The Socioeconomic Impact of Disability Progression in Multiple Sclerosis: A Retrospective Cohort Study of the German NeuroTransData Registry

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BACKGROUND

- Disability progression on the Expanded Disability Status Scale (EDSS) is a common outcome measure of disease progression in clinical studies of multiple sclerosis (MS)[1,2]

- The socioeconomic burden of MS goes far beyond the costs arising from the healthcare setting[3]

- NeuroTransData (NTD) MS registry contains real-world data for patients with MS (PwMS) living in Germany[4]

- Disability progression leads to decreased quality of life (QoL) and increased socioeconomic costs[5]

The aim of this study was to evaluate the impact of disease progression on societal costs and QoL using data from the German NTD MS registry

METHODS

Evaluation

NTD MS registry
- Registry network comprises 66 neurology and psychiatry clinics in Germany[4]
- Database maintained since 2008[4]
- Includes 22,000 PwMS with an average observation period of 5 years[4]
- Routinely captures clinical and socioeconomic data, as well as patient-reported outcomes
- All PwMS, regardless of disease-modifying therapy (DMT) treatment and MS subtype, were eligible for inclusion
- Patients provided informed consent and explicitly agreed to secondary use of their data

Evaluation of HCRU and costs (Euro 2019)
- Full covariate information available for 7,286 patients*
- Analyses conducted from the societal perspective with costs derived from public sources
- Stratified Health care resource utilisation (HCRU) by EDSS including:
  - **Direct medical costs** (inpatient care, day admissions, consultation, tests, medication, DMTs)
  - **Direct non-medical costs** (investments, community services, informal care)
  - **Indirect costs** (short- and long-term employment absences, pension status)

Statistical analysis
- Multivariate linear mixed regression modelling evaluated the associations between EDSS and 1) QoL 2) Cost
- Results were adjusted for confounders
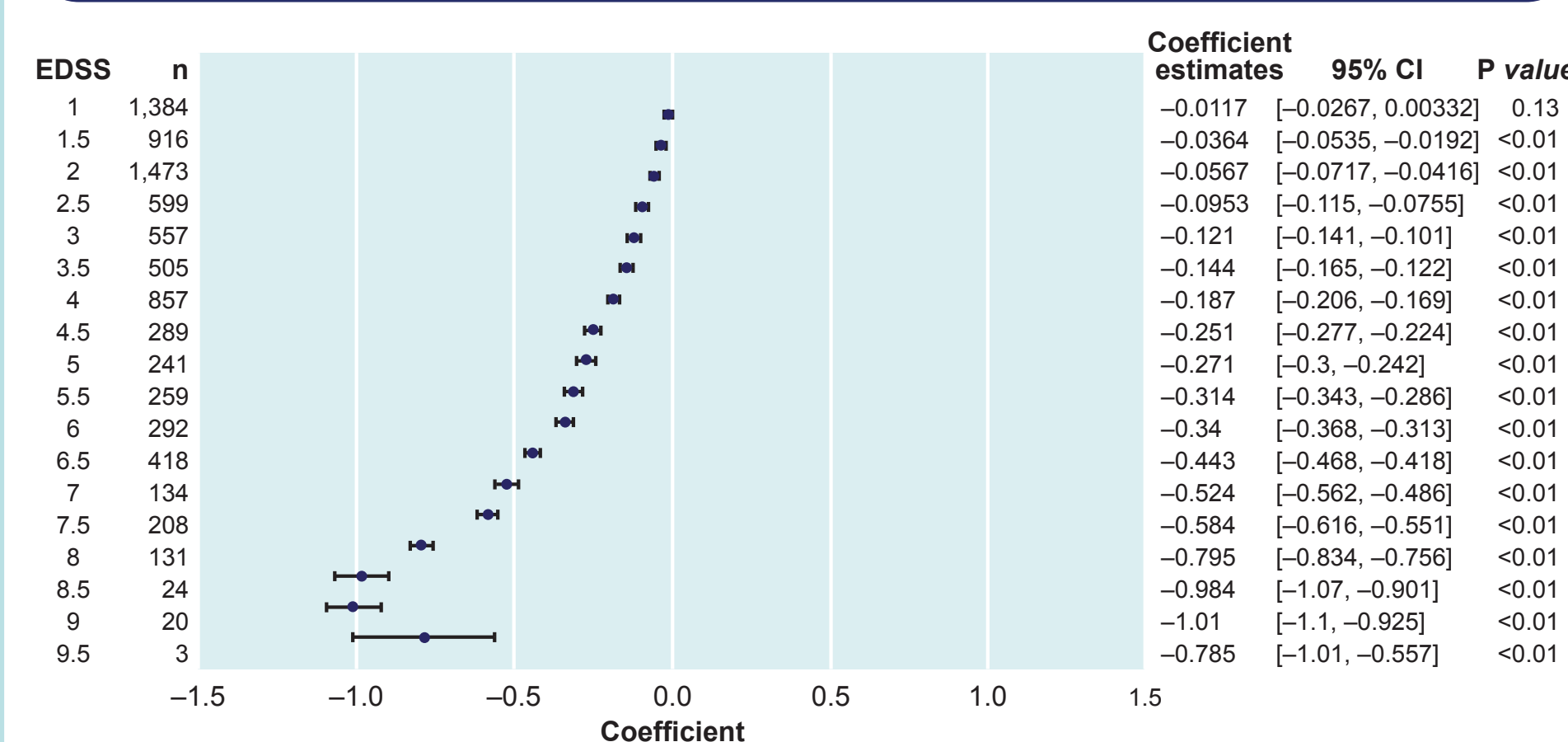- NTD treating center included as a random effect

