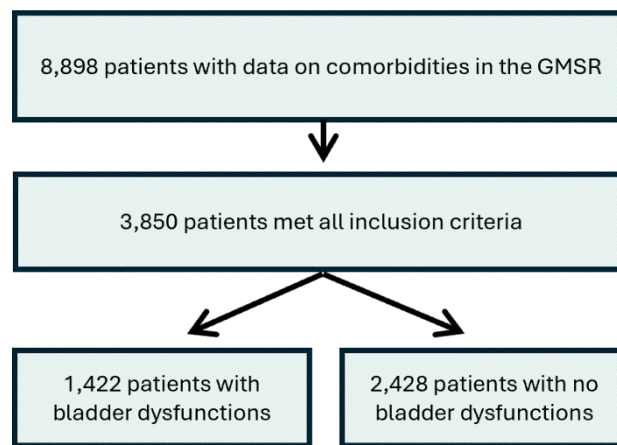




Supplementary Figure S1: Flowchart illustrating the data availability of comorbidities in the GMSR. Some data in the GMSR were only available for a specific subset of patients, either because their collection was optional or because they were part of the extended registry documentation, which not all MS centers participate in (e.g. disease-modifying therapies and comorbidities). The chart shows the number of patients, for whom information on comorbidities were available. This includes only patients who were part of the pharmacovigilance cohort of the GMSR. Of the 8,898 patients with data on comorbidities, 3,850 met all inclusion criteria.
GMSR, German Multiple Sclerosis Registry; MS, Multiple sclerosis.

Supplement Table S1: Comparison of the included ($N_v = 10,572$) and the excluded patients ($N_e = 11,900$) from the overall study population ($N_o = 22,472$).

Variables	Included patients ($N_v=10,572$)	Excluded patients ($N_e=11,900$)
Sociodemographics		
Sex, n (%)		
Female	7,584 (71.7)	8,520 (71.6)
Male	2,988 (28.3)	3,380 (28.4)
School level at last visit, n (%)*		
NSCE/CSE	1,470 (16.5)	1,933 (18.1)
GCSE	3,736 (41.9)	4,411 (41.3)
ATCEQ/A level	3,710 (41.6)	4,343 (40.6)
Educational level at last visit, n (%)*		
Completed vocational training	6,450 (70.0)	7,532 (69.6)
Completed university education	2,115 (22.9)	2,370 (21.9)
No completed/ongoing training	651 (7.1)	917 (8.5)
Employment status at last visit, n (%)*		
Employed - full-time	3,653 (40.5)	3,805 (36.2)
Employed - part-time	1,710 (19.0)	2,225 (21.2)
Retired - disability	2,146 (23.8)	2,643 (25.1)
Other	1,511 (16.8)	1,839 (17.5)
Partnership status at last visit, n (%)*		
Single	2,045 (21.2)	2,674 (24.3)
Any partnership	7,591 (78.8)	8,342 (75.7)
Age at last visit [years], <i>mean</i> (<i>SD</i>)	48.2 (12.6)	48.9 (12.6)
18–29, n (%)	774 (7.3)	904 (7.6)
30–39, n (%)	2,343 (22.2)	2,272 (19.1)
40–49, n (%)	2,643 (25.0)	2,814 (23.6)
50–59, n (%)	2,761 (26.1)	3,589 (30.2)
≥60, n (%)	2,051 (19.4)	2,321 (19.5)
Clinical variables		
Age at MS onset [years], <i>mean</i> (<i>SD</i>)*	32.3 (10.6)	34.0 (11.0)
<18, n (%)	608 (5.8)	504 (4.5)
18–29, n (%)	4,429 (41.9)	4,087 (36.2)
30–39, n (%)	3,029 (28.7)	3,407 (30.2)
40–49, n (%)	1,810 (17.1)	2,253 (20.0)
50–59, n (%)	603 (5.7)	869 (7.7)
≥60, n (%)	93 (0.9)	162 (1.4)
Disease duration from MS onset to last visit [years], <i>mean</i> (<i>SD</i>)* ^a	16.0 (10.0)	14.7 (10.9)
0–1, n (%)	121 (1.1)	1,032 (9.2)
2–9, n (%)	3,076 (29.1)	3,262 (28.9)
10–19, n (%)	4,032 (38.1)	3,522 (31.2)
20–29, n (%)	2,249 (21.3)	2,234 (19.8)
30–39, n (%)	820 (7.8)	975 (8.6)
≥40, n (%)	274 (2.6)	257 (2.3)
Time to diagnosis [years], <i>mean</i> (<i>SD</i>)*	1.24 (3.22)	1.30 (3.16)
Polysymptomatic at MS onset, n (%)	4,634 (43.8)	8,242 (69.3)
Bladder dysfunction at MS onset, n (%)*	489 (5.9)	1,406 (13.5)
Disease course at MS onset, n (%)*		
ROMS	9,853 (95.6)	10,307 (92.8)
POMS	451 (4.4)	797 (7.2)
Disease course at last visit, n (%)*		
CIS/ RRMS	8,671 (82.0)	8,941 (76.3)
SPMS	1,359 (12.9)	1,813 (15.5)
PPMS	542 (5.1)	965 (8.2)
EDSS score at last visit, <i>median</i> [<i>Q1</i> , <i>Q3</i>]*	2.0 [1.5;4.0]	3.0 [2.0;5.0]
Mild (0–2.5), n (%)	5,839 (56.8)	5,447 (47.0)
Moderate (3.0–5.5), n (%)	2,703 (26.3)	3,899 (33.6)
Severe (≥6.0), n (%)	1,738 (16.9)	2,249 (19.4)
Polysymptomatic at MS onset, n (%)	4,634 (43.8)	8,242 (69.3)

