

Predictors of ability to work in multiple sclerosis

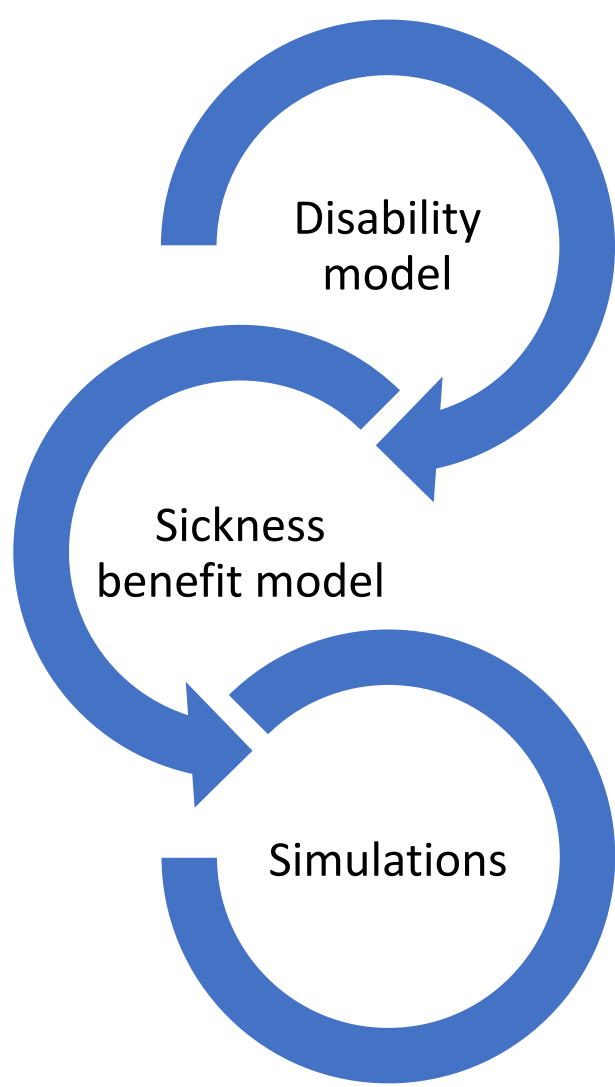
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Introduction

Multiple sclerosis (MS) is a chronic, progressive, disease that affects the ability to work. It is among the leading causes of disability in young adults in the world¹. Losing the ability to work has high personal and societal cost. Luckily, there are new disease-modifying therapies being developed²⁻⁴. However, as many of these are expensive biologic drugs, there is a need to evaluate their cost-effectiveness. Understanding who is at risk of disability to work is therefore important.

Using real-world data from Swedish registries, we investigated the quantitative link between number of days with MS-related sickness benefits and different assessments of disease severity.



Scales

The Expanded Disability Status Scale (EDSS)⁵ ranges from 0 (normal exam) to 10 (death due to MS) in steps of 0.5, and is rated by a physician.

The patient reported outcome (PRO) Multiple Sclerosis Impact Scale (MSIS-29)⁶ has 29 statements about the impact of the disease on daily life, all rated from 1 (not at all) to 5 (extremely). It can also be divided into two subscales: Psychological (MSIS-29 Psy) and Physical (MSIS-29 Phy). The score is reported as an average.

Another PRO is the Fatigue Scale for Motor and Cognitive Functions (FSMC)⁷, which has 20 statements about cognitive and motor fatigue related to MS, all rated from 1 (does not apply at all) to 5 (applies completely). It can also be divided into two subscales: Cognitive (FSMC Cog) and Motor (FSMC Mot). The total score is reported as the sum of scores.

Methods

An item response theory (IRT) model was developed to describe the disability, as assessed by EDSS, MSIS-29 Phy, MSIS-29 Psy, FSMC Mot and FSMC Cog. Each subscale was modeled with a separate latent variable and their respective correlations were estimated (see Figure 1).

Second, a 5-state Markov sickness benefit model was built, and the latent variables were tested as covariates to explain the probability of being on sickness benefits, along with age (see Figure 2).

Lastly, simulations from the sickness benefit model were performed to illustrate the impact in different scenarios.

