



HAL
open science

Impact of multiple sclerosis on employment and income: Insights from a random sample representative of private sector employees in France using longitudinal administrative data

Emmanuelle Leray, C. Regaert, E. Duguet, S. Guillaume, S. Pichetti, M.
Espagnacq

► To cite this version:

Emmanuelle Leray, C. Regaert, E. Duguet, S. Guillaume, S. Pichetti, et al.. Impact of multiple sclerosis on employment and income: Insights from a random sample representative of private sector employees in France using longitudinal administrative data. *Revue Neurologique*, 2024, 180 (8), pp.754-765. 10.1016/j.neurol.2024.02.389 . hal-04543869

HAL Id: hal-04543869

<https://ehesp.hal.science/hal-04543869v1>

Submitted on 29 Jan 2025

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0
International License



Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com



Original article

Impact of multiple sclerosis on employment and income: Insights from a random sample representative of private sector employees in France using longitudinal administrative data



E. Leray^{a,*}, C. Regaert^b, E. Duguet^c, S. Guillaume^b, S. Pichetti^b,
 M. Espagnacq^b

^a University of Rennes, EHESP, CNRS, Inserm, ARENES UMR 6051, RSMS U 1309, CS 74312, 15, avenue du Pr-Léon-Bernard, 35043 Rennes cedex, France

^b Institut de recherche et documentation en économie de la santé (IRDES), 21–23, rue des Ardennes, 75019 Paris, France

^c Faculté de sciences économiques et de gestion, Mail des mèches, Université Paris Est Créteil (UPEC), ERUDITE (EA 437), rue Poète et Sellier, 94010 Créteil cedex, France

INFO ARTICLE

Article history:

Received 29 August 2023

Received in revised form

30 December 2023

Accepted 6 February 2024

Available online 5 April 2024

Keywords:

Multiple sclerosis

Work trajectories

Administrative data

Difference in differences

ABSTRACT

In France, few data sources are available to estimate the impact of multiple sclerosis (MS) on job retention and its consequences on the level of resources, especially in large representative samples. The aim of the present study was to measure impact of MS on employment rates, wages and income (including unemployment benefit, sickness benefit and disability pension) by comparing work trajectories of people living with MS with those of a matched control group. We used the HYGIE database, which is the result of the linkage of two administrative databases in the private sector for a random sample of over 900,000 people. In order to identify the causal effect of MS on employment after 1 to 20 years, the difference-in-differences method with matching (age, sex, career and health history) was used, overall and in subgroups. The year of entry in long-term disease status for MS was used to approximate the onset of MS. Overall, 946 people with MS were included. Their situation was fairly favorable before MS (88.1% in employment, resources higher than the median for the general population), but MS had strong and continuous negative effects. Indeed, at 10 years, the employment rate fell by 28.6 percentage points (pp) and the disability pension allowance increased by 50.5 pp; the wage percentile fell by 19.2 pp and the replacement income accounted for a growing share of total income (+ 39.7 pp). Although administrative data had several strengths, clinical information on the severity of the disease or on its therapeutic management was not available. In conclusion, this study shows that the effects of MS on the employed population in the private sector occur early in the disease course and are cumulative, and that replacement income helps to reduce the loss of resources thanks to the French health and social system.

© 2024 The Authors. Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author.

E-mail address: emmanuelle.leray@ehesp.fr (E. Leray).

<https://doi.org/10.1016/j.neurol.2024.02.389>

0035-3787/© 2024 The Authors. Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Multiple sclerosis (MS) is a disease of the central nervous system that affects 2.8 million individuals in the world. It often begins between 20 and 40 years old and three quarters of cases are women [1]. About 120,000 people live with MS in France [2,3]. This chronic disease lasts for several decades and excess mortality compared with general population started 20 years after clinical onset [4,5]. For all of these reasons, employment and occupational trajectories are likely to be affected by the disease.

In the literature, few studies on the impact of MS on work including French data are available, and most of them are descriptive and cross-sectional: one European study [6], two national studies [7,8] and two regional studies [9,10]. Based on data from the French National Health Data System (SNDS) in 2013, 21% of people with MS had at least one sickness leave, with a median duration of 29 days [11].

In the international literature, the employment rate of people with MS varies widely between studies (range: 26–74%) [12], depending on the study populations (age, disease duration, level of education, etc.) and contexts (including legal and insurance systems). All the studies consistently show that MS has an impact on work, often early after disease onset. Even if disability does not seem visible, the consequences of the disease are present and lead to a lower employment rate than that in the general population. Few longitudinal studies are available, as highlighted in the first scoping review dedicated to the occupational outcomes in MS [12]. Indeed, among the 403 included studies, only 77 (19.1%) were longitudinal and 63 (15.6%) used a control group.

Thus, the main objective of the present study was to assess the impact of MS on employment status and income in the short and medium term (1 to 20 years) using French population-based data. By taking into account replacement income, i.e. unemployment benefit, sickness benefit and disability pension, the role of the French social protection system has been taken into account. The second objective was to perform subgroup analyses according to sex, age, period, and presence of comorbidities, to check whether the magnitude of the effects of MS differed according to these characteristics.

2. Material and methods

2.1. Data source

We used the HYGIE database, which results from the linkage of two French administrative databases for a random sample of private sector employees aged 22 to 70 years in 2005. Indeed, data from the National Pension Fund (CNAV) which contains detailed information on workers' status in the labor market (collected on a quarterly basis, from career onset) were linked to data from the National Health Insurance system which contained summarized data on health care use, health status and sick leaves. Linkage was performed using a unique identifier number (15-digit) available in both data sources. The CNAV data constituted the point of entry and a random

sample of beneficiaries aged 22 to 70 years who contributed to the general pension fund at least once in their life was included. The sample was randomly selected using specific values of the unique key identifier and the sampling rate was 1/50th. Information about sex came from the health insurance database and was collected as assigned at birth, i.e. as a binary variable. Health status was approximated through a list of long-term diseases (LTD) that are fully reimbursed by the health insurance system, MS being on the list (ICD-10 code G35). Thus, the HYGIE database offers the opportunity to study work trajectories and to identify occurrence of major health events.

2.2. Study population

From the entire population available in the HYGIE database ($n = 923,561$), people eligible to the present study fulfilled the following criteria: LTD registration for MS, between 1987 and 2013 (to get sufficient follow-up), having at least one year available before and after the LTD registration, and registered to the general insurance scheme before and after MS.

For each individual, follow-up started in the year prior to LTD registration for MS and ended either with death, with a change of insurance scheme, or the end of available data (31/12/2015). The year of LTD registration for MS (noted T) defined the index date.

2.3. Data

To measure the effect of MS on work trajectories, we built several annual indicators:

- three possible and mutually exclusive statuses: employment/unemployment/inactivity;
- two indicators related to health status: sick leave and disability pension;
- two indicators related to wages, the same for income, and the part of replacement income in total income.

Unemployment was defined as having at least one quarter of unemployment within a year without having any quarter in employment. Inactivity was defined as not having any quarter in employment or unemployment. Thus, the probability of being employed, unemployed or inactive was calculated every year, the sum of the three probabilities being equal to 100%.

Sickness leave and disability pension annual statuses were defined as having at least one quarter of sick leave or disability pension respectively. As those two statuses were based upon different kinds of information, they are not mutually exclusive, and it is therefore possible that an individual is considered as both “receiving sick leave” and “receiving disability pension”, either simultaneously or in two separate quarters in the same year.

