ReMuS MULTIPLE SCLEROSIS PATIENT REGISTRY

Regular Output from ReMuS Registry

Data export updated on 31.12.2016

– Summary Report

In Prague, 6th March 2017

Endowment fund IMPULS
Kateřinská 30, Praha 2, ID: 26169428
www.multiplesclerosis.cz

Contents

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1 Introduction

Czech National Registry of Multiple Sclerosis (ReMuS) was mainly created to obtain data on the prevalence, incidence, severity at the time of diagnosis and clinical course of multiple sclerosis (MS), its clinical symptoms, relapses, progression, MS treatment, disability development, comorbidities and causes of death. The objective is to provide outputs for cost and effectiveness monitoring of health care and medicinal products, assessment of information to be provided to health care payers, other public institutions and manufacturers of medicinal products, to assess the seriousness of MS and its socioeconomic impacts from the scientific, epidemiologic and statistical perspective.

Based on acquired data, it will be possible to look for possible risk factors both for the development of MS itself and lack of effectiveness its treatment or more rapid progression of the disease. Information on course of MS will enable health care payers to better plan the allocation of financial means necessary for the treatment of this disease. Information on treatment effectiveness are instrumental in the selection of the therapy and implementation of changes or modifications when relevant.

The registry now includes multiple sclerosis patients who:

- undergo treatment in one of the participating MS treatment centres
- have signed informed consent with processing their personal and clinical data in ReMuS registry.

The detailed analysis includes only patients who attended their appointment within the second half of 2016 or anytime in 2016 in case of non-DMD patients. The analysis is presented in two sections; the main part treats uniformly DMD/IVIG patients from all centres while the second part summarizes preliminary results for non-DMD patients who are entered only by some of the centres.

2 Results – DMD/ IVIG patients

As of 31. 12. 2016, ReMuS registry included data of patients from fifteen MS treatment centres – General University Hospital in Prague (VFN), Hospital in Teplice, Hospital in Jihlava, University Hospital Motol in Prague, University Hospital in Plzeň, Hospital of Pardubice Region, University Hospital in Ostrava, University Hospital Královské Vinohrady in Prague, Thomayer University Hospital Krč in Prague, University Hospital in Hradec Králové, University Hospital in Brno (Bohunice), University Hospital in Olomouc, Hospital in České Budějovice, University Hospital St. Anna in Brno and Regional Hospital T. Baťa in Zlín. For the main analysis, we included data of patients who were treated in the period from 1. 1. 2013 with one of the DMD and IVIG preparations reported below and for whom current data were available:

- DMDs – Aubagio, Avonex, Betaferon, Copaxone[20], Copaxone[40], Extavia, Gilenya, Lemtrada, Plegridy, Rebif[22], Rebif[44], Tecfidera, Tysabri
- IVIGs – Endobulin, Flebogamma, Gammagard, Kiovig, Octagam.

Patients classified as „non-DMD“ are also included into the present analysis. These patients had been treated with DMD or/and IVIG only before 1. 1. 2013 or haven´t used these products at all. Non-DMD patients were included only from the centres where such data was available.

Table 1 gives the final number of DMD/ IVIG patients included in ReMuS registry as of 31. 12. 2016. The first column contains total number of DMD/ IVIG patients in the registry (patients satisfying the condition of informed consent and treatment with DMDs or IVIGs), while the number of patients with current data (last visit in the second half of 2016) who were included in the current analysis is given in the second column.

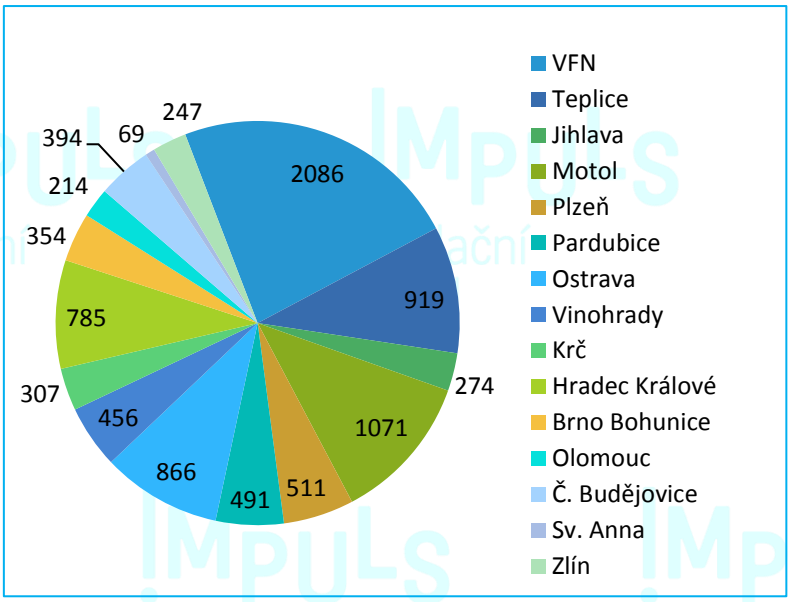

Figure 1 Total number of analysed patients by centres

Table 1 Total number of DMD/ IVIG patients by centres

Centre	Patients in the registry	Analysed patients	Percentage in the analysis
VFN	2166	2086	23.1%
Teplice	943	919	10.2%
Jihlava	283	274	3.0%
Motol	1112	1071	11.8%
Plzeň	538	511	5.7%
Pardubice	508	491	5.4%
Ostrava	880	866	9.6%
Vinohrady	475	456	5.0%
Krč	317	307	3.4%
Hradec Králové	807	785	8.7%
Brno Bohunice	364	354	3.9%
Olomouc	223	214	2.4%
České Budějovice	411	394	4.4%
Sv. Anna	69	69	0.8%
Zlín	247	247	2.7%
Total	9343	9044	100.0%

The table and figure below illustrate the evolution of the number of patients and centres participating in ReMuS registry since its creation. The first data export in summer 2013 analysed data originating from three centres – a total of 1501 patients. Now, in December 2016, the registry has expanded and include 15 MS treatment centres. The data on 9044 patients from all over the Czech Republic enter the analysis.

