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Title: 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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ABSTRACT:

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

Design: Population-based cohort study, with follow-up of annual sums of incomes from seven years before to four years after diagnosis.

Setting: Swedish general population with data linked from two nationwide registers.

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

Primary and secondary outcome measures: The primary outcome measure, DI was defined as the annual sum of total net incomes (earnings and benefits) minus taxes. Three main components of DI were also separately analysed as annual sums: earnings; sickness absence benefits; and disability pension benefits.

Results: We found no differences in mean annual DI between the people with and without MS by independent t-tests at each follow-up year. Significant differences were found for the annual levels of components of DI from diagnosis year by independent t-tests. A generalised estimating equation evaluated the differences in the DI trajectory development between people with and without MS with the result that the trajectory of MS patients developed in parallel to the references'. No association with MS and economic welfare, as measured by DI, was found.

Conclusions: The key finding that the DI trajectory was unchanged around the years of MS diagnosis despite differences in components highlights the disease's distinct financial burdens. The Swedish welfare system was responsive to the decreased earnings through balancing DI by the morbidity-related benefits around time of MS diagnosis.

ARTICLE SUMMARY:

Strengths and limitations

- The main strengths of this study include both the population-based design and use of nationwide registers with high completeness and validity, which enabled measurement of multiple sources of income including disposable income.
- The longitudinal study design with repeated measures of disposable income enabled the study of the development of DI over 12 years, in addition to the difference in levels.
- While residual confounding cannot be excluded, the reference group was a randomised stratified matched group from the general population at a ratio of 1:10.
- This study does not address the long-term association between economic welfare and MS as the follow-up was only four years in the post diagnosis period.

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

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

This study aimed to describe the development of disposable income (DI) and three main components (SA, DP, and earnings), among people diagnosed with MS in the years before and after diagnosis and compare with people without MS, in order to gain knowledge on the economic welfare of people diagnosed with MS in a welfare state.

2. METHODS

2.1 Study design

We conducted a cohort study to measure the levels and development of mean annual DI and its main components (SA, DP, and earnings) among PwMS in relation to matched references without MS from the Swedish population. The index year of diagnosis, 2009, was defined as time point T_0, and the seven years of observation before and four years after diagnosis as T_{-7} to T_{-1} and T_{+1} to T_{+4}, respectively.

2.2 Data sources

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

1) **Statistics Sweden**: *Longitudinal Integration Database for Health Insurance and Labour Market Studies* (LISA), to obtain sociodemographic variables and the sums of annual income from the different sources across follow-up.

2) **National Board of Health and Welfare:** *National Patient Registers*, to identify all people with an MS diagnosis, from inpatient hospital treatment by the International Classification (ICD) codes, ICD-9 (340) and 10 (G35) (1987-2009), and specialised outpatient treatment by ICD-10 (2001-2009).

2.3 Study population

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

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

The maximum number of years of observation was 12, with 97.3% (n= 764) of the PwMS and 97.8% (n=7671) of the reference group in the study at the end of follow-up (T_{+4}). Missing income data in LISA, which could be due to migration before/after the index year or death after T_0, led to small proportions of individuals across both groups not being followed for the entirety of follow-up.

2.4 Variables

Our main outcome measure was annual **disposable income** (DI). We used the DI measure constructed by Statistics Sweden, contained in LISA. This was the sum of incomes after tax, with sources including: income from work and public benefits such as disability pension; sickness absence; disability allowance; unemployment compensation; old-age pension; and social assistance.[34] DI was an individualised measure of household DI, calculated as the sum of household incomes, adjusted for household size and the individual's consumption weight to produce a continuous variable.[34]

The three main components of DI for working-aged PwMS were also included as alternative economic outcome variables in analyses as the mean annual sum:

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

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

- **Earnings**: Income from work was in the form of gross earnings. This included the sick pay provided by the employer during the first 14 days of a sick-leave spell.

All monetary values were presented in Swedish Krona (SEK) and adjusted for inflation by the Statistics Sweden Harmonised Consumer Price Index (HCPI) by the annual average 2016 value.[35]

The following combination of sociodemographic variables sourced from LISA were included in the analyses as explanatory variables:

- **Age** (continuous, time variant): In addition, age was also computed into a new continuous variable to control for curvilinearity in the statistical analyses by squaring the values for age;
- **Gender** (binary);
- **Educational level** (categorical, time variant: elementary; high school; college or university; and missing); and
- **Birth country** (categorical: Sweden; Other Nordic Countries; Other EU25 Countries; Rest of World; and missing).

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

2.5 Ethical approval

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

2.6 Statistical analyses

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

In our data management, we set 337 negative DI values between 2004 and 2013 to zero to prevent distortion of the DI means over time. This was required as Statistics Sweden changed how they coded DI in LISA; earlier years of follow-up had a lower limit of zero but from 2004, there was possibility of negative values. We trimmed extreme outlier DI values at 566,100 SEK, representing the 99th

percentile of annual DI across all study years. This made the distribution of DI reasonably normal for statistical analyses. Individuals with missing values in LISA for DI and the secondary outcome variables, in years other than T_0, were excluded in descriptive statistics for the respective years, but were included in the GEE model. We capped earnings at the 99th percentile to control for extreme outliers, which resulted in a maximum possible annual value of 810,400 SEK.

