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## Trajectories of disposable income before and after being diagnosed with multiple sclerosis: A nationwide register-based cohort study in Sweden with a population-based reference group

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1 **Title:** Trajectories of disposable income before and after being diagnosed with multiple sclerosis: A  
2 nationwide register-based cohort study in Sweden with a population-based reference group

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24

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2  
3 25 **ABSTRACT:**

4 26 **Objectives:** Disposable income (DI) encompasses multiple income sources and is a pertinent indicator  
5  
6 of an individual's economic welfare, particularly in welfare states. We described how DI and three  
7  
8 main components developed among people with multiple sclerosis (MS) in Sweden before and after  
9  
10 diagnoses, and analysed whether their DI trajectory differed to a reference group.

11 29  
12 30 **Design:** Population-based cohort study, with follow-up of annual sums of incomes from seven years  
13  
14 before to four years after diagnosis.

15 31  
16 32 **Setting:** Swedish general population with data linked from two nationwide registers.

17 33 **Participants:** All residents diagnosed with MS in 2009, aged 25-59 (n=785) and a reference group  
18  
19 without MS randomly selected with stratified matching by four sociodemographic variables (n=7847):  
20  
21 sex; age; education level; and country of birth.

22 34  
23 35  
24 36 **Primary and secondary outcome measures:** The primary outcome measure, DI was defined as the  
25  
26 annual sum of total net incomes (earnings and benefits) minus taxes. Three main components of DI  
27  
28 were also separately analysed as annual sums: earnings; sickness absence benefits; and disability  
29  
30 pension benefits.

31 37  
32 38  
33 39  
34 40 **Results:** We found no differences in mean annual DI between the people with and without MS by  
35  
36 independent t-tests at each follow-up year. Significant differences were found for the annual levels of  
37  
38 components of DI from diagnosis year by independent t-tests. A generalised estimating equation  
39  
40 evaluated the differences in the DI trajectory development between people with and without MS with  
41  
42 the result that the trajectory of MS patients developed in parallel to the references'. No association  
43  
44 with MS and economic welfare, as measured by DI, was found.

45 41  
46 42  
47 43  
48 44 **Conclusions:** The key finding that the DI trajectory was unchanged around the years of MS diagnosis  
49  
50 despite differences in components highlights the disease's distinct financial burdens. The Swedish  
51  
52 welfare system was responsive to the decreased earnings through balancing DI by the morbidity-  
53  
54 related benefits around time of MS diagnosis.  
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3 50 **ARTICLE SUMMARY:**

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5 51 **Strengths and limitations**

- 6  
7 52 • The main strengths of this study include both the population-based design and use of nationwide  
8  
9 53 registers with high completeness and validity, which enabled measurement of multiple sources of  
10  
11 54 income including disposable income.
- 12  
13 55 • The longitudinal study design with repeated measures of disposable income enabled the study of  
14  
15 56 the development of DI over 12 years, in addition to the difference in levels.
- 16  
17 57 • While residual confounding cannot be excluded, the reference group was a randomised stratified  
18  
19 58 matched group from the general population at a ratio of 1:10.
- 20  
21 59 • This study does not address the long-term association between economic welfare and MS as the  
22  
23 60 follow-up was only four years in the post diagnosis period.
- 24  
25  
26 61

## 1. INTRODUCTION

The chronic and progressive disease multiple sclerosis (MS) is the leading cause of non-traumatic neurological disability in younger adults.[1-5] People with MS (PwMS) in Sweden have a mean onset age of 32, but experience a time-lag before receiving a formal diagnosis.[6] Previous research has found MS to be associated with progressive work incapacity.[7-13] The indirect costs of PwMS of working age become a dominating cost as the disease progresses from a societal perspective, however, the impact of MS on the individual's economic welfare is relatively unknown.[6 14-16]

The wider socioeconomic context can mediate the economic impact of MS on the individual.[17 18] Sweden has a largely tax-financed universal healthcare system and welfare benefits to compensate a proportion of lost earnings due to morbidity-related work incapacity. The most substantial of these protections for PwMS are the temporary sickness absence (SA) and permanent disability pension (DP) benefits; both designed to compensate previous earnings reduced by morbidity-related absence. A higher proportion of PwMS receive the morbidity-related benefits, SA and DP, in comparison to the general population.[3 19] Studies show trends of PwMS experiencing differences in sources of income within a few years of symptom onset, indicating that morbidity-related benefits are an important source of income for PwMS to consider when investigating their economic situation.[20-23] Thus, earnings alone provides an incomplete picture of an individual's economic welfare; only that of the individual's labour market participation and income generation.[3 20] However, it is unclear what the collective impact of these changes in income sources are on the individual's economic welfare as earnings remain an important income source.[3] Thorough investigation on how MS affects the economic resources available to PwMS in Sweden necessitates the need to assess multiple sources of income in totality, and longitudinally, as effects between health status and economic welfare are not always manifested immediately.[3 19 24-29]

Disposable income (DI) is comprised of multiple income sources, allowing for a comprehensive description of economic welfare.[3 30] DI is the "sum of factor income (income from work and capital) and net income from transfers (government benefits), income taxes, and fees paid to the

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3 88 government".[20] An individual's consumption potential is better reflected with DI, than the  
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5 89 individual income sources.[30] DI is more nuanced than earnings or dichotomous employment status,  
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7 90 and can reflect the complexity of contemporary labour markets, employment patterns and multiple  
8  
9 91 income sources.[31] With 62% of PwMS in Sweden receiving partial or full DP in 2005, compared to  
10  
11 92 14% of a matched reference group, there is a need for a composite income indicator to consider  
12  
13 93 PwMS' financial welfare.[26] Despite an increasing number of studies on PwMS receiving SA and DP  
14  
15 94 benefits or about earnings, little is known about how MS impacts one's DI trajectory development in a  
16  
17 95 welfare state.[3 19 32] Recent longitudinal Danish studies applied DI concepts by combining both  
18  
19 96 earnings and DP benefits, but not income from SA benefits, to suggest similar trajectories, while  
20  
21 97 remaining in employment.[22 33] The full magnitude of the economic consequences for individuals  
22  
23 98 with MS remains unknown in the welfare state.[3 32]

24  
25 99 This study aimed to describe the development of disposable income (DI) and three main components  
26  
27 100 (SA, DP, and earnings), among people diagnosed with MS in the years before and after diagnosis and  
28  
29 101 compare with people without MS, in order to gain knowledge on the economic welfare of people  
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31 102 diagnosed with MS in a welfare state.

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## 35 36 37 38 104 **2. METHODS**

### 39 40 41 105 **2.1 Study design**

42  
43 106 We conducted a cohort study to measure the levels and development of mean annual DI and its main  
44  
45 107 components (SA, DP, and earnings) among PwMS in relation to matched references without MS from  
46  
47 108 the Swedish population. The index year of diagnosis, 2009, was defined as time point  $T_0$ , and the  
48  
49 109 seven years of observation before and four years after diagnosis as  $T_{-7}$  to  $T_{-1}$  and  $T_{+1}$  to  $T_{+4}$ ,  
50  
51 110 respectively.

### 52 53 54 55 111 **2.2 Data sources**

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3 112 Person-level data, linked by the unique personal identity numbers assigned to every resident in  
4  
5 113 Sweden, were obtained from the following two nationwide Swedish registers:

6  
7  
8 114 **1) Statistics Sweden:** *Longitudinal Integration Database for Health Insurance and Labour*  
9  
10 115 *Market Studies* (LISA), to obtain sociodemographic variables and the sums of annual income  
11  
12 116 from the different sources across follow-up.

13  
14  
15 117 **2) National Board of Health and Welfare:** *National Patient Registers*, to identify all people  
16  
17 118 with an MS diagnosis, from inpatient hospital treatment by the International Classification  
18  
19 119 (ICD) codes, ICD-9 (340) and 10 (G35) (1987-2009), and specialised outpatient treatment by  
20  
21 120 ICD-10 (2001-2009).

### 22 23 121 **2.3 Study population**

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25  
26 122 The study population was sourced from the total population registered as living in Sweden on 31  
27  
28 123 December 2009 (from LISA). The cohort of PwMS included all 785 PwMS with an incident MS  
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30 124 diagnosis in 2009 and aged 25-59 years (that is, of working ages in all studied years, 65 years being  
31  
32 125 the customary age for old-age pension in Sweden). All people with their first MS diagnosis according  
33  
34 126 to the national patient registers in 2009 were included, excluding all with a previous MS diagnosis  
35  
36 127 (according to both the in- and specialised out-patient registers).[26]

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39 128 We established a matched reference cohort of people who before 2010, according to the in- and  
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41 129 specialised out-patient registers, were not diagnosed with MS. Among all without MS, who according  
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43 130 to LISA, lived in Sweden 31 December 2009, we randomly selected ten references for each PwMS,  
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45 131 matched on age, gender, educational level, and birth country in 2009 ( $T_0$ ). This produced a stratified  
46  
47 132 matched reference group, which was similar to the MS cohort with relation to the distribution of the  
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49 133 selected sociodemographic variables at the point of diagnosis. The 1:10 ratio of references could not  
50  
51 134 be met for one individual with MS, with only seven possible references in the general Swedish  
52  
53 135 population matching the particular combination of sociodemographic variables. In all, 7847 references  
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55 136 were included at  $T_0$ .



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3 137 The maximum number of years of observation was 12, with 97.3% (n= 764) of the PwMS and 97.8%  
4 138 (n=7671) of the reference group in the study at the end of follow-up (T<sub>+4</sub>). Missing income data in  
5  
6 139 LISA, which could be due to migration before/after the index year or death after T<sub>0</sub>, led to small  
7  
8 140 proportions of individuals across both groups not being followed for the entirety of follow-up.  
9

## 10 11 141 **2.4 Variables**

12  
13  
14 142 Our main outcome measure was annual **disposable income** (DI). We used the DI measure constructed  
15  
16 143 by Statistics Sweden, contained in LISA. This was the sum of incomes after tax, with sources  
17  
18 144 including: income from work and public benefits such as disability pension; sickness absence;  
19  
20 145 disability allowance; unemployment compensation; old-age pension; and social assistance.[34] DI was  
21  
22 146 an individualised measure of household DI, calculated as the sum of household incomes, adjusted for  
23  
24 147 household size and the individual's consumption weight to produce a continuous variable.[34]  
25

26  
27 148 The three main components of DI for working-aged PwMS were also included as alternative economic  
28  
29 149 outcome variables in analyses as the mean annual sum:  
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- 31  
32 150 • **Sickness absence** (SA): All people living in Sweden above the age of 16 are covered by  
33  
34 151 public sick-leave insurance if they receive income from work or unemployment benefits and,  
35  
36 152 if due to disease or injury, have work incapacity. The Social Insurance Agency pays the  
37  
38 153 granted sickness absence benefits, of up to 80% of lost earnings, at 100, 75, 50 or 25% of  
39  
40 154 ordinary working hours. Among employees, the employer provides sick pay the first 13 days  
41  
42 155 of a sick-leave spell after the first uncompensated day;  
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44  
45 156 • **Disability pension** (DP): All residents aged 19-64 can be granted disability pension if disease  
46  
47 157 or injury leads to long-term or permanent work incapacity. Benefits of up to 64% of the lost  
48  
49 158 earnings are paid by the Social Insurance Agency, at 100, 75, 50 or 25% of ordinary working  
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51 159 hours; and  
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54 160 • **Earnings**: Income from work was in the form of gross earnings. This included the sick pay  
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56 161 provided by the employer during the first 14 days of a sick-leave spell.  
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3 162 All monetary values were presented in Swedish Krona (SEK) and adjusted for inflation by the  
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5 163 Statistics Sweden Harmonised Consumer Price Index (HCPI) by the annual average 2016 value.[35]  
6

