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RESEARCH ARTICLE

Meaningful benefit of disease-modifying treatment: Evaluating changes in health-related resource use

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Abstract

INTRODUCTION: Are reductions in the rate of decline from the new disease-modifying treatments (DMTs) in early Alzheimer's disease (AD) meaningful? We examined whether such reductions may be reflected in changes in health-related resource use.

METHODS: Patients with Clinical Dementia Rating (CDR) = 0.5 or 1 with a clinical diagnosis of mild cognitive impairment or AD, reflecting clinical trial populations. Health-related resource use was reported using the Resource Use Inventory (RUI) including direct medical care, non-medical care, unpaid informal care, and time use.

RESULTS: Faster decline in CDR–Sum of Boxes (CDR-SB) from baseline was independently associated with higher likelihood and hours of informal care received, and lower likelihood of employment/volunteer work, but not with direct medical care.

DISCUSSION: Reductions in the rate of decline in CDR-SB seen from DMTs significantly affect patients' work capacity and need for informal care, indicators of economic impact meaningful to patients, families, and health systems. These measures are not readily captured in administrative data sets.

KEYWORDS
clinical trials, dementia, disease-modifying treatment, health-related resource use

Highlights

- Following a cohort of participants with MCI or mild dementia due to AD that mimics participants targeted for AD trials, this study showed slower decline in CDR-SB have significant effects on patients' work capacity and need for informal care, but not on their direct medical care utilization such as hospitalizations, ED use, and doctors' visits.
- Capturing potential benefits in health-related resource use may require direct measures of informal care and work/volunteer effort which are meaningful outcomes to patients, families and health systems.

- Caution is needed in our effort to assess benefits of recently developed disease modifying treatment in AD using electronic health records and administrative data from which utilization of direct medical care are routinely collected as these data sources may not capture the most apparent changes in resource utilization during early disease stages.

1 | BACKGROUND

The approval of lecanemab in July of 2023, a new disease-modifying treatment (DMT) for Alzheimer's disease (AD) was based on results from randomized controlled trials (RCTs) in reducing the rate of decline on Clinical Dementia Rating–Sum of Boxes (CDR-SB), a measure of cognition and function.[1] The small effect size and the lack of familiarity with the outcome have heightened the discussions around the meaningfulness of the effects to patients, families, and payers. This has led to increasing calls to expand trial outcomes beyond the core dementia outcomes of cognition and function to encompass measures such as socioeconomic burden including health-related resource use and costs of care.[2–4]

Tremendous costs of care for AD during the symptomatic phases of the disease accrue in all aspects of care, including direct medical care, direct non-medical care, informal care, and intangible costs.[5,6] Direct medical costs associated with the management and treatment of AD include costs from physician visits, emergency department and hospital admissions, long-term care or skilled nursing facility care, and medications. Direct non-medical costs include all costs not directly related to medical services such as home health care, respite care, and transportation to medical visits. Indirect costs include lost productivity measured in lost income from wages. Intangible costs refer to costs associated with the loss of well-being, including pain and suffering, and premature mortality. As the field continues to move into the earlier stages of disease, studies have shown increased health-care use and costs around the onset of clinical symptoms when patients are experiencing early-stage mild cognitive impairment (MCI) or early symptomatic dementia.[6]

It is unclear how best to incorporate measures of health-related resource use and costs in AD trials. RCTs in AD targeting patients in early disease stages are typically performed over the course of 18 to 24 months. When trials are initiated at pre-clinical stages of AD in patients with little or no cognitive impairment, study length may be 4 years or more.[2] During these early stages of the disease, outcomes in health-related resource use that may be associated with treatment, such as potential reductions in direct medical cost, may not be apparent.[7,8] In addition, patients in early disease stages with mild or subtle cognitive and functional impairment often continue to work and participate in productive activities such as volunteering. As the number of older adults who participate in employment or volunteering activities continues to grow,[9] potential reductions in costs associated with the reduced loss in employment/volunteering time from treatments may be an important dimension of health-related resource use that have been overlooked.