Wages (issued from work) and income were also studied, income being equal to the sum of wages and replacement income, and replacement income being composed of daily allowances for sickness leaves, unemployment benefits and disability pensions. Two indicators were considered: the percentile and the relative value to the median. Thus, the

wage (respectively income) percentile corresponds to the distribution of wages (respectively income) of the MS population in relation to all workers included in the HYGIE database. The relative wage, calculated as the ratio to the median, gives the position of the MS population in relation to the median wage of the HYGIE database (same for income).

2.4. Statistical analysis

We aimed to perform a dynamic analysis of the relationship between health and occupation, through a before-after analysis where the break date is the date of health event, here LTD registration for MS. We used an approach based upon difference-in-differences (DiD) with exact matching [13,14]. We selected controls having no long-term disease at index date, matched for sex, and using caliper matching for the continuous variables: age (2 years), starting wage quartile (5 points), past stable employment rate (5 points), past illness rate (5 points). All eligible individuals were included in the control group and each control could be matched several times, to increase both the matching rate and the statistical power. In order to limit the bias of selecting “never sick” controls (not representative of the general population i.e. would lead to an overestimation of the effects of MS), controls could also have registered for a LTD (other than MS) over time, but only after the end of the analysis period. Thus, controls could have a LTD from T + 2 for the effects measured in T + 1, from T + 3 for the effects measured in T + 2, etc.

The results obtained from the DiD method are presented as variations over time measured in the MS population and attributable to MS due to the use of a comparable control

population [15]. Effects of MS were evaluated at different time points: 1 year to 20 years after LTD registration for MS and are expressed as percentage points (pp). Analyses were performed on the overall population, then stratified according to categories defined by: sex, age at and year of LTD registration MS, and presence of comorbidities.

2.5. Ethics

In accordance with the French legislation, the present study was approved by the national data protection agency (Commission Nationale Informatique et Libertés [CNIL]; approval DR-2019-152).

Table 1 – Characteristics of people living with multiple sclerosis included in the present study.

	Number	%
Number of people with MS	946	
Sex		
Men	299	31.7%
Women	644	68.3%
Age at LTD registration for MS		
< = 38 years old	491	51.9%
> 38 years old	455	48.1%
Comorbidities		
No	731	81.5%
Yes	166	18.5%
Year of LTD registration for MS		
< = 1998	245	27.3%
> 1998	652	72.7%

LTD: long-term disease.

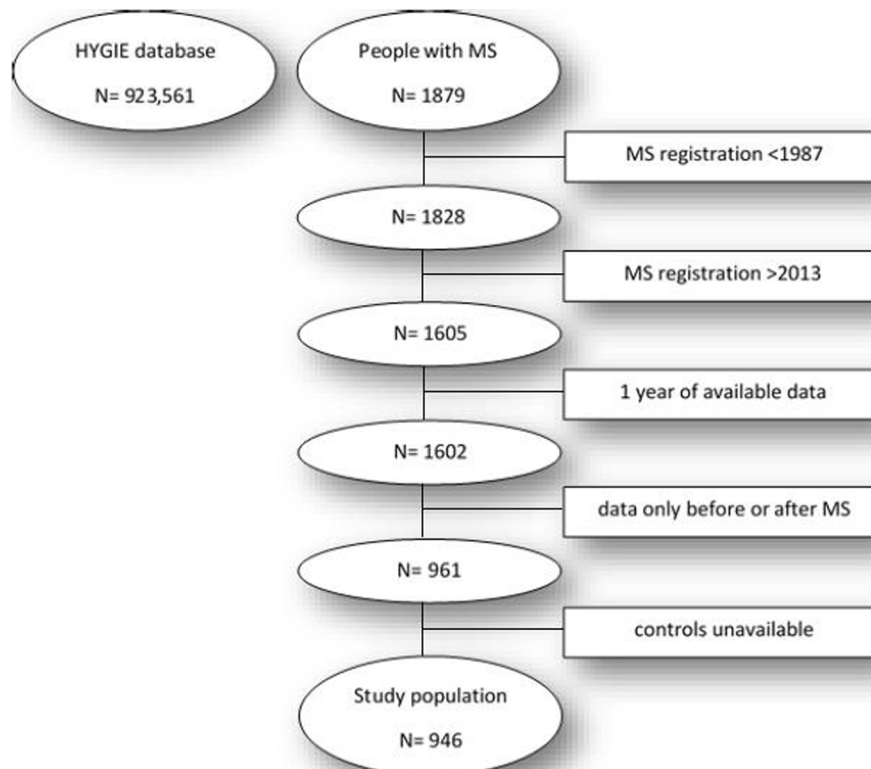


Fig. 1 – Flowchart of the study population.

3. Results

3.1. Characteristics of the study population

The study population was composed of 946 people with MS (Fig. 1) and their characteristics are presented in Table 1.

3.2. Effects of MS on employment

In the year preceding LTD registration for MS (T-1), 88.1% of people were employed, 4.5% unemployed and 7.4% inactive (Table 2). In addition, 13.0% had sickness leave for at least one quarter and 7.3% received disability pension.

In the year following LTD registration for MS (T + 1), the employment rate significantly decreased by 6.6 percentage points (pp). The significant negative effects of MS on employment persisted and even increased over time: -12.1 pp at 2 years, -22.4 pp at 5 years, -28.6 pp at 10 years, -35.1 pp at 15 years, and -46.2 pp at 20 years (T-1 always being the reference). On the other hand, the proportion of people being unemployed remained relatively stable (between 3 and 5%) and was not significantly affected by MS. The decline in employment was therefore translated into an increase of inactivity. Indeed, in the year following LTD registration for MS, the proportion of inactive persons increased by 6.9 pp. Over the 20 years of follow-up, this proportion increased regularly and significantly, reaching +21.1 pp at 5 years, +29.6 pp at 10 years, +36.7 pp at 15 years, and +48.9 pp at 20 years (Fig. 2).

3.3. Effects of MS on sickness leave and disability pension

Regarding sick leave (Table 2 and Fig. 3), the effect of MS was very strong (significantly different from 0) in the first 3 years following LTD registration. Indeed, the proportion of individuals being in sick leave increased by +23.6 pp at T + 1, +17.6 pp at T + 2 and +10.0 pp at T + 3. From the 4th year onwards, the effect became almost null and then went in the opposite direction.

Conversely, the proportion of people receiving disability pension (Table 2 and Fig. 4) rose steadily from 7.3% in T-1 to +5.4 pp at T + 1, +50.5 pp at T + 10 and +68.3 pp at T + 20.

3.4. Effects of MS on wages and income

These changes had an impact on wages and income (Table 2). Before the disease, the relative income of people with MS was 51% higher than the median (value 151), and then has fallen strongly and steadily: -14 pp at T + 1, -32 pp at T + 5, -44 pp at T + 10 and even -75 pp at T + 20. In terms of income percentiles, people with MS fell from the 64th percentile, well above the median, to the 46th percentile (64-18) after 20 years.