7  
8 164 The following combination of sociodemographic variables sourced from LISA were included in the  
9  
10 165 analyses as explanatory variables:

- 11  
12 166 • **Age** (continuous, time variant): In addition, age was also computed into a new continuous  
13  
14 167 variable to control for curvilinearity in the statistical analyses by squaring the values for age;  
15  
16  
17 168 • **Gender** (binary);  
18  
19  
20 169 • **Educational level** (categorical, time variant: elementary; high school; college or university;  
21  
22 170 and missing); and  
23  
24  
25 171 • **Birth country** (categorical: Sweden; Other Nordic Countries; Other EU25 Countries; Rest of  
26  
27 172 World; and missing).  
28  
29

30 173 The study cohort had near complete data with less than 0.25% missing values for country of birth, and  
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32 174 0.5% for educational level.  
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## 35 175 **2.5 Ethical approval**

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37  
38 176 The project was approved by the Regional Ethical Review Board of Stockholm, Sweden.  
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40

## 41 177 **2.6 Statistical analyses**

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44 178 Data management and statistical analyses were conducted in SAS v.9.4, with the exception of  
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46 179 generalised estimating equation (GEE) models, which were calculated in SPSS v.24.  
47  
48

49 180 In our data management, we set 337 negative DI values between 2004 and 2013 to zero to prevent  
50  
51 181 distortion of the DI means over time. This was required as Statistics Sweden changed how they coded  
52  
53 182 DI in LISA; earlier years of follow-up had a lower limit of zero but from 2004, there was possibility of  
54  
55 183 negative values. We trimmed extreme outlier DI values at 566,100 SEK, representing the 99<sup>th</sup>  
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3 184 percentile of annual DI across all study years. This made the distribution of DI reasonably normal for  
4  
5 185 statistical analyses. Individuals with missing values in LISA for DI and the secondary outcome  
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7 186 variables, in years other than  $T_0$ , were excluded in descriptive statistics for the respective years, but  
8  
9 187 were included in the GEE model. We capped earnings at the 99<sup>th</sup> percentile to control for extreme  
10  
11 188 outliers, which resulted in a maximum possible annual value of 810,400 SEK.

12  
13 189 Descriptive statistics were performed to describe the distribution of sociodemographic variables and  
14  
15 190 summarise the levels of the different income variables. Categorical data were expressed as frequency  
16  
17 191 distributions with the number and percentage. Continuous data were reported for both the PwMS and  
18  
19 192 the reference group, expressed by the mean, standard deviation and both the number and proportion  
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21 193 with annual sums >0.

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23  
24 194 The means of annual DI of PwMS was calculated for each year,  $T_{-7}$  to  $T_{+4}$ . The differences in mean  
25  
26 195 annual DI of PwMS were tested for statistical significance by dependent *t*-tests between the following  
27  
28 196 three time points:  $T_{-7}$  to  $T_0$ ;  $T_0$  to  $T_{+4}$ ; and  $T_{-7}$  to  $T_{+4}$ . Independent two-tailed *t*-tests with Cochran  
29  
30 197 approximation for the unequal variance were performed for each year of follow-up to test the  
31  
32 198 difference in mean annual DI between PwMS and the references. The mean differences in annual sums  
33  
34 199 of earnings, SA benefits, and DP benefits between PwMS and references were calculated at three time  
35  
36 200 points:  $T_{-7}$ ;  $T_0$ ; and  $T_{+4}$ .

37  
38  
39 201 Lastly, we conducted linear regression analyses, using the generalised estimating equation (GEE)  
40  
41 202 method to gain insight on how MS influenced the DI trajectory development over the study  
42  
43 203 period.[36] The GEE model described the difference in the slopes of the DI trajectories from 2002 to  
44  
45 204 2013 between PwMS and the reference group as the method allowed for the dependent repeated  
46  
47 205 measures of DI by accounting for the clustering of observations at both the individual and group levels  
48  
49 206 that violated the independence assumptions of other methods.[36-38] The dependent variable, DI, was  
50  
51 207 analysed as a continuous measure. The DI distribution was slightly right skewed, but GEE is a robust  
52  
53 208 method.[37] The GEE model was computed with the following specifications: a normal distribution;  
54  
55 209 identity link; and autoregressive within-subject correlation. The within-subject correlation structure  
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210 was selected because of the reasonable assumption that the correlation between an individual's annual  
211 DI values diminished over time. The models were adjusted for gender, age, education level, and  
212 country of birth. An additional age variable was included to account for curvilinearity. All variables  
213 were entered simultaneously with an interaction term of MS and year to evaluate whether PwMS had a  
214 different DI trajectory than the reference population. The periods pre and post diagnosis were assessed  
215 in separate models. The GEE model results were presented as un-standardised Beta regression  
216 coefficients with 95% confidence intervals (CI), which can be interpreted as values in SEK. The  
217 significance level for all analyses was  $\alpha=0.05$ .

218

### 219 3 RESULTS

220 We observed growth of annual DI experienced by both the PwMS and the reference group over the  
221 study period. There were significant differences between PwMS and the reference group in mean  
222 annual sums of SA benefits, DP benefits and earnings along the disease trajectory, but there were no  
223 differences in either the levels or development of mean annual DI between  $T_{-7}$  and  $T_{+4}$ .

224 Table 1 contains a basic description of the study population and shows that the reference group (n=  
225 7847) was representative of the PwMS cohort (n=785) on the distribution of these sociodemographic  
226 variables. The descriptive results revealed that the PwMS diagnosed in 2009 had a mean age of 41  
227 (95% CI: 40.7-42.0). The cohort had a female to male ratio of 2.17. At the end of follow-up,  $T_4$ , there  
228 were 97.3% (n=764) PwMS and 97.8% (n=7671) references with data available in LISA.

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**Table 1:** Sociodemographic characteristics of the study population at year of diagnosis (2009)

	<b>MS<sup>b</sup></b>		<b>References<sup>b</sup></b>	
	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>
	785	(100)	7847	(100)
<b>Sex</b>				
Men	248	(31.6)	2480	(31.6) <sup>a</sup>
Women	537	(68.4)	5367	(68.4) <sup>a</sup>
<b>Age Group</b>				
25-34	213	(27.1)	2130	(27.1) <sup>a</sup>
35-44	279	(35.5)	2790	(35.6) <sup>a</sup>
45-54	208	(26.5)	2077	(26.5) <sup>a</sup>
55-64	85	(10.8)	850	(10.8) <sup>a</sup>
<b>Education (in years)</b>				
≤9 (elementary) <sup>c</sup>	111	(14.1)	1107	(14.1) <sup>a</sup>
10 -12 (high school)	355	(45.2)	3550	(45.2) <sup>a</sup>
>12 (college or university)	319	(40.6)	3190	(40.7) <sup>a</sup>
<b>Country of Birth</b>				
Sweden	677	(86.2)	6770	(86.3) <sup>a</sup>
Nordic countries (except Sweden)	23	(2.9)	230	(2.9) <sup>a</sup>
EU25 (except Nordics)	27	(3.4)	270	(3.4) <sup>a</sup>
Rest of the world <sup>c</sup>	58	(7.4)	577	(7.4) <sup>a</sup>
<sup>a</sup> Reference group matched to MS cohort on these variables.				
<sup>b</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 in nationwide in- and specialised out-patient registers. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before 2010.				
<sup>c</sup> Individuals with missing variables added to lowest category (<0.5% of both study cohorts).				

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3 233 In  $T_0$ , PwMS had a mean annual DI of 177,000 SEK (95% CI: 170,200-183,900) (Figure 1). PwMS  
4  
5 234 experienced a mean increase in annual DI over the 12-year study period of 51,400 SEK (95% CI:  
6  
7 235 43,330-59,510). This increase in mean annual DI was observed in both the periods before (32,360  
8  
9 236 SEK, 95% CI: 26,360-38,360) and after diagnosis (19,390 SEK, 95% CI: 12,760-26,010) by  
10  
11 237 dependent t-tests. While there was a steady increase in mean annual DI throughout the study, the  
12  
13 238 distribution of annual DI of PwMS widened over follow-up.

14  
15 239 To further investigate the mean annual DI of PwMS, comparison was made to the reference group.  
16  
17 240 Figure 2 suggests there were differences in mean annual DI between PwMS and the reference group,  
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19 241 where the reference group consistently had higher annual DI means, starting from four years prior to  
20  
21 242 MS diagnosis. The gap between PwMS and references mean annual DI widened over time. However,  
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23 243 independent t-tests revealed that these differences were statistically non-significant (not presented).

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25  
26 244 Table 2 displays the differences in the mean annual sums of the main components of DI (earnings, SA  
27  
28 245 benefits, and DP benefits) between PwMS and references in  $T_{-7}$ ,  $T_0$ , and  $T_{+4}$ . In every year, both SA  
29  
30 246 and DP had a median of zero; indicating that most individuals in both groups did not receive either  
31  
32 247 benefit (not presented). The proportion of PwMS who received SA or DP increased over time, which  
33  
34 248 resulted in a higher proportion of PwMS than references receiving these morbidity-related benefits.  
35  
36 249 Accordingly, in every year, the mean SA and DP amounts were higher for PwMS than for the  
37  
38 250 reference group. These mean differences were highly significant, apart from SA benefits in 2002 ( $T_{-7}$ ).  
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40 251 From the time of diagnosis  $T_0$ , PwMS had significantly lower earnings than the reference group.