Data

The Swedish MS registry (SMSreg) and the Swedish Social Insurance Agency's Micro Data for Analyzes of Social Insurance registry were linked to create a dataset with both measures of disease severity and information about the level of sickness benefits related to MS on every day. Patients were 18-62 years old, with at least one record in the SMSreg in the 5-year period starting from the beginning of 2014 to the end of 2018. Benefits were collected and assigned one of 5 states: 0%, 25%, 50%, 75% or 100%, for each day. The first 14 days, paid by the employer, were not used.

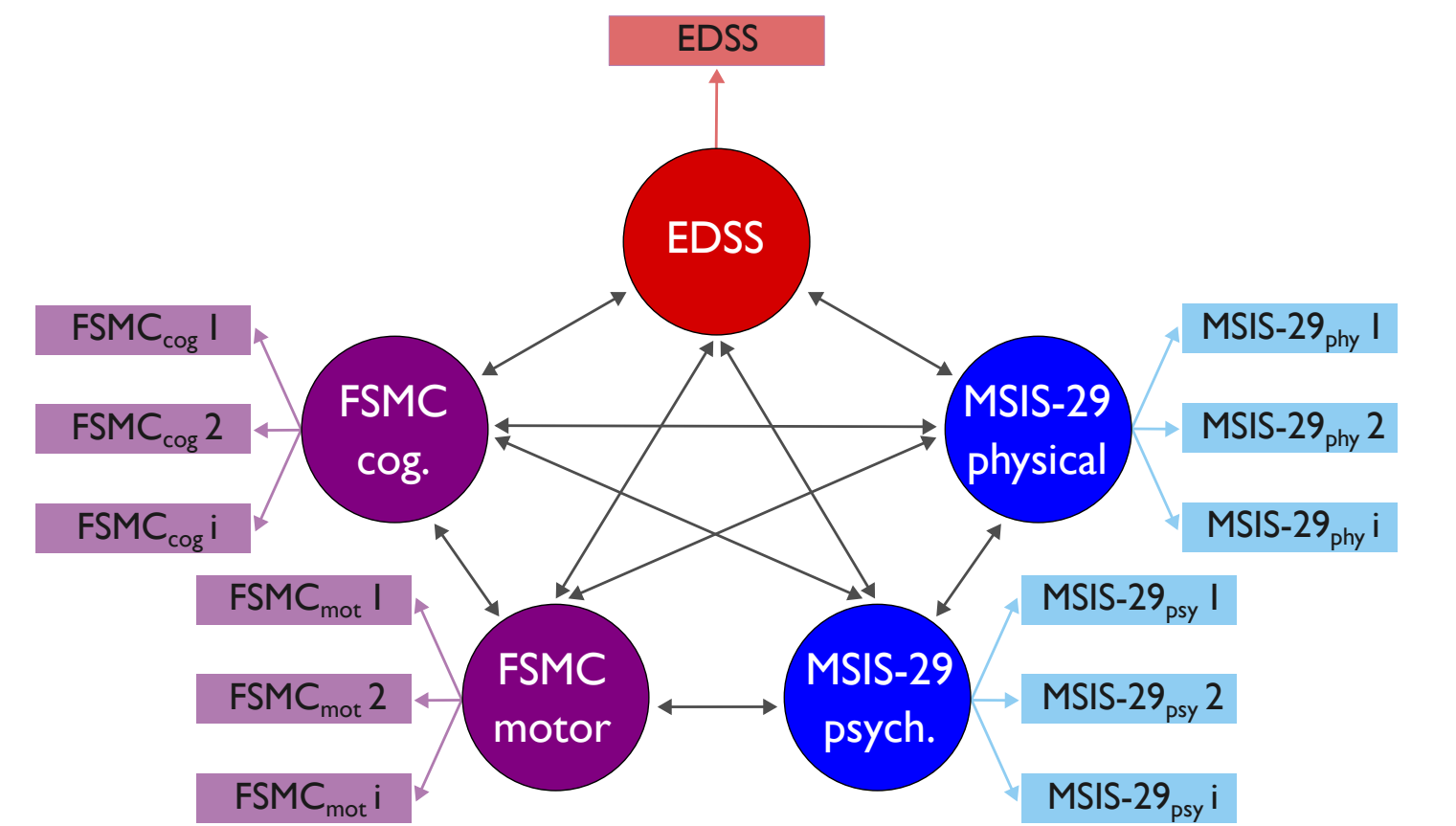


Figure 1. Schematic of the disability model, an item response theory model.

