patients entered the coverage gap, that their risk of entering the gap was doubled, and that their risk of entering within the first six months of the year was tripled.[20]

The causal link from coinsurance rates to OOP spending has been demonstrated in previous studies, and our findings support this link. In two studies examining the effects of Part D coverage gap closure and comparing non-LIS and LIS beneficiaries, Liu *et al.* found that OOP spending substantially decreased after enactment of the ACA, driven mainly by reduced spending on branded drugs.[13,14] While we did not explore the individual impact of branded and generic drugs, the observed decrease in spending is in line with our findings. Furthermore, an AHRQ study of Medicare Part D OOP spending using MEPS data from 2009 to 2018 found that median out-of-pocket drug spending fell by $181.[49]

The age-related results showed a reduction in Medicare Part D OOP spending with coverage gap closure and a more pronounced effect for older subgroups, as expected. A Kaiser Family Foundation report on Medicare Part D conducted in 2007, prior to the ACA, concluded that enrollee likelihood of reaching the coverage gap increased with age, going from 25% of Part D enrollees aged 65-74 to 33% of those age 85 and older.[50] In their study, Liu *et al.* included the

same age subgroups and found similar heterogeneous effects by age group, with reductions in OOP spending increasing with age.[14]

The analysis of sex subgroups was important because previous studies of Medicare enrollees have shown sex-related disparities with women having disproportionately higher rates of some especially costly health conditions, such as Alzheimer's disease.[51] Because of this, it is expected that women will benefit more from Part D benefit design changes that reduce cost-sharing. The substantially greater proportion of women in our study (63.6%), and the significant and sustained reduction in OOP spending are therefore in line with expectations.[41]

An important strength of this study is the linkage of HRS survey data, which provides an additional layer of information that Medicare claims alone do not allow. The HRS Langa-Weir Classification allows for the identification of beneficiaries with dementia or cognitive impairment without dementia who do not yet have a diagnosis claim, as cognitive impairment and dementia can often go undetected in early stages.[15,39,40]

All results must be interpreted considering this study's limitations. First, quasi-experimental designs can be subject to threats of internal validity due to residual confounding, which hinders strong causal conclusions. DID is limited by the need to find comparison groups that are as similar as possible.[52,53] The treated and control groups should be so similar that the only difference between them is exposure to the policy, after controlling for potential confounders. While DID accounts for time-invariant unobserved confounders, it does not account for those that are time-variant. Our choice of the LIS and non-LIS as our treatment groups is supported by

our results showing non-significant OOP spending changes in the pre-ACA period from 2006-2010.[54–59] Another limitation is that the use of HRS-Medicare linked data can introduce potential selection bias, as Medicare beneficiaries who took part in HRS and who consent to linkage between their HRS and Medicare data may be inherently different from individuals who did not. Therefore, our findings may not be generalizable to all Medicare patients or people without insurance. However, HRS features a nationally representative sample of US older adults, and consent rate of data linkage is over 85%, mitigating the concerns for selection bias.

1.5. Conclusion

In this large quasi-experimental study of Medicare beneficiaries with cognitive impairment, closure of the Medicare Part D coverage gap was associated with lower OOP spending on medications. This study yields insight into the economic and health burden of the coverage gap for cognitively impaired Medicare beneficiaries. It also lays a foundation for further investigation into other chronic diseases, such as cancers and rheumatoid arthritis, which are often managed by prescription medication and result in high OOP spending for the Medicare population.[60] Our findings can serve as support for considering changes to prescription drug coverage and cost, which is timely in the context of the Inflation Reduction Act, which will have profound effects on OOP spending.[21]

2. THE EFFECTS OF CLOSING THE MEDICARE PART D COVERAGE GAP ON MEDICATION USE IN OLDER ADULTS WITH ALZHEIMER'S DISEASE AND RELATED DEMENTIAS

ABSTRACT

Background

The Affordable Care Act gradually eliminated the Medicare Part D coverage gap between 2011 and 2020 by reducing coinsurance from 100% to 25% to reduce the cost burden of prescription drug costs. Medication discontinuation rates are high among individuals with cognitive impairment, due to both cost and their decline in cognitive and functional status. We evaluated the effects of reduced coinsurance on medication use for beneficiaries with Alzheimer's disease and related dementias (ADRD).

Methods

The study sample was Health and Retirement Study respondents with ADRD, linked to Medicare claims (2006-2018). The outcome of interest was the annual probability of Alzheimer's disease (AD) medication use. Using difference-in-differences and event study approaches, we estimated the differential change in the probability of AD medication use for non-low-income subsidy (LIS) respondents, as compared to LIS respondents, who were not subject to the coverage gap.

Results

A total of 10,830 non-LIS and 7163 LIS person-years were included (66.8% female, mean age 79.9 years), with 21.9% and 25.6% on AD medication, respectively. Closure of the coverage gap

resulted in an increase in the probability of AD medication use in beneficiaries with ADRD (4.3 percentage points; 95% CI: 1.2-7.4; p=0.017). Closure had significant associations among younger beneficiaries and males.

Conclusion

In beneficiaries with ADRD, closure of the Medicare Part D coverage gap increased AD medication use on average, indicating that patient financial responsibility in prescription drug insurance design drives use in this population.

2.1. Background

Medicare launched its Part D prescription drug benefit in 2006 with the goal of reducing financial barriers to facilitate the use of drugs that would not have been used in the absence of coverage.[2] In other words, Part D aimed to increase the affordability of and access to medications. The benefit was a success, as studies on the overall effect of Part D have found that the policy resulted in a 5.9-12.8% increase in prescription drug use and a 13.1-15.6% decrease in OOP spending.[3,4] Established through Part D in partnership with state Medicaid programs, the low-income subsidy (LIS) helps beneficiaries with limited income by assisting with the premiums and cost-sharing associated with the Part D benefit. Beneficiaries receiving the LIS have never been subject to Part D coinsurance.[14]

Despite this progress, the Part D coverage gap remained an important financial barrier due to its 100% coinsurance rate. Previous studies have found that the coverage gap was associated with lower medication use and adherence; whereas others saw no change for essential drugs.[5–7]

Adherence is defined as a patient taking a prescribed medicine or following the provider's instructions for taking the medicine.[61] The high OOP expenses from drugs often results in individuals delaying or skipping necessary treatment.[26,27] Lower adherence due to increased cost is not unique to Medicare as it has been shown that beneficiaries of private drug benefit plans with annual coverage limits are also more likely to discontinue their medications.[62,63]

Alzheimer's disease and related dementias (ADRD) affects up to 36% of US adults over 65,[29] making them among the most common chronic conditions for Medicare beneficiaries. ADRD are progressed forms of cognitive impairment as individuals experience more severe symptoms and lose their ability to take care of themselves or conduct their daily activities.[64,65] Alzheimer's disease alone is expected to affect 13.8 million older Americans by 2060,[30] making it an important public health concern.[15,16] People with ADRD often have impaired healthcare decision-making resulting in challenges with medication management and an increase in their risk for non-adherence.[18,19,66,67] Understanding the effects of coverage gap closure on adherence to commonly used, oral Alzheimer's disease medications is especially important because changes in benefits and coverage may be more difficult to track for this vulnerable population.[18–20] A prior study of Medicare beneficiaries with dementia found that, among new antidementia medication users, 23% discontinued within one month and 62% discontinued within one year.[68] A pragmatic clinical trial with 18 weeks of follow-up found that discontinuation rates for antidementia medications ranged from 39-59%, with 29.4% of individuals citing cost as their reason for discontinuing.[35] In addition to cost barriers, experiences of side effects or adverse drug events, perceived decline in cognitive/functional status, and worsening behavioral symptoms have been associated with non-adherence to antidementia medication.[68]

The effects of the Part D coverage gap closure are of interest to patients, providers, and policy makers. The objective of this study was to evaluate the effects of the gradual Medicare Part D coverage gap closure over a 10-year period on the utilization of and adherence to Alzheimer's disease (AD) medication in beneficiaries with ADRD. This topic is especially relevant today in the context of the Inflation Reduction Act (IRA), which will lead to lower drug costs and capped OOP spending for beneficiaries, and hopefully improve adherence.[21]

2.2. Materials & Methods

2.2.1. Data Sources

We used the Health and Retirement Study (HRS)–Medicare Linked Data from 2006 to 2018. These datasets include HRS survey information linked to the Centers for Medicare and Medicaid Services (CMS) claims and assessment data for the HRS study population. Of the Medicare data files, those of interest were beneficiary summary files, fee-for-service (FFS) inpatient and outpatient files, and Part D event files. The HRS has been fielded since 1992 and surveys more than 30,000 people aged 50 and older. To obtain zip code level income data, we used the Agency for Healthcare Research and Quality (AHRQ) Social Determinants of Health data. We used the Marketscan Redbook® to identify Alzheimer's disease drugs of interest by connecting it to the Medicare Part D event file via National Drug Classification codes. Part D pharmacy claims were included for the following AD drugs of interest: donepezil, galantamine, rivastigmine, memantine, and combination donepezil+memantine.

2.2.2. Sample Selection

Individuals eligible for inclusion in the primary analysis had a diagnosis of ADRD. They were identified using Medicare claims Chronic Conditions Warehouse variables, International Classification of Disease codes 9th (ICD-9) and 10th (ICD-10) versions and the HRS Langa-Weir Classification of Cognitive Function (Appendix A2. 1).[27,28] A sensitivity analysis expanded the criteria to a broader definition of cognitive impairment and added senile dementia, MCI, memory loss, other types of dementia, or cognitive deficit (see Appendix A2. 2 for results). We required continuous Medicare enrollment for at least one year before initiation of coverage gap closure (January 1, 2011) and one continuous calendar year after closure initiation, and at least one non-zero dollar Part D claim (see Appendix A2. 2 for sample selection details). The control group was comprised of person-waves for individuals either deemed eligible for or enrolled in the LIS, as these beneficiaries were never subject to the coverage gap.

2.2.3. Measures

Individuals were considered exposed to the policy if they experienced the effects of Part D coverage gap closure, as defined by not receiving LIS. Initiation of coverage gap closure occurred in 2011, with coinsurance rates dropping from 100% to 50% (93%) for branded (generic) drugs (Table 2.1).

Table 2.1. Coinsurance* rates in the Medicare Part D coverage gap over time.

