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## Assessing likelihood of secondary progressive multiple sclerosis in Sweden and Denmark: A federated learning analysis unveiling modestly higher odds in Sweden

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### Introduction:

A recent study reported a higher proportion of Secondary Progressive Multiple Sclerosis (SPMS) patients in Sweden than in Denmark. However, the results were limited to descriptive statistics since data could not be pooled. Therefore, the reasons behind this difference remain unclear. One hypothesis is that it might be linked to differences in age and sex distribution between the two Multiple Sclerosis (MS) populations.

### Objectives/Aims:

To investigate if the likelihood of being assigned with SPMS remains higher for patients in Sweden compared to Denmark when adjusting for age and sex distribution using a novel federated learning method.

### Methods:

We used data from MS registries in Sweden and Denmark on patients (i) alive at April 3, 2023 (index date); (ii) clinically assigned relapsing remitting MS (RRMS) or SPMS, and (iii) with complete data on birth date and MS onset date. A total of 30,475 patients were included (12,667 RRMS and 4,122 SPMS in Sweden, 10,681 RRMS and 3,005 SPMS in Denmark). A federated learning method using gradient descent for logistic regression across many iterations was developed in R. This allowed the use of a shared model for both registries without pooling data. The outcome variable was SPMS (TRUE/FALSE), and explanatory variables were age at index date, sex (female = TRUE), and country (Sweden = TRUE).

### Results:

Proportions of SPMS patients were 24.6% in Sweden and 22.0% in Denmark. Mean age (SD) for SPMS was 64.4 (10.6) years in Sweden and 62.3 (10.1) years in Denmark. For RRMS, the mean age (SD) was 47.1 (12.7) years in Sweden and 47.6 (12.1) years in Denmark. Female patients constituted 71.3% (Sweden) and 70.1% (Denmark) of the total population. The odds ratios with 95% confidence intervals for the logistic model were 1.120 [1.117 - 1.124] for age, 0.824 [0.769 - 0.883] for sex (females had lower odds), and 1.067 [1.002 - 1.136] for country (Sweden had higher odds).

### Conclusion:

These findings indicated a significantly higher likelihood of SPMS in Sweden compared to Denmark after adjusting for age and sex distributions. However, the observed difference between the countries was modest, and the age and sex descriptive data for the various subtypes were strikingly similar. Given these similarities, the higher odds ratio may be partly attributable to delays in recognising SPMS in clinical practice. The novel federated learning method utilised in this study demonstrates the potential for cross-national research collaborations without compromising data privacy.

### Disclosures:

Lars Forsberg: nothing to disclose Jan Hillert: JH has received honoraria for serving on advisory boards for Biogen, Bristol-Myers-Squibb, Janssen, Merck KGaA, Novartis, Sandoz and Sanofi-Genzyme and speaker's fees from Biogen, Janssen, Novartis, Merck, Teva, Sandoz and Sanofi-Genzyme. He has served as P.I. for projects sponsored by, or received unrestricted research support from, Biogen, Bristol-Myers-Squibb, Janssen, Merck KGaA, Novartis, Roche, and Sanofi-Genzyme. His MS research is funded by the Swedish Research Council and the Swedish Brain foundation. Elena Mouresan: nothing to disclose. Anna Glaser: nothing to disclose. Melinda Magyari: MM has served on scientific advisory board, as consultant for , received support for congress participation or speaker honoraria from Biogen, Sanofi, Roche, Novartis, Merck, Alexion, Bristol Myers Squibb .The Danish MS Registry received research support from Biogen, Genzyme, Roche, Merck, Novartis. Luigi Pontieri: nothing to disclose.