Table 2 Number of DMD/ IVIG patients in the ReMuS registry and its evolution in time

Data export date	Number of centres	Number of patients to be analysed	Data export date	Number of centres	Number of patients to be analysed
30. 06. 2013	3	1501	30. 06. 2015	13	7099
31. 12. 2013	7	2920	31. 12. 2015	13	7786
30. 06. 2014	12	4715	30. 06. 2016	14	8353
31. 12. 2014	12	5639	31. 12. 2016	15	9044

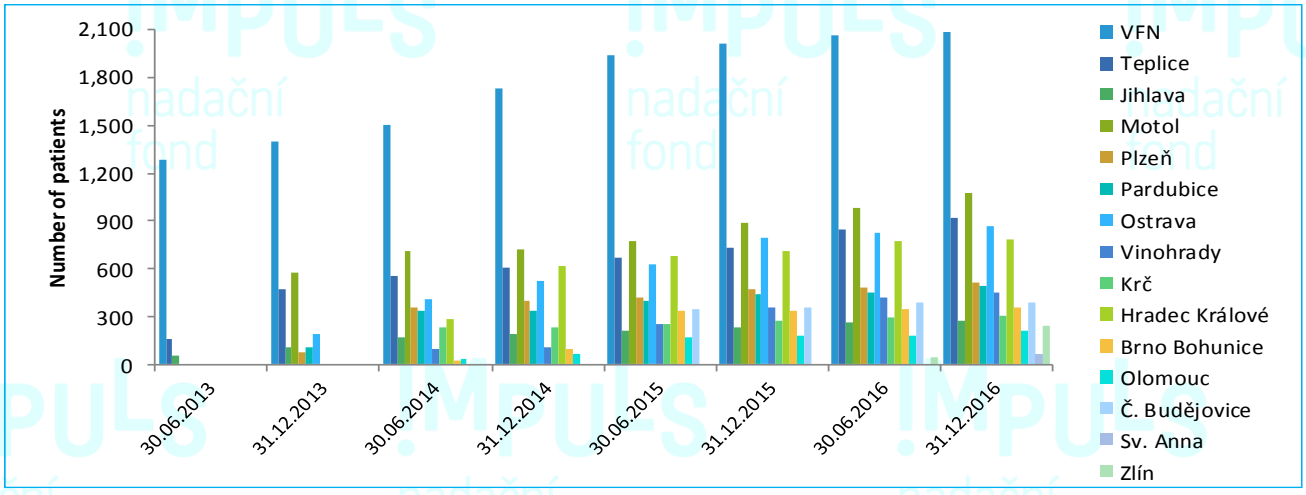

Figure 2 Number of DMD/ IVIG patients in the registry by individual centres – evolution in time

2.1 Demographic data

2.1.1 Sex

Taken together, all centres treat 71.5% women and 28.5% men.

Table 3 Patient distribution by sex

Sex	All centres	
	Number	Percentage
Females	6464	71.5%
Males	2580	28.5%

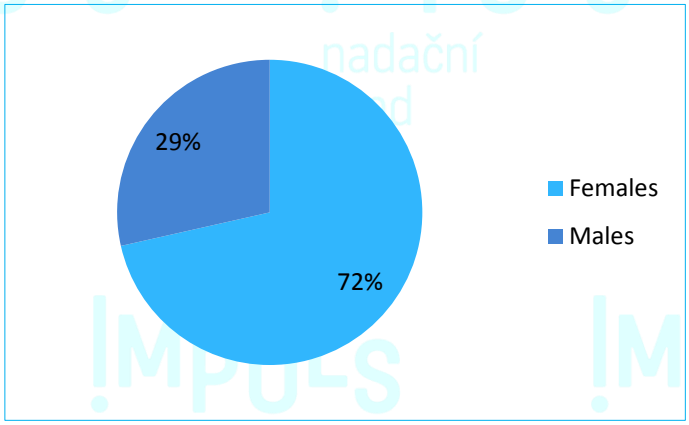

Figure 3 Patient distribution by sex

2.1.2 Age at last patient visit

Mean age at last visit is 41.3 years. For females, mean age was slightly higher than in men. Overall, the registry now includes 34 patients younger than 18 years, and 6 of these are younger than 15 years. When all MS treatment centres are taken together the most represented age group is that of patients aged 40 – 50 and 30 – 40 years.

Table 4 Patient age in years at last visit

Centre	Mean	Median	Minimum	Maximum	SD	Number of missing values
All centres	41.3	40.8	10.3	79.1	10.4	0

Table 5 Patient age in years at last visit by sex

Centre	Sex	Mean	Median	Minimum	Maximum	SD	Number of missing values
All centres	Females	41.6	41.2	10.5	75.1	10.5	0
	Males	40.6	39.9	10.3	79.1	10.0	0

Table 6 Number of patients younger than 15 and 18 years, respectively

Age	All centres	
	Number	Percentage
< 15 years	6	0.1%
< 18 years	34	0.4%

Table 7 Number of patients in individual groups by decades

Age	All centres	
	Number	Percentage
0 – 10	0	0.0%
10 – 20	85	0.9%
20 – 30	1224	13.5%
30 – 40	2903	32.1%
40 – 50	2933	32.4%
50 – 60	1477	16.3%
60 – 70	402	4.4%
70 – 80	20	0.2%
80 – 90	0	0.0%
90 – 100	0	0.0%

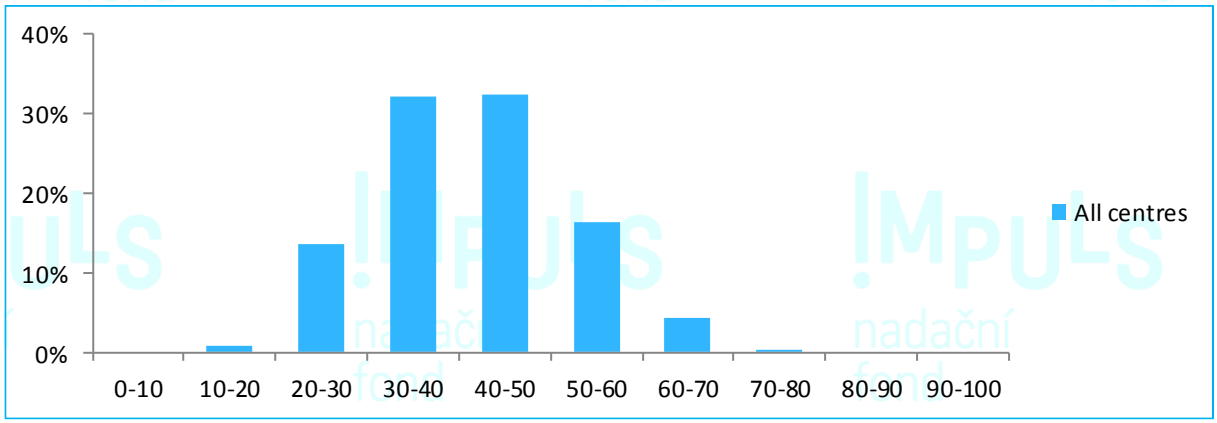

Figure 4 Patient distribution by age

2.1.3 Age at disease onset

Date of disease onset is an important parameter that is used to calculate patient age at disease onset and disease duration period.

