

Supplementary Online Content

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eAppendix. Details of Study Outcomes and Analyses

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Details of the National Registers in Sweden and How They Were Used in this Study

Register data	Details	Availability of data	Data used in Study
<i>The Swedish MS Registry (SMSreg)</i>	Introduced at the national scale in 2000. All neurology clinics in Sweden contribute clinical information to the platform. Prevalent MS cases were included, such that persons whose MS began prior to 2000 are also registered. The registry is estimated to capture 80% of all MS cases in Sweden.	2000 to 2016	All pediatric-onset MS patients were derived from this registry. Clinical details, including MS onset and diagnosis age, disease course, and therapy use were provided in the SMSreg.
<i>The Total Population Register and the Multigenerational Register</i>	Contains information on birthdate, sex, country of birth, and familial relations for all residents of Sweden.	1968 - 2016	The parents of PoMS and the general population cohort were linked to include parental education as a covariate in analyses of educational achievements of the child.
<i>The Longitudinal Integration Database for Health Insurance and Labor Market studies (LISA)</i>	Includes information on highest educational level and earnings from work (from 1990), as well as net annual sickness absence and disability pension days (from 1994). All measures are recorded annually for all residents of Sweden from age 16.	1990 - 2016	The matched references were drawn from LISA, as all persons needed to have data available in LISA in the final year (2016) to be included.
<i>The National Patient Register</i>	Includes information on all hospitalizations (from 1987) and outpatient visits in specialized healthcare (from 2001) nationwide. Date of visit and primary and secondary diagnoses (up to 30 diagnoses) are recorded according to the International Classification of Diseases (ICD) coding system	1987 - 2016	To ensure that the general population references did not include cases of MS or any demyelinating disorder. We excluded all persons with ≥ 1 of the following ICD codes: ICD-9: 340, 377, 367, 323, 341 or ICD-10: G35, G36, G37, H46.

eAppendix. Details of Study Outcomes and Analyses

Education and Parental Education: Highest educational level achieved is recorded in LISA, annually. We used the level from the most recent year of data availability, 2016, for all persons in the cohort. All included individuals were linked to their parents in LISA, to obtain information on the parent's highest educational level. The highest educational level of the two parents was selected in the year that the child was 18 years old. If the educational data were missing for both parents, we categorized them as elementary level education.

Earnings: All earnings were recorded in Swedish Kroner (SEK) and were converted to US Dollar (USD), using the average exchange rate in January 2010, which was 1 US dollar = 7.25 SEK.

Sickness absence and disability pension: Sickness absence may be granted to all residents of Sweden aged ≥ 16 years with income from work or unemployment benefits, if their work capacity is reduced due to disease or injury. The first 14 days of a sickness absence spell is paid by the employer, so there is no information regarding these days for employed people. Sickness absence spells ≥ 14 days are paid by the Social Insurance Agency. For unemployed persons, sickness absence spells are paid from the second day by the Social Insurance Agency. Moreover, all residents in Sweden aged 19-64 with long-term or permanent work incapacity due to disease or injury can be granted disability pension. Sickness absence and disability pension can be granted for part- or full-time (25%, 50%, 75%, or 100% of ordinary work hours), thus a person can have partial sickness absence and disability pension at the same time.

All outcomes related to income (earnings, sickness absence, and disability) were analysed within 4 distinct age periods. To be included in each analysis, a person must have had at least one year of data available for the corresponding outcome during that period. Moreover, only persons eligible to receive benefits were included in each analysis. For instance, a person receiving full-

time disability pension (360+days per year), is not eligible to receive sickness absence benefits, therefore, they were not included in the analysis of sickness absence.

Statistical analyses were performed using R Version 3.4.3 (Vienna, Austria; R-project. org/) and SAS Statistical Software Package 9.4 (SAS Institute Inc., Cary, NC). The project was approved by the Regional Ethical Review Board of Stockholm.

eTable 2. Educational Achievement in PoMS vs the General Population Reference Cohort

	Crude odds ratio (95%CI)	Adjusted odds ratio (95%CI)*
High school or higher vs. elementary school		
Matched References	1	1
PoMS	0.80 (0.59 – 1.01)	0.80 (0.58 – 1.01)
University vs. elementary or high school		
Matched References	1	1
PoMS	0.81 (0.67 – 0.98)	0.80 (0.66 to 0.97)

* Adjusted for matching factors plus highest parental education level achieved. CI = confidence interval. PoMS = pediatric-onset multiple sclerosis.

eTable 3. Earnings Among the PoMS and Matched Reference Cohort Over the Four Age Periods