In this study, we assess health-related resource use in a cohort of participants at early disease stages of AD and examine the relationship between health-related resource use and changes in dementia severity over time. By examining a cohort of well-characterized participants whose cognition and function are similar to those who are eligible to participate in AD trials and targeted for DMT, our study sheds light on whether changes in the rate of decline that result from DMTs may be able to capture potential economic impact, a meaningful measure to many stakeholders. By examining multiple dimensions of resource use separately, our study also sheds light on how to capture data on health-related resource use and costs.

2 | METHODS

2.1 | Resource Use Instrument

The Resource Use Instrument (RUI) was designed to be a self-administered questionnaire to be completed by study participant and/or partner to assess health-related service use and time use.[10] The RUI consists of questions that aim to reflect the most important aspects of direct medical care (hospitalizations, emergency care, doctor's visits); direct non-medical care (home health aides, attendants, companions); and unpaid, informal care provided by family and friends. In addition to these traditional measures of health-related resource items, the RUI also collects data on participants' time spent in paid employment and volunteer work. Assessment interval for hospitalizations was 1 year, and emergency care and doctors' visits were past 3 months. For home health care, informal care, and employment/volunteering, participants and their study partners were asked to recall use during the past 3 months and provide average weekly hours.

2.2 | Data source and sample derivation

Participants were enrolled in the National Alzheimer's Coordinating Center Uniform Data Set (NACC-UDS) at the Icahn School of Medicine at Mount Sinai (ISMMS) Alzheimer's Disease Research Center (ADRC), one of the longest-running National Institute on Aging (NIA)–funded Alzheimer's Disease Centers (ADCs). Recruitment, evaluation, and follow-up for the NACC-UDS have been detailed elsewhere.[11,12] Since

January 15, 2017, at each NACC-UDS visit, the ISMMS ADRC additionally collected participants' health-related resource use with the RUI. Data used in the present study included all participants who had at least one NACC-UDS visit since the start of RUI data collection and included annual follow-up visits until April 30, 2023. Because enrollment into the NACC-UDS for some participants predated the administration of the RUI, the NACC-UDS visit in which the RUI was first administered was considered a baseline for the current study. To mimic the participants who are likely to be enrolled in AD trials, we included in our analysis sample participants who were CDR = 0.5 or 1 at baseline with a clinical diagnosis of MCI or AD. Written informed consent was provided by all participants and informants and approved by ISMMS Institutional Review Board (IRB). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

2.3 | Dementia severity

Dementia severity was assessed using the CDR,[13] an integrated measure of both cognition and function in AD that has been most commonly used as an endpoint in RCTs.[14] The CDR assesses six domains including memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care, and yields a Sum of Boxes score ranging from 0 to 18 and a global score ranging from 0 to 3. Higher scores indicate greater impairment.

Because DMTs slow disease progression and change the slope of the disease trajectory, we focus on change in CDR-SB from baseline as a measure of change in dementia severity as has been used in many clinical trials.[15] Larger change scores reflect greater worsening.

2.4 | Other clinical and demographic variables

Demographic characteristics included age, sex, race (White, Black, Asian, other), ethnicity (Hispanic/Latino vs. other), and years of education. Per NACC-UDS protocol, patients' cognition was assessed by the Mini-Mental State Examination (MMSE),[16] daily living activities with the Functional Assessment Questionnaire (FAQ),[17] behavioral symptoms with the Neuropsychiatric Inventory–Questionnaire short form (NPI-Q),[18] and depressive symptoms with the Geriatric Depression Scale (GDS, 15-item version).[19,20] Participants' comorbidities were assessed using the Cumulative Illness Rating Scale (CIRS).[21]

2.5 | Statistical analysis

We first described participant demographics and health-related resource use at baseline for the entire sample and by dementia severity. We examined three outcomes of direct medical care: number of hospitalizations, number of emergency care visits, and number of doctors' visits; two outcomes of direct non-medical care: hours of home health care, hours of unpaid informal care; and an outcome in time use: hours employment/volunteer work. All outcomes are for the participant.