Descriptive statistics were performed to describe the distribution of sociodemographic variables and summarise the levels of the different income variables. Categorical data were expressed as frequency distributions with the number and percentage. Continuous data were reported for both the PwMS and the reference group, expressed by the mean, standard deviation and both the number and proportion with annual sums >0.

The means of annual DI of PwMS was calculated for each year, T_{-7} to T_{+4}. The differences in mean annual DI of PwMS were tested for statistical significance by dependent *t*-tests between the following 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 approximation for the unequal variance were performed for each year of follow-up to test the difference in mean annual DI between PwMS and the references. The mean differences in annual sums of earnings, SA benefits, and DP benefits between PwMS and references were calculated at three time points: T_{-7}; T_0; and T_{+4}.

Lastly, we conducted linear regression analyses, using the generalised estimating equation (GEE) method to gain insight on how MS influenced the DI trajectory development over the study period.[36] The GEE model described the difference in the slopes of the DI trajectories from 2002 to 2013 between PwMS and the reference group as the method allowed for the dependent repeated measures of DI by accounting for the clustering of observations at both the individual and group levels that violated the independence assumptions of other methods.[36-38] The dependent variable, DI, was analysed as a continuous measure. The DI distribution was slightly right skewed, but GEE is a robust method.[37] The GEE model was computed with the following specifications: a normal distribution; identity link; and autoregressive within-subject correlation. The within-subject correlation structure

was selected because of the reasonable assumption that the correlation between an individual's annual DI values diminished over time. The models were adjusted for gender, age, education level, and country of birth. An additional age variable was included to account for curvilinearity. All variables were entered simultaneously with an interaction term of MS and year to evaluate whether PwMS had a different DI trajectory than the reference population. The periods pre and post diagnosis were assessed in separate models. The GEE model results were presented as un-standardised Beta regression coefficients with 95% confidence intervals (CI), which can be interpreted as values in SEK. The significance level for all analyses was α=0.05.

3 RESULTS

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

Table 1 contains a basic description of the study population and shows that the reference group (n= 7847) was representative of the PwMS cohort (n=785) on the distribution of these sociodemographic variables. The descriptive results revealed that the PwMS diagnosed in 2009 had a mean age of 41 (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 were 97.3% (n=764) PwMS and 97.8% (n=7671) references with data available in LISA.

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

	MS [b] n	(%)	References [b] n	(%)
	785	(100)	7847	(100)
Sex				
Men	248	(31.6)	2480	(31.6) [a]
Women	537	(68.4)	5367	(68.4) [a]
Age Group				
25-34	213	(27.1)	2130	(27.1) [a]
35-44	279	(35.5)	2790	(35.6) [a]
45-54	208	(26.5)	2077	(26.5) [a]
55-64	85	(10.8)	850	(10.8) [a]
Education (in years)				
≤9 (elementary) [c]	111	(14.1)	1107	(14.1) [a]
10 -12 (high school)	355	(45.2)	3550	(45.2) [a]
>12 (college or university)	319	(40.6)	3190	(40.7) [a]
Country of Birth				
Sweden	677	(86.2)	6770	(86.3) [a]
Nordic countries (except Sweden)	23	(2.9)	230	(2.9) [a]
EU25 (except Nordics)	27	(3.4)	270	(3.4) [a]
Rest of the world [c]	58	(7.4)	577	(7.4) [a]

[a] Reference group matched to MS cohort on these variables.
[b] 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.
[c] Individuals with missing variables added to lowest category (<0.5% of both study cohorts).

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

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

Table 2 displays the differences in the mean annual sums of the main components of DI (earnings, SA benefits, and DP benefits) between PwMS and references in T_{-7}, T_0, and T_{+4}. In every year, both SA and DP had a median of zero; indicating that most individuals in both groups did not receive either benefit (not presented). The proportion of PwMS who received SA or DP increased over time, which resulted in a higher proportion of PwMS than references receiving these morbidity-related benefits. Accordingly, in every year, the mean SA and DP amounts were higher for PwMS than for the reference group. These mean differences were highly significant, apart from SA benefits in 2002 (T_{-7}). From the time of diagnosis T_0, PwMS had significantly lower earnings than the reference group.

