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Real-world operation of multiple sclerosis centres in Central-Eastern European countries covering 107 million inhabitants

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ABSTRACT

Background: In 2018 multiple sclerosis (MS) care unit (MSCU) recommendations were defined. Nevertheless, the information on MS care, and whether MS centres fulfil the international recommendation is limited. Thus our objectives were to assess whether centres meet the MSCU recommendations and gain a comprehensive overview of MS care in Central-Eastern European countries.

Methods: A self-report questionnaire assessing aspects of the MSCU recommendations, disease-modifying therapy (DMT) and registry use and the patient number was assembled and sent to nine Central-Eastern European countries. Furthermore, one Danish and one German centre were contacted as a reference.

Results: In 9/9 countries, MS care was pursued in centres by MS neurologists and MS nurses. In Austria and the Czech Republic, management of MS was conducted under strict regulations displaying a referral centre system, fundamentally similar to but independent of the MSCU criteria. Several centres fulfilled all aspects of the MSCU criteria, while others had similar insufficiencies consisting of a speech therapist, continence, pain and spasticity specialist, neuro-ophthalmologist, and oto-neurologist. In 9/9 countries, DMTs were reimbursed. However, some centres did not provide every available DMT. A national registry was available in 4/9 countries with mandatory registry use only in Austria and the Czech Republic.

Conclusion: In countries where MSCU recommendations are not fulfilled, a strictly regulated centre system similar to the Austrian and Czech model with a registry-based quality control might ensure appropriate care for people with MS.

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1. Introduction

Multiple Sclerosis (MS) is an autoimmune neurodegenerative disorder of the central nervous system that usually affects young adults at onset, causing physical and cognitive impairment (Thompson et al., 2018). According to estimates 2.8 million people live with MS worldwide, and approximately one million persons are affected in Europe alone (Walton et al., 2020).

Nowadays, many disease-modifying therapies (DMTs) are available; thus, with timely diagnosis and proper treatment, the patients' physical and cognitive status, as well as their quality of life can be preserved (Cerqueira et al., 2018). Nevertheless, due to the rapidly evolving therapeutic options and guidelines, general practitioners (GP) and general neurologists (GN) cannot keep up with brain-health focused care (Hobart et al., 2019). Therefore, defining the cornerstone of MS care was necessary. In 2018 the latest therapeutic guideline was created for European neurologists; subsequently, recommendations to a well-developed comprehensive multiple sclerosis care unit (MSCU) were also determined, suggesting that each country should adapt to these criteria depending on the specific health care circumstances in that country (Table 1) (Montalban et al., 2018, Montalban et al., 2018, Soelberg Sorensen et al., 2019).

The first and so far only adaptation stems from Latin America (Cristiano et al., 2021). Except for our previous work conducted in Hungary, no surveys assessed whether the existing centres fulfil the MSCU criteria (Kokas et al., 2022). Presumably, in some countries, medical care of persons with MS (pwMS) is part of general neurology. In others, MS care is pursued in specialised centres; nevertheless, the information on this is limited. Thus, our main objective is to extend our previous assessment to a larger region to gain a comprehensive overview of MS care. Therefore, Central-Eastern European countries partaking in the Danube Symposium for Neurological Sciences (DSNS) were contacted, covering a region over 107 million inhabitants, accounting for approximately 15% of the European population. In addition, the largest Danish and one German centre were also contacted as a reference.

Considering each country's different economic, financial and health care systems, our conception was not to compare the results but to establish a "starting point" for future surveys examining MS care, serving as a baseline to follow the improvement. Since this assessment is reproducible, the same countries could also participate in the 5-to-10-year follow-up study to determine the changes. Furthermore, as this investigation could be reproduced in other regions as well, an even more comprehensive overview of MS care may be achievable. We intended to assess whether MSCU criteria are fulfilled, investigate which personnel and infrastructural criteria are least prevalent, provide information regarding DMT use, and gather information on patient numbers, registry use in clinical settings, and management of MS in DSNS countries.

2. Materials and methods

2.1. Study design and participants

The survey was conducted at the Department of Neurology, Albert Szent-Györgyi Faculty of Medicine, Albert Szent-Györgyi Health Centre, University of Szeged, Szeged, Hungary with the contribution of MS centres from the following DSNS countries: Austria, Croatia, Czech Republic, Hungary, Poland, Romania, Serbia, Slovakia, and Slovenia. In addition, a centre from Denmark and Germany also participated in the survey.

According to primarily the MSCU recommendation and the therapeutic guideline, a questionnaire was assembled focusing on four main aspects: instrumental and personnel requirements of an MSCU, DMT use, patient number, and registry use (Kokas et al., 2022; Montalban et al., 2018a,b; Soelberg Sorensen et al., 2019).