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254**Table 2:** Annual mean components of disposable income (DI) for the cohort of people with MS (N=785) and the cohort of references (N=7847) at T<sub>-7</sub>, T<sub>0</sub> and T<sub>+4</sub><sup>e</sup>

	MS <sup>c</sup>				References <sup>c</sup>				Mean difference (100 SEK <sup>a</sup> )	p-value for difference
	Mean sum (100 SEK <sup>a</sup> )	Std Deviation	n <sup>d</sup>	% <sup>d</sup>	Mean sum (100 SEK <sup>a</sup> )	Std Deviation	n <sup>d</sup>	% <sup>d</sup>		
<b>T<sub>-7</sub></b>			<b>747</b>				<b>7457</b>			
Sickness absence	108	342	147	20	85	273	1289	17	23	0.078
Disability pension	140	513	63	8	84	348	383	5	56	0.004
Earnings <sup>b</sup>	1842	1598	645	86	1939	1566	6653	89	-97	0.1
Disposable income <sup>b</sup>	1491	679	-	-	1501	697	-	-	-10	0.686
<b>T<sub>0</sub></b>			<b>785</b>				<b>7847</b>			
Sickness absence	267	500	347	44	40	202	811	10	227	0.001
Disability pension	136	382	103	13	86	316	629	8	50	0.001
Earnings <sup>b</sup>	2078	1771	651	83	2484	1718	6791	87	-405	0.001
Disposable income <sup>b</sup>	1770	981	-	-	1820	1025	-	-	-50	0.178
<b>T<sub>+4</sub></b>			<b>764</b>				<b>7671</b>			
Sickness absence	292	553	220	29	79	305	963	13	213	0.001
Disability pension	293	553	210	28	79	305	558	7	214	0.001
Earnings <sup>b</sup>	2144	1928	582	76	2793	1895	6719	88	-649	0.001
Disposable income <sup>b</sup>	1994	1100	-	-	2055	1117	-	-	-61	0.1
<sup>a</sup> Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.										
<sup>b</sup> Trimmed at the 99 percentile.										
<sup>c</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 in national in- and specialised out-patient registers. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before 2010.										
<sup>d</sup> Number count or proportion receiving annual sums > 0.										
<sup>e</sup> T <sub>-7</sub> = 2002, T <sub>0</sub> = 2009 and T <sub>+4</sub> = 2013.										

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3 257 Potential differences in the development of the mean annual DI trajectory of PwMS from that of the  
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5 258 matched references were assessed with a GEE model. In Figure 2, there were indications of the slopes  
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7 259 both diverging prior to diagnosis and realigning to develop more in parallel in the years after  
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9 260 diagnosis. All results from the GEE model provided non-significant differences between the  
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11 261 development of the DI trajectories of PwMS and the reference group. Table 3 contains the differences  
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13 262 in DI development after diagnosis in relation to the year of diagnosis and shows that between  $T_0$  and  
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15 263  $T_{+4}$  was on an average 781 SEK (95% CI: -6922-3133) less for PwMS than for the reference group.  
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17 264 Analysis of the pre-diagnosis period is contained in Table 4, where from  $T_{-7}$  to  $T_0$  the development of  
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19 265 mean annual DI for PwMS was on an average 4039 SEK (95% CI:-10,536 -3315) lower than the  
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21 266 reference group.  
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**Table 3:** Disposable Income (DI) trajectory post diagnosis from T<sub>0</sub> (2009) to T<sub>+4</sub> (2013) in the cohort of people with MS (N=785) compared to the cohort of references (N=7847)<sup>a,b</sup>

Year	adjusted regression coefficient <sup>c,d,e</sup>	95% CI <sup>e</sup>
2013	-7.81	-69.22-31.33
2012	16.23	-38.39-27.87
2011	12.00	-41.20-27.14
2010	17.10	-32.26-25.19

<sup>a</sup> Reference groups for analysis: 2009 (T<sub>0</sub>) and reference group.  
<sup>b</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 in national in- and specialised out-patient registers, n=785 in 2009. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before and including 2009, n=7847 in 2009.  
<sup>c</sup> Adjusted for age, gender, education level and country of birth.  
<sup>d</sup> Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.  
<sup>e</sup> 100 SEK.

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**Table 4:** Disposable Income (DI) trajectory prior to diagnosis from T<sub>-7</sub> (2002) to T<sub>0</sub> (2009) in the cohort of people with MS (N=785) compared to the cohort of references (N=7847)<sup>a,b</sup>

Year	adjusted regression coefficient <sup>c,d,e</sup>	95% CI <sup>e</sup>
2009	-40.39	-105.36-33.15
2008	3.04	-61.35-32.85
2007	-7.14	-68.83-31.47
2006	-20.60	-75.88-28.20
2005	-8.63	-60.85-26.64
2004	2.58	-46.80-25.20
2003	-15.15	-48.44-16.98

<sup>a</sup> Reference groups for analysis: 2002 (T<sub>-7</sub>) and reference group.  
<sup>b</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 (T<sub>0</sub>), in national in- and specialised out-patient registers n=785 in 2009. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before 2010, n=7847 in 2009.  
<sup>c</sup> Adjusted for age, gender, education level and country of birth.  
<sup>d</sup> Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.  
<sup>e</sup> 100 SEK.

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## 278 4 DISCUSSION

### 279 4.1 Principal findings

280 We have presented the mean DI development for PwMS from seven years prior to four years after  
281 diagnosis, in comparison to the trajectory of a population-based stratified matched reference group  
282 without MS. This is the first Swedish study to analyse the DI trajectory of PwMS, and builds upon  
283 previous research of the individual components of DI. Our principal finding was that within the first  
284 four years after diagnosis there was little change to PwMS' DI trajectory in comparison to those  
285 without MS. Both groups' trajectories developed in parallel despite significant differences for  
286 individual component sources of income: earnings; SA benefits; and DP benefits. The morbidity-  
287 related benefits balanced the expected gap from reduced earnings to maintain the economic welfare of  
288 PwMS. The result that both DI levels and development are similar can be plausibly interpreted as the  
289 Swedish welfare system is responsive to the economic consequences of work incapacity through the  
290 SA and DP benefits around diagnosis with MS.

### 291 4.2 Interpretation of findings in context of previous research

292 To situate our findings on DI, distinct differences in the levels of mean annual gross income (earnings  
293 and benefit payments, but excluding SA benefits) were found in a Danish study by Hilt Pflieger et al,  
294 where 20-years after diagnosis, PwMS received 70% of the mean annual gross income of matched  
295 references.[22] The difference was attributed to DP benefits becoming the dominating source of  
296 income for PwMS in this longer follow-up, and compensated as a proportion of previous earnings.[22]  
297 Similarly to our results, Hilt Pflieger et al. found that both PwMS and references prior to diagnosis had  
298 an almost equal level of gross income.[22] Notable differences between the Danish and Swedish social  
299 security systems exist, for example, the lengths and entitlements for SA benefits and transition to DP  
300 benefits.[39] However, they are similar enough that it is likely that a longer follow-up period in our  
301 study would have reflected some differences in mean annual DI as found by Hilt Pflieger et al.,  
302 especially as previous research in Sweden, albeit non-specific on diagnosis, suggested that SA benefits  
303 were associated with lower subsequent DI levels.[20 22]

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3 304 In line with previous research, we identified a larger proportion of PwMS receiving income from  
4 305 morbidity-related benefits than references.[3 13 40] Trends from previous findings were reflected in  
5 306 the increased proportions of PwMS receiving DP benefits along the disease trajectory.[19 40] SA  
6 307 benefits are designed to compensate periods of temporary absence from work, and following the  
7 308 progressive chronic characteristics of MS, permanent DP can be expected to increase with time.[3 14  
8 309 19 40] We observed DP surpassing SA benefits four years post-diagnosis. This shift should plausibly  
9 310 reduce DI development because DP is compensated at a lower rate than SA. Such patterns were not  
10 311 found for the reference group; the proportions of references receiving SA benefits were larger than DP  
11 312 for all years.

12 313 Similarly to Wiberg et al., we found that PwMS had lower mean annual earnings than the references  
13 314 from diagnosis, with the mean difference increasing as the disease progressed.[3] This trend of  
14 315 increasing heterogeneity of PwMS' earnings has been postulated to be due to the disparate levels of  
15 316 work incapacity influenced by symptom severity, and variations in workplace and occupation  
16 317 flexibility to adapt.[15 29 41] Pearson et al. suggested ill health may reduce the level of earnings of  
17 318 those who remain economically active due to truncated careers and underemployment.[12] Therefore,  
18 319 further changes can be expected as time from diagnosis advances.[12 40] Both Wiberg et al. and our  
19 320 findings show that despite changes in income sources, earnings remain the dominating income source  
20 321 for PwMS; 76% of the PwMS in our study remained in paid work 4 years after diagnosis.[3] Hilt  
21 322 Pflieger et al., remarked that PwMS maintained similar levels of gross income to the references if  
22 323 remaining in paid work, which supports our finding of similar DI trajectories.[22]

#### 23 324 **4.3 Strengths and limitations**

24 325 A distinctive characteristic of this explorative study that adds to its strength and external validity was  
25 326 the use of nationwide registers. The registers provided the most complete data available and enabled  
26 327 both full inclusion of incident cases and use of DI. Larger study populations have been observed in  
27 328 prevalence-based studies; however, such designs were incompatible with our aim. Our study reflects  
28 329 common methodological characteristics of register-based income studies of PwMS. Formal diagnosis

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3 330 by ICD code was indicative of MS status, and despite the possibility for miscoding. ICD codes remain  
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5 331 more objective than the alternative, onset of symptoms, which suffer inaccuracies from recall bias and  
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7 332 attribution to MS.[40 42] The longitudinal design included both pre- and post-diagnosis periods, to  
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9 333 observe earlier progressive aspects of MS prior to diagnosis, such as relapses and resultant changes in  
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11 334 income sources.[4]

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13 335 Limitations of our study include that short SA spells (<14 days) were missing and the SA analyses  
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15 336 may therefore be underestimated. However, the DI analyses were unaffected, as these days were  
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17 337 included within the composite indicator under earnings because such spells are usually employer  
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19 338 compensated except for the first uncompensated day. Our analyses assumed homogeneity within  
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21 339 PwMS and did not consider the variation by either sociodemographic or disease characteristics. An  
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23 340 additional assumption in our interpretation of economic welfare was that DI was distributed evenly  
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25 341 within households according to need, but the actual distribution of income within households was  
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27 342 unknown.[27 30] Further, some informal support by increased earnings of household members was  
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29 343 also plausible.

