PANGAEA 2.0 EVOLUTION: Unraveling patient and treatment characteristics for SPMS and at risk for SPMS patients in clinical routine

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Disclosure || Background and objective

DISCLOSURE

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- 85% of MS patients are diagnosed with RRMS[1]
- 60% will convert to SPMS within 20 years due to evolvement of the disease over time[2,3]
- Currently, there are no reliable biomarkers or immunologic, pathologic or imaging based diagnostic markers to predict the transition of RRMS to SPMS[4,5]
- Unclear criteria to define the transition from RRMS to SPMS lead to late and mostly retrospective diagnosis of SPMS[4,5]
- Diagnosis of SPMS is still difficult due to a lack of clear diagnostic criteria[3]
- The PANGAEA 2.0 study is a post-authorization, non-interventional, German, treatment benefit study in MS patients. The study aims to better understand the disease progression of MS and especially the conversion from RRMS to SPMS with the goal to develop new diagnostic tools. A new study arm was added to PANGAEA 2.0, termed PANGAEA 2.0 EVOLUTION focusing on RRMS-patients with high-risk for SPMS and SPMS patients

Objective	**Aim of this interim analysis is to show differences in demographic and baseline characteristics of RRMS-patients with risk for SPMS vs SPMS-patients and present first follow-up data**

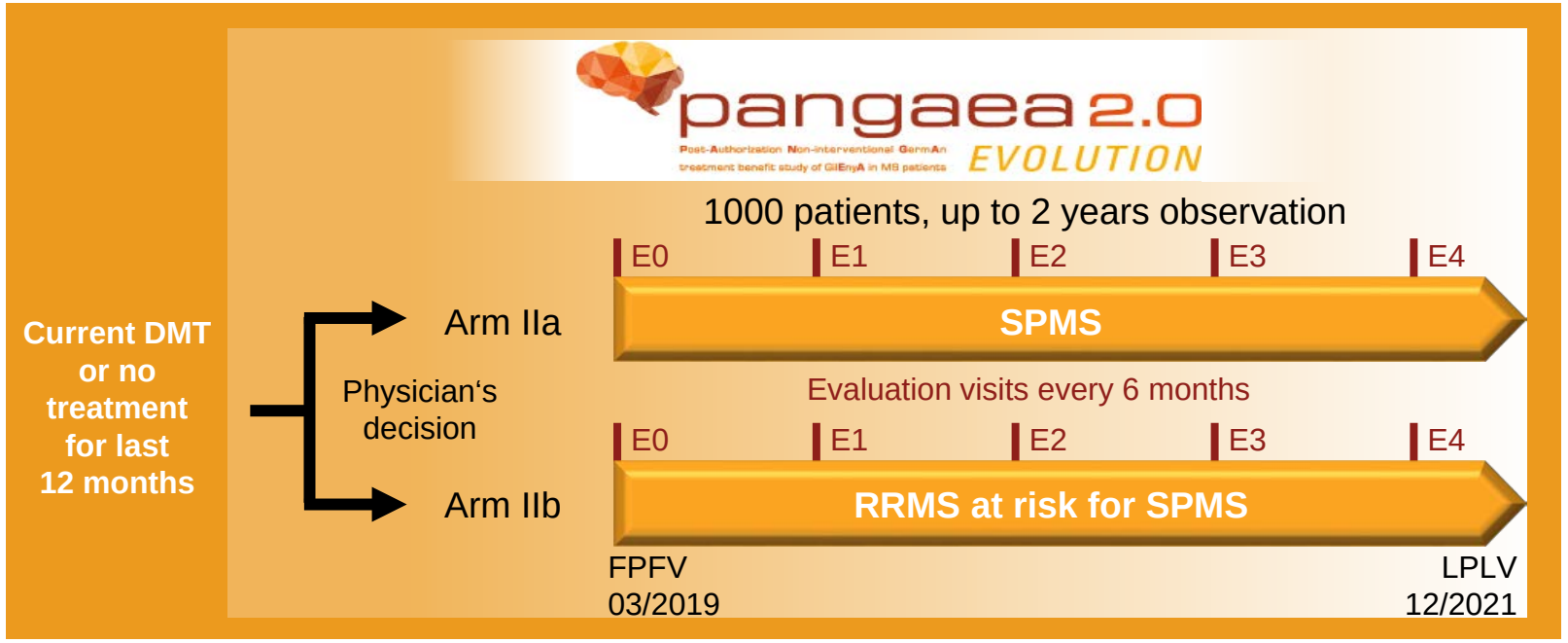
MS: Multiple Sclerosis; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS

[1] Rio J, et el. 2011; *Curr Opin Neurol*. 24(3), 230-237 | [2] Tremlett H, et al. *Mult Scler*. 2008;14:314–24 | [3] Scalfari A, et al. *J Neurol Neurosurg Psychiatry*. 2014;85:67–75 | [4] Lublin FC, et al. *Neurology*. 2014 | [5] Shirani A, et al. *Neurotherapeutics*. 2016; 13(1): 58–69

Methods

Study design

Figure 1. Study design



Inclusion criteria

- Age 18 to 65
- EDSS 3.0 – 6.5
- Prior RRMS diagnosis (McDonald criteria 2010)
- Current diagnosis based on physician's evaluation:
  - SPMS
  - RRMS at risk for SPMS
- On current DMT or no treatment for the last 12 months

Exclusion criteria

- Patients likely not being able to participate in this study for 24 months based on physicians evaluation

As of July 21, 2020 453 patients were enrolled in PANGAEA 2.0 EVOLUTION and included in this analysis

Results

Demography and Baseline Characteristics

Table 1. Baseline characteristics of patients included in this interim analysis

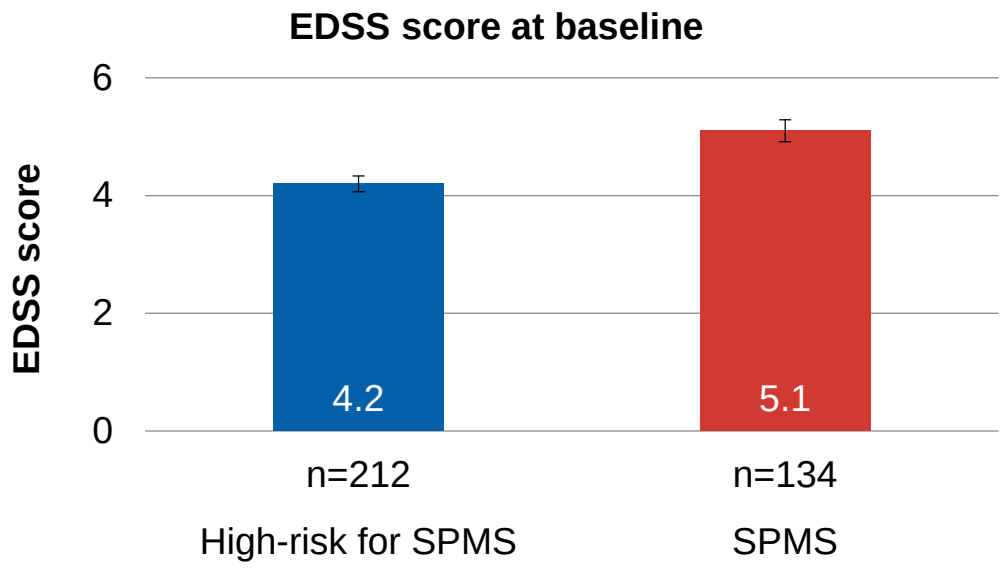
Variable		High risk for SPMS	SPMS
Number of patients	n	258	158
Age	years [mean ± SD]	49.8 ± 8.5	53.6 ± 7.3
Sex	female [n (%)]	187 (72.5%)	119 (75.3%)
	male [n (%)]	71 (27.5%)	39 (24.7%)
Disease and treatment history			
Time since diagnosis	years [mean ± SD]	13.9 ± 8.1	17.1 ± 9.0
Time since first symptoms	years [mean ± SD]	16.7 ± 8.9	21.1 ± 8.9
Time from first symptoms to diagnosis	years [mean ± SD]	2.9 ± 5.4	4.0 ± 6.8
Number of pretreatments	mean ± SD	2.0 ± 1.7	2.0 ± 1.4
Last treatment at inclusion			
No treatment at inclusion (total)		**23.6%**	**16.5%**
Baseline therapies (total)		**50.8%**	**59.4%**
Azathioprin		0.4%	1.9%
Cladribin		0.0%	0.0%
Dimethylfumarate		12.0%	5.7%
Glatirameracetate		11.6%	10.1%
Interferone		20.9%	25.9%
Mitoxantron		1.6%	13.9%
Teriflunomide		4.3%	1.9%
Escalation therapies (total)		**21.7%**	**16.4%**
Daclizumab		2.7%	0.0%
Fingolimod		10.5%	3.8%
Lemtrada		0.4%	0.6%
Ocrevus		1.9%	3.2%
Rituximab		0.0%	2.5%
Tysabri		6.2%	6.3%
Cannot be defined (total)		**3.9%**	**7.6%**

