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Longitudinal Adherence Trajectories of Patients with Multiple Sclerosis Initiating Once- or Twice-Daily Oral Disease-modifying Therapies

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SUMMARY



- The objective of this study was to elucidate longitudinal adherence trajectories of patients with MS initiating once-/twice-daily oral DMTs using group-based trajectory modeling (GBTM)

- GBTM can provide detailed information about longitudinal adherence patterns



- Administrative claims and merged sociodemographic data from commercial and MAPD enrollees in the Optum Research Database were utilized
- The trajectory analysis revealed three distinct longitudinal patterns of adherence
- There were several statistically significant factors predicting group membership
- Different groups may warrant different clinical interventions to address non-adherence



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BACKGROUND INFORMATION



- Patients with MS with the same aggregate adherence may exhibit different patterns of adherence
- GBTM can provide detailed information about longitudinal adherence patterns



OBJECTIVE



- To elucidate longitudinal adherence trajectories of patients with MS initiating once-/twice-daily oral DMTs using GBTM



METHODS

- This retrospective study used administrative claims and merged sociodemographic data from commercial and MAPD enrollees in the Optum Research Database
- Eligibility criteria were:
 - ≥ 1 once-/twice-daily oral DMT claim between January 1, 2014–July 31, 2018 (index);
 - ≥ 3 of the following: (1) MS-related (ICD-9-CM code 340 or ICD-10-CM code G35) ambulatory visits, (2) MS-related inpatient stays, or (3) DMT claims during a 12-month period;
 - Continuous 12-month eligibility with commercial/MAPD insurance before/after index;
 - No baseline oral DMT;
 - Age ≥ 18 years; and
 - No claims with diagnosis or procedure codes indicating pregnancy in the pre- or post-index periods
- Individuals following similar longitudinal progressions of adherence (PDC) were “clustered” together using GBTM
- The optimal number of groups best representing the heterogeneity in trajectories was selected considering log-likelihood, Akaike information criterion, Bayesian information criterion, and visual assessment of the resulting trajectory groups
- Multivariable polychotomous logistic regression was used to identify predictors of adherence group membership

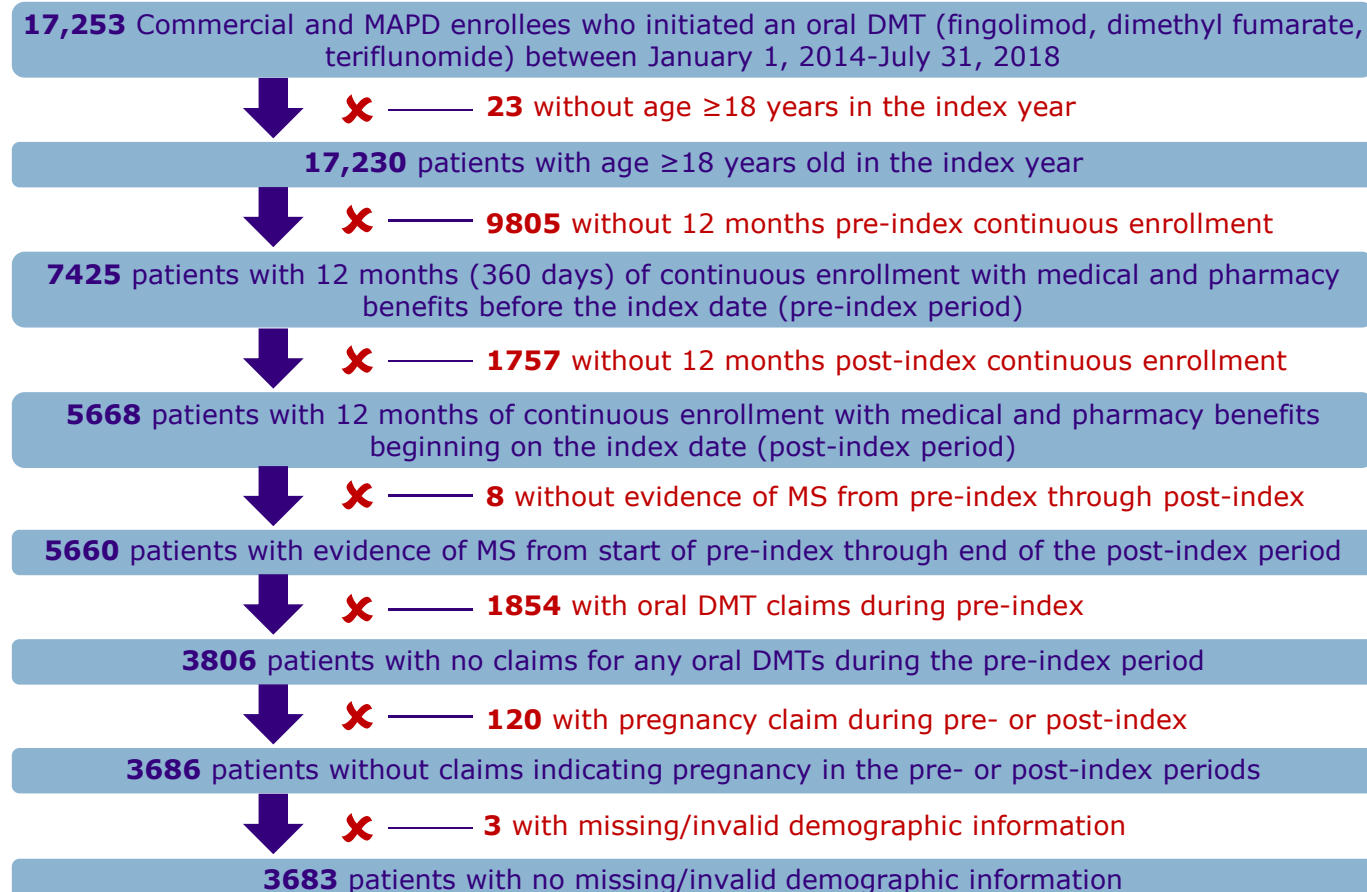
*In addition to main study inclusion criteria



