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RESEARCH ARTICLE

Disease severity at the time of initial cognitive assessment is related to prior health-care resource use burden

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Abstract

Introduction: Research has shown increased health-care resource use (HRU) among patients with Alzheimer's disease and related disorders (ADRD) well before diagnosis, but the degree to which HRU is correlated with disease severity at the time of initial assessment is not well documented.

Methods: Retrospective analysis of linked medical records and claims data for three cohorts: mild ADRD (first [index] Mini-Mental State Examination [MMSE] ≥20), moderate/severe ADRD (index MMSE < 20), controls without cognitive impairment. HRU during the pre-index year was compared using multivariate regressions.

Results: ADRD cohorts had significantly ($P < .01$) higher HRU than controls. Compared to mild ADRD patients, moderate/severe ADRD patients had higher rates of hospitalizations (relative risk [RR]: 1.57), emergency department visits (RR: 1.36), potentially avoidable hospitalizations (RR: 1.72), and accidental falls (RR: 1.58).

Discussion: HRU before initial assessment increases with disease severity at the time of assessment, highlighting the need for timely evaluation and improved management in the earliest stages of ADRD.

KEYWORDS
Alzheimer's disease, cognitive assessment, disease severity, MMSE, MoCA

1 | INTRODUCTION

Dementia, including Alzheimer's disease (AD), exerts substantial burden on patients and caregivers, resulting in increased costs to the health-care system.[1–3] The symptoms of AD and related disorders (ADRD) often present several years before a formal diagnosis is made,[4–8] resulting in complexities in clinical management and monitoring of not only ADRD but also other comorbidities that disproportionately affect this population.[9,10]

Indeed, recent studies have documented that patients with ADRD have substantially higher medical resource use and costs not only after, but also several years before—and particularly the year before—the diagnosis of ADRD. For example, in a study using Medicare data, it was found that even before diagnosis, AD patients had more hospitalizations and emergency department (ED) visits than matched controls, 33% to 40% of which could be considered potentially avoidable according to established quality metrics.[11] AD patients were also twice as likely to have accidental falls in the 3 years prior to their formal diagnosis as matched controls. In another study using the same data source, Lin et al. also found that during the 2 years before diagnosis, the costs for patients with ADRD, including mild cognitive impairment (MCI), were more than 40% higher than costs for matched controls with no dementia.[12] In a different study involving state Medicaid enrollees, Geldmacher et al. reported that compared to matched

controls without dementia, AD patients incurred $5549 more in total medical costs during the 12 months leading up to their diagnosis.[13] Similarly, Nair et al. found that patients with AD had increased medical resource use and costs during the 6 months prior to a confirmatory diagnosis of AD.[14] A prospective multi-ethnic, population-based study of cognitive aging among Medicare beneficiaries also reported that demand for medical care and associated costs increased during the 2 years before the incident dementia diagnosis.[15]

If indeed the presence of ADRD is the driver of the increased resource use observed among the ADRD patients in the pre-diagnosis period, one would expect the degree of resource use to be correlated with disease severity—patients with more advanced disease at the time of initial evaluation should incur greater resource use prior to the evaluation compared to those with lesser disease severity. However, empirical evidence regarding the association between disease severity and the trajectory of resource use leading up to the initial assessment is limited. In a recent study, Rosenbloom et al. reported that compared to patients who screened negative for cognitive impairment, those who screened positive had 32% higher rates of ED visits and 39% higher rates of hospitalization in the 18 months prior to the screening.[16] While not stratified by disease severity, these findings suggest that at least some of the patients in this study may have progressed to advanced stages of the disease at the time of the initial evaluation.

To address this gap in the literature, this study evaluated metrics related to medical resource use in the year prior to initial cognitive assessment among patients with ADRD. The results were stratified by disease severity defined by their first observed cognitive assessment score and compared to similar controls with no evidence of cognitive impairment.