- SPMS patients are older (53.6 ± 7.3 vs. 49.8 ± 8.5)
- SPMS patients have a longer disease history (time since first symptoms: 21.1 ± 8.9 vs. 16.7 ± 8.9)
- Higher proportion of patients without treatment in high risk for SPMS cohort at baseline compared to SPMS patients (23.6% vs. 16.5%)
- Compared to SPMS patients, a lower proportion of high risk for SPMS patients receive baseline therapies (50.8% vs. 59.4%)
- Only a minority of patients receives escalation therapies at baseline (High risk for SPMS: 21.7% vs SPMS: 16.4%)

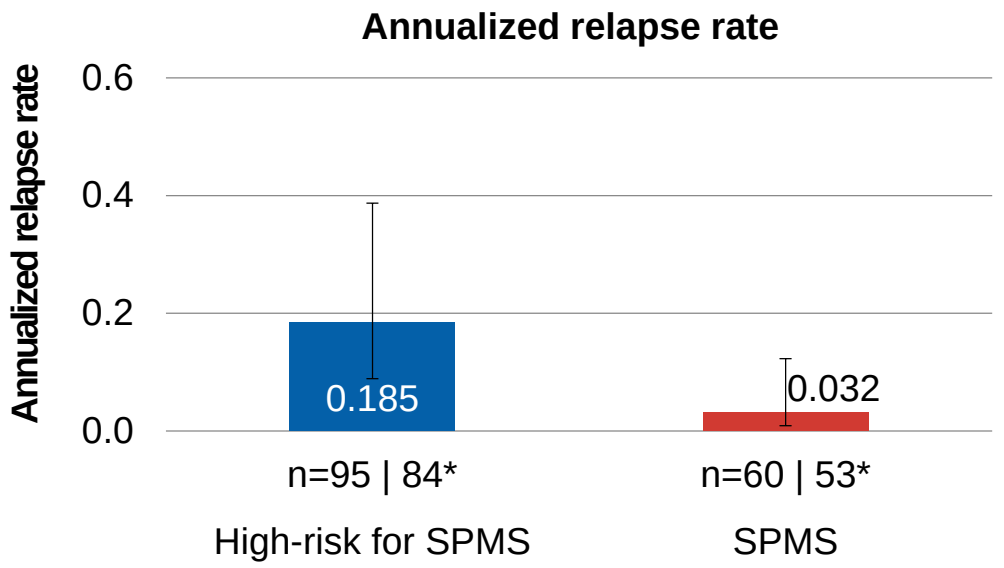
Results

EDSS and relapse activity

Figure 2. Assessment of disease burden by EDSS and annualized relapse rate



Values are mean ± 95% CI



Values show estimate ± 95% CI; estimates for ARR are calculated for the first six months of the study for the Follow-up Set; *Number of observations used