Evaluation of QoL
- Full covariate information available for 9,821 patients*
- Utilities estimated from the EQ-5D-5L values recorded in the NTD database using the German value set published in Ludwig et al. (2018)[6]

*Additional characteristics describing the patient population can be found in the Supplement.

RESULTS
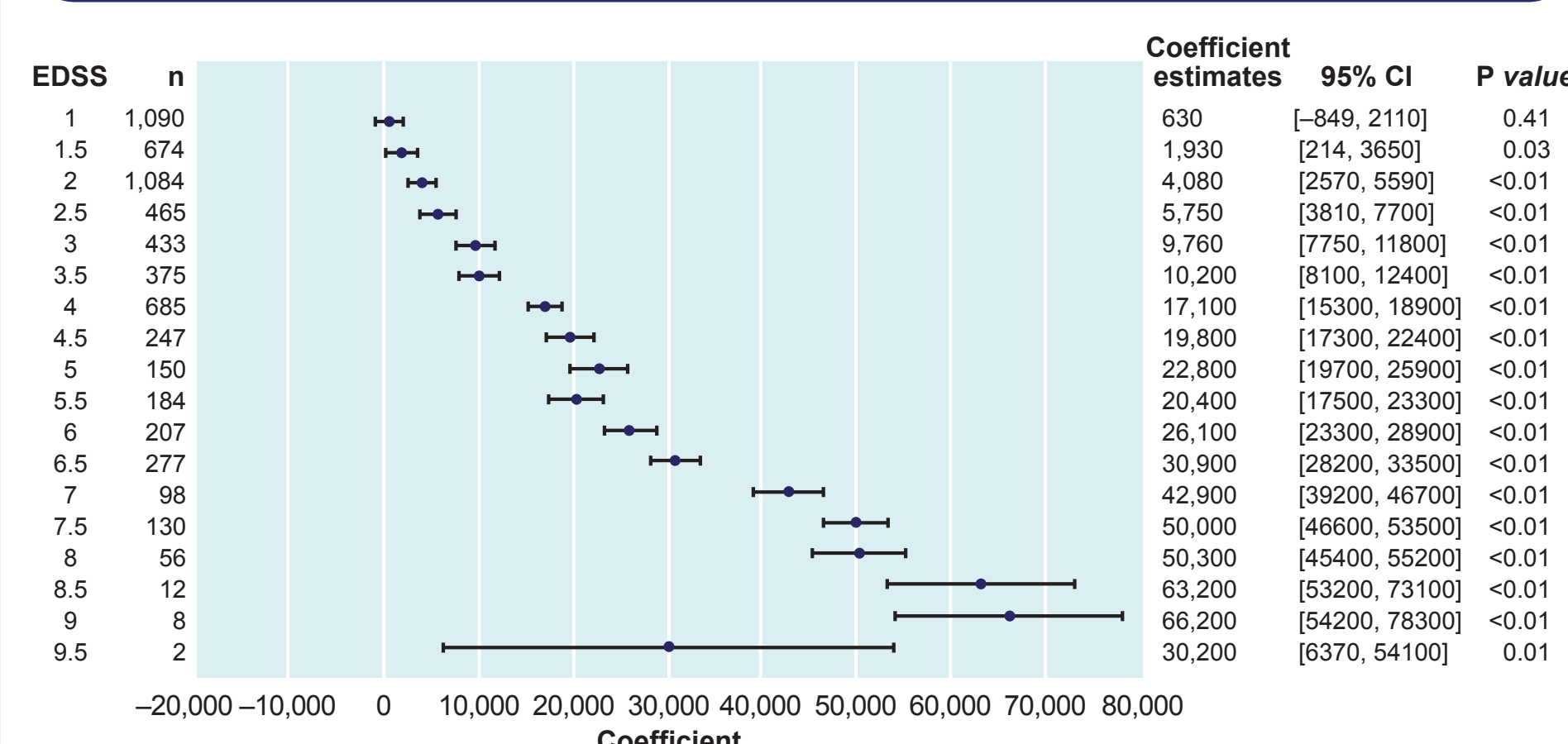
Association Between EDSS and QoL