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_{-7}, T_0 and T_{+4} [e]

	MS [c]				References [c]				Mean difference (100 SEK[a])	*p*-value for difference
	Mean sum (100 SEK[a])	Std Deviation	n [d]	% [d]	Mean sum (100 SEK [a])	Std Deviation	n [d]	% [d]		
T_{-7}			**747**				**7457**			
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 [b]	1842	1598	645	86	1939	1566	6653	89	-97	0.1
Disposable income [b]	1491	679	-	-	1501	697	-	-	-10	0.686
T_0			**785**				**7847**			
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 [b]	2078	1771	651	83	2484	1718	6791	87	-405	0.001
Disposable income [b]	1770	981	-	-	1820	1025	-	-	-50	0.178
T_{+4}			**764**				**7671**			
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 [b]	2144	1928	582	76	2793	1895	6719	88	-649	0.001
Disposable income [b]	1994	1100	-	-	2055	1117	-	-	-61	0.1

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

[b] Trimmed at the 99 percentile.

[c] 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.

[d] Number count or proportion receiving annual sums > 0.

[e] T_{-7} = 2002, T_0 = 2009 and T_{+4} = 2013.

Potential differences in the development of the mean annual DI trajectory of PwMS from that of the matched references were assessed with a GEE model. In Figure 2, there were indications of the slopes both diverging prior to diagnosis and realigning to develop more in parallel in the years after diagnosis. All results from the GEE model provided non-significant differences between the development of the DI trajectories of PwMS and the reference group. Table 3 contains the differences in DI development after diagnosis in relation to the year of diagnosis and shows that between T_0 and T_{+4} was on an average 781 SEK (95% CI: -6922-3133) less for PwMS than for the reference group. Analysis of the pre-diagnosis period is contained in Table 4, where from T_{-7} to T_0 the development of mean annual DI for PwMS was on an average 4039 SEK (95% CI:-10,536 -3315) lower than the reference group.

Table 3: Disposable Income (DI) trajectory post diagnosis from T_0 (2009) to T_{+4} (2013) in the cohort of people with MS (N=785) compared to the cohort of references (N=7847) [a b]

Year	adjusted regression coefficient [c d e]	95% CI [e]
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

[a] Reference groups for analysis: 2009 (T_0) and reference group.
[b] 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.
[c] Adjusted for age, gender, education level and country of birth.
[d] Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.
[e] 100 SEK.

Table 4: Disposable Income (DI) trajectory prior to diagnosis from T_{-7} (2002) to T_0 (2009) in the cohort of people with MS (N=785) compared to the cohort of references (N=7847) [a b]

Year	adjusted regression coefficient [c d e]	95% CI [e]
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

[a] Reference groups for analysis: 2002 (T_{-7}) and reference group.
[b] MS: Multiple sclerosis (MS) diagnosis first registered in 2009 (T_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.
[c] Adjusted for age, gender, education level and country of birth.
[d] Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.
[e] 100 SEK.

4 DISCUSSION

4.1 Principal findings

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

4.2 Interpretation of findings in context of previous research

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

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

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

4.3 Strengths and limitations

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

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

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

4.5 Implications for policy and research

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

to differ much between the groups implies that that the flexible system of morbidity-related benefits that differentiate morbidity situations and levels of work incapacity is necessary for PwMS to maintain similar levels of economic welfare to the general population along the disease trajectory, as there are no curative treatment options available.

Future research is required as unanswered questions remain; we did not have the opportunity to capture DI changes that may occur as MS progresses further from diagnosis. Additionally, future studies should be designed to investigate whether DI trajectories of PwMS are patterned by sociodemographic characteristics or disease severity.

5. CONCLUSIONS

Our results indicate that PwMS as a group have similar DI growth to those without MS in Sweden. We found significant differences between PwMS and the population-based reference group in the proportions receiving and levels of individual income sources along the disease trajectory. However, no differences were found in the levels or development of the composite measure, annual DI, at least for the first four years post-diagnosis. In line with its intentions, the welfare system appears to be responsive to the individuals' economic welfare through the balancing of reduced annual earnings by compensation with the SA and DP benefits.

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Data Statement: No additional data available. The authors of this study are not permitted to make the micro-level data in this study publically available due to its sensitive nature. According to the Swedish Ethical Review Act, the Personal Data Act, and the Administrative Procedure Act, data can be made available after legal review for researchers who meet the criteria for access to this type of sensitive and confidential data. For questions about this, please contact Professor Kristina Alexanderson, responsible for the data set.