RESEARCH IN CONTEXT

1. **Systematic review**: Prior studies have documented that even before diagnosis, people with Alzheimer's disease and related disorders (ADRD) have increased health-care resource use (HRU) compared to similar people with no cognitive impairment. However, empirical evidence regarding the association between disease severity and the trajectory of HRU leading up to the initial cognitive assessment is limited.
2. **Interpretation**: We find that intensity of HRU before initial cognitive assessment is correlated with disease severity as captured by impairment in cognitive abilities. Importantly, we find that among people with ADRD, those with moderate/severe ADRD have the highest rates of HRU across all outcomes.
3. **Future directions**: Future research should explore (a) the specific mechanisms behind these findings, (b) health-care costs associated with these findings, and (c) the implications of timely evaluation and management of ADRD patients in the earliest stages of the disease.

2 | METHODS

2.1 | Data sources

The study used the electronic medical records (EMR) and claims database from Geisinger Health System (MedMining), which is an integrated health network that serves millions of patients in north-eastern and central Pennsylvania. The database contains longitudinal (January 2004–August 2017), de-identified, EMR-based data extracts, with information on diagnoses, procedures, medications, vital signs, and select laboratory services for patients of all ages and with any insurance coverage. Additional data elements, including documented office tests such as cognitive assessments, are also available upon special request.

Furthermore, the database contains administrative claims data for a subset of patients insured by the Geisinger Health Plan (GHP; ≈450,000 enrollees), with information on patient demographics, enrollment history, diagnoses, medical resource use, and prescription drug use.

This retrospective study used pre-existing de-identified EMR and claims data. Therefore, an institutional board review was not required.

2.2 | Sample selection and study design

The sample selection criteria used in this study are outlined in Figure 1. The analytic sample was limited to patients enrolled in the GHP—and therefore who had both EMR and claims data available—for ≥2 years before the study index date, and who were ≥55 years throughout this time period. Patients with ≥1 valid cognitive assessment score (Mini-Mental State Examination [MMSE] or Montreal Cognitive Assessment [MoCA]) were included in the ADRD cohort. The first documented score was considered the study index date. ADRD patients were also required to have ≥1 relevant diagnoses (AD, memory loss, amnestic disorder in conditions classified elsewhere, dementia [unspecified], dementia [including vascular dementia], dementia in conditions classified elsewhere, mild memory disturbance, or MCI), or ≥1 prescriptions for cholinesterase inhibitors or memantine. The control cohort included patients who did not meet the criteria for the ADRD cohort, and had no diagnosis of cognitive impairment or dementia of any type in the observable medical history. The study index date for this cohort was selected at random from all eligible medical and pharmacy claims. Patients were also required to have ≥1 electronic medical records during the year starting 2 years before the index date.

The ADRD patients were further stratified into two cohorts based on the severity of cognitive impairment at the time of the first documented cognitive assessment. Specifically, patients with an MMSE score of 20 to 30, or MoCA score of 15 to 30, at the index evaluation were considered to have cognitive impairment of milder severity ("mild

