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LETTER TO THE EDITORS

Symptomatology of MS: results from the German MS Registry

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Abstract Since 2002, an MS Registry has been implemented by the German MS Society in more than 100 German MS centres. The objective is to provide information about disease characteristics, and to monitor the health care situation in a large population of patients. The aim of this report is to give detailed results on MS symptoms. By October 2008, data sets from 16,554 patients were recorded by 86 centres. A strikingly high number of persons suffered from fatigue and other "invisible" symptoms during early and late stages of the disease, underscoring the negative impact of these symptoms on quality of life in MS patients.

Keywords Multiple sclerosis · Databases · Register · Epidemiology · Health care · MS-symptoms

Sirs,

In Germany, a national MS registry was initiated in 2001 under the auspices of the German MS Society (DMSG Bundesverband e.V.) in order to collect epidemiological data on the number of patients with MS, course of the disease, and information on the healthcare and social situation of MS patients in Germany. In this paper, we aim to give an overview about the symptomatology of MS.

Patients are entered into the registry if they (1) suffer from MS (according to the McDonald criteria) or clinically isolated syndromes suggestive of MS and (2) gave written informed consent for collecting pseudonymous data. Data sets are documented on-site in the study centres by participating physicians and pooled and analysed by the MS Forschungs- und Projektentwicklungs-gGmbH (MSFP-gGmbH), a non-profit company associated to the German MS Society. Before analysis, a search for doubloons is performed in order to identify patients that could have been registered either multiple times in one centre or at more than one centre, using a unique pseudonym number. Data sets are checked for completeness (age, gender, degree of disability [EDSS], and diagnostic accuracy) and consistency, and those with missing data or inconsistencies are returned for completion or correction to the centres. A

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detailed description of the methodology of the German MS registry is given elsewhere [2, 3].

During a two-year period (2002/2003), a pilot phase has been taking place in five MS centres representing different levels of health care. Within this period, 3,458 data sets were obtained from which 3,223 (93.2%) passed quality checks and remained for further analysis [3, 4]. Based on the results of the pilot phase, the Minimal Data Set (MDS) was modified: unnecessary parameters were excluded, incomplete parameters were specified, and mistakable parameters were supplemented. These modifications resulted in the shortening of the MDS on the one hand, and a more accurate description of the included parameters on the other hand [2]. Since March 2005, new centres are continuously recruited and their number steadily increases: from five in the pilot phase, 15 in 2005, 57 in 2006, 86 in 2007, to 103 by 31 October 2008 (Fig. 1a). These centres represent a network of MS neurologists at university and acute care hospitals, rehabilitation clinics, and specialised or regional medical neurological practices across Germany. Selection criteria for the centres include a minimum number of MS patients treated (between 120 and 400 per year according to level of health care), long-standing experience in the treatment of MS patients, and obligation to follow treatment guidelines (the complete list of criteria can be seen on www.dmsg.de). By 31 October 2008, standardised data sets of 18,029 patients in 86 MS centres have been recorded, and 16,554 of them (91%) passed the above mentioned quality checks (Fig. 1b).

The demographic data of these patients were similar to those obtained from epidemiological studies [8–10]: 71% of the patients were female, mean age (±standard deviation) was 44.1 ± 11.7 years, mean disease duration was 12.5 ± 9.4 years, and 55% suffered from the relapsing–remitting form of the disease (as defined by Lublin and Reingold [6]). Median EDSS was 3.5, and 24% of MS patients scored ≥6.0 on the EDSS. Strikingly, the time until diagnosis lasted about 3.1 years from the occurrence of the first symptoms. Around one-third (35.1%) of all patients were prematurely retired due to MS, and a considerable proportion of these patients (20%) lost work capacity despite still being able to walk independently (EDSS ≤ 3.5). The majority of patients received immunomodulatory therapies (69.5%). The distribution within the individual therapeutic strategies reflects the recommendations made by the Multiple Sclerosis Therapy Consensus Group [7] and is comparable to that obtained in the NARCOMS registry [5].

The most frequent symptoms that were reported by the patients or revealed by neurological examination obtained during the last visit were fatigue, spasticity, bladder dysfunction, and ataxia. Likewise, pain, depression, and cognitive dysfunction occurred rather frequently (Table 1). Patients with disease duration less than two years suffered mainly from fatigue, whereas spasticity, bladder dysfunction, ataxia, and pain appeared considerably less often. The rate of fatigue even increased in patients with MS duration of more than 15 years; yet, these patients suffered eminently from spasticity, bladder dysfunction, ataxia, and pain (Table 1).

