



## DISEASE OBSERVATIONAL STUDY REPORT SYNOPSIS

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**Study Title: Involvements of MS patients in treatment switch decision making process in Slovakia**

**Study number: OBS15829**  
**Study name: ENGAGE**

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**Study initiation date [date first patient in (FPI)]: 01-Mar-2019**

**Study completion date [last patient completed/last patient out (LPO)]: 30-Nov-2020**

**Study design: Non-interventional, prospective, national, multicentre, non-product based biomedical research**

**Report date: 06-Aug-2021**

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This registry was performed in compliance with the guidelines for Good Epidemiology Practice. This report has been prepared based on the publication 'Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) – Guidelines for reporting observational studies – Ann Intern Med. 2007'.

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<b>SYNOPSIS</b>	
<b>Title of the registry:</b>	ENGAGE - Involvements of MS patients in treatment switch decision making process in Slovakia (OBS15829)
<b>Design:</b>	Non-interventional, prospective, national, multicentre, non-product based biomedical research
<b>Objectives:</b>	<p><b>Primary objective</b></p> <p>To determine the relationship between patient satisfaction with the treatment and the extent of patient engagement in decision-making related to treatment (TSQM-9 versus SDM-Q-9 questionnaires filled in by patients)</p> <p><b>Secondary objectives</b></p> <ol style="list-style-type: none"> <li>1. Identify the relationship between patient satisfaction with treatment and control preferences that suit both the patient and their physician when engaging in the decision-making process related to treatment (TSQM-9 questionnaires versus concordance score of CPS questionnaires filled in by the patient and their physician)</li> <li>2. Determine the relationship between patient satisfaction with treatment and their knowledge about MS (TSQM-9 versus MS Knowledge Test developed for the Engage study)</li> <li>3. Determine the acceptability of an electronic device for filling in questionnaires by patients, which will immediately send the resulting score to the physician during day-to-day practice at MS-specialized centres</li> <li>4. Collect data to validate the MS Knowledge Test for patients already receiving DMT</li> </ol>
<b>Participants:</b>	<p>Planned number of enrolled patients: 430</p> <p>Planned number of participating sites: 12</p> <p>Planned number of participating countries: 1 (Slovakia)</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Age ≥18 years</li> <li>• The patient has read, understood, signed, and dated the patient informed consent form.</li> <li>• Patient with RRMS treated with registered DMT drugs within usual medical care and in accordance with a SPC approved in Slovakia that is being switched from one type of DMT to another. (Note: Engage study may also include a patient who has been off DMT for the past 3 months.)</li> <li>• Ability to independently fill in patient questionnaires.</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Patient on their first DMT</li> <li>• Patient already included in this study.</li> </ul>
<b>Scientific committee and members:</b>	Not applicable
<b>Publications (reference):</b>	Not applicable
<b>Introduction - Background/rationale:</b>	In recent years, there has been a significant increase in the number of DMDs - disease modifying drugs or DMTs- disease modifying therapies - for the treatment of patients with relapsing-remitting multiple sclerosis (RRMS). To maximize the efficacy of DMT in RRMS, patient satisfaction with treatment is important, as it is reflected in patient adherence, which is, according to WHO definition, the extent to which the behavior of the patient (relating to drug use, compliance with treatment regimens) coincides with recommendations