In the questionnaire 22 aspects of the MSCU recommendation were included. These aspects, later referred to as "minimum criteria" (MS

nurse, secretary, neuropsychologist, pharmacist, dietitian, speech therapist, pain specialist, continence specialist, spasticity specialist) and "recommended criteria" (neuro-radiologist, microbiology, laboratory, electrophysiology, ophthalmology, internal medicine specialist,

Table 1

Concise summary of theECTRIMS/EAN therapeutic guideline and the multiple sclerosis care unit recommendations.

	ECTRIMS/EAN therapeutic guideline (Montalban et al., 2018, Montalban et al., 2018)	Multiple Sclerosis Care Unit recommendations (Soelberg Sorensen et al., 2019)
Brief summary of the key aspects of the international recommendations	The entire spectrum of DMTs should be available in care units with appropriate infrastructure to provide proper monitoring, detection, and management of possible side effects. DMT prescribing should be individualized (it should depend on patient characteristics, disease activity, safety, and accessibility). SPMS and PPMS patients should be treated. MRI examination should take place 6 months after new DMT initiation, then every 12 months except for natalizumab (every 3-6 months) or in case of disease reactivity (promptly). MRI scans should be of high-quality standards interpreted by qualified MS-radiologists. In case of an ineffective DMT, a more efficacious therapy should be offered. Switching to another DMT should also be individualized. In case of a highly effective DMT is stopped (because of side effects or disease reactivity), treatment with another highly efficacious therapy should be considered, if not possible, rebound might occur. Women of childbearing age should consider disease activity and accessibility of "pregnancy-safe" DMTs when planning pregnancy.	Since GPs and GNs are not able to keep up with the latest guidelines, advanced multidisciplinary and, thus comprehensive units according to local conditions should be established. The entire spectrum of DMTs should be available in care units with appropriate infrastructure to provide proper monitoring, detection, and management of possible side effects. The core of the MSCU is the patient, MS neurologist, MS nurse, complemented by the secretary (having a role in patient documentation and data recording), and at least three of the following: pharmacist, neuropsychologist, speech therapist, dietitian, continence specialist, pain specialist, spasticity specialist (the latter 3 can be provided by the MS nurse or the MS specialist). To ensure accurate diagnostics and differential diagnostics, a qualified neuro-radiologist, laboratory, electrophysiology, ophthalmology, and MRI services should also be promptly accessible. A fully developed MSCU should collaborate with many other neighbouring specialties as well: neuro-ophthalmologist, otoneurologist, neurorehabilitation, neurosurgeon, surgeon, obstetrician-gynaecologist, internal medicine specialist, and psychiatrist to treat complications and manage comorbidities. A multidisciplinary approach that focuses on patient-tailored management would enhance therapeutic efficacy, quality of life and satisfaction.

Abbreviations: DMT: disease-modifying therapy,ECTRIMS/EAN: European Committee for Treatment and Research/European Academy of Neurology, GN: general neurologist, GP: general practitioner, MS: multiple sclerosis, MSCU: multiple sclerosis care unit, MRI: magnetic resonance imaging, PPMS: primary progressive multiple sclerosis, SPMS: secondary progressive multiple sclerosis

surgeon, neurosurgeon, obstetrician-gynaecologist, neuro-ophthalmologist, oto-neurologist, psychiatrist, neurorehabilitation), were based on the original paper's definition of the "core of the MSCU" and "fully developed MSCU". The appellation "minimum criteria" might suggest aspects that are easier to fulfil. However, in case of the MSCU minimum criteria, explicitly MS-specific specialties were included, which aspects distinguish MSCUs from other facilities providing non-MS-specific care, thus they might be more difficult to fulfil. On the other hand, recommended criteria rather include aspects that are important in either the diagnosis of MS or the management of comorbidities that may accompany MS, thus they might be easier to access even in smaller facilities.

The second portion of the questionnaire assessed DMT use, as the MSCU recommendation states that the entire spectrum of DMTs should be available in care units. While the third and fourth portion investigated patient care capacity and data recording.

The questionnaires were sent via e-mail to the participating centres (Kokas et al., 2022; Montalban et al., 2018a,b; Soelberg Sorensen et al., 2019). Parallel to collecting and summarizing data from questionnaires, information regarding the management of MS, DMT reimbursement, prevalence estimates and country population data were also researched. Data were acquired between December 2020 and December 2021.

2.2. Statistical analysis

Descriptive statistics were used to summarize data. All questionnaires were included in the analysis, regardless of being completely or incompletely filled.

