

Additional Table 1: Charlson-Comorbidity-Index (CCI) and its components

No	Comorbidity	Charlson Score	ICD-10 Code
1	Coronary artery disease	1	I20%, I21%, I22%, I23%, I24%, I25%
2	Congestive heart failure	1	I11%, I50%
3	Peripheral vascular disease	1	I73%, I74%, I77%
4	Cerebrovascular disease	1	G45%, G46%, I6%
5	Dementia	1	F00%, F01%, F02%, F03%, G30%
6	Chronic pulmonary disease	1	J4%, J6% w/o J67%, J68%, J69%
7	Connective tissue disorder	1	M05%, M06%, M07%, M08%, M3%
8	Peptic ulcer disease	1	K25%, K26%, K27%, K28%
9	Mild liver disease	1	B18%, K70%, K73%, K75%
10	Diabetes mellitus without complications	1	E109%, E119%, E129%, E139%, E149%
11	Hemiplegia	2	G81%, G82%
12	Moderate or severe renal disease	2	N17%, N18%, N19%
13	Diabetes mellitus with end-organ damage	2	E10%, E11%, E12%, E13%, E14% w/o [No 10]
14	Tumor without metastases, leukemia, lymphoma, multiple myeloma	2	C% w/o [No 16]
15	Moderate or severe liver disease	3	K72%, K74%, I85%
16	Metastatic solid tumor	6	C77%, C78%, C79%, C80%
17	AIDS	6	B20%, B21%, B22%, B23%, B24%

Additional Table 2: Proxies used to identify symptom related treatment of MS-related symptoms

Group	Identification of medication related to symptom groups	Identification of invasive treatment of symptoms	
	ATC-Codes	ICD-10 GM	OPS
<i>Spasticity</i>	M03BX01, M03BX02, M03CA01, M03BX04, N05BA01, N02BG10, N07XX07	M24.5.- or M72.0 in conjunction with an OPS-Code 5-	6-003.8, 5-038.4
<i>Ataxia</i>	N03AF01		8-631/5-028.2/.3/.9/.a/.c
<i>Fatigue</i>	N04BB01, N06BA07		5-579.6, 5-578.6, 5-577
<i>Bladder dysfunction</i>	G04BD04, G04BD07, G04BD08, G04BD10, G04BD11, G04BD06, G04BX18, H01AB02, G04BD59, G04BD20, G04BD02, G04CA01, G04CA02, G04CA52, G04CA03, N07AA03		
<i>Sexual dysfunction</i>	G04BE01, G04BE01, G04BE01		5-649.5
<i>Depression</i>	N06AX26, N06AA02, N06AA04, N06AA06, N06AA09, N06AA10, N06AA12, N06AA16, N06AA21, N06AA25, N06AB03, N06AB04, N06AB05, N06AB06, N06AB08, N06AB10, N06AF04, N06AG02, N06AX03, N06AX05, N06AX11, N06AX12, N06AX14, N06AX16, N06AX18, N06AX21, N06AX22, N05AN01, N06AP01		
<i>Pain</i>	N02A-, N02B-, M02A-, M02B-		
<i>Intestinal disorder</i>	A06AD11, A06AD15, A06AD65, A06AG04, A06AX01, A03FA01, A03FA51, A03FA03		
<i>Systemic corticoids</i>			5-311.0; 5-431.2-;
<i>Dysphagia</i>			8-125-

Additional Table 3: Description of drug treatment of all MS-prevalent patients and respective MS subtype groups in 2015.