Regarding wages, prior to LTD registration, the MS population was at the 56th percentile of salary (i.e. 6 ranks above the median). Over time, MS caused this position to fall steadily (Table 2): from -6 ranks in the first year (i.e. at the median of the HYGIE population) to -19 ranks in the tenth year and -28 ranks after 20 years. The relative wage of the MS population also fell significantly over the period, from 126

Table 2 – Effects of multiple sclerosis on employment and income in the study population.

Time to/from MS	T-1 (reference)		T + 1		T + 2		T + 3		T + 4		T + 5		T + 10		T + 15		T + 20	
	%	Percentage points (pp)	pp	pp	pp	pp	pp	pp	pp	pp	pp	pp	pp	pp	pp	pp	pp	pp
Number of people with MS		946	919	856	793	714	436	218	82									
Number of controls		11730877	11397264	10662384	9951219	9261384	6145994	3644694	1802908									
Employment	88.1	-6.6	*** -12.1	*** -17.2	*** -20.6	*** -22.4	*** -28.6	*** -35.1	*** -46.2									
Unemployment	4.5	-0.3	ns +0.7	ns +3.0	*** +1.3	ns +1.4	ns -1.0	ns -1.6	ns -2.7									
Inactivity	7.4	+6.9	*** +11.4	*** +14.2	*** +19.3	*** +21.1	*** +29.6	*** +36.7	*** +48.9									
Sickness leave	13.0	+23.6	*** +17.6	*** +10.0	*** +2.4	ns +2.3	ns -4.6	** -5.9	* -11.7									
Disability pension	7.3	+5.4	*** +16.2	*** +27.7	*** +33.4	*** +36.4	*** +50.5	*** +58.5	*** +68.3									
Relative income (median = 100)	151	-14	*** -19	*** -24	*** -31	*** -32	*** -44	*** -63	*** -75									
Income percentile	64.1	-3.9	*** -4.8	*** -6.0	*** -7.9	*** -8.4	*** -11.1	*** -15.2	*** -18.0									
Part of replacement income in total income	16.2	+11.4	*** +15.8	*** +22.9	*** +25.6	*** +28.7	*** +39.7	*** +47.7	*** +58.6									
Relative wage (median = 100)	126	-25	*** -32	*** -39	*** -47	*** -50	*** -65	*** -87	*** -96									
Wage percentile	56.8	-6.3	*** -8.3	*** -10.9	*** -13.5	*** -14.5	*** -19.2	*** -24.5	*** -28.4									

*, P < 0.1; **, P < 0.05; ***, P < 0.01; ns: not significant at 10% threshold. Interpretation: one year before MS (T-1), 88.1% of people who will have MS are in employment. This rate falls by 6.6 percentage points one year after MS (T + 1). This difference is statistically significant at the 1% threshold. There are 946 people with MS present in both T-1 and T + 1.

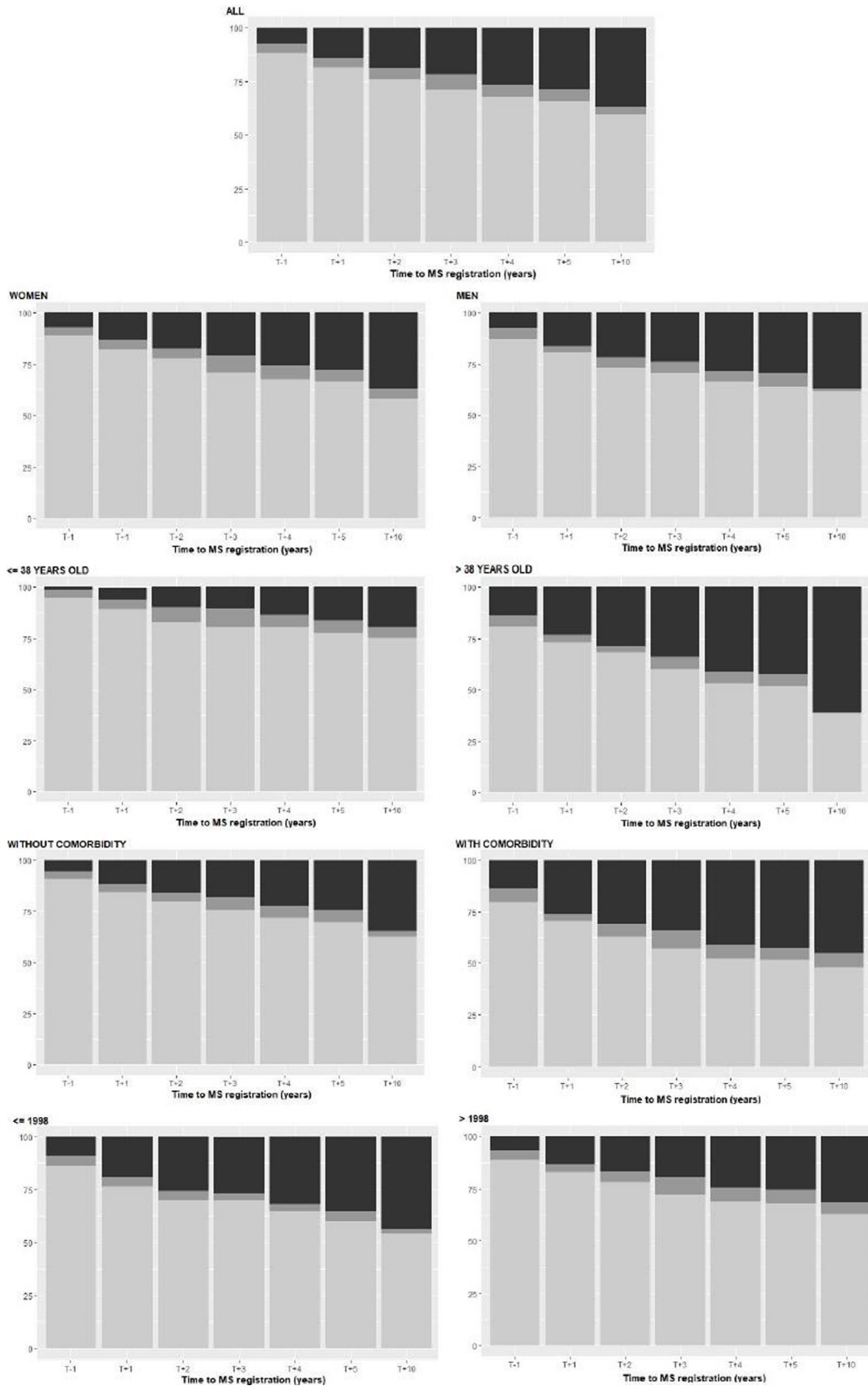


Fig. 2 – Effects of MS on employment according to time from/to MS registration (T, years), overall and by subgroups (black: inactivity; dark grey: unemployment; light grey: employment).