Homogeneity and heterogeneity were defined by calculating the percentile proportion of the centres fulfilling each criterion, in each country, resulting in a scale ranging from 0-100%. This scale was then divided to four equal parts: four quadrants – Q1, Q2, Q3, Q4. Q1 represents that 100-76% of centres fulfil the condition, Q2 means that in 75-51% of centres the criterion is ensured, Q3 implies that 50-26% of centres fulfil the condition, and Q4 indicates that the criterion is available in 25-0% of centres. Thereafter the quadrant proportions were further dissected, and three categories were created. First category: homogeneously available in 9/9 countries – if each country reached level Q1 in the fulfilment of the criterion. Second category: slightly heterogeneous availability among countries – if at least 1, but not more than 3 countries reached either level Q2, Q3 or Q4 in the fulfilment of the criterion. Third category: high heterogeneity in the availability among countries – if 4 or more countries reached either level Q2, Q3 or Q4 in the fulfilment of the criterion.

Most recent prevalence estimates were searched on multiple platforms. Current population data were uniformly collected in March 2022. The "number of patients according to prevalence estimates" was calculated by using the following formula:

$$\frac{\text{current population (number of people in the country)}}{100\,000} \times \text{most recent prevalence data (number of cases per 100\,000 people)}.$$

These numbers were then compared to the sum of "number of patients reported by centres" using the following formula:

$$\frac{\text{number of patients according to prevalence data (number)}}{\text{Number of patients reported by centres (number)}}$$

Resulting in the "difference between estimated and the actual number of patients" outcomes with a negative or positive sign, with the negative sign indicating how many patients do not get access to MS-specific treatment. In some countries, official and/or non-official data regarding patient numbers were available, which data were also considered during comparison. These outcomes were then interpreted in light of the participation rate of centres in the given country.

2.3. Ethical approval

The study was approved by the Hungarian Medical Research Council (reference number IV/5139-1/2021/EKU), and conducted in accordance with the Declaration of Helsinki.

3. Results

3.1. Participation rate

In total, 103 centres participated in the survey, 101 from DSNS countries, and 1 Danish and 1 German reference centre. From Austria, three questionnaires were received, two questionnaires representing two university centres and one representing the Austrian MS Centre Network of the Austrian Society of Neurology (ASN), consisting of 132 centres. Since the Austrian Centre Network operates under strict conditions, the Austrian participation rate can be considered 100%. In Romania (15/15) and Serbia (5/5), the participation rate was also 100%, whereas 94% of Hungarian (29/31), 90% of Slovakian (9/10), 67% of Slovenian (2/3), 60% of Czech (9/15), 50% of Croatian (5/10), and 19% of Polish (24/129) centres sent back questionnaires.

3.2. Management of multiple sclerosis and disease-modifying therapy reimbursement in participating countries

In all participating countries, management of MS was pursued in specialized MS centres, and all available DMTs were reimbursed by the countries' Health Insurance Funds (HIFs). (Berger et al., 2018, <https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, https://www.oegn.at/wp-content/uploads/2015/07/%C3%96GN_Kriterien_MSZentrum_18Februar2014.pdf, <https://neuro-hr.org/Content/Documents/Kriteriji%20za%20lijecenje%20RRMS-a%202021.pdf> 2022, Benjak et al., 2018, https://www.czech-neuro.cz/content/uploads/2020/04/rs_odborna-2.0_final_pub_web-2.pdf, https://nfimpuls.cz/images/docs/remus_zaverecne-zpravy/aj_zaverecna_zprava_2020_12_souhrna_web.pdf, Kapica-Topczewska et al., 2020, Broła et al., 2015, https://www.braincouncil.eu/wp-content/uploads/2020/06/ROMANIA_DEF_EBC_pp_03122019.pdf, Magyari et al., 2021, Ohle et al., 2021, <https://www.dmsg.de/service/kliniken-und-praxen/dmsg-ausgezeichnete-zentren>.) Of the participating countries, Hungary was the first to establish MS centre conditions in 1996. A similar approach was also applied in the Czech Republic in the same year to control the prescription of DMTs. These conditions were redefined in 2019 to suit the current requirements of MS care better. (https://nfimpuls.cz/images/docs/remus_zaverecne-zpravy/aj_zaverecna_zprava_2020_12_souhrna_web.pdf.) In Austria, specialized MS centre conditions were determined in 2000 and redefined in 2014. (https://www.oegn.at/wp-content/uploads/2015/07/%C3%96GN_Kriterien_MSZentrum_18Februar2014.pdf, https://nfimpuls.cz/images/docs/remus_zaverecne-zpravy/aj_zaverecna_zprava_2020_12_souhrna_web.pdf.) Similarly, in Germany and Denmark, MS centres operate under predetermined conditions (Table 2) (Magyari et al., 2021, Ohle et al., 2021, <https://www.dmsg.de/service/kliniken-und-praxen/dmsg-ausgezeichnete-zentren>).