#### 32 344 **4.5 Implications for policy and research**

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35 345 MS was not associated with economic welfare in Sweden. This suggests that the morbidity-related  
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37 346 transfer payments buffered the economic consequences of MS as the disease progressed around  
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39 347 diagnosis, compensating for the reduced earnings to ensure unchanged levels and development of the  
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41 348 DI trajectory.[28 43] Our results reflect the combination of a responsive welfare system and the  
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43 349 incremental progression of MS morbidity. Furthermore, our study provides support to the suggestion  
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45 350 that the effect of health status on income is less pronounced than the relationship's reciprocal direction  
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47 351 within welfare state contexts.[44] As the disease progresses, differences in DI trajectories may become  
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49 352 more apparent and reflect the findings of Hilt Pflieger et al.[22] Current focus of MS treatment is on  
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51 353 early intervention to delay disease progression, which should further preserve work capacity.[15 42]  
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53 354 Our results suggest that society is bearing some of the economic burden associated with MS, which  
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55 355 the individual would otherwise experience. The observation that the economic situation does not seem

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3 356 to differ much between the groups implies that that the flexible system of morbidity-related benefits  
4 357 that differentiate morbidity situations and levels of work incapacity is necessary for PwMS to maintain  
5 358 similar levels of economic welfare to the general population along the disease trajectory, as there are  
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7 359 no curative treatment options available.  
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11 360 Future research is required as unanswered questions remain; we did not have the opportunity to  
12 361 capture DI changes that may occur as MS progresses further from diagnosis. Additionally, future  
13 362 studies should be designed to investigate whether DI trajectories of PwMS are patterned by  
14 363 sociodemographic characteristics or disease severity.  
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## 21 22 23 365 **5. CONCLUSIONS**

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26 366 Our results indicate that PwMS as a group have similar DI growth to those without MS in Sweden. We  
27 367 found significant differences between PwMS and the population-based reference group in the  
28 368 proportions receiving and levels of individual income sources along the disease trajectory. However,  
29 369 no differences were found in the levels or development of the composite measure, annual DI, at least  
30 370 for the first four years post-diagnosis. In line with its intentions, the welfare system appears to be  
31 371 responsive to the individuals' economic welfare through the balancing of reduced annual earnings by  
32 372 compensation with the SA and DP benefits.  
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8  
9 377 CM performed data management, and MW, OM, CM and PT were involved in the data analyses. All  
10  
11 378 authors (CM, OM, MW, KA, KK, EF and PT) contributed to interpretation of results, participated in  
12  
13 379 the writing and reviewing of the drafts, and have approved the final version of the manuscript.  
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17 381 **Competing interests statement:** We have read and understood the BMJ policy on declaration of  
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19 382 interests. All authors have completed the ICMJE uniform disclosure  
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21 383 at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare the following interests with respect to the research,  
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32  
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35 390 writing of manuscript was performed without involvement of the funding bodies.  
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40 392 **Data Statement:** No additional data available. The authors of this study are not permitted to make the  
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42 393 micro-level data in this study publically available due to its sensitive nature. According to the Swedish  
43  
44 394 Ethical Review Act, the Personal Data Act, and the Administrative Procedure Act, data can be made  
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46 395 available after legal review for researchers who meet the criteria for access to this type of sensitive and  
47  
48 396 confidential data. For questions about this, please contact Professor Kristina Alexanderson,  
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50 397 responsible for the data set.  
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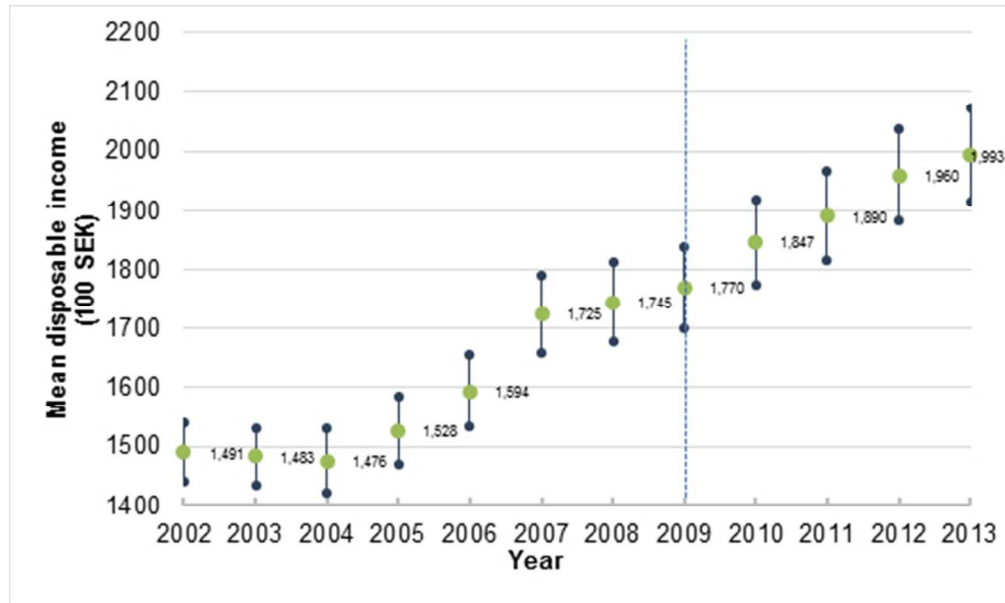


Figure 1: Mean disposable income (DI) in 2002-2013 among people diagnosed with multiple sclerosis (MS) in 2009. Mean annual disposable (DI) sum labelled to the right with the 95% confidence interval illustrated. DI inflated to 2016 values in Swedish Krona (SEK) with Harmonised Consumer Price Index. In 2017, 100 SEK  $\approx$  10.5 Euros. MS: individuals with first registered multiple sclerosis (MS) diagnosis in 2009 in national in- and specialised out-patient registers. Year of diagnosis (2009): dashed vertical line.

139x83mm (96 x 96 DPI)

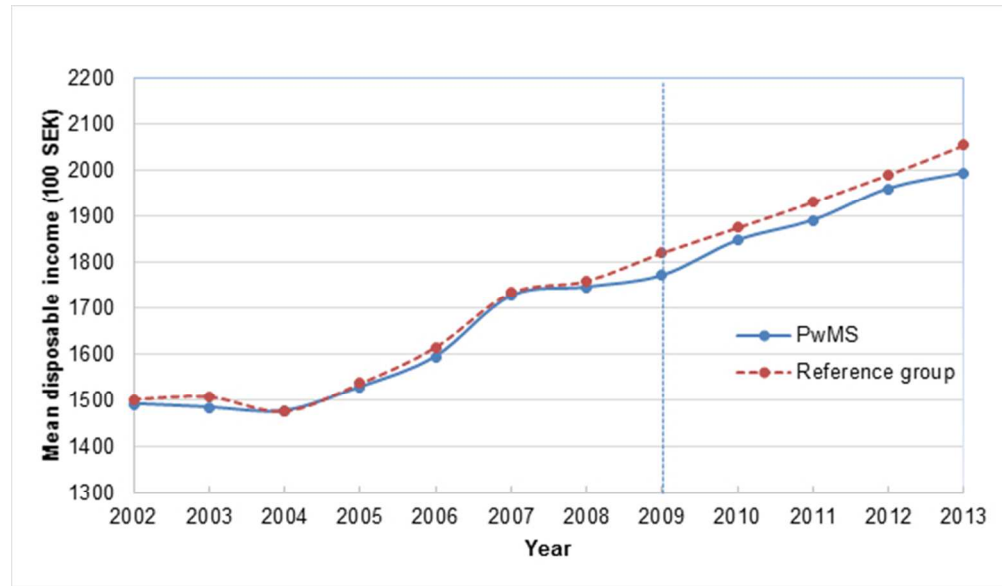


Figure 2: Mean disposable income (DI) in 2002-2013 among people diagnosed with multiple sclerosis (MS) in 2009 (N= 785) compared to references (N=7847). Annual disposable income (DI) inflated to 2016 values in Swedish Krona (SEK) with Harmonised Consumer Price Index. In 2017, 100 SEK  $\approx$  10.5 Euros. MS: individuals with first registered multiple sclerosis (MS) diagnosis in 2009 in national in- and specialised out-patient registers, solid line. References: matched on four variables (1→10) with no MS diagnosis registered in years before 2010. Year of diagnosis (2009): dashed vertical line.

165x96mm (96 x 96 DPI)

**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies***

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(b) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5, 7-9
		(b) Describe any methods used to examine subgroups and interactions	9
		(c) Explain how missing data were addressed	6 & 8
		(d) If applicable, explain how loss to follow-up was addressed	6 & 8
		(e) Describe any sensitivity analyses	N/A
<b>Results</b>			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	6 & 9
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9 & 10
		(b) Indicate number of participants with missing data for each variable of interest	9
		(c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-14
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	15
<b>Limitations</b>			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Trajectories of disposable income among people of working ages diagnosed with multiple sclerosis: A nationwide register-based cohort study in Sweden 7 years before to 4 years after diagnosis with a population-based reference group

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1 **Title:** Trajectories of disposable income among people of working ages diagnosed with multiple  
2 sclerosis: A nationwide register-based cohort study in Sweden 7 years before to 4 years after diagnosis  
3 with a population-based reference group

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24 status, Income

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3 26 **ABSTRACT:**

4 27 **Objectives:** To describe how disposable income (DI) and three main components changed, and  
5  
6 28 analyse whether DI development differed from working-aged people with multiple sclerosis (MS) to a  
7  
8 29 reference group from 7 years before to 4 years after diagnosis in Sweden.

9  
10 30 **Design:** Population-based cohort study, 12 years follow-up (seven years before to four years after  
11  
12 31 diagnosis).

13  
14 32 **Setting:** Swedish working-age population with microdata linked from two nationwide registers.

15  
16 33 **Participants:** Residents diagnosed with MS in 2009 aged 25-59 (n=785), and references without MS  
17  
18 34 (n=7847) randomly selected with stratified matching (sex; age; education; and country of birth).

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20 35 **Primary and secondary outcome measures:** DI was defined as the annual after tax sum of incomes  
21  
22 36 (earnings and benefits), to measure individual economic welfare. Three main components of DI were  
23  
24 37 analysed as annual sums: earnings; sickness absence benefits; and disability pension benefits.

25  
26 38 **Results:** We found no differences in mean annual DI between people with and without MS by  
27  
28 39 independent t-tests (p-values between 0.15-0.96). Differences were found for all studied components  
29  
30 40 of DI from diagnosis year by independent t-tests, for example in the final study year (2013): earnings  
31  
32 41 (-64,867SEK; 95% CI:-79,203--50,528); sickness absence benefits (13,330SEK; 95% CI:10,042-  
33  
34 42 16,500); and disability pension benefits (21,360SEK; 95% CI:17,380-25,350). A generalised  
35  
36 43 estimating equation evaluated DI trajectory development between people with and without MS to find  
37  
38 44 both trajectories developed in parallel, both before (-4039SEK; 95% CI:-10,536-2458), and after (-  
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40 45 781SEK; 95% CI:-6988-5360) diagnosis.

41  
42 46 **Conclusions:** The key finding of parallel DI trajectory development between working-aged MS and  
43  
44 47 references suggests minimal economic impact within the first four years diagnosis. The Swedish  
45  
46 48 welfare system was responsive to the observed reductions in earnings around MS diagnosis through  
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48 49 balancing DI with morbidity-related benefits. Future decreases in economic welfare may be  
49  
50 50 experienced as the disease progresses, although thorough investigation with future studies of modern  
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52 51 cohorts are required.



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1415 **ARTICLE SUMMARY:**16  
17 **Strengths and limitations**

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- 20 • The main strengths of this study include both the population-based design and use of nationwide
- 
- 21 registers with high completeness and validity, which enabled measurement of multiple sources of
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- 22 income of a recently diagnosed MS cohort.
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- 25 • The longitudinal study design with repeated measures enabled the study of the development of
- 
- 26 disposable income for working-aged people with MS pre- and post-diagnosis, in addition to the
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- 27 difference in annual levels of different income sources to a population-based reference group.
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- 30 • While residual confounding cannot be excluded, the reference group was a randomised stratified
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- 31 matched group from the general population at a ratio of 1:10.
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- 34 • An important limitation is that this study does not address the long-term association between
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- 35 economic welfare and MS, as the follow-up was only four years in the post-diagnosis period.
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## 1. INTRODUCTION

Multiple sclerosis (MS) is the leading cause of non-traumatic neurological disability in younger adults.<sup>1-4</sup> People with MS (PwMS) in Sweden have a mean onset age of 33 for first symptoms, but experience a time-lag of 6-7 years before receiving a formal diagnosis with this chronic and progressive disease.<sup>5</sup> Previous research has found MS to be associated with progressive work incapacity, due to physical disability worsening as time from onset increases.<sup>5-11</sup> Therefore, levels of absenteeism, with high proportions working part-time and exiting paid work, and presenteeism, with reduced work productivity, increase over the disease course.<sup>5 9</sup> However, there is uncertainty and variability among PwMS in progression to disability milestones.<sup>12</sup> The indirect costs of working-aged PwMS become a dominating cost as the disease progresses from a societal perspective.<sup>5 13-15</sup> Nonetheless, the impact of MS on the individual's economic welfare remains relatively unknown.