Each 0.5 step increase in EDSS correlates with significant decreases in QoL

EDSS	n	Coefficient estimates	95% CI	P value
1	1,384	−0.0017	[−0.0267, 0.00332]	0.13
1.5	916	−0.0364	[−0.0535, −0.0192]	<0.01
2	1,473	−0.0567	[−0.0717, −0.0416]	<0.01
2.5	599	−0.0953	[−0.115, −0.0755]	<0.01
3	557	−0.121	[−0.141, −0.101]	<0.01
3.5	505	−0.144	[−0.165, −0.122]	<0.01
4	857	−0.187	[−0.206, −0.169]	<0.01
4.5	289	−0.251	[−0.277, −0.224]	<0.01
5	241	−0.271	[−0.3, −0.242]	<0.01
5.5	259	−0.314	[−0.343, −0.286]	<0.01
6	292	−0.34	[−0.368, −0.313]	<0.01
6.5	418	−0.443	[−0.468, −0.418]	<0.01
7	134	−0.524	[−0.562, −0.486]	<0.01
7.5	208	−0.584	[−0.616, −0.551]	<0.01
8	131	−0.795	[−0.834, −0.756]	<0.01
8.5	24	−0.984	[−1.07, −0.901]	<0.01
9	20	−1.01	[−1.1, −0.925]	<0.01
9.5	9	−0.785	[−1.01, −0.557]	<0.01

QoL (measured using German value set); multivariate regression model was adjusted for age, living status, sex, time since last relapse, time since MS diagnosis, time since last confirmed progression event, current DMT use, educational attainment, MS subtype and included NTD centre as a random effect.
CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; NTD, NeuroTransData; QoL, quality of life.

### Association Between EDSS and Socioeconomic Costs

Each 0.5 step increase in EDSS correlates with significant increases in costs

EDSS	n	Coefficient estimates	95% CI	P value
1	1,090	630	[−849, 2110]	0.41
1.5	674	1,930	[214, 3650]	0.03
2	1,084	4,080	[2570, 5590]	<0.01
2.5	465	5,750	[3810, 7700]	<0.01
3	433	9,760	[7750, 11800]	<0.01
3.5	375	10,200	[8100, 12400]	<0.01
4	685	17,100	[15300, 18900]	<0.01
4.5	247	19,800	[17300, 22400]	<0.01
5	150	22,800	[19700, 25900]	<0.01
5.5	184	20,400	[17500, 23300]	<0.01
6	207	26,100	[23300, 28900]	<0.01
6.5	277	30,900	[28200, 33500]	<0.01
7	98	42,900	[39200, 46700]	<0.01
7.5	130	50,000	[46600, 53500]	<0.01
8	56	50,300	[45400, 55200]	<0.01
8.5	12	63,200	[53200, 73100]	<0.01
9	6	66,200	[54200, 78300]	<0.01
9.5	2	30,200	[6370, 54100]	0.01

QoL (measured using German value set); multivariate regression model was adjusted for age, living status, sex, time since last relapse, time since MS diagnosis, time since last confirmed progression event, current DMT use, educational attainment, MS subtype and included NTD centre as a random effect.
CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; NTD, NeuroTransData; QoL, quality of life.