	<p>made by the health care provider or treatment standards (Scolding et al., 2003). Non-adherence has not only an impact on the course of the patient's disease (more frequent and more severe relapses, progression of neurological deficit), but also significant socio-economic consequences (Steinberg et al., 2010).</p> <p>In order to achieve high adherence, the choice of long-term administered DMT for a particular patient should include, apart from medical considerations, the patient's personal values and preferences (Cofield et al., 2017). In addition, shared patient decision-making (SDM) has led to better compliance and better treatment outcome related to patient satisfaction in the treatment of various diseases (Elwyn et al, 2012), thus reducing the cost of therapy provided to the patient.</p> <p>Degner et al. (1997) introduced a Control Preference Scale (CPS) related to the preferred role in decision-making, which is the most widely used tool to determine the patient's preferred extent of engagement in health-related decision-making and its use in electronic form has been further described by Solari et al. (2013). The SDM-Q-9 questionnaire (which has already been validated in patients with multiple sclerosis (Ballesteros et al., 2017) was introduced to evaluate the extent to which the patient was truly engaged (Kriston et al., 2009). However, in order to engage in decision-making, the patient needs to have a good understanding of their disease and the benefit / risk ratio of the individual treatment options (Heesen et al., 2004; Giordano et al, 2008; Solari et al., 2007).</p> <p>The main objective of the Engage study is to determine the relationship between treatment satisfaction according to the TSQM-9 (Treatment Satisfaction Questionnaire for Medication) questionnaire and the extent of patient engagement in the patient-assessed SDM-Q-9 questionnaire.</p> <p>The study will also use an innovative approach to informing the physician about the resulting CPS questionnaire score - the patient's preferred role in decision-making - and a MS Knowledge Test just prior to a patient interview, at which they will decide on the choice of DMT. Since patient engagement in treatment-related decision-making places great demands on the collaboration between the patient and the physician, it is in practice necessary to introduce measures that could facilitate this cooperation (Tintore et al, 2017).</p> <p>Other Engage study objectives include verifying whether, in MS patient care, an electronic device that delivers information about the patient's preferred role as well as their level of MS knowledge facilitates physician-to-patient communication, and whether this procedure will result in patient engagement in decision-making and, above all, their higher satisfaction with the treatment chosen.</p>
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<p><b>Methodology:</b></p>	<p>Site and patient selection: Approximately 12 neurological centres specializing in MS treatment in Slovakia. The selection of centres took into account the representation of all regions in the Slovak Republic. Physicians offered study participation to all consecutive patients meeting the inclusion criteria. The aim was to recruit 430 patients, allowing for competitive recruitment. Data collection: Data were recorded in an electronic case report form (eCRF). There are 2 planned visits: V0: inclusion visit - after signing the patient informed consent form, the patient was asked to fill in the CPS, the MS Knowledge Test, and the TSQM-9 questionnaire using the electronic device. The resulting questionnaire score was immediately sent to the physician. After the physician gets acquainted with the results of the questionnaires, the patient was invited to the office where a new DMT was selected for the patient. V1: 3 months after the start of a new DMT, the patient was asked to again use the electronic device to fill in the SDM-Q-9 and TSQM-9m questionnaires Physicians completed the CPS and VAS questionnaire only once, using the electronic device Safety data collection: The aim of the registry was not to collect safety data. According to legislative requirements, physicians have to report all severe or unexpected adverse reactions to appropriate health authority without delay. Data management, review, validation: Before gaining access to eCRF, participating physician had to be trained. It was physicians' responsibility that entered data are complete and accurate. Data management could raise queries in order to resolve discrepancies resulting from the data review. Random data quality control performed by qualified sponsor designee was planned in 5% of sites which enrolled at least 1 patient. Statistical considerations: Pearson's correlation coefficient was calculated for the main observed parameters (TSQM versus SDM Q 9) and for the relationship between TSQM 9 versus the patient / physician CPS concordance and the correlation between TSQM 9 versus the Knowledge Test. All data were processed using descriptive statistics. For continuous variables, the number of patients selected, the mean, the standard deviation and other variance markers (median, interquartile range, and possibly other percentiles as appropriate) were to be determined. For categorical variables, the absolute number and percentage was to be given. All missing data were accounted for each analysis. No imputation of missing data was performed.</p>
<p><b>Registry period:</b></p>	<p>This report includes data reported to the Engage study from 01 March 2019 to 30 Nov 2020.</p>
<p><b>RESULTS</b></p>	
<p><b>Participants (actual):</b></p>	<p>Overall participation status: The ENGAGE study was a national study conducted in Slovakia only. Overall, 315 patients were enrolled at 9 participating sites. Participation per period of the study: Out of 315 enrolled patients, 288 patients completed the study. 27 patients (8.6%) terminated their study participation prematurely and their data were missing for analysis of data collected at V1 (TSQM-9 and SDM-Q-9 questionnaires). Overall, 315 patients were included into analysis of data from V0 and 288 patients were included into analysis of data from V1.</p>
<p><b>Participant characteristics and primary analyses:</b></p>	<p>There were 226 females (71.7%) and 89 males (28.3%) in the study population. With respect to level of education, most patient had secondary education – 155 (49.2%). University degree had 110 patients (34.9%), vocational school finished 44 patients (14.0%) and 4 patients had elementary education (1.3%). <b>Error! Reference source not found.</b> (Appendix II) summarizes treatments before V0 (previous) and treatment to which patient is switched to (new). As previous treatment most patients used Copaxone 40 mg – 71 patients (22.5%), Rebiff 44 – 54 patients (17.1%) and Gilenya – 46 patients (14.6%). Among the most frequently used new treatment was Aubagio – 89 patients (28.7%), Tecfidera – 50 patients (16.1%), and</p>

Ocrevus – 46 patients (14.8%).

Continuous baseline characteristics are described in detail in the table below.