Earnings remain an important income source for PwMS.<sup>3 16</sup> However, earnings alone provide an incomplete picture of an individual's economic welfare; limited to describing the individual's labour market participation and income generation.<sup>3 16</sup> A recent Swedish survey found that 77% of PwMS worked part-time, and participation in paid work rapidly decreased with advancing disease.<sup>5</sup>

The wider socioeconomic context can mediate the economic impact of MS on the individual.<sup>17 18</sup> The Swedish welfare state aims to protect individuals with chronic disease from economic pressure through universal healthcare and social insurance benefits. The most substantial of these benefits for PwMS are the temporary sickness absence (SA) and permanent or long-term disability pension (DP) benefits; both designed to compensate a proportion of previous earnings reduced by morbidity-related absence.

There is a growing body of evidence of the positive associations between MS progression in terms of physical disability and cognitive function with the morbidity-related benefits.<sup>19-22</sup> Furthermore, a substantially higher proportion of PwMS receive SA and DP, in comparison to the general population.<sup>3 21 23</sup> These changes in sources of income are observed to often occur within a few years of symptom onset, indicating that morbidity-related benefits are necessary to consider when investigating

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3 95 the economic situation of working-aged PwMS.<sup>16 24-26</sup> However, the collective impact of these changes  
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5 96 in incomes to the individual's economic welfare is largely unknown. Thorough investigation on how  
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7 97 MS affects the economic resources available to PwMS in Sweden necessitates the need to  
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9 98 longitudinally assess multiple sources of income in totality.<sup>3 21 23 27-30</sup>

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11 99 Disposable income (DI) is comprised of multiple income sources, enabling a comprehensive nuanced  
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13 100 description of economic welfare that better reflects an individual's consumption potential than the  
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15 101 individual income sources.<sup>3 31</sup> DI is the "sum of factor income (income from work and capital) and net  
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17 102 income from transfers (government benefits), minus income taxes, and fees paid to the government".<sup>16</sup>  
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19 103 Despite an increasing number of studies on PwMS receiving SA and DP benefits or about earnings,  
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21 104 little is known about how MS impacts one's DI trajectory development in a welfare state.<sup>3 20 21</sup>  
22  
23 105 Longitudinal Danish studies have applied DI concepts by combining both earnings before tax and DP  
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25 106 benefits, but not income from SA benefits, to suggest PwMS maintain similar trajectories while  
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27 107 remaining in paid work.<sup>25 32</sup> Nevertheless, the full magnitude of the current economic consequences for  
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29 108 individuals with MS remains unknown in the Swedish welfare state where the context for MS has  
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31 109 changed substantially in recent years due to treatments delaying disability progression and policy  
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33 110 environments for SA and DP grants.<sup>33-35</sup>

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36 111 This study aimed to describe the development of disposable income (DI) and three main components  
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38 112 (SA, DP, and earnings), among working-aged people diagnosed with MS in the years immediately  
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40 113 before and after diagnosis and compare with people without MS, in order to gain knowledge on the  
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42 114 economic welfare of working-aged people diagnosed with MS in a welfare state.

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## 116 2. METHODS

### 117 2.1 Study design

118 We conducted a cohort study to measure the levels and development of mean annual DI and its main  
119 components (SA, DP, and earnings) among PwMS aged 25-59 at diagnosis in Sweden, in relation to  
120 matched references without MS. The index year of diagnosis, 2009, is presented as  $Y_0$ , with the seven  
121 years of observation before and four years after diagnosis as  $Y_{-7}$  to  $Y_{-1}$  and  $Y_{+1}$  to  $Y_{+4}$  respectively.

### 122 2.2 Data sources

123 Person-level data were obtained from the following two nationwide Swedish registers:

- 124 1) *Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA)*,  
125 held by Statistics Sweden, was used to obtain sociodemographic variables and the sums of  
126 annual income from the different sources across follow-up.
- 127 2) *National Patient Registers*, held by the National Board of Health and Welfare, enabled  
128 identification of all people with an MS diagnosis. The registers contain healthcare visits for  
129 inpatient treatment by the International Classification (ICD) codes, ICD-9 (340) and 10 (G35)  
130 (1987-2009), and specialised outpatient treatment by ICD-10 (2001-2009).

131 The linkage of data was performed using the unique personal identity numbers assigned to every  
132 resident in Sweden.

### 133 2.3 Study population

134 The study population was sourced from the total population registered as living in Sweden on 31  
135 December 2009 (from LISA). The cohort of PwMS included all 785 PwMS identified with an incident  
136 MS diagnosis in 2009 and on 31 December 2009 aged 25-59 years. The age range allowed for the  
137 cohort to be of working ages in all studied years, with 65 years being the customary age for old-age  
138 pension in Sweden. All people with their first MS diagnosis according to the national patient registers

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3 139 in 2009 were included, excluding all with a previous MS diagnosis (according to the in- and  
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5 140 specialised out-patient registers).<sup>23</sup>  
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7 141 We established a matched reference cohort of people who before 2010, according to the in- and  
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9 142 specialised out-patient registers, were not diagnosed with MS. Among all without MS, who according  
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11 143 to LISA, lived in Sweden 31 December 2009, we randomly selected ten references for each PwMS,  
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13 144 matched on age, gender, educational level, and birth country in 2009 ( $Y_0$ ). This produced a stratified  
14  
15 145 matched reference group with the same distribution of the selected sociodemographic variables in  $Y_0$   
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17 146 to the MS cohort. The 1:10 ratio of references could not be met for one individual with MS, with only  
18  
19 147 seven possible references in the general Swedish population matching the particular combination of  
20  
21 148 sociodemographic variables. In all, 7847 references were included at  $Y_0$ .  
22

23  
24 149 The maximum number of years of observation was 12, with 97.3% ( $n=764$ ) of the PwMS and 97.8%  
25  
26 150 ( $n=7671$ ) of the reference group in the study at the end of follow-up ( $Y_{+4}$ ). Missing income data in  
27  
28 151 LISA, due to migration before/after the index year or death after  $Y_0$ , led to small proportions of  
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30 152 individuals across both groups not being followed for the entirety of follow-up.  
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## 32 33 153 **2.4 Patient and Public Involvement**

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36 154 This was a study based on national register data and there was no patient or public involvement.  
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## 38 39 155 **2.5 Variables**

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42 156 Our main outcome measure was annual **disposable income** (DI). We used the DI measure constructed  
43  
44 157 by Statistics Sweden, contained in LISA. This was the sum of incomes after tax, with sources  
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46 158 including: income from work and public benefits such as disability pension; sickness absence;  
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48 159 disability allowance; unemployment compensation; old-age pension; and social assistance.<sup>36</sup> DI was  
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50 160 an individualised measure of household DI, calculated as the sum of household incomes, adjusted for  
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52 161 household size and the individual's consumption weight to produce a continuous variable.<sup>36</sup>  
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3 162 The three main components of DI for working-aged PwMS were also included as secondary economic  
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5 163 outcomes in analyses as the mean annual sum:

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8 164 • **Sickness absence (SA):** All people living in Sweden above the age of 16 are covered by  
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10 165 public sick-leave insurance if they receive income from work or unemployment benefits and,  
11  
12 166 if due to disease or injury, have work incapacity. The Social Insurance Agency pays the  
13  
14 167 granted sickness absence benefits, of up to 80% of lost earnings, at 100, 75, 50 or 25% of  
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16 168 ordinary working hours. Among employees, the employer provides sick pay the first 13 days  
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18 169 of a sick-leave spell after the first uncompensated day;

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20 170 • **Disability pension (DP):** All residents aged 19-64 can be granted disability pension if disease  
21  
22 171 or injury leads to long-term or permanent work incapacity. Benefits of up to 64% of the lost  
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24 172 earnings are paid by the Social Insurance Agency, at 100, 75, 50 or 25% of ordinary working  
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26 173 hours; and

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29 174 • **Earnings:** Income from work was in the form of gross earnings (before tax deductions). This  
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31 175 included the sick pay provided by the employer during the first 14 days of a sick-leave spell.

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33  
34 176 Earnings were presented in gross form and only two potential public benefit payments were included  
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36 177 in the analyses, therefore, one cannot sum the three components to the presented DI values. All  
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38 178 monetary values were presented in Swedish Krona (SEK) and adjusted for inflation by the Statistics  
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40 179 Sweden Harmonised Consumer Price Index (HCPI) by the annual average 2016 value.<sup>37</sup>

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43 180 The following sociodemographic variables, sourced from LISA, were included in the analyses as  
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45 181 explanatory variables:

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48 182 • **Age** (continuous, time variant): In addition, age was also computed into a new continuous  
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50 183 variable to control for curvilinearity in the statistical analyses by squaring the values for age;

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53 184 • **Gender** (binary);

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3 185     • **Educational level** (categorical, time variant: elementary; high school; college or university;  
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5 186           and missing); and  
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8 187     • **Birth country** (categorical: Sweden; Other Nordic Countries; Other EU25 Countries; Rest of  
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10 188           World; and missing).

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12 189   The study cohort had near complete data with less than 0.25% missing values for country of birth, and  
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14 190   0.5% for educational level.

## 15 16 17 191     **2.6 Ethical approval**

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20 192   The project was approved by the Regional Ethical Review Board of Stockholm, Sweden.

## 21 22 23 193     **2.7 Statistical analyses**

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26 194   Data management and statistical analyses were conducted in SAS v.9.4, with the exception of  
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28 195   generalised estimating equation (GEE) models, which were calculated in SPSS v.24.

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31 196   In our data management, we set 337 negative DI values between 2004 and 2013 to zero to prevent  
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33 197   distortion of the DI means over time. This was required as Statistics Sweden changed how they coded  
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35 198   DI in LISA; earlier years of follow-up had a lower limit of zero, but negative values were possible  
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37 199   from 2004. We trimmed extreme outlier DI values at 566,100 SEK, representing the 99<sup>th</sup> percentile of  
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39 200   annual DI across all study years. This made the distribution of DI reasonably normal for statistical  
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41 201   analyses. Individuals with missing values in LISA for DI and the secondary outcomes, in years other  
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43 202   than  $Y_0$ , were excluded in descriptive statistics for the respective years, but were included in the GEE  
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45 203   model. Earnings were also capped at the 99<sup>th</sup> percentile (810,400 SEK) to control for extreme outliers.