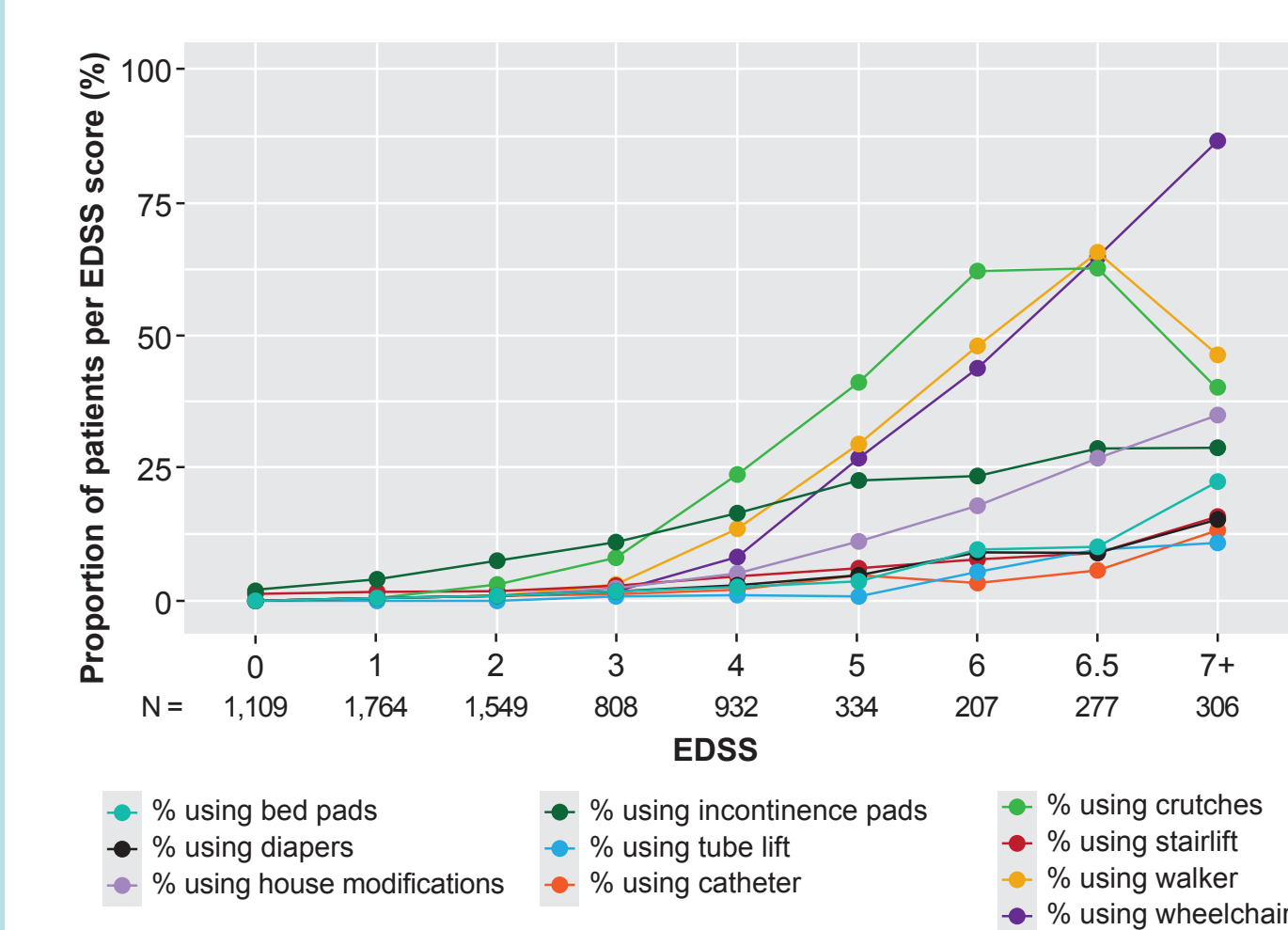### Mean Healthcare Resource Utilisation Costs per EDSS Category