We followed the health econometrics literature and used the two-part model to examine the continuous outcomes (hours of home health care, informal care, and employment/volunteer work).[22] We used the hurdle model, the analog of the two-part model for count data to examine number of hospitalizations, emergency care, and doctors' visits. The two-part and hurdle models allow for separate estimation of the effect of independent variables on the extensive margin (if any use) and on the intensive margin (amount or level of use conditional on any use) as well as an overall effect. In the first part of the two-part model, a logit model was used to estimate the probability of using a resource item.[22] In the second part of the two-part model, a generalized linear model was used to estimate the amount (level) of use in the subset of individuals who used a resource item. Our main independent variables were changes in CDR-SB from baseline and baseline CDR-SB. All models included age, sex, race, ethnicity, education, comorbidities, and follow-up years as covariates. The same covariates were included in both parts of the model. Cluster-robust standard errors were reported. All analyses were performed using Stata 17.0.[23] Statistical significance was set a priori at $P < 0.05$.

We conducted a set of secondary analyses using change in CDR global score instead of CDR-SB to examine its relationship with health-related resource use items. Results were substantively the same and are reported in Table S1 in supporting information.

RESEARCH IN CONTEXT

1. **Systematic review**: Recently several disease-modifying treatments (DMTs) in early Alzheimer's disease have shown effectiveness over placebo in reducing rate of decline on Clinical Dementia Rating Sum of Boxes (CDR-SB). However, questions have been raised about the meaningfulness of these effects to patients, families, and payers.
2. **Interpretation**: Change in CDR-SB seen with DMTs may have significant effects on patients' work capacity and need for informal care, which are indicators of potential economic impact and are meaningful outcomes to patients, families, and health systems that are not readily captured in administrative data sets.
3. **Future directions**: While we selected our sample to mimic participants who are likely to be targeted for clinical trial participation and treatment, amyloid pathology was not confirmed in all participants in our cohort. Because disease courses differ between those with and without amyloid, future studies that examine the relationship between amyloid burden and health-related resource use are urgently needed.

TABLE 1 Characteristics of participants by baseline CDR.

	Total sample		CDR 0.5		CDR 1		
N	291 (100%)		222 (76.3%)		69 (23.7%)		*P* value
Age, mean (SD)	76.7	(9.1)	76.1	(9.0)	78.6	(9.1)	0.036
Male, (%)	51.2		53.2		44.9		0.233
Race/ethnicity, (%)							
Non-Hispanic White	50.5		50.5		50.7		0.010
Non-Hispanic Black	17.2		20.3		7.3		
Hispanic	24.1		20.3		36.2		
Asian	8.3		9.0		5.8		
Marital status, (%)							0.947
Married/living as partners	54.6		55.0		53.6		
Widowed	17.5		17.1		18.8		
Divorced/separated	27.8		27.9		27.5		
Years of schooling, mean (SD)	14.7	(3.7)	14.9	(3.5)	14.3	(4.2)	0.519
Diagnosis, (%)							
MCI	61.2		79.7		1.4		<0.001
AD	38.8		20.3		98.6		
MMSE, mean (SD)	24.5	(4.4)	25.9	(3.4)	19.6	(3.9)	<0.001
NPI-Q, mean (SD)	3.5	(3.9)	2.9	(3.7)	5.2	(4.1)	<0.001
GDS, mean (SD)	3.1	(3.3)	3.3	(3.4)	2.4	(2.9)	0.034
FAQ, mean (SD)	6.5	(7.9)	3.1	(4.2)	17.8	(6.7)	
CIRS, mean (SD)	6.5	(3.5)	6.5	(3.6)	6.6	(3.4)	0.700
Number of follow-up visits, mean (SD)	2.1	(1.4)	2.0	(1.3)	2.3	(1.5)	0.187
CDR-SB, mean (SD)	2.7	(2.3)	1.6	(1.1)	6.1	(1.4)	<0.001
Change in CDR-SB from baseline, mean (SD)	2.7	(3.7)	1.89	(3.4)	5.1	(3.8)	<0.001

Abbreviations: AD, Alzheimer's disease; CDR, Clinical Dementia Rating; CDR-SB, CDR Sum of Boxes; CIRS, Cumulative Illness Rating Scale; FAQ, Functional Activities Questionnaire; GDS, Geriatric Depression Scale; MCI, mild cognitive impairment, MMSE, Mini-Mental State Examination; NPI-Q, Neuropsychiatric Inventory Questionnaire; SD, standard deviation.

