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HEALTHCARE ORGANIZATION

The management of multiple sclerosis by reference centers in south of Italy: a 2011 survey on health demands and needs in Campania region

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Abstract This cross-sectional study has investigated the diagnostic and therapeutic management of patients suffering from multiple sclerosis (MS) in the Campania Region (Italy). A survey involving all the reference centers for MS in Campania Region was conducted from March to August 2011. Centers responded to a web-administered questionnaire on management and clinical characteristics of MS patients. In the study period, 3263 patients (mean age 37 years, 66 % females) accessed the centers. Patients received a first diagnosis of MS in 161 cases (4.9 %). About 37 % of the subjects without a previous diagnosis came to the centers on their own initiative. All patients underwent a complete neurological examination and expanded disability status scale. The other most common investigations were magnetic resonance imaging (44.0 %) and evoked potentials (22.1 %). The number of treated patients was 2797 (87.1 %). The most used drugs were interferon β and glatiramer acetate. The time between diagnosis and initiation of therapy exceeded 6 months in 32 % of cases. Second-line drugs were under-used: 16 % of patients who might benefit from them show high clinical and radiological disease activity despite treatment with immunomodulant drugs. The MS care management of the surveyed centers showed consistent margins for improvement in 2011. Even though these data do not represent the current situation, they can be used to monitor improvements in MS care.

Keywords Multiple sclerosis · Disease management · Health services needs and demand

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Introduction

Multiple sclerosis (MS) is a chronic immune-mediated neurologic disease that results in progressive disability over time and affects approximately 1–2.5 million people around the world [1, 2]. Women are more likely to develop the disease than men with a clinical presentation usually between 20 and 50 years of age [3]. The goals of the symptomatic and disease-modifying therapies are to improve quality of life, reduce relapse rate, prolong remission, limit the onset of new MS lesions, and postpone the development of long-term disabilities. [1] The availability of new disease-modifying therapies has improved the natural course of the disease, but it can be affected by the different reimbursement policies of healthcare plans, and this may lead to unequal access to these drugs [4].

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A timely access to care and drugs is important because as it is widely recognized that "what is lost, is not regained" [5]. There are also strong evidences from large clinical studies demonstrating that early and proper immunomodulatory treatment is effective in reducing relapse activity, magnetic resonance imaging (MRI) lesion load, and disability progression, even though it is also expensive and potentially toxic [6, 7].

Furthermore, with the introduction of a highly sensitive brain MRI, the fraction of milder MS cases, and thus patients to be addressed to early therapies, will likely increase [8].

Taking into consideration all these aspects, it should bear in mind the importance of a multidimensional approach which ought to be coordinated in a dynamic process provided by well-organized care centers. In Italy, MS patients may refer to centers which are devoted to their care. Despite the recent incorporation of new treatment approaches early in the disease course, care providers still face difficult decisions on the therapeutic approach and when to initiate or escalate therapies. Such decisions require a proper assessment of relative risks, costs, and benefits of new and emerging therapies, as well as addressing challenges with adherence to achieve optimal management and outcomes [9]. All centers should agree on protocols and procedures in order to provide patients with an optimal care according to the available resources.

This pilot study, conducted in 2011 in Campania, the third Italy region in terms of resident inhabitants, (a) investigates the diagnostic and therapeutic pathways and the demographic and clinical characteristics of patients with MS and (b) aims to provide evidence about health demands and needs to address health care planning. The year 2011 was important because of the dawn of a new era in the management and treatment of the MS. Before that year, the Italian Medicines Agency (AIFA) had already authorized reference centers to prescribe and administrate under the "MS therapy" label the interferons and glatiramer acetate. Natalizumab and per os immunosuppressive drugs were prescribed as second-line drugs. Among immunosuppressant drugs, only mitoxantrone has an indication for MS as it is approved for patients with aggressive forms with frequent relapses and progressive forms with relapses during the progression of the disease. In 2012, AIFA authorized prescribing fingolimod [10]. In 2014, AIFA authorized prescribing teriflunomide [11] and in 2015 it authorized prescribing dimethyl fumarate [12], both with the same indication. Moreover, also diagnostic criteria and phenotypic classifications had recently evolved [13–15]. Even the England's National Institute for Health and Care Excellence (NICE) guidelines were recently updated (in 2014), an important fact considering that Italy never adopted any official guidelines and that in Europe only a few other countries have guidelines for the management of MS [16]. Therefore, year 2011 can be considered a sort of "baseline situation" before all these considerable changes occurred.