Average total socioeconomic costs per year increased with increasing EDSS
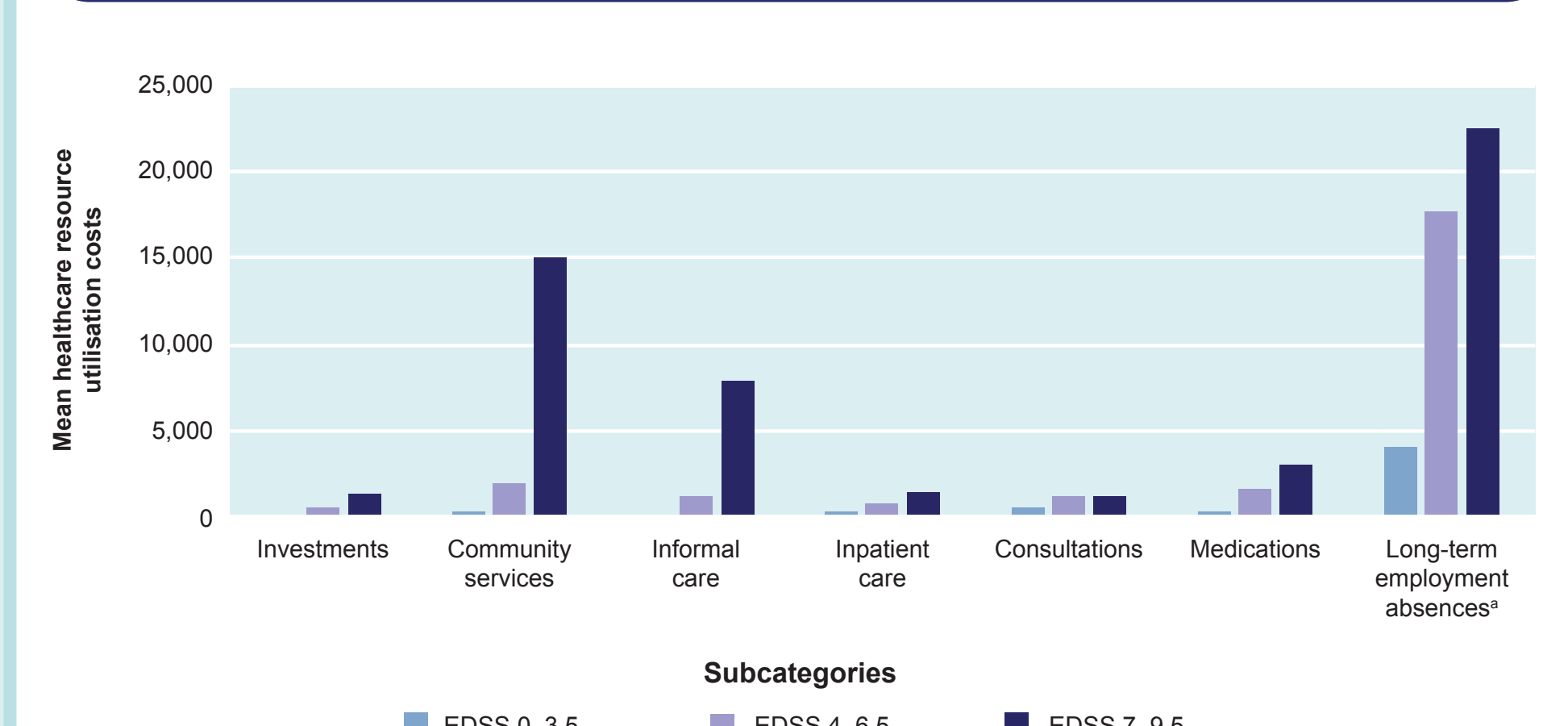
Costs are 2019 costs in Euro. [a]Includes pay for extended periods of work absence (long-term sick leave) and disability pensions.
EDSS, Expanded Disability Status Scale.

