

Supplementary Material

Treatment Status and Healthcare Cost Trends for Patients with Multiple Sclerosis in Japan: A Claims Database Analysis

Author details:

Izumi Kawachi^{1,2}, Hiromichi Otaka^{3*}, Kosuke Iwasaki⁴, Tomomi Takeshima⁴, Kengo Ueda³

¹Department of Neurology, Brain Research Institute, Niigata University, 1-757 Asahimachidori, Chuo-ku, Niigata, Japan

²Comprehensive Medical Education Center, Niigata University School of Medicine, 1-757 Asahimachidori, Chuo-ku, Niigata, Japan

³Neuroscience Medical Franchise, Medical Division, Novartis Pharma K.K., 1-23-1 Toranomom, Minato-ku, Tokyo, Japan

⁴Milliman Inc., 1-6-2 Kojimachi, Chiyoda-ku, Tokyo, Japan

Correspondence details:

Hiromichi Otaka

Neuroscience Medical Franchise, Medical Division, Novartis Pharma K.K., 1-23-1 Toranomom, Minato-ku, Tokyo, Japan

Email: hiromichi.otaka@novartis.com

Table S1. Classification and definition of treatments

Classification	Treatment name	Definition*
DMT	Interferon - β 1a	Interferon Beta-1a (Genetical Recombination)
	Dimethyl fumarate	Dimethyl Fumarate
	Interferon- β 1b	Interferon Beta-1b (Genetical Recombination)
	Glatiramer acetate	Glatiramer Acetate
	Fingolimod hydrochloride	Fingolimod Hydrochloride
	Natalizumab	Natalizumab (Genetical Recombination)
Oral steroid	Prednisolone	Excluding prednisolone prescribed within 3 months of prescription of other relapse treatment drug(s)
Immunosuppressant	Azathioprine	Azathioprine
	Tacrolimus Hydrate	Tacrolimus Hydrate
	Ciclosporin	Ciclosporin
	Mycophenolate Mofetil	Mycophenolate Mofetil
	Cyclophosphamide Hydrate	Cyclophosphamide Hydrate
	Methotrexate	Methotrexate
	Mitoxantrone Hydrochloride	Mitoxantrone Hydrochloride
Relapse treatment	Prednisolone	Prednisolone prescribed within 3 months of prescription with other relapse treatment drug(s)
	Prednisolone Sodium Succinate	Prednisolone Sodium Succinate
	Dexamethasone Sodium Phosphate	Dexamethasone Sodium Phosphate
	Methylprednisolone Sodium Succinate	Methylprednisolone Sodium Succinate
	plasma purification therapy	J039, J041

*General name for drugs or procedure price table code for procedures.

DMT: disease-modifying therapy

Table S2. Definition of comorbidities

Disease Name	Definition (ICD-10 code)
Constipation	K59.0
Polyneuropathy, unspecified	G62.9
Depressive episode, unspecified	F32.9
Epilepsy, unspecified	G40.9
Neuromuscular dysfunction of bladder, unspecified	N31.9
Headache	R51
Dizziness and giddiness	R42
Rheumatoid arthritis, unspecified	M06.9
Other epilepsy	G40.8
Generalized anxiety disorder	F41.1
Migraine, unspecified	G43.9
Neurotic disorder, unspecified	F48.9
Sicca syndrome	M35.0
Trigeminal neuralgia	G50.0

ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th revision

Table S3. Definition of clinical tests

Name of clinical test	Definition (procedure price table code)
MRI	E202
clinical psychological or neuropsychological test	D283-D285
neurological test	D239-3
ophthalmologic test	D255-D282-3
cerebrospinal fluid test	D403
visual evoked potential test	D2362
somatosensory evoked potential test	D2361

MRI: magnetic resonance imaging.

Figure S1. Treatment pattern by age (2017)

The percentage for no treatment refers to the percentage of patients without any treatment listed below per patient month, and for each treatment per patient per month.

*Oral steroid is prednisolone excluding those prescribed within 3 months of prescription with other relapse treatment drug(s) than prednisolone.

The colors are assigned for all drugs as below.



