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## **Delay in the diagnosis of multiple sclerosis in Croatia**

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### **Authors' contributions**

Study concept and design: Adamec, Habek. Acquisition of data: Adamec, Barun, Gabelić, Zadro, Habek. Analysis and interpretation of data: Adamec, Habek. Drafting of the manuscript: Habek. Critical revision of the manuscript for important intellectual content: Adamec, Barun, Gabelić, Zadro, Habek. Administrative, technical, and material support: Adamec, Barun, Gabelić, Zadro,.

**Conflict of interest statement:** There is no conflict of interest.

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## **Abstract**

### **Background**

The National Institute for Health and Clinical Excellence (NICE) guidelines for multiple sclerosis (MS) recommend the time from initial presentation to first neurological evaluation to be no longer than 6 weeks, and a further six weeks until any necessary investigations are completed. The aim of this study was to evaluate how many patients with MS are diagnosed within the NICE timelines in two settings specific for Croatia.

### **Patients and methods**

All patients with the final diagnosis of clinically isolated syndrome (CIS) or MS in a six months period were retrospectively reviewed. We calculated time from first symptom to first neurological evaluation, time from first symptom to MRI scan, time from first neurological evaluation to MRI scan, time from first neurological evaluation to lumbar puncture (LP), time from first symptom to diagnosis and time from first neurological evaluation to diagnosis. We also calculated the percentage of patients fulfilling the NICE timelines.

### **Results**

This study showed that only 61.5% of MS patients in Croatia see neurologist within 6 weeks of first symptoms, and 64.1% are diagnosed within next 6 weeks. However, 80% and 100% of patients presented to the emergency room of our hospital (where a visit to a MS clinic can be automatically made) met the NICE guidelines for time from first symptom to first neurological evaluation and time from first neurological evaluation to diagnosis, respectively.

### **Conclusion**

A specifically designed demyelinating disease diagnostic clinic offers a better service than other existing models in the diagnosis and management of MS patients.

**Key words:** Multiple sclerosis, time to diagnosis, MRI, lumbar puncture, delay

## **Introduction**

The National Institute for Health and Clinical Excellence (NICE) guidelines for multiple sclerosis (MS) recommend the time from initial presentation to first neurological evaluation to be no longer than 6 weeks, and a further six weeks until any necessary investigations are completed. [1] The aim of this study was to evaluate the time from first clinical presentation, first neurological evaluation, MRI, lumbar puncture and final diagnosis in a specialized MS clinic in Croatia and to calculate how many patients are diagnosed within timelines in two settings specific for Croatia.

## **Patients and methods**

All patients with the final diagnosis of clinically isolated syndrome (CIS) or MS in a six months period (April-October 2011) who were treated in the Referral Center for Demyelinating Diseases of the Central Nervous System in Zagreb were retrospectively reviewed. The diagnosis of CIS and MS was based on the 2010 revision of the McDonald's criteria.[2] Data on clinical symptoms, type of first presentation (optic neuritis, transverse myelitis, brainstem/cerebellar symptoms, hemispherical symptoms and multifocal symptoms), final diagnosis (CIS, RRMS, PPMS), CFS findings, number of lesions on the brain MRI and VEP findings were gathered. We calculated time from first symptom to first neurological evaluation, time from first symptom to MRI scan, time from first neurological evaluation to MRI scan, time from first neurological evaluation to lumbar puncture (LP), time from first symptom to diagnosis and time from first neurological evaluation to diagnosis. We also calculated the percentage of patients fulfilling the NICE timelines. Furthermore we divided patients in two groups. The first group consisted of patients who presented to the emergency room of our Department of Neurology and the second group consisted of patients who were

referred to our Center outpatient clinic from other regional hospitals or general practitioners. The differences between groups for all parameters were calculated by using t-test for independent samples. P value < 0.05 was considered as statistically significant. For the statistics SPSS (Chicago, Il) software was used.

## **Results**

In the study period we identified 39 patients, 26 females and 13 males. There were 5 patients with optic neuritis, 8 with transverse myelitis, 15 with brainstem/cerebellar symptoms, 6 with hemispherical symptoms and 5 with multifocal symptoms. The diagnosis of RRMS was made in 16, PPMS in 1 and CIS in 22 patients. Brain MRI was normal in one patient, 3 had one lesion and 35 patients had more than 2 lesions. CSF analysis revealed oligoclonal bands in all patients and VEP was positive in 15 patients.

