



Productivity Losses Associated with Adult Spinal Muscular Atrophy (SMA) Patients who are not Treated with Disease Modifying Therapies: A Population-Based Study in Sweden

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Background

- Spinal muscular atrophy (SMA) is a rare, progressive, neuromuscular disorder that leads to loss of motor function and respiratory failure.¹
- Medical absenteeism manifested as sickness absence and disability pension may be substantial in adults with SMA who experience significant morbidity that affects their ability to work.^{2,3}
- Premature mortality that occurs before retirement results in decreased labour supply, which may lead to slow economic growth.⁴
- The magnitude of productivity losses due to medical absenteeism and premature death associated with SMA is unknown.⁵

Objective

- The study aimed to quantify morbidity- and mortality-induced productivity losses associated with SMA as compared with references from the general Swedish population.

Methods

Study Design

- Matched-reference cohort study included adult patients with SMA aged 18 to 65 years identified in the Swedish National Patient Registry (NPR) and National Registry for Neuromuscular Disorders (NMIS)⁶ from 1 January 2007 to 31 December 2018. Patients were identified with a first ever SMA-related inpatient or outpatient care event coded as International Classification of Diseases, 10th classification (ICD-10) codes (G12.0 or G12.1).
- A working age SMA population (i.e., 18–64 years) was selected. Patients with SMA were matched 1:4 based on sex, age, and county of residence to a reference cohort from the Total Population Registry.
- The index date was 1 January 2007 for prevalent patients and their matches or the date of the first diagnosis for incident cases and their matches.
- NPR data were linked to MiDAS (Mikrodata för analys av socialförsäkringen) to identify medical absenteeism and the Cause of Death Registry [Dödsorsaksregistret] (CDR) to identify premature death.

Morbidity and mortality-induced productivity losses

- Morbidity-induced productivity losses were estimated as the number of workdays lost attributable to SMA (difference in annual mean number between cohorts estimated using generalised estimating equations [GEE]) and were monetised using national mean income. Productivity losses included net days (gross total) of sickness absence and disability pensions.
- Synthetic cohorts were created to assess the time-varying effects of SMA on workdays lost and medical absenteeism since first SMA diagnosis over the course of the disease in the presence of differential follow-up and left and right truncation. These synthetic cohorts were created by aggregating data into cells corresponding to the time units that would be studied if a single cohort could be observed longitudinally.
- Mortality-induced productivity losses were estimated as foregone lifetime earnings due to premature deaths in the SMA cohort compared with the reference cohort, after adjusting for age- and sex-specific background unemployment.

Results

- One hundred and seventy-two adult patients with SMA were identified and matched to 688 references.
- At index, 67.6% of patients with SMA participated in the labour force, which was significantly lower than their reference cohorts (86.5%, p<0.0001; **Table 1**).
- Annual productivity losses due to medical absenteeism were 100 (95% confidence interval [CI]: 61.5, 138.1) days higher for each adult patient with SMA than the reference (**Table 2**).
- Morbidity-induced productivity losses (in Euro [EUR]) were on average €24,795 for adult patients with SMA per-patient per-year.
- Adults with SMA missed more days than their references through the entire period and the difference grew from year 2 and 3 respectively (**Figure 1 and 2**).
- Foregone lifetime earnings due to premature mortality were on average €89,360 and €79,150 for men and women with SMA, respectively.