Mean age at disease onset is 30.8 years. Table 8 shows, however, that patient age at disease onset ranged from 3 years to 67 years.

Table 8 Patient age in years at the time of disease onset

Centre	Mean	Median	Minimum	Maximum	SD	Number of missing values
All centres	30.8	29.6	3.3	67.3	9.6	4

2.1.4 Patient distribution by individual healthcare insurance companies

Table 9 and Figure 5 show the distribution of patients in the registry by individual health insurance companies. 58.4% patients are insured with the General Health Insurance Company (code: 111). 13.0% are insured with Health Insurance Company of the Ministry of Internal Affairs (code: 211) and 9.6% with Business Health Insurance Company (code: 207).

Table 9 Patient distribution by health insurance companies

Health Insurance Co.	All centres	
	Number	Percentage
111	5278	58.4%
201	498	5.5%
205	825	9.1%
207	872	9.6%
209	135	1.5%
211	1178	13.0%
213	254	2.8%
Other	4	0.0%

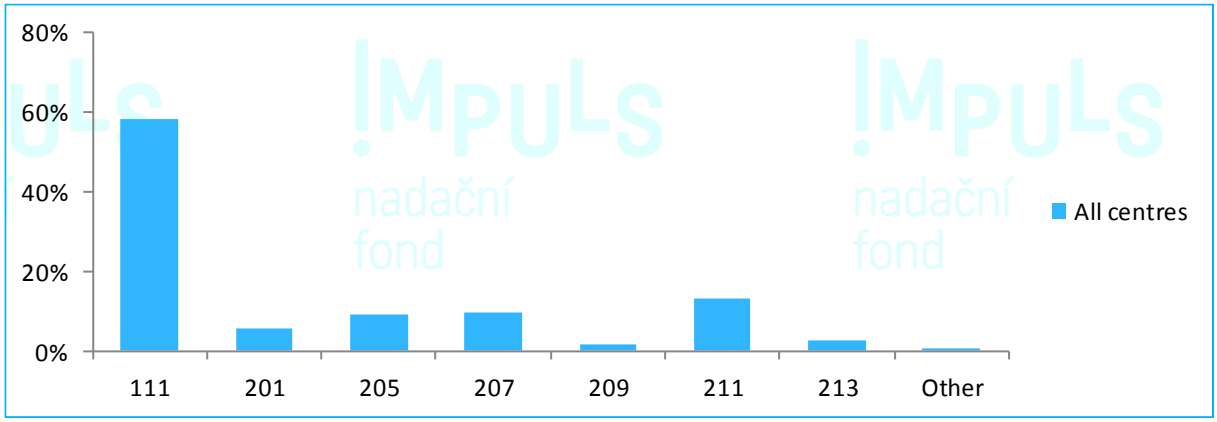

Figure 5 Patient distribution by health insurance companies

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2.1.5 Patient distribution by regions

The registry makes it possible to obtain data on patient distribution by individual Czech Republic regions based on ZIP codes attached to patient residence addresses. ZIP codes assigned to communities that were part of two regions were assigned to the region that included most of the included communities. ZIP codes not found in the ZIP code registry of the Czech National Postal Office (Czech Post) were interpreted as incorrect.

The registry includes patients from all Czech Republic regions.

Table 10 Patient distribution by regions of their residence

Regions	All centres	
	Number	Percentage*
South Bohemia	562	6.2%
South Moravia	383	4.2%
Karlovy Vary	240	2.7%
Vysočina	489	5.4%
Hradec Králové	599	6.6%
Liberec	412	4.6%
Moravia-Silesia	825	9.1%
Olomouc	217	2.4%
Pardubice	586	6.5%
Plzeň	434	4.8%
Prague	1722	19.0%
Central Bohemia	1454	16.1%
Ústí nad Labem	731	8.1%
Zlín	385	4.3%

* 4 patients have permanent residence in Slovakia and 1 patient in Poland

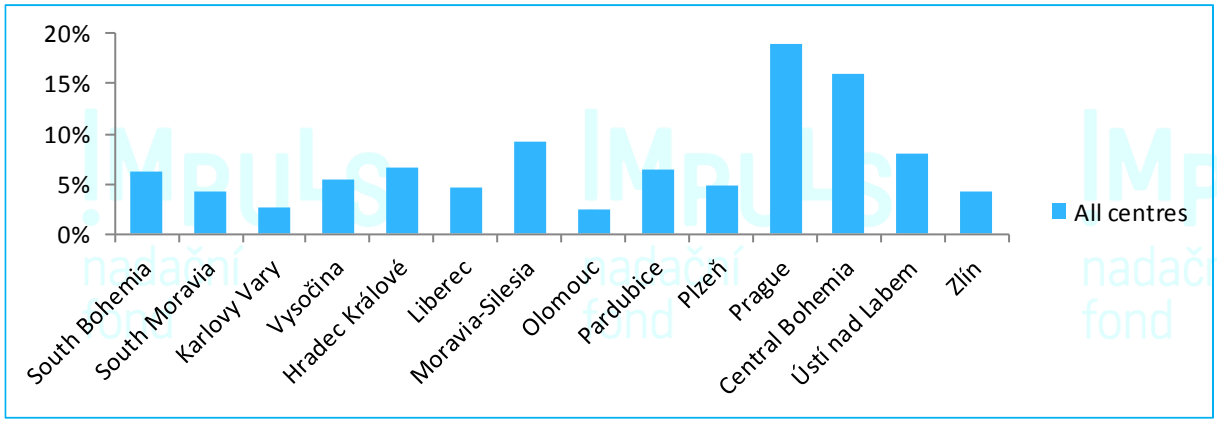

Figure 6 Patient distribution by regions of their residence

2.2 Employment and social benefits

Employment and provision of social benefits are evaluated based on data obtained at last visit. These parameters must be completed at each visit even when the condition remains the same.

It should be noted that all possibilities and combinations of employment and especially those for social benefits cannot be appreciated and the clarity and purposefulness of the output is preserved at the same time. It was thus necessary to introduce certain preference criteria so the physicians be able to complete the data and decide what options to choose in unclear combined cases. These preference criteria (that is that the type of disability pension [DP] takes precedence over unemployment benefits or maternal leave [ML]) must be taken into account when interpreting and presenting this type of data.