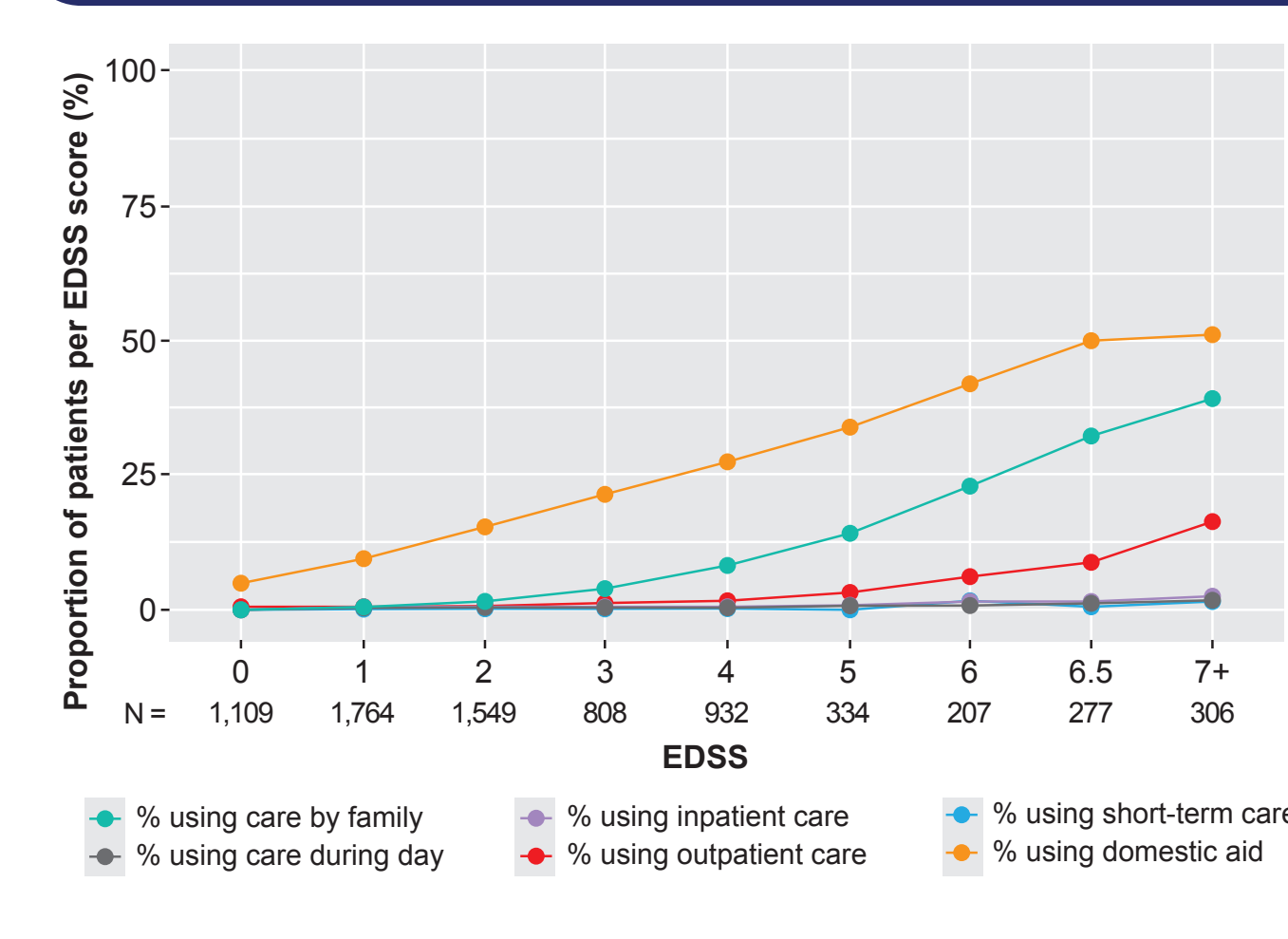### Proportion of Patients Requiring Direct Investments (by EDSS)

Increase in use of supporting tools and investments from EDSS score 3 onwards

N = 1,109, 1,764, 1,549, 808, 932, 334, 207, 277, 306

% using bed pads, % using diapers, % using home modifications, % using incontinence pads, % using tube lift, % using catheter, % using crutches, % using stairlift, % using walker, % using wheelchair

NTD cost population (2019) N=7,286.
EDSS, Expanded Disability Status Scale; NTD, NeuroTransData.