Results continued

Table 1. Baseline Characteristics of Adults with SMA and Their Matched Reference Cohort

Patient disposition, demographics and clinical characteristics	Adult SMA N = 172	Reference N = 688	P-value
SMA status at SMA index date, n (%)			1 ¹
Incident	39 (22.7%)	156 (22.7%)	
Prevalent	133 (77.3%)	532 (77.3%)	
Age at index (years), Mean (SD)	40.2 (20.0)	40.2 (20.0)	1 ²
Male sex, n (%)	107 (62.2%)	428 (62.2%)	1 ¹
Charlson score^a, Mean (SD)	0.2 (0.6)	0.1 (0.7)	0.0373 ³
Follow-up time (years), Mean (SD)	9.3 (4.3)	8.9 (4.4)	0.3470 ³
Duration of disease at index (years), Mean (SD)	6.2 (6.2)	6.2 (6.2)	1 ²
Dead at the end of follow-up, n (%)	26 (15.1%)	39 (5.7%)	<.0001 ¹
Socioeconomic characteristics at Index			
Highest level of education at end of follow-up, n (%)			0.6078 ¹
N evaluated	167	667	
Compulsory (i.e., ≤9 years)	69 (41.3%)	281 (42.1%)	
High school (i.e., 10–12)	51 (30.5%)	222 (33.3%)	
University (i.e., >12 years)	47 (28.1%)	164 (24.6%)	
Participating in the labour force^b	75 / 111 (67.6%)	383 / 443 (86.5%)	<.0001 ¹
Skill levels for occupation^c, n (%)			0.0043 ¹
N evaluated	51	284	
Level 1	n < 5	21 (7.4%)	
Level 2	15 (29.4%)	149 (52.5%)	
Level 3	15 (29.4%)	59 (20.8%)	
Level 4	19 (37.3%)	55 (19.4%)	
Annual work-related income (€), Mean (SD)	27,610 (17,283)	31,039 (19,914)	0.3504 ³
Annual family disposable income (€), Mean (SD)	45,159 (35,207)	47,041 (38,301)	0.3114 ³

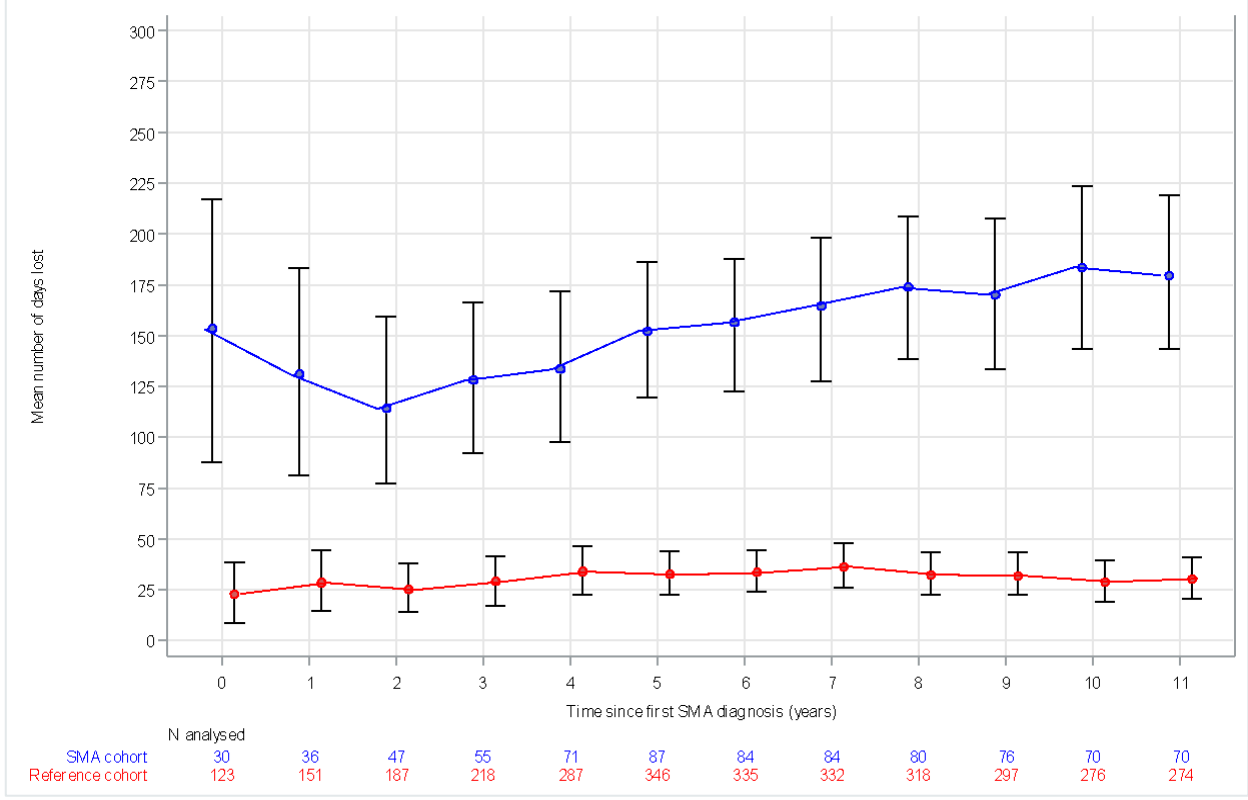
Abbreviations: SD = standard deviation; SEK = Swedish krona; SMA = spinal muscular atrophy
a Charlson Score was estimated using the updated and validated weights from Quan et al. 2011
b Restricted to those aged 18 to 65. Definitions based on Statistics Sweden, Employment and Education Statistics, for the Labour Force Surveys (LFS) described in “Concepts and definitions LFS”. The labour force includes people who are either employed or unemployed. Not in the labour force are persons aged 18–65 who are neither employed nor unemployed, including full-time students and pensioners, and those with unpaid domestic work or a long-term illness. Socioeconomic and sociodemographic characteristics measured on December 31 of the year before the index date.
c Definitions in accordance with the International Standard Classification of Education, UNESCO 1997 (ISCED-97), and based on Statistics Sweden, Standard for Swedish occupational classification (SSYK), SSYK 2012. Standard for Swedish occupational classification 2012. Only presented for those who are in the labour force. Level 1 = No or a low formal education requirement; Level 2 = Education programs at upper secondary and tertiary level of no more than two years in length; Level 3 = Practical or vocational tertiary education programs of two to three years in length; Level 4 = Theoretical or research-oriented tertiary education programs and third-cycle programs of at least three years, normally four years or longer in length.
1 Chi-square p-value; 2 Fisher’s exact p-value; 3 Wilcoxon p-value; 4 Equal variance t-test; 5 Unequal variance t-test