2.2.1 Employment

As part of entering employment data, the selection must be made among the options PTE – part-time employment, FTE – full-time employment, DNW – does not work (irrespective of the reasons for employment/unemployment and possible social benefits) and STUDENT – studies (social and health insurance is paid for by the state).

More than one half of the patients have full-time employment (57.0%), followed by 13.5% patients who work part-time.

Table 11 Patient distribution by employment

Employment	All centres	
	Number	Percentage*
PTE	1217	13.5%
FTE	5158	57.0%
DNW	2114	23.4%
STUDENT	246	2.7%

* 3.4% patients did not have data on employment correctly completed

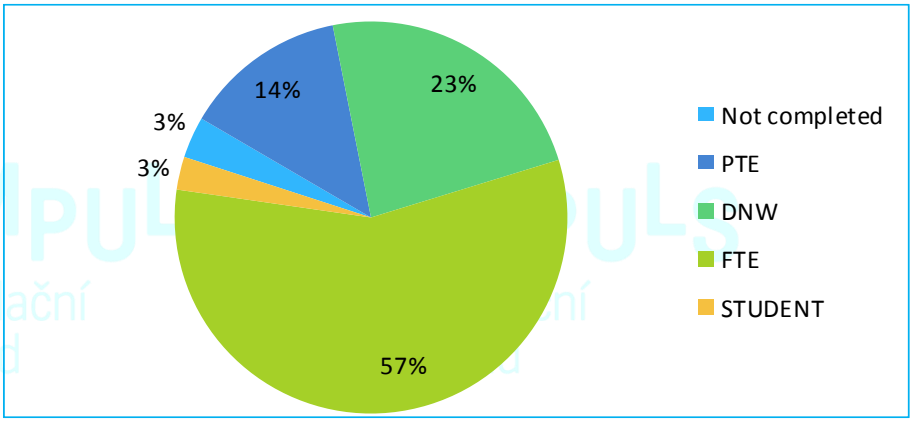

Figure 7 Patient distribution by employment

2.2.2 Social benefits

The structure of social benefits is based on simplified data as the completer had always to choose one, "most important" benefit in cases where a patient was receiving more benefits. DP1, DP2 and DP3 are social benefits that were of most interest to us - these codes denote 3 degrees of disability pension. ML – maternity leave is only reported as secondary information, as are unemployment benefits (UNEMPL). OAP codes for old-age pension.

55.5% patients do not receive any social benefit.

Table 12 Patient distribution by type of social benefit

Social benefit	All centres	
	Number	Percentage*
DP1	1207	13.3%
DP2	676	7.5%
DP3	1023	11.3%
ML	534	5.9%
UNEMPL	73	0.8%
OAP	201	2.2%
Does not receive (X)	5021	55.5%

* 3.4% patients had no data completed for social benefits

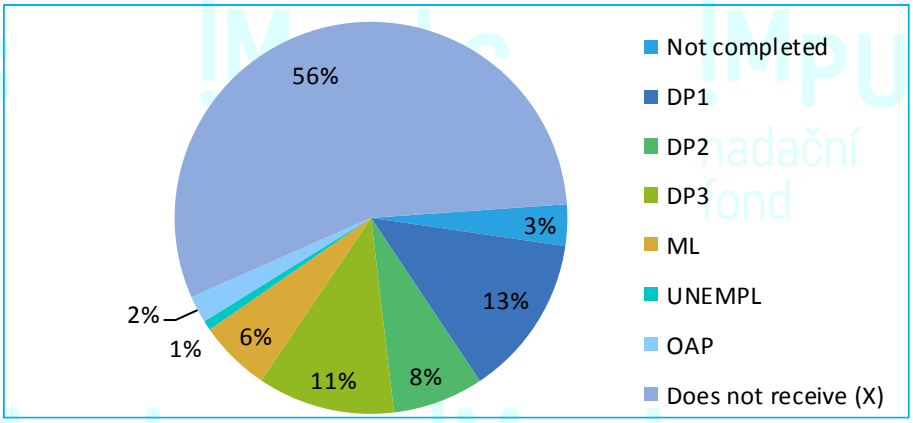

Figure 8 Patient distribution by type of social benefit

2.3 Disease duration period

Mean disease duration period is 10.5 years.

Table 13 Disease duration period (from disease onset to last visit)

Centre	Mean	Median	Minimum	Maximum	SD	Number of missing values
All centres	10.5	8.9	0.0	46.5	7.7	4

2.4 Degree of damage

Degree of damage is assessed using EDSS (Expanded Disability Status Scale) assigned value at each visit. Degree of damage is analysed as that found at the last available patient visit.

EDSS ranges from 0 to 10, where 0 means healthy patient without complaints, degree 5 corresponds to considerable damage, inability to work and ability to walk for a distance less than 500 metres, and degree 10 means death due to MS.

Median EDSS value is 2.5. Most patients are in the EDSS group between 1.5 – 2.

Table 14 Degree of damage (EDSS value) at last visit

Centre	Mean	Median	Minimum	Maximum	SD	Number of missing values
All centres	2.7	2.5	0.0	10.0	1.5	6

Table 15 Degree of damage (EDSS value) at last visit

EDSS	All centres	
	Number	Percentage*
0 – 1	1305	14.4%
1.5 – 2	3280	36.3%
2.5 – 3	1580	17.5%
3.5 – 4	1308	14.5%
4.5 – 5	844	9.3%
5.5 – 6	511	5.7%
6.5 – 7	189	2.1%
7.5 – 8	17	0.2%
8.5 – 9	3	0.0%
9.5 – 10	1	0.0%

