Long-Term Economic Impact of Non-Persistence to Disease Modifying Therapies in a Cohort of German Patients with Multiple Sclerosis

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OBJECTIVE

To assess the long-term societal costs associated with non-persistence to Disease-Modifying Therapies (DMTs) in Multiple Sclerosis (MS) by comparing economic outcomes between persistent and non-persistent patients.

KEY TAKEAWAYS

Non-persistence to DMTs in MS is associated with a higher risk of earlier disability pension, greater use of walking aids, and substantially higher societal costs vs. persistence, driven mainly by indirect and direct medical costs

Considering treatment persistence into DMTs decision-making may help reduce the overall economic burden of MS from a societal perspective

INTRODUCTION

- Non-persistence to disease-modifying therapies (DMTs) for multiple sclerosis (MS) may compromise treatment efficacy for controlling disease course
- A significant knowledge gap exists regarding the full spectrum of costs (medical/non-medical and indirect) associated with non-persistence

OUTCOMES

- Primary Outcomes: cumulative total costs (direct and direct non-medical, indirect costs) up to 4 years
  - Direct medical costs: inpatient care/day admissions, consultations, tests
  - Direct non-medical costs: investments, community services, informal care
  - Indirect costs: short-term absence, long-term absence, invalidity, early retirement
- Secondary outcomes:
  - Disability pension: Full or partial disability pension
  - 3-month Expanded Disability Status Scale (EDSS) score confirmed disability progression (CDP)
  - Walking aids: Use of crutches, ambulators, or wheelchairs

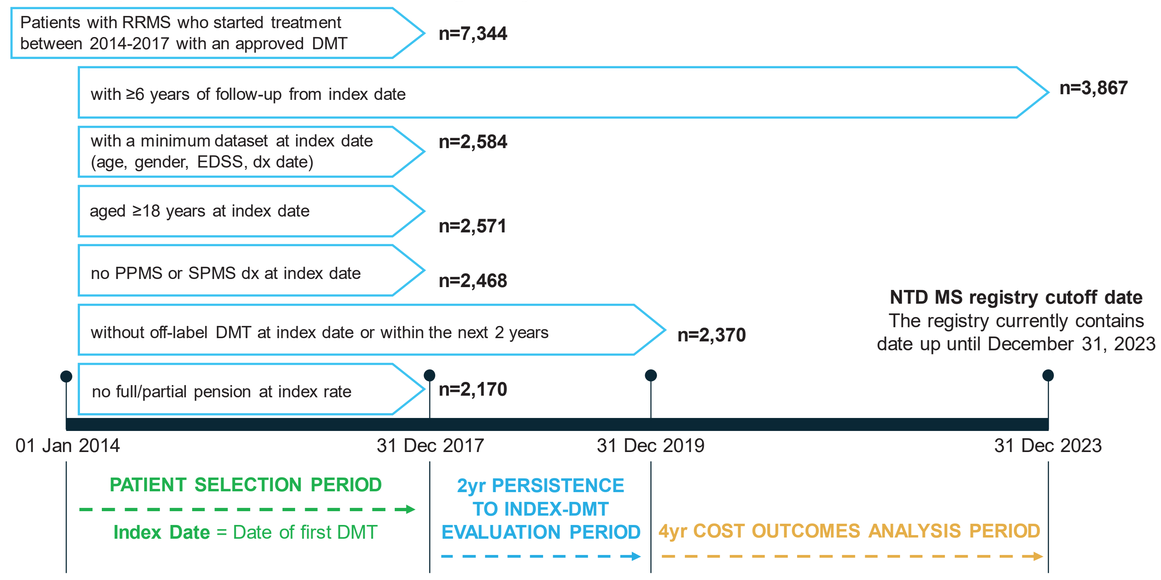
STATISTICAL ANALYSIS

- Marginal structural models fitted with Inverse Probability of Treatment Weighting (IPTW) to balance baseline and time-varying confounders (see online suppl. material)
  - Gamma distribution utilized with a log link to relate mean costs to covariates
  - Estimated coefficients, 95% CIs, and p-values calculated with bias-corrected and accelerated bootstrap.
  - P-values adjusted for multiple testing by cost category using the Holm-Bonferroni procedure
- Time-to-event analysis for secondary outcomes performed using Kaplan-Meier estimators and Cox regression models, both accounting for estimated IPTW weights

METHODS

- Retrospective cohort study using data from the German NeuroTransData MS registry (Fig 1.)
- DMTs grouped by route of administration, mechanism of action, and efficacy based on German MS therapy guidelines
- Non-persistence defined as discontinuation or switching to a different DMT group within 2 years post-index DMT

