

Electronic Supplementary Material

Cost-of-Illness Progression Before and After Diagnosis of Multiple Sclerosis: A Nationwide Register-Based Cohort Study in Sweden of People Newly Diagnosed with Multiple Sclerosis and a Population-Based Matched Reference Group

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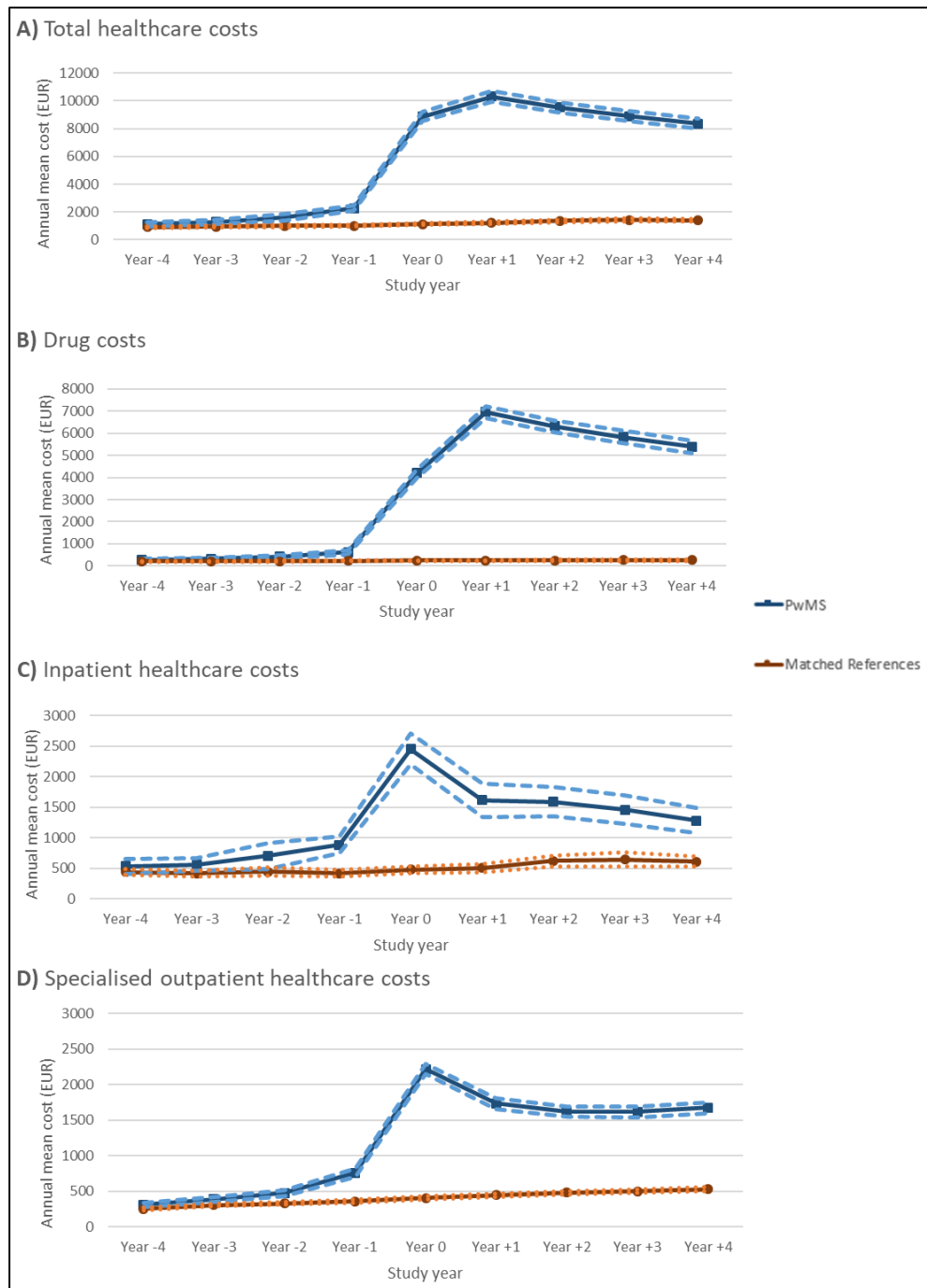


Figure 1: Unadjusted mean per person annual healthcare costs and the respective component costs with 95% confidence intervals for the PwMS (n=1988) compared with the population-based matched references without MS (n=7981) [(a) Total healthcare costs (b) Drug costs, (c) Inpatient healthcare costs, (d) Specialised outpatient healthcare costs] from Y₋₄ to Y₊₄.

Notes: Costs are presented as Euros with 2019 values. Y₀ represents the year of diagnosis with MS.