Baseline characteristics (n=315)

Variable	Mean	95%CI for mean	SD	Median	Minimum	Maximum
Age (years)	40.50	39.32 41.69	10.70	40.00	18	68
Period from MS diagnosis (years)	7.61	6.94 8.27	5.97	6.00	0	42
EDSS	2.81	2.65 2.97	1.44	2.50	0	6.5
Number of relapses during the last 12 months	0.71	0.63 0.79	0.75	1.00	0	4
Number of relapses during the last 24 months	0.96	0.85 1.07	0.98	1.00	0	6

The primary objective of the study was to determine the relationship between patient satisfaction with treatment evaluated through TSQM-9 questionnaire and the extent of patient engagement in decision-making related to treatment (SDM-Q-9 questionnaires filled in by patients). Table below summarizes scores of TSQM-9 from V0 and V1 and SDM-Q-9 from V1.

Summary of TSQM-9 from V0 and V1 and SDM-Q-9 from V1:

Variable	Mean	95%CI for mean	SD	Median	Minimum	Maximum
V0 (n=315)						
TSQM-9 Global satisfaction	54.76	52.61 56.91	19.37	57.00	0	100
TSQM-9 Effectiveness	58.39	56.56 60.22	16.52	61.00	0	100
TSQM-9 Convenience	67.44	65.45 69.43	17.93	67.00	17	100
V1 (n=288)						
TSQM-9 Global satisfaction	65.72	63.63 67.81	18.02	71.00	7	100
TSQM-9 Effectiveness	65.10	63.20 66.99	16.33	67.00	0	100
TSQM-9 Convenience	79.86	78.12 81.60	15.01	83.00	11	100
SDM-Q-9	79.00	76.93 81.06	17.79	81.00	13	100

Spearman's correlation coefficient was calculated to determine the TSQM-versus SDM-Q-9 and it is summarized in the table below.

Spearman correlation between TSQM-9 and SDM-Q-9 filled by a patient (n=288)

Variable	Correlation Coefficient	Sig. (2-tailed)
V0		
TSQM-9 Global satisfaction	0.109	0.064
TSQM-9 Effectiveness	0.062	0.292
TSQM-9 Convenience	0.189**	0.001
V1		
TSQM-9 Global satisfaction	0.211**	<0.001