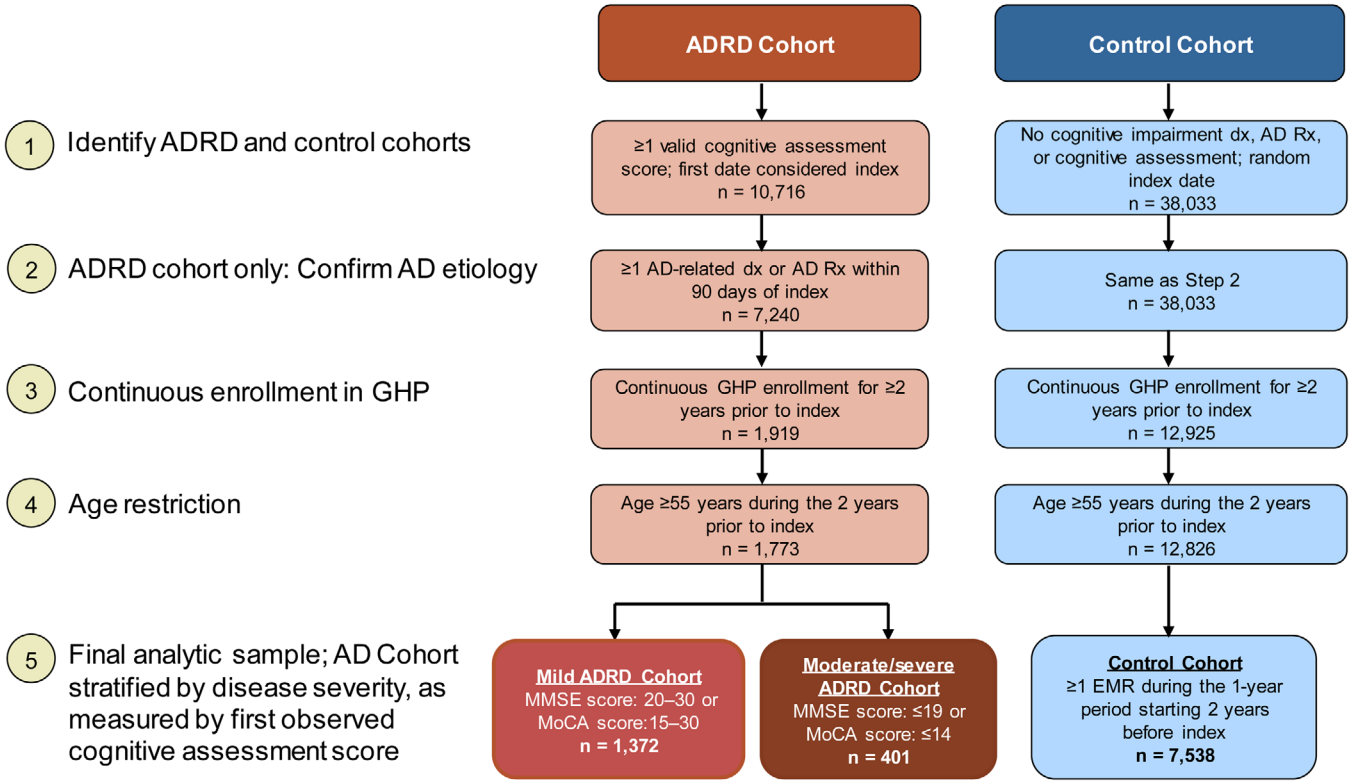

FIGURE 1 Sample selection and resulting patient counts. ADRD, Alzheimer's disease and related disorders; dx, diagnosis; GHP, Geisinger Health Plan; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; Rx, prescription

ADRD"), while those with an MMSE score ≤19, or MoCA score ≤14, were considered to have cognitive impairment of a greater severity ("moderate/severe ADRD").[17] In the event that a patient met the criteria for both mild ADRD and moderate/severe ADRD on the index date (eg, based on different MMSE vs MoCA scores), the patient was classified as moderate/severe ADRD.

For all cohorts, patient characteristics were evaluated during the year starting 2 years before the index date (baseline period) whereas outcomes were evaluated during the year immediately preceding the index date (observation period; Figure S1 in supporting information).

2.3 | Patient characteristics

Patient characteristics during the baseline period were compared among the three cohorts. These included demographics (age, sex, race), year of index date, Charlson Comorbidity Index (CCI) and its components,[18,19] select additional comorbidities (hyperlipidemia, hypertension, depression, psychosis, anxiety, and bipolar disorders), medical resource use (proportions of patients with ≥1 hospitalizations, ED visits, outpatient/physician office visits, skilled nursing facility [SNF] visits, nursing facility, or home health-care visits), and select prescription drug use (proportions of patients prescribed an antihypertensive, antihyperlipidemic, antidiabetic, opioid, antidepressant, antipsychotic, and/or anxiolytic).

2.4 | Outcomes

Rates of all-cause ED visits and hospitalizations, potentially avoidable hospitalizations (PAH) for select acute and chronic conditions, and accidental falls during the year before the index date were compared among the three cohorts. Additionally, proportions of patients with all-cause hospitalizations who also had a PAH were estimated for all cohorts. Furthermore, the relative risks of experiencing the outcomes were estimated for the following comparisons: mild ADRD versus controls, moderate/severe ADRD versus controls, and moderate/severe ADRD versus mild ADRD.