Abbreviations: EUR: Euros; MS: multiple sclerosis; PwMS: People with multiple sclerosis

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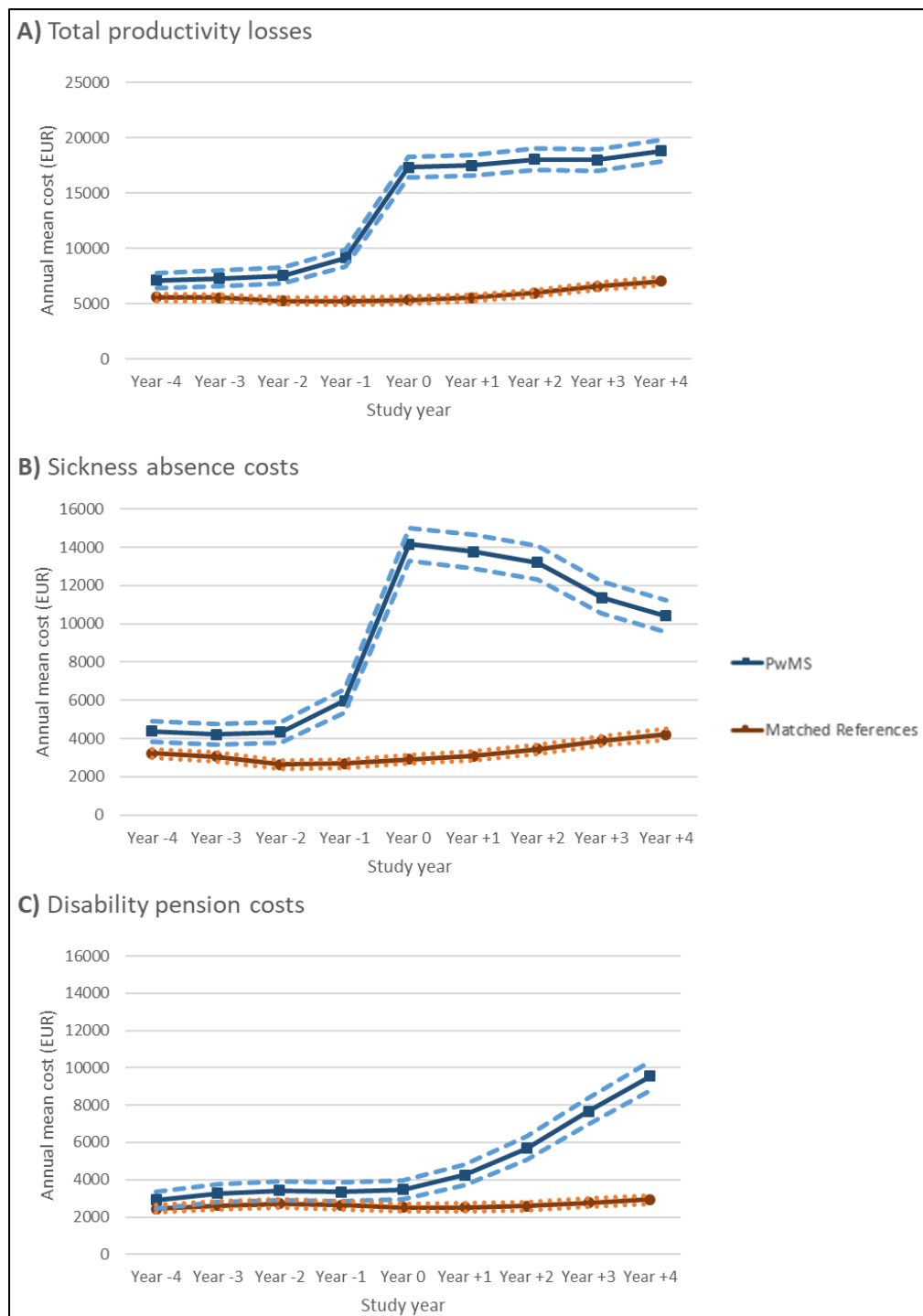


Figure 1: Unadjusted mean per person annual productivity losses and the respective component costs with 95% confidence intervals for the PwMS (n=1988) compared with the population-based matched references without MS (n=7981) [(a) Total productivity losses (b) Sickness absence costs, (c) Disability pension costs] from Y₋₄ to Y₊₄.

Notes: Costs are presented as Euros with 2019 values. Y₀ represents the year of diagnosis with MS.

Abbreviations: EUR: Euros; MS: Multiple sclerosis; PwMS: People with multiple sclerosis

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Table 1: The proportions of annual total costs, healthcare costs, and productivity losses that the cost components contribute to among the people with multiple sclerosis (PwMS) (n=1988) and the population-based matched references without multiple sclerosis (n=7981)