3.3. Multiple sclerosis care unit criteria

In total 97/103 centres completed the part of the questionnaire surveying MSCU criteria: data from 2/29 Hungarian, 1/24 Polish, and 1/9 Slovakian centres were missing, whereas 3/24 Polish and 1/5 Croatian questionnaires were incompletely filled.

According to the three questionnaires received from Austria

Table 2

Management of multiple sclerosis in participating countries.

Management of multiple sclerosis and disease-modifying therapy reimbursement in participating countries

Austria (Berger et al., 2018, <https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, https://www.oegn.at/wp-content/uploads/2015/07/%C3%96GN_Kriterien_MSZentrum_18Februar2014.pdf.)

Since 2000, pwMS have received medical care in the Austrian Centre Network. The latest version of the MS Centre Network Conditions was composed in 2013. Currently, the Centre Network consists of 132 centres, which Network is strictly regulated by the ASN. Conditions to become a centre:

- The head of the institute should be a board-certified neurologist who has expertise in the field of MS.
- Knowledge of the latest clinical, diagnostic, and therapeutic guidelines, capability to perform a standard neurologic examination supplemented with EDSS scores, and capability to interpret MRI results should be ensured.
- Capability to treat pwMS according to the latest therapeutic guidelines.
- Personnel and instrumental conditions should be guaranteed (medical assessment within 14 days, relapse treatment within 48 hours, at least 60-minute-long therapeutic visits, separate examination room, room to collect CSF samples, infusion room, waiting room etc.).
- As centres are part of a network, treatment of other aspects of the disease is ensured.
- Documentation should include patient history, EDSS, MRI results, therapeutic indication, relapse, adherence to therapy, and data entry of pwMS receiving DMTs is mandatory in the Austrian Treatment Registry.

Application to obtain centre status should be filed in writing to the ASN, including evidence that the conditions mentioned above are fulfilled. Certification needs to be renewed every 2 years, conditioned to participation in CME approved MS training and Centre Network conferences as provided by the ASN. DMTs are available free of charge.

Croatia (<https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, <https://neuro-hr.org/Content/Documents/Kriteriji%20za%20lijecenje%20RRMS-a%202021.pdf> 2022, Benjak et al., 2018)

Medical care of pwMS is pursued in 10 institutes. Diagnostic and therapeutic guidelines are accessible on the website of the Croatian Association of Neurology. Different DMTs can be commenced if pwMS fulfil initiation criteria:

- EDSS scores are in the therapeutic range of the DMT.
 - Disease activity is in the therapeutic range of the DMT.
 - Approval of the institutional pharmacy to begin treatment.
- DMTs are available free of charge.

Czech Republic (<https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, https://www.czech-neuro.cz/content/uploads/2020/04/rs_odborna-2.0_final_pub_web-2.pdf, https://nimpuls.cz/images/docs/remus_zaverecne-zpravy/aj_zaverecna_zprava_2020_12_souhrna_web.pdf.)

In most cases, medical care of pwMS is ambulatory and explicitly takes place in specialized centres. Still, in severe cases, the centre should provide inpatient care: either the centre itself guarantees the appropriate conditions or is in close contact with a hospital to which pwMS can be referred to. A system of specialised MS centres was established in the Czech Republic in 1996, but the main aim of this system was to control the prescription of DMTs. Thanks to the systematic efforts of the Neurological Society, an agreement was then reached with the Ministry of Health in 2019, and highly specialised care centres were redefined, containing the latest applicable diagnostic and therapeutic guidelines. Currently, 15 centres are responsible for the medical care of pwMS, and the number of centres is maximized; it may not exceed 17. Application to achieve the centre status should be filed in writing to the Czech Ministry of Health, including evidence that the conditions mentioned above are fulfilled, and quality control should be ensured. The Czech health care provider regularly monitors quality indicators of the centres, including:

- Highly specialized medical staff (multidisciplinary team with working hours adjusted to patient number, additionally, the head of the institute should be a board-certified neurologist).
- Number and proportion of patients receiving DMT.
- Instrumental background (MRI, OCT, evoked potentials, EEG, EMG, ECG, CSF analysis, laboratory, examination room, infusion room, number of infusion pumps adjusted to patient number).
- Availability of treatment options.