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48 204   Descriptive statistics were performed to describe the distribution of sociodemographic variables and  
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50 205   summarise the levels of the different incomes. Categorical data were expressed as frequency  
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52 206   distributions with the number and percentage. Continuous data were reported for both the PwMS and  
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54 207   the reference group, expressed by the mean, 95% confidence intervals (95% CI), and both the number  
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56 208   and proportion with annual sums  $>0$ .<sup>38</sup>

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3 209 The means of annual DI of PwMS was calculated for each year,  $Y_{-7}$  to  $Y_{+4}$ . The differences in mean  
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5 210 annual DI of PwMS were tested for statistical significance by dependent t-tests between the following  
6  
7 211 three time points:  $Y_{-7}$  to  $Y_0$ ;  $Y_0$  to  $Y_{+4}$ ; and  $Y_{-7}$  to  $Y_{+4}$ . Independent two-tailed t-tests with Satterthwaite  
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9 212 approximation for unequal variance were performed for each year of follow-up to test the difference in  
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11 213 mean annual DI between PwMS and the references. The mean differences in annual sums of earnings,  
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13 214 SA benefits, and DP benefits between PwMS and references were calculated with 95% CI at three  
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15 215 time points:  $Y_{-7}$ ;  $Y_0$ ; and  $Y_{+4}$ .

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17 216 Lastly, we conducted linear regression analyses, using the generalised estimating equation (GEE)  
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19 217 method to analyse how MS influenced the DI trajectory development over the study period.<sup>39</sup> The  
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21 218 GEE model described the difference in the slopes of the DI trajectories from  $Y_{-7}$  to  $Y_{+4}$  between PwMS  
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23 219 and the reference group. The method allowed for the dependent repeated measures of DI by  
24  
25 220 accounting for the clustering of observations at both the individual and group levels that violated  
26  
27 221 independence assumptions.<sup>39-41</sup> The dependent variable, DI, was analysed as a continuous measure.  
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29 222 The DI distribution was slightly right skewed, but GEE is a robust method.<sup>40</sup> The GEE model was  
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31 223 computed with the following specifications: a normal distribution; identity link; and autoregressive  
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33 224 within-subject correlation. The within-subject correlation structure was selected because of the  
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35 225 reasonable assumption that the correlation between an individual's annual DI values diminished over  
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37 226 time. The models were adjusted for gender, age, education level, and country of birth. An additional  
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39 227 age variable was included to account for curvilinearity. All variables were entered simultaneously with  
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41 228 an interaction term of MS and year to evaluate whether PwMS had a different DI trajectory than the  
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43 229 references. The periods pre- and post-diagnosis were assessed in separate models. The GEE model  
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45 230 results were presented as un-standardised Beta regression coefficients with 95% CI, which can be  
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47 231 interpreted as values in SEK. The significance level for all analyses was  $\alpha=0.05$ .

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3 233 **RESULTS**  
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6 234 We observed growth of annual DI experienced by both the PwMS and the reference group over the  
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8 235 study period. There were significant differences between PwMS and the reference group in mean  
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10 236 annual sums of SA benefits, DP benefits, and earnings along the disease trajectory. No differences in  
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12 237 either the levels or development of mean annual DI between  $Y_{.7}$  and  $Y_{+4}$  were observed.  
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14 238 Table 1 contains a basic description of the study population and shows that the reference group (n=  
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16 239 7847) was representative of the PwMS cohort (n=785) on the distribution of these sociodemographic  
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18 240 variables. The MS cohort had a mean age of 41 (95% CI: 40.7-42.0) in  $Y_0$ , and a female to male ratio  
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20 241 of 2.17.  
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**Table 1: Sociodemographic characteristics of the study population at year of diagnosis (2009)**

	MS <sup>b</sup>		References <sup>b</sup>	
	n	(%)	n	(%)
	785	(100)	7847	(100)
<b>Sex</b>				
Women	537	(68.4)	5367	(68.4) <sup>a</sup>
Men	248	(31.6)	2480	(31.6) <sup>a</sup>
<b>Age Group</b>				
25-34	213	(27.1)	2130	(27.1) <sup>a</sup>
35-44	279	(35.5)	2790	(35.6) <sup>a</sup>
45-54	208	(26.5)	2077	(26.5) <sup>a</sup>
55-59	85	(10.8)	850	(10.8) <sup>a</sup>
<b>Education (in years)</b>				
≤9 (elementary) <sup>c</sup>	111	(14.1)	1107	(14.1) <sup>a</sup>
10-12 (high school)	355	(45.2)	3550	(45.2) <sup>a</sup>
>12 (college or university)	319	(40.6)	3190	(40.7) <sup>a</sup>
<b>Country of Birth</b>				
Sweden	677	(86.2)	6770	(86.3) <sup>a</sup>
Nordic countries (except Sweden)	23	(2.9)	230	(2.9) <sup>a</sup>
EU25 (except Nordics)	27	(3.4)	270	(3.4) <sup>a</sup>
Rest of the world <sup>c</sup>	58	(7.4)	577	(7.4) <sup>a</sup>

<sup>a</sup> Reference group matched to MS cohort on these variables.

<sup>b</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 in nationwide in- and specialised out-patient registers. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before 2010.

<sup>c</sup> Individuals with missing variables added to lowest category (<0.5% of both study cohorts).

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3 245 In  $Y_0$ , PwMS had a mean annual DI of 177,040 SEK (95% CI: 170,170-183,920) (Figure 1). PwMS  
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5 246 experienced a mean increase in annual DI over the 12-year study period of 51,400 SEK (95% CI:  
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7 247 43,330-59,510). This increase in mean annual DI was observed in both the periods before (32,360  
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9 248 SEK; 95% CI: 26,360-38,360) and after diagnosis (19,390 SEK; 95% CI: 12,760-26,010) by  
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11 249 dependent t-tests.

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13 250 **(INSERT FIGURE ONE)**

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16 251 To further investigate the mean annual DI of PwMS, comparison was made to the reference group.  
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18 252 **Figure 2** suggests there were differences in mean annual DI between PwMS and the reference group,  
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20 253 where the reference group consistently had higher annual DI means, from four years prior to MS  
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22 254 diagnosis. This suggested gap widened over time. However, independent t-tests suggested that these  
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24 255 differences were statistically non-significant (p-values ranged between 0.15-0.96) (not presented).

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27 256 **(INSERT FIGURE TWO)**

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30 257 Table 2 displays the differences in the mean annual sums of the main components of DI (earnings, SA  
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32 258 benefits, and DP benefits) between PwMS and references in  $Y_{-7}$ ,  $Y_0$ , and  $Y_{+4}$ . In every year, both SA  
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34 259 and DP had a median of zero; indicating that most individuals in both groups did not receive either  
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36 260 benefit (not presented). A trend for PwMS to have greater sums of income from morbidity-related  
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38 261 benefits than the references was present from  $Y_{-7}$  (DP mean difference: 5571 SEK; 95% CI: 1773-  
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40 262 9369). The proportion of PwMS who received each of the benefits, SA and DP, increased over time.  
41  
42 263 However, substantial skewedness of income from these morbidity-related sources remained even  
43  
44 264 among PwMS; in each year less than 30% of PwMS had annual income from each benefit (except SA  
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46 265 in  $Y_0$ , 44%). This skewness was larger among the references (<17 %). Notwithstanding, in every year  
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48 266 studied, the mean SA and DP amounts were higher for PwMS than for the reference group with  
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50 267 differences in all years, apart from SA benefits in 2002 ( $Y_{-7}$ ). PwMS had a peak in SA in  $Y_0$  with the  
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52 268 DP benefits increasing in the post-diagnosis period, whereas the references had stable DP sums and  
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54 269 proportions across follow-up. From the time of diagnosis  $Y_0$ , PwMS had significantly lower earnings  
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56 270 than the reference group, with this trend continuing throughout the post-diagnosis period.

271 **Table 2:** Annual mean sums of income for the cohort of people with MS (N=785) and the cohort of references (N=7847) at Y<sub>-7</sub>, Y<sub>0</sub> and Y<sub>+4</sub><sup>e</sup>

	<u>MS</u> <sup>c</sup>				<u>References</u> <sup>c</sup>				<b>Mean difference</b>	<b>95%CI</b>
	<u>Mean sum</u> <sup>a</sup>	<u>95% CI</u>	<u>n</u> <sup>d</sup>	<u>%</u> <sup>d</sup>	<u>Mean sum</u> <sup>a</sup>	<u>95% CI</u>	<u>n</u> <sup>d</sup>	<u>%</u> <sup>d</sup>		
<b>Y<sub>-7</sub><sup>e</sup></b>			<b>747</b>				<b>7457</b>			
Sickness absence	10,829	(8369-12,293)	147	20	8523	(7804-9243)	1289	17	2306	(-257-4868)
Disability pension	13,966	(10,281-17,654)	63	8	8396	(7480-9312)	383	5	5571	(1773-9369)
Earnings <sup>b</sup>	184,174	(172,691-195,658)	645	86	193,918	(190,357-197,467)	6653	89	-9742	(-21,763-2275)
Disposable income <sup>b f</sup>	149,060	(144,180-153,940)	-	-	150,110	(148,530-151,700)	-	-	-1051	(-6184-4073)
<b>Y<sub>0</sub><sup>e</sup></b>			<b>785</b>				<b>7847</b>			
Sickness absence	26,685	(23,178-30,179)	347	44	3995	(3549-4442)	811	10	22,693	(19,155-26,220)
Disability pension	13,548	(10,866-16,230)	103	13	8571	(7871-9270)	629	8	4977	(2208-7745)
Earnings <sup>b</sup>	207,834	(195,427-220,242)	651	83	248,352	(244,339-252,365)	6791	87	-40,517	(-53,558- -27,476)
Disposable income <sup>b f</sup>	177,040	(170,170-183,920)	-	-	182,010	(179,750-184,280)	-	-	-4971	(-12,210-2266)
<b>Y<sub>+4</sub><sup>e</sup></b>			<b>764</b>				<b>7671</b>			
Sickness absence	19,597	(16,363-22,831)	220	29	6263	(5664-6862)	963	13	13,330	(10,042-16,500)
Disability pension	29,269	(25340-33,199)	210	28	7908	(7226-8590)	558	7	21,360	(17,380-25,350)
Earnings <sup>b</sup>	214,426	(200,723-228,119)	582	76	279,298	(275,050-283,534)	6719	88	-64,867	(-79,203- -50,528)
Disposable income <sup>b f</sup>	199,350	(191,540-207,160)	-	-	205,450	(202,950-207,950)	-	-	-6098	(-14,300-2103)

<sup>a</sup> Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.

<sup>b</sup> Trimmed at the 99 percentile.

<sup>c</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 in national in- and specialised out-patient registers. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before 2010.

<sup>d</sup> Number count or proportion receiving annual sums > 0.

<sup>e</sup> Y-7 = 2002, Y0 = 2009 and Y+4 = 2013.

<sup>f</sup> Disposable income is the sum of incomes from earnings and benefits (in addition to SA and DP presented) after tax (net). Earnings are presented as gross (amount paid before taxable deductions) and therefore are higher than the DI presented.