* 0.1% patients had no data completed about EDSS degree

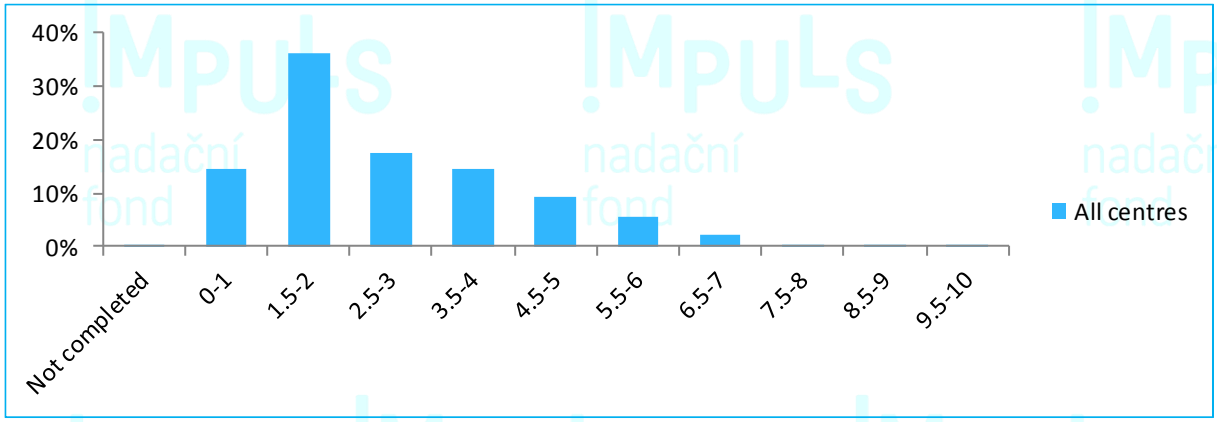

Figure 9 Patient distribution by EDSS degree

2.5 Relapse

Over the last 6 months, relapse of the disease (recurrence of symptoms) was recorded in 8.7% patients, and 22.0% over the period of 12 months. What should be taken into account is that the number of relapses reported here is an overall number including multiple relapses in one patient. Mean number of relapses annually (ARR, annualized relapse rate) is 0.220.

Table 16 Relapse occurrence over last 6 and 12 months

Relapse	All centres	
	Number	Percentage
Over 6 months	787	8.7%
Over 12 months	1986	22.0%

Relapse severity is defined as mild, moderate or severe. Mild relapse intensity means that the relapse does not impact negatively on activities of daily life (ADLs). Moderate intensity does impact on activities of daily life already, while the severe form is recorded in cases where the relapse is associated with severe discomfort of the patients, deteriorates their activities of daily life significantly and results in their inability to work, or hospital admission.

Severity of most relapses was mild or moderate. Mild relapses account for 39.6% of all recorded relapses over the last 6 months, while this rate is 39.9% over the last 12 months. Moderate-intensity relapses was 55.4%, or 55.6% and severe relapses was 4.8%, or 4.4%.

Table 17 Relapse severity over last 6 and 12 months

Relapse over 6 months	All centres	
	Number	Percentage*
Mild	312	39.6%
Moderate	436	55.4%
Severe	38	4.8%
Relapse over 12 months	**Number**	**Percentage***
Mild	793	39.9%
Moderate	1105	55.6%
Severe	87	4.4%

* In 0.1% of the recorded relapses data on relapse severity over last 6 months were missing
In 0.1% of the recorded relapses data on relapse severity over last 12 months were missing

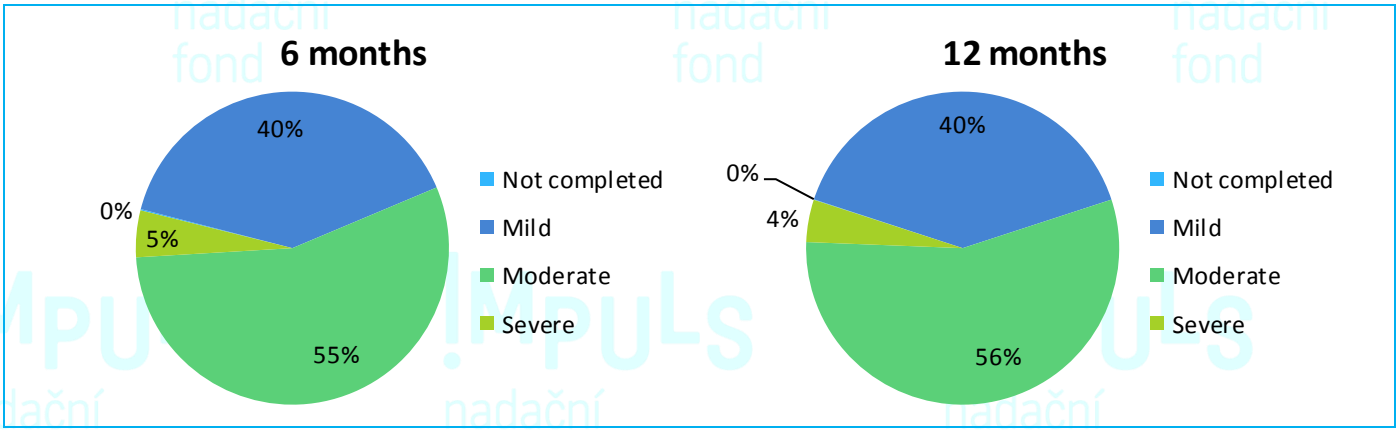

Figure 10 Relapse severity over last 6 and 12 months

The last analysed parameter was the form of relapse treatment – outpatient vs. inpatient treatment. Vast majority of the relapses was treated on outpatient basis. Rates of hospital treatments in individual centres were around 10 percent.

Table 18 Type/form of relapse treatment over last 6 and 12 months

Relapse over 6 months	All centres Number	Percentage*
Outpatient	710	90.2%
Hospital stay	60	7.6%
Relapse over 12 months	**Number**	**Percentage***
Outpatient	1723	86.8%
Hospital stay	217	10.9%

* 2.2% of relapses recorded over the last 6 months data on type of treatment were missing
2.3% of relapses recorded over the last 12 months data on type of treatment were missing