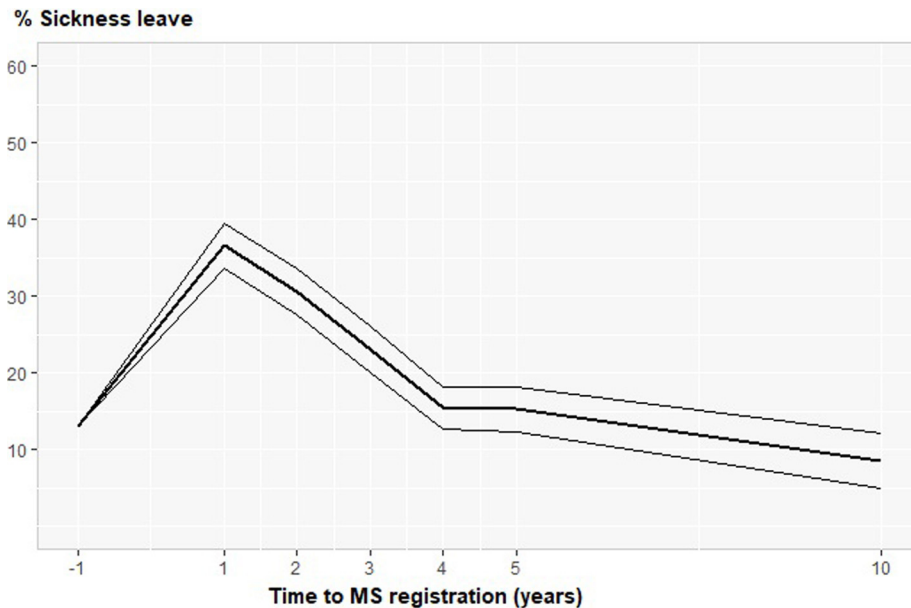


Fig. 3 – Effects of multiple sclerosis on sickness leave according to time from/to MS registration (T, years).

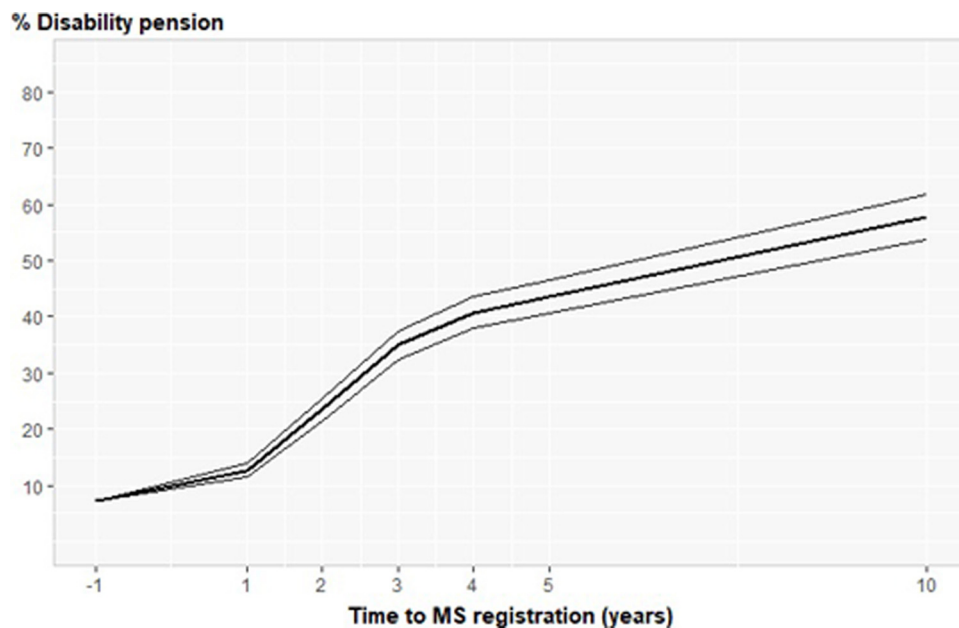


Fig. 4 – Effects of multiple sclerosis on disability pension according to time from/to MS registration (T, years).

initially (26 points above the median) to 61 (126–65) after 10 years and 30 (126–96) after 20 years. This sharp downgrading was consistent with the decline in the ability to work and we observed a radical shift in the composition of income, with the part of replacement income in the total income rising from 16.2% to about 75%.

3.5. Subgroup analyses

Sex differences were relatively marginal regarding employment (Table 3). The employment rate in T-1 was similar

between men and women (around 88%) and decreased in the same proportions over time (except in year 10).

The situation differed according to the age of LTD registration for MS (Table 4). Indeed, fewer people > 38 years old were working in T-1 (80.7% vs. 94.9% for those under 38), and the drop in employment rate was much more pronounced: -7.6 pp in T-1 to -42.3 pp in T+10 (versus -5.6 pp and -19.6 pp respectively in younger people).

People with MS and comorbidity (Table 5) had a lower percentage of employment than those without comorbidity before MS (79.6% vs. 90.6% at T-1), and the effects of MS were

Table 3 – Effects of multiple sclerosis on employment and income in the study population according to sex.

Time to MS	T-1 (reference)	T + 1	T + 2	T + 3	T + 4	T + 5	T + 10	
MEN								
Number of people with MS		299	292	271	251	220	150	
Employment	87.2	-6.6	*** -14.2	*** -16.7	*** -20.9	*** -23.5	*** -25.7	***
Unemployment	5.2	-2.3	* +0.2	ns +0.3	ns -0.3	ns +1.6	ns -3.9	*
Inactivity	7.5	+9.0	*** +14.0	*** +16.4	*** +21.1	*** +21.9	*** +29.7	***
Sickness leave	9.5	+25.0	*** +19.9	*** +10.9	*** +2.2	ns +0.3	ns -1.8	ns
Disability pension	7.5	+4.6	*** +16.4	*** +28.5	*** +34.2	*** +34.8	*** +48.4	***
Relative income (median = 100)	164	-20	*** -31	*** -35	*** -46	*** -42	*** -53	***
Income percentile	67.0	-5.0	*** -6.3	*** -7.6	*** -9.6	*** -10.6	*** -12.5	***
Part of replacement income in total income	15.8	+10.4	*** +16.8	*** +23.0	*** +26.5	*** +29.1	*** +38.7	***
Relative wage (median = 100)	167	-31.4	*** -45	*** -52	*** -64	*** -61	*** -76	***
Wage percentile	65.4	-7.6	*** -10.3	*** -13.3	*** -15.6	*** -16.7	*** -20.9	***
WOMEN								
Number of people with MS		644	627	587	540	494	288	
Employment	88.6	-6.3	*** -10.8	*** -17.8	*** -20.8	*** -22.1	*** -30.3	***
Unemployment	4.1	+0.4	ns +0.9	ns +4.5	*** +2.5	* +1.5	ns +0.6	ns
Inactivity	7.3	+5.9	*** +9.9	*** +13.4	*** +18.3	*** +20.6	*** +29.7	***
Sickness leave	14.6	+22.8	*** +17.1	*** +9.7	*** +2.3	ns +3.7	ns -5.7	**
Disability pension	7.2	+5.7	*** +16.0	*** +27.3	*** +32.8	*** +36.9	*** +51.5	***
Relative income (median = 100)	108	-11	*** -13	*** -19	*** -26	*** -29	*** -37	***
Income percentile	53.8	-3.2	*** -3.8	*** -5.2	*** -7.1	*** -7.9	*** -10.8	***
Part of replacement income in total income	16.3	+11.6	*** +15.5	*** +23.1	*** +25.7	*** +28.7	*** +39.6	***
Relative wage (median = 100)	107	-21.0	*** -25	*** -33	*** -41	*** -46	*** -56	***
Wage percentile	52.8	-5.6	*** -7.3	*** -9.8	*** -12.6	*** -14.0	*** -18.6	***

*: P < 0.1; **: P < 0.05; ***: P < 0.01; ns: not significant.