Materials and methods

This survey collected aggregate data on the activity of the MS centers of Campania region during a 6-month period from March to August 2011. Referents of all the MS centers were contacted and were asked to complete a questionnaire ("Appendix") form through a dedicated Web portal. The questionnaire, including 30 questions, was developed by the Institute of Public Health of the Catholic University of the Sacred Heart, Rome, and validated by clinical key opinion leaders. The survey investigated the diagnostic and therapeutic management of MS (5 and 11 questions, respectively), but also the demographic and clinical characteristics of patients followed at the reference centers (6 and 5 questions, respectively), as well as logistics (2 questions). Data were collected from patients who have been diagnosed with MS in different years, and therefore different diagnostic criteria have probably been used in order to make the diagnosis. However, all patients were classified according to the McDonald criteria delivered in 2010 [13].

One other question was conceived to classify patients by clinical picture according to the main clinical indications of the new available drugs used in the MS treatment, aiming to identify subjects who may benefit from them and subsequently assess missed therapeutic opportunities. In particular, centers were asked to report the following information:

- number of patients suffering from an RR-MS with expanded disability status scale (EDSS) between 1 and 5.5;
- number of patients suffering from secondary progressive MS (SP-MS) with EDSS between 3 and 6.5 and at least 2 relapses or 1 point increase in EDSS in the previous 2 years;
- number of patients suffering from RR-MS who were treated with interferon or glatiramer acetate and had at least 1 relapse or showed at least 9 hyperintense lesions on T2-weighted MRI or at least a gadolinium (Gd)-enhanced lesion in the previous year;
- number of patients with high disease activity (defined as the presence of at least 2 relapses or 1 relapse in therapy with incomplete recovery and residual disability not inferior to 2, and the presence of at least 9 hyperintense lesions on T2-weighted MRI or the presence of at least one Gd + lesion in the last year) despite at least 12 months of treatment with interferon or glatiramer acetate;

- number of patients with the increase of brain MRI lesion load and at least 1 among unchanged or increased relapse rate and the presence of severe relapses despite treatment with interferon or glatiramer acetate in the previous year; and
- number of patients who could benefit from a symptomatic therapy aimed at relieving fatigue and improving motor impairment.

The reference centers were subjected to a first call and to a second recall to adhere to the survey. During the two calls, ad hoc requests were sent to every single center in case of inconsistencies. A descriptive statistical analysis of the sample was performed with SPSS 12.0 software for Windows. Analyses were weighted for the number of patients followed by each center. Inconsistent data for which no clarification came from the reference centers, even after solicitations, were considered missing. When data were missing, the absolute number of subjects with available data was specified. In such cases, relative frequencies were calculated based on the number of available records.

Results

Main demographic and clinical characteristics of the population

Overall, 3263 patients suffering from MS were observed at least once in the reference centers of the Campania region during the 6-month study period. The median number of patients seen per center was 136.5 (range 30–1286). The average patients' age was 37 years, and the ages ranged from 5 to 75 years for males and from 10 to 74 for females. At onset, 2273 (71.7 % out of 3170 with onset data available) were aged between 20 and 39 years, with a wide majority of patients being diagnosed in the 20–29 age class (1392 patients, 43.9 %). The number of females was 2167 (66 % of the sample) and that of males was 1096 (34 %). Data on residency were only available for 2858 subjects (87.6 % of the sample). All these patients, except 162 (5.7 %), were residents in Campania Region. All nonresident patients came from bordering or other southern regions of Italy. At diagnosis, 70 % of patients presented with an EDSS between 1.5 and 3 (data available on 3114 patients). Twelve point five percent of patients had a score of less than 1.5 and 17.5 % had a score greater than 3. The majority of patients had a disease lasting between 2 and 10 years (28.7 % between 2 and 5 years and 34.2 % between 6 and 10 years), and only 10.0 % of patients had a disease duration of less than 2 years. At the time of last visit, 2925 patients had a clear distinguishable clinical picture. In particular, there were 137 (4.7 %) patients suffering from clinically isolated syndrome (CIS), 1904 (65.1 %) RR-MS, 344 (11.8 %) SP-MS with relapses, 332 (8.4 %) SP-MS with no relapses, 141 (4.8 %) primary progressive MS (PP-MS) with no relapse, and 67 (2.3 %) PP-MS with relapses.