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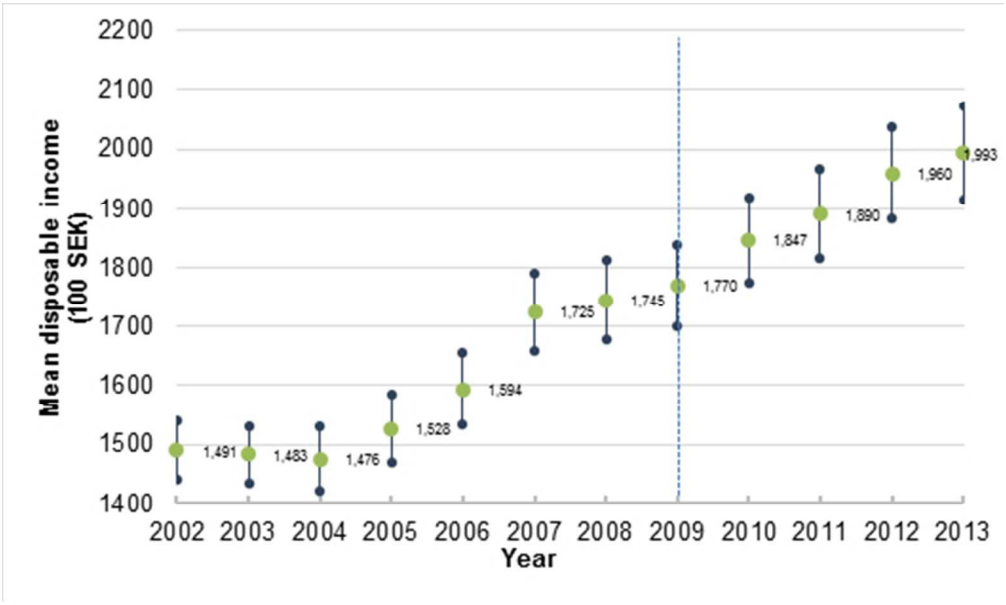

Figure 1: Mean disposable income (DI) in 2002-2013 among people diagnosed with multiple sclerosis (MS) in 2009. Mean annual disposable (DI) sum labelled to the right with the 95% confidence interval illustrated. DI inflated to 2016 values in Swedish Krona (SEK) with Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 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.

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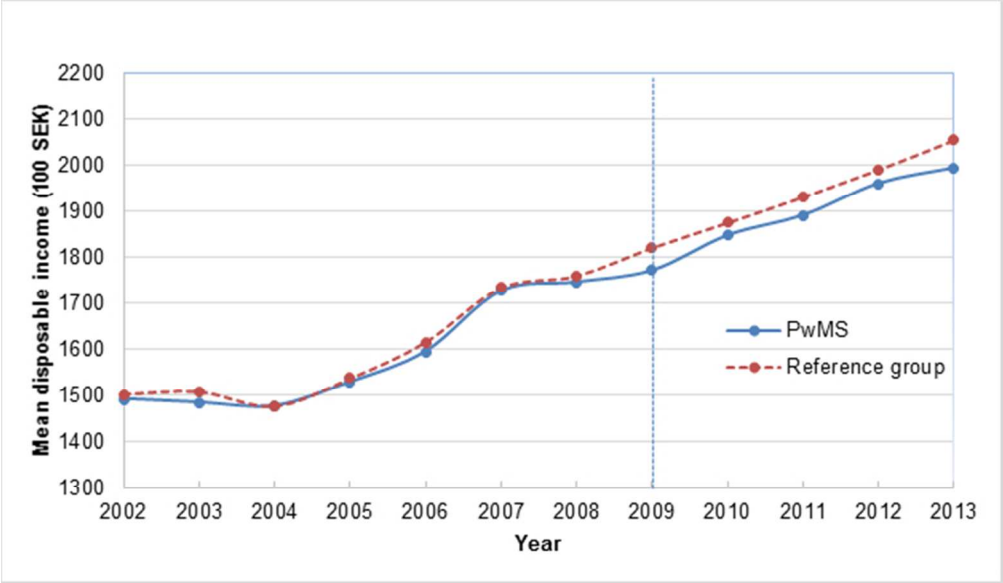

Figure 2: Mean disposable income (DI) in 2002-2013 among people diagnosed with multiple sclerosis (MS) in 2009 (N= 785) compared to references (N=7847). Annual disposable income (DI) inflated to 2016 values in Swedish Krona (SEK) with Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros. MS: 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
Introduction			
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
Methods			
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
Results			

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
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations			
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
Other information			
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.

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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Title: 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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ABSTRACT:

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

Design: Population-based cohort study, 12 years follow-up (seven years before to four years after diagnosis).

Setting: Swedish working-age population with microdata linked from two nationwide registers.

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

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

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

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

ARTICLE SUMMARY:

Strengths and limitations

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

1. INTRODUCTION

Multiple sclerosis (MS) is the leading cause of non-traumatic neurological disability in younger adults.[1-4] 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.[5] Previous research has found MS to be associated with progressive work incapacity, due to physical disability worsening as time from onset increases.[5-11] 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.[5 9] However, there is uncertainty and variability among PwMS in progression to disability milestones.[12] The indirect costs of working-aged PwMS become a dominating cost as the disease progresses from a societal perspective.[5 13-15] Nonetheless, the impact of MS on the individual's economic welfare remains relatively unknown.