	<p>TSQM-9 Effectiveness 0.266** &lt;0.001</p> <p>TSQM-9 Convenience 0.223** &lt;0.001</p> <p>** . Correlation is significant at the 0.01 level (2-tailed).</p> <p>Spearman’s correlation showed that with very strong statistical significance (p&lt;0.001), there is only mild correlation between TSQM-9 and SDM-Q-2 scores as expressed by correlation coefficient from 0.211 to 0.266.</p>																																																	
<p><b>Other analyses:</b></p>	<p>The study used an innovative approach to informing the physician about the resulting Control preference scale (CPS) questionnaire score - the patient's preferred role in decision-making just prior to a patient interview, at which they decided on the choice of DMT. Each physician also completed CPS to reflect their overall approach to include a patient into decisions</p> <p>Table below summarizes CPS completed by each patient and CPS completed by their physician. However, physicians answered CPS questionnaire only once to assess their overall approach to treatment decision process, therefore their answers do not refer to actual decision process during V0. All physicians chose from only two answers (shared responsibility vs the doctor's decision after considering the patient's opinion). These two options were also the most frequently answered by patients [141 patients (44.8%) for doctor's decision after considering the patient's opinion and 88 patients (27.9%) for sharing responsibility], followed by option the decision made solely by the doctor [64 patients (20.3%)]. Only 22 patients preferred to be involved more in decision making process [15 patients (2.2%) for patient decision only and 15 patients (4.8%) for patients' decision after considering the doctor's opinion]. Physicians also completed CPS (only once during the study) to collect their preferred role. Out of 15 physicians, 5 (33.3%) preferred shared responsibility and 10 (66.7%) chose the doctor's decision after considering the patient's opinion.</p> <p>To determine the relationship between patient satisfaction with treatment and control preference that suits the patient and their physician when engaging in the decision-making process related to the treatment, the analysis of TSQM-9 questionnaires versus concordance score of CPS questionnaires filled on by the patient and their physician was performed.</p> <p>Concordance rate was assessed as consensus between physician and patient. It can be “Agreement”, “Partial agreement”, or “Disagreement”. Agreement means the same answers from investigator and subject. Partial agreement means combination of answers “The Patient decision” and “The Patient decision after considering the doctor's opinion”, or combination “The doctor's decision” and “The doctor's decision after considering the patient's opinion”. Disagreement means other combination of answers.</p> <p>Overall, agreement was observed in 132 patients (41.9%), partial agreement as described above in 129 patients (41.0%) and disagreement in 54 patients (17.1%).</p> <p>As described in the table below, no significant differences (as per mean 95% CI intervals) in TSQM-9 and concordance categories were observed. Only lower median in TSQM-9 Global Satisfaction in subgroup with disagreement (64 vs 71) and lower median in TSQM-9 Convenience in subgroup with agreement (78 vs 83) were observed in comparison to the other subgroups.</p> <p>Table CPS patient-physician concordance vs TSQM-9 at V1 (n=288)</p> <table border="1" data-bbox="443 1522 1487 1879"> <thead> <tr> <th>Variable</th> <th>Mean</th> <th>95%CI for mean</th> <th>SD</th> <th>Median</th> <th>Minimum</th> <th>Maximum</th> </tr> </thead> <tbody> <tr> <td colspan="7" style="text-align: center;">TSQM-9 Global satisfaction</td> </tr> <tr> <td>Agreement</td> <td>64.64</td> <td>61.23 - 68.06</td> <td>18.74</td> <td>71.00</td> <td>14</td> <td>100</td> </tr> <tr> <td>Partial agreement</td> <td>67.57</td> <td>64.31 - 70.84</td> <td>17.98</td> <td>71.00</td> <td>7</td> <td>100</td> </tr> <tr> <td>Disagreement</td> <td>63.86</td> <td>59.29 - 68.44</td> <td>16.27</td> <td>64.00</td> <td>21</td> <td>100</td> </tr> <tr> <td>Total</td> <td>65.72</td> <td>63.63 - 67.81</td> <td>18.02</td> <td>71.00</td> <td>7</td> <td>100</td> </tr> <tr> <td colspan="7" style="text-align: center;">TSQM-9 Effectiveness</td> </tr> </tbody> </table>	Variable	Mean	95%CI for mean	SD	Median	Minimum	Maximum	TSQM-9 Global satisfaction							Agreement	64.64	61.23 - 68.06	18.74	71.00	14	100	Partial agreement	67.57	64.31 - 70.84	17.98	71.00	7	100	Disagreement	63.86	59.29 - 68.44	16.27	64.00	21	100	Total	65.72	63.63 - 67.81	18.02	71.00	7	100	TSQM-9 Effectiveness						
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Partial agreement	66.74	63.75	69.73	16.45	67.00	17	100																																																																																																							