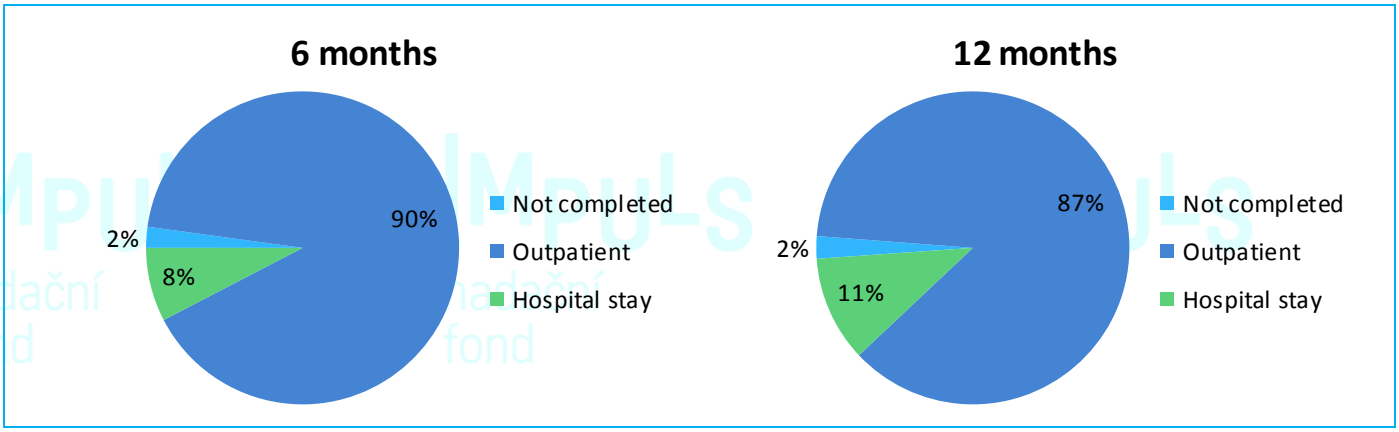

Figure 11 Type/form of treatment over last 6 and 12 months

2.6 Treatment

Evaluation of MS treatment included the preparation used at last visit, a DMD or IVIG. Five patients did not terminate their treatment for 2 preparations, so the numbers for these patients are included twice. In these cases, it is a parallel treatment with two medicines.

Patients receiving IVIG preparations were included by very few centres in this phase. 422 patients (4.7%) did not receive any DMD or IVIG preparation at their last visit (their treatment was temporarily or permanently discontinued). These 422 patients are not included in Table 19, but are included in Table 20.

Most patients received Copaxone (22.6%). 26.0% patients used the escalation therapy (Gilenya, Lemtrada, Tecfidera, Tysabri) at the time of the last visit.

Table 19 Patient distribution by the preparation used at last visit

Treatment	All centres	
	Number	Percentage
DMD		
Aubagio	424	4.9%
Avonex	1400	16.2%
Betaferon	745	8.6%
Copaxone [20]	311	3.6%
Copaxone [40]	1642	19.0%
Extavia	141	1.6%
Gilenya	859	10.0%
Lemtrada	76	0.9%
Plegridy	0	0.0%
Rebif[22]	550	6.4%
Rebif[44]	999	11.6%
Tecfidera	530	6.1%
Tysabri	780	9.0%
IVIG	6	0.1%
Flebogamma	103	1.2%
Gammagard	5	0.1%
Kiovig	42	0.5%
Octagam	14	0.2%

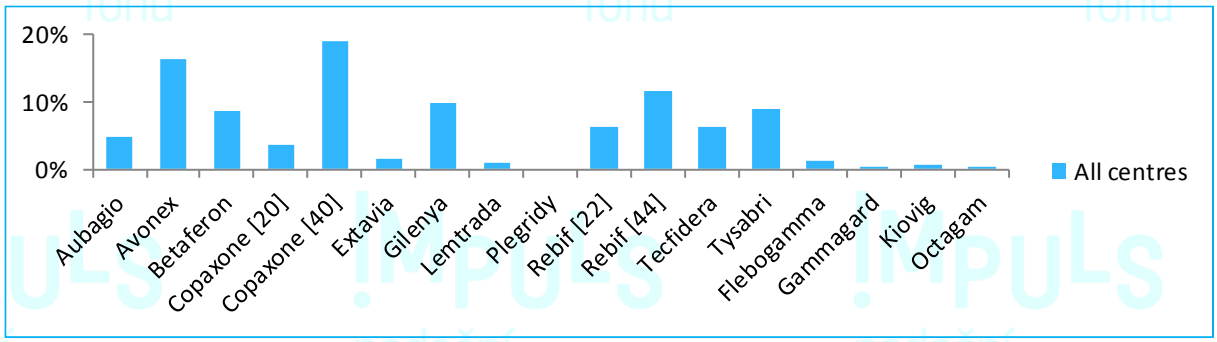

Figure 12 Medicinal preparations used - DMDs and IVIGs

2.6.1 New initiations, terminations or change of therapy with DMDs/ IVIGs

As part of a more detailed analysis of patient treatment the proportion of patients was determined who initiated treatment with new DMD/ IVIG preparations over the last half year and whole year prior to data export on 31. 12. 2016. 3.5% or 7.5% initiated treatment with these preparations, respectively.

The number of patients who terminated treatment with DMDs over the period of interest cannot be exactly determined at present. At their last visit, 422 patients (4.7%) received no treatment. 120 of these patients (1.3%) terminated/discontinued treatment over the half year of interest, and the remaining 302 patients (3.3%) had terminated treatment earlier and did not initiate new treatment over the period of interest.

The last recorded parameter was the number of patients who changed their DMD or IVIG preparation over the period of interest. Over the last half year, the number of these patients was 4.9% while it was 14.7% over the last year.

Table 20 Number of patients who initiated new treatment with DMDs/ IVIGs, terminated or changed these preparations over the period of interest

Treatment - over last 6 months	All centres	
	Number	Percentage
Initiation	315	3.5%
New termination	120	1.3%
Earlier termination	302	3.3%
Termination overall	422	4.7%
Change	443	4.9%
Treatment - over last 12 months	**Number**	**Percentage**
Initiation	681	7.5%
New termination	220	2.4%
Earlier termination	202	2.2%
Termination overall	422	4.7%
Change	1332	14.7%