Earnings remain an important income source for PwMS.[3 16] 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.[3 16] A recent Swedish survey found that 77% of PwMS worked part-time, and participation in paid work rapidly decreased with advancing disease.[5]

The wider socioeconomic context can mediate the economic impact of MS on the individual.[17 18] 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.[19-22] Furthermore, a substantially higher proportion of PwMS receive SA and DP, in comparison to the general population.[3 21 23] 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

the economic situation of working-aged PwMS.[16 24-26] However, the collective impact of these changes in incomes to the individual's economic welfare is largely unknown. Thorough investigation on how MS affects the economic resources available to PwMS in Sweden necessitates the need to longitudinally assess multiple sources of income in totality.[3 21 23 27-30]

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

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

2. METHODS

2.1 Study design

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

2.2 Data sources

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

1) *Longitudinal Integration Database for Health Insurance and Labour Market Studies* (LISA), held by Statistics Sweden, was used to obtain sociodemographic variables and the sums of annual income from the different sources across follow-up.

2) *National Patient Registers*, held by the National Board of Health and Welfare, enabled identification of all people with an MS diagnosis. The registers contain healthcare visits for inpatient treatment by the International Classification (ICD) codes, ICD-9 (340) and 10 (G35) (1987-2009), and specialised outpatient treatment by ICD-10 (2001-2009).

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

2.3 Study population

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

in 2009 were included, excluding all with a previous MS diagnosis (according to the in- and specialised out-patient registers).[23]

We established a matched reference cohort of people who before 2010, according to the in- and specialised out-patient registers, were not diagnosed with MS. Among all without MS, who according to LISA, lived in Sweden 31 December 2009, we randomly selected ten references for each PwMS, matched on age, gender, educational level, and birth country in 2009 (Y_0). This produced a stratified matched reference group with the same distribution of the selected sociodemographic variables in Y_0 to the MS cohort. The 1:10 ratio of references could not be met for one individual with MS, with only seven possible references in the general Swedish population matching the particular combination of sociodemographic variables. In all, 7847 references were included at Y_0.

The maximum number of years of observation was 12, with 97.3% (n=764) of the PwMS and 97.8% (n=7671) of the reference group in the study at the end of follow-up (Y_{+4}). Missing income data in LISA, due to migration before/after the index year or death after Y_0, led to small proportions of individuals across both groups not being followed for the entirety of follow-up.

2.4 Patient and Public Involvement

This was a study based on national register data and there was no patient or public involvement.

2.5 Variables

Our main outcome measure was annual **disposable income** (DI). We used the DI measure constructed by Statistics Sweden, contained in LISA. This was the sum of incomes after tax, with sources including: income from work and public benefits such as disability pension; sickness absence; disability allowance; unemployment compensation; old-age pension; and social assistance.[36] DI was an individualised measure of household DI, calculated as the sum of household incomes, adjusted for household size and the individual's consumption weight to produce a continuous variable.[36]

The three main components of DI for working-aged PwMS were also included as secondary economic outcomes in analyses as the mean annual sum:

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

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

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

Earnings were presented in gross form and only two potential public benefit payments were included in the analyses, therefore, one cannot sum the three components to the presented DI values. All monetary values were presented in Swedish Krona (SEK) and adjusted for inflation by the Statistics Sweden Harmonised Consumer Price Index (HCPI) by the annual average 2016 value.[37]

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

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

- **Gender** (binary);

- **Educational level** (categorical, time variant: elementary; high school; college or university; and missing); and
- **Birth country** (categorical: Sweden; Other Nordic Countries; Other EU25 Countries; Rest of World; and missing).

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

2.6 Ethical approval

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

2.7 Statistical analyses

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

In our data management, we set 337 negative DI values between 2004 and 2013 to zero to prevent distortion of the DI means over time. This was required as Statistics Sweden changed how they coded DI in LISA; earlier years of follow-up had a lower limit of zero, but negative values were possible from 2004. We trimmed extreme outlier DI values at 566,100 SEK, representing the 99th percentile of annual DI across all study years. This made the distribution of DI reasonably normal for statistical analyses. Individuals with missing values in LISA for DI and the secondary outcomes, in years other than $Y_{0,}$ were excluded in descriptive statistics for the respective years, but were included in the GEE model. Earnings were also capped at the 99th percentile (810,400 SEK) to control for extreme outliers.

Descriptive statistics were performed to describe the distribution of sociodemographic variables and summarise the levels of the different incomes. Categorical data were expressed as frequency distributions with the number and percentage. Continuous data were reported for both the PwMS and the reference group, expressed by the mean, 95% confidence intervals (95% CI), and both the number and proportion with annual sums >0.[38]

The means of annual DI of PwMS was calculated for each year, Y_{-7} to Y_{+4}. The differences in mean annual DI of PwMS were tested for statistical significance by dependent t-tests between the following 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 approximation for unequal variance were performed for each year of follow-up to test the difference in mean annual DI between PwMS and the references. The mean differences in annual sums of earnings, SA benefits, and DP benefits between PwMS and references were calculated with 95% CI at three time points: Y_{-7}; Y_0; and Y_{+4}.