All-cause hospitalizations and ED visits were identified based on the definitions suggested by the Centers for Medicare and Medicaid Services (CMS).[20,21] Falls were identified as hospitalizations or ED visits with the following diagnosis codes: International Statistical Classification of Diseases and Related Health Problems (ICD) 9 CM - E880-E888; ICD 10 CM - V00.1x-V00.8x, W00.x-W18.x (A and D subcodes). PAHs for serious short-and long- term complications of diabetes, chronic obstructive pulmonary disease or asthma, hypertension, and heart failure were identified based on criteria defined by the Medicare Ambulatory Care Indicators for the Elderly (MACIEs) and Prevention Quality Indicators (PQI).[22,23] For acute conditions, hospitalizations associated with dehydration, urinary tract infection, and bacterial pneumonia as the primary admission diagnoses were considered PAHs. These conditions were selected because they are common acute and chronic conditions among the older population that are sensitive to

ambulatory care in the most recent MACIE guidance, and are readily identifiable in the EMR and/or claims data. See Tables S1 and S2 in supporting information for additional details regarding PAH identification.

2.5 | Statistical analyses

The analyses were conducted in three steps. First, statistical significance of differences in underlying baseline characteristics was assessed using chi-square tests for categorical measures. Next, to account for differences in underlying patient characteristics in subsequent analyses, sampling weights were estimated using inverse probability of treatment weighting (IPTW)—a multi-treatment extension of propensity score-based methods.[24] Propensity scores were estimated using a multinomial logistic regression model with cohort assignment as the dependent variable and the following patient characteristics as independent variables: demographics, year of index, total CCI score, select additional comorbidities, select prescription drug use, and rates of medical resource use with ≥1% prevalence in all cohorts. After this, the inverse of the estimated propensity scores were used as weights to account for differences across the three cohorts. The weights were adjusted for sample size, to account for leverage issues.[25] ADRD-related comorbidities (depression, psychosis, bipolar disorder, anxiety) and prescription drugs (antidepressant, antipsychotic, anxiolytic) were excluded from the adjustment factor because these may be correlated with cognitive impairment, either as independent contributing factors, or as a result of unresolved diagnosis and/or inadequate management. The baseline characteristics of the three cohorts were then compared using logistic regression models for categorical measures and generalized linear models with normal distributions for age, CCI, and year of index to ensure no important differences remain across cohorts. Finally, statistical significance of differences in outcomes were compared using logistic regression models. In addition to the key independent variable of cohort assignment, all regression models included sampling weights to account for differences in underlying patient characteristics.

All statistical analyses were performed using SAS Enterprise Guide version 7.1 (SAS Institute Inc., Cary, NC). A *P*-value < .05 was considered statistically significant.

3 | RESULTS

The selection criteria identified 1372 mild ADRD, 401 moderate/severe ADRD patients, and 7538 control patients (Figure 1).

3.1 | Baseline characteristics

The characteristics of the three cohorts before and after weighting are described in Table 1.

Before weighting, compared to controls, patients in the mild ADRD and moderate/severe ADRD cohorts were older than controls (78 and 82 years vs 72 years, respectively), and had higher comorbidity burden, prescription drug use, as well as medical resource use ($P < .05$ for all comparisons). In addition, the differences between the mild and moderate/severe ADRD cohorts with respect to age, comorbidity burden, and resource use were also statistically significant ($P < .05$; Table 1).

After weighting, the three cohorts were similar on most characteristics (Table 1). However, as expected, substantial differences remained between the cohorts in the rates of all ADRD-associated comorbidities and medication use; with the rates being the highest among the moderate/severe ADRD cohort. Additionally, patients in the moderate/severe ADRD cohort had significantly higher rates of all-cause hospitalizations, ED visits, and home health care compared to controls (hospitalizations: 21% vs 17%, ED: 33% vs 25%, home health care: 26% vs 22%).

3.2 | Relative risks and frequencies of experiencing the outcomes over time after weighting

During the observation period (ie, the year before the index date), patients in the mild ADRD and moderate/severe ADRD cohorts had significantly ($P < .01$) higher rates of all outcomes than the control cohort; the rates being the highest among the moderate/severe ADRD cohort (Figure 2 and Table 2). Specifically, 30% of the mild ADRD and 46% of the moderate/severe ADRD patients had an inpatient stay compared to 22% among the control patients. Similarly, the rates of ED visits were 47%, 65%, and 28% among the mild ADRD, moderate/severe ADRD, and control cohorts, respectively. The risks of PAH were also higher among the two ADRD cohorts than controls—relative risk (RR) for mild ADRD cohort: 1.46, RR for moderate/severe ADRD cohort: 2.52. Relatedly, the proportions of patients with all-cause hospitalizations that were attributable to PAH were higher among the moderate/severe ADRD cohort than controls (62% vs 45%). Results were also similar for falls—RR for mild ADRD cohort: 2.48, RR for moderate/severe ADRD cohort: 3.91 (Table 2).