Table 4 – Effects of multiple sclerosis on employment and income in the study population according to age at long-term disease registration for multiple sclerosis.

Time to MS	T-1 (reference)	T + 1	T + 2	T + 3	T + 4	T + 5	T + 10	%
<= 38 years old								
Number of people with MS		491	479	454	420	387	263	
Employment	94.9	-5.6	*** -11.6	*** -14.2	*** -14.3	*** -17.1	*** -19.6	***
Unemployment	3.6	+1.0	ns +3.6	** +5.4	*** +2.4	* +2.3	ns +1.7	ns
Inactivity	1.6	+4.6	*** +8.1	*** +8.9	*** +11.9	*** +14.7	*** +17.8	***
Sickness leave	13.5	+22.3	*** +18.1	*** +12.1	*** +5.5	** +6.6	*** +0.3	ns
Disability pension	2.2	+1.8	*** +8.7	*** +18.6	*** +23.4	*** +26.7	*** +41.7	***
Relative income (median = 100)	119	-12	*** -14	*** -14	*** -19	*** -21	*** -33	***
Income percentile	56.8	-3.2	*** -3.8	*** -3.8	*** -5.2	*** -5.5	*** -8.0	***
Part of replacement income in total income	11.4	+9.3	*** +12.9	*** +18.3	*** +19.2	*** +23.0	*** +33.4	***
Relative wage (median = 100)	120	-20.5	*** -23	*** -25	*** -30	*** -34	*** -51	***
Wage percentile	56.5	-4.9	*** -6.1	*** -7.0	*** -8.8	*** -9.8	*** -14.8	***
> 38 years old								
Number of people with MS		455	440	402	373	327	173	
Employment	80.7	-7.6	*** -12.6	*** -20.5	*** -27.7	*** -28.8	*** -42.3	***
Unemployment	5.5	-1.8	ns -2.5	* +0.3	ns +0.1	ns +0.2	ns -5.1	**
Inactivity	13.8	+9.3	*** +15.1	*** +20.2	*** +27.7	*** +28.6	*** +47.4	***
Sickness leave	12.5	+25.0	*** +17.0	*** +7.6	*** -1.1	ns -2.9	ns -12.0	***
Disability pension	12.9	+9.3	*** +24.3	*** +38.0	*** +44.7	*** +47.9	*** +63.9	***
Relative income (median = 100)	134	-16	*** -24	*** -35	*** -45	*** -45	*** -61	***
Income percentile	59.3	-4.6	*** -5.8	*** -8.4	*** -10.9	*** -11.9	*** -15.9	***
Part of replacement income in total income	21.5	+13.5	*** +19.0	*** +28.1	*** +32.9	*** +35.4	*** +49.2	***
Relative wage (median = 100)	133	-29.5	*** -41	*** -56	*** -66	*** -68	*** -85	***
Wage percentile	57.1	-7.9	*** -10.8	*** -15.4	*** -18.9	*** -20.2	*** -25.8	***

*: P < 0.1; **: P < 0.05; ***: P < 0.01; ns: not significant.

systematically stronger in that group (-9.1 pp vs. -6.3 pp at T + 1, and -31.8 pp vs. -27.9 pp at T + 10).

Regarding the year of LTD registration (Table 6), the most recent MS (> 1998) seemed to remain employed more often than the oldest MS (<= 1998) (respectively 88.9% vs. 86.0% at

T-1, -5.9 pp vs. -9.4 pp at T + 1, and -26.0 pp vs. -31.8 pp at T + 10).

Regarding the effects of MS on sickness leave, all the subgroups showed a profile similar to the overall study population (Fig. 3): a significant increase in the year following

Table 5 – Effects of multiple sclerosis on employment and income in the study population according to presence of comorbidity.

Time to MS	T-1 (reference)	T + 1	T + 2	T + 3	T + 4	T + 5	T + 10	%
WITHOUT COMORBIDITY								
Number of people with MS		731	711	657	607	547	341	
Employment	90.6	-6.3 ***	-10.9 ***	-15.1 ***	-18.7 ***	-21.1 ***	-27.9 ***	
Unemployment	3.8	+0.1 ns	+0.6 ns	+2.7 **	+1.7 ns	+2.1 *	-0.9 ns	
Inactivity	5.6	+6.2 ***	+10.3 ***	+12.5 ***	+17.0 ***	+19.0 ***	+28.8 ***	
Sickness leave	10.3	+23.8 ***	+19.3 ***	+11.7 ***	+3.7 **	+3.9 **	-4.9 **	
Disability pension	5.6	+4.2 ***	+13.3 ***	+25.0 ***	+30.4 ***	+33.3 ***	+48.1 ***	
Relative income (median = 100)	132	-14 ***	-18 ***	-23 ***	-30 ***	-31 ***	-44 ***	
Income percentile	59.4	-3.7 ***	-4.3 ***	-5.3 ***	-7.4 ***	-8.1 ***	-11.5 ***	
Part of replacement income in total income	13.4	+10.7 ***	+14.7 ***	+21.8 ***	+24.6 ***	+27.9 ***	+39.6 ***	
Relative wage (median = 100)	134	-24.6 ***	-30 ***	-38 ***	-46 ***	-48 ***	-65 ***	
Wage percentile	58.5	-6.1 ***	-7.5 ***	-9.9 ***	-12.6 ***	-13.7 ***	-19.2 ***	
WITH COMORBIDITY								
Number of people with MS		166	161	157	151	145	91	
Employment	79.6	-9.1 ***	-16.8 ***	-22.8 ***	-27.4 ***	-27.9 ***	-31.8 ***	
Unemployment	6.9	-3.4 ns	-0.6 ns	+2.2 ns	-0.3 ns	-1.5 ns	-0.2 ns	
Inactivity	13.4	+12.6 ***	+17.5 ***	+20.6 ***	+27.7 ***	+29.4 ***	+32.0 ***	
Sickness leave	22.2	+29.0 ***	+18.6 ***	+8.7 **	+0.6 ns	-2.7 ns	-2.8 ns	
Disability pension	13.0	+7.2 ***	+24.3 ***	+36.8 ***	+43.4 ***	+46.4 ***	+59.5 ***	
Relative income (median = 100)	104	-20 ***	-25 ***	-32 ***	-37 ***	-37 ***	-44 ***	
Income percentile	53.1	-6.3 ***	-7.2 ***	-9.1 ***	-10.4 ***	-9.9 ***	-10.8 ***	
Part of replacement income in total income	25.8	+11.5 ***	+19.8 ***	+27.5 ***	+31.0 ***	+31.7 ***	+41.6 ***	
Relative wage (median = 100)	98	-31.2 ***	-41 ***	-50 ***	-56 ***	-57 ***	-68 ***	
Wage percentile	50.7	-8.5 ***	-12.2 ***	-15.5 ***	-17.7 ***	-17.7 ***	-19.9 ***	

*: P < 0.1; **: P < 0.05; ***: P < 0.01; ns: not significant.

Table 6 – Effects of multiple sclerosis on employment and income in the study population according to year of long-term disease registration for multiple sclerosis.