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4 273 Potential differences in the development of the mean annual DI trajectory of PwMS from that of the  
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6 274 matched references were assessed with a GEE model. In Figure 2, there were indications of the slopes  
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8 275 both diverging prior to diagnosis and realigning to develop more in parallel in the years after  
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10 276 diagnosis. All results from the GEE model provided non-significant differences between the  
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12 277 development of the DI trajectories of PwMS and the reference group. Table 3 contains the differences  
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14 278 in DI development after diagnosis in relation to the year of diagnosis, and shows that between  $Y_0$  and  
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16 279  $Y_{+4}$  was on an average 781 SEK (95% CI: -6922-5360) less for PwMS than for the reference group.  
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18 280 Analysis of the pre-diagnosis period is contained in Table 4, where from  $Y_{-7}$  to  $Y_0$  the development of  
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20 281 mean annual DI for PwMS was on an average 4039 SEK (95% CI:-10,536-2458) lower than the  
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22 282 reference group.  
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**Table 3:** Disposable Income (DI) trajectory post-diagnosis from  $Y_0$  (2009) to  $Y_{+4}$  (2013) in the cohort of people with MS (N=785) compared to the cohort of references (N=7847)<sup>a,b</sup>

Year	adjusted regression coefficient <sup>c,d</sup>	95% CI
$Y_{+4}$ (2013)	-781	-6922-5360
$Y_{+3}$ (2012)	1623	-3839-7085
$Y_{+2}$ (2011)	1200	-4120-6520
$Y_{+1}$ (2010)	1710	-3226-6646

<sup>a</sup> Reference groups for analysis: 2009 ( $Y_0$ ) and reference group.

<sup>b</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 ( $Y_0$ ), in national in- and specialised out-patient registers, n=785 in 2009. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before and including 2009, n=7847 in 2009.

<sup>c</sup> Adjusted for age, gender, education level and country of birth.

<sup>d</sup> Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.

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**Table 4:** Disposable Income (DI) trajectory pre-diagnosis from  $Y_{-7}$  (2002) to  $Y_0$  (2009) in the cohort of people with MS (N=785) compared to the cohort of references (N=7847)<sup>a,b</sup>

Year	adjusted regression coefficient <sup>c,d</sup>	95% CI
$Y_0$ (2009)	-4039	-10,536-2458
$Y_{-1}$ (2008)	304	-6135-6742
$Y_{-2}$ (2007)	-715	-6883-5454
$Y_{-3}$ (2006)	-2060	-7588-3468
$Y_{-4}$ (2005)	-863	-6085-4358
$Y_{-5}$ (2004)	258	-4681-5197
$Y_{-6}$ (2003)	-1515	-4844-1813

<sup>a</sup> Reference groups for analysis: 2002 ( $Y_{-7}$ ) and reference group.

<sup>b</sup> MS: Multiple sclerosis (MS) diagnosis first registered in 2009 ( $Y_0$ ), in national in- and specialised out-patient registers n=785 in 2009. References: matched on variable distribution (1→10) with no registered MS diagnosis in years before 2010, n=7847 in 2009.

<sup>c</sup> Adjusted for age, gender, education level and country of birth.

<sup>d</sup> Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.

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## 293 4. DISCUSSION

### 294 4.1 Principal findings

295 We have presented the mean DI development for working-aged PwMS from seven years before to four  
296 years after diagnosis, in comparison to a population-based stratified matched reference group without  
297 MS. Our principal finding was that within the first four years after diagnosis there was little change to  
298 PwMS' DI trajectory in comparison to those without MS. Both groups experienced parallel trajectory  
299 development despite substantial differences in the individual component sources of income: earnings;  
300 SA benefits; and DP benefits. Changes in morbidity-related benefits balanced the expected gap from  
301 reduced earnings to maintain the economic welfare of PwMS over follow-up. The result that both DI  
302 levels and development are similar can be interpreted as responsiveness of the Swedish welfare system  
303 to the potential economic consequences of work incapacity through benefit payments in the first years  
304 after MS diagnosis.

### 305 4.2 Interpretation of findings

306 Our interpretations are contextualized within the short-term, with observation pertaining to the years  
307 early in the disease course. This is of importance in the context of a heterogeneous and progressive  
308 disease, where baseline disability and age at onset are predictive of progression to milestones of  
309 irreversible physical disability.<sup>35 42</sup>

310 To situate our findings of DI, a Danish study found differences in the levels of mean annual gross  
311 income (pre-tax sums of earnings and benefit payments, but excluding SA benefits) only after 20-  
312 years post-diagnosis, where PwMS received 70% of the mean annual gross income of matched  
313 references.<sup>25</sup> The difference was attributed to DP benefits (compensated as a proportion of previous  
314 earnings) becoming the largest source of income for PwMS by the end of this longer follow-up which  
315 allowed for increasing severity of disability and consequent morbidity-related absence from work.<sup>25</sup>  
316 Notable differences exist between the Danish and Swedish social security systems and labour  
317 markets.<sup>43</sup> However, is likely that PwMS in Sweden would also experience reduced DI after a

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3 318 substantially longer follow-up allowing for further disease progression, as long-term DP benefits  
4 319 compensate lost earnings to a lower proportion than short-term SA benefits.<sup>10 25</sup> Earnings remained the  
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6 320 main income source for our MS cohort, where 76% cohort still participated in paid work to some  
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8 321 degree at the end of follow-up, reflecting findings of Wiberg et al. that notwithstanding changes in  
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10 322 sources of income around diagnosis, earnings remain the dominant source.<sup>3</sup> Furthermore, Hilt Pflieger  
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12 323 et al. concluded that PwMS maintained similar levels of gross income to the references while  
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14 324 remaining in paid work.<sup>25</sup> The combination of which supports our findings of similar DI trajectories  
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16 325 between PwMS and the references in the short-term.

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19 326 Despite the importance of earnings for maintaining economic welfare of working-aged PwMS,  
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21 327 reductions in comparison to references were observed to begin early in the disease course. Similarly to  
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23 328 Wiberg et al., we found that PwMS had lower mean annual earnings than the references from  
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25 329 diagnosis, with the mean difference increasing with time from diagnosis.<sup>3</sup> This trend of early and  
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27 330 increasing heterogeneity of PwMS' earnings has been postulated to be due to the disparate levels of  
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29 331 work incapacity, influenced by severity of physical disability and cognitive function independently,  
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31 332 and variations in flexibility of occupations and workplaces to adapt.<sup>14 20 30 44-46</sup> Furthermore, the level  
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33 333 of earnings may be reduced of those who remain economically active due to truncated careers and  
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35 334 underemployment.<sup>9</sup> The accumulation of irreversible physical disability of MS is highly variable and  
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37 335 related to both age of clinical onset and current age.<sup>42</sup> As the disease progresses, future unbalanced  
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39 336 changes in the component sources of DI may therefore occur through further reduced earnings due to  
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41 337 increasing levels of work incapacity.<sup>5 9 25 47</sup>

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44 338 In line with previous research, we identified a larger proportion of PwMS receiving income from  
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46 339 morbidity-related benefits than references, and PwMS transitioning from SA to DP benefits.<sup>3 10 47</sup>  
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48 340 These patterns were not found for the reference group; the proportions of references receiving SA  
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50 341 benefits were larger than DP for all years. Nevertheless, most PwMS were observed to not be on either  
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52 342 benefit within our study period, further suggesting that early stages of MS morbidity were observed.  
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54 343 These morbidity-related benefits have an increasing role in consideration of the progressive nature of  
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56 344 MS.<sup>10 20</sup> SA benefits are designed to compensate periods of temporary absence from work, and



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3 345 following the progressive chronic characteristics of MS, permanent DP can be expected to increase  
4 346 with time.<sup>3 13 21 47</sup> Consistent with the trends we observed, the literature suggests that while SA is  
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6 347 highest among PwMS around diagnosis years, DP grants continue to increase with time.<sup>10 47</sup> We  
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8 348 observed DP surpassing SA benefits post-diagnosis. This increase of DP benefits can accordingly be  
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10 349 expected to continue with time.<sup>10 22 47</sup> Such a continuation would plausibly reduce future DI  
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12 350 development due to the lower reimbursement by DP compared to SA benefits. Furthermore, previous  
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14 351 research in Sweden, non-specific on diagnosis, suggested an association between SA benefits and  
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16 352 lower subsequent DI levels.<sup>16</sup>

### 19 353 **4.3 Strengths and limitations**

22 354 A distinctive characteristic of this explorative study that adds to its strength and external validity was  
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24 355 the use of nationwide registers. The registers provided the most complete data available and enabled  
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26 356 both full inclusion of incident cases, and use of DI which could capture the complexity of incomes  
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28 357 available to PwMS in Sweden including part-time SA and DP grants alongside earnings. Such  
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30 358 complex combinations are important to acknowledge, especially with the early focus of our  
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32 359 observation period.<sup>10</sup> Our study reflects common methodological characteristics of register-based  
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34 360 income studies of PwMS. MS status was ascertained by formal diagnosis by ICD codes. Despite the  
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36 361 possibility for miscoding, this method was more objective than the alternative, onset of symptoms,  
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38 362 which suffer inaccuracies from recall bias and attribution to MS.<sup>47 48</sup> The longitudinal design included  
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40 363 both pre- and post-diagnosis periods, to observe earlier progressive aspects of MS prior to diagnosis,  
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42 364 such as relapses and resultant changes in income sources.<sup>4</sup>

45 365 An important limitation of our analyses and interpretations of economic welfare is the short-term  
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47 366 perspective. Data was available up to 31 December 2013. The diagnosis year 2009 was selected to  
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49 367 balance considerations of follow-up length (both before and after diagnosis), and to have a cohort  
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51 368 reflecting current treatments and policy environments, especially regarding stricter requirements for  
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53 369 SA and DP grants.<sup>33 34</sup> Further, short SA spells (<14 days) were missing and the SA analyses may  
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55 370 therefore be underestimated. However, the DI analyses were unaffected, as short spells were included

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3 371 within the composite indicator under earnings, because such spells are usually employer compensated  
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5 372 except for the first uncompensated day. Our analyses assumed homogeneity within PwMS and did not  
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7 373 consider the variation within the cohort by either sociodemographic or disease characteristics. We did  
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9 374 not differentiate between the different grades of SA or DP benefits which are a unique feature of the  
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11 375 Swedish social insurance system. The cohort being early in the disease course and with high  
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13 376 proportions still engaged in paid work, such benefits were likely to be part-time for many in the cohort  
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15 377 <sup>20 22 30</sup>. An additional assumption in our interpretation of economic welfare was that DI was distributed  
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17 378 evenly within households according to need, but the actual distribution was unknown.<sup>28 31</sup> Further,  
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19 379 informal support by increased earnings of household members was also plausible.