The differences in outcomes between the two ADRD cohorts were also significant. Specifically, compared to mild ADRD patients, the moderate/severe ADRD patients had significantly ($P < .01$) higher rates of all-cause hospitalizations (RR vs mild ADRD: 1.57), all-cause ED visits (RR: 1.36), any PAH (RR: 1.72), and falls (RR: 1.58) (Table 2). Additionally, the proportion of patients with an all-cause hospitalization that could be attributed to PAH was higher among the moderate/severe ADRD cohort than the mild ADRD cohort (62% vs 48%).

The aggregate trends observed for PAH across the control, mild ADRD, and moderate/severe ADRD cohorts also applied to most of the individual PAH conditions (Table 2). However, small sample sizes made interpretation challenging.

4 | DISCUSSION

During the year leading up to the first cognitive assessment (MMSE or MoCA), patients with ADRD were significantly more likely to have

TABLE 1 Baseline patient characteristics before and after weighting

	Before weighting						After weighting					
Characteristic	Control (n = 7,538)	Mild ADRD N = 1,372)	$P^{Mvs.C}$	Moderate/ Severe ADRD (n = 401)	$P^{Svs.C}$	$P^{Svs.M}$	Control (n = 7,538)	Mild ADRD N = 1,372)	$P^{Mvs.C}$	Moderate/ Severe ADRD (n = 401)	$P^{Svs.C}$	$P^{Svs.M}$
Age, mean (SD)	72.2 (7.59)	77.8 (7.59)	*	81.7 (6.46)	*	*	73.3 (7.98)	73.2 (8.48)		73.7 (8.2)		
Male, %	46.5	41.2	*	40.6	†		45.5	48.1		51.0	†	
CCI score, mean (SD)	1.1 (1.55)	1.3 (1.61)	*	1.6 (1.74)	*	*	1.2 (1.60)	1.2 (1.55)		1.4 (1.67)	†	
Select comorbidities, %												
Hypertension	69.4	74.5	*	81.3	*	*	70.9	69.3		70.8		
Hyperlipidemia	72.3	75.2	†	70.1		†	73.0	72.0		68.7		
Depression	9.3	22.7	*	22.4	*		9.6	23.7	*	20.6	*	
Psychosis	0.3	3.9	*	7.7	*	*	0.3	3.4	*	7.6	*	*
Bipolar disorder	0.3	0.9	*	1.0	†		0.3	1.1	*	1.8	*	
Anxiety	11.7	21.7	*	20.0	*		12.4	20.1	*	16.4	†	
Any ADRD, %	n/a	21.9	-	41.4	-	*	n/a	18.8	-	39.2	–	*
Prescription drug use, %												
Antihypertensive	38.6	37.4		40.1			38.7	38.6		38.7		
Antihyperlipidemic	40.5	44.8	*	43.4			41.7	41.8		43.0		
Antidiabetic	15.4	15.3		23.4	*	*	16.0	17.5		19.0		
Opioid	21.7	26.7	*	22.7			22.7	23.1		22.4		
Antidepressant	12.9	27.6	*	28.2	*		13.2	28.4	*	37.5	*	*
Antipsychotic	1.2	2.7	*	8.0	*	*	1.3	3.3	*	7.2	*	*
Anxiolytic	8.3	9.0		10.5			8.3	9.6		14.6	*	*
Health-care resource use, % with ≥1 visit												
Inpatient	15.0	20.8	*	21.9	*		16.6	16.5		20.7	†	
ED	21.6	35.3	*	41.6	*	†	24.7	23.7		33.2	*	*
Outpatient	94.9	96.9	*	93.8		*	95.0	94.5		95.0		
Physician office	93.5	93.1		90.3	†		93.4	93.3		95.5		
SNF	1.2	3.9	*	10.7	*	*	2.2	2.0		2.2		
Other nursing facility	0.6	2.5	*	6.7	*	*	1.2	1.2		1.5		
Home healthcare	19.7	25.2	*	33.9	*	*	21.5	22.8		26.0	†	

Abbreviations: ADRD, Alzheimer's disease and related disorders; CCI, Charlson Comorbidity Index; ED, emergency department; $P^{Mvs.C}$, *P*-value for mild ADRD vs control; $P^{Svs.C}$, *P*-value for moderate/severe ADRD vs control; $P^{Svs.M}$, *P*-value for moderate/severe ADRD vs mild ADRD; SD, standard deviation; SNF, skilled nursing facility.