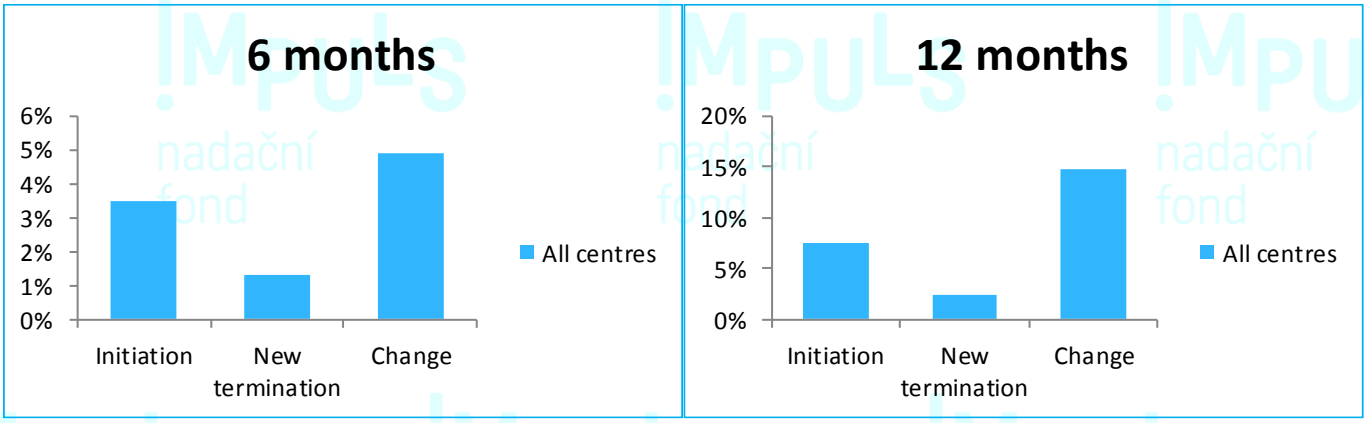

Figure 13 New initiation, termination or change of therapy with DMDs/ IVIGs

2.7 Health-related events

2.7.1 Pregnancy

Over the evaluated period of 6 months prior to data export on 31. 12. 2016 a total of 60 MS patients delivered children (0.9%). 58 of these gave birth to 1 child, 2 patients had twins. In the course of whole 2016 child deliveries were reported in a total of 137 patients (2.1%). 132 of these patients delivered 1 child, 4 patients had twins, and 1 had triplets.

Table 21 Number of deliveries over the period of interest

Pregnancies - last 6 months	All centres	
	Number	Percentage
Number of deliveries	60	0.9%
Pregnancies - last 12 months	Number	Percentage
Number of deliveries	137	2.1%

2.7.2 Adverse events

Very few adverse events were recorded. Some centres had not yet started to complete this parameter in more detail. These results cannot thus be reliably interpreted so far. There is no correction in place for data expression in percentages for the case of multiple AEs in one patient.

There have been 1 serious adverse event reported in the previous 6 months. Medicinal product Tysabri was associated to the development of infection. The relevant information was communicated to the marketing authorization holder by the MS treatment centre. Earlier in the first half of 2016, 1 serious adverse event was reported in relation to the product Rebif [44]. Details about local necrosis in the site of injection was forwarded to the national authority SÚKL by the MS treatment centre.

Table 22 Number of adverse events with first occurrence in the period of interest

Adverse events - last 6 month	All centres	
	Number	Percentage
Number of AEs	70	0.8%
Number of predefined AEs	25	0.3%
Number of severe AEs	1	0.0%
Adverse events - last 12 month	Number	Percentage
Number of AEs	194	2.1%
Number of predefined AEs	61	0.7%
Number of severe AEs	2	0.0%

3 Results – Non-DMD patients

Data on non-DMD patients represent an integral part of ReMuS if available. Patients are classified "non-DMD" provided that they have not been administered DMD and/or IVIG either at all or only before 1. 1. 2013. Following a 2-year initial phase, each centre starts to enter additional data on these patients. In the reporting period up to 31. 12. 2016, only 3 centres were in the 2-year initial phase; Hospital České Budějovice, University Hospital St. Anna in Brno and Regional Hospital of T. Baťa in Zlín. These centres delivered information about DMD/IVIG patients only.

The centres that provided data on less than 20 non-DMD patients were excluded from the analysis albeit not in the initial phase for this sample size would not allow appropriate statistical analysis and interpretation. It was the case of University Hospital Motol in Prague, Regional Hospital Pardubice, University Hospital Královské Vinohrady in Prague, University Hospital in Brno Bohunice and University Hospital Olomouc.

Taken together, 7 MS centres were considered in the present analysis of non-DMD patients - General University Hospital in Prague, Hospital Teplice, Hospital Jihlava, University Hospital Plzeň, Univeristy Hospital Ostrava, Thomayer Hospital Krč in Prague, University Hospital Hradec Králové. Patients were included on condition that they completed at least one appointment in the course of 2016.

Table 23 shows the final number of non-DMD patients enrolled into the ReMuS registry up to 31. 12. 2016. The first column represents a total of all patients in the registry having signed informed consent who do not fulfil the criteria for DMDM/IVIG. Number of patients whose data entered the present analysis (completed at least 1 appointment in 2016 in the centre that reported more than 20 subjects) is shown in the second column.

Table 23 Total number of non-DMD patients per centre

Centre	Non-DMD patients in the registry (centres with less than 20 non-DMD patients were not included)	Analysed Non-DMD patients	Percentage of Non-DMD patients in the analysis
VFN	1042	876	44.8%
Teplice	366	364	18.6%
Jihlava	109	102	5.2%
Motol	– (13)	–	–
Plzeň	209	206	10.5%
Pardubice	– (0)	–	–
Ostrava	68	67	3.4%
Vinohrady	– (7)	–	–
Krč	52	52	2.7%
Hradec Králové	288	288	14.7%
Brno Bohunice	– (0)	–	–
Olomouc	– (1)	–	–
Total	2134	1955	100.0%

The following tables outline characteristics of non-DMD patients coming from the 7 abovementioned centres compared to DMD/IVIG patients from all 15 centres participating in ReMuS.

The mean age of non-DMD patients is higher than in DMD/IVIG patients (53.3 years vs. 41.3 years) and they appear to be elder at the onset of the disease (34.9 years vs. 30.8 years). Significantly smaller portion of non-DMD patients were working compared to DMD/IVIG patients. There is the similar result in case of social benefits too. 40.2% non-DMD patients were entitled invalidity pension stage 3 at the time of the last appointment, 17.0% were retired and only 28.3% non-DMD patients were allocated no social benefits. In contrast, only 11.3% DMD/IVIG patients were entitled invalidity pension stage 3, 2.2% were retired and 55.5% non-DMD patients did not receive any social benefits.