Management of multiple sclerosis

One hundred sixty-one patients received a diagnosis of MS or CIS among 293 who had their first visit during the study period (54.9 % of all the newly observed patients). Table 1 represents data on the origin of patients referring to the centers. Of the 445 patients receiving a diagnosis at one of the reference centers, 166 patients (37.3 %) came by their own initiative and 165 (37.1 %) were addressed by a specialist doctor. Of the 210 patients who received a diagnosis of MS elsewhere, 120 (57.1 %) came to the centers by their

Table 1 Origin of patients referring to the centers

Subject/institution sending to the reference center	First diagnosed with MS at the center ($N = 445$)	First diagnosed with MS elsewhere ($N = 210$)
Patient's own initiative	166 (37.3 %)	120 (57.1 %)
Emergency departments	35 (7.9 %)	0 (0 %)
General practitioners	79 (17.8 %)	33 (15.7 %)
Specialist doctor	165 (37.1 %)	57 (27.1 %)
Ophthalmologist	91 (55.2 %)*	20 (35.1 %)*
Urologist	5 (3 %)*	0 (0 %)*
Orthopedic	7 (4.2 %)*	6 (10.5 %)*
Neurologist	59 (35.6 %)*	22 (38.6 %)*
Psychologist/psychiatrist	0 (0 %)*	0 (0 %)*
Other specialists	3 (1.8 %)*	4 (7 %)*
Missing data	0 (0 %)*	5 (8.8 %)*

* Percentage among specialist doctors

own initiative and 57 (27.1 %) were sent by a specialist doctor. In both situations, medical specialists addressing patients to the centers were mainly ophthalmologists, followed by neurologists. Table 2 summarizes the proportion of patients investigated by medical and instrumental examination. All patients underwent a complete neurological examination and evaluation with EDSS during each visit. MRI and sensory and motor visual evoked potentials were the most commonly performed instrumental examinations (44.0 and 22.1 %, respectively).

Regarding the treatment, 2797 patients (87.1 % of 3211 patients for whom data on treatment were available) underwent drug therapy. The median number of treated patients per center was 113 (range 19–1150), and the percentage of patients in treatment varied between 56.9 and 100 % among different centers. During the study period, 235 out of 3263 patients (7.2 %) started a drug therapy, with a median of 16 patients per center (range 1–65); the percentage varied between 2.5 and 21.1 % among the different centers. Table 3 shows absolute and relative frequencies of 2797 patients categorized by drug treatment. Interferon and glatiramer acetate were the most prescribed drugs, while per os and intravenous immunosuppressant drugs and natalizumab were administered in only 3.3, 1.8, and 5.4 % of patients, respectively. The elapsed time between diagnosis and initiation of therapy has been reported for 241 patients in total (10.5 % of the sample) and was between 1 and 3 months in 48.1 %, between 4 and 6 months in 19.9 %, and between 7 and 12 months in 20.3 % of cases. In the remaining 11.6 % of cases, the therapy started after at least 1 year from the diagnosis (data not shown).

During the 6-month study period, 140 patients (5 % of the treated subjects) changed therapy (Fig. 1). The percentage varied between 2.2 and 14.9 % among different centers. In 63.2 % of the patients, the reason for the change was intolerance, while in 33.1 % ineffectiveness addressed to a different drug approach. Only in 3.7 % of the patients, a switch was observed because of low treatment compliance. Data on changed drug were available only for 103 patients (73.6 % of the 140 patients who changed therapy). The higher frequency of drug switch was documented for patients in treatment with natalizumab (9.2 %), followed by patients treated with intravenous and per os immunosuppressive drugs, 6.1 and 4.4 %, respectively (Table 4). In the same period, 40 patients discontinued any therapy (1.4 % of 2797 in treatment subjects, with values ranging from 0 to 5.3 % according to the center). Discontinuation was attributable to ineffectiveness in 20.0 % of cases, intolerance in 32.5 %, pregnancy in 25.0 %, patient's own choice in 5.0 %, and to other reasons in 17.5 % of cases (Fig. 1). Overall, 229 patients (8.2 % of subjects in treatment) suffered from a disease relapse during treatment, of