Disagreement	64.90	61.40	68.41	12.49	67.00	33	94																																																																																																							
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Agreement	77.58	74.53	80.62	16.70	78.00	11	100																																																																																																							
Partial agreement	81.71	79.13	84.30	14.23	83.00	39	100																																																																																																							
Disagreement	80.80	77.47	84.14	11.86	83.00	44	100																																																																																																							
Total	79.86	78.12	81.60	15.01	83.00	11	100																																																																																																							
<p>MS knowledge test (MSKT) was developed specifically for this study to verify whether the level of patients' MS knowledge facilitates physician-to-patient communication. Table below summarizes number of patients by achieved scores in individual domains and total score. In comparison to MSTK total score, patients were more successful in completing domains 2 (MS impact on family planning), 3 (MS relapse) and 5 (DMTs), while more mistakes were made in domains 1 (MRI findings) and 4 (MS disability). Of note, no patient correctly answered all questions (grade 1), only 3 (1.0%) patients achieved grade 2, while distribution of grade 3, 4 and 5 was 25.1%/55.6%/18.4% respectively. As a result, 74.0% of patients fell into grade 4 and 5, that are considered as not successful marks. On top of that, there were huge differences among individual questions in frequency of correct (1.3% to 59.4%)/wrong (14.3% to 84.8%) /I don't know answers (2.2% to 49.2%).</p> <p>Summary of MSKT scores by domains and in total.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th rowspan="2"></th> <th colspan="2">Domain 1</th> <th colspan="2">Domain 2</th> <th colspan="2">Domain 3</th> <th colspan="2">Domain 4</th> <th colspan="2">Domain 5</th> <th colspan="2">Total</th> </tr> <tr> <th>n</th> <th>%</th> <th>n</th> <th>%</th> <th>n</th> <th>%</th> <th>n</th> <th>%</th> <th>n</th> <th>%</th> <th>n</th> <th>%</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>2</td> <td>0.6%</td> <td>19</td> <td>6.0%</td> <td>7</td> <td>2.2%</td> <td>0</td> <td>0.0%</td> <td>8</td> <td>2.5%</td> <td>0</td> <td>0.0%</td> </tr> <tr> <td>2</td> <td>6</td> <td>1.9%</td> <td>32</td> <td>10.2%</td> <td>47</td> <td>14.9%</td> <td>1</td> <td>0.3%</td> <td>53</td> <td>16.8%</td> <td>3</td> <td>1.0%</td> </tr> <tr> <td>3</td> <td>28</td> <td>8.9%</td> <td>70</td> <td>22.2%</td> <td>101</td> <td>32.1%</td> <td>29</td> <td>9.2%</td> <td>92</td> <td>29.2%</td> <td>79</td> <td>25.1%</td> </tr> <tr> <td>4</td> <td>130</td> <td>41.3%</td> <td>84</td> <td>26.7%</td> <td>102</td> <td>32.4%</td> <td>46</td> <td>14.6%</td> <td>131</td> <td>41.6%</td> <td>175</td> <td>55.6%</td> </tr> <tr> <td>5</td> <td>149</td> <td>47.3%</td> <td>110</td> <td>34.9%</td> <td>58</td> <td>18.4%</td> <td>239</td> <td>75.9%</td> <td>31</td> <td>9.8%</td> <td>58</td> <td>18.4%</td> </tr> <tr> <td>Total</td> <td>315</td> <td>100.0%</td> <td>315</td> <td>100.0%</td> <td>315</td> <td>100.0%</td> <td>315</td> <td>100.0%</td> <td>315</td> <td>100.0%</td> <td>315</td> <td>100.0%</td> </tr> </tbody> </table> <p>On top of that, domain 2 with questions regarding impact of MS on family planning was more successfully (achieved grade 1, 2 or 3) answered by women (38.4%) then men (11.4%).</p> <p>No significant correlation between patient satisfaction with treatment on V1 and patient knowledge about MS evaluated by Spearman correlation test between TSQM-9 scores versus MS Knowledge Test total scores was detected.</p> <p>Use of electronic device for questionnaires completion by patients, when resulting scores are sent immediately to the physician during the day-to-day practice at MS-specialized clinic was highly appreciated by physicians and nurses. The median score reported thought Visual Analogue Scale (VAS) 0-10 on the satisfaction with the use of an electronic device was 10.0.</p>									Domain 1		Domain 2		Domain 3		Domain 4		Domain 5		Total		n	%	n	%	n	%	n	%	n	%	n	%	1	2	0.6%	19	6.0%	7	2.2%	0	0.0%	8	2.5%	0	0.0%	2	6	1.9%	32	10.2%	47	14.9%	1	0.3%	53	16.8%	3	1.0%	3	28	8.9%	70	22.2%	101	32.1%	29	9.2%	92	29.2%	79	25.1%	4	130	41.3%	84	26.7%	102	32.4%	46	14.6%	131	41.6%	175	55.6%	5	149	47.3%	110	34.9%	58	18.4%	239	75.9%	31	9.8%	58	18.4%	Total	315	100.0%	315	100.0%	315	100.0%	315	100.0%	315	100.0%	315	100.0%
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1	2	0.6%	19	6.0%	7	2.2%	0	0.0%	8	2.5%	0	0.0%																																																																																																		
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Total	315	100.0%	315	100.0%	315	100.0%	315	100.0%	315	100.0%	315	100.0%																																																																																																		