A. Earnings among the full cohort				
Age period		Median earnings in USD (IQR)	Beta-coefficient (95% CI)	*Adjusted beta-coefficient (95%CI)
19 – 24	PoMS	7634 (2390 to 15,586)	-1544 (-2493 to -594)	-1618 (-2558 to -678)
	References	10,959 (4894 to 18,152)		
25 – 34	PoMS	16,362.07 (3991 to 29,248)	-4321 (-5975 to -2667)	-4226 (-5861 to -2592)
	References	22,838 (11,766 to 34,038)		
35 – 44	PoMS	16,219 (26 to 37,106)	-8586 (-12,621 to -4551)	-8654 (-12,583 to -4724)
	References	34,903 (22,223 to 47,747)		
45 – 54	PoMS	10,651 (0 to 43,200)	-10,720 (-18,650 to -2790)	-10,683 (-18,187 to -3178)
	References	44,894 (32,740 to 59,832)		
B. Earnings among persons with >0 earnings within each age period				
Age period		Median earnings in USD (IQR)	Beta-coefficient (95% CI)	*Adjusted beta-coefficient (95% CI)
19 – 24	PoMS	9170 (3908 to 16,458)	-1713 (-2690 to -737)	-1768 (-2732 to -803)
	References	11,451 (5761 to 18,589)		
25 – 34	PoMS	18,516 (7935 to 30,773)	-4640 (-6338 to -2943)	-4598 (-6276 to -2920)
	References	24,131 (14,088 to 34,979)		
35 – 44	PoMS	27,385 (10,411 to 43,927)	-10,322 (-14,818 to -5827)	-10,661 (-15,075 to -6248)
	References	35,852 (24,841 to 48,400)		
45 – 54	PoMS	30,386 (15,387 to 48,179)	-14,124 (-23,756 to -4492)	-15,264 (-24,556 to -5973)
	References	45,320 (35,356 to 60,411)		

A: Annual median net earnings among the PoMS and matched reference cohort over the four age periods and the results of the Tobit regression models comparing the two groups (PoMS versus reference cohort).

B: Annual median net earnings among the PoMS and matched references over the four age periods and the results of the linear regression models comparing the two groups, including only persons with non-zero earnings. USD = United States Dollar. *Adjusted models based on matching factors plus highest educational level. PoMS = pediatric-onset multiple sclerosis.

eTable 4. Number and Percentage of Persons in the PoMS Group and the Reference Cohort Who Had Zero Earnings, ≥ 1 Sickness Absence Day, or ≥ 1 Disability Pension Day in Each of the Four Age Periods

Age period		N*	Number (%) with zero earnings	Number (%) with ≥ 1 sickness absence day	Number (%) with ≥ 1 disability pension day
19 – 24	PoMS	413	42 (10.2)	133 (32.6)	78 (18.9)
	References	3696	178 (4.8)	594 (15.2)	121 (3.1)
25 – 34	PoMS	388	41 (10.6)	218 (60.2)	121 (31.2)
	References	3849	220 (5.7)	1236 (34.9)	126 (3.3)
35 – 44	PoMS	193	46 (23.8)	88 (62.4)	101 (52.3)
	References	1829	96 (5.2)	517 (37.4)	91 (4.7)
45 – 54	PoMS	73	29 (39.7)	27 (62.8)	45 (61.6)
	References	730	37 (5.1)	128 (30.6)	45 (6.2)

* The number of persons refers to those in the earnings analysis. Only persons eligible for sickness absence or disability pension days in each age period were included in these proportions. PoMS = pediatric-onset multiple sclerosis.

Stratified analyses by childhood- and adolescent-onset MS

We stratified our analyses by onset age, to separately analyse the association between childhood-onset (<13 years of age) and adolescent-onset MS (≥ 13 & <18 years of age). There were 55 persons with childhood-onset MS and 430 persons with adolescent-onset MS. Results are shown in eTables 5-7.

eTable 5. Educational Level Among PoMS Compared to the Matched Reference Cohort in Childhood-Onset and Adolescent-Onset Cases

	Childhood-onset PoMS	Adolescent-onset PoMS
Outcome	Adjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)
High School or higher (vs elementary)	0.60 (0.27 – 1.34)	0.91 (0.66 – 1.28)
University (vs high school or elementary)	0.69 (0.38 – 1.25)	0.82 (0.66 – 1.00)

Odds ratios represent the odds of the childhood or adolescent cases compared to the references, matched on age, sex, country of birth, and adjusted for parental educational level. PoMS = pediatric-onset multiple sclerosis.