Since 2013 patient data should be recorded in the ReMus registry from which annual reports, and regular epidemiological and financial statistics can be obtained. Certification should be renewed every 5 years; moreover, the Czech Ministry of Health should be notified in writing in case of changing conditions. DMTs are available free of charge.

Hungary (Kokas et al., 2022, <https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>.)

Specialized MS centre conditions were established by the Hungarian Neurological Professional College in 1996:

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Table 2 (continued)

Management of multiple sclerosis and disease-modifying therapy reimbursement in participating countries

- The designated hospitals' neurological departments should provide a separate outpatient unit dedicated to pwMS, granting a minimum of 6 consulting hours/week.
- The institute where the centre is located, should have the conditions to examine, diagnose, and treat pwMS.
- The MS care team should consist of at least 2 neurologists experienced in the field of MS and one specially trained MS nurse.
- Documentation should include patient history, ARR during DMT, and physical status including EDSS.

These conditions were determined over 20 years ago due to the high retail price of the only therapeutic option available at the time (IFN- β). Since treatment resources were limited, the insurance would only fund treatment under strictly regulated and regularly monitored conditions. However, these criteria have not evolved in accordance with the changing circumstances experienced in the past years. Currently 31 centres are responsible for the medical care of pwMS, 11 hospitals located in the capital city and generally 1-1 located in each county. MS centres are responsible for the medical care of pwMS in their region. Patient documentation is not standardized across centres, and a national registry is not available. However, the regional registry of Szeged and the G35H0 ICD-10 code were valuable tools in providing information on MS epidemiology. DMTs are available free of charge.

In Poland management of MS is undertaken in 129 centres (65 specialised MS centres and 64 general MS centres).

- Specialised MS centres provide the full spectrum of Ist and IInd line drugs, and in total, are based within regional hospital facilities.
- In addition, general MS centres provide basic diagnostic options and manage patients using first-line drugs.
- All centres have more or less even regional distribution in 16 voivodeships.

A national registry is available in Poland, with a two-sided data platform (MS neurologists and patients can also enter data); however, data entry is voluntary. DMTs are available free of charge.

- All drugs are dispensed within state-funded treatment programmes based on locally calculated budgets.

In most cases, MS management is carried out in outpatient facilities but with regular access to hospital wards. The Polish Neuroscience Society (PoNS) provides training, and conferences in MS and is responsible for developing diagnostic and therapeutic guidelines, and epidemiological analyses. Future prospects: PoNS has worked out a strategy for Polish neurology, proposing new care system, giving stronger position for MS centres within the national healthcare system and focusing on shortening diagnostic and therapeutic pathways for MS patients. MS care in Romania is going through changes. Past-present:

- 15 centres were responsible for the care of pwMS, 9 located in the capital city; thus, regional care of patients was not possible, resulting in inequality in access to treatment.
- Due to the more advanced technical and personnel background, mainly university hospitals were designated as centres; however, rehabilitation was not solved in most of them, or it was not MS-specific.
- Suspected cases of MS were referred to a neurologist by a GP, who referred the patient to an MS centre, and only neurologists experienced in MS could request diagnostic tests. Otherwise, costs had to be covered by the patient.
- High costs of diagnostic tests and limited financial resources, absence of standard MRI protocols, and shortage of neuroradiologists lead to delays in the diagnosis.
- Generally, neurologists experienced in the MS field provided medical care for pwMS, yet in some centres, care was the responsibility of the general neurologist.

Present-future: recently published MS centre conditions:

- Provides an opportunity for accreditation for all county hospitals; thus, the number and distribution of MS centres should ensure equality of access to care.
- Suggests that multidisciplinary care should be adapted to outpatient care (it was usually solved within the framework of inpatient care, resulting in more costs).
- Advocates the development of rehabilitation opportunities.

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Poland (Berger et al., 2018, <https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, Kapica-Topczewska et al., 2020, Broła et al., 2015)

<https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, https://www.braincouncil.eu/wp-content/uploads/2020/06/ROMANIA_DEF_EBC_pp_03122019.pdf).

Romania (<https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, https://www.braincouncil.eu/wp-content/uploads/2020/06/ROMANIA_DEF_EBC_pp_03122019.pdf).

Table 2 (continued)

Management of multiple sclerosis and disease-modifying therapy reimbursement in participating countries

- Suggests the use of the national register (although a Romanian MS register has existed since 2013, it has been used voluntarily thus far).

DMTs are available free of charge.

Management of pwMS is pursued in 10 specialized centres.

DMTs are available free of charge.

In Slovenia, management of pwMS is pursued in 3 MS centres.

Shortage of MS nurses and neurologists specialized in MS.