	<p>Furthermore, TSQM-9 questionnaires from V0 and V1 visit, CPS completed by a patient, MS Knowledge Test, and SDM-Q-9 were evaluated separately by the following characteristics: for single demographic groups, (gender, age, education), for different EDSS score values, for different groups according to the duration of the disease (0-1 years, 2-3 years, 4-5 years, 6-10 years, 11 years and more), based on the new DMT treatment introduced at V0, based on the number of previous DMTs used before V0.</p> <p>Based on the above mentioned review of individual characteristics, the following potential relationships were observed:</p> <ul style="list-style-type: none"><li>• The higher is the achieved level of education, the more successful was result of MSKT and the higher was SDM-Q-9 score.</li><li>• The higher is EDSS, the higher is TSQM-9 Convenience score from V0 and the lower is the same parameter from V1.</li><li>• The longer is the duration of the disease, the higher was TSQM-9 Global Satisfaction score from V0 and V1.</li><li>• The higher was the number of previous DMTs, the higher was the SDM-Q-9 score and lower TSQM-9 Efficacy score from V0.</li><li>• During the Engage study, 18 adverse events (AEs) considered to be associated with Sanofi Product and related to the treatment at the same time were reported. Details of all reported AEs are provided in Appendix 3.9 AEs/SAEs Summary.</li></ul>
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<b>Discussions:</b>	<p>Engage patient population is similar to population of MS patients described in previous studies (Ballesteros et al., 2017; Brola et al., 2016), when MS predominantly affects females and young people. In the Engage study, females have superiority in numbers to males (71.7% of women) and average age was 40.5 years in comparison to Polish study of Brola et al, (2016) with 69.7% of women and average age 37.8 years, or Spanish study with 68.3 % of women and average age 42.1 years (Ballesteros et al., 2017). Mean EDSS and duration of MS are also comparable as follows – Engage study: EDSS 2.8, duration 7.6 years; Brola et al. (2016): EDSS 3.2, duration of MS 14.5 years; Ballesteros et al. (2017) EDSS 2.5, duration of MS 9.1 years. For the Engage study, the need of switch from one type of DMT to another was an inclusion criterion.</p> <p>In the Engage study, TSQM-9 scores (mean, 95% confidence interval – CI) collected at V0 [Global satisfaction 54.76, 52.61-56.91, Effectiveness 58.39, 56.56-60.22, Convenience 67.44, 65.45-69.43] are lower in comparison to TSQM-9 scores from V1 [Global satisfaction 65.72, 63.63-67.81, Effectiveness 65.10, 63.20-66.99, Convenience 79.86, 78.12-81.60]. Overall, V1 TSQM-9 scores in the Engage study, reflect the data from Skarlet study – non-interventional cross-sectional study to evaluate treatment satisfaction and quality of life in patients with RRMS with current DMT in clinical practice [Global satisfaction 66.99, 65.32-68.67, Effectiveness 68.07, 66.47-69.66, Convenience 75.05, 73.49-76.60] (Turcani et al., 2020).</p> <p>Median SDM-Q-9 in cross-sectional study in RRMS patients was 93.3% (Ballesteros et al., 2017), what is higher than in the Engage study - 81.0%. On the opposite, the reported mean sum SDM-Q-9 scores ranged from 42 to 75 in several studies of various designs and in different diseases reviewed by Doherr et al. (2017).</p> <p>The primary objective of the study was to determine the relationship between patient satisfaction with treatment evaluated through TSQM-9 questionnaire and the extent of patient engagement in decision-making related to treatment (SDM-Q-9 questionnaires filled in by patients). Spearman’s correlation showed that with very strong statistical significance (&lt;0.001), there is only mild correlation between TSQM-9 and SDM-Q-2 scores as expressed by correlation coefficient from 0.211 to 0.266. To our knowledge, no study has performed such correlation to date, but positive effect of shared decision-making on patient adherence to DMT in MS care (Ben-Zacharia et al., 2018) was already established. In the setting of the elderly patients on dialysis as optional treatment to prolong survival, Ladin et al. (2017) investigated the relationship between patient engagement in treatment modality selection and treatment satisfaction. As a result, many older patients did not perceive dialysis as their choice, did not actively engage in decision-making and remained unaware of conservative management. However, patients who engaged in SDM (mostly modality selection) described greater satisfaction with the process and outcomes, exhibiting confidence and pride in their thorough, deliberative decision-making process.</p> <p>In the Engage study, preferred role in treatment decision making was assessed by CPS, when only 7% of patients reported active role (patient decision only or patient decision after consideration of physician’s opinion), 28% would share the responsibility and 65% would prefer passive role (physician’s decision after consideration of patient’s opinion or physician’s decision only). In the extensive American NARCOMS registry of 7009 adult patients with MS, the corresponding (active/shared/passive) CPS scores were 47.9%/42.8%/10.3% (Cofield et al., 2017). According to Solari et al. (2013), the most important factor associated with role preference is a country of a patient (with active/collaborative/passive roles reported by 15%/55%/30% of Italian vs. 70%/30%/0% of German patients - p=0.016) when cultural characteristics and country-specific variations in health system organization might contribute to these differences. Also, familiarity with a clinical condition increases desire for a shared (as opposed to passive) role and older and less educated individuals were most likely to prefer passive roles (Deber et al., 2007).</p> <p>No differences in TSQM-9 from V1 and CPS patient/physician concordance categories were observed. Only lower median in TSQM-9 Global Satisfaction in subgroup with disagreement (64 vs 71) and lower median in TSQM-9 Convenience in subgroup with agreement (78 vs 83) were observed in comparison to the other subgroups. These results suggest that disagreement in treatment decision making approach between patient and physician might affect future patient satisfaction with this treatment, while patients would be happy with less convenient treatment if the patient role in treatment decision making was in accordance</p>
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	<p>with their preference. To our knowledge, no study has performed correlation such to date.</p> <p>In the Engage study, huge gaps in patient education on their disease assessed by MSKT questionnaire were observed as no patient correctly answered all questions (grade 1), only 3 (1.0%) patients achieved grade 2, while distribution of grade 3, 4 and 5 was 25.1%/55.6%/18.4% respectively. As a result, 74.0% of patients fell into grade 4 and 5, that are considered as not successful marks. Good understanding of a disease is important prerequisite for patient involvement into treatment decision process. Interventions - patient education programmes led to significantly more participants with informed choice (Köpke et al., 2017) and to more autonomous decision making in patients with relapsing MS (Köpke et al, 2009). As there is no comparable questionnaire, MSKT might be an important tool to measure the level of patient knowledge.</p> <p>Although no significant correlation between patient satisfaction with treatment on V1 and patient knowledge about MS evaluated by Spearman correlation test between TSQM-9 scores versus MSKT was detected in the Engage study, Yeh et al. (2018) observed that sufficient patient education and patient satisfaction were positively related to patient empowerment, but to our knowledge, no study has performed such correlation specifically in MS patients to date.