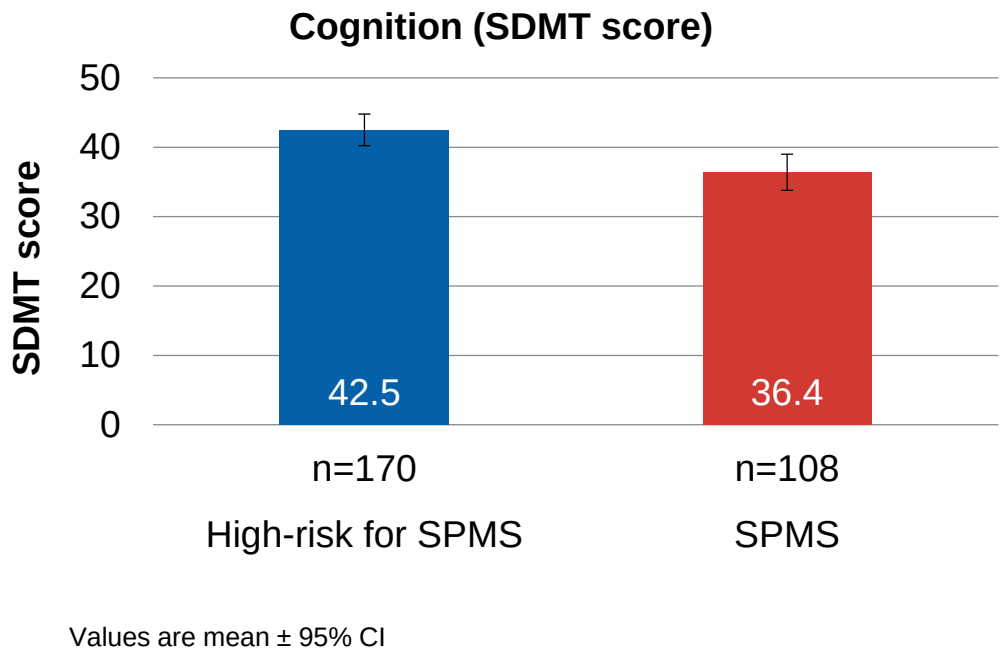
Disease burden: SPMS patients have a higher EDSS score, lower annualized relapse rate

EDSS: Expanded Disability Status Scale (the higher the score the higher the impairment)