Age		~9	10~19	20~29	30~39	40~49	50~59	60~69	70~79	80~89	90~
Number of patients (patient month): denominator		175	846	3502	8568	13955	10890	8069	5098	1606	136
No treatment	No treatment patients	64.6%	71.3%	65.2%	65.2%	64.6%	70.1%	74.4%	83.4%	88.7%	97.1%
DMT	Dimethyl fumarate	0.000	0.052	0.117	0.075	0.068	0.059	0.020	0.009	0.002	0.000
	IFN-β1a	0.320	0.025	0.059	0.062	0.062	0.058	0.025	0.004	0.000	0.000
	IFN-β1b	0.000	0.024	0.043	0.046	0.054	0.049	0.035	0.012	0.001	0.000
	Glatiramer acetate	0.000	0.040	0.021	0.029	0.018	0.016	0.004	0.000	0.000	0.000
	Fingolimod	0.000	0.040	0.130	0.126	0.148	0.093	0.050	0.012	0.002	0.000
	Natalizumab	0.000	0.025	0.014	0.013	0.009	0.009	0.003	0.000	0.000	0.000
	DMT total	0.320	0.206	0.383	0.352	0.360	0.284	0.136	0.037	0.005	0.000
Oral steroid*	Prednisolone	0.246	0.143	0.062	0.119	0.118	0.157	0.222	0.184	0.119	0.000
	Oral steroid total	0.246	0.143	0.062	0.119	0.118	0.157	0.222	0.184	0.119	0.000
Immunosuppressant	Azathioprine	0.183	0.000	0.014	0.007	0.018	0.023	0.025	0.009	0.000	0.000
	Tacrolimus	0.000	0.053	0.013	0.013	0.008	0.016	0.036	0.018	0.019	0.000
	Cyclosporine	0.000	0.000	0.000	0.004	0.004	0.006	0.009	0.001	0.006	0.000
	Mycophenolate mofetil	0.000	0.011	0.003	0.006	0.000	0.005	0.002	0.000	0.000	0.000
	Cyclophosphamide	0.000	0.012	0.009	0.000	0.001	0.001	0.001	0.001	0.001	0.000
	Methotrexate	0.000	0.000	0.000	0.001	0.002	0.018	0.018	0.006	0.011	0.000
	Mitoxantrone	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	Immunosuppressant total	0.183	0.076	0.041	0.031	0.033	0.068	0.091	0.035	0.037	0.000
Relapse treatment drugs	Prednisolone (relapse therapy)	0.149	0.183	0.095	0.084	0.061	0.052	0.059	0.063	0.017	0.044
	prednisolone sodium succinate	0.006	0.018	0.007	0.006	0.006	0.003	0.007	0.006	0.000	0.000
	Dexamethasone phosphate ester sodium	0.000	0.009	0.000	0.004	0.001	0.005	0.023	0.028	0.006	0.000
	Methylprednisolone sodium ester succinate	0.171	0.136	0.160	0.107	0.094	0.057	0.033	0.025	0.016	0.081
	Relapse treatment drugs total	0.326	0.346	0.262	0.201	0.162	0.118	0.122	0.122	0.039	0.125
Relapse treatment	Plasma purification therapy	0.000	0.000	0.012	0.003	0.002	0.004	0.004	0.001	0.001	0.000

DMT: disease-modifying therapy, IFN: interferon

Figure S2. Prevalence of comorbidities by age (2017)

The colors are assigned as below.