3 | RESULTS

3.1 | Baseline characteristics and health-related resource use

The sample included 291 participants who were followed for an average of 2.1 ± 1.4 years (range = 1–6; Table 1). Average age was 76.7 ± 9.1, 49% female, average education was 14.7 ± 3.7 years. At baseline, mean CDR-SB was 2.7 ± 2.3, 76.3% had CDR global score of 0.5; 61.2% had MCI and 38.8% AD. On average, MMSE = 24.5 ± 4.4, NPI-Q = 3.5 ± 3.9, FAQ = 6.5 ± 7.9, GDS = 3.1 ± 3.3, and CIRS = 6.5 ± 3.5, consistent with mild cognitive and functional impairment and comorbidities. In the sample, 50.5% participants were non-Hispanic White, 17.2% non-Hispanic Black, 24.1% Hispanic, and 8.3% Asian and other races. Compared to those with CDR = 0.5, participants with CDR = 1 were older, more likely to be female, and with lower education and worse clinical profiles. The two groups had similar levels of comorbidities and lengths of follow-up.

At baseline, use rates were: hospitalization (17.9%), emergency department (ED; 21.0%), doctors' visit (89.3%), home health care (16.8%), informal care (33.3%), and participation in employment/volunteering work (26.5%; Table 2). Compared to those with CDR = 0.5, participants with CDR = 1 had similar rates of use of direct medical care, but higher use rates of direct non-medical care and lower rates of participation in employment/volunteering.

Table 2 also shows average level of use of each resource item among those who used the respective item. Informal care was higher (19.0 ± 14.9 vs. 11.9 ± 11.8 hours per week) and employment/volunteering was lower (13.3 ± 18.5 vs. 18.8 ± 19.0 hours per week) in CDR = 1 compared to CDR = 0.5 (both $P < 0.01$). Use of other resources was similar between the two groups.

3.2 | Association between change in CDR-SB from baseline with resource use items

Estimation results on direct medical care use of hospitalizations, ED, and doctors' visits from the hurdle models are shown in Table 3. Results

TABLE 2 Baseline resource use by CDR.

		All sample		CDR 0.5		CDR 1		
N	Number of individuals	291		222		69		*P* value
Any use (%)	Hospitalizations	17.9		17.1		20.3		0.548
	ED use	21.0		20.3		23.2		0.603
	Doctors' visits	89.3		90.1		87.0		0.461
	Home health care	16.8		11.7		33.3		<0.001
	Informal care	33.3		18.5		81.2		<0.001
	Paid employment/volunteering	26.5		32.4		7.3		<0.001
Per "user" use	# hospitalizations	1.35	(0.76)	1.26	(0.76)	1.57	(0.76)	0.105
	# ED admissions	1.26	(0.60)	1.31	(0.63)	1.13	(0.50)	0.145
	# Doctors' visits	1.92	(2.15)	1.85	(2.05)	2.13	(2.46)	0.456
	Hours of home health care	33.2	(49.5)	23.6	(33.3)	44.0	(62.1)	0.120
	Hours of informal care	16.00	(14.00)	11.90	(11.80)	19.00	(14.90)	0.013
	Hours volunteer/employment	18.40	(18.90)	18.80	(19.00)	13.30	(18.50)	0.277
Per person use	# hospitalizations	0.24	(0.61)	0.22	(0.57)	0.32	(0.72)	0.366
	# ED admissions	0.27	(0.58)	0.27	(0.60)	0.26	(0.53)	0.708
	# Doctors' visits	1.71	(2.12)	1.67	(2.03)	1.86	(2.40)	0.770
	Hours of home health care	5.59	(23.7)	2.77	(13.5)	14.7	(41.0)	<0.001
	Hours of informal care	5.33	(11.10)	2.19	(6.81)	15.40	(15.30)	0.005
	Hours of volunteer/employment	4.87	(12.70)	6.08	(13.90)	0.96	(5.68)	0.006