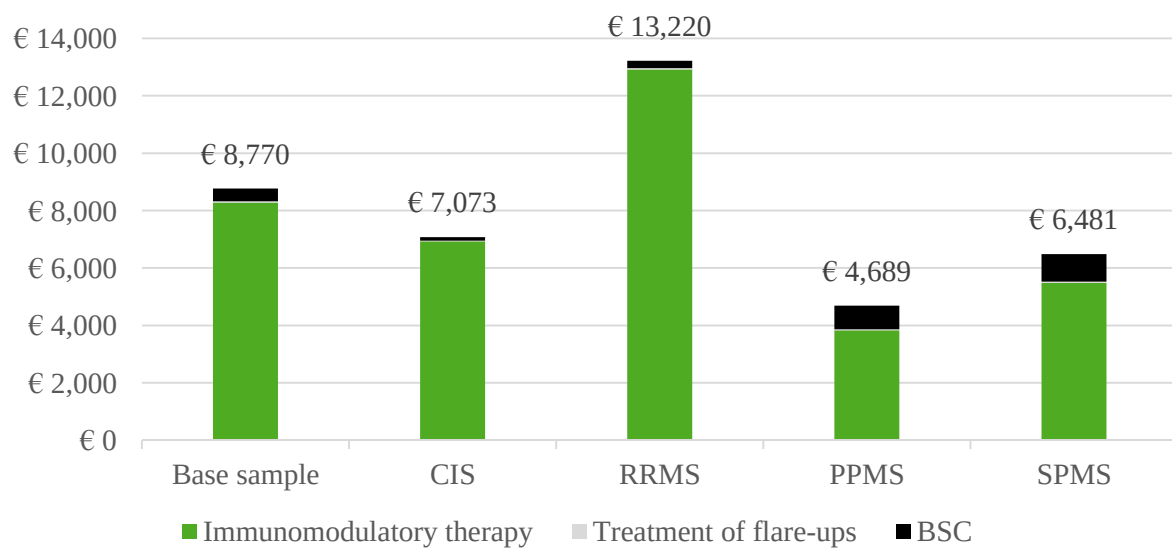
			Base sample	CIS	RRMS	PPMS	SPMS
N			13,133	1,398	5,498	2,247	2,042
Immuno- modulatory therapy	No therapy	N%	54.16%	61.66%	30.41%	77.57%	66.06%
	Interferon beta-1a	N% (DDD)	11.30% (275.16)	8.73% (261.94)	17.19% (280.05)	4.76% (280.71)	6.95% (267.65)
	Interferon beta-1b	N% (DDD)	4.71% (300.55)	4.01% (325.43)	6.09% (296.59)	2.67% (318.24)	6.07% (302.29)
	Glatiramer acetate	N% (DDD)	8.21% (278.68)	10.52% (281.04)	12.39% (277.41)	3.25% (306.43)	4.51% (285.13)
	Peginterferon beta-1a	N% (DDD)	2.45% (390.05)	3.58% (454.68)	3.71% (388.06)	1.11% (376.97)	1.22% (403.17)
	Dimethyl fumarate	N% (DDD)	7.88% (287.92)	9.30% (291.26)	12.57% (289.07)	3.25% (314.26)	3.72% (280.86)
	Teriflunomide	N% (DDD)	3.24% (274.62)	1.93% (254.83)	5.31% (274.94)	1.56% (276.47)	1.91% (284.61)
	Fingolimod	N% (DDD)	5.98% (317.06)	2.22% (337.10)	10.40% (317.22)	2.49% (350.56)	4.55% (301.02)
	Natalizumab	N% (DDD)	3.64% (299.42)	0.64% (314.48)	6.38% (304.17)	1.56% (283.78)	2.84% (280.31)
	Azathioprine	N% (DDD)	1.92% (212.51)	0.36% (143.15)	1.22% (221.23)	2.94% (208.70)	3.72% (212.76)
Treatment of flare-ups	Methyl- prednisolone	N% (DDD)	8.13% (271.85)	5.72% (272.86)	9.86% (252.84)	7.39% (298.70)	9.30% (332.33)
	Other glucocorticoids	N% (DDD)	12.21% (309.93)	9.73% (427.32)	11.57% (272.05)	12.19% (280.29)	14.25% (485.74)
	No therapy	N%	81.06%	85.48%	80.12%	81.53%	78.50%

Additional Table 4: Agents used as first, second and third lines of therapy for MS