RESULTS

- **A total of 3683 patients met eligibility criteria** (mean [SD] age: 48.8 [11.8] years; female: 74.8%; commercial insurance: 69.6%; MAPD: 30.4%)
- Mean (SD) PDC was 0.71 (0.32) for commercial and 0.70 (0.33) for MAPD enrollees
- **GBTM revealed 3 distinct adherence groups:**
 - 'Immediately Non-adherent' (mean PDC <0.3 by Month 3),
 - 'Gradually Non-adherent' (mean PDC ≥0.8 at Month 3 but ≤0.4 by Month 8), and
 - 'Adherent' (mean PDC ≥0.8 through the 12-month post-index period), comprising 18.7%, 18.3%, and 62.9% of patients, respectively

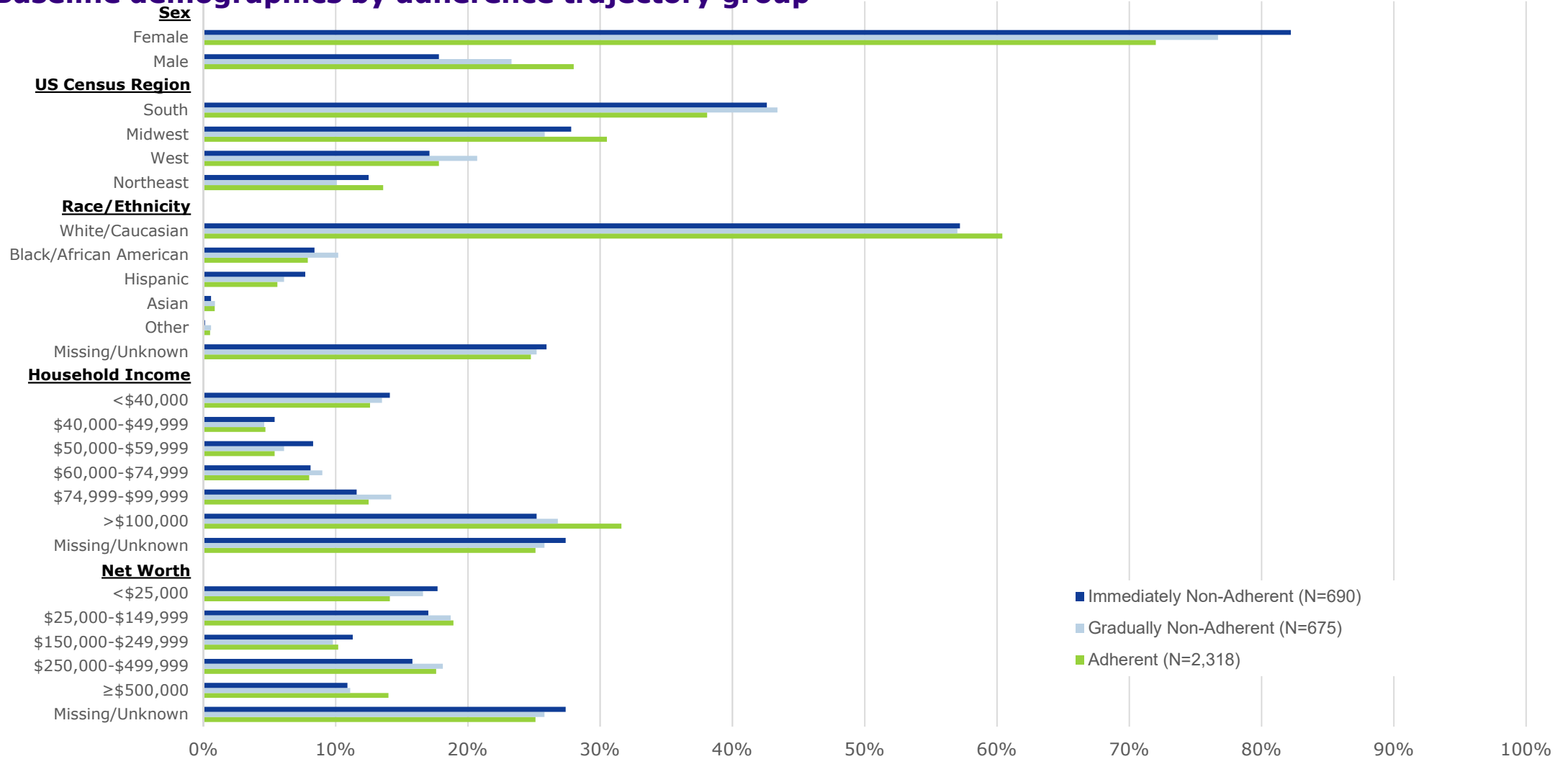
Patient selection





RESULTS

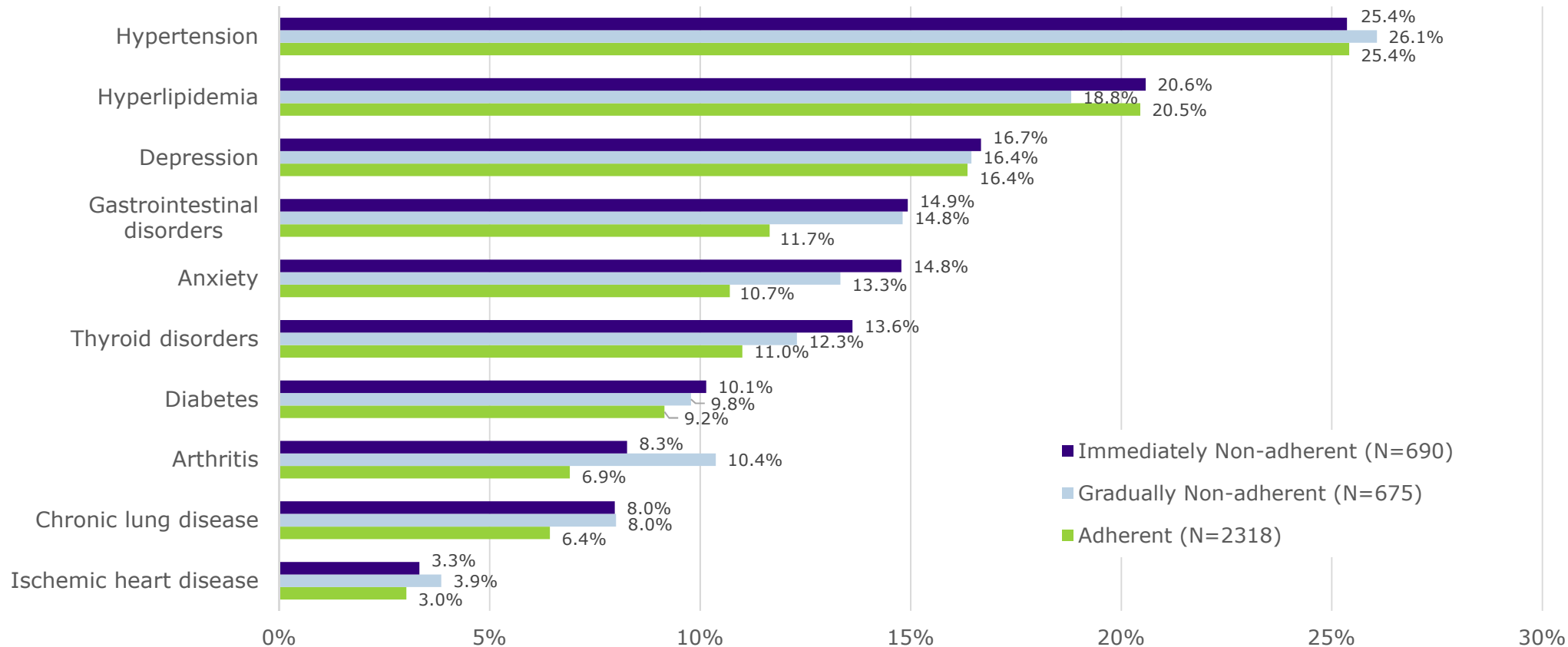
Baseline demographics by adherence trajectory group





RESULTS