Note: Assessment interval for hospitalizations was 1 year, emergency care and doctors' visits the past 3 months. For home health care, informal care, and employment/volunteering, participants and their study partners were asked to recall use during the past 3 months and provide average weekly hours.
Abbreviations: CDR, Clinical Dementia Rating; ED, emergency department.

showed that controlling for other covariates, change in CDR-SB and baseline CDR-SB were largely unassociated with the likelihood of use in any of these resources. Among those who used the resource item, changes in CDR-SB and baseline CDR-SB also were largely unassociated with the level of use.

Table 3 also showed estimation results on use of direct non-medical care, informal care, and employment/volunteering work estimated from two-part models. For home health care, the logit model showed that change in CDR-SB from baseline was not associated with higher likelihood of receiving care although baseline CDR-SB was (odds ratio [OR] = 1.424 ± 0.141, $P < 0.001$). Among those who received care, neither change in CDR-SB from baseline nor baseline CDR-SB was associated with hours of home health care received. For informal care, both change in CDR-SB from baseline (OR = 1.284 ± 0.090, $P < 0.001$) and baseline CDR-SB (OR = 1.794 ± 0.186, $P < 0.001$) were associated with higher likelihood of receiving care. The generalized linear model showed that among those who received care, a one-point increase in baseline CDR-SB was associated with 0.098 ± 0.033 additional hours of informal care ($P < 0.01$). For employment/volunteering, a one-point increase in change in CDR-SB from baseline was associated with lower likelihood of participation (OR = 0.468 ± 0.101, $P < 0.001$).

We computed average overall effects of change in CDR-SB from baseline and baseline CDR-SB by combining estimates from both parts of the two-part models (Table 4). Results showed that the overall effect from a one-point increase in the change in CDR-SB from baseline was associated with an increase of 0.9 ± 0.3 hours per week of informal care ($P < 0.001$), an increase of 1.3 ± 0.7 hours per week of home health care ($P = 0.094$), and a decrease of 0.7 ± 0.4 hours of employment/volunteering ($P = 0.05$). The overall effect from a one-point increase in baseline CDR-SB was an increase in home health care hours of 3.9 ± 1.2 hours a week ($P < 0.001$) and an increase of 2.2 ± 0.4 hours per week of informal care ($P < 0.001$), but no statistically significant effect on hours of employment/volunteering (Table S2 in supporting information).

4 | DISCUSSION

In this study, we followed a cohort of well-characterized research participants who were in mild and early dementia stages and examined multiple dimensions of health-related resource use over time as disease progressed. We used the same inclusion criteria often used in AD trials and selected participants with MCI or mild dementia due to AD at baseline so that our cohort mimics dementia severity in participants targeted for AD trials. Average MMSE and distribution of CDR in our study fell in between the Clarity AD trial[15] and the TRAILBLAZER-ALZ 2 trial.[24] Specifically, average MMSE score in our cohort at baseline was 24.5, compared to average MMSE = 25.5 reported in the Clarity AD trial[15] and MMSE = 22.2 in the TRAILBLAZER-ALZ 2 trial.[24] In our study, 76% of the participants were CDR = 0.5 and 24% CDR = 1

TABLE 3 Estimation results from two-part models for all resource use items.