	PwMS									Matched References								
	Year ₋₄	Year ₋₃	Year ₋₂	Year ₋₁	Year ₀	Year ₊₁	Year ₊₂	Year ₊₃	Year ₊₄	Year ₋₄	Year ₋₃	Year ₋₂	Year ₋₁	Year ₀	Year ₊₁	Year ₊₂	Year ₊₃	Year ₊₄
Percentage of total costs																		
Drug costs	3.3%	3.8%	4.6%	5.5%	16.0%	25.0%	22.9%	21.7%	19.8%	3.2%	3.3%	3.5%	3.7%	3.8%	3.6%	3.5%	3.4%	3.1%
Inpatient healthcare costs	6.5%	6.6%	7.7%	7.7%	9.3%	5.8%	5.8%	5.4%	4.7%	6.8%	6.4%	7.2%	6.7%	7.5%	7.5%	8.5%	8.1%	7.2%
Specialised outpatient healthcare costs	3.8%	4.5%	5.2%	6.7%	8.5%	6.2%	5.9%	6.0%	6.2%	3.9%	4.8%	5.3%	5.8%	6.3%	6.7%	6.6%	6.3%	6.3%
Healthcare costs subtotal	13.6%	15.0%	17.5%	19.9%	33.9%	37.1%	34.5%	33.1%	30.7%	14.0%	14.5%	16.0%	16.2%	17.6%	17.8%	18.7%	17.9%	16.6%
Sickness absence costs	50.9%	46.8%	45.1%	50.9%	52.9%	47.6%	44.9%	38.4%	34.1%	48.1%	45.2%	40.6%	41.6%	43.5%	44.8%	45.8%	47.3%	48.7%
Disability pension costs	35.4%	38.3%	37.4%	29.2%	13.3%	15.3%	20.6%	28.5%	35.2%	37.9%	40.3%	43.4%	42.2%	38.9%	37.4%	35.5%	34.8%	34.7%
Productivity losses subtotal	86.4%	85.0%	82.5%	80.1%	66.1%	62.9%	65.5%	66.9%	69.3%	86.0%	85.5%	84.0%	83.8%	82.4%	82.2%	81.3%	82.1%	83.4%
Percentage of healthcare costs																		
Drug costs	24.5%	25.6%	26.1%	27.6%	47.4%	67.5%	66.3%	65.5%	64.6%	23.1%	22.8%	21.8%	23.0%	21.3%	20.4%	19.0%	19.2%	18.7%
Inpatient healthcare costs	47.6%	44.1%	44.1%	38.8%	27.6%	15.6%	16.7%	16.4%	15.3%	48.9%	44.3%	44.9%	41.2%	42.7%	42.3%	45.6%	45.4%	43.3%
Specialised outpatient healthcare costs	27.9%	30.3%	29.9%	33.5%	25.0%	16.8%	17.0%	18.1%	20.1%	27.9%	32.9%	33.3%	35.8%	36.0%	37.3%	35.4%	35.3%	38.0%
Percentage of productivity losses																		
Sickness absence costs	59.0%	55.0%	54.7%	63.5%	80.0%	75.7%	68.5%	57.4%	49.2%	56.0%	52.8%	48.4%	49.7%	52.8%	54.4%	56.4%	57.7%	58.4%
Disability pension costs	41.0%	45.0%	45.3%	36.5%	20.0%	24.3%	31.5%	42.6%	50.8%	44.0%	47.2%	51.6%	50.3%	47.2%	45.6%	43.6%	42.3%	41.6%

Notes: Proportions of the total productivity losses were adjusted for maximum possible net days of sickness absence and disability pension for the respective year. Accordingly, the sickness absence subtotal was adjusted to sum to the total productivity losses sum, rather than using the sickness absence costs presented in Table 3.

Abbreviations: PwMS: People with multiple sclerosis

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Table 1: Results from the GEE models assessing the association between MS and cost of illness (total costs, healthcare costs and productivity losses) among the people with multiple sclerosis (n=1988) compared with population-based matched references without multiple sclerosis (n=7981) with log link, Poisson distribution, and autoregressive correlations.

