

Multi-state Modelling Accurately Characterises the Persistence to Distinct Preventive Treatment Lines in patients with migraine in Spain

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BACKGROUND AND OBJECTIVE

- Migraine is a highly prevalent and burdensome disease characterized by recurrent moderate-to-severe headaches [1-3].
- The goals of migraine preventive treatment are to reduce the headache-related disability as well as the economic and healthcare burden of the disease [4].
- Despite the wide range of available preventive medications, a large proportion of people with migraine do not receive optimal prophylaxis [5]:
 - In Spain, it is as low as 13.7% [6].
- Among those who initiate it, poor adherence and persistence have been reported [5,7], but the number of studies addressing these matters is still limited.
- To help improve persistence to migraine prophylaxis, the aim of this analysis was to provide insights into discontinuation patterns and associated risk factors in patients who started their first preventive treatment.

METHODS

- Design:** Retrospective observational study of migraine preventive treatment persistence.
- Inclusion criteria:** adults with a diagnosis of migraine and first preventive treatment (oral agents or botulinum toxin) initiated between 01/01/2016 and 30/06/2018.
- Data source:** One-year follow-up information of 7,866 patients from the BIG-PACTM database (Spain) [8].
- Outcome measures:**
 - Persistence to treatment
 - Maintenance
 - Switching (<60 days since the last prescription)
 - Discontinuation:
 - Reinitiation of the same or another treatment (≥60 days)
 - Permanent withdrawal
- Statistical analysis:** Discontinuation patterns across multiple treatment lines and the influence of several covariates (age, gender, CCI and time since diagnosis) were analyzed by a Multi-state Model (MSM) of proportional hazards [9]. The mstate package in R was used [10].

KEY RESULT

The risk of discontinuing migraine prophylaxis was higher from the first line of treatment than the successive ones

- A possible association between age and non-persistence was also identified.

	From the 1 st line			From the 2 nd line			From the 3 rd line		
Covariates	HR	SD	P	HR	SD	P	HR	SD	P
Age ^a	5.06	<0.001	<0.001	5.10	<0.001	<0.001	5.09	0.01	0.237
Gender	0.98	0.03	0.526	0.87	0.19	0.455	1.09	0.55	0.882
CCI	1.01	0.01	0.516	0.95	0.09	0.582	1.01	0.28	0.96
Time since diagnosis	0.99	0.01	0.048	0.97	0.04	0.432	1.04	0.11	0.730
Disc. (vs. 1 st line)	n/a			0.24	0.35	<0.001	0.21	0.98	0.110

^a5-year HR

CONCLUSIONS

- MSM better describes complex real-world clinical scenarios whereby medication drop-out events are state-dependent, i.e., they depend on the treatment line.
- Patients with migraine tend to discontinue the first line of preventive treatment more often than the other lines.
- Increasing age may be a risk factor for abandoning migraine prophylaxis.
- People with migraine who were prescribed preventive medication for the first time showed poor persistence to it:
 - About a third of them persisted after one year of treatment;
 - Discontinuation mostly occurred during the first six months;
 - Treatment switching and reinitiation were common events.
- Intervention measures towards improving persistence to migraine preventive medication will require further studies that pinpoint the reasons behind medication drop-out events, including migraine severity, efficacy and tolerability issues as well as patient satisfaction.