Real-world data on the prevalence and therapy of symptomatic bladder dysfunction in people with multiple sclerosis. Submitted to: Therapeutic Advances in Neurological Disorders. Corresponding author: Mathia Kirstein (kirstein@msregister.de)

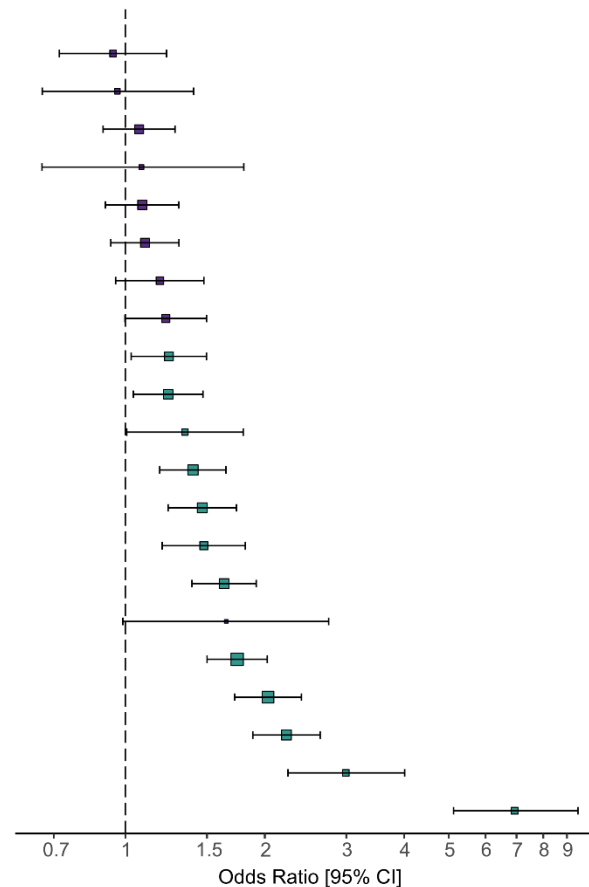
Bladder dysfunction at MS onset, <i>n</i> (%) [*]	489 (5.9)	1,406 (13.5)
Number of comorbidities, <i>n</i> (%) [*]	1.69 (2.11)	1.42 (1.97)
0	1,444 (37.5)	1,150 (43.1)
1	884 (23.0)	634 (23.7)
2-4	1,137 (29.5)	695 (26.0)
≥5	385 (10.0)	192 (7.2)
Disease-modifying therapy at last visit, <i>n</i> (%) [*]	8,644 (82.4)	8,342 (71.3)

^{*}Denominators may deviate from the sample sizes of the subgroups due to missing values.