Lastly, we conducted linear regression analyses, using the generalised estimating equation (GEE) method to analyse how MS influenced the DI trajectory development over the study period.[39] The GEE model described the difference in the slopes of the DI trajectories from Y_{-7} to Y_{+4} between PwMS and the reference group. The method allowed for the dependent repeated measures of DI by accounting for the clustering of observations at both the individual and group levels that violated independence assumptions.[39-41] The dependent variable, DI, was analysed as a continuous measure. The DI distribution was slightly right skewed, but GEE is a robust method.[40] The GEE model was computed with the following specifications: a normal distribution; identity link; and autoregressive within-subject correlation. The within-subject correlation structure was selected because of the reasonable assumption that the correlation between an individual's annual DI values diminished over time. The models were adjusted for gender, age, education level, and country of birth. An additional age variable was included to account for curvilinearity. All variables were entered simultaneously with an interaction term of MS and year to evaluate whether PwMS had a different DI trajectory than the references. The periods pre- and post-diagnosis were assessed in separate models. The GEE model results were presented as un-standardised Beta regression coefficients with 95% CI, which can be interpreted as values in SEK. The significance level for all analyses was α=0.05.

RESULTS

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

Table 1 contains a basic description of the study population and shows that the reference group (n= 7847) was representative of the PwMS cohort (n=785) on the distribution of these sociodemographic 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 of 2.17.

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

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

[a] Reference group matched to MS cohort on these variables.
[b] 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.
[c] Individuals with missing variables added to lowest category (<0.5% of both study cohorts).

In $Y_{0,}$ PwMS had a mean annual DI of 177,040 SEK (95% CI: 170,170-183,920) (Figure 1). PwMS experienced a mean increase in annual DI over the 12-year study period of 51,400 SEK (95% CI: 43,330-59,510). This increase in mean annual DI was observed in both the periods before (32,360 SEK; 95% CI: 26,360-38,360) and after diagnosis (19,390 SEK; 95% CI: 12,760-26,010) by dependent t-tests.

(INSERT FIGURE ONE)

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

(INSERT FIGURE TWO)

Table 2 displays the differences in the mean annual sums of the main components of DI (earnings, SA benefits, and DP benefits) between PwMS and references in Y_{-7}, Y_0, and Y_{+4}. In every year, both SA and DP had a median of zero; indicating that most individuals in both groups did not receive either benefit (not presented). A trend for PwMS to have greater sums of income from morbidity-related benefits than the references was present from Y_{-7} (DP mean difference: 5571 SEK; 95% CI: 1773-9369). The proportion of PwMS who received each of the benefits, SA and DP, increased over time. However, substantial skewedness of income from these morbidity-related sources remained even among PwMS; in each year less than 30% of PwMS had annual income from each benefit (except SA in $Y_{0,}$ 44%). This skewness was larger among the references (<17 %). Notwithstanding, in every year studied, the mean SA and DP amounts were higher for PwMS than for the reference group with differences in all years, apart from SA benefits in 2002 (Y_{-7}). PwMS had a peak in SA in Y_0 with the DP benefits increasing in the post-diagnosis period, whereas the references had stable DP sums and proportions across follow-up. From the time of diagnosis Y_0, PwMS had significantly lower earnings than the reference group, with this trend continuing throughout the post-diagnosis period.

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_{-7}, Y_0 and Y_{+4} [e]

	MS [c]				References [c]				Mean difference	95%CI
	Mean sum [a]	95% CI	n[d]	%[d]	Mean sum [a]	95% CI	n[d]	%[d]		
Y_{-7} [e]			**747**				**7457**			
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 [b]	184,174	(172,691-195,658)	645	86	193,918	(190,357-197,467)	6653	89	-9742	(-21,763-2275)
Disposable income [b f]	149,060	(144,180-153,940)	-	-	150,110	(148,530-151,700)	-	-	-1051	(-6184-4073)
Y_0 [e]			**785**				**7847**			
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 [b]	207,834	(195,427-220,242)	651	83	248,352	(244,339-252,365)	6791	87	-40,517	(-53,558- -27,476)
Disposable income [b f]	177,040	(170,170-183,920)	-	-	182,010	(179,750-184,280)	-	-	-4971	(-12,210–2266)
Y_{+4} [e]			**764**				**7671**			
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 [b]	214,426	(200,723-228,119)	582	76	279,298	(275,050-283,534)	6719	88	-64,867	(-79,203- -50,528)
Disposable income [b f]	199,350	(191,540-207,160)	-	-	205,450	(202,950-207,950)	-	-	-6098	(-14,300-2103)

[a] Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.
[b] Trimmed at the 99 percentile.
[c] 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.
[d] Number count or proportion receiving annual sums > 0.
[e] Y-7 = 2002, Y0 = 2009 and Y+4 = 2013.
[f] 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.

Potential differences in the development of the mean annual DI trajectory of PwMS from that of the matched references were assessed with a GEE model. In Figure 2, there were indications of the slopes both diverging prior to diagnosis and realigning to develop more in parallel in the years after diagnosis. All results from the GEE model provided non-significant differences between the development of the DI trajectories of PwMS and the reference group. Table 3 contains the differences in DI development after diagnosis in relation to the year of diagnosis, and shows that between Y_0 and Y_{+4} was on an average 781 SEK (95% CI: -6922-5360) less for PwMS than for the reference group. Analysis of the pre-diagnosis period is contained in Table 4, where from Y_{-7} to Y_0 the development of mean annual DI for PwMS was on an average 4039 SEK (95% CI:-10,536-2458) lower than the reference group.

