EE340

Real-world healthcare resource utilization and costs of patients with Alzheimer's disease by stage: a retrospective observational study

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Background

- Alzheimer's Disease (AD) is a progressive neurodegenerative disorder that is the leading cause of dementia in adults 65 years and older, accounting for up to 75% of dementia cases in this population.[1]
- The healthcare and economic burden of patients living with AD is considerable, especially once a patient progresses to a more advanced stage.[2]
- Identifying specific cost drivers during the progressive stages of AD is a crucial step in understanding the overall economic burden associated with AD and the potential impact of new interventions and therapies in the earlier stages of AD.

Objectives

- To compare the AD-related healthcare resource utilization (HCRU) and the associated costs by AD stage.
- To identify predictors of high AD-related costs among patients living with AD.

Methods

- **Design:** A retrospective observational study
- **Data Source:** HealthVerity (HV) insurance claims data linked to electronic medical records
- **Observation Period:** From 01/01/2015 to 12/31/2021
- **Index date:** Date of first cognitive assessment test (Mini-mental state examination [MMSE] or Montreal cognitive assessment [MoCA])
- **Study Population:** Patients with ≥1 cognitive assessment and with ≥1 medical or pharmacy claim for AD diagnosis or AD medication within 120 days of an index date were included. **(Figure 1)**
- **Exclusion Criteria:**
  - <12 months of continuous enrollment prior to the index date
  - <120 days of follow-up after the index date
- **Comparison Groups: (Table 1)**
  - Early AD (EAD: mild cognitive impairment [MCI] due to AD/mild AD dementia)
  - Advanced AD (AAD: moderate/severe AD dementia)
- **Statistical Analyses**
  - Inverse probability of treatment weighting (IPTW) was used to control for confounding by baseline characteristics.
  - IPTW-weighted generalized linear regression models (GLMs) with a negative binomial distribution were used to compare AD-related HCRU and IPTW-weighted GLMs with gamma distribution and log-link function were used to compare the costs between the groups.
  - Least Absolute Shrinkage and Selection Operator (LASSO) regression with three-fold cross-validation was used to identify predictors of high AD-related costs (defined as the 80th percentile of costs).
  - Multivariable logistic regression models were used to estimate the likelihood of high AD-related costs based on identified predictors; odds Ratios (OR) and 95% confidence intervals (CI) were reported.

Table 1: MMSE and MoCA scores corresponding to AD stages

Cohort	AD Stage	MMSE score	MoCA score
Early AD	MCI due to AD	26-28	24-25
	Mild AD dementia	21-25	18-23
Advanced AD	Moderate AD dementia	11-20	10-17
	Severe AD dementia	0-10	0-9

Results

Patient Characteristics

- A total of 193 patients were included (108 with EAD and 85 with AAD). Overall median age was 82 years and 63% of the study population were female. **(Table 2)**
- There were 46 (23.8%) patients categorized as having MCI due to AD, 62 (32.1%) as having mild AD dementia, 52 (26.9%) as having moderate AD dementia, and 33 (17.1%) as having severe AD dementia.
- Patients were followed for a mean of 2.43 years (standard deviation [SD]: 1.38).
- The MMSE was more common (91.7%) than the MoCA (8.3%) as an AD staging tool.
- Several key baseline characteristics were unbalanced (i.e., standardized difference ≥10%) prior to IPTW including comorbidity score, frailty score, and emergency department visits. However, after applying IPTW, all characteristics were well-balanced (i.e., standardized difference <10%). **(Table 2)**