Table 2. Expected Number of Annual Workdays Lost (Per Patient) due to Medical Absenteeism Including SA and DP^a

Population	Mean Annual Workdays Lost (95% CIs)		Difference in Mean Annual Workdays Lost (95% CIs) Attributable to SMA
	SMA Cohorts	Matched Reference Cohorts	
Adult SMA	123.1 (85.7–160.6)	23.3 (16.9–29.8)	99.8 (61.5 – 138.1)

Abbreviations: CI = confidence interval; DP = disability pension; SA = sickness absence; SMA = spinal muscular atrophy
a A generalized estimating equations (GEE) with gamma distribution model was used. workdays lost = intercept + SMA + disease duration + SMA*disease duration + sex + age (pooled analysis; model run assuming exchangeable correlation matrix; marginal mean evaluated at each level of subtype)

Figure 1. Synthetic Cohorts Depicting the Evolution of Medical Absenteeism over Time since First Diagnosis in Adults with SMA



Analysis restricted to time accrued between 18 and 65 years of age. 95% CIs constructed using bootstrapping methods.
Note: since these are synthetic cohorts individuals can enter a leave the annual cohorts each year, therefore, the numbers at risk fluctuates between the years.
Abbreviation: SMA = spinal muscular atrophy.

Conclusions

- Productivity losses amongst adults with SMA in Sweden are substantial (an average of 100 more workdays [€24,795] lost per patient per year compared with non-SMA adults) and are endured by the patient and society as a whole.
- Gains from improving the lives of these patients will have more than just a clinical benefit.

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