Figure 1. Study design and eligibility criteria



RESULTS

Patient characteristics

- Prior to weighting, Non-Persisters cohort had systematic differences from Persisters cohort in several baseline characteristics, including age, gender and index DMT group
- Weighting successfully eliminated differences across baseline confounders (standardized mean differences <0.1) between cohorts

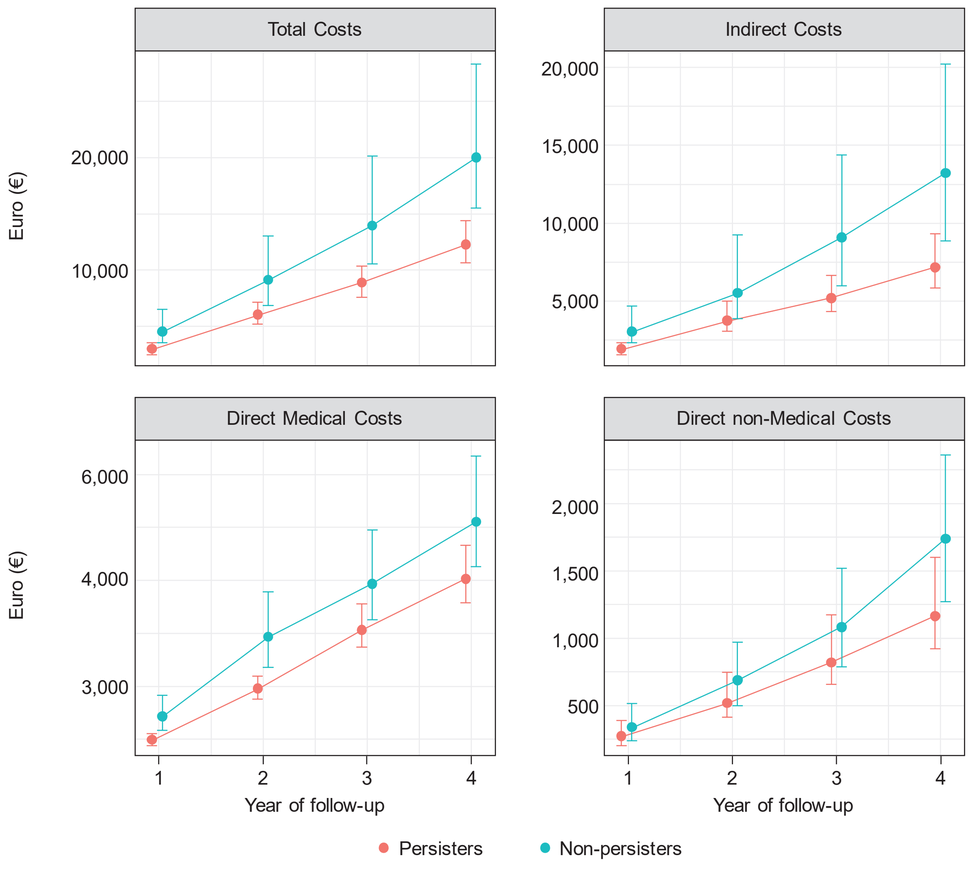
Table 1. Baseline patient characteristics before IPTW

Characteristic	Overall (N=2,170)	Non-Persisters (N=648)	Persisters (N=1,522)
Age, years, mean (SD)	39.3 (10.8)	37.1 (10.4)	40.2 (10.8)
Female, n (%)	1,561 (71.9%)	519 (80.1%)	1,042 (68.5%)
EDSS score, mean (SD)	1.6 (1.4)	1.6 (1.4)	1.6 (1.5)
Relapses before index date, mean (SD)	0.6 (0.7)	0.7 (0.8)	0.6 (0.7)
Time since diagnosis, mean (SD)	6.1 (6.5)	5.7 (6.1)	6.3 (6.7)
% DMT naive at index	888 (40.9%)	280 (43.2%)	608 (39.9%)
MRI with Gd+ lesions at index, n (%)	1,181 (54.4%)	360 (55.6%)	821 (53.9%)

Annual cost increase (Fig. 2)

- Cost differences accumulated over time for total, indirect, and direct medical expenses, underscoring the long-term impact of non-persistence