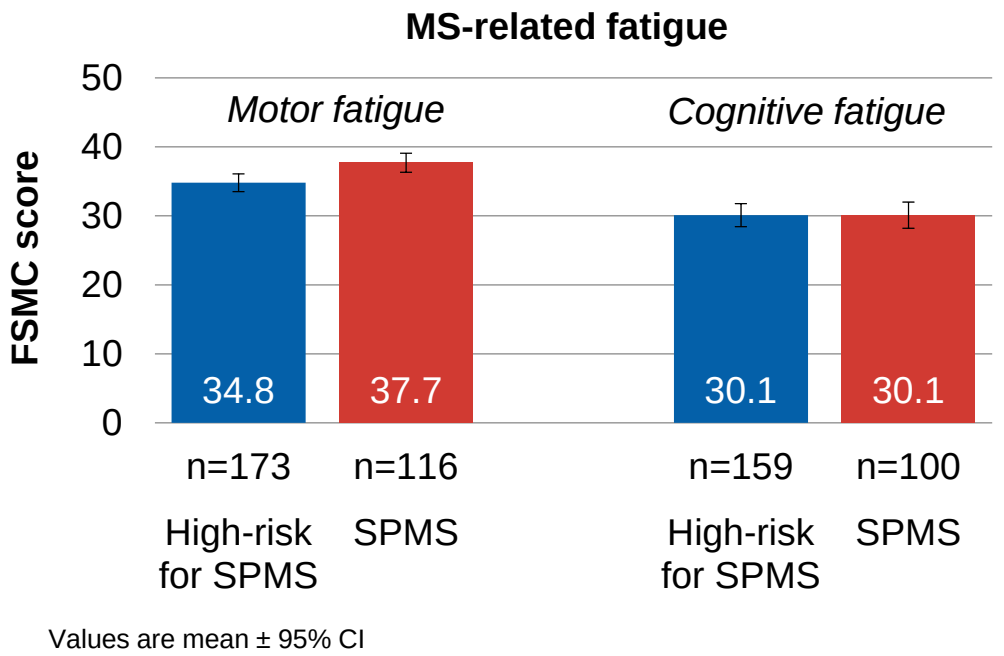
Results

Cognition and Fatigue

Figure 3. Assessment of cognition and fatigue by SDMT and FSMC



Values are mean ± 95% CI



Values are mean ± 95% CI

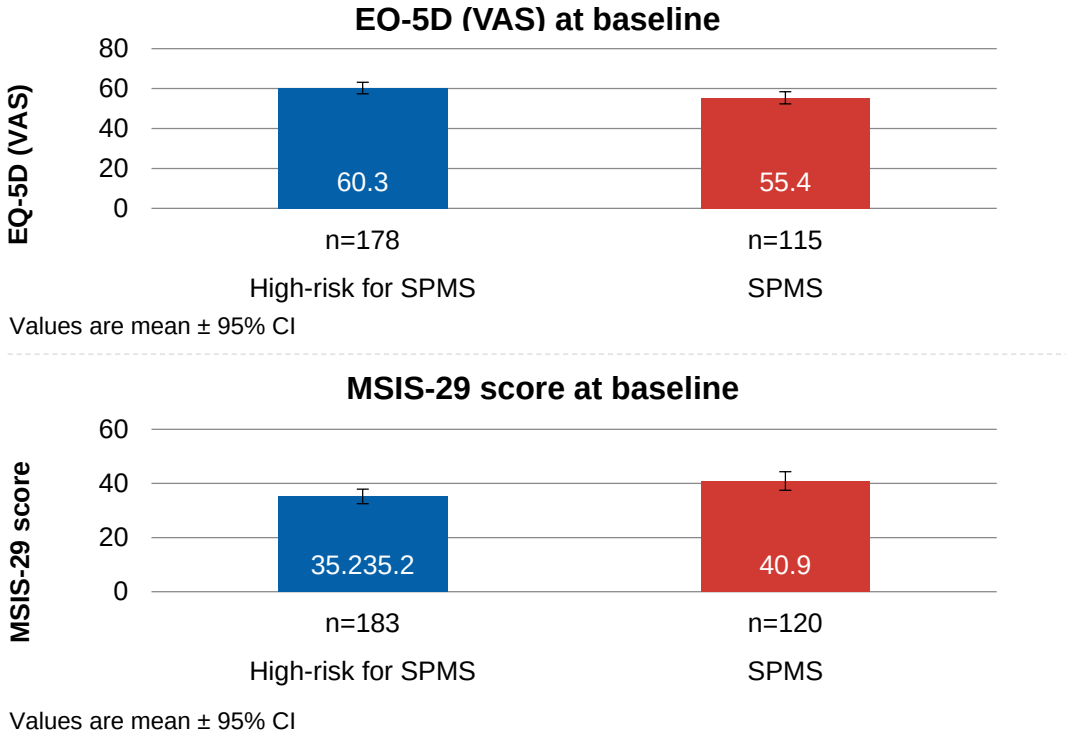
Impairment of cognition and motor fatigue are more pronounced in SPMS patients. Cognitive fatigue is comparable in both populations*

*Note: Whereas “impairment in cognition” refers to a decrease in patient's mental processing speed, “cognitive fatigue” describes mental impairment caused by the patient’s state of exhaustion. FSMC: Fatigue Scale for Motor and Cognitive Functions (the higher the score the higher the impairment); SDMT: Symbol Digit Modalities Test (the lower the numbers the higher the impairment)