	Hospitalization		ED		Doctor's visit		Home health care		Informal care		Employment /volunteering	
	Logit	Truncated Poisson	Logit	Truncated Poisson	Logit	Truncated negative binomial	Logit	GLM	Logit	GLM	Logit	GLM
	OR (SE)	IRR (SE)	OR (SE)	IRR (SE)	OR (SE)	IRR (SE)	OR (SE)	Coef. (SE)	OR (SE)	Coef. (SE)	OR (SE)	Coef. (SE)
Change in CDR-SB from baseline	1.007	1.082	0.924	0.994	1.035	1.011	1.093	0.048	1.284***	0.039+	0.468***	0.141
	(0.058)	(0.077)	(0.054)	(0.076)	(0.059)	(0.047)	(0.072)	(0.040)	(0.090)	(0.022)	(0.101)	(0.100)
Baseline CDR-SB	0.994	0.968	0.928	1.068	1.021	0.934	1.424***	0.102	1.794***	0.098**	0.823	−0.202
	(0.067)	(0.102)	(0.065)	(0.155)	(0.079)	(0.045)	(0.141)	(0.072)	(0.186)	(0.033)	(0.119)	(0.153)

Note: All models controlled for baseline age, sex, race, ethnicity, education, marital status, and number of comorbid conditions. Full model results in Table S2 in supporting information.
Abbreviations: GLM, generalized linear model; IRR, incident rate ratio; OR, odds ratio; SE, standard error.
$+P < 0.10$, $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

compared to 81% CDR = 0.5 and 19% CDR = 1 in the Clarify AD Trial, and 61% CDR = 0.5, 36% CDR = 1, and 3% CDR = 2 in the combined tau population in the TRAILBLAZER-ALZ 2 Trial. Our cohort was followed for an average of 2 years as is typical in AD trials. Results showed that use of direct medical care were largely unassociated with change in CDR-SB from baseline. However, independent of patients' demographic and clinical characteristics, the likelihood of receiving informal care and participation in employment/volunteering were significantly associated with baseline dementia severity. Among those who received some informal care, change in CDR-SB from baseline was associated with more hours of informal care. These results are consistent with findings of several recent studies examining potential cost savings from delayed AD progression. In an observational study of resource use and costs in community-dwelling patients with mild AD and their caregivers, Wessels et al. showed changes in the Integrated Alzheimer's Disease Rating Scale (iADRS), a measure of cognition and function constructed as a linear combination of the Alzheimer's Disease Assessment Scale–Cognitive subscale[25] and the Alzheimer's Disease Cooperative Study–Instrumental Activities of Daily Living,[26] were associated with higher non-medical costs and caregiving time but not direct medical costs.[27] Studies using GERAS-US data also showed delaying disease progression as measured by MMSE was associated with reductions in caregiver hours.

Our results have several important implications in the current discussions on measuring meaningful changes in AD trials in which DMTs have modest effects in reducing rate of decline. First, the relationships between the rate of changes in CDR and use of informal care and participation in employment/volunteering suggest that reductions in the rate of decline from DMT would have implications on health-related resource use on these dimensions. Specifically, our results showed that on average, a one-point reduction in the change in CDR-SB from baseline was associated with a reduction of almost an hour per week of informal care, a reduction of 1.3 hours per week of home health care, and an increase of 0.7 hours (45 minutes) per week in employment/volunteering, although the association with home health care was statistically significant only at the 10% level. Recent trials reported significant though modest differences in the rate of change in CDR-SB between DMT and placebo at 18 months of 0.45 (95% confidence interval = [−0.67, −0.23], $P < 0.001$).[15] Applying these estimates with our results suggests that such reductions in change in CDR-SB would translate to an estimated reduction of 32 hours of informal care, 46 hours of home health care, and an increase of 26 hours of employment/volunteering per patient during an 18-month period. These differences may seem modest at first. However, they are likely to be meaningful to at least some patients and families.[2] Because DMTs slow disease progression and change the slope of the disease trajectory, it is likely that greater benefits will accrue over time. Additionally, while much work has examined caregivers' time spent on providing care to dementia patients and time lost from employment and wages from caregivers of patients with dementia, loss from participation in employment and volunteering in dementia patients themselves during early stages of the diseases may have been overlooked.