	2006-2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Branded	100%	50%	50%	47.5%	47.5%	45%	45%	40%	35%	30%	25%
Generic	100%	93%	86%	79%	72%	65%	58%	51%	44%	37%	25%

*The proportion of the medication cost borne by the beneficiary.

Medication use was defined as the presence of any Part D event claim for an AD drug in a given year. Our covariates included the following time-varying measures: a categorical count (0, 1, 2, 3+) of high-priority chronic conditions defined by CMS, and median income by zip code.[42] Median income by zip code from 2011 to 2018 was directly available from AHRQ. Median income was imputed for prior years (2006 to 2010) by deflating AHRQ income values using the US Bureau of Labor and Statistics Employment Cost Index.[43] Income values were inflation adjusted to 2018 USD.

2.2.4. Statistical Analyses

We examined the extensive margin of use (probability of any AD medication use) by estimating the association between closure of the Part D coverage gap and any AD medication use.[32,33] Using the difference-in-differences (DID) method with a linear probability model, we assessed the effect of coverage gap closure on the average probability of AD medication use between non-LIS and LIS groups, comparing years after gap closure (2011-2018) to those before closure (2006-2010) (Equation 2.1).

To gain insight into how coverage gap closure effects changed in each year of the study period, we used a DID event study approach with a linear probability model. We estimated the change in the beneficiary-level probability of AD medication use between the non-LIS and LIS groups in each year from 2006 to 2018 compared to 2010 (Equation 2.2).

$$Y_{it} = \beta_0 + \alpha_i + \theta_t + \beta_1 Post_t + \beta_2 nonLIS_i + \beta_3 nonLIS_i \cdot Post_t + \beta_4 X'_{it} + \epsilon_{it}, \quad (2.1)$$

$$Y_{it} = \beta_0 + \alpha_i + \sum_t \beta_1 Year_t + \sum_t \beta_2 nonLIS_i + \sum_t \beta_3 nonLIS_i \cdot Year_t + \beta_4 X'_{it} + \epsilon_{it}, \quad (2.2)$$

where Y_{it} represents the outcome, the probability of medication use, for beneficiary i; α_i and θ_t are sets of indicator variables for individual and year fixed effects, respectively; *Post* is an indicator variable for periods before (Post=0) or after (Post=1) gap closure; $Year_t$ is a set of year indicator variables; $nonLIS_i$ is an indicator variable for assignment of beneficiary i to the treatment ($nonLIS_i$ =1) or control group ($nonLIS_i$ =0) based on receipt of the LIS; X'_{it} is a set of time-varying covariates (a categorical count of chronic conditions and median income by zip code); and ε_{it} is the error term. The β_3 coefficients estimated the effect of coverage gap closure on medication use probability between the treatment and control groups. In Equation (2.1), it is the overall effect in the post-period (years 2011-2018) relative to the pre-period (2006-2010). In Equation (2.2), coefficients are generated for each year relative to the reference year (2010), one year prior to the policy implementation. Standard errors were clustered at the state level.

2.2.4.1. Subgroup analyses

The following subgroup analyses were conducted to explore heterogeneity in the effects of coverage gap closure among beneficiaries with ADRD: age (65-74, 75-84, 85+), sex (females and males).

The statistical analyses were performed using R Studio, version 4.3.2 (RStudio, PBC, Boston, MA, US).

2.3. Results

2.3.1. Study Sample

A total of 1807 individuals accounting for 17,993 person-years over the study period were included in the analysis (Appendix A2. 2). There were 10,830 and 7163 person-year observations in the non-LIS (treated) and LIS (control) arms, respectively. The mean age of all individuals was 79.9 years (standard deviation [SD], 8.54), 66.8% were female, 57.3% had three or more chronic conditions, the average median income by zip code was $50,200 (SD, 20,200) (Table 2.2). Descriptive statistics demonstrated differences between the two arms. The LIS group had a larger proportion of females and individuals under age 65 years, and more chronic conditions compared to the non-LIS arm (Table 2.2). Of the 17,993 total observations, 4210 had a claim for an AD drug of interest, including 2312 for donepezil, 127 for galantamine, 1369 for memantine, 21 for the combination of donepezil and memantine, and 381 for rivastigmine (10 individuals). Only 6.8% of the sample exclusively used branded drugs in a given calendar year. See Appendix A2. 3 for sample sizes by year and subgroup, Appendix A2. 4 for beneficiary-level sample characteristics, Appendix A2. 5 for broader cognitive impairment beneficiary-level sample characteristics, and Appendix A2. 6 for broader cognitive impairment person-year-level sample characteristics.

Table 2.2. ADRD person-year sample characteristics.

	LIS	**non-LIS**	**Overall**
N	7163	10,830	17,993
Age			
Mean (SD)	78.4 (10.2)	80.8 (7.10)	79.9 (8.54)
Median [Min, Max]	79.0 [34.0, 110]	81.0 [53.0, 110]	80.0 [34.0, 110]
Age Group			
<65	639 (8.9%)	51 (5.1%)	690 (3.8%)

65-74	1637 (22.9%)	2105 (19.4%)	3742 (20.8%)
75-84	2896 (40.4%)	5314 (49.1%)	8210 (45.6%)
85+	1991 (27.8%)	3360 (31.0%)	5351 (29.7%)
Sex			
Male	1755 (24.5%)	4215 (38.9%)	5970 (33.2%)
Female	5408 (75.5%)	6615 (61.1%)	12,023 (66.8%)
Chronic Conditions			
0	839 (11.7%)	2486 (23.0%)	3325 (18.5%)
1	471 (6.6%)	786 (7.3%)	1257 (7.0%)
2	558 (7.8%)	931 (8.6%)	1489 (8.3%)
3+	5295 (73.9%)	6627 (61.2%)	11,922 (66.3%)
Income, Median by Zip			
Mean (SD)	$45,800 (18,200)	$53,100 (20,900)	$50,200 (20,200)
Median [Min, Max]	$41,600 [13,200, 172,000]	$48,600 [12,500, 250,000]	$45,800 [12,500, 250,000]
Income Quintiles by Zip			
1st	106 (1.5%)	76 (0.7%)	182 (1.0%)
2nd	3247 (45.3%)	2189 (29.4%)	6436 (35.8%)
3rd	2842 (39.7%)	5209 (48.1%)	8051 (44.7%)
4th	867 (12.1%)	2111 (19.5%)	2978 (16.6%)
5th	98 (1.4%)	224 (2.1%)	322 (1.8%)
Missing	3 (0.0%)	21 (0.2%)	24 (0.1%)
Medication			
Donepezil	972 (13.6%)	1340 (12.4%)	2312 (12.8%)
Donepezil + Memantine	13 (0.2%)	8 (0.1%)	21 (0.1%)
Galantamine	28 (0.4%)	99 (0.9%)	127 (0.7%)
Memantine	605 (8.4%)	764 (7.1%)	1369 (7.6%)
Rivastigmine	215 (3.0%)	166 (1.5%)	381 (2.1%)
None	5530 (74.4%)	8453 (78.1%)	13,783 (76.6%)

Branded drug only			
No	6596 (92.1%)	10,168 (93.9%)	16,764 (93.2%)
Yes	567 (7.9%)	662 (6.1%)	1229 (6.8%)

Notes: Characteristics of person-years in the study sample (2006-2018). Individuals had a diagnosis of ADRD. We required continuous enrollment for the entire year, enrollment in at least one year before and one year after initiation of coverage gap closure, and at least one non-zero Part D claim. The control group was person-waves for individuals either deemed eligible for or enrolled in the LIS.
LIS: Low-income subsidy.

2.3.2. Overall effect

The average effect of coverage gap closure on the probability of AD medication use is represented by the estimated β_3 coefficient from Equation (2.1) and annual effects by the estimated β_3 coefficients from Equation (2.2). Among Medicare beneficiaries with ADRD, the fully adjusted DID model showed that coverage gap closure led to a significant increase in the probability of AD medication use of 4.3 percentage points (95% CI: 1.2-7.4; p=0.017) (Table 2.3). This translates into a 19.6% increase in the probability of use. Event study results showed non-significant increases in the annual probability of use from 2011 to 2016 (2011 vs. 2010: 1.2 percentage points; 95% CI: -2.0-4.3). There were eventual significant increases in 2017 and 2018 (2017 vs. 2010: 9.1 percentage points; 95% CI: 1.6-16.6; p=0.02), once coinsurance rates fell to 40% (51%) for branded (generic) drugs (Figure 2.1). The parallel trends assumption is validated, demonstrated by non-significant changes in OOP from 2006 to 2009.

Table 2.3. Effect of coverage gap closure on the probability of medication use among beneficiaries with ADRD.

	Estimate	**95% CI**	**p-value**
Overall			
ADRD only	0.043	0.012, 0.074	0.017*

Subgroups			
Ages 65-74	0.030	0.0057, 0.053	0.015*
Ages 75-84	0.0033	-0.035, 0.042	0.86
Ages 85+	0.027	-0.022, 0.76	0.28
Males	0.056	0.017, 0.094	<0.01*
Females	0.026	-0.0012, 0.052	0.061

This table reports the coefficients on non-LIS*post using Equation (2.1), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.
ADRD: Alzheimer's disease and related dementias; CI: Confidence interval

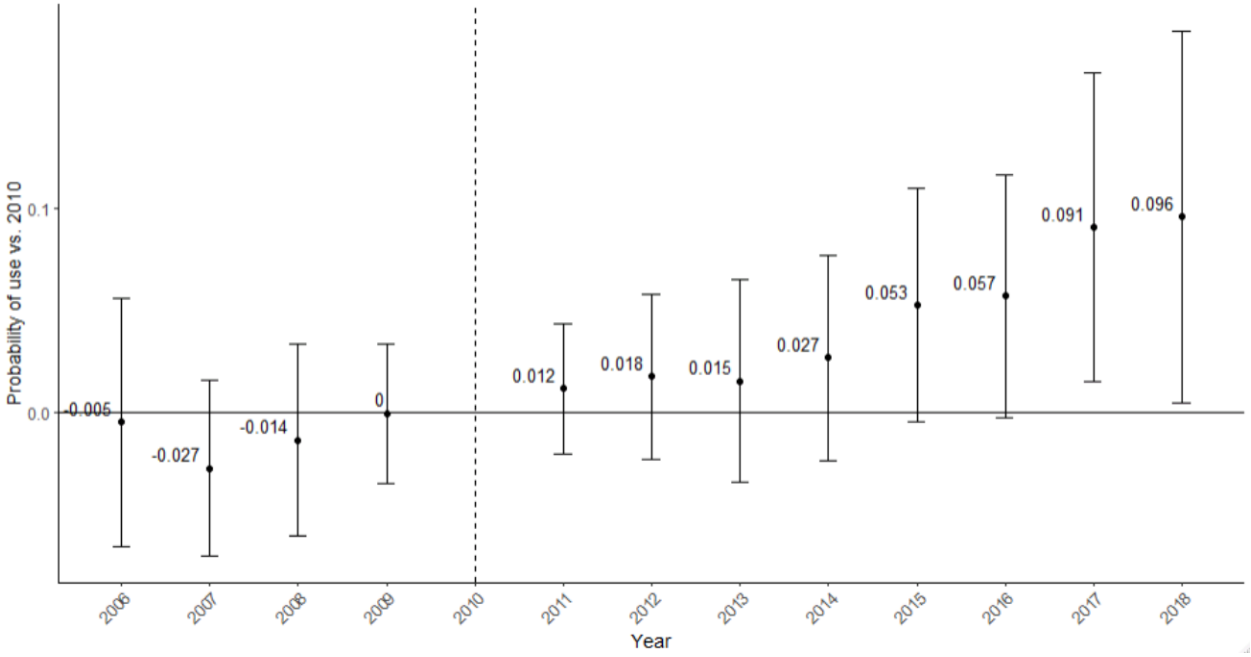

Figure 2.1. Effects of coverage gap closure on the probability of medication use compared to 2010 in beneficiaries with ADRD.