Results

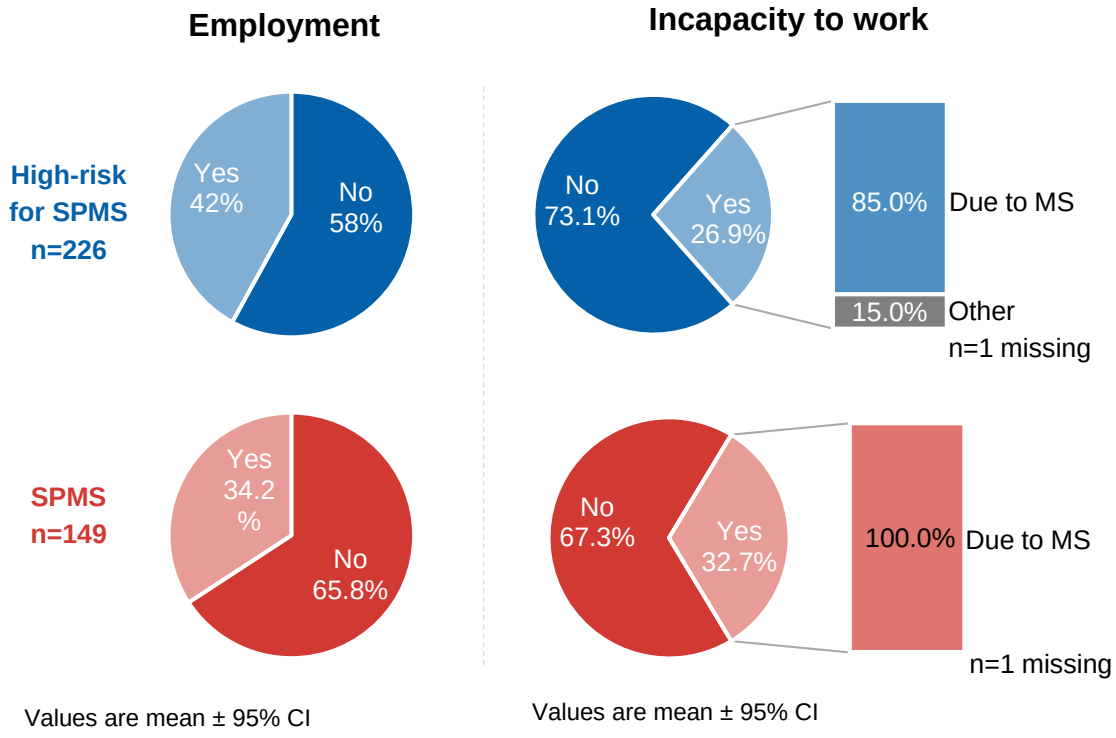
Quality of Life || Working status

Figure 4. Assessment of quality of life by EQ-5D (VAS) and MSIS-29



Quality of life assessments show higher impairment in SPMS patients

Figure 5. Assessment of working status and incapacity



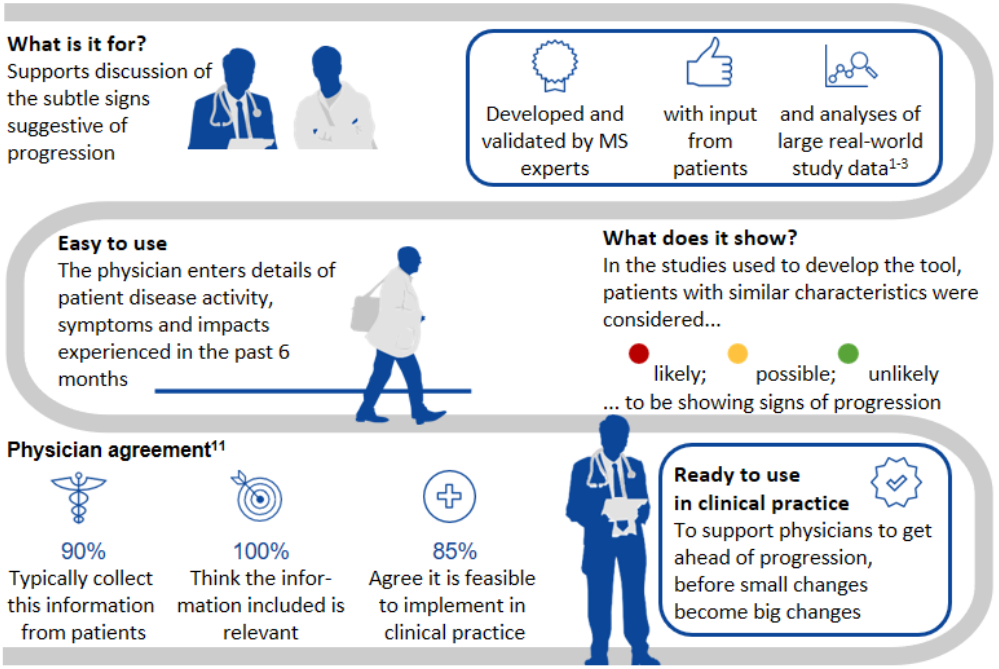
SPMS patients face higher unemployment rate and incapacity to work due to MS when compared to patients at high-risk for SPMS