Table 2 Medical and instrumental examinations carried out at each visit to the reference centers in the study period

	N (%)
Complete neurological examination	3263 (100)
Expanded disability status scale (EDSS)	3263 (100)
Magnetic resonance (MRI)	1436 (44.0)
Sensory and motor visual evoked potentials	721 (22.1)
Ophthalmologic evaluation	491 (15.0)
Paced auditory serial addition test (PASAT)	445 (13.6)
Short form (36) health survey (SF-36)	319 (9.8)
Multiple sclerosis functional composite (MSFC)	311 (9.5)
Fatigue severity scale (FSS)	281 (8.6)
Beck depression inventory test (BDI)	247 (7.6)
Nine-hole peg test	219 (6.7)
Timed 25-foot walk (T25FW)	213 (6.5)
Ashworth scale	73 (2.2)
Electroencephalogram	61 (1.9)

Table 3 Absolute and relative frequencies of 2797 patients* stratified by drug treatment

Therapy	*N* of patients in treatment*	Relative frequency on patients in treatment (%)	Maximum duration of treatment (months)
Per os immunosuppressive drugs (azathioprine, methotrexate)	91	3.3	252
Intravenous immunosuppressive drugs (cyclophosphamide, mitoxantrone)	49	1.8	72
Subcutaneous interferon β 1a	987	35.3	180
Intramuscular interferon β 1a	568	20.3	180
Subcutaneous interferon β 1b	537	19.2	180
Glatiramer acetate	606	21.7	242
Natalizumab	152	5.4	48
Steroids	2	0.1	12
Others	90	3.2	–

* Sum exceeds 2797 patients because some patients were in treatment with more than one drug at the same time

whom 201 (87.1 %) needed corticosteroids and 42 (18.3 %) were hospitalized. Two hundred and seventy-seven patients (9.9 % out of 2797 patients in treatment) had disease activity signs at MRI in the absence of clinical manifestations, 309 (11.0 %) suffered from any degree of cognitive impairment, and 1259 (45.0 %) suffered from any degree of motor impairment. Tolerability issues were documented in 1046 patients (37.4 % of the subjects in treatment). According to the clinical picture and therapeutic management, the patients were classified as shown in Table 5.

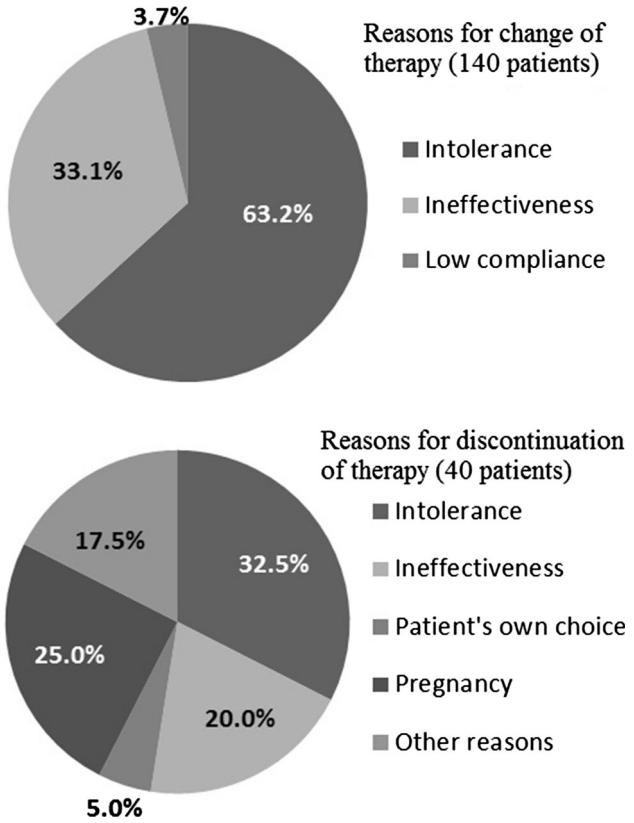

Fig. 1 Reasons for change and discontinuation of therapy in the studied population