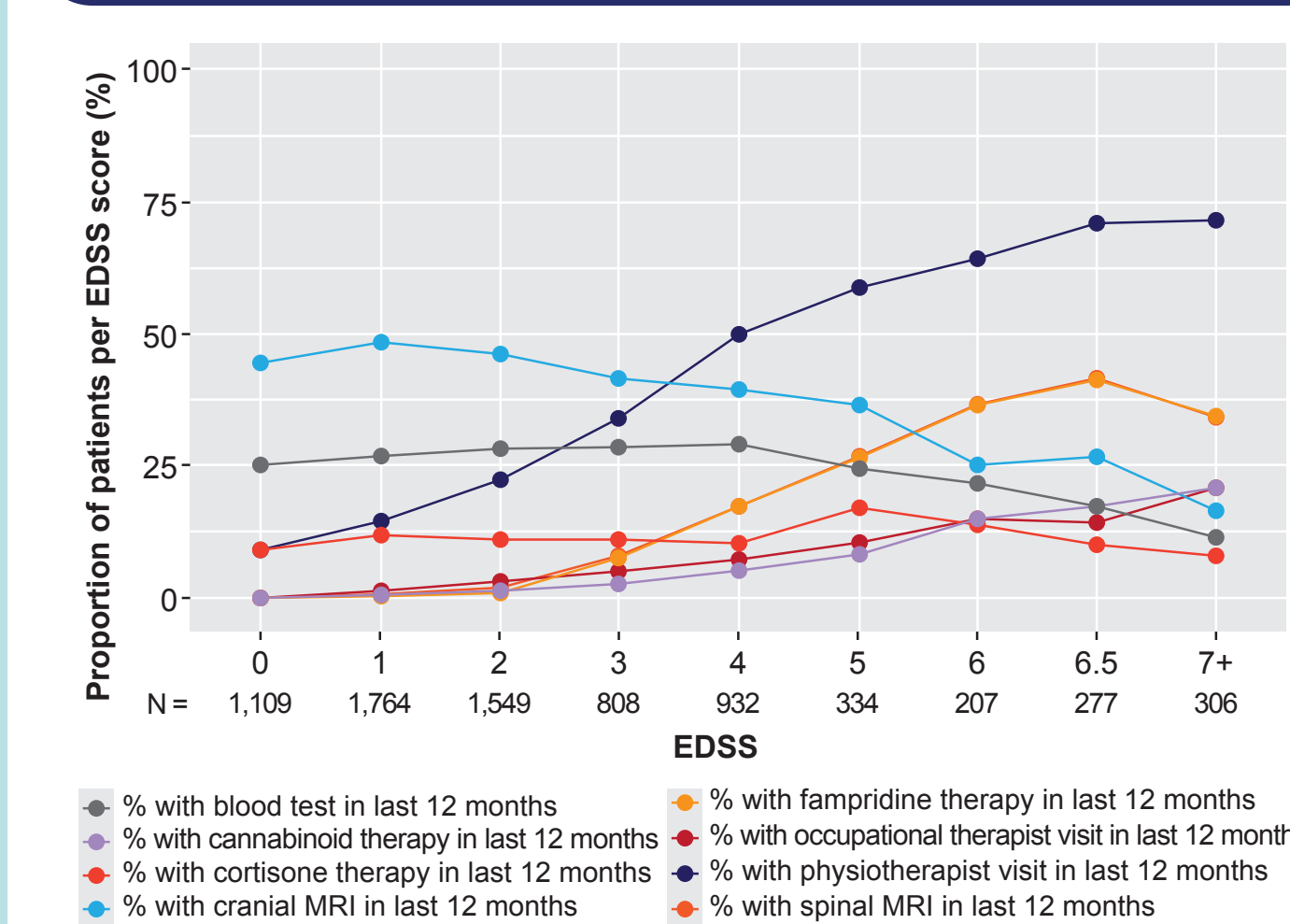### Proportion of Patients Requiring Different Types of Care (by EDSS)

Requirement for domestic aid, family care and then outpatient care increased with higher EDSS levels

N = 1,109, 1,764, 1,549, 808, 932, 334, 207, 277, 306

% using care by family, % using care during day, % using inpatient care, % using outpatient care, % using short-term care, % using domestic aid

NTD cost population (2019) N=7,286.
EDSS, Expanded Disability Status Scale; NTD, NeuroTransData.

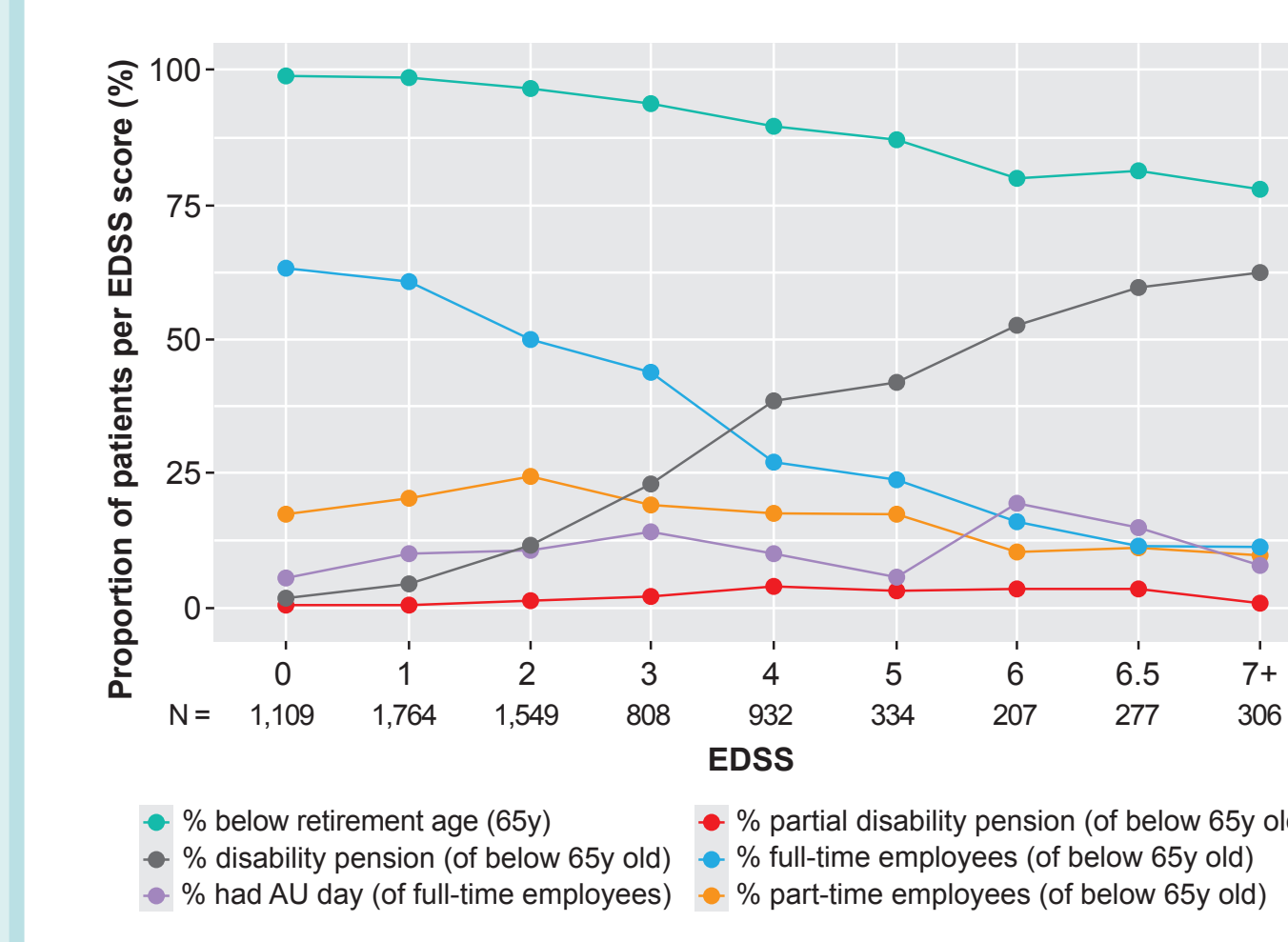### Proportion of Patients Incurring Direct Medical Costs (by EDSS)