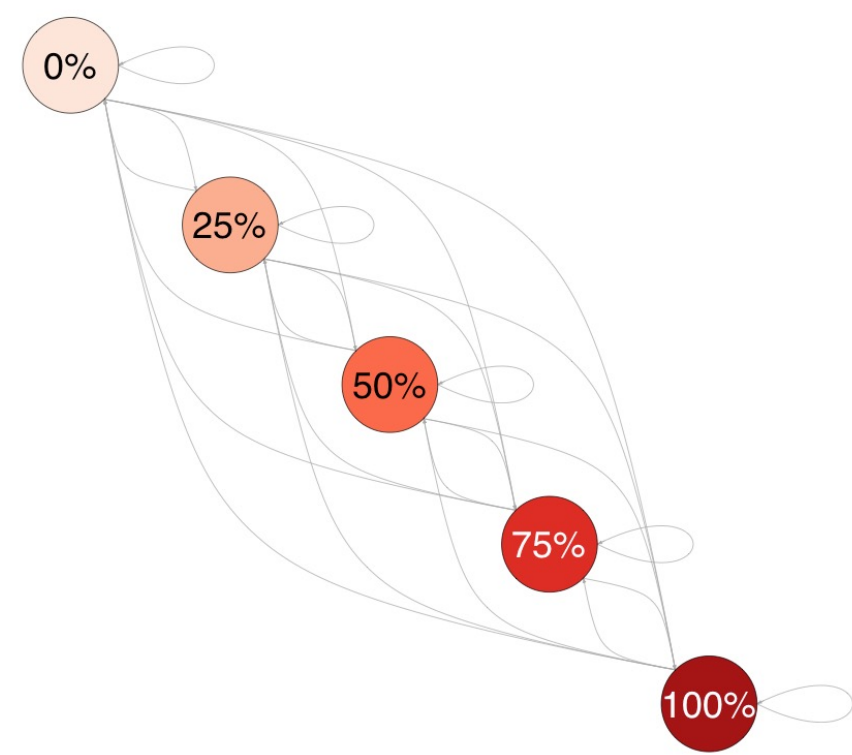


Figure 2. Schematic of the sickness benefit model, showing the 5 possible states of sickness benefit for each day.

Results

The IRT disability model with 5 latent variables showed high correlation (≥ 0.7) between EDSS and MSIS-29 Phy, as well as between FSMC Mot and MSIS-29 Phy, as shown in Table 1. The lowest correlations, on the other hand, were between EDSS and MSIS-29 Psy and EDSS and FSMC Cog. This shows that the EDSS mainly captures the physical aspects of MS.

Table 1. Correlation between latent variables.

	EDSS	MSIS-29 PHY	MSIS-29 PSY	FSMC MOT	FSMC COG
EDSS	1				
MSIS-29 PHY	0.73	1			
MSIS-29 PSY	0.30	0.71	1		
FSMC MOT	0.47	0.72	0.59	1	
FSMC COG	0.28	0.57	0.60	0.92	1

The developed Markov model allows patient-level predictions for the number of days on sickness benefits, based on age, EDSS, MSIS-29 and/or FSMC. As seen in Figure 3, there is a large difference in the number of predicted days with sickness benefits based on EDSS alone. At severe symptoms (EDSS 6-9.5), patients are predicted to spend >50% of the days on MS-related sickness benefits, while patients with mild symptoms (0-2.5) hardly have any days. High MSIS-29 phy (2.55-5) also leads to almost half a year of sickness benefit, as well as high age (46-62 years).

Conclusions

- The number of days with MS-related sickness benefit varied strongly with disease severity
- EDSS was the overall strongest predictor for number of sickness days
- MSIS-29 physical had an impact when EDSS was low, meaning that PROs can be particularly useful in early disease stages
- This model can be used to quantify the societal and individual cost for different MS treatments, as it shows who is at what risk of work disability.

