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Real-World Patterns of Outcomes in Patients with Multiple Sclerosis Who Are Adherent versus Non-Adherent to Disease Modifying Treatments over 6 Years

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CONCLUSIONS

- Out of 15,617 people with MS, 42% were adherent over a median of 5.6 years, while 43.3% were non-adherent, and 14.7% were non-DMD-treated
- Adherent patients showed significantly lower ARR and longer time to first relapse, cane/walker use, and wheelchair use when compared with non-adherent patients
- These results highlight the importance of DMD adherence in slowing disease progression. Indicators of MS-related disability were found to be related to adherence, suggesting a lower rate of disability progression over time
- Further analyses are planned to understand barriers to adherence and comparisons by DMD route of administration

INTRODUCTION

- MS is a chronic disease often requiring long-term treatment with DMDs
- Non-adherence to maintenance therapy regimens is a risk factor for poor outcomes, which for people with MS may lead to increased relapse frequency as well as disease progression[1-3]
- The impact of long-term DMD adherence on clinical outcomes has not yet been adequately quantified

OBJECTIVE

- To assess the impact of long-term DMD adherence to maintenance therapies on MS disease progression in the real world retrospective claims analysis

METHODS

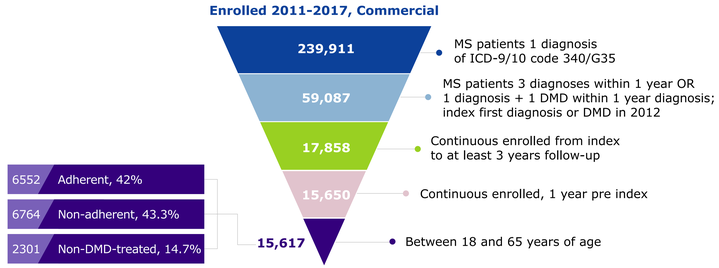
- This was a retrospective administrative claims analysis of the 2011–2017 US MarketScan Commercial database records
- Patients included in the analysis:
  - Were aged 18–65 years
  - Were diagnosed with MS as defined by ≥3 ICD-9/10 340/G35 diagnosis claims or ≥1 diagnosis and >1 DMD claim within 1 year (i.e. index-date was the first MS diagnosis or DMD claim in 2012)
  - Demonstrated continuous eligibility of 1-year baseline prior to index-date and ≥3 years follow-up (up to 6 years)
- Adherent patients were those with a PDC ≥0.8 and non-adherent patients were those with PDC <0.8, considered overall and as two non-adherent subgroups (PDC ≥0.6 – <0.8 and PDC <0.6). PDC was calculated as the total of the supply days that DMDs were prescribed in follow-up, divided by the total number of follow-up days with the consideration of the DMD route of administration[4]
- PS greedy matching was used to balance population characteristics (age, gender, geography, comorbidities, relapses) 1 year pre-index
- Average number of relapses were compared between the two cohorts using a Poisson regression model adjusted for PS and route of DMD administration with an offset on follow-up time
  - Relapse was defined as a hospitalization with a primary diagnosis of 340/G35 or an outpatient visit with diagnosis of 340/G35 plus a pharmacy or medical claim for a qualifying corticosteroid within 7 days. Two or more relapses occurring within 30 days will be considered one relapse[5]
- Time to first relapse, time to cane/walker use, and time to wheelchair use were also compared between the two cohorts using a Cox-proportional hazard model adjusted for PS and route of DMD administration
  - Time to cane/walker/wheelchair are defined as the number of days after index when first claims occurred that associated with cane/walker/wheelchair use, the patients who had any claims in 1-year pre-index period that were associated with cane/walker/wheelchair use were excluded

RESULTS

Patients

- A total of 15,617 patients met eligibility criteria (**Figure 1**). Median duration of follow-up was 5.6 years

Figure 1. Population Selection



- After PS matching, 6121 matched pairs were analyzed. Both patient cohorts had similar baseline characteristics for each analysis, with standardized differences of all baseline characteristics between two comparison groups of <0.1 (**Table 1**)

