# Relapse rates and disability progression in paediatric onset MS patients during the course of the disease

A comparative study with adult onset MS

P104

**D. Ellenberger[1*], P. Flachenecker[2], J. Haas[3], K. Hellwig[4], D. Pöhlau[5], A. Stahmann[1], C. Warnke[6], U.K. Zettl[7], P.S. Rommer[8,7]**

for the German Multiple Sclerosis Register of the German National MS Society

1: MS-Forschungs- und Projektentwicklungs-gGmbH, German MS Register, Hannover, Germany
2: Neurological Rehabilitation Center Quellenhof, Bad Wildbad, Germany
3: Deutsche Multiple Sklerose Gesellschaft, Bundesverband e.V., Hanover, Germany
4: St. Joseph and St. Elisabeth Hospital, Ruhr University, Department of Neurology, Bochum, Germany
5: German Red Cross-Kamillus-Clinic, Department of Neurology, Asbach, Germany
6: University Hospital of Cologne, Department of Neurology, Cologne,Germany,
7: University Medical Center Rostock, Department of Neurology, Rostock, Germany
8: Medical University of Vienna, Department of Neurology, Vienna, Austria

## Background

Paediatric onset MS (PaedOMS) patients form a subgroup within MS characterized by disease onset in childhood, i.e., before 18 years of age. Relapse rates seem to be higher and disease progression – as assessed by the Expanded Disability Status Scale (EDSS) – may be faster in PaedOMS than in patients with adult onset (AOMS).

## Objectives

In a retrospective cohort study we evaluated relapse rates and progression to an EDSS ≥3 in MS patients 5-40 years after disease onset, stratified by PaedOMS and AOMS.

## Methods

The German MS register was used to identify subgroups of patients with a relapsing MS type by age at disease onset, categorized into paediatric (<18 years) or adult onset (18-29y, 30-39y, >40y). Patients with less than 5 years of MS duration at the time of the last recorded follow-up were excluded. The groups were further categorized into disease duration epoques, e.g. 5-10 year interval since disease onset. Patients' most recent annual relapse rates (ARR) including 95% confidence intervals as well as EDSS milestones (≥3) were calculated.

## Results

The analysis included 15,912 patients among them 965 with a paediatric onset. In the years 5 to 10 after onset, ARRs were higher in PaedOMS (<18y: 0.263 [0.187,0.360]) compared to AOMS (18-30y: 0.155 [0.136,0.176], 30-40y: 0.127 [0.108,0.150] and >40y: 0.094 [0.079,0.112]).