		Model 1a ¹			Model 2a ²			Model 3a ³			Model 4a ⁴		
		IRR ⁵	95% CI	p-value	IRR ⁵	95% CI	p-value	IRR ⁵	95% CI	p-value	IRR ⁵	95% CI	p-value
Total costs													
MS	MS (ref = no MS)	2.94	[2.78-3.10]	<0.001	2.93	[2.77-3.09]	<0.001	2.79	[2.65-2.94]	<0.001	2.76	[2.62-2.90]	<0.001
Study Year	Year-3 (ref = Year-4)	1.01	[0.98-1.05]	0.431	1.01	[0.98-1.05]	0.437	1.02	[0.98-1.06]	0.300	1.02	[0.98-1.05]	0.379
	Year-2	1.06	[1.02-1.10]	0.005	1.06	[1.02-1.10]	0.005	1.06	[1.02-1.10]	0.004	1.06	[1.02-1.10]	0.004
	Year-1	1.08	[1.03-1.13]	0.001	1.08	[1.03-1.13]	0.001	1.08	[1.04-1.13]	0.001	1.08	[1.03-1.13]	0.001
	Year0	1.49	[1.42-1.56]	<0.001	1.49	[1.42-1.56]	<0.001	1.50	[1.43-1.57]	<0.001	1.49	[1.42-1.56]	<0.001
	Year+1	1.62	[1.54-1.71]	<0.001	1.63	[1.55-1.71]	<0.001	1.63	[1.56-1.71]	<0.001	1.63	[1.55-1.71]	<0.001
	Year+2	1.68	[1.60-1.76]	<0.001	1.68	[1.60-1.76]	<0.001	1.69	[1.61-1.77]	<0.001	1.69	[1.61-1.77]	<0.001
	Year+3	1.71	[1.63-1.79]	<0.001	1.71	[1.63-1.79]	<0.001	1.72	[1.64-1.80]	<0.001	1.71	[1.64-1.80]	<0.001
	Year+4	1.77	[1.69-1.86]	<0.001	1.77	[1.69-1.86]	<0.001	1.79	[1.71-1.87]	<0.001	1.78	[1.70-1.87]	<0.001
Age	Age (years)				1.03	[1.03-1.03]	<0.001	1.03	[1.03-1.04]	<0.001	1.02	[1.01-1.02]	<0.001
Birth country	Not in Sweden (ref = Sweden)				1.25	[1.15-1.36]	<0.001	0.93	[0.86-1.02]	0.107	1.18	[1.09-1.28]	<0.001
Living area	Other large cities (ref = Stockholm)				1.05	[0.96-1.15]	0.295	1.02	[0.93-1.11]	0.660	1.05	[0.97-1.15]	0.234
	Medium-sized towns				1.03	[0.95-1.11]	0.532	0.96	[0.89-1.03]	0.269	1.05	[0.98-1.14]	0.182
	Rural				1.17	[1.08-1.27]	<0.001	1.05	[0.98-1.14]	0.179	1.18	[1.09-1.28]	<0.001
Sex	Men (ref = Women)				0.67	[0.63-0.72]	<0.001	0.66	[0.62-0.71]	<0.001	0.78	[0.73-0.83]	<0.001
Cohort	2011 (ref= 2010)				1.05	[0.99-1.13]	0.122	1.07	[1.00-1.13]	0.051	1.05	[0.99-1.12]	0.131
	2012				1.01	[0.94-1.08]	0.840	1.03	[0.97-1.10]	0.300	1.01	[0.95-1.08]	0.729
Work	Manager (ref= Office work)							0.57	[0.46-0.69]	<0.001			
	Manual labour/customer service							1.32	[1.23-1.42]	<0.001			
	Unclassified work							1.33	[1.17-1.50]	<0.001			
	Not in paid work							3.15	[2.90-3.41]	<0.001			
Family composition	Children living at home (ref= No)							1.00	[0.94-1.07]	0.880			
	Cohabiting/married (ref = No)							0.85	[0.79-0.90]	<0.001			
Educational level	University/college (ref = No)							0.72	[0.68-0.77]	<0.001			
Comorbidity	1-2 categories (ref=0)										1.59	[1.47-1.71]	<0.001

3-4 categories											3.23	[2.96-3.52]	<0.001
5+ categories											4.89	[4.43-5.39]	<0.001
Healthcare costs													
MS	MS (ref = no MS)	5.26	[4.97-5.55]	<0.001	5.25	[4.97-5.55]	<0.001	5.20	[4.92-5.49]	<0.001	5.06	[4.79-5.34]	<0.001
Study Year	Year-3 (ref = Year-4)	1.10	[1.03-1.18]	0.007	1.10	[1.03-1.18]	0.007	1.10	[1.03-1.18]	0.007	1.10	[1.03-1.18]	0.007
	Year-2	1.28	[1.18-1.39]	<0.001	1.28	[1.18-1.39]	<0.001	1.28	[1.18-1.39]	<0.001	1.28	[1.18-1.39]	<0.001
	Year-1	1.35	[1.24-1.47]	<0.001	1.35	[1.24-1.47]	<0.001	1.35	[1.24-1.47]	<0.001	1.35	[1.24-1.47]	<0.001
	Year0	2.77	[2.55-3.00]	<0.001	2.77	[2.55-3.00]	<0.001	2.77	[2.56-3.00]	<0.001	2.77	[2.56-3.00]	<0.001
	Year+1	3.26	[3.01-3.54]	<0.001	3.26	[3.01-3.54]	<0.001	3.27	[3.01-3.54]	<0.001	3.27	[3.01-3.54]	<0.001
	Year+2	3.24	[2.99-3.51]	<0.001	3.24	[2.99-3.51]	<0.001	3.24	[3.00-3.51]	<0.001	3.24	[3.00-3.51]	<0.001
	Year+3	3.13	[2.88-3.39]	<0.001	3.12	[2.88-3.39]	<0.001	3.13	[2.88-3.39]	<0.001	3.13	[2.88-3.39]	<0.001
	Year+4	2.98	[2.75-3.23]	<0.001	2.98	[2.75-3.23]	<0.001	2.98	[2.75-3.23]	<0.001	2.98	[2.75-3.23]	<0.001
	Age	Age (years)				1.00	[1.00-1.00]	0.146	1.00	[1.00-1.01]	0.001	0.99	[0.99-1.00]
Birth country	Not in Sweden (ref = Sweden)				1.01	[0.93-1.10]	0.818	0.90	[0.83-0.98]	0.014	0.97	[0.89-1.05]	0.425
Living area	Other large cities (ref = Stockholm)				0.92	[0.85-1.00]	0.048	0.91	[0.84-0.98]	0.014	0.94	[0.87-1.02]	0.141
	Medium-sized towns				0.88	[0.82-0.95]	0.001	0.86	[0.80-0.92]	<0.001	0.91	[0.85-0.98]	0.012
	Rural				0.89	[0.83-0.96]	0.004	0.86	[0.79-0.93]	<0.001	0.91	[0.84-0.98]	0.013
Sex	Men (ref = Women)				0.85	[0.80-0.90]	<0.001	0.84	[0.80-0.90]	<0.001	0.93	[0.88-0.99]	0.023
Cohort	2011 (ref= 2010)				1.00	[0.94-1.07]	0.890	1.01	[0.95-1.08]	0.787	0.99	[0.93-1.06]	0.863
	2012				0.98	[0.92-1.05]	0.564	0.99	[0.93-1.06]	0.816	0.99	[0.93-1.05]	0.700
Work	Manager (ref= Office work)							0.83	[0.72-0.96]	0.010			
	Manual labour/customer service							1.12	[1.05-1.19]	<0.001			
	Unclassified work							1.16	[1.04-1.29]	0.007			
	Not in paid work							1.71	[1.54-1.90]	<0.001			
Family composition	Children living at home (ref= No)							0.99	[0.92-1.06]	0.804			
	Cohabiting/married (ref = No)							0.95	[0.88-1.02]	0.167			
Educational level	University/college (ref = No)							0.95	[0.89-1.01]	0.095			
Comorbidity	1-2 categories (ref=0)										1.28	[1.20-1.36]	<0.001
	3-4 categories										1.97	[1.81-2.15]	<0.001
	5+ categories										3.40	[3.00-3.86]	<0.001
Productivity losses													
MS	MS (ref = no MS)	2.38	[2.25-2.52]	<0.001	2.38	[2.24-2.54]	<0.001	2.29	[2.16-2.43]	<0.001	2.25	[2.12-2.39]	<0.001
Study Year	Year-3 (ref = Year-4)	1.00	[0.97-1.04]	0.924	1.00	[0.96-1.04]	0.934	1.01	[0.97-1.05]	0.743	1.00	[0.97-1.04]	0.881