DMTs are available free of charge.

In Serbia, management of MS is pursued in 5 MS centres.

DMTs are available free of charge.

The country is divided into four main regions. In these regions, the health care system and financial background differ significantly.

Management of MS is pursued in 13 MS clinics, the only units authorized to prescribe DMTs.

MS clinics predominantly provide outpatient care for pwMS.

However, when inpatient care is needed, hospitalization of patients is ensured by close collaboration with inpatient departments.

Use of the national Danish Multiple Sclerosis Registry is mandatory for all centres.

DMTs are available free of charge, and it is the Danish Medicines Council's role to provide national treatment recommendations.

Management of MS is pursued in 187 centres (70 specialized MS centres, 95 MS centres, and 22 MS rehabilitation centres), certified by the German Multiple Sclerosis Society (DMSG).

However, DMSG certification is voluntary, and it is not necessary to provide MS care and receive reimbursement for medications. In fact, many, even large (university) MS centres are not certified.

Centre types operate under specified conditions, determined by DMSG, consisting of 4 main sections:

- Expertise and training
 - Continuous management of pwMS should be performed by board-certified neurologists who have at least 5 years of experience in the management of MS
 - The healthcare professionals involved in MS management should also have at least 2 years of experience in MS care.
 - Regular training and education opportunities should be ensured for MS neurologists, healthcare professionals, and neighbouring specialties partaking in the management of MS and pwMS.
 - The pre-determined minimum number of patients managed in outpatient and inpatient facilities is established (specific to each centre category). MS centres should manage at least 80-120 pwMS, while specialized MS centres and MS rehabilitation centres should care for at least 400 and 120 pwMS, respectively.
- Diagnostics
 - The very first consultation at the centre should last for at least 1 hour.
 - Patient examination, assessment of physical status, determination of deficits, and evoked potentials should be executed and documented according to standardized manners.
 - CSF examination conducted by a certified laboratory, and MRI examination conducted by an MS-familiar neuroradiologist using standardized protocols should be available in MS centres and specialized MS centres but not in rehabilitation centres (in MS rehabilitation centres fundamental laboratory examinations should be available, cooperation with an external laboratory is a feasible option as well).
- Management of MS
 - MS centres and specialized MS centres
 - Criteria of diagnostic and therapeutic guidelines should be fulfilled and implemented in everyday clinical practice.
 - Treatment with DMTs and relapse treatment should be ensured (cooperation with inpatient facilities might be a feasible option).
 - Symptomatic treatment (management of bladder dysfunction) and rehabilitation (physiotherapy, ergotherapy, speech therapy) of MS should be ensured.
 - Emergency care should be provided.
 - Premises should be disability accessible.

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Slovakia (Berger et al., 2018, <https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>).

Slovenia (Berger et al., 2018, <https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>).

Serbia (<https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>).

Denmark (<https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, Magyari et al., 2021)

Germany (<https://www.emsp.org/wp-content/uploads/2021/03/MS-Barometer2020-Final-Full-Report-Web.pdf>, Ohle et al., 2021, <https://www.dmsg.de/service/kliniken-und-praxen/dmsg-ausgezeichnete-zentren>).

Table 2 (continued)

Management of multiple sclerosis and disease-modifying therapy reimbursement in participating countries
<ul style="list-style-type: none"> ○ MS rehabilitation centres <ul style="list-style-type: none"> ■ Physiotherapy, occupational therapy, speech therapy, and consultation with a psychologist and neuropsychologist should be ensured with an individualized treatment approach. ■ Individualized consultations regarding disease information, coping strategies, and self-catheterization should be ensured. Furthermore, consultation with social workers and the supply of medical aids should be guaranteed. ■ Emergency care should be provided, and cooperation with inpatient facilities might be a feasible option. ● Cooperation within DMSG <ul style="list-style-type: none"> ○ Centres should participate in research, medical training and should publish in DMSG forums and journals. ○ Patient information should be recorded in the German Multiple Sclerosis Registry <p>DMTs are available free of charge.</p>

Abbreviation: ASN: Austrian Society of Neurology, ARR: annualized relapse rate, CME: continuing medical education, CSF: cerebrospinal fluid, DMSG: Deutsche Multiple Sklerose Gesellschaft (German Multiple Sclerosis Society), DMT: disease-modifying therapy, ECG: electrocardiography, EDSS: expanded disability status scale, EEG: electroencephalography, EMG: electromyography, GP: general practitioner, ICD: international classification of diseases, MRI: magnetic resonance imaging, MS: multiple sclerosis, OCT: optical coherence tomography, PolNS: Polish Neuroscience Society, pwMS: people with multiple sclerosis

(including one covering the entire Austrian MS Centre Network of 132 centres), all aspects of the minimum and recommended criteria were fulfilled.