Note: Before weighting, statistical significance was evaluated using chi-square tests for categorical measures and Wilcoxon rank-sum tests for continuous measures. After weighting, statistical significance was assessed using generalized linear models for age and CCI (using a normal distribution) and logistic regression models for categorical variables. Models accounted for differences in baseline patient characteristics using the weights generated from the propensity score-based inverse probability treatment weighting approach.

*$P < .01$.

†$P < .05$.

all-cause hospitalizations and ED visits, PAHs, and accidental falls requiring medical care compared to similar control patients with no cognitive impairment. More importantly, after accounting for baseline differences across the ADRD cohorts, the degree of resource use increased with disease severity at the time of initial assessment, with the rates of all outcomes being the highest among the moderate/severe ADRD cohort. Additionally, the proportions of patients with ≥1 hospitalization who also had ≥1 PAH were higher among the

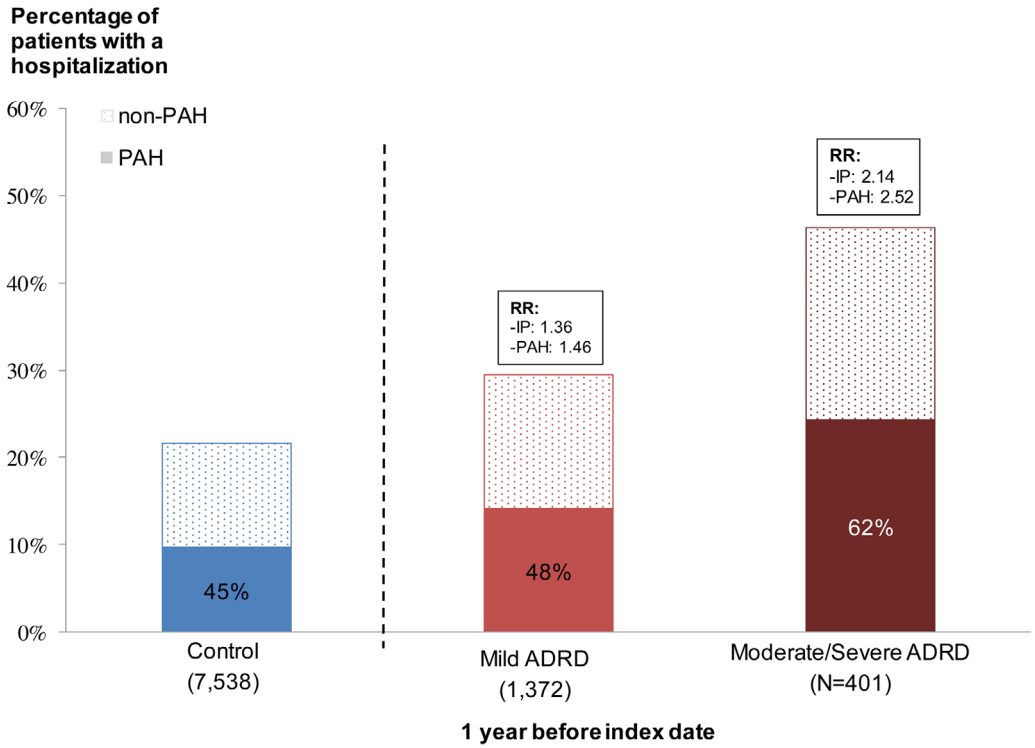

FIGURE 2 Rates of all-cause hospitalizations and proportions attributable to PAH after weighting. ADRD, Alzheimer's disease and related disorders; IP, inpatient; PAH, potentially avoidable hospitalization; RR, relative risk (estimated vs the control cohort). Note: Statistical significance of difference was assessed using logistic regression models. Models were fitted on cohort assignment and accounted for differences in baseline patient characteristics using the weights generated from the propensity score-based inverse probability treatment weighting approach

moderate/severe ADRD cohort (62%) compared to the control (45%) and mild ADRD cohorts (48%); $P < .01$ for both comparisons.