Table 2: Baseline characteristics before and after IPTW

Patient characteristics	Unweighted Sample			IPTW weighted sample		
	EAD, N = 108	AAD, N = 85	Std. Diff %	EAD, N = 105	AAD, N = 84	Std. Diff %
Age at index date						
Mean ± SD [median]	81.63 ± 9.23 [82.00]	82.32 ± 8.51 [83.00]	8.0	81.73 ± 9.17 [82.00]	81.40 ± 9.71 [82.00]	3.0
Sex, n (%)						
Male	40 (37.04)	31 (36.47)	1.0	40 (37.00)	32 (38.03)	2.0
Female	68 (62.96)	54 (63.53)	1.0	67 (63.00)	52 (61.97)	2.0
Elixhauser comorbidities score						
Mean ± SD [median]	6.81 ± 8.04 [5.00]	8.95 ± 9.67 [5.00]	24.0 *	7.31 ± 8.11 [5.00]	7.28 ± 9.23 [5.00]	0.0
Claims-based frailty index score, n (%)						
Non-frail (frailty score <0.15)	22 (20.37)	10 (11.76)	24.0 *	17 (15.89)	13 (15.43)	1.0
Prefrail (frailty score ≥0.15 and <0.25)	55 (50.93)	48 (56.47)	11.0 *	59 (55.59)	47 (56.34)	2.0
Frail (frailty score ≥0.25)	31 (28.70)	27 (31.76)	7.0	30 (28.52)	24 (28.23)	1.0
All-cause HCRU						
Number of visits, mean ± SD [median]						
Inpatient	0.31 ± 0.70 [0.00]	0.39 ± 0.84 [0.00]	10.0	0.31 ± 0.70 [0.00]	0.32 ± 0.79 [0.00]	1.0
Emergency department	0.45 ± 0.97 [0.00]	0.93 ± 1.73 [0.00]	34.0 *	0.60 ± 1.19 [0.00]	0.65 ± 1.32 [0.00]	4.0
Outpatient	14.22 ± 9.46 [13.00]	13.33 ± 9.74 [12.00]	9.0	14.09 ± 8.98 [13.00]	14.89 ± 12.31 [13.00]	7.0
Skilled nursing facility	2.04 ± 8.93 [0.00]	2.05 ± 7.04 [0.00]	0.0	1.84 ± 8.13 [0.00]	1.89 ± 6.47 [0.00]	1.0
Other	6.26 ± 10.42 [1.00]	7.96 ± 16.75 [1.00]	12.0 *	6.51 ± 10.62 [1.00]	6.52 ± 15.08 [0.00]	0.0
Pharmacy						
Prescriptions, mean ± SD [median]	26.98 ± 17.84 [25.00]	25.64 ± 17.60 [22.00]	8.0	26.48 ± 16.99 [25.00]	26.69 ± 18.32 [23.00]	1.0

An absolute standardized difference (Std. Diff) more than 10% was considered to be an imbalance between the two cohorts and is denoted with "*".

HCRU and Costs

- Only 27.78% of patients with EAD had an AD-related encounter during the follow-up period, compared to 57.65% of patients with AAD.
- The higher AD-related HCRU for the AAD cohort was driven by outpatient visits (mean ±SD: 1.37 ±2.37 vs. 0.49 ±0.99 in EAD cohort). **(Figure 2)**

Figure 1: Sample selection

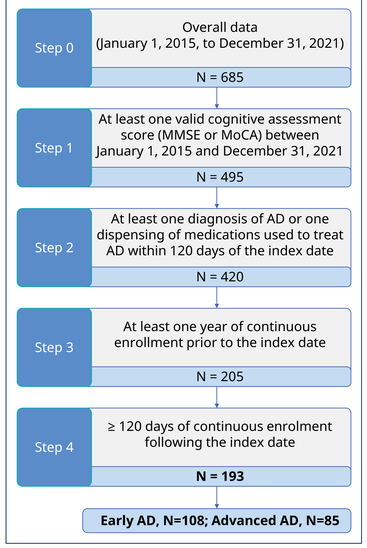
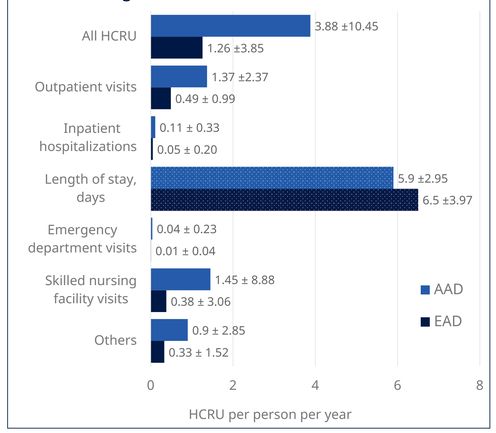


Figure 2: Mean AD-related healthcare resource use during follow-up period per person per year by AD stage



Length of stay (per episode) represents mean length of stay for patients with at least one inpatient stay during follow up. Denominator for the rest of the outcomes is whole AD population; Other visits include "other place of service".