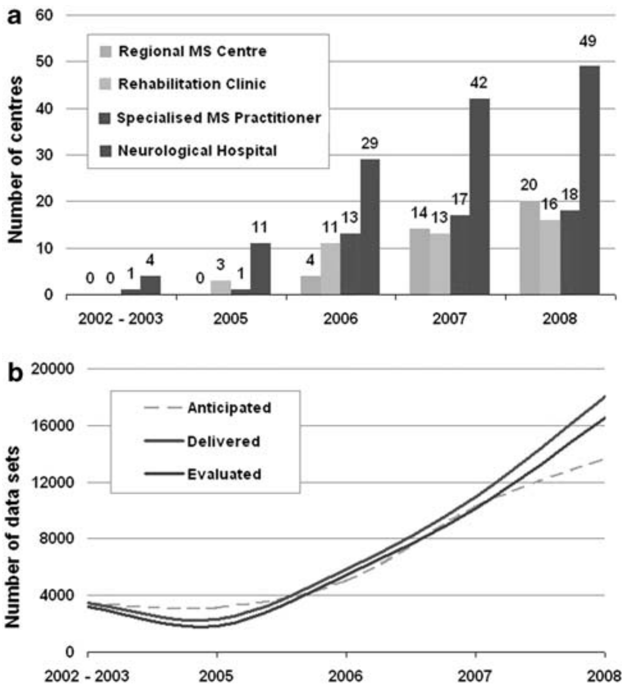

Fig. 1 Development of the number of documentation centres (**a**) and data sets (**b**) in the German MS Register. The total number of centres increased from five in the pilot phase (2002–2003) to 15 in 2005, 57 in 2006, 86 in 2007 and 103 until October 2008. By 31 October 2008, a total of 16,554 data sets have passed quality control. Data sets from the pilot phase were not eligible for inclusion, because the structure of the data sets was modified prior to the extension phase

The most frequent initial symptoms that were reported by the patients were sensory problems (43.1%), paresis (37.0%), and visual dysfunction (30.1%). The frequencies of symptoms were similar in the subgroup of patients with disease duration of less than 2 years, indicating that initial symptoms have been reliably recorded. Compared to people with disease onset after the age of 50 years, patients who developed MS before the age of 20 experienced more often visual dysfunction (34.2 vs. 15.4%) and sensory problems (44.2 vs. 32.7%), and less frequently paresis (32.8 vs. 54.1%) and motor incoordination (19.8 vs. 28.8%). These differences were statistically significant ($p < 0.001$, chi-square test).

Some limitations need to be considered: due to a centre-based approach, our findings may not be representative for the MS population as a whole. The above mentioned comparability to other epidemiological studies, however, makes this possibility unlikely. There may be a

Table 1 Symptoms of MS obtained during the last visit

	n	Frequency	DD < 2 years	DD > 15 years
Number	16,554		1,052	4,747
Spasticity	7,012	4,142 (59.1%)	68 (17.3%)	1,796 (75.8%)
Fatigue	6,726	4,245 (63.1%)	167 (40.6%)	1,461 (67.6%)
Pain	6,548	3,399 (36.6%)	100 (24.6%)	902 (42.2%)
Bladder dysfunction	6,573	3,723 (56.6%)	79 (20.5%)	1,619 (74.0%)
Dysfunction of defecation	6,040	1,260 (20.9%)	18 (4.8%)	613 (31.1%)
Sexual dysfunction	4,951	1,073 (21.7%)	28 (8.0%)	409 (27.3%)
Ataxia/tremor	6,384	2,985 (46.8%)	96 (24.4%)	1,181 (56.5%)
Cognitive dysfunction	6,239	2,244 (36.0%)	76 (19.6%)	823 (40.6%)
Depression	6,632	2,411 (36.4%)	96 (23.6%)	806 (38.0%)
Oculomotor dysfunction	6,542	1,268 (19.4%)	60 (14.6%)	506 (24.3%)
Dysarthria/dysphonia	6,189	901 (14.6%)	18 (4.6%)	410 (20.4%)
Dysphagia	6,183	485 (7.8%)	5 (1.3%)	256 (12.7%)
Epileptic seizures	6,215	188 (3.0%)	6 (1.6%)	75 (3.7%)
Other paroxysms	5,980	219 (3.7%)	8 (2.1%)	76 (3.9%)

DD (disease duration) = time since onset of MS

The first line of the table gives the total number of patients recorded in the data set

The column "*n*" shows the number of patients for whom data on a particular symptom were available

The numbers in the "Frequency" column give the absolute number of patients with this particular symptom. The percentages refer to the total number of entries per symptom shown in column "*n*"

The columns "DD < 2 years" and "DD > 15 years" denote the numbers of recorded symptoms according to disease duration of patients. The percentages refer to those patients with a particular disease duration for whom data on this symptom were available (not shown)

selection bias since patients with early MS might be less enthusiastic to participate although the burden for enrolled patients is low, as is the number of patients refusing consent (less than 10%). There was no quality control of EDSS measurement, but the centres had long-standing (more than 5 years) experience in the care of MS patients. Another limitation may be that symptoms were recorded as they are reported by the patients and/or revealed by neurological examination and thus, some symptoms, particularly depression, fatigue and cognitive dysfunction may be underestimated.

Despite these shortcomings, the German MS Registry resulted in a broad registration of MS patients from across the country within a relatively short time period, allowing for an estimate on the health care situation of MS patients in Germany. With more than 16,000 data sets, the German MS Registry belongs to one of the largest databases of MS worldwide [1]. The impact of the disease on quality of life is underscored by the high number of persons who suffered from "invisible" symptoms, such as fatigue, cognitive dysfunction and depression during both, early and late stages of the disease. This underscores the high impact of the disease on quality of life. The data of the German MS Registry may help to monitor the provision of services, therapies, and treatments which may in the long-term improve quality of life for MS patients.

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