This figure reports the coefficients on non-LIS*Year using Equation (2.2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.

2.3.3. Subgroup analyses

Closure of the coverage gap was associated with significant increases in the probability of AD medication use in beneficiaries aged 65-74 years (3.0 percentage points; 95% CI: 0.57-5.3%; p=0.015) and males (5.6 percentage points; 95% CI: 1.7-9.4%; p<0.01) (Table 2.3). See Appendices A2.7, A2.7.1, A2.7.2 for difference-in-differences and event study results for the broader cognitive impairment sample.

2.4. Discussion

We conducted a quasi-experimental study using difference-in-differences and event study approaches to examine the effect of Medicare Part D coverage gap closure from 2011 to 2018 on medication use among beneficiaries with ADRD. We found that coverage gap closure led to a significant 19.6% increase in the average probability of medication use, mostly due to increases that occurred in 2017 and 2018. Coverage gap closure led to significant increases in the probability of use among the younger beneficiaries and males.

Our findings indicate that cost-sharing has important effects on medication use in individuals with ADRD. As was intended by the ACA, lowering Part D coinsurance rates increased the affordability of medications, which encouraged beneficiaries to fill their prescriptions. Our results also showed that the annual increases in use were not statistically significant until 2017. This finding may align with other studies showing no change in generic drug use with closure of the coverage gap, as all of our drugs of interest were off patent by 2010, except memantine.[4,34]

Furthermore, the decreases in the coinsurance rate are larger in later years compared to 2010, which likely contribute to the larger responses.

While there have been many studies examining Medicare Part D, most have focused on the effect of launching Part D on use and adherence; few have examined the effects of coverage gap closure.[2,3,5,7,35–37] Furthermore, only one study has used an event study approach to observe the annual effects of gap closure.[4] Liu et al. explored the effects of coverage gap closure on medication use in 10 drug classes and found an increase in the likelihood of monthly drug initiation at the extensive margin ranging from 0.2 to 1.6 percentage points.[4] This supports our finding of a significant increase in the probability of use after coverage gap closure. The same study included an event study examining supply counts and concluded that total supply counts of prescription drugs increased gradually following the coverage gap closure initiation, with more pronounced effects in the first two years of policy implementation. While our event study found no change in the probability of use immediately following the initiation of gap closure, our study focused on any medication use and not the number of claims, so these results cannot be directly compared. However, it is possible that patients who were already taking medication filled more prescriptions than they would have prior to gap closure; while patients who were not taking drugs before gap closure did not change their habits despite lower prices.

Our analysis of age subgroups found a significant change in the average probability of use for the younger subgroup of ADRD beneficiaries aged 65-74 years. A study by Liu *et al*. observed that the increase in branded drug use after the ACA was due to younger Medicare beneficiaries,

indicating a higher price sensitivity among this group.[4] Our results are consistent with this, though we did not explore trends in branded versus generic drugs. [37]

There were important strengths to this study. First is the linkage of HRS survey data, which provides an additional layer of information that Medicare claims alone do not allow. The HRS Langa-Weir Classification allowed for the identification of beneficiaries with ADRD who do not yet have a diagnosis claim, as there is a considerable amount of off-label medication use in this population.[39,40,71] Second, our use of the event study approach is unique as most research has examined average changes before and after Part D launch or ACA enactment. Finally, the proportion of our sample with a diagnosis of ADRD who used a medication matches that of other studies using HRS data.[72]

All results must be interpreted considering this study's limitations. First, quasi-experimental designs can be subject to threats of internal validity due to residual confounding, which hinders strong causal conclusions. DID is limited by the need to find comparison groups that are as similar as possible.[52,53] The treated and control groups should be so similar that the only difference between them is exposure to the policy, after controlling for potential confounders. While DID accounts for time-invariant unobserved confounders, it does not account for those that are time-variant. Our choice of the LIS and non-LIS as our treatment groups is supported by our results showing non-significant OOP spending changes in the pre-ACA period from 2006-2010.[54–59] Another limitation is that the use of HRS-Medicare linked data can introduce potential selection bias, as Medicare beneficiaries who took part in HRS and who consent to linkage between their HRS and Medicare data may be inherently different from individuals who did not.

Therefore, our findings may not be generalizable to all Medicare patients or people without insurance. However, HRS features a nationally representative sample of US older adults, and consent rate of data linkage is over 85%, mitigating the concerns for selection bias. A third limitation is the small number of beneficiaries on each AD drug of interest, which prevented us from conducting the adherence analysis. A possible solution to this issue would be to use 100% Medicare data, which would allow us to tackle an important question that has not yet been explore as studies have focused on utilization instead of adherence.

2.5. Conclusions

In this quasi-experimental study of Medicare beneficiaries with ADRD and cognitive impairment, closure of the Medicare Part D coverage gap led to significant changes in AD medication use. This study yields insight into the role coinsurance plays in the use of medications among Medicare beneficiaries with ADRD. It is important to explore this topic for other chronic conditions because nonadherence to medications for these conditions could have consequences for morbidity, mortality, and healthcare costs.[44–46] Better management of comorbidities, such as diabetes, heart failure, and hypertension, can allow healthier aging for vulnerable older adults. Our findings can serve as support for considering changes to prescription drug coverage and cost, which is timely in the context of the Inflation Reduction Act, which will have profound effects on medication use.[21]

3. THE ASSOCIATION BETWEEN MEDICATION ADHERENCE AND HEALTHCARE COSTS AND UTILIZATION AMONG COGNITIVELY IMPAIRED OLDER ADULTS

ABSTRACT

Background

Medication discontinuation rates are high among individuals with cognitive impairment, due to both cost and their decline in cognitive and functional status. Adherence is essential in this population for managing their disease and comorbidities to reduce their healthcare use and expenditures. We evaluated the association between medication adherence and inpatient (IP) and emergency department (ED) related healthcare costs and visits.

Methods

The study sample was Health and Retirement Study respondents with cognitive impairment taking medication for Alzheimer's disease (AD), linked to Medicare claims (2006-2018). The outcomes of interest were total healthcare costs and visit counts for IP and ED hospitalizations. Using a two-part model approach, adjusting for year and individual fixed effects, chronic conditions, and median income by zip code, we estimated the association between adherence to AD medication (binary with proportion of days covered threshold at 80% and continuous) and the probability of incurring healthcare costs for IP and ED hospitalizations and the amount of those costs, as well as the probability of having an IP or ED hospitalization and the number of such visits.

Results

A total of 4511 person-years were included (68.9% female, mean age 81.7 years). Adherence to AD drugs was associated with significant reductions in the probability of incurring IP healthcare costs (-2.4 percentage points [ppts]; 95% CI: -4.3 to -0.55 ppts; p=0.011) and of having an IP hospitalization (-2.3 ppts; 95% CI: -4.26 to -0.40 ppts; p=0.018). However, adherence was not significantly associated with the amount of IP costs incurred conditioning on incurring any costs (4.0 ppt increase; 95% CI: -20.2 to 35.3 ppts) or the number of hospitalizations conditioning on having any hospitalizations (0.2 ppt increase; 95% CI: -14.4 to 17.5ppts). Adherence was significantly associated with a 6.4 ppt reduction in the probability of incurring ED costs (95% CI: -9.8 to -2.9 ppts; p<0.001) and a 6.5 ppt reduction in the probability of an ED visit (95% CI: -10.1 to -2.8 ppts; p<0.001). Additionally, adherence resulted in a 19.3 ppt reduction in total non-zero ED costs (95% CI: -30.2 to -6.7 ppts; p<0.01) and a 15.9 ppt reduction in the number of ED visits (95% CI: -22.7 to -8.2 ppts; p<0.01). Individuals 85 years or older and females had a lower probability of incurring costs or having an ED or IP visit.

Conclusion

In beneficiaries with cognitive impairment, adherence to AD medication was associated with a reduction in the independent probability of incurring IP and ED healthcare costs, as well as the occurrence of IP and ED hospitalizations, indicating that improved adherence might lead to better management of symptoms requiring costly care.