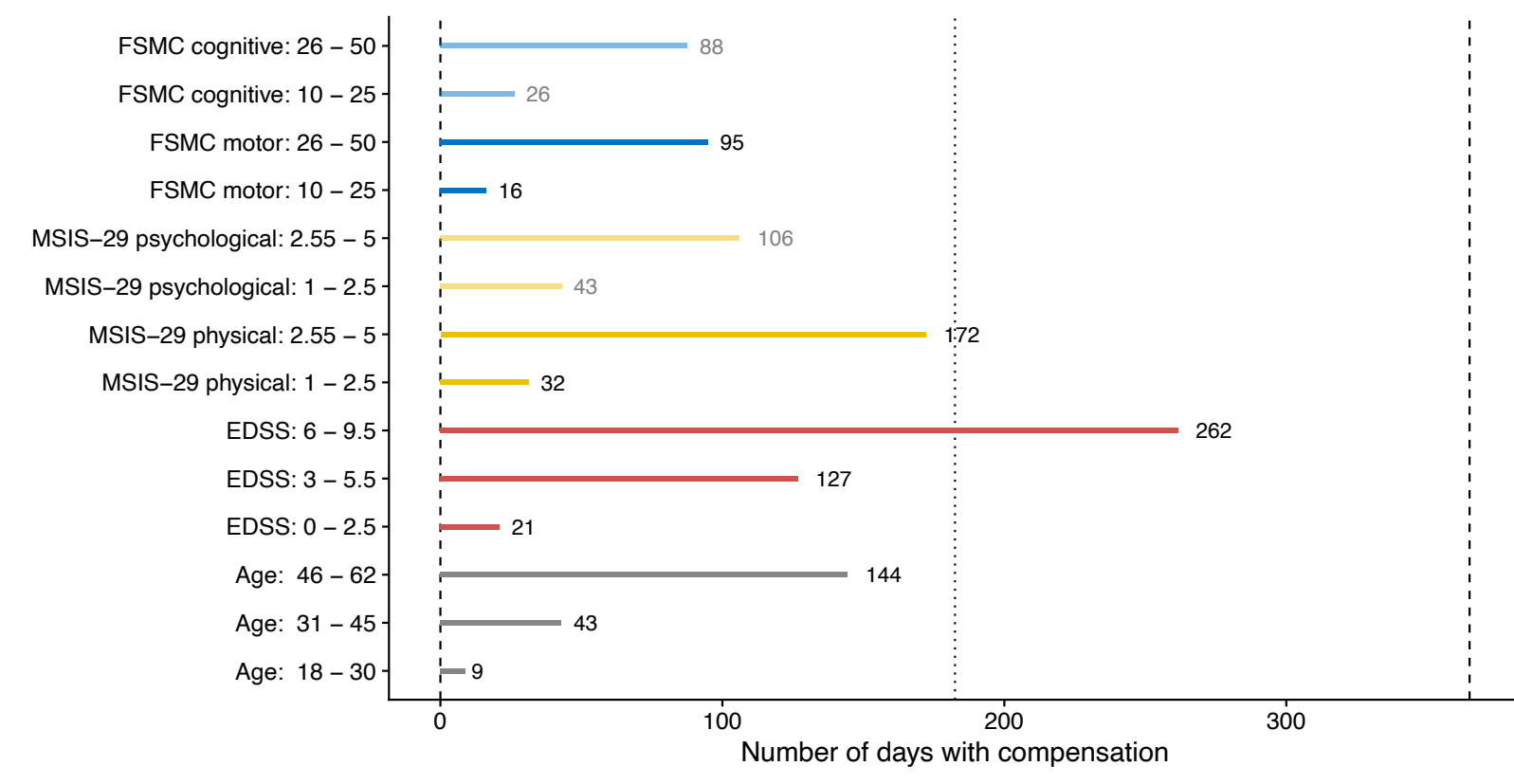


Figure 3. Expected number of days with benefits per year for different score and age ranges. The dashed lines indicate 0 and 365 days, the dotted line indicates 182.5 days, i.e., half a year.

In Figure 4, the importance of MSIS-29 Phy is further demonstrated as a strong predictor in the group of low EDSS, where a high value (2.55-5) leads to 3 times more days with sickness benefit than low (1-2.5).