CIS, Clinically isolated syndrome; EDSS, Expanded Disability Status Scale; MS, Multiple sclerosis; *N*, Number of patients; *p*, *p*-value; POMS, Progressive-onset MS; PPMS, Primary progressive MS; Q1, First quartile; Q3, Third quartile; ROMS, Predominantly relapse-onset MS; RRMS, Relapsing-remitting MS; school levels (A level, Advanced level; ATCEQ, Advanced technical college entrance qualification; CSE/GCSE, Certificate of secondary education/ general CSE; NSCE, No school-leaving certificate); SD, Standard deviation; SPMS, Secondary progressive MS.

Variable: OR [95% CI], *p*-value)

Restless legs syndrome	0.94 [0.72;1.23], <i>p</i> =0.646)
Dysarthria	0.96 [0.66;1.40], <i>p</i> =0.832)
Pain	1.07 [0.89;1.28], <i>p</i> =0.459)
Dysphagia	1.08 [0.66;1.80], <i>p</i> =0.758)
Fine motor dysfunction	1.09 [0.90;1.30], <i>p</i> =0.371)
Depression	1.10 [0.93;1.30], <i>p</i> =0.264)
Visual dysfunction	1.19 [0.95;1.48], <i>p</i> =0.127)
Uhthoff's phenomenon	1.22 [1.00;1.50], <i>p</i> =0.053)
Paresthesia	1.24 [1.03;1.50], <i>p</i>=0.024)
Cognitive dysfunction	1.24 [1.04;1.47], <i>p</i>=0.016)
Ocular motor disorder	1.34 [1.01;1.80], <i>p</i>=0.046)
Sensory dysfunction	1.40 [1.19;1.65], <i>p</i><0.001)
Balance disorder	1.47 [1.24;1.74], <i>p</i><0.001)
Sleep disorder	1.48 [1.20;1.81], <i>p</i><0.001)
Movement disorder	1.63 [1.39;1.92], <i>p</i><0.001)
Epileptic seizure	1.65 [0.99;2.75], <i>p</i> =0.055)
Fatigue	1.74 [1.50;2.02], <i>p</i><0.001)
Mobility impairment/paresis	2.03 [1.72;2.40], <i>p</i><0.001)
Spasticity	2.23 [1.88;2.63], <i>p</i><0.001)
Sexual dysfunction	2.99 [2.25;4.01], <i>p</i><0.001)
Bowel dysfunction	6.94 [5.12;9.51], <i>p</i><0.001)



Supplementary Figure S2: sub-analysis of MS symptoms. A multivariable logistic regression model was used to identify if specific MS symptoms are associated with the occurrence of bladder dysfunctions among 7,379 pwMS with complete data. The model was adjusted for sex, age, disease duration and disease course. The forest plot contains colored boxes indicating the ORs of the variables analyzed for the occurrence of bladder dysfunction. Green boxes and bold fonts indicate statistical significance and boxes with no statistical significance are colored purple. Box size is proportional to the number of patients included. Whiskers symbolize the 95% CIs of the ORs. Twelve out of 21 analyzed MS symptoms were identified as statistically significant associated with the occurrence of bladder dysfunctions. PwMS diagnosed with bowel or sexual dysfunctions have a particularly high risk of experiencing bladder dysfunctions. CI, Confidence interval; CIS, Clinically isolated syndrome; MS, Multiple sclerosis; OR, Odds ratio; *p*, *p*-value; people with MS, pwMS