Table 1. Baseline Characteristics, All Patients and Matched Patients

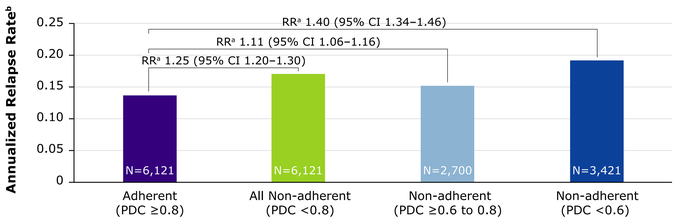
	All Patients		1:1 Matched Patients		
Match Variables	**Adherent (PDC ≥0.8)**	**Non-Adherent (PDC <0.8)**	**Adherent (PDC ≥0.8)**	**Non-Adherent (PDC <0.8)**	**Standardized Mean Difference**
N	6,552	6,764	6,121	6,121	
Age at index, year (SD)	47.7 (8.8)	46.2 (9.2)	47.2 (8.8)	47.0 (8.7)	-0.0220
CCI score (SD)	0.06 (0.26)	0.09 (0.32)	0.06 (0.26)	0.06 (0.26)	-0.0006
≥ 1 relapse in prior year	9.2%	11.9%	9.7%	9.4%	0.0111
Female	76.3%	78.8%	77.7%	77.7%	-0.0006
Region					0.0289
Northeast region	23.2%	25.3%	24.1%	24.5%	
North Central region	25.9%	21.9%	24.0%	23.5%	
South region	35.4%	39.0%	36.8%	37.4%	
West region	15.5%	13.7%	15.1%	14.6%	
Unknown region	0.1%	0.1%	0.1%	0.0%	

RESULTS (cont.)

Number of Relapses

- Adherent users had significantly lower ARRs compared with all non-adherent users, as well as each subgroup of non-adherent users (**Figure 2**)

Figure 2. Annualized Relapse Rate

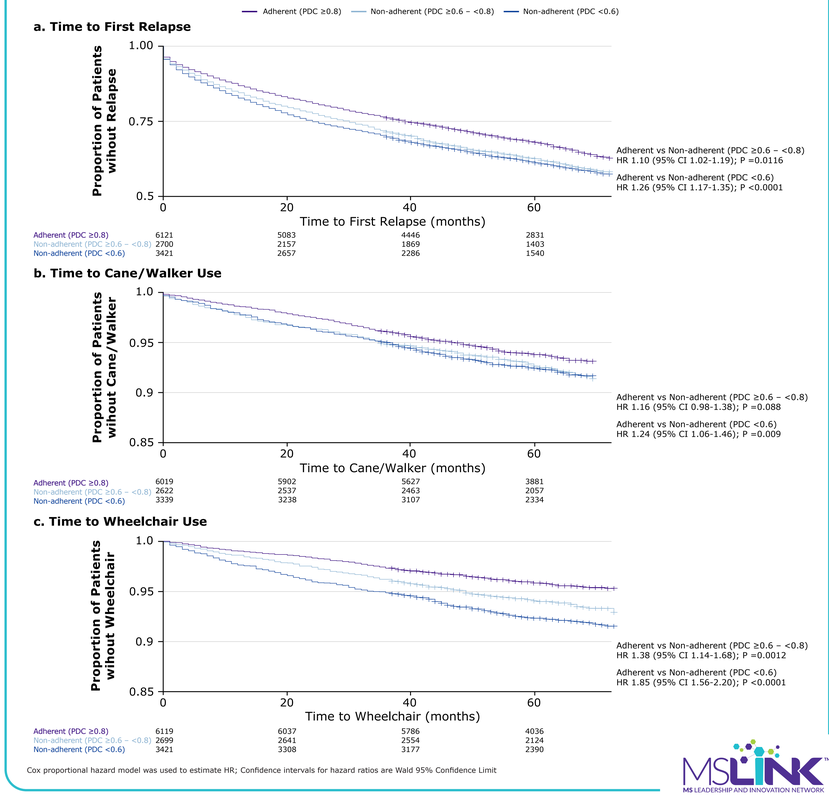


P<0.0001 for adherent vs. nonadherent in all three analyses
[a]RR was estimated using GEE Poisson model adjusted for route of DMD administration with an offset on follow-up time; [b]ARR was estimated based on the total number of relapses during the follow-up time; P values are from a Wald chi-square test.

Time to Disease Progression

- For all comparisons but one, adherent users had significantly longer time to first relapse, cane/walker use, and wheelchair use compared with both groups of non-adherent users, with larger differences found between adherent and highly non-adherent users (**Figure 3**)

Figure 3. Kaplan Meier Plots Showing Time to Outcomes



Cox proportional hazard model was used to estimate HR; Confidence intervals for hazard ratios are Wald 95% Confidence Limit

Abbreviations: ARR, annualized relapse rate; **CCI,** Charlson Comorbidity Index; **CI,** confidence interval; **DMD**, disease modifying drug; **GEE,** generalized estimating equation; **HR,** hazard ratio; **MS,** multiple sclerosis; **PDC,** proportion of days covered; **PS,** propensity score; **RR,** rate ratio

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