3.1. Background

Cognitive impairment, including Alzheimer's disease and related dementias (ADRD), affects up to 36% of US adults over 65,[1] making them among the most common chronic conditions for Medicare beneficiaries. Alzheimer's disease alone is expected to affect 13.8 million older Americans by 2060,[30] making it an important public health concern.[15,16] People with cognitive impairment often have impaired healthcare decision-making resulting in challenges with medication management and an increase in their risk for non-adherence.[18,19,66,67]

Medication adherence is defined as a patient taking a prescribed medicine per their healthcare provider's instructions.[9] Good adherence is associated with improved health outcomes and lower health care utilization, whereas avoidable health care costs due to non-adherence are estimated between $100-300 billion per year in the US.[8–12] Studies have shown that adherence to medications for chronic conditions is poor.[15] Barriers such as adverse drug events, perceived decline in cognitive/functional status, worsening behavioral symptoms, and out-of-pocket costs have been associated with non-adherence to antidementia medication.[68] A prior study of Medicare beneficiaries with dementia found that, among new antidementia medication users, 23% discontinued their medication within one month and 62% within one year.[68] A pragmatic clinical trial with 18 weeks of follow-up found that discontinuation rates for antidementia medications ranged from 39-59%.[35]

Improved medication adherence can reduce the need for expensive acute care. Examining older adults with dementia and major depressive disorder, Bhattacharjee et al. concluded that adherence was associated with reductions in all-cause hospitalization risk.[18] A study of Medicare

Advantage enrollees with chronic conditions found that adherence to maintenance medications during the first year of treatment was significantly associated with lower likelihood of hospitalization and ED encounters in the first two years of treatment.[10]

As the prevalence of ADRD continues to increase and national healthcare expenditures are on the rise, it is important to understand the association between adherence to Alzheimer's disease (AD) medications that treat these conditions and healthcare resource utilization and cost. While AD medications may not be expected to have direct health effects that influence healthcare resource use, adherence to them may help symptom management, and serve as a proxy for better management of comorbidities; effects on healthcare costs and utilization are therefore plausible. Utilization and cost are expected to be correlated in most cases, but there are health insurance reimbursement schemes and contractual agreements that result in differences in the occurrence of these two outcomes, thereby impacting patients and payers groups differently. Therefore, we will examine both in order to create more comprehensive policy recommendations. The objective of this study was to evaluate the association between AD medication adherence and inpatient (IP) and emergency department (ED) related healthcare costs and visits among Medicare beneficiaries with cognitive impairment.

3.2. Materials & Methods

3.2.1. Data Sources

We used the Health and Retirement Study (HRS) linked to Medicare claims from 2006 to 2018.[37] The HRS has been fielded since 1992 and surveys more than 30,000 people aged 50 and older every two years. Of the Medicare data files, we used the beneficiary summary files, fee-for-

service inpatient and outpatient files, and Part D event files. To obtain zip code level income data, we used the Agency for Healthcare Research and Quality (AHRQ) Social Determinants of Health data (2011-2020).[38] We used the Marketscan Redbook® to identify National Drug Classification codes for Alzheimer's disease drugs of interest.

3.2.2. Sample Selection

Our analytic sample included person-waves in which the respondent had a diagnosis of either ADRD, senile dementia, MCI, memory loss, other types of dementia, or cognitive deficit. These conditions were identified using Medicare claims Chronic Conditions Warehouse variables, International Classification of Disease codes 9th (ICD-9) and 10th (ICD-10) versions and the HRS Langa-Weir Classification of Cognitive Function (Appendix A3. 1).[39,40] To maintain a consistent selection approach across aims, we required continuous Medicare enrollment for at least one year prior to January 1, 2011 and one year after, and at least one non-zero dollar Part D claim (Appendix A3. 2). Part D pharmacy claims were included for the following AD drugs of interest: donepezil, galantamine, rivastigmine, memantine, and combination donepezil+memantine.

3.2.3. Measures

The exposure was adherence to the AD drugs of interest, measured by proportion of days covered (PDC). PDC is the proportion of days in the measurement period (one year) covered by prescription claims for the same medication or another in its therapeutic category.[75] Adherence was calculated using the prescription service dates and days supply for each Part D event claim, and the PDC time period began at first fill and ended at the end of the year. The primary measure of adherence was binary, with a PDC threshold at 80%, where beneficiaries were considered

adherent if PDC ≥ 80% and non-adherent otherwise. Sensitivity analyses used a continuous measure of adherence with PDC ranging from 0% to 100%.

The outcomes of interest were the probability of a visit or incurring costs, and the amount of each, analyzed separately for IP hospitalizations and ED visits. IP hospitalizations were obtained from the Medicare FFS inpatient files and ED visits from both the Medicare FFS inpatient and outpatient files (See Appendix A3. 2 for ED revenue center codes). All costs were inflation-adjusted to 2018 US dollars using the medical care component of the Consumer Price Index from the US Bureau of Labor and Statistics.[41]

In addition to year and individual fixed effects, the following time-varying covariates were included in the model: a categorical count (0, 1, 2, 3+) of high-priority chronic conditions defined by CMS, and median income by zip code.[42] Median income by zip code from 2011 to 2018 was directly available from AHRQ. Median income was imputed for prior years (2006 to 2010) by deflating AHRQ income values using the US Bureau of Labor and Statistics Employment Cost Index.[43] Income values were inflation adjusted to 2018 USD.

3.2.4. Study Design & Analysis

3.2.4.1. Two-part model

A two-part model estimated the association between adherence to AD medication and the odds of incurring healthcare costs for IP and ED hospitalizations and the amount of those costs, as well as the odds of having an IP or ED hospitalization and the number of such visits. The first part modelled the probability of incurring costs or experiencing a hospitalization (linear probability

model, Equation 3.1). The second part assessed the magnitude of the costs among those who incurred costs (generalized linear model with log link and gamma distribution, Equation 3.2) or the number of hospitalizations among those who experienced a hospitalization (negative binomial regression, Equation 3.2).

$$Y = \gamma_0 + \gamma_1 A_{it} + \gamma_2 W'_{it} + \alpha_i + \theta_t \quad (3.1)$$

$$\log [E(Z)] = \beta_0 + \beta_1 A_{it} + \beta_2 W'_{it} + \alpha_i + \theta_t \,, \quad (3.2)$$

where Y is the first outcome, probability of incurring IP or ED hospitalizations or costs comparing adherent to non-adherent beneficiaries; Z is the second outcome, the number of IP or ED hospitalizations or costs among beneficiaries with non-zero outcomes from part one; A_{it} represents exposure, adherence; W'_{it} is a set of time-varying covariates (a categorical count of chronic conditions and median income by zip code); α_i is a set of indicator variables for individual fixed effects; and θ_t is a set of indicator variables for year fixed effects. The γ_1 coefficient will estimate the difference in the probability of having a hospitalization or of incurring costs due to IP or ED visits, and the β_1 coefficient will estimate the difference in the number of visits or difference in costs if non-zero between adherent and non-adherent beneficiaries. Standard errors were clustered at the state level.

To examine heterogeneity in the association between adherence and utilization, we performed subgroup analyses according to age (65-74, 75-84, 85+ years) and sex, as defined by the Medicare beneficiary summary file. We also conducted sensitivity analyses for the binary

measure of adherence by varying the PDC threshold from 80% to 60% and 90%. The statistical analyses were performed using R Studio, version 4.3.2 (RStudio, PBC, Boston, MA, US).

3.3. Results

3.3.1. Study Sample

A total of 4511 patient-years accounting for 892 individuals over the study period were included in the analysis (Appendix A3. 3). There were 1800 and 2711 patient-years in the non-adherent and adherent groups, respectively. The mean age of all patient-years was 81.7 years (standard deviation [SD], 7.20), 68.9% were female, 65.2% had three or more chronic conditions, and the average median income by zip code was $50,900 (SD 21,300) (Table 3.1). Descriptive statistics demonstrated differences between the two arms. The adherent group had a larger proportion over age 85 years, less chronic conditions, more ADRD diagnoses, and less rivastigmine claims (Table 3.1). Of the 4511 total observations, 2518 (55.8%) had a claim for donepezil, 127 (2.8%) for galantamine, 1449 (32.1%) for memantine, 392 (8.7%) for rivastigmine, and 25 (0.6%) for the combination of donepezil and memantine (Table 3.1). The majority of observations did not experience an IP hospitalization (89.8%) or ED visit (57.7%), and the mean among those who did was 1.3 (SD 0.7) and 2.1 (SD 1.9) visits, respectively. See Appendix A3. 4 for sample sizes for each statistical model and subgroup.

Table 3.1. Patient-year characteristics.

	Non-Adherent (PDC<80%)	**Adherent (PDC≥80%)**	**Overall**
Unique patients, N	703	697	892
Patient-years, N	1800	2711	4511
Age			
Mean (SD)	80.9 (7.55)	82.3 (6.90)	81.7 (7.20)

Median [Min, Max]	81.0 [50.0, 107]	82.0 [52.0, 106]	82.0 [50.0, 107]
Age Group			
<65	47 (2.6%)	25 (0.9%)	72 (1.6%)
65-74	277 (15.4%)	314 (11.6%)	591 (13.1%)
75-84	907 (50.4%)	1315 (48.5%)	2222 (49.3%)
85+	569 (31.6%)	1057 (39.0%)	1626 (36.0%)
Sex			
Male	585 (32.5%)	820 (30.2%)	1405 (31.1%)
Female	1215 (67.5%)	1891 (69.8%)	3106 (68.9%)
Chronic Conditions			
0	401 (22.3%)	544 (20.1%)	945 (20.9%)
1	116 (6.4%)	117 (6.5%)	293 (6.5%)
2	124 (6.9%)	207 (7.6%)	331 (7.3%)
3+	1159 (64.4%)	1783 (65.8%)	2942 (65.2%)
Income, Median by Zip			
Mean (SD)	$50,400 (20,500)	$51,200 (21,900)	$50,900 (21,300)
Median [Min, Max]	$45,500 [13,200, 155,000]	$46,000 [15,000, 250,000]	$45,700 [13,200, 250,000]
Income, Quintiles by Zip			
1st	17 (0.9%)	26 (1.0%)	43 (1.0%)
2nd	677 (37.6%)	1051 (38.8%)	1728 (38.3%)
3rd	770 (42.8%)	1151 (42.5%)	1921 (42.6%)
4th	296 (16.4%)	414 (15.3%)	710 (15.7%)
5th	36 (2.0%)	61 (2.3%)	97 (2.2%)
Missing	4 (0.2%)	8 (0.3%)	12 (0.3%)
Hospice			
Yes	123 (6.8%)	96 (3.5%)	219 (4.9%)
Diagnosis			
ADRD	1648 (91.6%)	2562 (94.5%)	4210 (93.3%)
Dementia, other	78 (4.3%)	92 (3.4%)	170 (3.8%)
MCI	70 (3.9%)	55 (2.0%)	125 (2.8%)
Other	4 (0.2%)	2 (0.1%)	6 (0.1%)
Medication			
Donepezil	969 (53.8%)	1549 (57.1%)	2518 (55.8%)
Donepezil + Memantine	12 (0.7%)	13 (0.5%)	25 (0.6%)
Galantamine	47 (2.6%)	80 (3.0%)	127 (2.8%)
Memantine	571 (31.7%)	878 (32.4%)	1449 (32.1%)
Rivastigmine	201 (11.2%)	191 (7.0%)	392 (8.7%)
PDC			