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) [a b]

Year	adjusted regression coefficient [c d]	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

[a] Reference groups for analysis: 2009 (Y_0) and reference group.
[b] 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.
[c] Adjusted for age, gender, education level and country of birth.
[d] Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.

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) [a b]

Year	adjusted regression coefficient [c d]	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

[a] Reference groups for analysis: 2002 (Y_{-7}) and reference group.
[b] 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.
[c] Adjusted for age, gender, education level and country of birth.
[d] Un-standardised beta. Inflated to 2016 Swedish Krona (SEK) values by the Harmonised Consumer Price Index. In 2017, 100 SEK ≈ 10.5 Euros.

4. DISCUSSION

4.1 Principal findings

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

4.2 Interpretation of findings

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

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

substantially longer follow-up allowing for further disease progression, as long-term DP benefits compensate lost earnings to a lower proportion than short-term SA benefits.[10 25] Earnings remained the main income source for our MS cohort, where 76% cohort still participated in paid work to some degree at the end of follow-up, reflecting findings of Wiberg et al. that notwithstanding changes in sources of income around diagnosis, earnings remain the dominant source.[3] Furthermore, Hilt Pfleger et al. concluded that PwMS maintained similar levels of gross income to the references while remaining in paid work.[25] The combination of which supports our findings of similar DI trajectories between PwMS and the references in the short-term.

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

In line with previous research, we identified a larger proportion of PwMS receiving income from morbidity-related benefits than references, and PwMS transitioning from SA to DP benefits.[3 10 47] These patterns were not found for the reference group; the proportions of references receiving SA benefits were larger than DP for all years. Nevertheless, most PwMS were observed to not be on either benefit within our study period, further suggesting that early stages of MS morbidity were observed. These morbidity-related benefits have an increasing role in consideration of the progressive nature of MS.[10 20] SA benefits are designed to compensate periods of temporary absence from work, and

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

4.3 Strengths and limitations

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

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

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

4.5 Implications for policy and research

Our results reflect the combination of a responsive welfare system and the incremental progression of MS morbidity. The finding of unchanged levels and development of economic welfare, as measured by DI, in the presence of MS suggests that the morbidity-related transfer payments buffered the economic consequences of MS of reduced earnings in the years directly after diagnosis.[29] Our results suggest that society is bearing much of the economic burden associated with MS, which the individual would otherwise experience. The observation that the economic situation does not seem to differ much between the groups implies that that the flexible system of morbidity-related benefits that differentiate morbidity situations and levels of work incapacity in allowing part-time grants is necessary for PwMS to maintain similar levels of economic welfare to the general population early in the disease trajectory.

Moreover, current focus of MS treatment is on early intervention to delay disease progression, which should further preserve work capacity for longer periods post-diagnosis.[14 22 35 48] These delaying effects of early initiated treatments have been found to extend to socioeconomic outcomes and reduce the risk of full-time DP, which in light of the lower compensation for DP benefits, could provide further protections of economic welfare.[22]

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

PwMS older than 65, who may experience different DI development to our study cohort as a consequence of different income sources and benefit entitlements. This would be of particular interest in the Swedish context where the prevalent MS population is comparatively older than in other European countries.[5] Our interpretations for working-aged persons with MS focused on the role of DP benefits, which are not available for older adults.

5. CONCLUSIONS

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

Figure Legends

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

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 ≈10.5 Euros. MS: Individuals with first registered MS diagnosis in 2009 (Y_0) in national in- and specialised out-patient registers.

Figure 2 Mean disposable income (DI) Y_{-7} to Y_{+4} among people diagnosed with multiple sclerosis (MS) in Y_0 (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=Y_0). MS (solid blue line): Individuals with first registered MS diagnosis in 2009 (Y_0) 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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Data Statement: No additional data available. The authors of this study are not permitted to make the micro-level data in this study publically available due to its sensitive nature. According to the Swedish Ethical Review Act, the Personal Data Act, and the Administrative Procedure Act, data can be made available after legal review for researchers who meet the criteria for access to this type of sensitive and confidential data. For questions about this, please contact Professor Kristina Alexanderson, responsible for the data set.