Time to MS	T-1 (reference)	T + 1	T + 2	T + 3	T + 4	T + 5	T + 10	%
< = 1998								
Number of people with MS		245	239	239	234	236	201	
Employment	86.0	-9.4 ***	-16.2 ***	-16.1 ***	-21.2 ***	-25.8 ***	-31.8 ***	
Unemployment	4.8	-0.4 ns	-0.3 ns	-1.6 ns	-1.5 ns	0.0 ns	-2.7 ns	
Inactivity	9.2	9.8 ***	16.5 ***	17.6 ***	22.8 ***	25.8 ***	34.5 ***	
Sickness leave	15.2	22.4 ***	17.9 ***	13.3 ***	5.0 ns	5.3 ns	-5.7 *	
Disability pension	9.6	5.5 ***	15.9 ***	30.7 ***	35.6 ***	38.7 ***	53.4 ***	
Relative income (median = 100)	116	-22 ***	-23 ***	-26 ***	-35 ***	-40 ***	-50 ***	
Income percentile	57.4	-7.2 ***	-7.6 ***	-7.9 ***	-10.4 ***	-10.9 ***	-12.5 ***	
Part of replacement income in total income	18.2	5.9 ***	12.8 ***	24.3 ***	26.9 ***	32.2 ***	42.1 ***	
Relative wage (median = 100)	116	-26.8 ***	-32 ***	-41 ***	-51 ***	-58 ***	-72 ***	
Wage percentile	55.8	-7.7 ***	-9.6 ***	-12.6 ***	-15.4 ***	-16.8 ***	-20.7 ***	
> 1998								
Number of people with MS		652	633	575	524	456	231	
Employment	88.9	-5.9 ***	-10.5 ***	-16.8 ***	-20.1 ***	-20.8 ***	-26.0 ***	
Unemployment	4.4	-0.6 ns	0.6 ns	4.3 ***	2.6 *	2.1 ns	1.0 ns	
Inactivity	6.8	6.5 ***	9.8 ***	12.5 ***	17.6 ***	18.7 ***	25.1 ***	
Sickness leave	12.2	25.6 ***	19.7 ***	10.2 ***	2.2 ns	1.0 ns	-3.3 ns	
Disability pension	6.5	4.4 ***	15.1 ***	25.8 ***	31.9 ***	34.7 ***	48.0 ***	
Relative income (median = 100)	129	-13 ***	-18 ***	-24 ***	-30 ***	-29 ***	-39 ***	
Income percentile	58.2	-3.0 ***	-3.8 ***	-5.3 ***	-6.9 ***	-7.2 ***	-10.3 ***	
Part of replacement income in total income	15.4	12.8 ***	16.7 ***	22.3 ***	25.4 ***	26.9 ***	38.2 ***	
Relative wage (median = 100)	130	-25.4 ***	-32 ***	-40 ***	-47 ***	-46 ***	-60 ***	
Wage percentile	57.1	-6.1 ***	-7.9 ***	-10.3 ***	-12.8 ***	-13.3 ***	-18.2 ***	

*: P < 0.1; **: P < 0.05; ***: P < 0.01; ns: not significant.

LTD registration, persisting over 3 years and then reducing over time. The same profile, i.e. a sharp increase over time, was also systematically observed regarding the effects of MS on disability pension (Fig. 4). People > 38 years old at LTD

registration for MS had a higher increase of disability pension over time (+63.9 pp vs. +41.7 pp at T + 10), which seems consistent with the fact that they were less likely to remain employed. The part of disability pension among people with

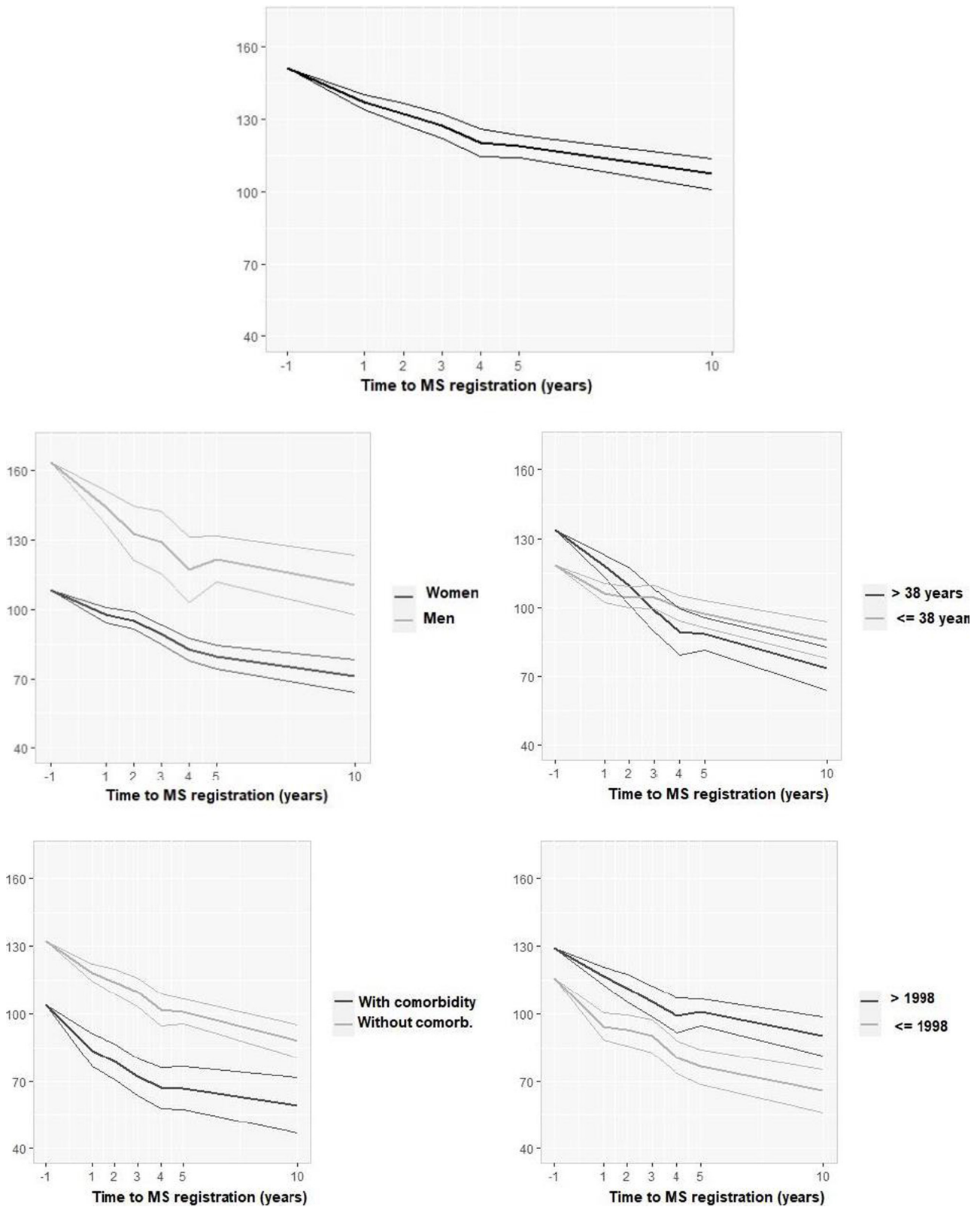


Fig. 5 – Effects of multiple sclerosis on relative income (median = 100) according to time from/to MS registration (T, years), overall and by subgroups.

comorbidities increased by +59.5 pp after 10 years, compared with +48.1 pp in the absence of comorbidity.