	Year-2	1.02	[0.98-1.06]	0.344	1.02	[0.98-1.06]	0.392	1.02	[0.98-1.06]	0.377	1.02	[0.98-1.06]	0.387
	Year-1	1.04	[1.00-1.09]	0.078	1.04	[0.99-1.09]	0.093	1.04	[1.00-1.10]	0.067	1.04	[0.99-1.09]	0.084
	Year0	1.29	[1.23-1.35]	<0.001	1.29	[1.23-1.36]	<0.001	1.30	[1.24-1.36]	<0.001	1.30	[1.23-1.36]	<0.001
	Year+1	1.36	[1.30-1.43]	<0.001	1.36	[1.30-1.44]	<0.001	1.37	[1.30-1.44]	<0.001	1.37	[1.30-1.44]	<0.001
	Year+2	1.43	[1.36-1.51]	<0.001	1.43	[1.36-1.51]	<0.001	1.44	[1.37-1.51]	<0.001	1.43	[1.36-1.51]	<0.001
	Year+3	1.49	[1.41-1.57]	<0.001	1.49	[1.41-1.56]	<0.001	1.50	[1.43-1.57]	<0.001	1.49	[1.42-1.57]	<0.001
	Year+4	1.58	[1.50-1.67]	<0.001	1.59	[1.51-1.67]	<0.001	1.60	[1.52-1.68]	<0.001	1.59	[1.52-1.67]	<0.001
Age	Age (years)				1.04	[1.03-1.04]	<0.001	1.04	[1.04-1.05]	<0.001	1.02	[1.02-1.03]	<0.001
Birth country	Not in Sweden (ref = Sweden)				1.32	[1.21-1.45]	<0.001	0.94	[0.86-1.03]	0.207	1.25	[1.14-1.37]	<0.001
Living area	Other large cities (ref = Stockholm)				1.09	[0.98-1.22]	0.121	1.06	[0.95-1.18]	0.275	1.09	[0.98-1.21]	0.111
	Medium-sized towns				1.07	[0.98-1.18]	0.142	0.99	[0.91-1.09]	0.902	1.10	[1.00-1.20]	0.044
	Rural				1.27	[1.16-1.40]	<0.001	1.12	[1.03-1.23]	0.011	1.28	[1.17-1.40]	<0.001
Sex	Men (ref = Women)				0.62	[0.58-0.68]	<0.001	0.62	[0.57-0.66]	<0.001	0.74	[0.68-0.79]	<0.001
Cohort	2011 (ref= 2010)				1.07	[0.99-1.16]	0.092	1.08	[1.01-1.16]	0.033	1.07	[0.99-1.15]	0.081
	2012				1.02	[0.94-1.10]	0.707	1.05	[0.97-1.13]	0.211	1.02	[0.94-1.10]	0.635
Work	Manager (ref= Office work)							0.49	[0.37-0.65]	<0.001			
	Manual labour/customer service							1.39	[1.28-1.52]	<0.001			
	Unclassified work							1.36	[1.17-1.59]	<0.001			
	Not in paid work							3.68	[3.35-4.03]	<0.001			
Family composition	Children living at home (ref= No)							1.02	[0.95-1.09]	0.645			
	Cohabiting/married (ref = No)							0.82	[0.76-0.88]	<0.001			
Educational level	University/college (ref = No)							0.66	[0.61-0.71]	<0.001			
Comorbidity	1-2 categories (ref=0)										1.73	[1.57-1.91]	<0.001
	3-4 categories										3.78	[3.40-4.20]	<0.001
	5+ categories										5.57	[4.97-6.24]	<0.001

¹ Model 1a: Cost = MS + year.