Table 24 Comparison of parameters of DMD/ IVIG and non-DMD patients – part 1

		DMD/ IVIG patients		Non-DMD patients	
Parameter		Number/ Mean	Percentage/ SD	Number/ Mean	Percentage/ SD
Sex	Female	6464	71.5%	1397	71.5%
	Male	2580	28.5%	558	28.5%
Age		41.3	10.4	53.3	11.6
Age	0 – 10	0	0.0%	0	0.0%
	10 – 20	85	0.9%	1	0.1%
	20 – 30	1224	13.5%	55	2.8%
	30 – 40	2903	32.1%	214	10.9%
	40 – 50	2933	32.4%	457	23.4%
	50 – 60	1477	16.3%	581	29.7%
	60 – 70	402	4.4%	529	27.1%
	70 – 80	20	0.2%	113	5.8%
	80 – 90	0	0.0%	5	0.3%
	90 – 100	0	0.0%	0	0.0%
Age at disease onset		30.8	9.6	34.9	11.3
Employment	PTE	1217	13.5%	147	7.5%
	FTE	5158	57.0%	585	29.9%
	DNW	2114	23.4%	1219	62.4%
	STUDENT	246	2.7%	4	0.2%
Social benefits	DP1	1207	13.3%	123	6.3%
	DP2	676	7.5%	125	6.4%
	DP3	1023	11.3%	785	40.2%
	ML	534	5.9%	26	1.3%
	UNEMPL	73	0.8%	10	0.5%
	OAP	201	2.2%	333	17.0%
	Does not receive (X)	5021	55.5%	553	28.3%
Disease duration period		10.5	7.7	18.4	10.7

Non-DMD patients in the registry have higher mean EDSS compared to DMD/ IVIG patients (4.7 vs. 2.7) whilst the most frequent are those with EDSS stage 6.5 – 7 (23.7%). 5.3% of non-DMD patients experienced relapses and 10 non-DMD patients (0.7%) gave birth in 2016.

Table 25 Comparison of parameters of DMD/ IVIG and non-DMD patients – part 2

		DMD/ IVIG patients		Non-DMD patients	
Parameter		Number/ Mean	Percentage/ SD	Number/ Mean	Percentage/ SD
EDSS		2.7	1.5	4.7	2.2
EDSS	0 – 1	1305	14.4%	140	7.2%
	1.5 – 2	3280	36.3%	286	14.6%
	2.5 – 3	1580	17.5%	178	9.1%
	3.5 – 4	1308	14.5%	215	11.0%
	4.5 – 5	844	9.3%	166	8.5%
	5.5 – 6	511	5.7%	315	16.1%
	6.5 – 7	189	2.1%	463	23.7%
	7.5 – 8	17	0.2%	156	8.0%
	8.5 – 9	3	0.0%	34	1.7%
	9.5 – 10	1	0.0%	1	0.1%
Relapse occurrence over 6 months		787	8.7%	46	2.4%
Relapse occurrence over 12 months		1986	22.0%	103	5.3%
Pregnancies Last 6 months	Number of deliveries	60	0.9%	3	0.2%
Pregnancies Last 12 months	Number of deliveries	137	2.1%	10	0.7%

4 Conclusion

On 31. 12. 2016, the eight data export into ReMuS registry was delivered, followed by regular interim data analysis from the registry focusing on the period from 1. 1. 2016 to 31. 12. 2016. Over the evaluated period data of DMD/ IVIG patients from fifteen MS treatment centres included in ReMuS registry were available - General University Hospital in Prague (VFN), Hospital in Teplice, Hospital in Jihlava, University Hospital Motol in Prague, University Hospital in Plzeň, Hospital of Pardubice Region, University Hospital in Ostrava, University Hospital Královské Vinohrady in Prague, Thomayer University Hospital Krč in Prague, University Hospital in Hradec Králové, University Hospital in Brno (Bohunice), University Hospital in Olomouc, Hospital in České Budějovice, University Hospital St. Anna in Brno and Regional Hospital T. Baťa in Zlín. Information about non-DMD patients was provided by 7 centres - General University Hospital in Prague (VFN), Hospital in Teplice, Hospital in Jihlava, University Hospital in Plzeň, University Hospital in Ostrava, Thomayer University Hospital Krč in Prague and University Hospital in Hradec Králové. These MS treatment centres are no more in the initial phase (they have been entering data for more than 2 years) and were eligible to enter the analysis by providing data on more than 20 non-DMD patients. These centres enter data on their patients in the registry on continual basis, and as of the day of export on 31. 12. 2016 data on the treatment of 9343 DMD/ IVIG patients and 2134 non-DMD patients has been collected. After the exclusion of patients missing recent data, data of the total of 9044 DMD/ IVIG and 1955 non-DMD patients from the whole Czech Republic were processed for the purpose of the present analysis.

The main analysis was performed on the data from DMD/ IVIG patients. 71.7% of them were of female gender, mean age at the last visit was 41.3 years and the mean age at the disease onset was 30.8 years. 99.6% patients were over 18 and 58.4% patients were insured with the General Health Insurance Company (VZP). The registry includes data of patients from all regions of the Czech Republic. 70.5% patients are able to work (they work full-time or part-time) and 32.1% receive stage 1-3 disability pensions. The most frequent degree of impairment are patients with EDSS between 1.5 and 2. Mean number of relapses in one year (ARR, annualized relapse rate) is 0.220. 55.4% relapses over the last 6 months and 55.6% relapses over the last 12 months were moderate intensity, and the vast majority was treated outpatient. Medicinal product used most often was Copaxone (22.6%). During the last 6 months, 3.5% of patients started with DMD treatment, 1.3% of patients completed or interrupted the DMD treatment and 4.9% patients changed DMD treatment. Over the last year, 7.5% patients started with DMD treatment, 2.4% of patients completed or interrupted the DMD treatment and 14.7% changed their DMD treatment. In the course of whole 2016 deliveries were reported in 137 patients with MS (2.1%). The suspicion for two severe adverse events were reported in the period under review for medicinal products indicated in MS (Tysabri and Rebif). Both events were forwarded to either the marketing authorization holder or SÚKL (State Institute for Drug Control) by both MS treatment centres.

Non-DMD patients were described in terms of demographic, working activity, social benefits, duration of the treatment, EDSS, frequency of relapses and pregnancy. Data from 7 contributing centres was processed indicating that these patients were elder in average compared to DMD/ IVIG patients (53.3 years vs. 41.3 years). Non-DMD patients were also elder at the onset of the disease (34.9 years vs. 30.8 years). Significantly smaller portion of non-DMD patients was active/ able to work. Their mean EDSS was higher compared to DMD/ IVIG patients (4.7 vs. 2.7). The most frequent level of disability EDSS ranged from 6.5 to 7 (23.7%). Relapses were reported in 5.3% of non-DMD patients in 2016. 10 non-DMD patients (0.7%) delivered during 2016.

Progressive engagement of the individual centres needs be considered for interpretation of the outcomes. Information from patients´ records started to be provided recently. The records are continuously corrected and amended based on the deviation reports in all participating centres. The results presented for non-DMD patients are to be regarded as a pilot analysis of the currently available information. The numbers are likely to rise in the future.

Compared to the first export in June 2013, the quantity of patients included in the registry has now increased more than 6-fold and the amount of incorrect or missing data declined. Finally, the involvement of new centres allows to highlight patient variability and diversity of the treatment of MS in the Czech Republic.