In terms of relative income, there were distinct trends among subgroups (Fig. 5). Firstly, according to sex (Fig. 5 and Table 3), we showed that the evolution of the employment rate was almost similar, whereas significant differences were observed between men and women for wages and income. Indeed, among women who had a lower initial income than men (108 compared with 164), relative income deteriorated less sharply than among men (−37 pp vs. −53 pp at T + 10). However, relative income at the end of the period remained in favor of men. As women were very close to the median income at the time they registered for MS, they fell below this level in the first year after LTD registration while men remained above the median income at 10 years. Older people at LTD registration had higher relative income before MS than younger people (134 vs. 119 at T−1) but experienced a stronger decrease over time (−61 vs. −33 at T + 10), putting them in a less favored situation (Fig. 5 and Table 4). People with comorbidity were less favored before MS compared to people without comorbidity (104 compared to 132), but MS reduced the relative income of both groups of same magnitude (−44 pp at T + 10), so that the gap between the two groups remained unchanged (Fig. 5 and Table 5). However, the situation of people with comorbidities was more worrying, since they received 60% of the median income at T + 10. For people with LTD registration before 1998, the drop in income was greater (−50 pp after 10 years) than for people with registration after 1998 (−39 pp), meaning that the level of income was better preserved in the recent period (Fig. 5 and Table 6).

4. Discussion

Using longitudinal administrative data from a French random sample of salaried workers, we found that MS had significant, strong and negative effects on work. From the first year following LTD registration, MS reduces the probability of being employed and increases the probability of being inactive and receiving disability pension.

The size of the HYGIE database allowed estimation by the DiD method with exact matching, to constitute a large control group that was fully comparable to MS population. This statistical method aimed to identify the specific effects of MS by neutralizing the other effects that can influence occupational trajectories, whether they are linked to the individuals or to the economic situation. Thus, the observed decline in the employment rate considers individual characteristics of age, sex, previous health status and previous employment, as well as changes in the labor market in France over time. Quantifying the effect of MS on occupational trajectories in comparison with a matched control group provides an opportunity to measure the direct and indirect effects of the disease. Indeed, the direct effects of the disease are the consequences of relapse occurrence, presence of symptoms, disability accumulation, etc., whereas the indirect effects can relate to the occurrence of comorbidities or lifestyle changes due to MS. The same type of questions about the direct and indirect effects of MS arises when studying other outcomes, such as mortality [5].

Some results are probably related to the French regulatory framework. The switch from sickness leave to disability pension in the first 3 years can be explained by changes in rights: transition to long illness after 6 months off work, then to disability within a maximum of 3 years. Similarly, the result showing that the impact of MS has no influence on unemployment, except in the third year, is certainly linked to the risk of dismissal for unfitness (medical reason) prior to initiation of disability pension.

The decrease of employment led to a sharp increase in inactivity and, in parallel, disability pension, overall and in the following subgroups: people who were older when they registered LTD for MS (> 38 years old), people who had oldest registration (< = 1998), and people with comorbidities. The issue of comorbidities is playing an increasing role in the field of MS [16], due to the multiple consequences: delay in diagnosis, complexity of management, progression of disability, etc. In a recent study from Northern Europe [17], the authors also showed a high level of disability pension in the MS population compared with the matched general population (50% vs. 20%) and observed that, in 15% of cases, disability pension depended not only on MS, but also on other diseases.

Subgroup analyses showed negative effects of MS of decreased magnitude in the most recent period (after 1998), which is consistent with findings from a Finnish study [18]. Among 484 people with MS, they found that the risk of getting disability pension was lower after 1995 than before (HR 0.41 [0.31–0.55]). The median time between diagnosis and onset of disability pension increased from 8.3 years for people diagnosed before 1995 to 11.1 years for those diagnosed more recently. These differences may reflect differences in diagnosis and/or treatment. Indeed, changes in MS management (such as new drugs, early treatment, and multidisciplinary care [19]) may have a positive effect on job retention for people with MS. Due to lack of information in the database, it was not possible to carry out analyses according to disease-modifying treatments or visits to MS expert centers.

Age had a significant effect. Indeed, the oldest people at LTD registration received more often disability pension at that time, and their proportion increased more sharply each year compared with younger patients. We do not know the age at MS diagnosis but it has been observed that late-onset MS has a poorer prognosis and is more often progressive [20].

Regarding sex, we observed that the employment rate was quite comparable between men and women before MS, and that the effects of MS were more or less the same in both groups.

The difference between relative wage and relative income indicates the level of financial compensation provided by replacement income. We found that the French social protection system limits the deterioration in people's financial situation by 20 points. Indeed, by comparing the effect of MS on relative indicators, we can see that replacement income avoids a drop of 21 ranks (−65 for wages vs. −44 for income at T + 10, and respectively −96 vs. −75 at T + 20). At 20 years, replacement income represents almost 75% of total income, which enables people to limit the loss of resources. However, both relative wage and relative income fall below the median. We do not have explanations regarding the fact that relative income (151) and relative wage (126) were so high at T−1.

Indeed, there is no clear relationship between socio-economic status and risk of MS, and we cannot rule out a risk of under-diagnosis or under-registration for LTD in people with low income.

Subgroup analyses have highlighted specific situations regarding wages and income. The effects known in the literature on sex differences (lower wages for women for equivalent tasks, less stable employment, part-time work and more frequent career breaks) were probably observed, as men have higher wages than women, and men were in a more favorable situation than the average French population of private-sector employees before MS. At 10 years, the financial situation was still more favorable for men. However, this difference in income was not linked to a higher retention job in men. Indeed, the proportion of replacement income was very similar according to sex, and has changed in the same way over time for men and women. Therefore, we do think that the better situation observed for men was related to their much higher initial wage than women.

The presence of comorbidity was the only situation that results in a worse financial situation than the average salaried population at the index date: their wage was below the median, but this phenomenon due to a lesser capacity to work was compensated by replacement income, so that income was above the median.

It is worth highlighting the strengths and weaknesses of our study. The use of administrative data has several advantages: there is no 'refusal' to participate, there is little or no missing data (and unlike surveys conducted directly with patients: no unavailability due to illness, refusal to respond or inability to be contacted), and there is little or no attrition. That being said, the lack of clinical data also leads to certain limitations. Firstly, the date of LTD registration for MS does not necessarily correspond to the date of diagnosis, and even less to MS clinical onset. We do not have a reference period for time before such registration, and it is likely to vary according to a number of factors such as the initial characteristics of the disease, in particular the severity of the first episode(s), the need for disease-modifying treatment, etc. It is probably the reason why the proportion of people being on sick leave or receiving disability pension was not null before LTD registration for MS (T-1). With regard to period effects, we are unable to test our hypotheses due to lack of data. Identification of MS cases relied on a unique criterion, namely "G35" ICD-10 code as the reason for LTD registration. Despite the medical validation of this registration by a doctor from the health insurance system, we cannot exclude a risk of false positives (i.e. the inclusion of people without MS in the MS population) or false negatives (i.e. the inclusion of people with MS in the control group). If it exists, we believe that this bias does not call into question the results or the message of this study.