In Croatia, 1/5 centres fulfilled both the minimum and recommended criteria. However, regarding minimum criteria in the rest of the centres, either secretary, spasticity, or pain specialist was lacking. On the other hand, recommended criteria were fulfilled by 2/5 centres, while in one centre, an oto-neurologist was not accessible.

In the Czech Republic, 5/9 centres fulfilled both the minimum and the recommended criteria, and 1/9 centres fulfilled only the minimum criteria. However, in the rest of the centres, the availability of either microbiology, speech therapist, continence and pain specialist, or oto-neurologist was not ensured.

In Hungary, 10/29 centres fulfilled all aspects of the minimum criteria, of which 7 centres also fulfilled all aspects of the recommended criteria. The least prevalent specialties were neuropsychologist, spasticity and pain specialist, oto-neurologist, and neuro-ophthalmologist.

In Poland, 2/24 centres fulfilled both the minimum and recommended criteria, 2/24 centres fulfilled only the minimum, and 5/24 centres fulfilled the recommended criteria. Secretary, microbiology, continence, spasticity, and pain specialists were the least prevalent among centres.

In Romania, 1/15 centres fulfilled recommended criteria; however, not a single centre managed to fulfil minimum criteria. Secretary, ophthalmology was often not ensured, and consultation with a speech therapist, pain, continence, and spasticity specialist was not guaranteed. Furthermore, consulting hours with a neurosurgeon, obstetrician-gynaecologist, neuro-ophthalmologist, and oto-neurologist was not ensured in many centres.

In Serbia, 1/5 centres fulfilled both the minimum and recommended criteria, and 2/5 centres fulfilled only the aspects of recommended criteria. Secretary employment, consultation with a speech therapist, continence specialist, spasticity specialist and neuro-ophthalmologist were often not ensured.

In Slovakia, no centre fulfilled all aspects of the minimum criteria, and only 3/9 centres fulfilled the recommended criteria. In addition, Slovakian centres rarely employed a secretary, and consultation with a neuropsychologist, speech therapist, pain, continence, and spasticity specialist was often not guaranteed. Furthermore, ophthalmology, neuro-rehabilitation, and consulting hours with a surgeon, neuro-ophthalmologist, oto-neurologist, and psychiatrist were not consistently guaranteed.

In Slovenia, neither of the centres fulfilled all aspects of the minimum or the recommended criteria. For example, a pain, continence, and spasticity specialist, surgeon, and oto-neurologist were not available in one of the centres. Whereas, in the other, pain and continence specialist, electrophysiology, and ophthalmology were not accessible (eTable1).

According to the questionnaires received from Denmark and Germany, both the minimum and recommended criteria were fulfilled in those particular centres.

As the above detailed listing suggests, there are homogeneities and heterogeneities in the fulfilment of the MSCU criteria between countries. In 4/9 countries more than 75% of MSCUs fulfilled at least 75% of the criteria (reaching level Q1 - homogenous availability). In the rest of the countries, criteria were heterogeneously fulfilled (reaching level Q2-Q3-Q4). Homogeneously available criteria were: MS nurse, pharmacist, dietitian, neuroradiologist, laboratory, internal medicine specialist, psychiatry, and neurorehabilitation. The availability of neuropsychologist, microbiology, electrophysiology, ophthalmology, surgeon, neurosurgeon, and obstetrician-gynaecologist was slightly heterogenous among countries. At the same time, in the availability of the administrator, speech therapist, pain, continence, and spasticity specialist, oto-neurologist, and neuro-ophthalmologist high heterogeneity was detected among countries, thus appeared to be homogeneous shortcomings (eTable2, Table 3).

3.4. DMT use

In total 96/103 centres completed the part of the questionnaire surveying DMT use. Data were missing from 1/9 Czech, 1/24 Polish, 1/15 Romanian, 2/29 Hungarian and 2/9 Slovakian centres.

Austrian and Slovenian centres administered the entire spectrum of DMTs. However, there were centres in all the remaining countries, where one or more DMTs were not accessible. For example, natalizumab (NTZ) was not used in 1/5 Croatian centres, the rest of the centres used the entire spectrum of DMTs. In the Czech Republic 7/9 centres used every DMT, and 1/9 centres did not use cladribine (CLA). In Serbia 4/5 centres administered every moderately and highly effective DMTs (HEDMTs), however, 1/5 centre did not administer dimethyl-fumarate (DMF) and NTZ. In 7/9 Slovakian centres the entire spectrum of DMTs was used. Only 15/29 Hungarian and 16/24 Polish centres provided all available DMTs. In Romania, no centre used all of the DMTs. CLA was not used at all, since it was not approved by Romanian Medication Authorities at the time of the survey. DMF and alemtuzumab (ALM) was

Table 3
Summary of homogeneity and heterogeneity in the fulfilment of MSCU criteria according to achieved quadrant levels.