Mean (SD)	50.1% (22.3)	93.3% (5.73)	76.1% (25.8)
IP costs			
No costs	1598 (88.8%)	2488 (91.8%)	4086 (90.6%)
Mean† (SD)	$18,857 (18,527)	$15,627 (13,808)	$17,162 (16,284)
ED costs			
No costs	1024 (56.9%)	1686 (62.2%)	2710 (60.1%)
Mean† (SD)	$9096 (13,572)	$8108 (14,476)	$8534 (14,098)
IP hospitalizations			
No visits	1584 (88.0%)	2469 (91.1%)	4053 (89.8%)
1 visit	156 (8.7%)	196 (7.2%)	352 (7.8%)
2 visits	43 (2.4%)	38 (1.4%)	81 (1.8%)
≥3 visits	17 (0.9%)	8 (0.3%)	25 (0.6%)
Mean† (SD)	1.4 (0.8)	1.2 (0.6)	1.3 (0.7)
ED visits			
No visits	975 (54.2%)	1630 (60.1%)	2605 (57.7%)
1 visit	404 (22.4%)	574 (21.2%)	978 (21.7%)
2 visits	185 (10.3%)	246 (9.1%)	431 (9.6%)
≥3 visits	236 (13.1%)	261 (9.6%)	497 (11.0%)
Mean† (SD)	2.3 (2.1)	2.0 (1.6)	2.1 (1.9)

Notes: Characteristics of individuals in the study sample (2006-2018). Individuals had a diagnosis of either ADRD, senile dementia, MCI, memory loss, other types of dementia (unspecified dementia without behavioral disturbance, corticobasal degeneration, other specified senile psychotic conditions, unspecified senile psychotic conditions), or cognitive deficit, or were classified as cognitive impairment with or without dementia according to the Langa-Weir algorithm. We required continuous enrollment for the entire year, enrollment in at least one year before and one year after initiation of coverage gap closure, and at least one non-zero Part D claim.
†Mean among individuals with non-zero costs or visits.
SD: Standard deviation; PDC: Proportion of days covered; IP: Inpatient; ED: Emergency department

3.3.2. Inpatient Hospitalizations

Overall, adherence to AD drugs, defined by a binary measure of PDC of 80% or greater, was associated with significant reductions in the probability of incurring IP healthcare costs (-2.4 percentage points [ppts]; 95% CI: -4.3 to -0.55 ppts; p=0.011) and of experiencing an IP hospitalization (-2.3 ppts; 95% CI: -4.26 to -0.40 ppts; p=0.018) compared to non-adherence. However, being adherent was not significantly associated with the amount of IP costs incurred conditioning on incurring any costs (4.0 ppt increase; 95% CI: -20.2 to 35.3 ppts) or the number

of hospitalizations conditioning on having any hospitalizations (0.2 ppt increase; 95% CI: -14.4 to 17.5 ppts). Similar results were observed when increasing the PDC threshold to 90%, among individuals aged 85 years or older, and among females (Table 3.2 and Table 3.3). See Appendix A3. 6 and A3. 7 for results with a continuous value of PDC.

Table 3.2. Two-part model results for IP hospitalization healthcare costs with a binary measure of adherence.

	Part 1: Linear Probability Model			**Part 2: Gamma Regression**		
Sample	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
Full	-0.0243	-0.0431, -0.00554	0.0112*	1.0396	0.798, 1.353	0.773
Full: PDC 60%	-0.0152	-0.0405, 0.010	0.239	1.154	0.903, 1.474	0.254
Full: PDC 90%	-0.0369	-0.0584, -0.0153	<0.001*	1.012	0.854, 0.1.218	0.827
Ages: 65-74	0.0113	-0.0663, 0.0888	0.776		Model did not converge	
Ages: 75-84	-0.0164	-0.0488, 0.0160	0.321	1.042	0.844, 1.285	0.705
Ages: 85+	-0.0524	-0.0900, -0.0149	<0.01*	0.808	0.506, 1.289	0.370
Sex: M	-0.0108	-0.0463, 0.0248	0.553	1.080	0.921, 1.267	0.344
Sex: F	-0.0305	-0.0524, -0.00861	<0.01*	0.932	0.681, 1.277	0.661

This table reports the coefficient on adherence from Equation (3.1) and the exponentiated coefficient on Ait from Equation (3.2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code. Unless otherwise specified, proportion of days covered threshold for adherence is 80%.
*Statistically significant result.

Table 3.3. Two-part model results for IP hospitalization counts with a binary measure of adherence.

	Part 1: Linear Probability Model			**Part 2: Negative Binomial**		
Sample	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
Full	-0.0233	-0.0426, -0.00404	0.0178*	1.002	0.856, 1.175	0.976
Full: PDC 60%	-0.0117	-0.0382, 0.0147	0.385	1.041	0.886, 1.224	0.623
Full: PDC 90%	-0.0382	-0.0589, -0.175	<0.001*	1.026	0.845, 1.245	0.796
Ages: 65-74	0.0175	-0.0619, 0.0970	0.665		Model did not converge	
Ages: 75-84	-0.0193	-0.0558, 0.0171	0.299	1.052	0.902, 1.225	0.516
Ages: 85+	-0.0513	-0.0901, -0.0125	<0.01*	1.0362	0.936, 1.146	0.491
Sex: M	-0.00748	-0.0418, 0.0268	0.669	0.981	0.878, 1.095	0.731
Sex: F	-0.0314	-0.0524, -0.0104	<0.01*	1.025	0.847, 1.240	0.799

This table reports the coefficient on adherence from Equation (3.1) and the exponentiated coefficient on Ait from Equation (3.2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code. Unless otherwise specified, proportion of days covered threshold for adherence is 80%.
*Statistically significant result.

3.3.3. Emergency Department Visits

A binary measure of medication adherence (PDC threshold at 80%) was significantly associated with a 6.4 ppt reduction in the probability of incurring ED costs (95% CI: -9.8 to -2.9 ppts; p<0.001) and a 6.5 ppt reduction in the probability of an ED visit (95% CI: -10.1 to -2.8 ppts; p<0.001) compared to non-adherence. Additionally, adherence resulted in a 19.3 ppt reduction in total non-zero ED costs (95% CI: -30.2 to -6.7 ppts; p<0.01) and a 15.9 ppt reduction in the number of ED visits (95% CI: -22.7 to -8.2 ppts; p<0.01). Similar significant results were observed when increasing the PDC threshold to 90%, among individuals aged 85 years or older, and among females (Table 3.4 and Table 3.5). See Appendix A3. 6 and A3. 7 for results with a continuous value of PDC, which are aligned with the main results.

Table 3.4. Two-part model results for ED visit healthcare costs with a binary measure of adherence.

	Part 1: Linear Probability Model			**Part 2: Gamma Regression**		
Sample	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
Full	-0.0636	-0.0981, -0.0291	<0.001*	0.807	0.698, 0.933	<0.01*
Full: PDC 60%	-0.0349	-0.0745, 0.00459	0.083	0.9720	0.790, 1.196	0.788
Full: PDC 90%	-0.0730	-0.107, -0.0390	<0.001*	0.681	0.568, 0.815	<0.0001*
Ages: 65-74	0.002	-0.117, 0.120	0.978		Model did not converge	
Ages: 75-84	-0.0392	-0.0944, 0.0161	0.165	0.865	0.644, 1.155	0.321
Ages: 85+	-0.0886	-0.127, -0.0505	<0.00001*		Model did not converge	
Sex: M	-0.0158	-0.0704, 0.0389	0.571		Model did not converge	
Sex: F	-0.0815	-0.124, -0.0388	<0.001*	0.839	0.691, 1.018	0.0747

This table reports the coefficient on adherence from Equation (3.1) and the exponentiated coefficient on Ait from Equation (3.2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code. Unless otherwise specified, proportion of days covered threshold for adherence is 80%.
*Statistically significant result.

Table 3.5. Two-part model results for ED visit counts with a binary measure of adherence.

	Part 1: Linear Probability Model			**Part 2: Negative Binomial**		
Sample	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
Full	-0.0646	-0.101, -0.0283	<0.001*	0.841	0.773, 0.918	<0.0001*
Full: PDC 60%	-0.0383	-0.0760, -0.000548	0.0468*	0.9050	0.784, 1.043	0.168
Full: PDC 90%	-0.0766	-0.112, -0.0416	<0.0001*	0.788	0.708, 0.876	<0.0001*
Ages: 65-74	0.009	-0.110, 0.127	0.887	1.107	0.815, 1.503	0.514
Ages: 75-84	-0.0365	-0.0891, 0.0161	0.174	0.846	0.712, 1.004	0.0556
Ages: 85+	-0.101	-0.144, -0.0591	<0.00001*		Model did not converge	
Sex: M	-0.0159	-0.0714, 0.0397	0.576	0.917	-0.783, 1.074	0.282
Sex: F	-0.0823	-0.127, -0.0379	<0.001*	0.843	0.746, 0.954	<0.01*

This table reports the odds ratio from Equation (3.1) and the exponentiated coefficient on Ait from Equation (3.2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code. Unless otherwise specified, proportion of days covered threshold for adherence is 80%.
*Statistically significant result.

3.4. Discussion

We examined the association between AD medication adherence and IP and ED healthcare costs and visits using two-part models among Medicare beneficiaries with cognitive impairment treated with AD medication. Using a binary definition of adherence, results showed a significant negative association between adherence and incurring any healthcare costs for both IP and ED visits, the occurrence of IP and ED visits, and the amount of ED healthcare costs and visits. This finding was consistent among females and beneficiaries aged 85 years or older, and when using at least 90% PDC as the alternative definition of adherence. The occurrence of IP and ED visits reinforces the importance of policies to promote adherence, and the costs incurred help to understand the implications of good adherence for Medicare and taxpayers.

We found reductions in hospitalizations and ED use; a possible reason for this is that medication adherence may allow better management of the symptoms of cognitive impairment, thus reducing the need for healthcare. Another possibility is that adherence may be a proxy for other good health behaviours, such as adherence to other medications that treat comorbidities, thus resulting in fewer IP or ED visits and a lower probability of incurring IP or ED related healthcare expenditures. [8,11,76,77]. Examples of AD-related comorbidities are hypertension and diabetes, which are on the list of AHRQ ambulatory care sensitive conditions for which proper management can prevent complications or the need for hospitalization.[78]

For IP care, we found no association between adherence and the amount of costs or visits among those admitted. The lack of change in IP costs might be explained by the level of illness severity required for an admission. Being admitted to the hospital means that the patient is experiencing severe symptoms or a decline in health status; therefore, conditioning on admission, adherence may not be playing a role in determining total cost. The non-significant difference in IP hospitalization counts may be due to the low variability in hospitalizations in our sample.