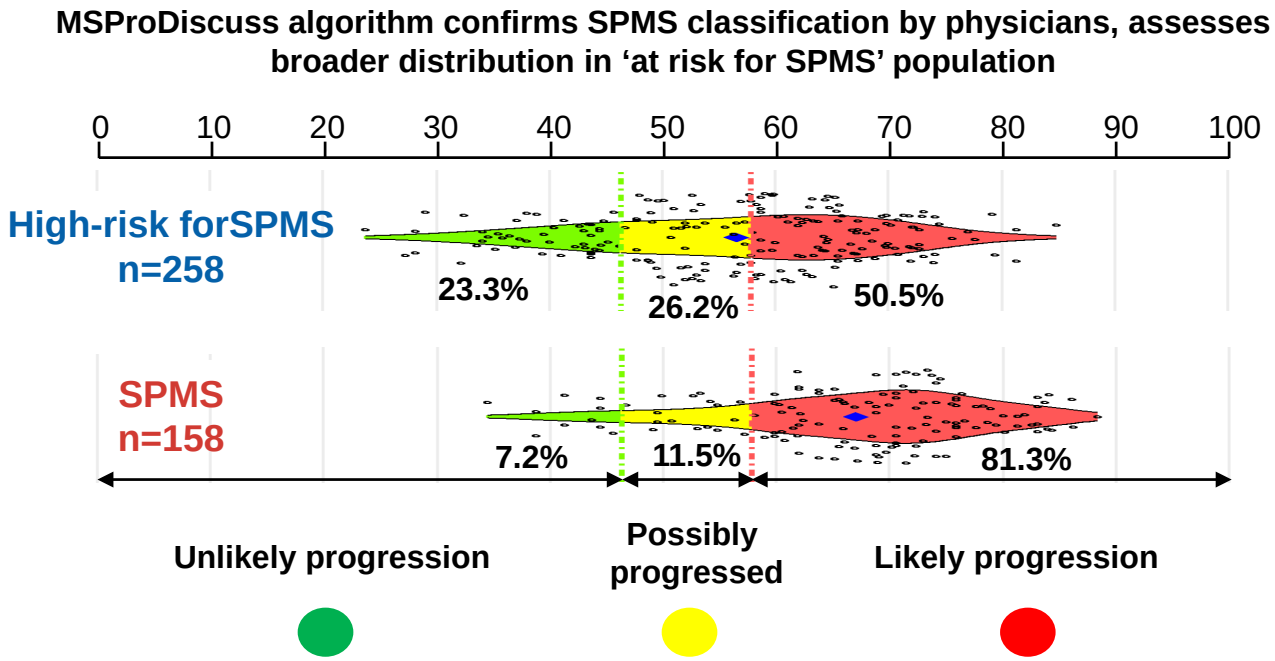
EQ-5D: EuroQol 5-dimension - visual analog scale: (the lower the number the higher the impairment); MSIS-29: Multiple sclerosis impact scale - 29 items (the higher the score the higher the impairment)

Results

Progression questionnaire - MSProDiscuss™

Figure 6. Assessment of progression by MSProDiscuss™ [1-6]