#### 20 21 380 **4.5 Implications for policy and research**

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24 381 Our results reflect the combination of a responsive welfare system and the incremental progression of  
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26 382 MS morbidity. The finding of unchanged levels and development of economic welfare, as measured  
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28 383 by DI, in the presence of MS suggests that the morbidity-related transfer payments buffered the  
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30 384 economic consequences of MS of reduced earnings in the years directly after diagnosis.<sup>29</sup> Our results  
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32 385 suggest that society is bearing much of the economic burden associated with MS, which the individual  
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34 386 would otherwise experience. The observation that the economic situation does not seem to differ much  
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36 387 between the groups implies that that the flexible system of morbidity-related benefits that differentiate  
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38 388 morbidity situations and levels of work incapacity in allowing part-time grants is necessary for PwMS  
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40 389 to maintain similar levels of economic welfare to the general population early in the disease trajectory.

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43 390 Moreover, current focus of MS treatment is on early intervention to delay disease progression, which  
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45 391 should further preserve work capacity for longer periods post-diagnosis.<sup>14 22 35 48</sup> These delaying effects  
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47 392 of early initiated treatments have been found to extend to socioeconomic outcomes and reduce the risk  
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49 393 of full-time DP, which in light of the lower compensation for DP benefits, could provide further  
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51 394 protections of economic welfare.<sup>22</sup>

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54 395 Future research is required; we did not have the opportunity to capture long-term DI changes that may  
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56 396 occur with further disease progression and increasing work incapacity. Lastly, we did not consider

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3 397 PwMS older than 65, who may experience different DI development to our study cohort as a  
4 398 consequence of different income sources and benefit entitlements. This would be of particular interest  
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6 399 in the Swedish context where the prevalent MS population is comparatively older than in other  
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8 400 European countries.<sup>5</sup> Our interpretations for working-aged persons with MS focused on the role of DP  
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10 401 benefits, which are not available for older adults.  
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## 13 402 **5. CONCLUSIONS**

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16 403 Our results indicate that working-aged PwMS as a group have similar DI growth to those without MS  
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18 404 in Sweden around time of diagnosis, and suggests that the potential economic impact of MS for the  
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20 405 individual may arise later in the disease course. We found significant differences between PwMS and  
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22 406 the population-based reference group in the individual income sources over the 12 year follow-up  
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24 407 within both the pre- and post-diagnosis periods. However, no differences were found in the levels or  
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26 408 development of the composite measure, annual DI, at least within the first four years post-diagnosis. In  
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28 409 line with its intentions, the welfare system appears to be responsive to the individuals' economic  
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30 410 welfare early in the disease course through balancing PwMS' DI, reflected in the reduced annual  
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32 411 earnings balanced by increased SA and DP benefits.  
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3 413 **Figure Legends**

4 414 Figure 1: Mean disposable income (DI)  $Y_{-7}$  to  $Y_{+4}$  among people diagnosed with multiple sclerosis  
5 415 (MS) in  $Y_0$

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7 416 *Notes:* Mean annual DI with 95% confidence intervals illustrated. DI sums are inflated to 2016 values  
8 417 in Swedish Krona (SEK) with the Harmonised Consumer Price Index. In 2017, 100 SEK  $\approx$ 10.5 Euros.  
9 418 MS: Individuals with first registered MS diagnosis in 2009 ( $Y_0$ ) in national in- and specialised out-  
10 419 patient registers.

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17 421 Figure 2 Mean disposable income (DI)  $Y_{-7}$  to  $Y_{+4}$  among people diagnosed with multiple sclerosis  
18 422 (MS) in  $Y_0$  (N=785) compared to references (N=7847)

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20 423 *Notes:* Mean annual DI inflated to 2016 values in Swedish Krona (SEK) with Harmonised Consumer  
21 424 Price Index In 2017, 100 SEK  $\approx$ 10.5 Euros. Year of diagnosis (2009= $Y_0$ ). MS (solid blue line):  
22 425 Individuals with first registered MS diagnosis in 2009 ( $Y_0$ ) in national in- and specialised out-patient  
23 426 registers. References (dashed red line: matched on four variables (1 $\rightarrow$ 10) with no MS diagnosis  
24 427 registered in years before 2010 in the national patient register.

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8  
9 432 MW performed data management, and CM, OM, MW and PT were involved in the data analyses. All  
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11 433 authors (CM, OM, MW, KA, KK, EF and PT) contributed to interpretation of results, participated in  
12  
13 434 the writing and reviewing of the drafts, and have approved the final version of the manuscript.  
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27 441 KK had no competing interests to declare.  
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35 445 writing of manuscript was performed without involvement of the funding bodies, however, Biogen  
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37 446 was invited to comment on the manuscript.  
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43 448 **Data Statement:** No additional data available. The authors of this study are not permitted to make the  
44  
45 449 micro-level data in this study publically available due to its sensitive nature. According to the Swedish  
46  
47 450 Ethical Review Act, the Personal Data Act, and the Administrative Procedure Act, data can be made  
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49 451 available after legal review for researchers who meet the criteria for access to this type of sensitive and  
50  
51 452 confidential data. For questions about this, please contact Professor Kristina Alexanderson,  
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53 453 responsible for the data set.  
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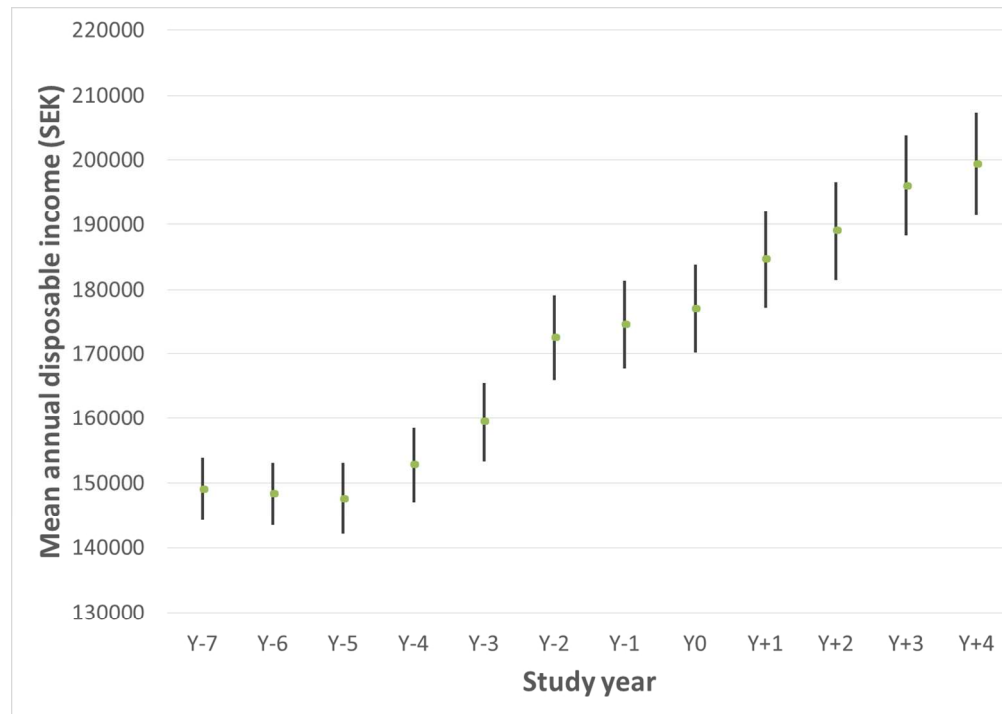


Figure 1: Mean disposable income (DI) Y-7 to Y+4 among people diagnosed with multiple sclerosis (MS) in Y0. Notes: Mean annual DI with 95% confidence intervals illustrated. DI sums are inflated to 2016 values in Swedish Krona (SEK) with the Harmonised Consumer Price Index. In 2017, 100 SEK  $\approx$  10.5 Euros. MS: Individuals with first registered MS diagnosis in 2009 (Y0) in national in- and specialised out-patient registers.

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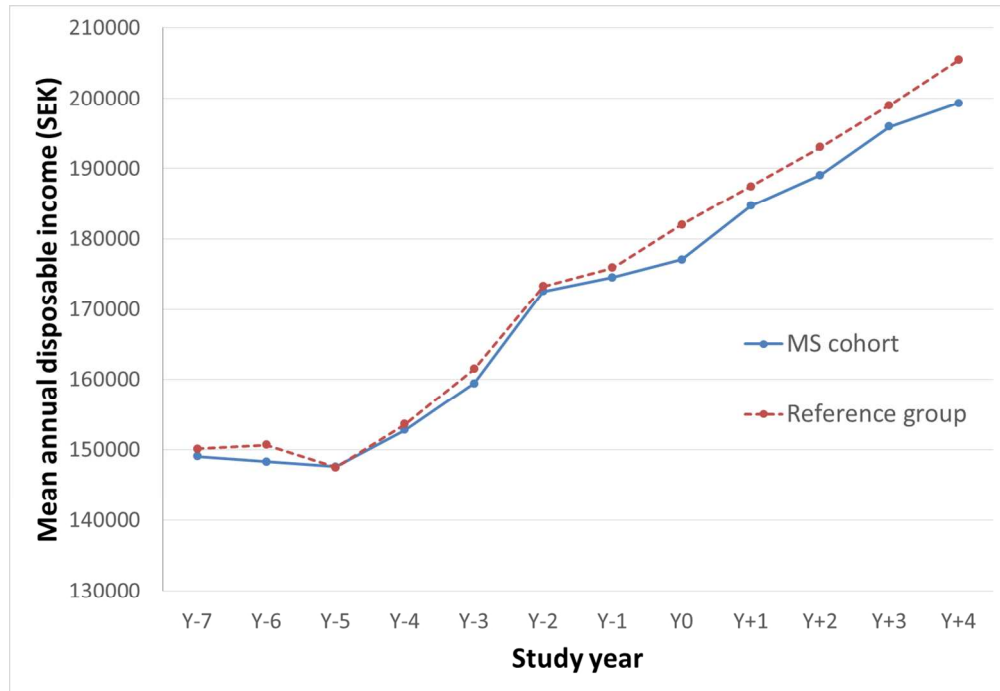


Figure 2 Mean disposable income (DI) Y-7 to Y+4 among people diagnosed with multiple sclerosis (MS) in Y0 (N=785) compared to references (N=7847). Notes: Mean annual DI inflated to 2016 values in Swedish Krona (SEK) with Harmonised Consumer Price Index In 2017, 100 SEK ≈10.5 Euros. Year of diagnosis (2009=Y0). MS (solid blue line): Individuals with first registered MS diagnosis in 2009 (Y0) in national in- and specialised out-patient registers. References (dashed red line: matched on four variables (1→10) with no MS diagnosis registered in years before 2010 in the national patient register.

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**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1 & 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(b) For matched studies, give matching criteria and number of exposed and unexposed	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7-10
		(b) Describe any methods used to examine subgroups and interactions	9
		(c) Explain how missing data were addressed	7 & 9
		(d) If applicable, explain how loss to follow-up was addressed	7 & 9
		(e) Describe any sensitivity analyses	N/A
<b>Results</b>			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9 & 10
		(b) Indicate number of participants with missing data for each variable of interest	9, 11-12
		(c) Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	Report numbers of outcome events or summary measures over time	13-14
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15-16
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	17
<b>Limitations</b>			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).