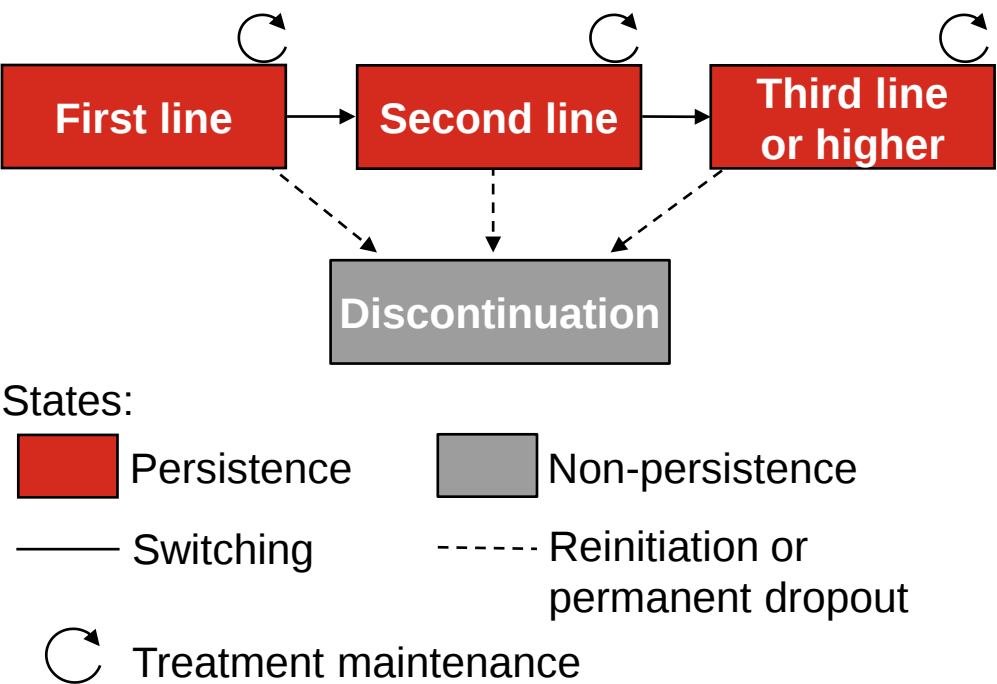
Patient characteristics

	N = 7866 (100%)			
Age (years), mean (SD)	48.2 (14.8)			
Gender (women), n (%)	6324 (80.4)			
Comorbidities ^a , n (%)				
Generalized anxiety dis.	2827 (35.9%)	Smokers	1426 (18.1%)	
Dyslipemia	2124 (27.0%)	Obesity	1161 (14.8%)	
Arterial hypertension	1724 (21.9%)	Depressive syndr.	890 (11.3%)	
CCI, mean (SD)	0.4 (0.9)			

^a≥10%

MSM: design

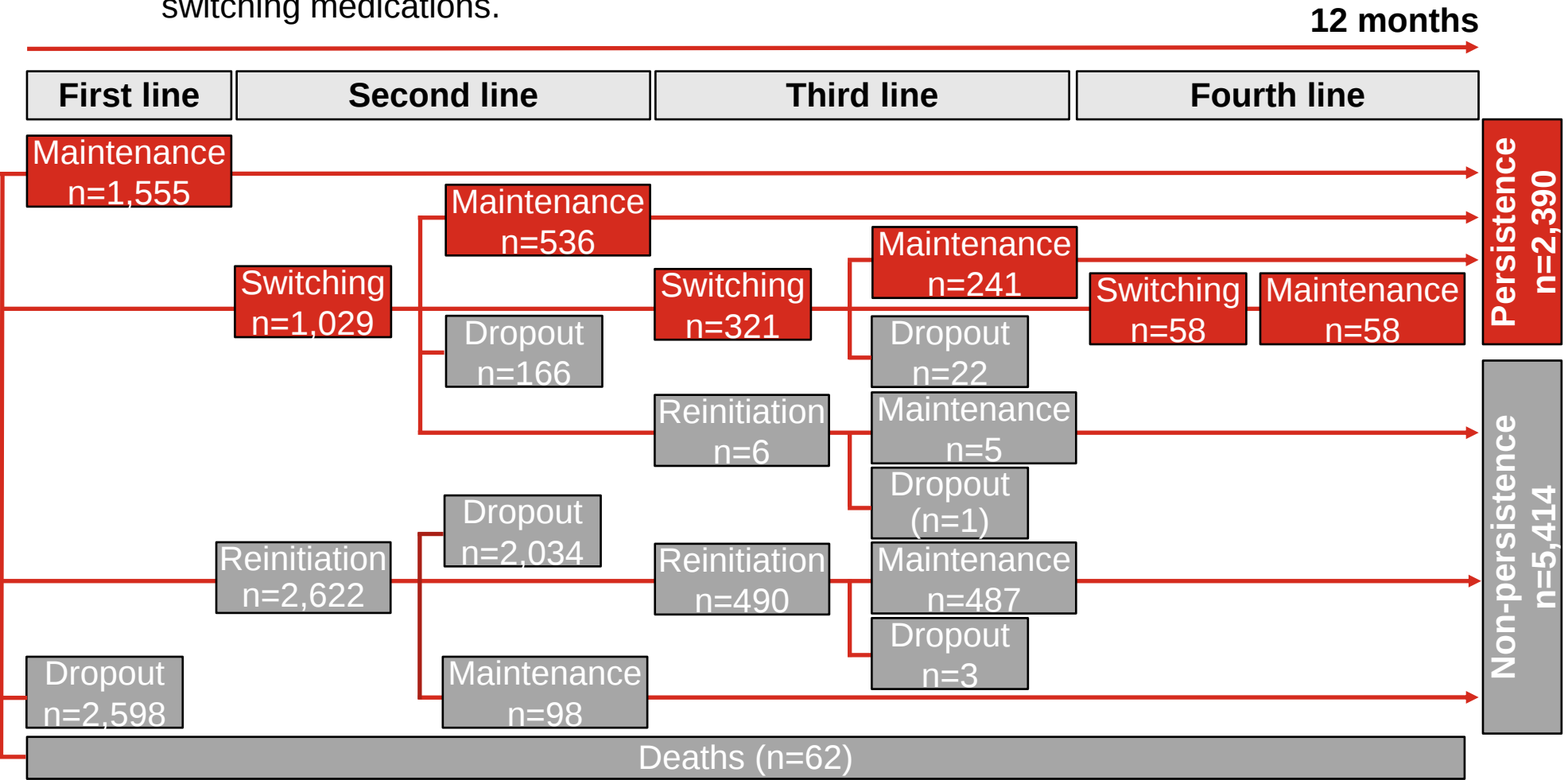
Patients with migraine under preventive treatment could transition across 4 possible therapeutic states