In contrast, we found significant associations for the magnitude of both ED costs and visits. Adherent individuals may be less likely to visit the ED compared to those who are non-adherent because of their symptom management. Moreover, adherent patients will likely be less costly once in the ED because the severity of their symptoms may be lower than that of non-adherent patients.

Proportion of days covered is a widely used measure for medication adherence and has an established threshold at 80% to define whether patients are adherent or not.[75,79] Through our sensitivity analyses varying the adherence threshold to 60% and 90%, we assessed how defining adherence affected the results. Increasing the threshold to 90% was associated with greater reductions in the probability of incurring IP and ED spending and utilization, and the probability of ED spending and use among those who visited the ED compared to the 80% threshold. However, decreasing the requirement to 60% resulted in non-significant findings except for a reduction in the probability of ED utilization. Our results show that adherence defined using the standard or more stringent criteria may have stronger relationships with disease management and lower IP and ED use. A continuous measure of PDC found that increases in adherence were associated with lowering the probability of incurring IP and ED costs, and with lower ED costs and use.

While there have been studies conducted among individuals with chronic conditions of the association between adherence and healthcare resource utilization and cost, ours addresses an important gap by focusing on older adults with cognitive impairment, a particularly vulnerable subgroup due to their often-impaired healthcare decision making. Prior research of patients with hematologic malignancies, diabetes, hyperlipidemia, and cardiovascular disease have found that patients with good medication adherence had a reduced risk of IP and ED utilization and costs compared to those who were non-adherent.[8,73,76] These studies, which used statistical models similar to ours and a PDC threshold at 80%, support our findings of a negative association between medication adherence and the probability of IP or ED utilization and costs. In two other studies, results showed that good adherence led to reduced emergency department visits and poor

adherence increased the likelihood of hospitalization.[10,46] These studies used measurements of adherence and statistical models different from ours, but arrived at similar conclusions.

This study had important strengths. First is the linkage of HRS survey data, which provides an additional layer of information that Medicare claims alone do not allow. The HRS Langa-Weir Classification allowed for the identification of beneficiaries with cognitive impairment who do not yet have a diagnosis claim, as there is a considerable amount of off-label medication use in this population.[39,40,71] Second, the proportion of our sample with a diagnosis of ADRD who used a medication matches that of other studies using HRS data.[72]

All results must be interpreted considering this study's limitations. First, the results may not be generalizable due to selection bias because Medicare beneficiaries who took part in HRS as survey respondents may be inherently different from individuals who did not take part in the survey, especially in terms of cognitive function. Moreover, the results may not be generalizable to all individuals with cognitive impairment because not everyone in the sample had a diagnosis that made them eligible for AD medication, and those eligible for treatment who did receive medication may have been different from those who did not. Second, adherence was measured using dispensing claims, which do not guarantee ingestion of the medication; however, this indirect measure has been used extensively in pharmacoepidemiologic research and is considered reliable. Third, this population often has multiple comorbidities and is taking multiple medications. Therefore, it is possible that adherence to AD medication specifically was not the reason for any IP hospitalizations or ED visits. Fourth, there is a potential for omitted variable bias, as we were unable to control for dementia severity. Individuals with lower severity typically

have better adherence, leading to generally better health and less healthcare resource utilization. Our inclusion of individuals fixed effects partially control for this, but cognitive decline across time could still drive both worse adherence and more IP and ED use within an individual. Finally, our analysis may be subject to reverse causality. For example, if an individual is hospitalized for reasons other than their cognitive impairment, they may be deprescribed from their AD medication to help optimize their pharmaceutical intake.

3.5. Conclusion

In this retrospective observational study of Medicare beneficiaries with cognitive impairment, adherence to AD medication was associated with lower probability of incurring IP and ED costs, the occurrence of IP and ED visits, and the amount of ED healthcare costs and visits. Our findings can serve as support for considering strategies to improve adherence to AD drugs to help reduce the burden of IP and ED visits for patients, health systems, and insurers.

CONCLUSION

In these three studies of Medicare beneficiaries with cognitive impairment, we examined the effect of Medicare Part D coverage gap closure from 2011 to 2018 on patient OOP spending, medication use, and the association between adherence and healthcare resource utilization. We found that closure of the Medicare Part D coverage gap led to significant decreases in OOP spending and increases AD medication use. We also concluded that adherence to AD medication was associated with lower probability of incurring IP and ED costs, the occurrence of IP and ED visits, and the amount of ED healthcare costs and visits.

This dissertation yields insight into the economic and disease management challenges that stem from Medicare benefit design for cognitively impaired beneficiaries. From a policy perspective, our findings of decreased OOP spending and increase in medication use in response to lower coinsurance rates suggest that affordable medication initiatives, such as the Inflation Reduction Act (IRA), can be successful in reducing the patient cost burden for vulnerable subpopulations and encourage beneficiaries to fill their prescriptions. With respect to healthcare resource utilization, the occurrence of IP and ED visits reinforces the importance of policies to promote adherence, and the costs incurred help to understand the implications of good adherence for Medicare and taxpayers. Our results can serve as support for considering strategies to improve adherence to AD drugs to help reduce the burden of IP and ED visits for patients, health systems, and insurers.

To our knowledge, these are the first analyses of the impact of Part D coverage gap closure on OOP spending, medication use, and the association between adherence and healthcare resource

utilization in cognitively impaired Medicare beneficiaries. We address an important gap by focusing on older adults with cognitive impairment, a particularly vulnerable subgroup due to their often-impaired healthcare decision making. This work will lay a foundation for further investigation into other chronic diseases, cancer, and rheumatoid arthritis, which are often managed by prescription medication and result in high OOP spending for the Medicare population.[60] It also provides a framework to examine the effects of the remaining years of gap closure in 2019 and 2020, and of the eventual OOP spending caps that the IRA will implement.

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SUPPLEMENTAL APPENDICES

A1. CHAPTER 1 APPENDIX

A1. 1. ICD-9 and ICD-10 codes for memory-related diagnoses.

ICD-9	ICD-10
290.8, 290.9, 294.9, 331.3, 331.4, 331.5, 331.6, 331.81, 331.82, 331.83, 331.89, 331.9, 438.0, 780.93	F03.90, F06.70, F06.71, F06.8, G91.0, G91.3, G91.8, G91.9, G91.1, G93.7, G31.83, G31.84, G31.85, G31.89, G31.9, I69.010, I69.011, R41.1, R41.2, R41.3

A1. 2. Sample selection.

Inclusion Criteria	N	Person-years
RAND HRS whole sample (2006-2018; waves 8-14)	31.282	135,079
lHRS linked to Medicare claims (2006-2018)	20,465	181,120
Diagnosis of ADRD, senile dementia, MCI, memory loss, other types of dementia, or cognitive deficit	14,011	122,786
Full year of enrollment	11,165	79,365
Enrollment in Medicare Parts A, B, and D	8621	52,568
Same treatment arm in the pre- and post-period	7851	46,681
At least one Medicare Part D claim	7669	44,689
No non-LIS beneficiary with non-zero LIS	7668	46,681
At least one observation in the pre- and post-periods	3252	29,841

A1. 3. Sample sizes.

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Full Sample													
nonLIS	644	1152	1446	1558	1845	1840	1723	1571	1436	1288	1155	1016	870
LIS	615	839	996	1063	1296	1281	1167	1059	950	881	809	681	660
Ages 65-74													
nonLIS	250	437	544	540	592	525	425	335	265	206	133	85	52
LIS	280	362	292	392	420	377	312	263	225	190	145	128	120
Ages 75-84													
nonLIS	312	538	649	699	824	819	789	763	720	659	609	550	495
LIS	186	257	323	359	422	435	435	425	387	373	375	307	297
Ages 85+													
nonLIS	75	163	228	292	392	464	486	458	445	416	406	375	319
LIS	71	119	156	185	226	255	223	204	195	195	179	165	170
Males													
nonLIS	261	464	603	663	787	781	720	658	588	525	463	393	329
LIS	161	219	252	273	352	341	311	288	250	225	219	178	172
Females													
nonLIS	383	688	843	895	1058	1059	1003	913	848	763	692	623	541
LIS	454	620	744	790	944	940	856	771	700	656	590	503	488

A2. CHAPTER 2 APPENDIX

A2. 1. ICD-9 and ICD-10 codes for memory-related diagnoses.

ICD-9	ICD-10
290.8, 290.9, 294.9, 331.3, 331.4, 331.5, 331.6, 331.81, 331.82, 331.83, 331.89, 331.9, 438.0, 780.93	F03.90, F06.70, F06.71, F06.8, G91.0, G91.3, G91.8, G91.9, G91.1, G93.7, G31.83, G31.84, G31.85, G31.89, G31.9, I69.010, I69.011, R41.1, R41.2, R41.3

A2. 2. Sample selection table.

Inclusion Criteria	N	Person-years
RAND HRS whole sample (2006-2018; waves 8-14)	31.282	135,079
HRS linked to Medicare claims (2006-2018)	20,465	181,120
Diagnosis of ADRD, senile dementia, MCI, memory loss, other types of dementia, or cognitive deficit	14,011	122,786
Full year of enrollment	11,165	79,365
Enrollment in Medicare Parts A, B, and D	8621	52,568
Same treatment arm in the pre- and post-period	7851	46,681
At least one Medicare Part D claim	7669	44,689
No non-LIS beneficiary with non-zero LIS	7668	46,681
At least one observation in the pre- and post-periods	3252	29,841
ADRD Diagnosis	1807	17,993

A2. 3. ADRD sample sizes by year and subgroup.