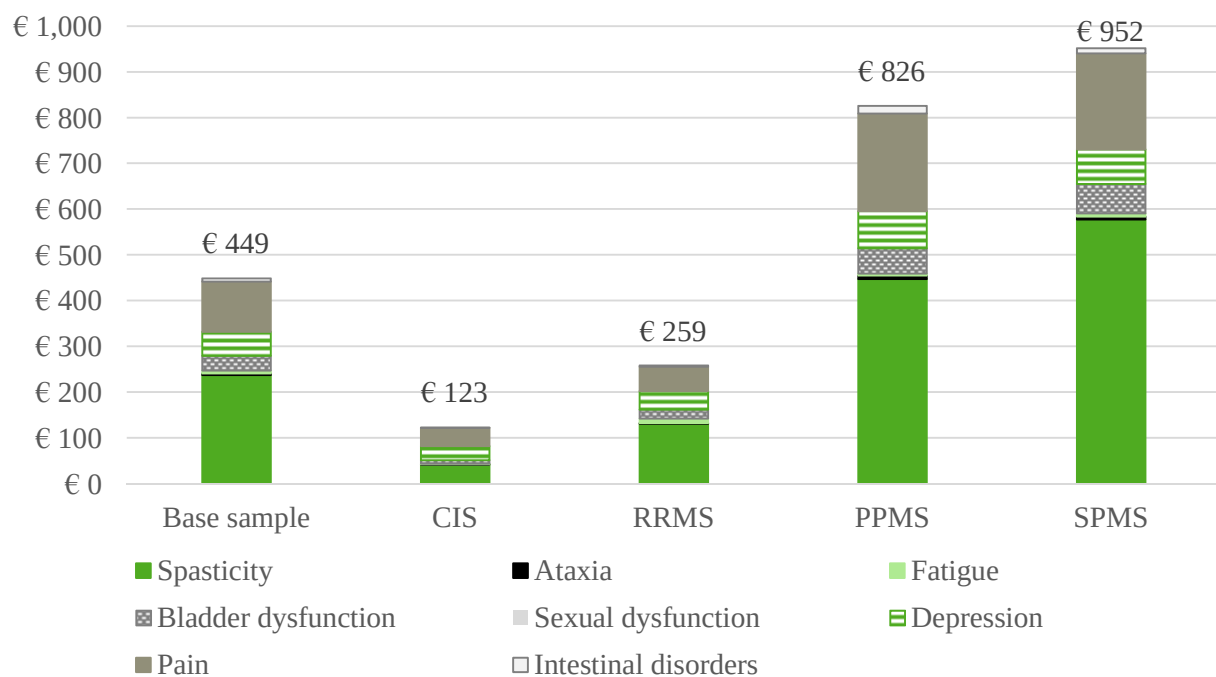
First-line agent	N (%)	Second-line agent	N (%)	Third-line agent N (%)
<i>Interferon beta-1a</i>	710 (40.57%)	Azathioprine	1 (0.14%)	1 (100.00%)
		Alemtuzumab	1 (0.14%)	-
		Mitoxantrone	1 (0.14%)	-
		Interferon beta-1b	2 (0.28%)	1 (50.00%)
		Natalizumab	24 (3.38%)	5 (20.83%)
		Peginterferon beta-1a	31 (4.37%)	3 (9.68%)
		Teriflunomide	35 (4.93%)	1 (2.86%)
		Glatiramer acetate	37 (5.21%)	14 (37.84%)
		Fingolimod	51 (7.18%)	5 (9.80%)
		Dimethyl fumarate	95 (13.38%)	11 (11.58%)
		No second-line agent	432 (60.85%)	-
<i>Glatiramer acetate</i>	470 (26.86%)	Rituximab	1 (0.21%)	-
		Azathioprine	2 (0.43%)	1 (50.00%)
		Peginterferon beta-1a	2 (0.43%)	-
		Interferon beta-1b	8 (1.70%)	5 (62.50%)
		Teriflunomide	15 (3.19%)	-
		Interferon beta-1a	18 (3.83%)	10 (55.56%)
		Natalizumab	21 (4.47%)	3 (14.29%)
		Fingolimod	40 (8.51%)	1 (2.50%)
		Dimethyl fumarate	64 (13.62%)	6 (9.38%)
		No second-line agent	299 (63.62%)	-
<i>Interferon beta-1b</i>	257 (14.69%)	Alemtuzumab	1 (0.39%)	-
		Mitoxantrone	1 (0.39%)	-
		Azathioprine	2 (0.78%)	2 (100.00%)
		Natalizumab	4 (1.56%)	1 (25.00%)
		Peginterferon beta-1a	6 (2.33%)	-
		Interferon beta-1a	9 (3.50%)	3 (33.33%)
		Glatiramer acetate	9 (3.50%)	3 (33.33%)
		Teriflunomide	11 (4.28%)	1 (9.09%)
		Fingolimod	16 (6.23%)	1 (6.25%)
		Dimethyl fumarate	28 (10.89%)	2 (7.14%)
		No second-line agent	170 (66.15%)	-
<i>Natalizumab</i>	103 (5.89%)	Teriflunomide	2 (1.94%)	-
		Glatiramer acetate	2 (1.94%)	1 (50.00%)
		Interferon beta-1a	4 (3.88%)	2 (50.00%)
		Dimethyl fumarate	11 (10.68%)	1 (9.09%)
		Fingolimod	17 (16.50%)	1 (5.88%)
		No second-line agent	67 (65.05%)	-
<i>Azathioprin</i>	97 (5.54%)	Peginterferon beta-1a	1 (1.03%)	1 (100.00%)
		Natalizumab	1 (1.03%)	-
		Rituximab	1 (1.03%)	-
		Interferon beta-1a	1 (1.03%)	1 (100.00%)