In table 1 data on all analyzed parameters are presented. The mean time from first symptom to first neurological evaluation was 21.5 weeks. NICE guidelines were fulfilled only for 24 (61.5%) patients. The reasons for delayed initial neurological evaluation were unrecognized clinical symptoms by general practitioner (GP) resulting in the delayed referral, non-specific symptoms resulting either in patients not seeking medical attention on time or delayed referral by the GP, patient not attending the first appointment and scheduling difficulties due to staffing shortages. The mean time from first neurological evaluation to MRI scan was 4.2 weeks. MRI scan was performed before first neurological visit in 13 (33.3%) patients. Only 4 patients had MRI scan performed more than 6 weeks after the initial neurological evaluation, one because he failed to attend the MRI appointment, two because they were not referred to the MRI by the neurologist because of unspecific clinical symptoms and one because of

scheduling difficulties. Reasons for the delay in CSF analysis were the same as for the delay in MRI.

The mean time from first symptom to diagnosis was 34.3 weeks and time from first neurological evaluation to diagnosis was 12.8 weeks. NICE guidelines were fulfilled only for 24 (61.5%) patients. The main reasons were due to delayed MRI or LP and clerical errors.

When we divided the patients in two groups, there were 10 patients in the group 1 and 29 patients in group 2 (Table 2). There was a statistically significant difference between groups in time from first symptom to first neurological evaluation, time from first symptom to MRI scan and time from first symptom to diagnosis. When looking at time from first symptom to first neurological evaluation and time from first neurological evaluation to diagnosis, NICE guidelines were fulfilled for 80.0% and 100.0% of patients in group 1 and 55.2% and 51.7% in group 2, respectively.

## **Discussion**

This study showed that only 61.5% of MS patients in Croatia see a neurologist within 6 weeks of first symptoms, and 64.1% are diagnosed within next 6 weeks. When considering these results specific condition of the Croatian healthcare system should be taken into account. The patients with neurological symptoms can without referral from a GP or emergency medicine specialist see a neurologist in an emergency room of a hospital that has a neurological service. This is the reason why we divided the patients into two groups. Although there was no difference between groups after the initial neurological evaluation (time to MRI, LP or diagnosis), 80% and 100% of patients presented to the emergency room of our hospital (where a visit to a MS clinic can be automatically made) met the NICE guidelines for time



from first symptom to first neurological evaluation and time from first neurological evaluation to diagnosis, respectively.

Compared to other European countries, time from first symptom to first neurological evaluation is longer in Croatia than in Ireland (NICE guidelines were met for 61.5% versus 78% patients) while time from first neurological evaluation and final diagnosis is shorter in Croatia than Ireland (NICE guidelines were met for 64.1% versus 52% patients).[3] On the other hand for Spanish versus Croatian MS patients both intervals are longer (median time of 15.6 versus 2 and 7.2 versus 2.3 weeks, respectively).[4] The reasons for these differences should be sought for in different organization of health care systems in Europe, but also in MS awareness among GPs and emergency medicine physicians. As well, our study supported the finding that specifically designed demyelinating disease diagnostic clinic offers a better service than other existing models.[5]

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## Tables

Table 1. Overall times from presentation to diagnosis.

	Mean time (weeks)	Median time (weeks)	Range (weeks)	Number (%) fulfilling NICE guidelines
Time from first symptom to first neurological evaluation	21.5	2	0-204.4	24 (61.5%)
Time from first symptom to MRI scan	25.7	5.1	0.3-206.9	NA
Time from first neurological evaluation to MRI scan	4.2	0.6	-10.1-100.9	NA
Time from first neurological evaluation to LP	11.3	1.1	0-197.7	NA
Time from first symptom to diagnosis	34.3	9.7	1.1-209.9	NA
Time from first neurological evaluation to diagnosis	12.8	2.3	0.4-198.7	25 (64.1%)

Table 2. Comparison of analyzed parameters between groups.

	Group	Mean time (weeks)	p value	Number (%) fulfilling NICE guidelines
Time from first symptom to first neurological evaluation	1	3.6	0.021	8 (80.0%)
	2	27.7		16 (55.2%)
Time from first symptom to MRI scan	1	4.3	0.008	NA
	2	33.1		NA
Time from first neurological evaluation to MRI scan	1	0.7	0.448	NA
	2	5.4		NA
Time from first neurological evaluation to LP	1	0.8	0.278	NA
	2	14.9		NA
Time from first symptom to diagnosis	1	5.5	0.002	NA
	2	44.2		NA
Time from first neurological evaluation to diagnosis	1	1.9	0.259	10 (100.0%)
	2	16.5		15 (51.7%)