eTable 6. Earnings Among the PoMS Compared to the Matched Reference Cohort in Childhood-Onset and Adolescent-Onset Cases

	Childhood-onset PoMS	Adolescent-onset PoMS
Age period	*Adjusted beta-coefficient (95% CI) of earnings in USD	*Adjusted beta-coefficient (95% CI) of earnings in USD
19 – 24	-2622 (-5194 to -49)	-1486 (-2495 to -477)
25 – 34	-6699 (-11,515 to -1882)	-3975 (-5708 to -2242)
35 – 44	-7872 (-23,112 to 7369)	-8612 (-12,643 to -4581)
45 – 54	2446 (-45,169 to 50,062)	-11,619 (-18,366 to -4870)

*Adjusted for matching factors and highest educational level. PoMS = pediatric-onset multiple sclerosis.

eTable 7. Sickness Absence and Disability Pension Days Among the PoMS Compared to the Matched Reference Cohort in Childhood- and Adolescent-Onset MS

Age Period	Childhood-onset PoMS		Adolescent-onset PoMS	
	*Adjusted rate ratio (95% CI) of annual net sickness absence days	*Adjusted rate ratio (95% CI) of annual net disability pension days	*Adjusted rate ratio (95% CI) of annual net sickness absence days	*Adjusted rate ratio (95% CI) of annual net disability pension days
19 – 24	2.85 (1.01 – 4.35)	0.97 (0.62 – 1.53)	3.26 (2.13 – 5.00)	0.96 (0.76 – 1.21)
25 – 34	3.00 (1.40 – 6.41)	0.99 (0.58 – 1.69)	3.07 (2.34 – 4.05)	0.94 (0.77 – 1.15)
35 – 44	0.72 (0.16 – 3.23)	1.06 (0.60 – 1.86)	1.93 (1.22 – 3.05)	1.46 (1.20 – 1.79)
45 – 54	‡	1.36 (0.90 – 2.04)	1.10 (0.53 – 2.26)	1.44 (1.10 – 1.90)

*Adjusted for matching factors and highest educational level. ‡ Insufficient number of cases for analysis. PoMS = pediatric-onset multiple sclerosis.

Stratified analyses of two eras (1980-1999 & 2000-2014)

We defined two periods of time and stratified the analyses by these eras. The first era included all persons with an MS onset between 1980 and 1999 (n= 239 cases and 2390 references) and the second era included all persons with an MS onset between 2000 and 2014 (246 cases and 2460 references). Because there were no persons from the second era who had data available in the older age periods (ages 35-54), only income results in the first two age periods are described. Results of education level, earnings, and disability benefits are shown in eTables 8-10.

eTable 8. Educational Level Among PoMS Compared to the Matched Reference Cohort in the Two Eras

	Era one (1980-1999)	Era two (2000 – 2014)
Outcome	*Adjusted odds ratio (95% CI)	*Adjusted odds ratio (95% CI)
High School or higher (vs elementary)	0.86 (0.55 – 1.36)	0.87 (0.57 – 1.31)
University (vs high school or elementary)	0.86 (0.65 – 1.13)	0.74 (0.56 – 0.97)

* Adjusted for matching factors plus highest parental education level achieved. CI = confidence interval.

eTable 9. Earnings Among PoMS Compared to the Matched Reference Cohort in the Two Eras

	Era one (1980-1999)	Era two (2000 – 2014)
Age period	*Adjusted beta-coefficient (95% CI) of earnings in USD	*Adjusted beta-coefficient (95% CI) of earnings in USD
19 – 24	-2223 (-3453 to -992)	-1116 (-2489 to 160)
25 – 34	-5114 (-7059 to -3169)	-2994 (-5820 to -168)

* Adjusted for matching factors plus highest education level achieved. CI = confidence interval.

eTable 10. Sickness Absence and Disability Net Days Among the PoMS Compared to the Matched Reference Cohort in Two Eras

	Era one (1980-1999)		Era two (2000 – 2014)	
Age period	Rate ratio (95% CI) of annual net sickness absence days	Rate ratio (95% CI) of annual net disability pension days	Rate ratio (95% CI) of annual net sickness absence days	Rate ratio (95% CI) of annual net disability pension days
19 – 24	4.22 (2.46 – 7.26)	1.13 (0.68 – 1.89)	2.24 (1.29 – 3.88)	0.95 (0.74 – 1.20)
25 – 34	3.41 (2.40 – 4.65)	1.19 (0.92 – 1.57)	2.53 (1.68 – 3.79)	0.84 (0.66 – 1.07)

* Adjusted for matching factors plus highest education level achieved. CI = confidence interval.