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Full sample (ADRD)													
nonLIS	494	896	978	1062	1098	1122	1048	937	844	749	652	542	408
LIS	446	603	649	702	746	739	673	594	525	465	403	326	292
Ages 65-74 years													

nonLIS	253	440	552	549	596	535	437	338	268	213	139	87	53
LIS	281	366	397	396	427	387	323	271	230	194	146	128	121
Ages 75-84 years													
nonLIS	316	545	606	726	851	855	818	790	752	690	640	580	523
LIS	189	265	336	380	447	451	454	448	415	398	390	324	311
Ages 85+ years													
nonLIS	75	166	233	300	409	489	517	486	465	441	429	396	331
LIS	74	124	167	199	246	278	246	227	209	207	192	177	181
Males													
nonLIS	264	470	611	679	808	811	748	683	607	555	491	410	343
LIS	162	223	259	279	362	350	321	298	257	234	227	187	183
Females													
nonLIS	387	695	859	924	1085	1100	1047	946	884	796	724	659	568
LIS	461	634	766	824	988	982	901	816	740	688	611	523	503
Donepezil													
nonLIS	10	25	39	73	97	93	71	58	46	39	31	21	16
LIS	21	43	48	62	92	89	70	54	39	29	24	23	20
Galantamine													
nonLIS	0	2	6	8	12	12	8	5	4	2	1	1	0
LIS	1	1	0	1	3	2	1	1	1	1	0	0	0
Memantine													
nonLIS	5	13	24	40	56	56	45	33	22	11	9	3	2
LIS	8	17	26	42	59	57	41	33	24	18	13	10	8
Rivastigmine													
nonLIS	1	1	4	8	14	15	10	6	3	1	1	1	1
LIS	3	6	10	11	17	17	10	10	8	8	4	2	2
Donepezil + Memantine													
nonLIS	0	0	0	0	0	0	0	0	0	0	0	0	0
LIS	0	0	0	0	0	0	0	0	0	0	0	0	0

A2. 4. ADRD beneficiary-level sample characteristics.

	LIS	non-LIS	Overall
N	710	1097	1807
Age			
Mean (SD)	74.6 (10.3)	76.7 (6.94)	75.9 (8.50)
Median [Min, Max]	75.0 [34.0, 105]	77.0 [53.0, 97.0]	7.60 [34.0, 105]
Age Group			
<65	84 (11.8%)	13 (1.2%)	97 (5.4%)
65-74	269 (37.9%)	417 (38.0%)	686 (38.0%)
75-84	237 (33.4%)	507 (46.2%)	744 (41.2%)
85+	120 (16.9%)	160 (14.6%)	280 (15.5%)
Sex			
Male	179 (25.2%)	436 (39.7%)	615 (34.0%)
Female	531 (74.8%)	661 (60.3%)	1192 (66.0%)
Chronic Conditions			
0	100 (14.1%)	310 (28.3%)	410 (22.7%)
1	72 (10.1%)	111 (10.1%)	183 (10.1%)
2	69 (9.7%)	110 (10.0%)	179 (9.9%)
3+	469 (66.1%)	566 (51.6%)	1035 (57.3%)
Income, Median by Zip			
Mean (SD)	45,200 (18,000)	45,100 (17,300)	45,100 (17,600)
Median [Min, Max]	40,900 [13,200, 121,000]	41,200 [12,500, 118,000]	41,100 [12,500, 121,000]
Income Quintiles by Zip			
1st	13 (1.8%)	18 (1.6%)	31 (1.7%)
2nd	298 (42.0%)	437 (39.8%)	735 (40.7%)
3rd	267 (37.6%)	456 (41.6%)	723 (40.0%)
4th	120 (16.9%)	172 (15.7%)	292 (16.2%)
5th	12 (1.7%)	14 (1.3%)	26 (1.4%)
Medication			
Donepezil	71 (10.0%)	58 (5.3%)	129 (7.1%)
Donepezil + Memantine	0 (0%)	0 (0%)	0 (0%)
Galantamine	3 (0.4%)	9 (0.8%)	12 (0.7%)
Memantine	11 (1.5%)	8 (0.7%)	19 (1.1%)
Rivastigmine	8 (1.1%)	1 (0.1%)	9 (0.5%)
None	617 (86.9%)	1021 (93.1%)	1638 (90.6%)
Branded drug only			
No	697 (98.2%)	1088 (99.2%)	1785 (98.8%)
Yes	13 (1.8%)	9 (0.8%)	22 (1.2%)

Notes: Characteristics of individuals in the study sample (2006-2018). Individuals had a diagnosis of ADRD. We required continuous enrollment for the entire year, enrollment in at least one year before and one year after initiation of coverage gap closure, and at least one non-zero Part D claim. The control group was person-waves for individuals either deemed eligible for or enrolled in the LIS.
LIS: Low-income subsidy.

A2. 5. Cognitively impaired beneficiary-level sample characteristics.

	LIS	non-LIS	Overall
N	1329	1923	3252
Age			
Mean (SD)	71.4 (10.4)	75.0 (7.27)	73.9 (8.92)
Median [Min, Max]	71.0 [34.0, 105]	75.0 [51.0, 97.0]	74.0 [34.0, 105]
Age Group			
<65	262 (19.7%)	49 (2.5%)	311 (9.6%)
65-74	578 (43.5%)	847 (44.0%)	1425 (43.8%)
75-84	349 (26.3%)	787 (40.9%)	1136 (34.9%)
85+	140 (10.5%)	240 (12.5%)	380 (11.7%)
Sex			
Male	366 (27.5%)	818 (42.5%)	1184 (36.4%)
Female	963 (72.5%)	1105 (57.5%)	2068 (63.6%)
Chronic Conditions			
0	224 (16.9%)	695 (36.1%)	919 (28.3%)
1	135 (10.2%)	201 (10.5%)	336 (10.3%)
2	151 (11.4%)	181 (9.4%)	332 (10.2%)
3+	819 (61.6%)	846 (44.0%)	1665 (51.2%)
Income, Median by Zip			
Mean (SD)	45,500 (18,000)	46,000 (17,700)	45,800 (17,800)
Median [Min, Max]	41,300 [12,600, 126,000]	41,600 [12,500, 127,000]	41,500 [12,500, 127,000]
Income Quintiles by Zip			
1st	25 (1.9%)	29 (1.5%)	54 (1.7%)
2nd	536 (40.3%)	730 (38.0%)	1266 (38.9%)
3rd	536 (40.3%)	832 (43.3%)	1368 (42.1%)
4th	206 (15.5%)	304 (15.8%)	510 (15.7%)
5th	23 (1.7%)	26 (1.4%)	49 (1.5%)
Missing	3 (0.2%)	2 (0.1%)	5 (0.2%)
Diagnosis			
ADRD	710 (53.4%)	1097 (57.0%)	1807 (55.6%)
Dementia, other	110 (8.3%)	73 (3.8%)	183 (5.6%)
MCI	495 (37.2%)	722 (37.5%)	1217 (37.4%)
Other	14 (1.1%)	31 (1.6%)	45 (1.4%)
Medication			
Donepezil	77 (5.8%)	63 (3.3%)	140 (4.3%)
Donepezil + Memantine	0 (0.0%)	0 (0.0%)	0 (0.0%)
Galantamine	3 (0.2%)	9 (0.5%)	12 (0.4%)
Memantine	12 (0.9%)	10 (0.5%)	22 (0.7%)
Rivastigmine	8 (0.6%)	2 (0.1%)	10 (0.3%)

None	1229 (92.5%)	1839 (95.6%)	3068 (94.3%)
Branded drug only			
No	1315 (98.9%)	1911 (99.4%)	3226 (99.2%)
Yes	14 (1.1%)	12 (0.6%)	26 (0.8%)

Notes: Characteristics of individuals in the study sample (2006-2018). Individuals had a diagnosis of either ADRD, senile dementia, MCI, memory loss, other types of dementia (unspecified dementia without behavioral disturbance, corticobasal degeneration, other specified senile psychotic conditions, unspecified senile psychotic conditions), or cognitive deficit, or were classified as cognitive impairment with or without dementia according to the Langa-Weir algorithm. We required continuous enrollment for the entire year, enrollment in at least one year before and one year after initiation of coverage gap closure, and at least one non-zero Part D claim. The control group was person-waves for individuals either deemed eligible for or enrolled in the LIS.
LIS: Low-income subsidy.

A2. 6. Cognitively impaired person-year sample characteristics.

	LIS	**non-LIS**	**Overall**
N	12,779	18,154	30,933
Age			
Mean (SD)	75.8 (10.3)	79.6 (7.36)	78.0 (8.91)
Median [Min, Max]	76.0 [34.0, 110]	79.0 [51.0, 102]	78.0 [34.0, 110]
Age Group			
<65	1777 (13.9%)	211 (1.2%)	1988 (6.4%)
65-74	3667 (28.7%)	4460 (24.6%)	8127 (26.3%)
75-84	4808 (37.6%)	8746 (48.2%)	13,554 (43.8%)
85+	2527 (19.8%)	4737 (26.1%)	7264 (23.5%)
Sex			
Male	3342 (26.2%)	7480 (41.2%)	10,822 (35.0%)
Female	9437 (73.8%)	10,674 (58.8%)	20,111 (65.0%)
Chronic Conditions			
0	2326 (18.2%)	6156 (33.9%)	8482 (27.4%)
1	945 (7.4%)	1267 (7.0%)	2212 (7.2%)
2	1043 (8.2%)	1442 (7.9%)	2485 (8.0%)
3+	8465 (66.2%)	9289 (51.2%)	17,754 (57.4%)
Income, Median by Zip			
Mean (SD)	44,900 (17,800)	52,700 (20,400)	49,500 (19,700)
Median [Min, Max]	41,000 [12,600, 172,000]	48,500 [12,500, 250,000]	45,300 [12,500, 250,000]
Income Quintiles by Zip			
1st	259 (2.0%)	124 (0.7%)	383 (1.2%)
2nd	6079 (47.6%)	5524 (30.4%)	11,603 (37.5%)
3rd	4913 (38.4%)	8803 (48.5%)	13,716 (44.3%)
4th	1373 (10.7%)	3348 (18.4%)	4721 (15.3%)
5th	143 (1.1%)	326 (1.8%)	469 (1.5%)
Missing	12 (0.1%)	29 (0.2%)	41 (0.1%)

Diagnosis			
ADRD	7163 (56.1%)	10,830 (59.7%)	17,993 (58.2%)
Dementia, other	1915 (15.0%)	1281 (7.1%)	3196 (10.3%)
MCI	3610 (28.2%)	5785 (31.9%)	9395 (30.4%)
Other	91 (0.7%)	258 (1.4%)	349 (1.1%)
Medication			
Donepezil	1051 (8.2%)	1467 (8.1%)	2518 (8,1%)
Donepezil + Memantine	17 (0.1%)	8 (0.0%)	25 (0.1%)
Galantamine	28 (0.2%)	99 (0.5%)	127 (0.4%)
Memantine	637 (5.0%)	812 (4.5%)	1449 (4.7%)
Rivastigmine	218 (1.7%)	174 (1.0%)	392 (1.3%)
None	10,828 (84.7%)	15,594 (85.9%)	26,422 (85.4%)
Branded drug only			
No	12,185 (95.4%)	17,462 (96.2%)	29,647 (95.8%)
Yes	594 (4.6%)	692 (3.8%)	1286 (4.2%)

Notes: Characteristics of person-years in the study sample (2006-2018). Individuals had a diagnosis of either ADRD, senile dementia, MCI, memory loss, other types of dementia (unspecified dementia without behavioral disturbance, corticobasal degeneration, other specified senile psychotic conditions, unspecified senile psychotic conditions), or cognitive deficit, or were classified as cognitive impairment with or without dementia according to the Langa-Weir algorithm. We required continuous enrollment for the entire year, enrollment in at least one year before and one year after initiation of coverage gap closure, and at least one non-zero Part D claim. The control group was person-waves for individuals either deemed eligible for or enrolled in the LIS.
LIS: Low-income subsidy.