² Model 2a: Included the covariates included in Model 1a + the matching variables (age + sex + country of birth + living area) + cohort.

³ Model 3a: Included the covariates included in Model 2a + educational level + children living at home + cohabiting/married + work.

⁴ Model 4a: Included the covariates included in Model 2a + comorbidity. Comorbidity is according to a modified RxRisk Comorbidity index constructed with ATC codes from the SPDR (excluding MS DMTs) or whether in the Swedish Cancer Register. Comorbidity refers to the number of condition categories within the calendar year of Y-4.

⁵ The coefficients are presented exponentiated as incidence rate ratios (IRRs) which can be interpreted as population averaged multipliers of the cost excess.

Abbreviations: ATC: Anatomical Therapeutic Chemical Classification System; DMT: Disease modifying therapy; CI: Confidence interval; GEE: Generalised estimating equation; IRR: Incidence rate ratio; MS: Multiple sclerosis; ref: Reference group in regression model

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Table 1: Time trends in the excess cost progression (total costs, healthcare costs and productivity losses) among the people with multiple sclerosis (n=1988) compared with the population-based matched references without multiple sclerosis (n=7981) from GEE models including an interaction term MS*year with log link, Poisson distribution, and autoregressive correlations.

		Model 1b ¹			Model 2b ²			Model 3b ³		
		IRR ⁴	95% CI	p-value	IRR ⁴	95% CI	p-value	IRR ⁴	95% CI	p-value
Total costs										
MS	MS (ref = no MS)	1.20	[1.07-1.34]	0.002	1.21	[1.08-1.35]	0.001	1.20	[1.08-1.32]	0.001
Study Year	Year-3 (ref = Year-4)	1.01	[0.97-1.05]	0.783	1.00	[0.97-1.05]	0.831	1.01	[0.97-1.05]	0.754
	Year-2	0.98	[0.93-1.02]	0.287	0.97	[0.93-1.02]	0.274	0.98	[0.93-1.02]	0.296
	Year-1	0.97	[0.92-1.03]	0.345	0.97	[0.93-1.03]	0.333	0.98	[0.93-1.03]	0.371
	Year0	0.98	[0.93-1.04]	0.489	0.98	[0.93-1.04]	0.490	0.99	[0.94-1.04]	0.588
MS*Year	Year+1	1.01	[0.96-1.07]	0.687	1.01	[0.96-1.07]	0.658	1.02	[0.97-1.08]	0.453
	Year+2	1.10	[1.04-1.16]	0.002	1.10	[1.04-1.16]	0.001	1.11	[1.05-1.17]	<0.001
	Year+3	1.20	[1.13-1.27]	<0.001	1.20	[1.13-1.27]	<0.001	1.21	[1.15-1.28]	<0.001
	Year+4	1.27	[1.20-1.35]	<0.001	1.27	[1.21-1.35]	<0.001	1.29	[1.22-1.36]	<0.001
	Year-3*MS (ref= ref= no MS Year-4)	1.05	[0.96-1.14]	0.311	1.05	[0.96-1.14]	0.310	1.04	[0.95-1.13]	0.381
	Year-2*MS	1.18	[1.06-1.30]	0.002	1.18	[1.06-1.30]	0.002	1.17	[1.06-1.29]	0.002
	Year-1*MS	1.51	[1.35-1.69]	<0.001	1.50	[1.35-1.68]	<0.001	1.49	[1.33-1.65]	<0.001
	Year0*MS	3.46	[3.10-3.86]	<0.001	3.44	[3.09-3.84]	<0.001	3.40	[3.06-3.78]	<0.001
MS*Year	Year+1*MS	3.60	[3.22-4.03]	<0.001	3.59	[3.21-4.01]	<0.001	3.52	[3.16-3.92]	<0.001
	Year+2*MS	3.29	[2.94-3.68]	<0.001	3.27	[2.93-3.65]	<0.001	3.20	[2.88-3.56]	<0.001
	Year+3*MS	2.90	[2.59-3.24]	<0.001	2.88	[2.58-3.22]	<0.001	2.82	[2.54-3.14]	<0.001
	Year+4*MS	2.75	[2.46-3.08]	<0.001	2.74	[2.46-3.06]	<0.001	2.69	[2.42-2.99]	<0.001
Age	Age (years)				1.03	[1.02-1.03]	<0.001	1.03	[1.03-1.04]	<0.001
Birth country	Not in Sweden (ref = Sweden)				1.25	[1.15-1.35]	<0.001	0.94	[0.86-1.02]	0.136
Living area	Other large cities (ref = Stockholm)				1.06	[0.97-1.16]	0.217	1.03	[0.94-1.12]	0.574
	Medium-sized towns				1.03	[0.95-1.11]	0.541	0.96	[0.89-1.03]	0.281
	Rural				1.17	[1.08-1.27]	<0.001	1.05	[0.98-1.14]	0.173
Sex	Men (ref = Women)				0.68	[0.64-0.73]	<0.001	0.67	[0.63-0.71]	<0.001
Cohort	2011 (ref= 2010)				1.06	[0.99-1.13]	0.111	1.07	[1.00-1.13]	0.049
	2012				1.01	[0.94-1.08]	0.795	1.03	[0.97-1.10]	0.298
Work	Manager (ref= Office work)							0.58	[0.47-0.70]	<0.001
	Manual labour/customer service							1.32	[1.23-1.41]	<0.001
	Unclassified work							1.31	[1.16-1.48]	<0.001
	Not in paid work							3.08	[2.84-3.34]	<0.001