Discussion

This paper focused on the management of MS patients admitted to the reference centers in the Campania region. The idea was to make a snapshot of the type of critical points and needs faced by reference centers in charge of MS patients' care. As emerged from the survey, a great number of patients suffering from MS (3263) accessed the reference centers in the 6-month period. According to the estimates of the Italian Association on MS (AISM) in 2010, the number of people affected by MS living in Campania region was 5990 [17]. Consequently, it is possible to suppose that approximately more than half of the patients suffering from MS in the region had access to one of the regional reference centers during the 6-month study period. This amount of patients, according to the follow-up schedule, translates into a significant impact both in terms of work time spent in medical examinations per each access and of instrumental diagnosis, as MRI and sensory and motor visual evoked potentials are frequently used to assess patients in their follow-up. The survey confirmed this trend of use, documenting how MRI was performed in 44 % of cases but evoked potentials in about 22 % of patients, leading to relevant costs. Another important effort made by reference centers is to strictly monitor MS patients' therapeutic approach, using drugs with documented potential side effects. This was confirmed by the proportion of patients experiencing problems with treatment: of the % of treated patients, a percentage ranging between 2.2 and 14.9 % across centers needed to change therapy during the study period, whereas from 0 to 5.3 %, depending on the center, required discontinuation of any therapy. Both change in therapeutic approach and discontinuation represent a critical point for physicians,

Table 4 Patients who changed drug treatment

Therapy	*N* of patients who changed therapy/*N* of patients in treatment (% of patients in treatment with the same drug)	Minimum duration of treatment (months)	Maximum duration of treatment (months)
Per os immunosuppressive drugs (azathioprine, methotrexate)	4/91 (4.4 %)	8	12
Intravenous immunosuppressive drugs (cyclophosphamide, mitoxantrone)	3/49 (6.1 %)	2	2
Subcutaneous interferon β 1a	25/987 (2.5 %)	1	24
Intramuscular interferon β 1a	20/568 (3.5 %)	2	72
Subcutaneous interferon β 1b	15/537 (2.8 %)	3	48
Glatiramer acetate	22/606 (3.6 %)	2	62
Natalizumab	14/152 (9.2 %)	2	24

Table 5 Classification of patients according to the clinical picture and therapeutic management

Condition	*N* patients	Notes
RR-MS with EDSS between 1 and 5.5	1854	97.4 % of 1904 patients suffering from RR-MS
SP-MS with EDSS between 3 and 6.5 and at least 2 relapses or 1 point increase in EDSS in the previous 2 years	323	47.8 % of 676 patients suffering from SP-MS
RR-MS treated with interferon or glatiramer acetate and at least 1 relapse or at least 9 hyperintense lesions on T2-weighted MRI or at least 1 Gd-enhanced lesion in the previous year	236	8.7 % or 2698 patients treated with interferon or glatiramer
High disease activity despite at least 12-month treatment with interferon or glatiramer acetate	158	5.8 % of 2698 patients treated with interferon or glatiramer
Increase of brain MRI lesion load and at least one among unchanged or increased relapse rate and the presence of severe relapses despite treatment with interferon or glatiramer acetate in the previous year	271	10.0 % of 2698 patients treated with interferon or glatiramer
Patients who could benefit from a symptomatic therapy aimed at relieving fatigue and improving motor impairment	1163	55.6 % of 2092 patients treated with interferon

EDSS expanded disability status scale, RR-MS relapsing-remitting multiple sclerosis, *SP-MS* secondary progressive multiple sclerosis, *MRI* magnetic resonance imaging

underlying how it is related to treatment intolerance or inefficacy. Indeed, the results of the survey showed that it is important for the reference centers to make a multidisciplinary approach and management of MS patients possible and timely.