Finally, we do not have characteristics of work (fixed-term or open-ended contract, full-time or part-time, type of tasks, etc.). The sample used in the HYGIE database is a random sample of private sector employees and is therefore representative of this sector. However, the results observed cannot be extrapolated to other sectors, particularly the public sector or that of self-employed workers. The final limitation was that only income from public social protection was taken into account, while people may benefit from additional income

from private insurance or company pension schemes. At present, no source can be used to estimate the number of people receiving this additional income, or the level of the amounts received.

To conclude, the present study demonstrated that MS has strongly negative and lasting effects on work in a large sample of private sector employees in France. The employment rate deteriorates rapidly after people had LTD registration for MS, overall and in all subgroups. While relative wage and relative income were above the median at the index date, all subgroups (except men) fall below the median income after 10 years. However, even if the losses of wages and income vary, the same gap of around 20 points at 10 years is found between wages and income in each subgroup. This highlights that the French social protection system is not more favorable to certain categories, which implies that initial inequalities are probably maintained [21].

Funding

This work was supported by Fondation pour l'Aide à la Recherche sur la Sclérose en Plaques (Fondation ARSEP). The funding agency had no role in the design nor execution of the study, including the collection, management, analysis or interpretation of the data; the preparation, review or approval of the manuscript; or decision to submit the manuscript for publication.

Disclosure of interest

The authors declare that they have no competing interest.

REFERENCES

- [1] Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie RA, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Mult Scler* 2020;26(14):1816-21. <http://dx.doi.org/10.1177/1352458520970841>.
- [2] Foulon S, Maura G, Dalichampt M, Alla F, Debouverie M, Moreau T, et al. Prevalence and mortality of patients with multiple sclerosis in France in 2012: a study based on French health insurance data. *J Neurol* 2017;264(6):1185-92.
- [3] Roux J, Guilleux A, Lefort M, Leray E. Use of health care services from patients with multiple sclerosis in France over 2010-2015: a nationwide population-based study using health administrative data. *Mult Scler J Exp Transl Clin* 2019;5(4). <http://dx.doi.org/10.1177/2055217319896090> [2055217319896090].
- [4] Leray E, Vukusic S, Debouverie M, Clanet M, Brochet B, de Sèze J, et al. Excess mortality in patients with multiple sclerosis starts at 20 years from clinical onset: data from a large-scale French observational study. *PLoS One* 2015;10(7):e0132033.
- [5] Rollot F, Fauvernier M, Uhry Z, Vukusic S, Bossard N, Remontet L, et al. Effects of age and disease duration on excess mortality in patients with multiple sclerosis from a French nationwide cohort. *Neurology* 2021;97(4):e403-13. <http://dx.doi.org/10.1212/WNL.0000000000001224>.

- [6] Lebrun-Frenay C, Kobelt G, Berg J, Capsa D, Gannedahl M, European Multiple Sclerosis Platform.. et al. New insights into the burden and costs of multiple sclerosis in Europe: Results for France. *Mult Scler* 2017;23(2_Suppl.):65-77. <http://dx.doi.org/10.1177/1352458517708125>.
- [7] http://www.rolche.fr/content/dam/rolche_france/fr_FR/doc/Impact%20psycho-social%20de%20la%20sclerose%20en%20plaques%20dans%20la%20sphere%20professionnelle.pdf [Accessed August 2023].
- [8] Fantoni-Quinton S, Kwiatkowski A, Vermersch P, Roux B, Hauteceur P, Leroyer A. Impact of multiple sclerosis on employment and use of job-retention strategies: The situation in France in 2015. *J Rehabil Med* 2016;48(6):535-40. <http://dx.doi.org/10.2340/16501977-2093>.
- [9] Ongagna JC, Passadori A, Pinelli J, Isner-Horobeti ME, Zaenker C, De Seze J. Difficulties experienced at work by patients with multiple sclerosis. *Rev Neurol (Paris)* 2015;171(11):782-6. <http://dx.doi.org/10.1016/j.neurol.2015.06.007>.
- [10] Kwiatkowski A, Marissal JP, Pouyfaucou M, Vermersch P, Hauteceur P, Dervaux B. Social participation in patients with multiple sclerosis: correlations between disability and economic burden. *BMC Neurol* 2014;14:115. <http://dx.doi.org/10.1186/1471-2377-14-115>.
- [11] Lefeuvre D, Rudant J, Foulon S, Alla F, Weill A. Healthcare expenditure of multiple sclerosis patients in 2013: A nationwide study based on French health administrative databases. *Mult Scler J Exp Transl Clin* 2017;3(3) [2055217317730421].
- [12] Vitturi BK, Rahmani A, Dini G, Montecucco A, Debarbieri N, Sbragia E, et al. Occupational outcomes of people with multiple sclerosis: a scoping review. *BMJ Open* 2022;12(7):e058948. <http://dx.doi.org/10.1136/bmjopen-2021-058948>.
- [13] Lechner M. The estimation of causal effects by difference-in-differences methods. *Found Trends Econometr* 2010;4:165-224.
- [14] Duguet E. Measuring the effect of health events in the labour market. In: Hashimzade N, Thornton MA, editors. *Handbook of research methods and applications in empirical microeconomics*. Cheltenham, UK: Edward Elgar Publishing; 2021.
- [15] <https://www.irdes.fr/recherche/2018/rapport-568-consequences-de-la-survenue-du-cancer-sur-les-parcours-professionnels.html> [Accessed August 2023].
- [16] Marrie RA, Fisk JD, Fitzgerald K, Kowalec K, Maxwell C, Rotstein D, et al. Etiology, effects and management of comorbidities in multiple sclerosis: recent advances. *Front Immunol* 2023;14:1197195. <http://dx.doi.org/10.3389/fimmu.2023.1197195>.
- [17] Murlay C, Karampampa K, Alexanderson K, Hillert J, Friberg E. Diagnosis-specific sickness absence and disability pension before and after multiple sclerosis diagnosis: An 8-year nationwide longitudinal cohort study with matched references. *Mult Scler Relat Disord* 2020;42:102077. <http://dx.doi.org/10.1016/j.msard.2020.102077>.
- [18] Heinonen T, Castrén E, Luukkaala T, Mäkinen K, Ruutiainen J, Kuusisto H. The retirement rate due to multiple sclerosis has decreased since 1995 – A retrospective study in a Finnish central hospital. *Mult Scler Relat Disord* 2020;45:102360. <http://dx.doi.org/10.1016/j.msard.2020.102360>.
- [19] Derache N, Dufay A, Lebarbey C. Organization of care for multiple sclerosis in France. *Rev Neurol (Paris)* 2018;174(6):475-9. <http://dx.doi.org/10.1016/j.neurol.2018.01.366>.
- [20] Naseri A, Nasiri E, Sahraian MA, Daneshvar S, Talebi M. Clinical features of late-onset multiple sclerosis: a systematic review and meta-analysis. *Mult Scler Relat Disord* 2021;50:102816. <http://dx.doi.org/10.1016/j.msard.2021.102816>.
- [21] Leray E, Espagnacq M, Duguet E, Guillaume S, Guilleux A, Pichetti S, et al. Conséquences de la sclérose en plaques sur les parcours professionnels en France. Étude EMOJI (Effects of Multiple Sclerosis on Occupational Trajectories), Rapport Irdes, 589. 2023, <https://www.irdes.fr/recherche/2023/rapport-589-consequences-de-la-sclerose-en-plaques-sur-les-parcours-professionnels-en-france.html>.