Table 3: AD-related HCRU comparison

HCRU	Adjusted IRR	95% CI	P-value
AD-related HCRU	3.64	[1.96, 6.75]	≤0.001*
Inpatient hospitalizations	1.88	[0.79, 4.50]	0.154
Emergency department visits	6.79	[0.75, 61.25]	0.088
Outpatient visits	2.76	[1.68, 4.54]	≤0.001*
Skilled nursing facility visits	29.92	[6.60, 135.54]	≤0.001*
Other	2.50	[0.95, 6.59]	0.065

Incidence Rate Ratios (IRRs); EAD as reference; Results for hospice/home care visits are not displayed due to the failure of the generalized linear model to converge. P-values less than <0.05 were considered to be significant and are denoted with "*".

Table 4: AD-related costs comparison

Costs	Adjusted Cost Ratio	95% CI	P-value
Total costs	3.26	[1.51, 7.04]	0.003*
Medical costs	3.24	[1.47, 7.13]	0.004*
Outpatient visits	3.42	[1.55, 7.53]	0.002*

EAD as reference; Results for inpatient, emergency department, skilled nursing facility, hospice/home care, and pharmacy costs are not displayed due to the failure of the generalized linear model to converge; Total costs are a sum of total medical and pharmacy costs; P-values less than <0.05 were considered to be significant and are denoted with "*".

- Inpatient costs were the highest type of AD-related costs, followed by outpatient and pharmacy costs.
- The AAD cohort had significantly higher overall AD-related HCRU (incidence rate ratio [IRR] [95% CI]=3.64 [1.96-6.75]) and outpatient visits (2.76 [1.68-4.54]) during follow-up period compared to the EAD cohort. **(Table 3)**
- Total AD-related costs (cost ratio=3.26, p=0.003), medical costs (cost ratio=3.24, p=0.004) and outpatient visits costs (cost ratio=3.42, p=0.002) were higher in the AAD cohort versus the EAD cohort. **(Table 4)**

Predictors of High Cost

- Among baseline factors considered, only AD stage and frailty score significantly contributed to the predictive value of the LASSO regression model for high AD-related costs. Patients who were frail (OR [95% CI] =2.12 [1.01-4.43]) or with AAD (2.43 [1.17-5.03]) were significantly more likely to incur high AD-related costs. **(Table 5)**

Table 5: Predictors of high AD-related total costs

Logistic Regression	3-Fold Cross-Validation	
Post-LASSO Variables	**OR (95% CI)**	**P-value**
AAD (ref: EAD)	2.43 (1.17, 5.03)	0.017*
Frail (ref: Non-frail or prefrail)	2.12 (1.01, 4.43)	0.047*

Predictors were identified using the LASSO model. P-values less than <0.05 were considered to be significant and are denoted with "*".

Discussion

- Results from the present study reported a higher AD-related HCRU and costs for the advanced versus early AD cohort, which is consistent with the current literature.[3,4]
- AD severity was associated with higher AD-related costs. Frailty was also found to be associated with high AD-related costs in the current study. This new finding contributes to advancing our understanding of the economic burden faced by patients with AD.

Limitations

- Administrative claims data are collected for payment rather than research purposes, and as such, there may be billing inaccuracies and missing data due to miscoding of medical diagnoses. The costs available within the HV data are proxy costs, with some level of missingness, and do not accurately reflect the real term costs associated with healthcare encounters across different health plans. The current research only includes patients' direct costs and HCRU and did not count for the burden from caregivers.
- There is the potential misclassification due to AD diagnoses, MMSE/MoCA disease severity changes overtime. Additionally, most of AD cases were based on clinical diagnosis (i.e., without biomarker confirmation). Therefore, some cases may be misclassified.

Conclusion

- Patients with AAD incurred higher AD-related HCRU and costs compared to those with EAD.
- AD severity and patient frailty were predictive factors for increased AD-related costs for patients with AD.
- Further research is necessary to determine whether interventions earlier in disease progression can mitigate these costs for patients with AAD.

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