# msregister Real-world data on relapse-independent worsening in MS

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## Background

- In recent years, disability progression independent of relapse activity (PIRA) has moved into the focus of research

## Objectives

- To examine the determinants of the time to PIRA events in relapsing MS patients

## Methods

- Use of recurrent events data from the German MS Registry ➔ prevalence and risk factors of confirmed PIRA (cPIRA)
- Index date: first visit since 2017
- Inclusion: relapsing onset MS including CIS patients (pwROMS) with complete relapse and DMT documentation
- Use of time-dependent Cox model ➔ assessment of confirmed EDSS progression in relapse absence between EDSS visits
- The Following confounders were used: age at MS onset, EDSS at index (≤3.5 [mild], 4.0-5.5 [moderate], ≥6.0 [severe]), periods of diagnosis (≤2007, 2008-2012, 2013-2017, 2018-2024), sex, time-varying DMT status (untreated, moderately efficient DMT [MDMT], highly efficient DMT [HDMT])

## Results

- 10,990 pwROMS included
- Estimated probability to experience cPIRA within 1 year after index date ➔ 6.23%
- When the current EDSS is controlled for by stratifying the baseline hazards by roving EDSS ➔ all effects remain
- No significant interaction effects of treatment efficacy and sex by means of a likelihood ratio test when controlling for roving EDSS

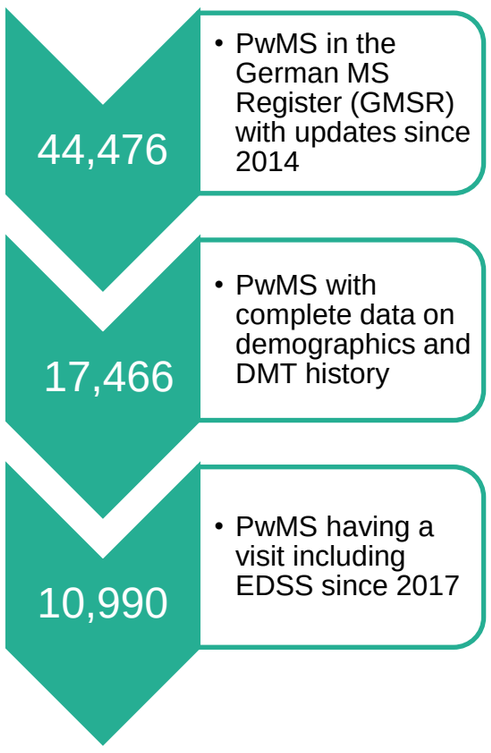


**Figure 1.** Flowchart of study inclusion criteria

| | ALL (N=10,990) |
|---|---|
| **Sex** | |
| Males | 3017 (27.5%) |
| Females | 7973 (72.5%) |
| **Age at MS onset [years], mean (sd)** | 31.8 (10.2) |
| **Disease course** | |
| CIS | 61 (0.56%) |
| RRMS | 9514 (87.2%) |
| SPMS | 1280 (11.7%) |
| **Time to first DMT [years], mean (sd)** | 5.3 (7.2) |
| **Family status** | |
| Living alone | 2377 (22.1%) |
| Living with a partner | 7305 (67.8%) |
| Unknown | 1089 (10.1%) |
| **Highest education** | |
| Higher education | 3453 (37.9%) |
| Lower education | 5653 (62.1%) |