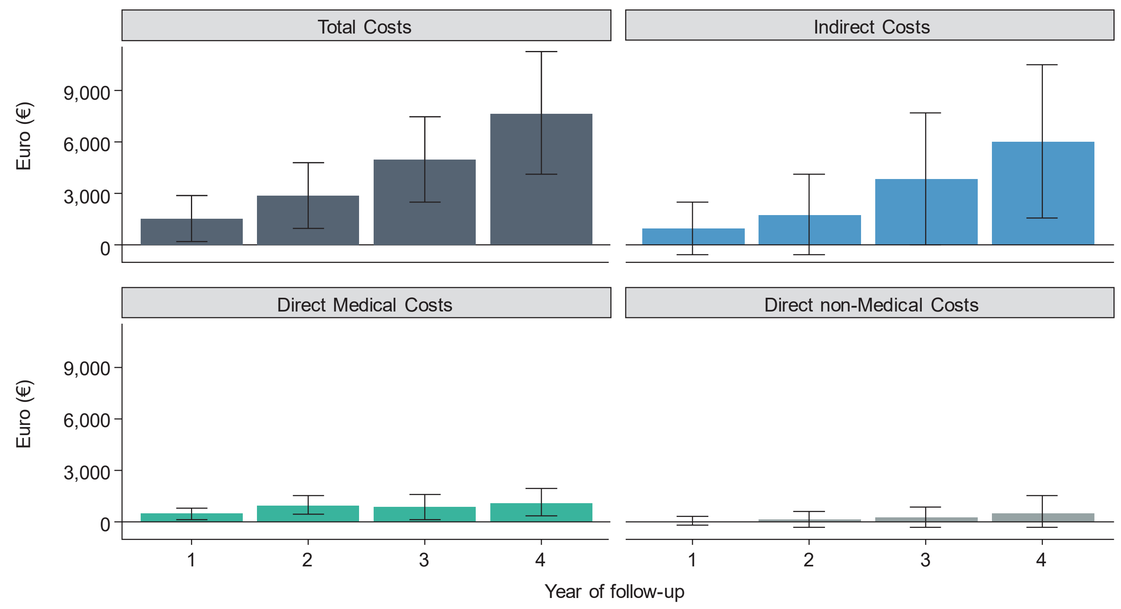
Figure 2. Estimated cumulative costs per patient by year and cost type



Impact of non-persistence on societal costs (Fig. 3)

- At the end of the 4-year follow-up, average excess cumulative costs per person incurred by the non-persisters group compared to persisters were:
  - € 7670 higher total costs (95% CI 2866-15908, p<0.001).
  - € 6001 higher indirect costs (95% CI 1384-13340, p<0.01)
  - € 1088 higher direct medical costs (95% CI 100-2366, p=0.03)
  - € 580 higher direct non-medical costs (95% CI -5-1248, p=0.05)

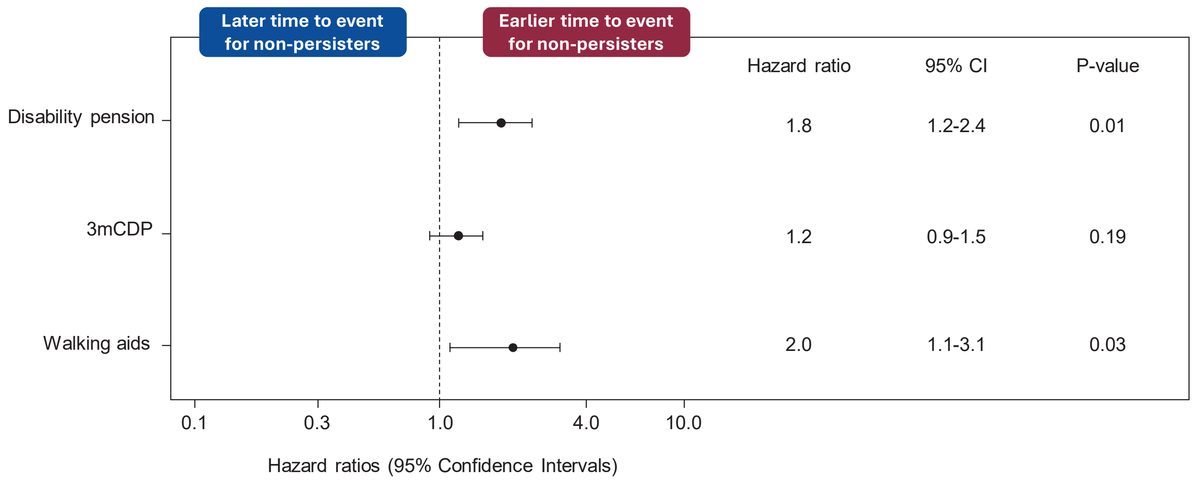
Figure 3. Estimated costs differences (non-persisters vs. persisters) by year



Impact of non-persistence on disability risk (Fig. 4)

- Over 4 years, Non-persisters had statistically significant higher risk of requiring earlier disability pension or greater use of walking aids compared to Persisters
- Non-persisters had higher risk of experiencing earlier 3mCDP (not statistically significant, p=0.19)

Figure 4. Hazard ratios for secondary disability outcomes



LIMITATIONS

- Cumulative cost outcomes may include non-causal recurring costs (e.g., wheelchairs, disability pensions) initiated during the cohort entry period that cannot be attributed to non-persistence.
- Residual confounding remains possible due to unmeasured factors, such as baseline comorbidities

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DISCLOSURES

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