MSM: persistence to migraine prophylaxis and treatment patterns

Approximately a third of patients who had started their first preventive treatment were persistent to it following the first year

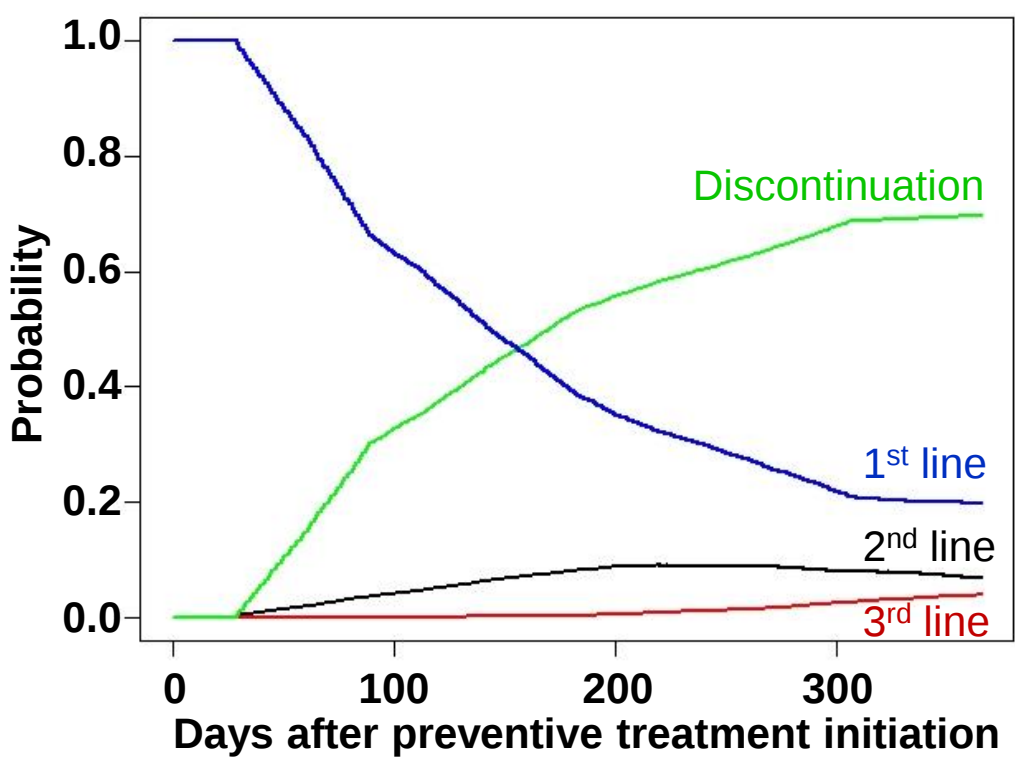
- Discontinuation mostly occurred during the first 6 months of the study.
 - Persistence rate at 6 months: 2,545 (32.4%) patients.
- At 12 months, 2,390 (30.4%) patients had persisted with the treatment by maintaining it or switching medications.



MSM: distribution of patients throughout the study

Persistence curves differ according to the treatment line

- For the second and third (or later) lines of treatment, the curves remained similar and stable throughout the study.
- First-line persistence curve decreased and was steeper in the first six months as a result of the increasing discontinuation rate in this time window.
 - Median persistence time in first-line was 162 (95%CI: 158-166) days.



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Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; Disc., discontinuation; HR, hazard ratio; MSM, Multi-state Model; n/a, not applicable; P, P value; SD, standard deviation

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