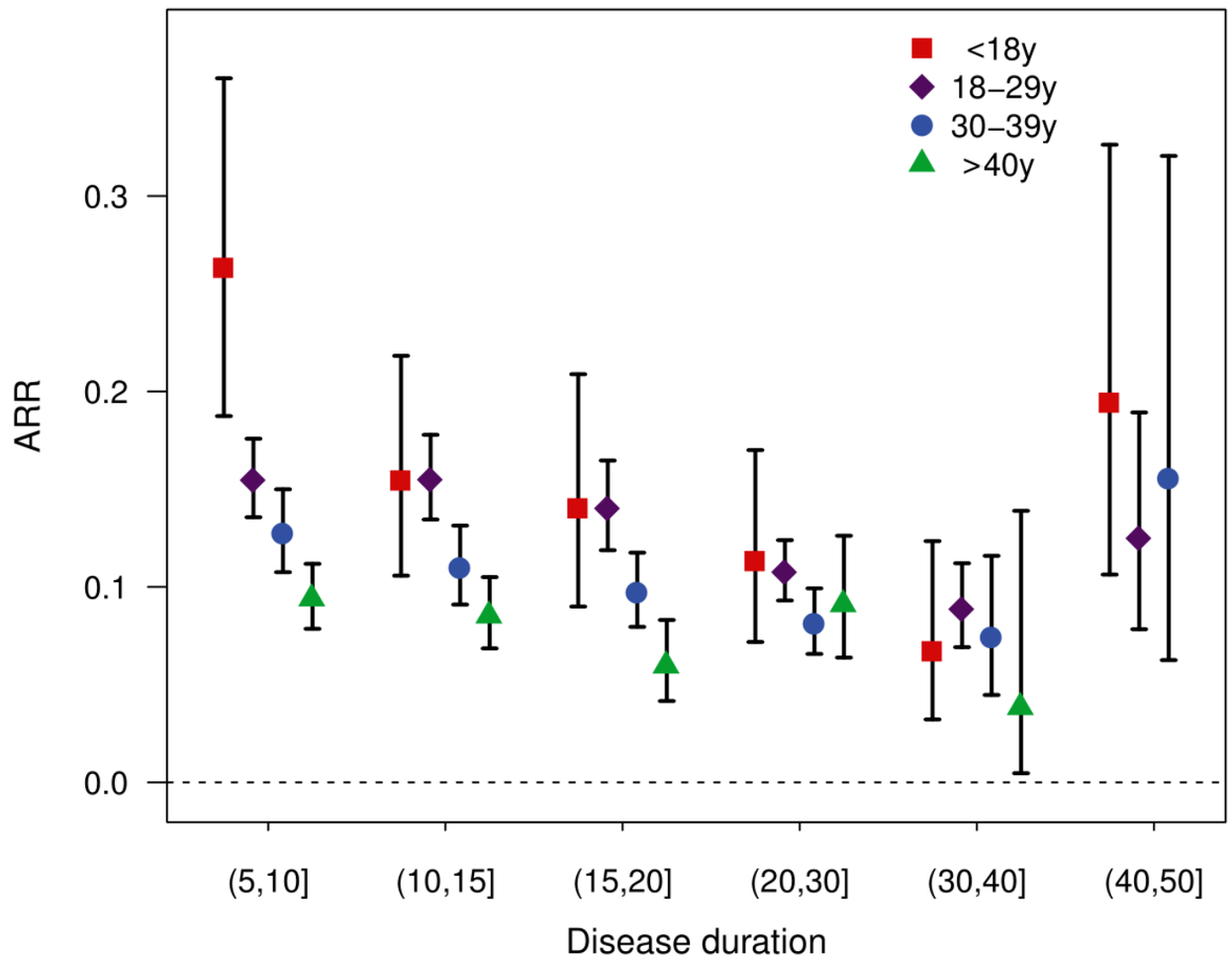


Figure 1: Annualized relapse rates (ARR) over duration of the disease (5-10y, 10-15y, 15-20y, 20-30y and 40-50y after MS onset) grouped by age of onset (pediatric onset: <18y, adult onset: 18-29, 30-39, >40). 95% confidence intervals are given by whisters.

| | Paediatric onset MS (< 18y) N = 965 | Adult onset MS 18-29y N=6711 | Adult onset MS 30-39y N=4784 | Adult onset MS >40y N=3450 |
|---|---|---|---|---|
| Gender [female, %] | 767 (79.5%) | 4936 (73.6%) | 3401 (71.1%) | 244 (70.8%) |
| Age last (y) | 37.3 (±11.8) | 43.4 (±10.3) | 51.4 (±8.2) | 59.1 (±7.3) |
| Disease duration last (y) | 21.6 (±11.9) | 18.9 (±10.0) | 16.6 (±8.0) | 12.8 (±6.1) |
| EDSS last (y) | 3.1 (±2.2) | 3.1 (±2.2) | 3.8 (±2.1) | 3.6 (±2.0) |
| Time to diagnosis: | | | | |
| <2 y | 58.0% | 67.5% | 71.7% | 77.2% |
| 2-5 y | 15.5% | 12.2% | 12.4% | 13.4% |
| >5 y | 26.4% | 20.3% | 15.9% | 9.4% |
| Symptoms at onset: | | | | |
| sensory | 57.5% | 59.2% | 60.1% | 60.4% |
| visus | 49.0% | 46.9% | 42.9% | 38.2% |
| pyramidal | 35.8% | 35.4% | 39.9% | 46.6% |

Table 1: Characteristics of patient groups by age of onset meeting study inclusion. Percentage (%) or mean (±SD) given.