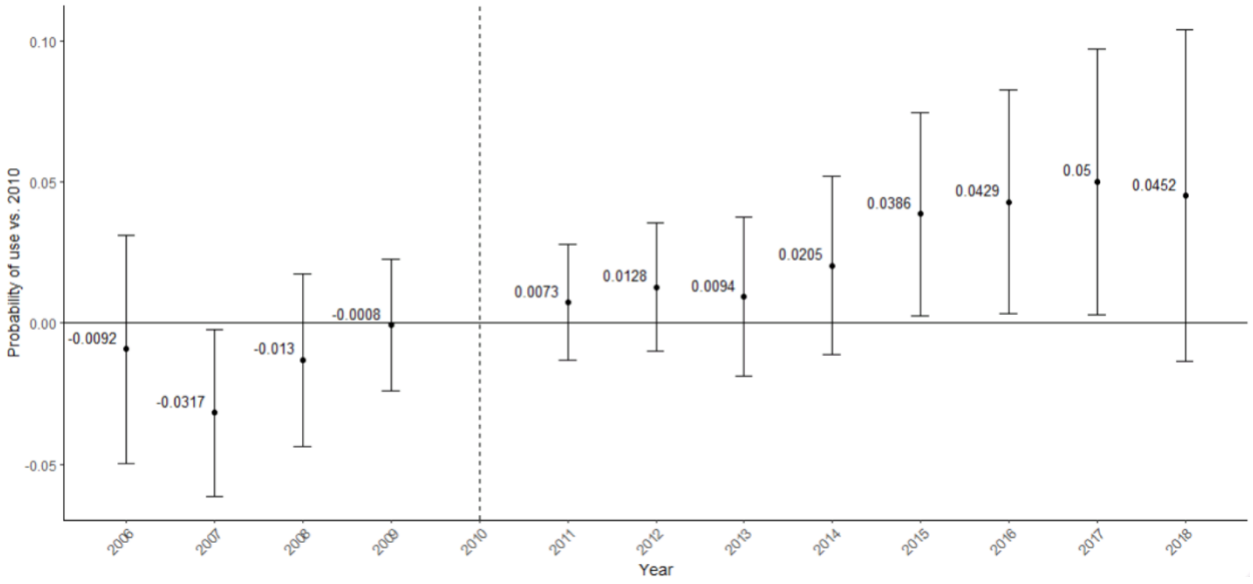
A2. 7. Difference-in-differences and event study results for beneficiaries with cognitive impairment.

Beneficiaries with ADRD or other cognitive impairment experienced a similar significant average increase in the probability of AD medication use (3.2 percentage points; 95% CI: 1.13-5.27; $p<0.01$) (Table 3). Event study results also showed a similar initial non-significant increase in the annual probability of use in the first four years after initiation of coverage gap closure (2011 vs. 2010: 0.73 percentage points; 95% CI: -1.3-2.8) followed by significant increases from 2015 to 2017 (2015 vs. 2010: 3.9 percentage points; 95% CI: 0.31-7.4; $p=0.033$) (Figure 2). The parallel trends assumption was validated.

A2.7.1. Effect of coverage gap closure on the probability of medication use among beneficiaries with cognitive impairment.

	Estimate	95% CI	p-value
ADRD+CI	0.032	0.011, 0.053	<0.01*

This table reports the coefficients on non-LIS*post using Equation (1), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.
ADRD: Alzheimer's disease and related dementias; CI: Confidence interval



A2.7.2. Effects of coverage gap closure on the probability of medication use compared to 2010 in beneficiaries with cognitive impairment. This figure reports the coefficients on non-LIS*Year using Equation (2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.

A3. CHAPTER 3 APPENDIX

A3. 1. ICD-9 and ICD-10 codes for memory-related diagnoses.

ICD-9	ICD-10
290.8, 290.9, 294.9, 331.3, 331.4, 331.5, 331.6, 331.81, 331.82, 331.83, 331.89, 331.9, 438.0, 780.93	F03.90, F06.70, F06.71, F06.8, G91.0, G91.3, G91.8, G91.9, G91.1, G93.7, G31.83, G31.84, G31.85, G31.89, G31.9, I69.010, I69.011, R41.1, R41.2, R41.3

A3. 2. Emergency department visit codes.

Outpatient and inpatient FFS file revenue center codes
Emergency room: 0450, 4051, 0452, 0453, 0454, 0455, 0456, 0457, 0458, 0459 Professional fees – Emergency room: 0981

A3. 3. Sample selection table.

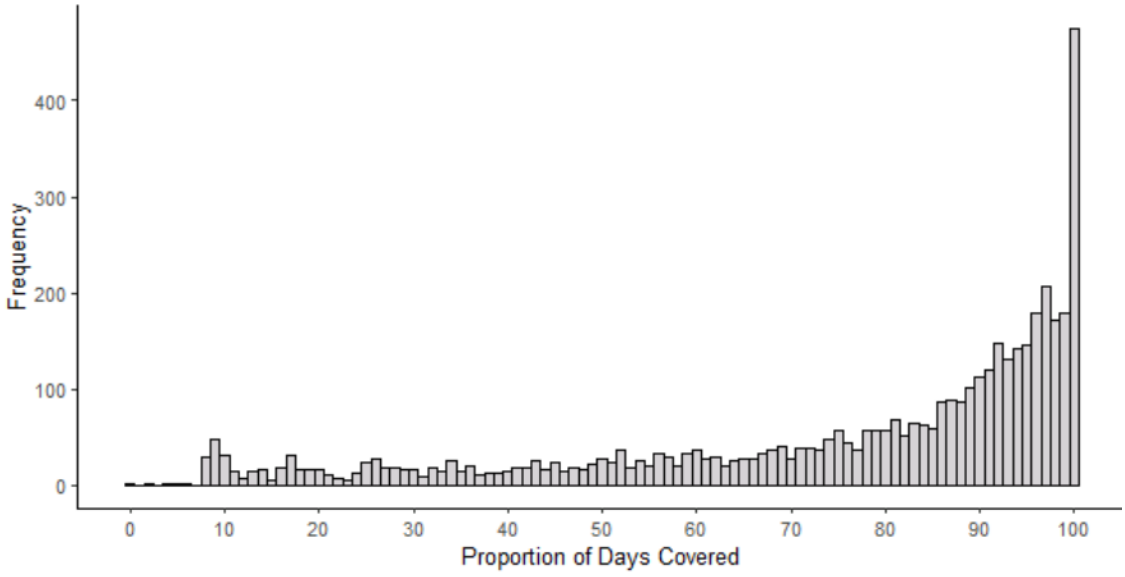
Inclusion Criteria	N	Person-years
RAND HRS whole sample (2006-2018; waves 8-14)	31.282	135,079
HRS linked to Medicare claims (2006-2018)	20,465	181,120
Diagnosis of ADRD, senile dementia, MCI, memory loss, other types of dementia, or cognitive deficit	14,011	122,786
Full year of enrollment	11,165	79,365
Enrollment in Medicare Parts A, B, and D	8621	52,568
Same treatment arm in the pre- and post-period	7851	46,681
At least one Medicare Part D claim	7669	44,689
No non-LIS beneficiary with non-zero LIS	7668	46,681
At least one observation in the pre- and post-periods	3252	29,841
Taking Alzheimer's disease medication	892	4511

A3. 4. Sample person-years per model.

	Part 1 (Expenditure & Counts)	Part 2 (Expenditure)	Part 2 (Visit counts)
IP: Full	4511	425	458
IP: Ages 65-74	591	52	54
IP: Ages 75-84	2222	227	245
IP: Ages 85+	1626	141	152
IP: Males	1405	157	157
IP: Females	3106	268	268
ED: Full	4511	1801	1906
ED: Ages 65-74	599	232	245
ED: Ages 75-84	2222	843	890
ED: Ages 85+	1626	704	748
ED: Males	1405	532	532
ED: Females	3106	1269	1335

IP: Inpatient; ED: Emergency department

A3. 5. Distribution of proportion of days covered.



A3. 6. Two-part model results for IP and ED healthcare costs with a continuous measure of adherence.

	Part 1: Linear Probability Model			Part 2: Gamma Regression		
Sample	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
IP	-0.00047	-0.00087, -0.000064	0.023*	1.00089	0.996, 1.0055	0.708
ED	-0.00101	-0.0017, -0.00027	<0.01*	0.997	0.993, 0.999	0.0391*

This table reports the estimates from Equation (1) and the exponentiated coefficient on Ait from Equation (2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.
IP: Inpatient; ED: Emergency department
*Statistically significant result.

A3. 7. Two-part model results for IP hospitalization and ED visit counts with a continuous measure of adherence.

	Part 1: Linear Probability Model			Part 2: Negative Binomial		
Sample	**Estimate**	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
IP	-0.00047	-0.00088, -0.000071	0.0213*	1.0003	0.997, 1.003	0.857
ED	-0.0011	-0.0018, -0.00036	<0.01*	0.996	0.995, 0.998	<0.001*

This table reports the estimate from Equation (1) and the exponentiated coefficient on Ait from Equation (2), along with 95% confidence intervals from state-level clustered standard errors. Covariates include individual and year fixed effects, chronic conditions, and median income by zip code.
IP: Inpatient; ED: Emergency department
*Statistically significant result.