Family composition	Children living at home (ref= No)							1.01	[0.95-1.08]	0.671
	Cohabiting/married (ref = No)							0.84	[0.79-0.90]	<0.001
Educational level	University/college (ref = No)							0.73	[0.69-0.78]	<0.001
Healthcare costs										
MS	MS (ref = no MS)	1.19	[1.00-1.40]	0.046	1.19	[1.00-1.40]	0.046	1.18	[1.00-1.39]	0.054
Study Year	Year-3 (ref = Year-4)	1.05	[0.97-1.13]	0.208	1.05	[0.97-1.13]	0.218	1.05	[0.97-1.13]	0.216
	Year-2	1.12	[1.03-1.22]	0.011	1.12	[1.03-1.22]	0.012	1.12	[1.03-1.22]	0.012
	Year-1	1.11	[1.00-1.23]	0.040	1.11	[1.00-1.23]	0.040	1.11	[1.01-1.23]	0.038
	Year0	1.23	[1.12-1.35]	<0.001	1.23	[1.12-1.35]	<0.001	1.23	[1.12-1.35]	<0.001
	Year+1	1.31	[1.18-1.45]	<0.001	1.31	[1.18-1.45]	<0.001	1.31	[1.19-1.45]	<0.001
	Year+2	1.49	[1.35-1.66]	<0.001	1.49	[1.35-1.66]	<0.001	1.49	[1.35-1.66]	<0.001
	Year+3	1.55	[1.38-1.74]	<0.001	1.55	[1.38-1.73]	<0.001	1.55	[1.38-1.74]	<0.001
	Year+4	1.52	[1.37-1.69]	<0.001	1.52	[1.37-1.69]	<0.001	1.52	[1.37-1.69]	<0.001
	Year-3*MS (ref= no MS Year-4)	1.11	[0.94-1.30]	0.228	1.11	[0.94-1.31]	0.223	1.11	[0.94-1.30]	0.230
MS*Year	Year-2*MS	1.33	[1.07-1.66]	0.009	1.33	[1.08-1.66]	0.009	1.33	[1.07-1.65]	0.009
	Year-1*MS	1.93	[1.60-2.33]	<0.001	1.93	[1.60-2.33]	<0.001	1.92	[1.59-2.32]	<0.001
	Year0*MS	6.66	[5.57-7.95]	<0.001	6.65	[5.57-7.94]	<0.001	6.65	[5.57-7.93]	<0.001
	Year+1*MS	7.28	[6.07-8.74]	<0.001	7.28	[6.07-8.74]	<0.001	7.27	[6.06-8.72]	<0.001
	Year+2*MS	5.90	[4.92-7.08]	<0.001	5.90	[4.92-7.08]	<0.001	5.89	[4.91-7.06]	<0.001
	Year+3*MS	5.33	[4.41-6.44]	<0.001	5.33	[4.41-6.44]	<0.001	5.32	[4.40-6.42]	<0.001
	Year+4*MS	5.07	[4.22-6.09]	<0.001	5.07	[4.22-6.09]	<0.001	5.06	[4.22-6.08]	<0.001
Age	Age (years)				1.00	[1.00-1.00]	0.161	1.00	[1.00-1.01]	0.001
Birth country	Not in Sweden (ref = Sweden)				1.02	[0.94-1.10]	0.719	0.90	[0.83-0.98]	0.019
Living area	Other large cities (ref = Stockholm)				0.93	[0.86-1.01]	0.074	0.91	[0.84-0.99]	0.022
	Medium-sized towns				0.88	[0.82-0.95]	0.001	0.86	[0.80-0.92]	<0.001
	Rural				0.89	[0.83-0.97]	0.004	0.86	[0.80-0.93]	<0.001
Sex	Men (ref = Women)				0.85	[0.80-0.90]	<0.001	0.85	[0.80-0.90]	<0.001
Cohort	2011 (ref= 2010)				1.00	[0.94-1.07]	0.912	1.01	[0.95-1.07]	0.809
	2012				0.98	[0.92-1.04]	0.501	0.99	[0.93-1.06]	0.746
Work	Manager (ref= Office work)							0.83	[0.72-0.95]	0.007
	Manual labour/customer service							1.12	[1.05-1.19]	0.001
	Unclassified work							1.15	[1.04-1.28]	0.009
	Not in paid work							1.71	[1.53-1.90]	<0.001
Family composition	Children living at home (ref= No)							0.99	[0.92-1.07]	0.824
	Cohabiting/married (ref = No)							0.95	[0.88-1.02]	0.155
Educational level	University/college (ref = No)							0.95	[0.89-1.01]	0.098
Productivity losses										
MS	MS (ref = no MS)	1.21	[1.08-1.36]	0.002	1.22	[1.09-1.37]	0.001	1.21	[1.09-1.34]	0.001