A further problem arises from the different clinical patterns observed in patients who had accessed the reference centers. Most of the patients were aged 20–49 years and suffered from a 1.5–3 EDSS disease (generally a RR-MS), but up to one-third of the cases showed a less typical clinical presentation when the first symptoms appeared. Our experience, documenting the use of many different treatment strategies, leads us to consider that physicians should be suggested to share as much as possible guidelines and recommendations for the management of the MS disease. Through the survey, it was observed that about one-third of all patients could benefit from a symptomatic therapy aimed at relieving fatigue and improving motor impairment and that the time between diagnosis and initiation of therapy exceeded 6 months in 32 % of cases. These results further support the need to improve sharing of therapeutic strategies. Another key aspect is the under-use of second-line drugs (around 16 % of patients who might benefit from them have high clinical and radiological disease activity despite treatment with immunomodulating drugs) which may be related to both high costs and need for monitoring possible side effects.

A high proportion of patients referring to the centers by their own initiative (37 % of the patients without a diagnosis and over 50 % of the patients who received a diagnosis elsewhere) was noticed. This phenomenon is quite surprising but has been observed with considerable heterogeneity among the analyzed centers, even if no associations were found with the number of patients followed or the type of center (data not shown). Probably, this can be explained by the fact that MS centers are often associated to neurological clinics or university hospitals, which may attract patients with neurological disorders but no MS diagnosis yet. However, the high proportion of patients referring to the centers by their own initiative may be considered a proxy of an overall inappropriate management of patients suffering from MS in the Campania region. In fact, if the management of MS patients was properly organized on regional base, a higher proportion of patients addressed to the reference centers by physicians/specialists would probably be observed. At the same time, the fact that about one patient in twenty was resident in other regions could indicate a potential attractiveness of the Campania MS reference centers with regard to southern region of Italy. Our work has some limits which should be addressed. Above all, this study was conducted in 2011, just before new drugs became largely available or received new indications. Therefore, trends in diagnosis, access to the centers, management, and treatment may have changed in the last few years, and the results of this study should not be considered generalizable to the current situation. Another important limit is the fact that data were collected in an aggregate way not allowing to study individual patients. Furthermore, data were not complete or consistent for all the considered centers, restricting some analyses to a limited number of centers. Moreover, because of the different number of patients accessing the reference centers, also practices and management were somehow heterogeneous. In particular, EDSS raters were different in each center and, subsequently, the EDSS assessment may have been affected by the expertise of the various operators. Similarly, centers did not share a methodology for identifying MS lesions at MRI and this could have impacted the results. Nevertheless, the possibility to describe the access to all reference centers in an aggregate way may be considered, at the same time, a point of strength because it

provided a regional and more consistent overview of the topic. Even if results represent a snapshot of the 2011 situation, these data can be used as a starting point to monitor the improvements in the management of MS following the introduction of new diagnostic criteria, drugs, and indications. Lastly, the paper could be considered as the first attempt to describe health demand and needs of MS patients in a whole region of the country.

Conclusion

The high number of patients suffering from MS admitted to the centers on their own initiative and the large proportion of those for whom a delay in the initiation of therapy was documented may indicate deficiencies in the system of MS care. Of interest, the results show an under-utilization of second-line drugs for the MS treatment in Campania. In fact, according to the survey, 16 % of patients (who might have benefit from second-line treatment) showed high clinical and radiological disease activity despite treatment with immunomodulant drugs. The survey led us to conclude that it is of strategic importance to provide the reference centers with the necessary resources to make a multidisciplinary approach and management of MS patients possible and timely. In the same direction, physicians should be supported to share as much guidelines and recommendations as possible for the disease management of patients with less common clinical characteristics.

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Compliance with ethical standards

Conflict of interest This study was funded by Biogen Idec, which owns and produces various drugs used in the treatment of multiple sclerosis. None of the authors are employed by Biogen Idec or by any other organization that might have an interest in the submitted work.

Appendix

See Table 6.