Age	0	10~19	20~29	30~39	40~49	50~59	60~69	70~79	80~89	90~
Number of patients (patient month): denominator	175	846	3502	8568	13955	10890	8069	5098	1606	136
Constipation	9.1%	8.0%	7.0%	13.3%	18.0%	21.4%	28.1%	28.9%	29.0%	11.0%
Polyneuropathy, unspecified	1.7%	3.7%	7.3%	9.9%	13.8%	15.1%	17.7%	14.9%	13.9%	14.7%
Depressive episode, unspecified	0.0%	0.8%	5.3%	6.2%	9.3%	10.4%	11.7%	7.8%	7.2%	0.0%
Epilepsy, unspecified	2.9%	6.7%	6.7%	5.7%	7.0%	9.6%	9.2%	8.3%	5.2%	1.5%
Neuromuscular dysfunction of bladder, unspecified	0.0%	1.4%	1.4%	3.8%	5.1%	8.0%	9.0%	8.9%	10.5%	8.8%
Headache	12.0%	5.8%	9.9%	8.5%	7.8%	6.6%	4.7%	3.3%	1.9%	0.0%
Dizziness and giddiness	0.0%	3.1%	3.7%	4.1%	5.1%	4.9%	5.0%	6.0%	2.4%	0.0%
Rheumatoid arthritis, unspecified	0.0%	0.6%	0.9%	1.8%	3.1%	4.4%	6.4%	6.3%	5.9%	1.5%
Other epilepsy	5.1%	4.4%	2.5%	2.7%	2.9%	3.8%	3.6%	3.5%	2.1%	0.0%
Generalized anxiety disorder	0.0%	3.1%	1.9%	2.8%	3.1%	3.4%	4.7%	3.5%	2.1%	0.0%
Migraine, unspecified	0.0%	3.4%	4.7%	3.6%	3.4%	3.6%	1.8%	1.2%	0.2%	0.0%
Neurotic disorder, unspecified	0.0%	0.0%	0.6%	2.5%	2.7%	2.4%	3.3%	2.0%	2.7%	0.0%
Sicca syndrome	0.0%	1.4%	0.9%	1.3%	2.6%	2.3%	3.9%	2.7%	2.7%	0.0%
Trigeminal neuralgia	0.0%	0.0%	0.8%	1.1%	1.8%	2.7%	4.0%	2.3%	0.9%	0.0%

Figure S3. Healthcare resource utilization and healthcare costs by age (2017)

The colors are assigned by each item group (clinical tests, hospitalization, relapse, hospital visit, or healthcare costs) as below.



Age		~9	10~19	20~29	30~39	40~49	50~59	60~69	70~79	80~89	90~
Number of patients (patient month): denominator		175	846	3502	8568	13955	10890	8069	5098	1606	136
Clinical tests (PPPM)	MRI	0.291	0.294	0.240	0.205	0.185	0.147	0.110	0.084	0.057	0.059
	Clinical psychological or neuropsychological test	0.011	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.008	0.000
	Neurological test	0.000	0.004	0.008	0.006	0.004	0.004	0.002	0.001	0.000	0.000
	Ophthalmologic test	0.549	0.755	0.371	0.313	0.346	0.320	0.378	0.377	0.270	0.015
	Cerebrospinal fluid test	0.023	0.026	0.021	0.012	0.009	0.006	0.007	0.010	0.009	0.007
	Visual evoked potential test	0.000	0.006	0.007	0.004	0.002	0.002	0.001	0.001	0.000	0.000
	Somatosensory evoked potential test	0.000	0.012	0.006	0.005	0.003	0.003	0.001	0.002	0.000	0.000
Hospitalization (PPPM)	Hospitalization	0.057	0.059	0.033	0.028	0.024	0.025	0.032	0.040	0.045	0.066
Relapse (PPPM)	Relapse	0.023	0.039	0.039	0.029	0.027	0.021	0.016	0.015	0.009	0.015
Hospital visit (PPPM)	Hospital visit	0.771	0.758	0.792	0.786	0.884	0.834	0.921	0.962	0.822	0.640
Healthcare costs (JPY, PPPM)	Total healthcare costs	96,475	138,026	114,216	122,478	116,799	102,481	88,618	72,789	78,541	68,576
	MS treatment cost	40,866	41,526	81,337	84,107	82,010	55,568	28,783	10,449	3,802	64
	Clinical test cost	3,627	4,112	3,086	2,626	2,438	2,010	1,667	1,411	995	848
	Other healthcare costs	51,982	92,388	29,793	35,744	32,351	44,903	58,169	60,929	73,743	67,664

JPY: Japanese yen, MRI: magnetic resonance imaging, MS: multiple sclerosis, PPPM: per patient per month.