TABLE 4 Estimated overall effects from change in CDR-SB from baseline and baseline CDR-SB on home health care, informal care, and employment/volunteering.

	Home health care (hours per week)		Informal care (hours per week)		Employment/volunteering (hours per week)	
	Overall effect	*P*	Overall effect	*P*	Overall effect	*P*
1-point change in CDR-SB from baseline	1.3	0.094	0.9	0.001	−0.7	0.050
	(0.8)		(0.3)		(0.4)	
1-point increase in baseline CDR-SB	3.9	0.001	2.2	<0.001	−0.8	0.145
	(1.2)		(0.4)		(0.6)	

Note: Parameter estimates from Table 3.
Abbreviation: CDR-SB, Clinical Dementia Rating Sum of Boxes.

Our results also shed light on potential sources of data on health-related resource use in AD trials. Much research on health-related resource use in AD has relied on electronic medical records (EMR) and administrative data sets from which data on use of direct medical care routinely collected, but we observe that these data sources may not capture the most apparent changes in resource use during early disease stages. At the same time, data on informal care or participation in employment/volunteering that showed changes during early disease stages are not readily available in these databases. These observations are consistent with other studies.[28] Capturing these benefits may require a direct measure of informal care and work/volunteer effort.

Our study has several limitations. First, while we selected our sample to mimic participants with MCI or mild dementia who are likely to be targeted for trial participation and treatment, we were unable to select those with evidence of amyloid or tau pathology because they were not confirmed in all participants in our cohorts. Mean CDR-SB score at baseline in our cohort was 2.7 ± 2.3, slightly lower than those who participated in the Clarity AD trial cohort in which mean CDR-SB score at baseline was approximately 3.2.[15] In our cohort, change in CDR-SB from baseline at an average of 2 years follow-up was 2.71 ± 3.7 points, or 1.93 points at 18 months assuming linearity in the rate of change, which is in line with reported adjusted mean change from baseline at 18 months of 1.66 points in the placebo group in the Clarity AD trial and 2.42 points in the placebo group in the TRAILBLAZER-ALZ 2 trial.[24] Compared to the participants in the Clarity and TRAILBLAZER-ALZ 2 trials, our cohort was older (average age = 77 vs. 71 and 73, respectively) and more racially/ethnically diverse (17% vs. 2.3% and 4% Black; 24% Hispanic vs. 12.5% and 6% Hispanic, respectively). While average follow-up duration was similar to recent AD trials, participants in our cohort were followed on an annual basis, yielding much less frequently observed data than those collected in AD trials. It is unclear how these differences may affect our results in resources use. Having a more racial/ethnically diverse cohort, however, provides more confidence that the primary outcome can be more meaningfully interpreted in a wide range of individuals. Because disease courses differ between those with/without amyloid, future studies that examine the relationship between amyloid burden and resource use are needed. Second, the participants in our study were at the earliest stages of the disease, all of whom lived in the community at baseline. Aside from home health care, few used other non-medical care, such as adult day care, or respite care. There was no institutional care use in this cohort yet. Future studies with longer follow-ups will need to include a more comprehensive set of resource items. Last, our cohort was relatively small and recruited from one ADRC in a major metropolitan area. Research participants in the ADRC tend to be better educated than the general population. Education and other socioeconomic factors are likely associated with health-care use and ability to volunteer and/or work that may not be correlated with disease severity. Caution is warranted in generalizing results to other populations.

5 | CONCLUSIONS

Here we demonstrate resource use and potential economic impact of the trajectory of the CDR-SB, a common outcome measure in clinical trials of DMTs with significant associations in informal care and work and volunteer time but not with direct medical costs. At this early stage of disease, administrative data and the EMR may not capture the most meaningful effects of treatment on resource use and economic impact. Further evidence is needed to determine the persistence of these effects and the meaningfulness that independence and work/volunteer hours hold for patients, their families, and communities.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

CONSENT STATEMENT

Written informed consent was provided by all participants and informants and approved by ISMMS Institutional Review Board (IRB).

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SUPPORTING INFORMATION

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

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