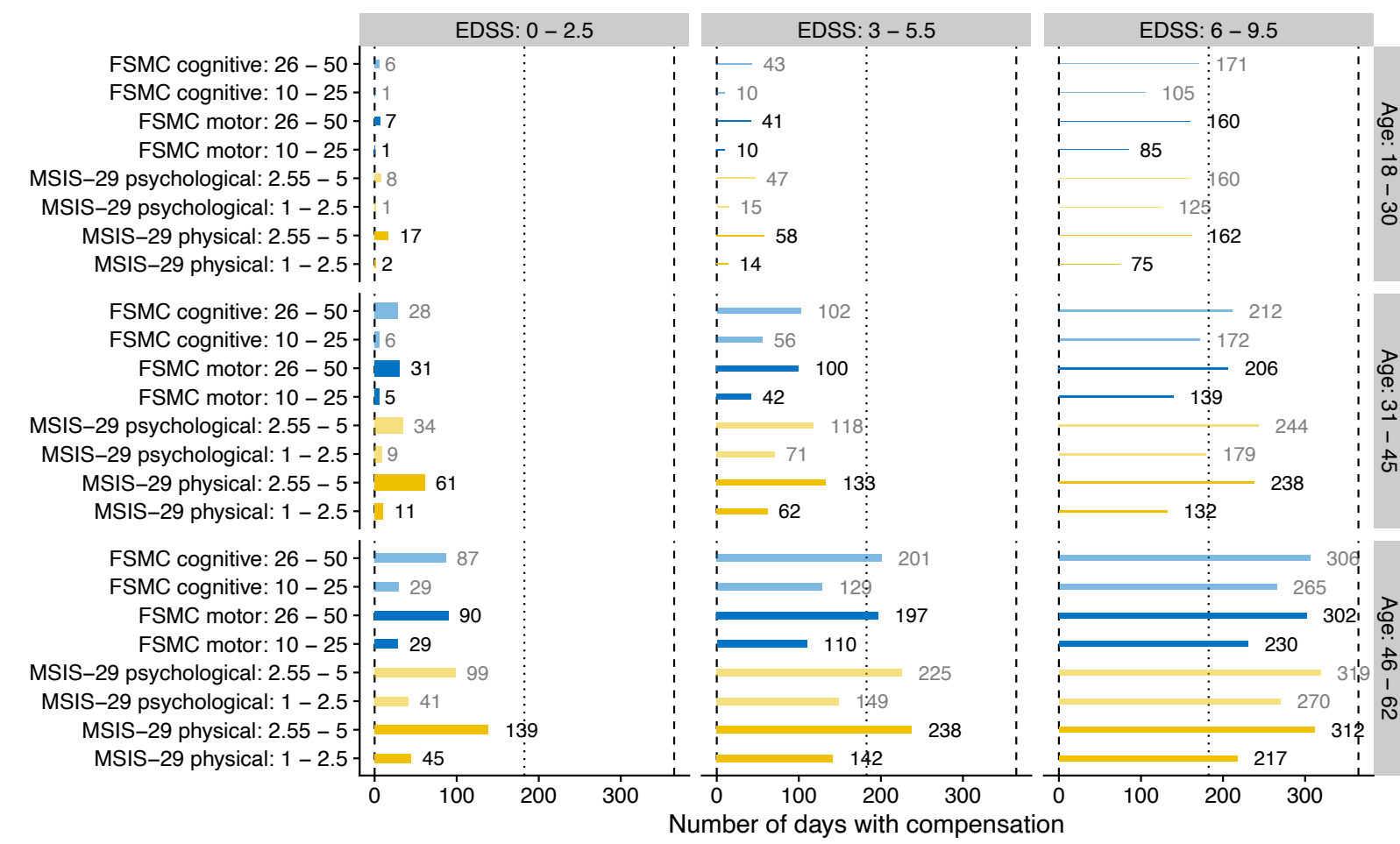


Figure 4. Expected number of days with benefits per year for different PRO score ranges, stratified by EDSS value and age. The dashed lines indicate 0 and 365 days, the dotted line indicates 182.5 days, i.e., half a year. The widths of the bars are proportional to the number of observations of each scenario.

The EDSS is physician-reported, and our analysis suggests that the disability evaluated by physicians is the most relevant for the ability to work. Especially, the physical disabilities had higher predictive value than the psychological ones. It should be noted that EDSS is assessed in the clinic, while MSIS-29 and FSMC are self-reported, which could be a source of bias. Further, it is natural that EDSS correlates best with the number of days with benefits, since a physician needs to support a sickness leave or sickness pension.

The current model can be used as part of an approach to compute costs of different treatments. It also showcases the usefulness of PROs as a complement to clinic visits, especially in the early stages of the disease.

In collaboration with



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