Table 6 Questionnaire

Questionnaire section (number of questions)	Aspects investigated
Logistics (2)	Number of patients with at least one access to the center in the study period
	New patients in the last 6 months
Demographics (6)	Age (mean and range)
	Age class distribution
	Gender
	Age class distribution stratified by gender
	Residency (Campania region or other origin)
	Origin if not Campania resident
Clinical characteristics (5)	Age at onset
	EDSS at disease onset
	Signs/symptoms at first visit
	Disease duration
	Disease classification (CIS, RR-MS, SP-MS with relapses; SP-MS without relapses; PP-MS with relapses; PP-MS without relapses)
Diagnostic management (5)	Patients who received a diagnosis of MS in the last 6 months
	Number of patients who received the diagnosis of MS at the center
	Origin of patients if having the diagnosis at the center
	Origin of patients if having the diagnosis elsewhere
	Medical and instrumental examinations carried out at the center in the study period
Therapeutic management (11)	Number of patients having at least one access to the center during treatment
	Patients who started treatment in the last 6 months
	Time between diagnosis and initiation of treatment
	Administered drugs
	Duration of administration
	Number of patients who changed drug therapy in the study period
	Reason for changing drug therapy
	Number of patients who interrupted any drug therapy in the study period
	Reason for discontinuation of drug therapy
	Number of patients who had relapses in the last 6 months
	Health issues emerged in the study period
Other (1)	Classification by clinical picture and treatment

CIS clinically isolated syndrome, RR-MS relapsing-remitting multiple sclerosis, *SP-MS* secondary progressive multiple sclerosis, *PP-MS* primary progressive multiple sclerosis

References

1. Compston A, Coles A (2008) Multiple sclerosis. Lancet 372(9648):1502–1517
2. Kantarci O, Wingerchuk D (2006) Epidemiology and natural history of multiple sclerosis: new insights. Curr Opin Neurol 19(3):248–254
3. Milo R, Kahana E (2010) Multiple sclerosis: geoepidemiology, genetics and the environment. Autoimmun Rev 9(5):A387–A394
4. Flachenecker P, Rieckmann P (2003) Early intervention in multiple sclerosis: better outcomes for patients and society? Drugs 63(15):1525–1533
5. Schwid SR, Bever CT (2001) The cost of delaying treatment in multiple sclerosis: what is lost is not regained. Neurology 56(12):1620
6. Comi G, Filippi M, Barkhof F et al (2001) Effect of early interferon treatment on conversion to definite multiple sclerosis: a randomised study. Lancet 357(9268):1576–1582
7. Kleinschmidt-DeMasters BK, Tyler KL (2005) Progressive multifocal leukoencephalopathy complicating treatment with natalizumab and interferon beta-1a for multiple sclerosis. N Engl J Med 353(4):369–374
8. Black WC, Welch HG (1997) Screening for disease. AJR Am J Roentgenol 168(1):3–11
9. Bandari DS, Sternaman D, Chan T, Prostko CR, Sapir T (2012) Evaluating risks, costs, and benefits of new and emerging therapies to optimize outcomes in multiple sclerosis. J Manag Care Pharm (JMCP) 18(9):1–17
10. AIFA: Nota 65. Available online: http://www.agenziafarmaco.gov.it/sites/default/files/determina_aifa_g.u._n._194_del_21_agosto_2012.pdf
11. AIFA: Regime di rimborsabilitá e prezzo del medicinale per uso umano «Aubagio» (teriflunomide). Available online: http://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario;jsessionid=AK13EUOFaFm271zcoDogAw__.ntc-as5-guri2a?atto.dataPubblicazioneGazzetta=2014-08-13&atto.codiceRedazionale=14A06412&elenco30giorni=false
12. AIFA: Rinegoziazione del medicinale per uso umano “Tecfidera (dimetilfumarato)”. Available online: http://www.gazzettaufficiale.biz/atti/2015/20150019/15A00394.htm
13. Polman CH, Reingold SC, Banwell B et al (2011) Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol 69(2):292–302
14. Lublin FD (2014) New multiple sclerosis phenotypic classification. Eur Neurol 72(Suppl 1):1–5
15. Lublin FD, Reingold SC, Cohen JA et al (2014) Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology 83(3):278–286
16. Maurice J (2014) Multiple sclerosis guideline production takes off. Lancet 384(9958):1914–1915
17. AISM: Bilancio sociale AISM 2010. Available online: http://allegati.aism.it/manager/trackdoc.asp?file=/manager/UploadFile/2/20110527_617.pdf&open