Therapies/non-DMT medications increase and MRI investigations decrease with increase in EDSS

N = 1,109, 1,764, 1,549, 808, 932, 334, 207, 277, 306

% with blood test in last 12 months, % with cannabinoid therapy in last 12 months, % with cortisone therapy in last 12 months, % with cranial MRI in last 12 months, % with fampridine therapy in last 12 months, % with occupational therapist visit in last 12 months, % with physiotherapist visit in last 12 months, % with spinal MRI in last 12 months

NTD cost population (2019) N=7,286.
EDSS, Expanded Disability Status Scale; NTD, NeuroTransData.

Proportion of Patients in Employment or with Disability pensions (by EDSS)

Employment decreased with increase in EDSS, whereas disability pensions increased

N = 1,109, 1,764, 1,549, 808, 932, 334, 207, 277, 306

% below retirement age (65y), % disability pension (of below 65y old), % had AU (of full-time employees), % partial disability pension (of below 65y old), % full-time employees (of below 65y old), % part-time employees (of below 65y old)

NTD cost population (2019) N=7,286. Note for those of working age less than 65 years, n=6,838, and for those of working age and working full time, n=3,195.
AU, sick day; EDSS, Expanded Disability Status Scale; NTD, NeuroTransData; y, years.

STRENGTHS & LIMITATIONS

- Data on the full range of medical and societal costs on the impact of MS disease progression are not systematically captured during routine clinical practice within the NTD registry
- With regard to historical data, to ensure generalisability of findings regarding HCRU and costs, this analysis has been limited to a single recent year (2019) while for utility analyses, it is not expected that temporal trends exist in the relation between QoL and EDSS and thus data from 2009–2019 are used
- Informal care was recorded as binary response ('yes'/'no') without hours of care being recorded, and this could have led to inaccurate assignment of costs. Also, costs for investments were not directly recorded and had to be estimated based on assigning unit costs per investment type
- A strength of our study is the representative sampling of PwMS patients overcoming limitations of prior studies relying on survey-based recruitment, which may have led to exclusion of healthier patients at low EDSS and sicker patients at high EDSS
- Sampling differences may have led to observation of lower costs at lower EDSS and lower QoL at higher EDSS, compared with a previous survey-based study[7]

CONCLUSIONS

Each 0.5 step increase in EDSS score correlates with significant increases in socioeconomic costs and decreases in QoL

- Within a clinically representative MS population, increases in EDSS scores lead to **decreases in QoL** and **increases in socioeconomic costs**
- These findings highlight the **socioeconomic burden of disease progression in MS**
- Such findings highlight the potential value of halting or delaying disease progression through the **early use of high efficacy therapies**

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