Recent studies have similarly reported that patients with ADRD experience increased health-care resource use, including potentially avoidable hospitalizations for ambulatory care–sensitive conditions, in the period leading up to the formal diagnosis.[12–16] Our findings are also consistent with the results reported by Rosenbloom et al., in which the authors found higher rates of ED visits and hospitalizations during the 18 months prior to initial screening for dementia.[16] Additionally, our results align with the findings of the prospective Adult Changes in Thought (ACT) cohort study, which found that cognitively normal adults who subsequently developed dementia had 41% higher likelihood of being hospitalized for any reason during the follow-up period, and 78% higher odds of hospitalizations for ambulatory care–sensitive conditions than those who did not develop dementia.[26] Note, however, that the findings of this study are not directly comparable to ours due to the differences in the study designs, particularly the time period over which study outcomes are assessed. Specifically, while the rates of acute care use (including PAH) for the control cohort in the Phelan et al. study were estimated over the entire observation period, the outcomes for the incident dementia cohort were limited to the post-dementia diagnosis period. By comparison, the outcomes reported in our study strictly precede a cognitive assessment.

Our results also add to these previous reports by providing additional insight into the correlation between disease severity at the time of initial cognitive assessment and metrics of health-care resource use leading up to that first evaluation. While conducting formal assessments of severity of impairment prior to or at the time of diagnosis is recommended to inform patient care management strategies, in our study, nearly a quarter of the patients with cognitive assessment did not have any evidence of such an evaluation until more advanced stages of the disease. Consequently, these patients had considerably greater likelihoods of costly medical resource use, some of which could potentially be prevented with better ambulatory care, compared to ADRD patients whose first observed cognitive evaluation was at milder stages of the disease. While costs were not directly assessed in this study, the fact that disease severity is correlated with the likelihood of experiencing these acute events suggests that delaying cognitive evaluation until the disease has progressed may result in increased costs to the health-care system. In addition, delays in cognitive evaluation create a missed opportunity for patients who might otherwise benefit from potential future therapies that increasingly target the earliest stages of the disease.

Taken together, our study findings underscore the need for efforts aimed at earlier detection of cognitive impairment and improving care management for these patients, which, in turn, could improve health outcomes and reduce the use of costly care. Recent initiatives such

TABLE 2 Relative risks of health service use, PAH, and falls in the year prior to index date, after weighting

	Control(n = 7,538)	Mild ADRD(n = 1,372)		Moderate/Severe ADRD(n = 401)		
Outcome	(%)	(%)	$RR^{Mvs.C}$	(%)	$RR^{Svs.C}$	$RR^{Svs.M}$
Any hospitalization	21.7	29.5	1.36*	46.4	2.14*	1.57*
Any ED visit	27.6	47.4	1.72*	64.5	2.34*	1.36*
Any PAH	9.7	14.2	1.46*	24.4	2.52*	1.72*
PAH for chronic conditions						
Short-term complications of diabetes	0.1	0.4	6.77*	2.2	34.73*	5.13*
Long-term complications of diabetes	3.3	5.1	1.58*	11.4	3.51*	2.22*
COPD/asthma	4.1	4.6	1.11	4.7	1.15	1.03
Hypertension	1.6	3.1	1.99*	3.9	2.48*	1.25
Heart failure	2.9	3.4	1.15	4.9	1.66†	1.44
PAH for acute conditions						
Dehydration	0.8	1.4	1.60	2.7	3.16*	1.97
Urinary tract infection	0.3	0.8	2.63*	1.3	4.50*	1.71
Bacterial pneumonia	0.3	0.4	1.11	1.2	3.47†	3.11
Any hospitalizations or ED visits for accidental falls	4.0	9.9	2.48*	15.6	3.91*	1.58*

Abbreviations: ADRD, Alzheimer's disease and related disorders; COPD, chronic obstructive pulmonary disease; ED, emergency department; PAH, potentially avoidable hospitalization; $RR^{Mvs.C}$, relative risk (mild ADRD vs control); $RR^{Svs.C}$, relative risk (moderate/severe ADRD vs control); $RR^{Svs.M}$, relative risk (moderate/severe ADRD vs mild ADRD)

Note: Statistical significance of difference was assessed using logistic regression models. Models were fitted on cohort assignment and accounted for differences in baseline patient characteristics using the weights generated from the propensity score-based inverse probability treatment weighting approach.