</p> <p>Use of electronic device for questionnaires completion by patients, when resulting scores are sent immediately to the physician prior the patient visit was highly appreciated by physicians and nurses. The median score reported thought Visual Analogue Scale (VAS) 0-10 on the satisfaction with the use of an electronic device was 10.0. Other successful use of real-time patient-reported outcomes has been reported in patients with heart failure (Stehlik et al., 2017), in postoperative follow-up after hepatectomy, distal pancreatectomy, or pancreaticoduodenectomy (Pickens et al., 2019), or in patients with rheumatoid arthritis (Forman et al., 2018). Methods of collecting patient-reported outcomes on electronic device, or web-based applications enable also remote data collection that could be used to support a more frequent assessment of diseases symptoms without over-burdening the healthcare system (Haylard, 2011). Positive results of remote symptom monitoring were already described by Sebastian et al., (2019) in patients with ulcerative colitis, or in oncology clinical practice by Halyard (2011).</p> <p>Implementation of an interactive online patient decision aid that informs patients of their options, considers their individual preferences and goals, and facilitates conversations with their physicians specifically for patients with relapsing forms of MS are also under investigation to facilitate patient engagement in evidence-based treatment decisions (Bansnack et al., 2019).</p> <p>Engage study also evaluated possible association of TSQM-9 scores, CPS completed by a patient, MSKT score and SDM-Q-9 score by various patient/disease characteristics, when the following potential relationships were observed:</p> <ul style="list-style-type: none"><li>• The higher is the achieved level of education, the more successful was result of MSKT (not that convincing) and the higher was SDM-Q-9 score.</li><li>• The higher is EDSS, the higher is TSQM-9 Convenience score from V0 and the lower is the same parameter from V1.</li><li>• The longer is the duration of the disease, the higher was TSQM-9 Global Satisfaction score from V0 and V1.</li><li>• The higher was the number of previous DMTs, the higher was the SDM-Q-9 score and lower TSQM-9 Efficacy score from V0.</li></ul> <p>Among 7009 participants of the NARCOMS Registry – adult patients with MS, Cofield et al. (2017) performed detailed analysis of associations between CPS selection and various patient/disease characteristics. According to CPS scores, active/shared/passive role was preferred by 47.9%/42.8%/10.3% of patients. Shared preference was higher for women and those taking DMTs and increased with age and disease duration (all <math>p &lt; 0.05</math>) while patient-centered decisions were most common for respondents not taking a DMT at the time of the survey and were preferred by those who had no DMT history compared with those who had previously taken a DMT (<math>p &lt; .0001</math>). There was no difference in shared decision making</p>
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	<p>preference by current MS disease course after adjusting for other disease-related factors.</p> <p>In the study of D'Amico et al. (2016), active/shared/passive role as assessed by CPS score was chosen by 25%/35%/40% of patients for the decision-making process on their first-line treatment. The patients showing an active attitude had a significantly higher EDSS score and a significantly higher number of relapses (<math>p &lt; 0.5</math> for both) than those who showed other attitudes. Therefore, those with higher disability preferred to be active in the decision-making process.</p> <p>As discussed above, the most important factor associated with role preference is a country of a patient when cultural characteristics and country-specific variations in health system organization might contribute to these differences Solari et al. (2013). Also, familiarity with a clinical condition increases desire for a shared (as opposed to passive) role and older and less educated individuals were most likely to prefer passive roles (Deber et al., 2007).</p> <p>Although no statistical analysis on individual factors associated with TSQM-9, CPS, MSKT and SDM-Q-9 was performed, results of the Engage study confirmed published findings that education and number of previous DMTs might impact patient willingness to be involved in treatment decision making. On top of that, Engage study brought novel observation of association between treatment satisfaction features and EDSS, MS duration and number of previous treatment. Individual factors associated with treatment satisfaction are needed to be investigated in future studies to help to improve patient empowerment, increase patient quality of life and potentially enhance efficacy of administered treatment and improve MS outcomes.</p> <p>There are several limitations associated with this study. First, the study was conducted within one country with traditionally quite passive patient role, which could limit the generalizability of the results for other countries. Second, physicians themselves preferred only two categories out of 5 in CPS. Third, a huge gap in patient education on their disease was observed while good understanding of a disease is an important prerequisite for patient involvement into treatment decision process.</p> <p>On the opposite, the important strength of the study is the implementation of treatment satisfaction evaluation in the context of treatment decision. Furthermore, the Engage study collected wide variety of parameters that helped to provide insight into role preference both by patient and physician, the extent to which patients are involved in the process of decision-making (SDM-Q-9) and MS Knowledge test – a tool to measure patient knowledge. The newly developed MSKT questionnaire was also helpful to identify areas of patient education that must be improved by the frequency of wrong/I don't know answers to each question.</p> <p>Patient engagement is vital in MS in order to optimize outcomes for patients, society and healthcare systems. Recently, the issues that influence patient engagement in MS were described in detail with elaborated strategies for overcoming these barriers (Rieckmann et al., 2015; Rieckmann et al., 2018). Of particular interest now is the development of patient-centred educational resources that can be used during consultations to enhance disease understanding and improve communication between patient and their physicians. This patient-centred approach not only allows patients to be more comfortable with the decisions they make but enables active participation in self-care. Use of an interactive online patient decision aid that informs patients of their options, considers their individual preferences and goals, and facilitates conversations with their physicians, could also improve how patients with relapsing forms of MS make evidence-based treatment decisions (Bansnack et al., 2019).</p> <p>Furthermore, training programs dedicated to healthcare professionals should be developed on shared decision making, patient-centered care, risk communication, and relation-building so that they are fully aware of the shared decision making process and can communicate effectively with persons with MS (Rahn et al., 2020). Even with difficult choices between modalities, patients appreciated the opportunity to deliberate, learn more through discussion and educational resources and to engage in discussions with clinicians and loved ones (Ladin et al., 2017).</p>
<p><b>Conclusions:</b></p>	<p>In conclusion, the results of this detailed survey increase our understanding of MS patient population characteristics, patient satisfaction with DMT treatment, extend of patient involvement in decision making,</p>