Baseline clinical characteristics by adherence trajectory group





RESULTS

Pre-index relapses and healthcare resource use by adherence trajectory group

	Immediately Non-adherent (N=690)	Gradually Non-adherent (N=675)	Adherent (N=2318)
Non-oral DMT utilization, n(%)	295 (42.8%)	280 (41.5%)	1194 (51.5%)
Relapses			
# of relapses, mean (SD)	0.50 (0.81)	0.50 (0.97)	0.41 (0.74)
Relapse within 12 months, n (%)	251 (36.4%)	224 (33.2%)	708 (30.5%)
Inpatient	38 (5.5%)	47 (7.0%)	136 (5.9%)
Emergency room	46 (6.7%)	51 (7.6%)	102 (4.4%)
Ambulatory	223 (32.3%)	192 (28.4%)	605 (26.1%)
Relapse within 90 days pre-index, n (%)	139 (20.1%)	146 (21.6%)	406 (17.5%)
Inpatient	22 (3.2%)	30 (4.4%)	69 (3.0%)
Emergency room	18 (2.6%)	25 (3.7%)	52 (2.2%)
Ambulatory	122 (17.7%)	119 (17.6%)	347 (15.0%)
MS-related visits/stays			
% with any visits/stays, n (%)			
Office visits	667 (96.7%)	625 (92.6%)	2196 (94.7%)
Outpatient facility visits	448 (64.9%)	423 (62.7%)	1450 (62.6%)
Emergency visits	148 (21.5%)	148 (21.9%)	397 (17.1%)
Inpatient stays	77 (11.2%)	90 (13.3%)	263 (11.4%)
# of visits/stays, mean (SD)			
Office visits	5.3 (4.6)	4.7 (4.7)	5.5 (6.0)
Outpatient facility visits	4.2 (12.9)	4.2 (11.0)	4.3 (13.3)
Emergency visits	0.4 (1.2)	0.4 (1.2)	0.3 (0.8)
Inpatient stays	0.2 (0.5)	0.2 (0.6)	0.1 (0.4)
Inpatient days	1.3 (6.9)	1.4 (6.9)	1.5 (9.2)

Note: Because patients may have >1 relapse and a single relapse may be treated in >1 venue, relapse venues are not mutually exclusive.