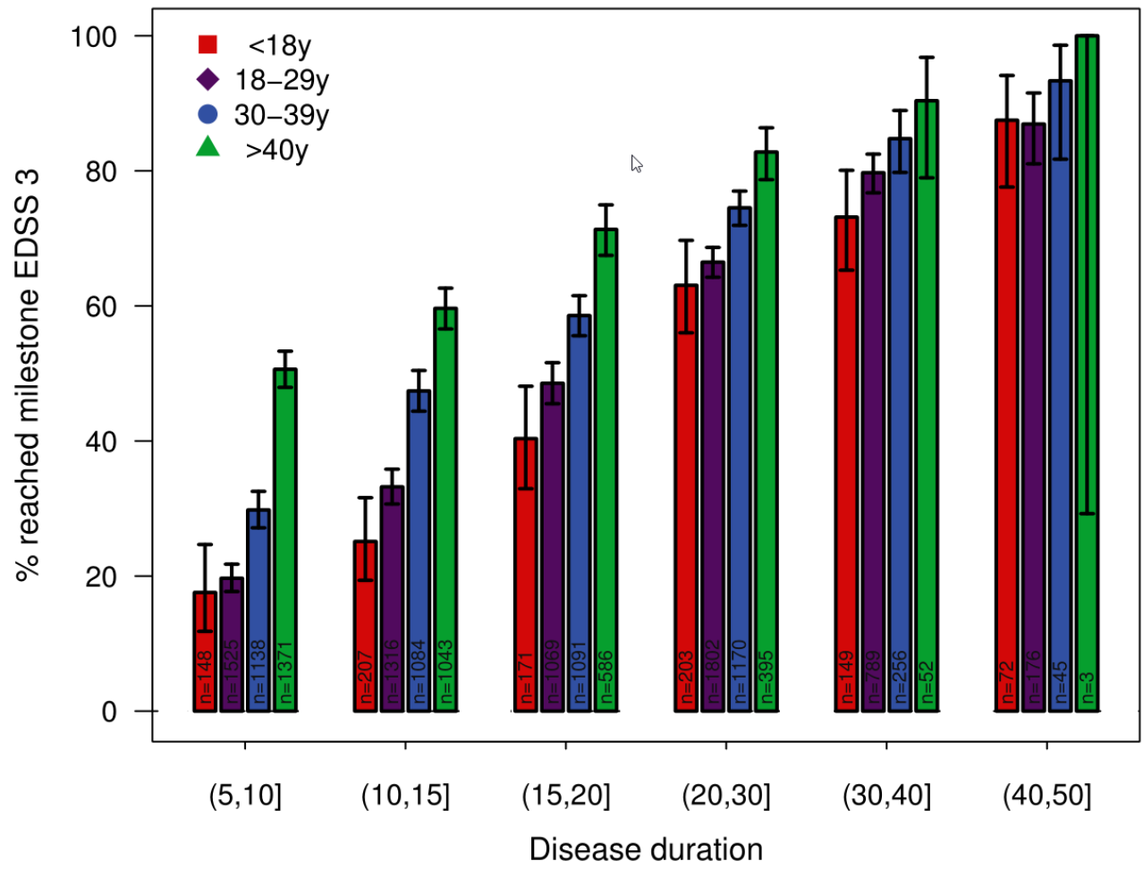


Figure 2: Proportion of patients who have reached EDSS milestone 3. 95% confidence intervals are given by whisters.

## Conclusions

Patients with paediatric onset MS have a higher ARR that is not attributable to the relapses that led to diagnosis. However, persistent disease activity may explain both the early manifestation/diagnosis of MS and the higher relapse rate seen in our follow-up. EDSS in contrast proved to be strongly age-related and not affected by the higher ARRs in PaedOMS. In the group suffering from MS for more than 40 years an increase in 'relapses' was seen, possibly due to a mischaracterization of relapses in the context of age-related neurological deficits/chronic diseases rather than an immunological cause. Further analyses of the effects of DMT at the different stages of the disease may be of interest.

## References

1. Tremlett, H., Zhao, Y., Joseph, J., & Devonshire, V. (2008). Relapses in multiple sclerosis are age-and time-dependent. Journal of Neurology, Neurosurgery & Psychiatry, 79(12), 1368-1374.
2. McKay, K. A., Hillert, J., & Manouchehrinia, A. (2019). Long-term disability progression of pediatric-onset multiple sclerosis. Neurology, 92(24), e2764-e2773.

## Disclosures - Declaration of interest:

DE and JH have nothing to disclose. PF has received speaker's fees and honoraria for advisory boards from Almirall, Bayer, Biogen, Celgene, Genzyme, Novartis, Merck, Roche, and Teva. None resulted in a conflict of interest. KH has received speaking fees, travel support, and research honoraria from Biogen, Teva, Sanofi Genzyme, Novartis, Bayer Healthcare, Merck Serono, and Roche. None resulted in a conflict of interest. DP received research grants from Sandoz, Schering, Biogen; speaker fees from Almirall, Bayer, Biogen, Merck, Novartis, Roche, Sanofi Genzyme and Teva. None resulted in a conflict of interest. AS has no personal pecuniary interests to disclose, other than being the lead of the German MS Registry, which receives (project) funding from a range of public and corporate sponsors, recently including The German Innovation Fund (G-BA), The German Retirement Insurance,The German MS Trust, German MS Society, Biogen, Celgene (BristolMyersSquibb), Merck, Novartis, Roche, and Sanofi. None resulted in a conflict of interest. CW has received institutional support from Novartis, Biogen, Alexion, Janssen, and Roche. None resulted in a conflict of interest. UKZ has received speaking fees, travel support and /or financial support for research activities from Alexion, Almirall, Bayer, Biogen, Janssen, Merck Serono, Novartis, Octapharm, Roche, Sanofi Genzyme, Teva as well as EU, BMBF, BMWi and DFG. None resulted in a conflict of interest. PSR has received speaking fees, honoraria from advisory boards, and/or financial support for research activities from Actelion (Johnson and Johnson), Almirall, Biogen, Merck Serono, Novartis, Roche, Sanofi Genzyme, and Teva. None resulted in a conflict of interest.