First-line agent	N (%)	Second-line agent	N (%)	Third-line agent N (%)
		Dimethyl fumarate	2 (2.06%)	1 (50.00%)
		Teriflunomide	3 (3.09%)	-
		Glatiramer acetate	3 (3.09%)	1 (33.33%)
		No second-line agent	85 (87.63%)	-
<i>Fingolimod</i>	85 (4.86%)	Interferon beta-1a	1 (1.18%)	1 (100.00%)
		Teriflunomide	1 (1.18%)	-
		Glatiramer acetate	2 (2.35%)	-
		Dimethyl fumarate	3 (3.53%)	-
		Natalizumab	4 (4.71%)	1 (25.00%)
		No second-line agent	74 (87.06%)	-
<i>Teriflunomide</i>	12 (0.69%)	Peginterferon beta-1a	1 (8.33%)	-
		Interferon beta-1a	2 (16.67%)	1 (50.00%)
		No second-line agent	9 (75.00%)	-
<i>Mitoxantrone</i>	10 (0.57%)	Interferon beta-1a	1 (10.00%)	1 (100.00%)
		No second-line agent	9 (90.00%)	-
<i>Rituximab</i>	6 (0.34%)	No second-line agent	6 (100.00%)	-

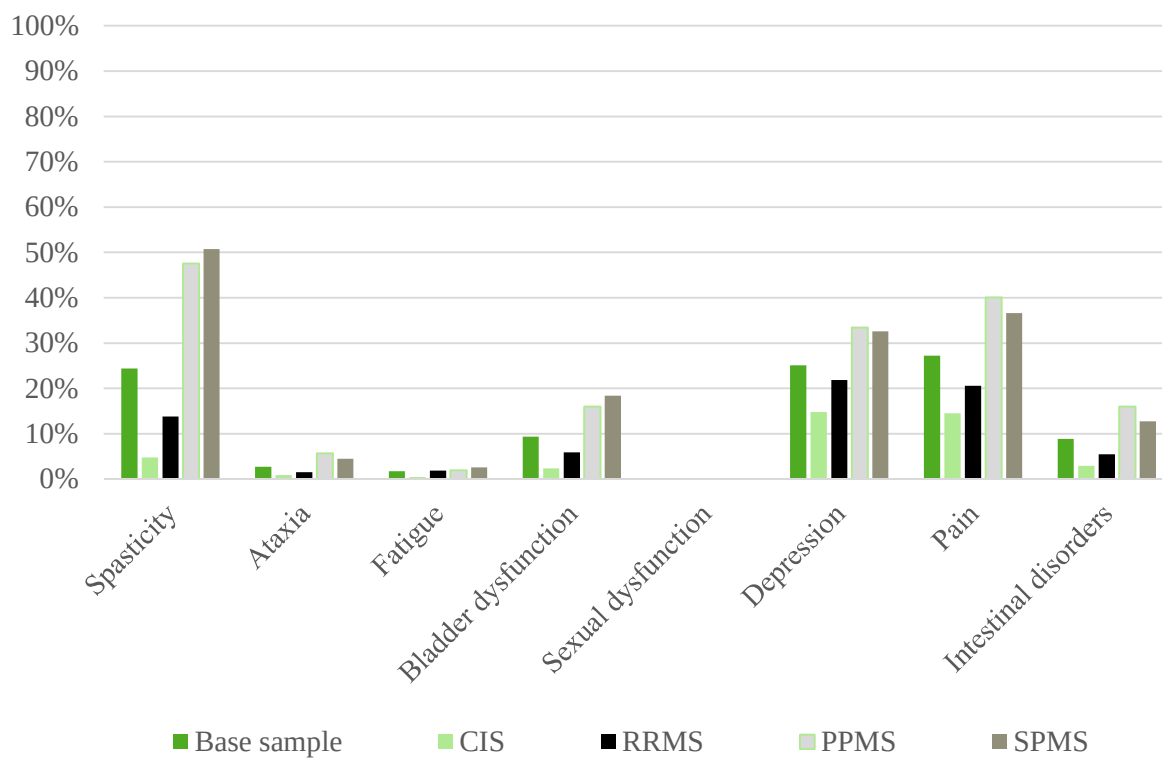
Additional Figure 1: Distribution of drug treatment costs per patient year in 2015



Additional Figure 2: Distribution of drug therapy costs per patient year for treatment of symptoms in 2015



Additional Figure 3: Percentage of patients with at least one prescription in symptom groups in the year 2015



Additional Figure 4: A Selection of the most common treatments in 2015

