Topic: Clinical aspects of MS - 5 Epidemiology

Title: Decline in PPMS Diagnosis? – The German View

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Text: **Background**: In Germany approximately 6-9% of the People with MS suffer from primary progressive MS (PPMS) (1). In 2016 Westerlind et al. (2) reported a significant decrease in diagnosis of PPMS in Sweden. In this abstract we analyse data in the German MS-Register with regard to the findings of Westerlind et al.

Methods: Data from the German MS-Registry was extracted in May 2017. Only patients with a confirmed disease course and who were born between 1946 and 1980 were analysed (N=33,804). Birth and diagnosis cohorts were defined in line with Westerlind et al.. Statistical analyses included Age-Period-Cohort Models based on cubic regression splines. Adjustment for sex, diagnosis delay and the date of entry into the registry was made.

Results: 57.3% of our analysed patients with PPMS were females and mean age was 51.2(±7.73) at time of analyses. Mean age at diagnosis was 42.7(±9.72). Crude estimates of PPMS prevalence ranges from 19% for the late 1940s birth cohort to less than 2% for the late 1970s birth cohort. Age-Period-Cohort modes reveal that this decline seems to be occurring due to a temporal trend (drift). The underlying temporal trend is described best by the birth cohort only ($p<0.001$). The 95%-confidence bounds for trends in the date of diagnosis however are too narrow to replicate the substantial effects reported by Westerlind et al ($p=0.71$). The variables age at diagnosis ($p<0.001$), gender (odds ratio 1.8;$p<0.001$) and diagnosis delay ($p<0.001$) were also found to be significant while the entry date into the register was not ($p=0.91$). Sensitivity analyses by regional strata show coherent results.

Conclusions: Our analyses found strong temporal trends as reported by Westerlind et al.. The causal reasons for these effects are still unclear. Since the Swedish and German data suggest that the date of birth is a strong explanatory variable, epidemiological reasons must be considered as causal factors. Conversely the date of diagnosis which was highly relevant in the Swedish data may also account for

epidemiological factors, but primarily for those related closely in time to the disease onset. Westerlind et al. also suggested clinical reasons like changing criteria to diagnose PPMS patients playing a role. That hypothesis was not supported by the German data. Our findings were adjusted by all relevant covariates, were homogeneous among regional strata, and did not depend on the collection date.

References:

1. Petersen G, Wittmann R, Arndt V, Göpffarth D. Epidemiologie der Multiplen Sklerose in Deutschland. Nervenarzt. 2014;85(8):990–998.

2. Westerlind H, Stawiarz L, Fink K, Hillert J, Manouchehrinia A. A significant decrease in diagnosis of primary progressive multiple sclerosis: A cohort study. Mult Scler J. 2016;1352458516643394.

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