*$P < .01$.

†$P < .05$

as the Medicare Annual Wellness Visit;[27] the National Alzheimer's Project Act;[28] and the Health Outcomes, Planning, and Education for Alzheimer's (HOPE) Act[29] are a step in the right direction. However, to date, no study has found beneficial effects of such interventions on medical resource use, particularly preventable hospitalizations.[30] Other studies—such as the post hoc physician panel review of hospitalizations and ED visits that was conducted as part of the government's large innovation project fund have similarly reported that not all hospitalizations or ED visits that might meet the CMS criteria for PAH may be actually preventable in practice.[31,32] Additionally, there may be systemic challenges in developing and implementing algorithms surrounding quality metrics such as PAH, which further limit the ability to improve ambulatory care provision and reduce acute care use.[33] Nonetheless, our study findings suggest that early knowledge of increased acute medical resource use, particularly as it relates to chronic and acute conditions common among older adults, may provide physicians an additional marker of undetected cognitive issues. Future studies aimed at assessing the disease trajectory at earlier stages of cognitive impairment and understanding the correlation between increased health-care resource use and subsequent detection of ADRD could help inform strategies for optimal evaluation and management of patients with evidence of cognitive impairment.

Our study had several limitations. First, it is possible that some patients received a cognitive assessment prior to the earliest observed evaluation in the database (eg, while insured with a different health plan, using a different instrument), and the effects of potential differences in disease severity at the time of that evaluation on study findings remain unknown. Second, the study relied on the ICD-9 and ICD-10 diagnosis codes to identify the overall ADRD and control cohorts, and the effects of any inaccuracies on the study findings are not known. Relatedly, the protocols around administering and documenting the findings of cognitive assessments among patients without suspected ADRD (eg, as part of routine care) are not clear. However, to the degree that patients in the control cohort had any cognitive issues that remained undetected, our study potentially underestimates the true economic burden leading up to the initial cognitive assessment. Additionally, while it was possible to quantify the differences in metrics of resource use by disease severity, further research is needed to estimate the associated cost burden, as this information is considered proprietary by the data provider and therefore not captured within the database. Third, while the study used rigorous statistical methods to account for heterogeneity in underlying characteristics of the three cohorts, it cannot account for unobserved factors such as attributes of care provision in the ambulatory settings. Finally, the study findings

are limited to patients enrolled in a regional health plan and may not generalize to other populations (eg, all Medicare beneficiaries).

In conclusion, consistent with prior analyses, our study found that ADRD patients had substantially higher rates of all-cause hospitalizations, ED visits, PAH, and accidental falls relative to similar controls in the year prior to their formal cognitive assessment. However, the magnitude of differences varies by degree of severity at the time of cognitive assessment, with increased overall and potentially avoidable health-care resource use among patients at more advanced stages of cognitive impairment. These findings suggest that health-care use patterns related to common chronic and acute conditions may be markers of underlying cognitive impairment and highlight the need for timely evaluation and improved management of ADRD patients in the earliest stages of the disease.

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CONFLICTS OF INTEREST

J. Scott Andrews is an employee of Eli Lilly and Company. Urvi Desai, Noam Y. Kirson, and Yao Lu are employees of Analysis Group, Inc., a company that received funding from Eli Lilly and Company to conduct this study. VB was an employee of Eli Lilly and Company at the time of the study.

AUTHOR CONTRIBUTIONS

Urvi Desai, Noam Y. Kirson, and J. Scott Andrews contributed to study concept and design, interpretation of results, study supervision, and critical revision of the manuscript for important intellectual content. Valerie Bruemmer contributed to study concept and design, interpretation of results, and critical revision of the manuscript for important intellectual content. Yao Lu contributed to statistical analyses, interpretation of the results, and critical revision of the manuscript for important intellectual content. The sponsor assisted in the study design, interpretation of results, and critical revision of the paper.

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SUPPORTING INFORMATION

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

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