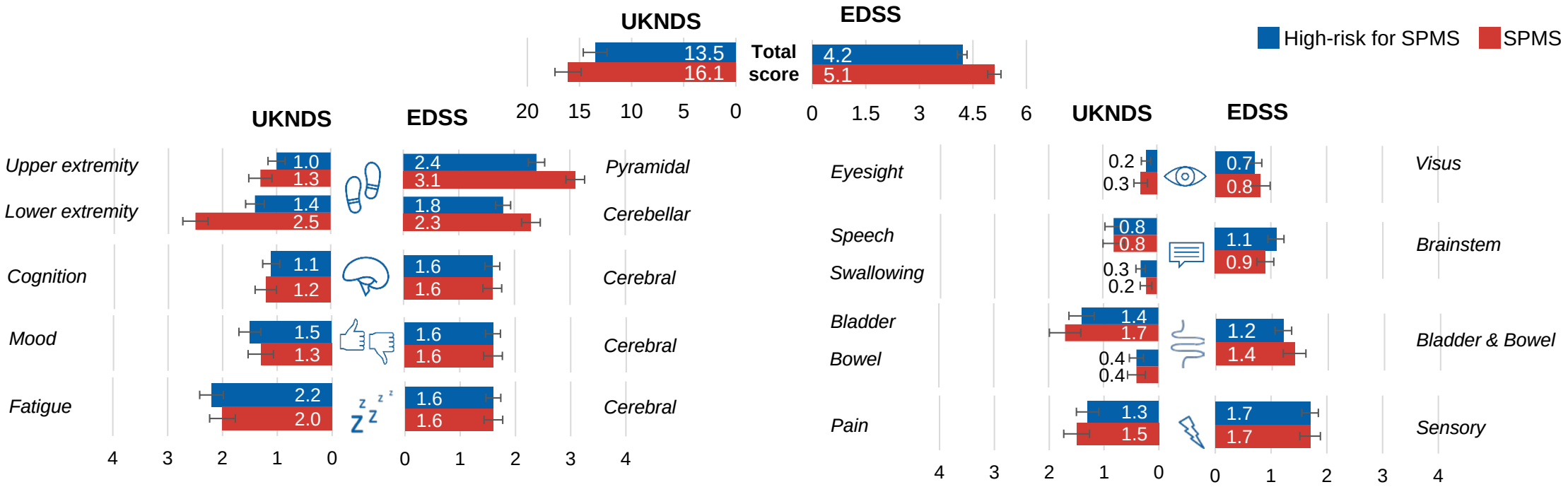
Algorithm highly correlates with physicians' decision to classify SPMS patients

[1]Ziemssen T, et al. Poster P2.156 presented at AAN 2016 | [2]Simsek D, et al. Poster P241 presented at ECTRIMS 2015 | [3]Piani-Meier D, et al. Poster EP1401 presented at ECTRIMS 2017 | [4]Tolley C, et al. JMIR Med Inform. 2020;8(4):e17592 | [5]Ziemssen T, et al. J Med Internet Res. 2020;22(2):e16932 | [6]Ziemssen T, et al. Mult Scler Relat Disord. 2020;38:101861

Results

Patients' and physicians' disability assessment

Figure 7. Assessment of disability by UKNDS vs. EDSS



Both UKNDS and EDSS show SPMS patients having higher disease burden which is mainly due to impairments in motoric and urogenital/gastrointestinal domains. In general, evaluations from patients' and physicians' perspective were in accordance.

Values are mean ± 95% CI; UKNDS domains "sexuality" and "other" were not compared as EDSS domain "other" was not evaluated;

n(UKNDS [High-risk SPMS/SPMS] || EDSS [High-risk SPMS/SPMS]): Total: ([171/110] || [212/134]); Movement: ([185/120; 187/120] || [212/136; 212/135]); Cognition: ([188/119] || [212/135]); Mood: ([187/120]) || ([212/135]); Fatigue: ([186/119] || [212/135]); Visus: ([186/120] || [212/134]); Speech and swallow: ([181/120; 182/118] || [212/135]); Bladder and bowel: ([185/120; 185/120] || [212/136]); Sensitivity and pain: ([181/117]) || ([212/136]); || EDSS: Expanded Disability Status Scale; UKNDS: United Kingdom neurological disability scale

Conclusions

- SPMS patients are older, have a longer disease history, more often received an induction therapy, while patients with high risk for SPMS received more often escalation therapies
- SPMS patients have higher EDSS score, but less relapses than risk patients
- Quality of life is more diminished in SPMS patients compared to patients at high risk for SPMS
- MSProDiscuss algorithm correlates with physicians‘ decision to classify SPMS patients in clinical routine
- Cognition and motor fatigue are more impaired in SPMS patients, while cognitive fatigue is similar in both populations
- Unemployment and retirement due to MS is increased in SPMS patients

Interim results of PANGAEA 2.0 EVOLUTION show different progressive patient profiles in a real world setting.

A longitudinal observation aims to identify key symptoms associated with the underlying progression and helps to define a more accurate and unified diagnosis for progression and SPMS and subsequently a better long-term outcome for these patients.

Thank you