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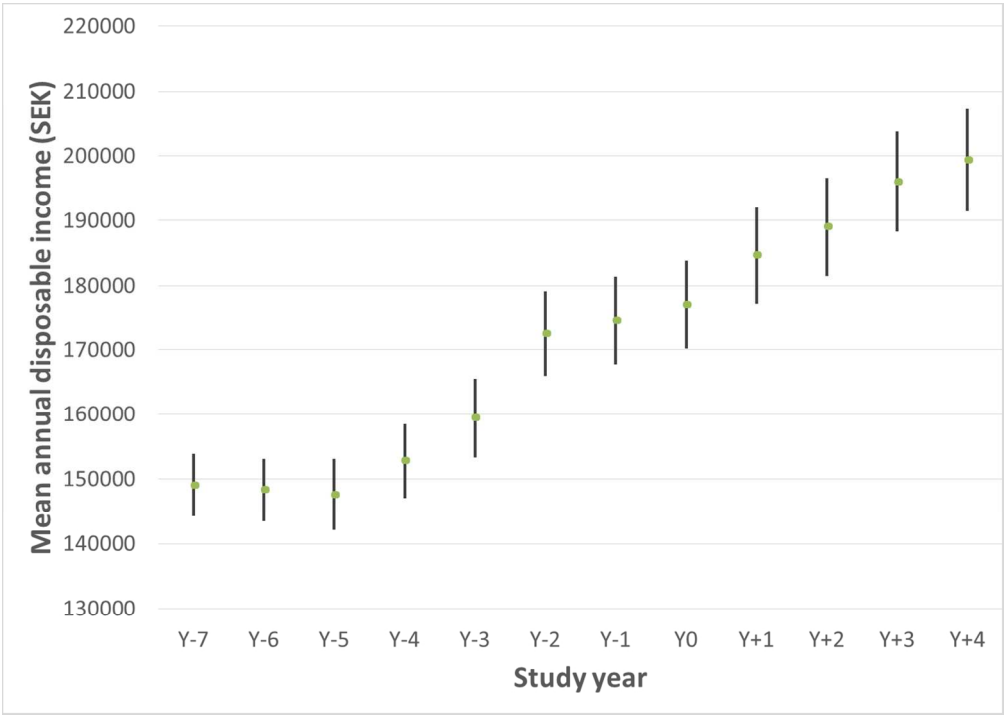

Figure 1: Mean disposable income (DI) Y-7 to Y+4 among people diagnosed with multiple sclerosis (MS) in Y0. Notes: Mean annual DI with 95% confidence intervals illustrated. DI sums are inflated to 2016 values in Swedish Krona (SEK) with the Harmonised Consumer Price Index. In 2017, 100 SEK ≈10.5 Euros.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

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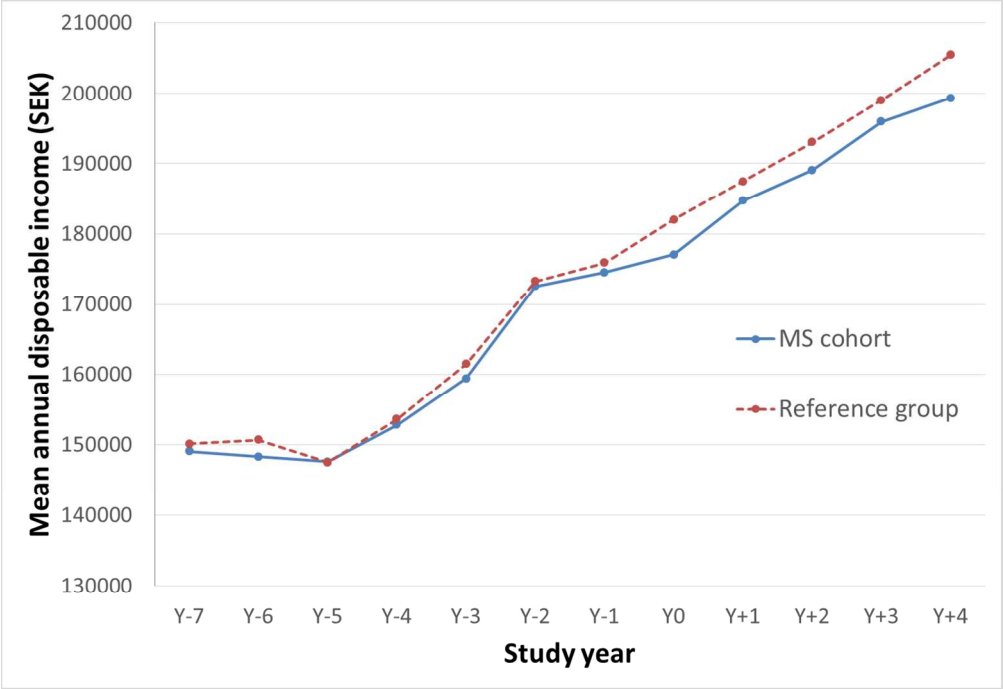

Figure 2 Mean disposable income (DI) Y-7 to Y+4 among people diagnosed with multiple sclerosis (MS) in Y0 (N=785) compared to references (N=7847). Notes: Mean annual DI inflated to 2016 values in Swedish Krona (SEK) with Harmonised Consumer Price Index In 2017, 100 SEK ≈10.5 Euros. Year of diagnosis (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
Introduction			
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
Methods			
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
Results			

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
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations			
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
Other information			
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.