**Table 1.** Characteristics of PwMS cohort

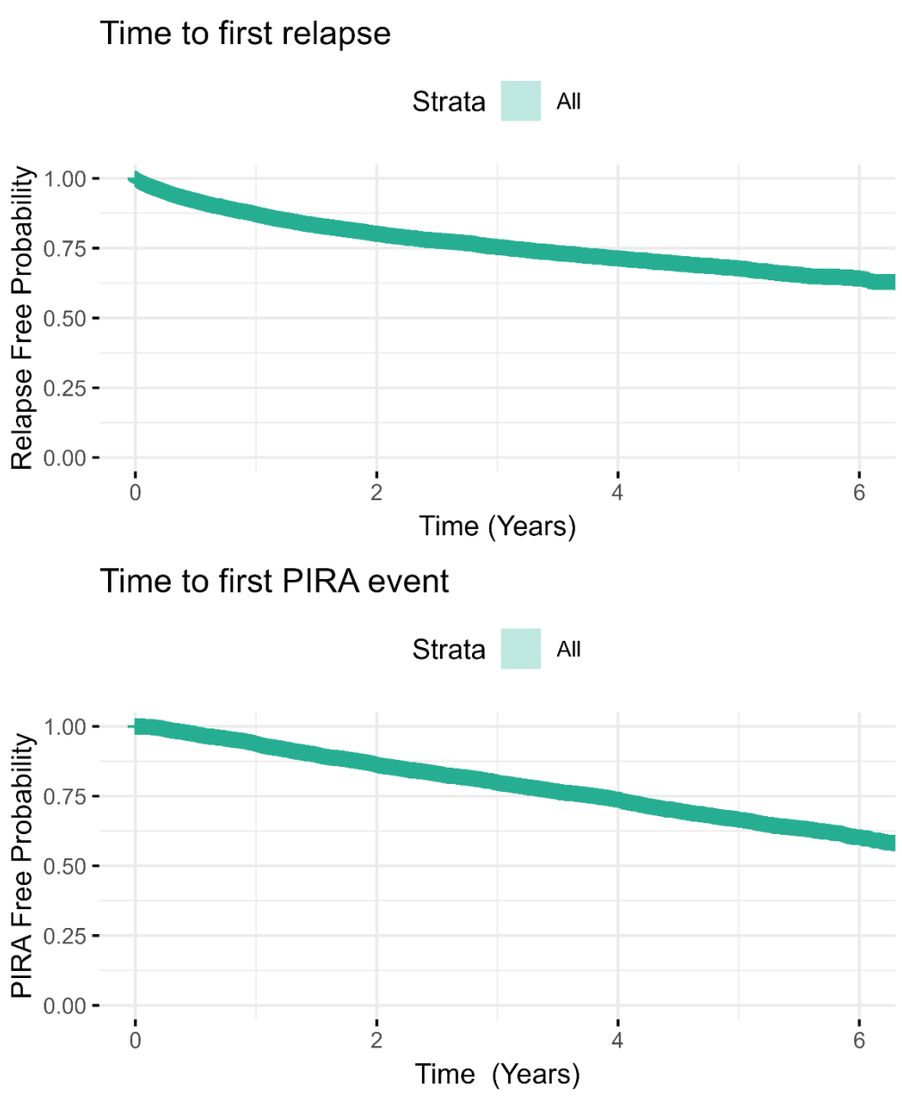


**Figure 2.** Kaplan-Meier curves for the time to first relapse and time to first PIRA in years

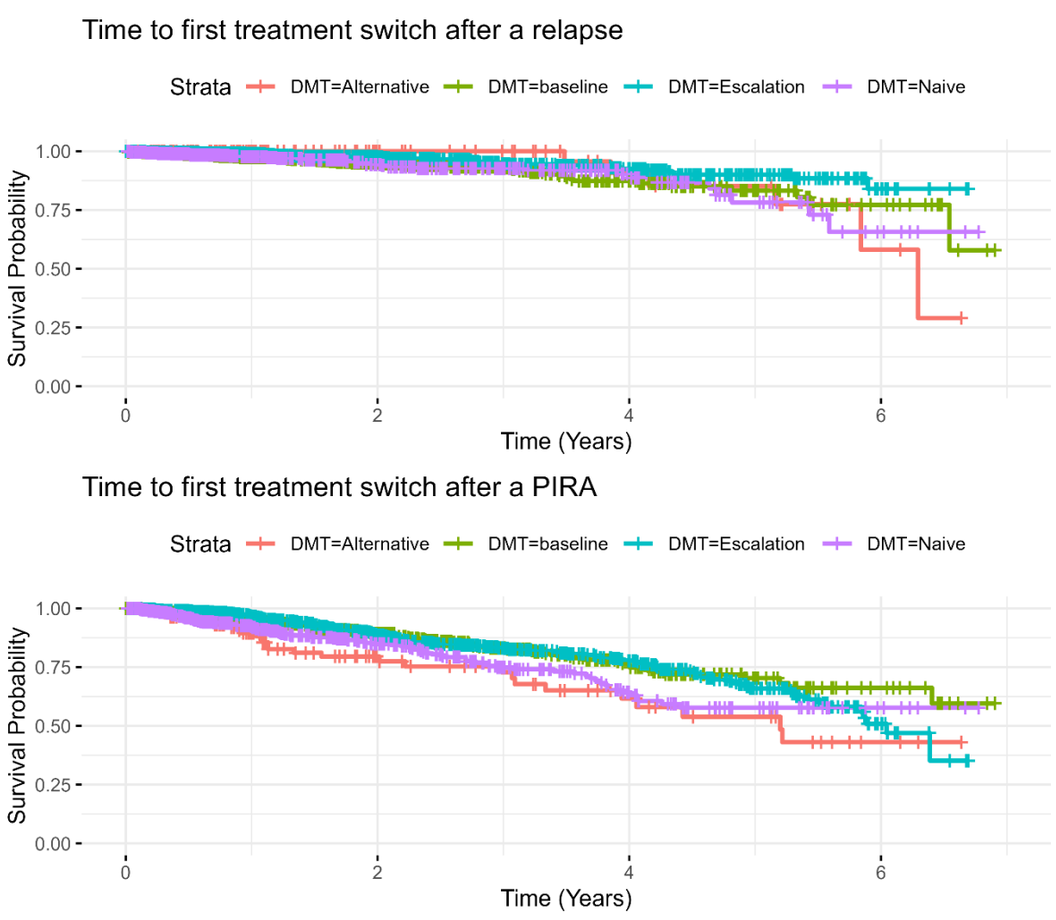


**Figure 3.** Kaplan-Meier curves up until first treatment switch after a relapse and PIRA events

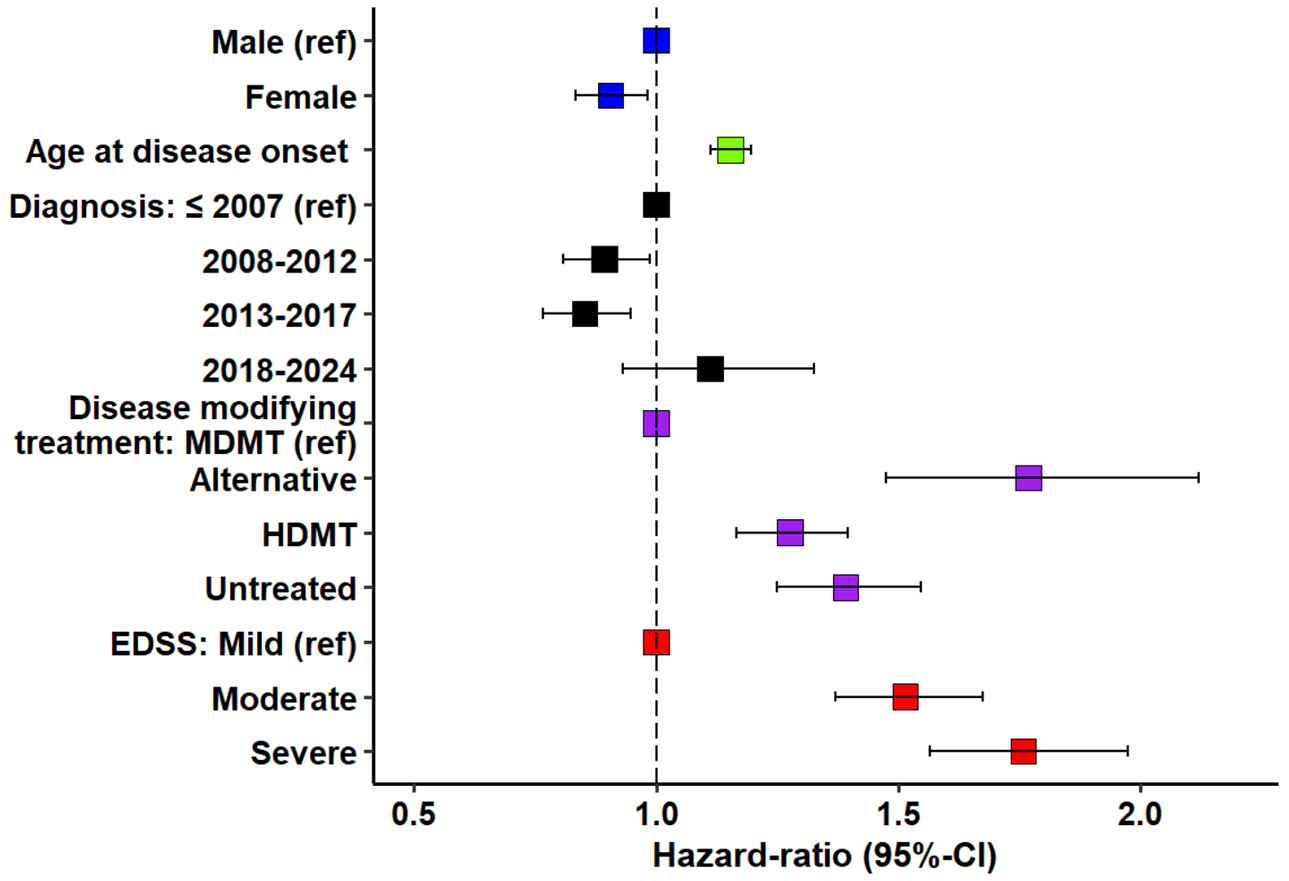


**Figure 4.** Forest plot of multivariable cox regression to determine risk factors of a PIRA event

## Conclusions

- No indication of sex-specific treatment effects if the current disease burden is controlled for
- Patients on MDMT were less prone to experience cPIRA than patients not receiving any treatment or HDMT
- Additional analyses regarding time to relapse and time to cPIRA jointly to quantify indirect subgroup effects resulting from relapse prevalence and direct subgroup effects that govern the susceptibility of PIRA in relapse absence

**Declaration of interest:** Niklas Frahm is an employee of the MSFP. Moreover, he is an employee of Rostock's University Medical Center and received travel funds for research meetings from Novartis. None resulted in a conflict of interest. Melanie Peters, David Ellenberger and Maximilian Bardo had no personal financial interests to disclose other than being employees of the German MS Registry. Alexander Stahmann has no personal financial interests to disclose, other than being the leader of the German MS Registry, which receives (project) funding from a range of public and corporate sponsors, recently including G-BA, The German Retirement Insurance, The German MS Trust, German MS Society, Biogen, Bristol Myers Squibb, Merck, Novartis and Roche. None resulted in a conflict of interest.