Study Year	Year-3 (ref = Year-4)	1.00	[0.96-1.04]	0.935	1.00	[0.96-1.04]	0.887	1.00	[0.96-1.04]	0.974
	Year-2	0.95	[0.91-1.00]	0.051	0.95	[0.91-1.00]	0.046	0.95	[0.91-1.00]	0.050
	Year-1	0.96	[0.90-1.01]	0.103	0.95	[0.90-1.01]	0.096	0.96	[0.91-1.01]	0.102
	Year0	0.94	[0.89-1.00]	0.051	0.94	[0.89-1.00]	0.049	0.95	[0.90-1.00]	0.060
	Year+1	0.97	[0.91-1.03]	0.283	0.97	[0.91-1.03]	0.293	0.98	[0.92-1.03]	0.410
	Year+2	1.04	[0.98-1.10]	0.235	1.04	[0.98-1.10]	0.213	1.05	[0.99-1.11]	0.104
	Year+3	1.15	[1.08-1.22]	<0.001	1.15	[1.08-1.22]	<0.001	1.16	[1.10-1.22]	<0.001
	Year+4	1.24	[1.17-1.31]	<0.001	1.24	[1.17-1.32]	<0.001	1.25	[1.19-1.32]	<0.001
MS*Year	Year-3*MS (ref= ref= no MS Year-4)	1.03	[0.94-1.13]	0.482	1.03	[0.94-1.13]	0.483	1.03	[0.94-1.12]	0.574
	Year-2*MS	1.14	[1.03-1.27]	0.012	1.14	[1.03-1.27]	0.012	1.14	[1.02-1.26]	0.015
	Year-1*MS	1.42	[1.26-1.60]	<0.001	1.41	[1.26-1.59]	<0.001	1.40	[1.25-1.56]	<0.001
	Year0*MS	2.76	[2.45-3.11]	<0.001	2.75	[2.44-3.09]	<0.001	2.71	[2.42-3.03]	<0.001
	Year+1*MS	2.76	[2.45-3.12]	<0.001	2.74	[2.44-3.09]	<0.001	2.69	[2.40-3.01]	<0.001
	Year+2*MS	2.65	[2.35-2.98]	<0.001	2.63	[2.34-2.96]	<0.001	2.57	[2.30-2.88]	<0.001
	Year+3*MS	2.33	[2.07-2.63]	<0.001	2.32	[2.06-2.61]	<0.001	2.27	[2.03-2.54]	<0.001
	Year+4*MS	2.26	[2.01-2.55]	<0.001	2.25	[2.00-2.53]	<0.001	2.20	[1.97-2.46]	<0.001
Age	Age (years)				1.04	[1.03-1.04]	<0.001	1.04	[1.04-1.04]	<0.001
Birth country	Not in Sweden (ref = Sweden)				1.32	[1.20-1.45]	<0.001	0.94	[0.86-1.04]	0.233
Living area	Other large cities (ref = Stockholm)				1.10	[0.98-1.23]	0.095	1.06	[0.96-1.18]	0.244
	Medium-sized towns				1.08	[0.98-1.18]	0.136	1.00	[0.91-1.09]	0.930
	Rural				1.27	[1.16-1.40]	<0.001	1.13	[1.03-1.23]	0.010
Sex	Men (ref = Women)				0.63	[0.58-0.68]	<0.001	0.62	[0.58-0.66]	<0.001
Cohort	2011 (ref= 2010)				1.07	[0.99-1.16]	0.073	1.08	[1.01-1.17]	0.029
	2012				1.02	[0.94-1.11]	0.584	1.05	[0.98-1.13]	0.185
Work	Manager (ref= Office work)							0.50	[0.38-0.66]	<0.001
	Manual labour/customer service							1.39	[1.28-1.51]	<0.001
	Unclassified work							1.35	[1.16-1.57]	<0.001
	Not in paid work							3.60	[3.29-3.95]	<0.001
Family composition	Children living at home (ref= No)							1.03	[0.96-1.10]	0.493
	Cohabiting/married (ref = No)							0.82	[0.76-0.88]	<0.001
Educational level	University/college (ref = No)							0.67	[0.62-0.72]	<0.001

¹ Model 1b: Cost = MS + year +MS*year.

² Model 2b: Included the covariates included in Model 1 + the matching variables (age + sex + country of birth + living area) + cohort. Model 2b was selected to inform the adjusted mean costs.

³ Model 3b: Included the covariates included in Model 2 + educational level + children living at home + cohabiting/married + work.

⁴ The coefficients are presented exponentiated as incidence rate ratios (IRRs) which can be interpreted as population averaged multipliers of the cost excess.

Abbreviations: CI: Confidence interval; GEE: Generalised estimating equation; IRR: Incidence rate ratio; MS: Multiple sclerosis; ref: Reference group in regression model