	<p>role preferred by both patient and physician and the level of patient knowledge of their disease. Although no evaluated correlation (TSQM-9 vs SDM-Q-9; TSQM-9 vs patient/physician concordance in CPS and TSQM-9 vs MSKT) was confirmed, Engage study revealed important information that will be helpful in improving the healthcare provided to patients with MS.</p> <p>Huge gaps in patient education on their disease were observed in the Engage study. However, no analogous tool to measure patient knowledge has been developed to date, therefore we are not able to compare Engage population with other study results. These gaps also bring opportunity to improve patient education that might increase their understanding to the treatment options and enhance their willingness to be engaged more in decision making.</p> <p>Engage study introduced an innovative approach when electronic device used by patients to complete questionnaires sent immediately patient scores (the preferred role in decision-making CPS and a MS Knowledge Test) to the physician just prior to a patient interview, at which they discussed the choice of DMT. Physicians and nurses highly appreciated the use of such device. In future perspective, methods of collecting patient-reported outcomes on electronic device, or web-based applications enable also remote data collection that could be used to support a more frequent assessment of diseases symptoms what might be safer and more comfortable for a patient and at the same time without over-burdening the healthcare system.</p> <p>Although no statistical analysis on factors associated with treatment satisfaction, preferred role in treatment decision, MS knowledge and the extend of patient involvement in decision making was performed, results of the Engage study confirmed published findings that education and number of previous DMTs might impact patient willingness to be involved in treatment decission making. On top of that, Engage study brought novel observation of a correlation of treatment satisfaction features and EDSS, MS duration and number of previous treatment. Individual factors associated with treatment satisfaction are needed to be investigated in future studies to help to improve patient empowerment, increase patient quality of life and potentially enhance efficacy of administered treatment and improve MS outcomes.</p>
<p><b>Date of report:</b></p>	<p>06-August-2021</p>