RESULTS

Several statistically significant factors predicted adherence group membership

- **Female** (vs. male) sex, **no pre-index DMTs**, ≥ 2 (vs. no) **pre-index emergency visits**, and **twice-** (vs. once-) **daily index DMT dosing** were associated with **higher odds** of being in the **Immediately Non-adherent** and **Gradually Non-adherent** groups compared with the Adherent group
- **Increasing age**, **pre-index headache**, **no pre-index eye disorders**, and **twice-daily dose** were **associated with** the **Immediately Non-adherent** group compared with both the Gradually Non-adherent and Adherent groups
- **Pre-index arthritis** was **associated with** the **Gradually Non-adherent** versus Adherent group

Factors associated with adherence trajectory group

Independent variables	Immediately Non-adherent vs. Adherent		Gradually Non-adherent vs. Adherent		Immediately Non-adherent vs. Gradually Non-adherent		Overall p-value
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	
Age	1.008 (1.000, 1.016)	0.041	0.994 (0.986, 1.001)	0.103	1.015 (1.005, 1.025)	0.003	0.012
Gender							
Male (vs. female)	0.588 (0.471, 0.736)	<0.001	0.772 (0.626, 0.952)	0.016	0.762 (0.579, 1.003)	0.052	<0.001
Region							
Northeast	ref.	–	ref.	–	ref.	–	
Midwest	1.052 (0.781, 1.415)	0.740	1.158 (0.845, 1.588)	0.362	0.908 (0.618, 1.335)	0.623	0.653
South	1.173 (0.884, 1.557)	0.268	1.464 (1.084, 1.977)	0.013	0.801 (0.556, 1.155)	0.235	0.038
West	1.024 (0.740, 1.417)	0.885	1.483 (1.063, 2.067)	0.020	0.691 (0.458, 1.042)	0.078	0.063
Race/Ethnicity							
White/Caucasian	ref.	–	ref.	–	ref.	–	
Black/African American	0.994 (0.711, 1.389)	0.970	1.176 (0.859, 1.611)	0.311	0.845 (0.569, 1.255)	0.403	0.571
Hispanic/Latino	1.413 (0.987, 2.023)	0.059	1.104 (0.757, 1.612)	0.607	1.279 (0.818, 2.001)	0.281	0.169
Other/unknown/missing	1.078 (0.876, 1.326)	0.480	0.992 (0.805, 1.224)	0.943	1.086 (0.839, 1.405)	0.531	0.756
Index DMT daily average consumption							
Once-a-day (vs. twice-a-day)	0.621 (0.514, 0.749)	<0.001	0.789 (0.656, 0.948)	0.011	0.787 (0.624, 0.993)	0.043	<0.001
Pre-index DMT utilization							
1+ (vs. 0)	0.705 (0.59, 0.843)	<0.001	0.691 (0.578, 0.827)	<0.001	1.02 (0.817, 1.273)	0.862	<0.001
Pre-index MS-related emergency visits							
0	ref.	–	ref.	–	ref.	–	
1	1.096 (0.84, 1.43)	0.499	1.192 (0.916, 1.552)	0.192	0.919 (0.664, 1.273)	0.613	0.398
2+	1.555 (1.092, 2.216)	0.014	1.922 (1.362, 2.713)	<0.001	0.809 (0.540, 1.212)	0.304	<0.001
Pre-index arthritis disorders							
Yes (vs. no)	1.03 (0.739, 1.437)	0.860	1.499 (1.096, 2.051)	0.011	0.687 (0.467, 1.012)	0.058	0.034
Pre-index headache, including migraine (AHRQ CCS condition)							
Yes (vs. no)	1.504 (1.232, 1.835)	<0.001	0.919 (0.743, 1.138)	0.439	1.636 (1.272, 2.104)	<0.001	<0.001
Pre-index eye disorders (AHRQ CCS condition)							
Yes (vs. no)	0.782 (0.653, 0.936)	0.007	1.031 (0.863, 1.233)	0.735	0.758 (0.607, 0.946)	0.014	0.017



CONCLUSIONS



- **This trajectory analysis in patients with MS receiving once- or twice-daily oral DMTs revealed three distinct longitudinal patterns of adherence**
- **There were several statistically significant factors predicting group membership**



- **Different groups may warrant different clinical interventions to address non-adherence**