	Homogenously available in 9 countries	High heterogeneity in the availability among countries	Slightly heterogeneous availability among countries	Homogenously available in 9 countries	Homogenously available in 9 countries	High heterogeneity in the availability among countries	High heterogeneity in the availability among countries	High heterogeneity in the availability among countries	High heterogeneity in the availability among countries	Homogenously available in 9 countries	Slightly heterogeneous availability among countries	Homogenously available in 9 countries	Slightly heterogeneous availability among countries	Slightly heterogeneous availability among countries	Homogenously available in 9 countries	Slightly heterogeneous availability among countries	Slightly heterogeneous availability among countries	High heterogeneity in the availability among countries	High heterogeneity in the availability among countries	Homogenously available in 9 countries	Homogenously available in 9 countries	In 4/9 countries more than 75% of MSCUs fulfilled at least 75% of the criteria (Q1) \vskip5\hfill\hbox\rot90{In 5/9 countries 7-12 criteria were heterogeneously fulfilled by MSCUs (Q2-Q3-Q4). \vskip5\hfill\hbox\rot90{Homogeneous shortcomings were: the administrator, speech therapist, pain, continence, and spasticity specialist, oto-neurologist, and neuro-ophthalmologist}				
Slo	Q1	Q1	Q1	Q1	Q1	Q1	Q4	Q4	Q2/Q3	Q1	Q1	Q1	Q2/Q3	Q1	Q2/Q3	Q1	Q1	Q1	Q2/Q3	Q1	Q1	Q1	68%	23%		9%
Sk	Q1	Q4	Q2	Q1	Q1	Q3	Q3	Q3	Q4	Q1	Q2	Q1	Q1	Q1	Q2	Q1	Q1	Q2	Q2	Q2	Q2	Q2	45%	32%	14%	9%
Srb	Q1	Q2	Q1	Q1	Q1	Q3	Q1	Q2	Q3	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q2	Q1	Q1	Q1	77%	14%	9%	0%	
Ro	Q1	Q2	Q1	Q1	Q1	Q3	Q4	Q4	Q4	Q1	Q1	Q1	Q1	Q2	Q1	Q1	Q2	Q3	Q4	Q1	Q1	55%	18%	9%	18%	
Pl	Q1	Q2	Q1	Q1	Q1	Q2	Q3	Q2	Q2	Q1	Q2	Q1	Q1	Q1	Q2	Q2	Q2	Q1	Q2	Q1	Q1	55%	36%	9%	0%	
Hu	Q1	Q2	Q2	Q1	Q1	Q2	Q2	Q1	Q3	Q1	Q1	Q1	Q2	Q1	Q1	Q1	Q1	Q2	Q2	Q1	Q1	63%	32%	5%	0%	
Cz	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q2	Q1	Q1	95%	5%	0%	0%	
Cr	Q1	Q2	Q1	Q1	Q1	Q1	Q1	Q1	Q3	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	90%	5%	5%	0%	
Au	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	Q1	100%	0%	0%	0%	
	MS nurse	Sec retary	Neuro psycho logist	Phar macist	Dietitian	Speech therapist	Pain specialist	Conti nence spe cialist	Spasticity specialist	Neuro- radio logist	Micro biology	Labo ratory	Electro physio logy	Ophthal mology	Internal medicine	Surgeon	Neuro surgeon	Obste tric- gynaeco logist	Neuro- ophthal mologist	Oto- neuro logist	Psychia trist	Neuro rehabi litation	Q1 percentile proportion	Q2 percentile proportion	Q3 percentile proportion	Q4 percentile proportion

Abbreviation: MSCU: Multiple Sclerosis Care Unit, Q1: first quadrant – 100-76% of centres fulfil the criteria, Q2: second quadrant – 75-51% of centres fulfil the criteria, Q3: third quadrant – 50-26% of centres fulfil the criteria, Q4: fourth quadrant – 25-0% of centres fulfil the criteria

Table 4
Comparison of patient numbers according to prevalence estimates and data reported by participating centres.

	Current population 2022	Prevalence /100 000 inhabitants	Methodology and date of the latest prevalence estimate	Number of patients according to prevalence estimate	Number of patients reported by centres	Difference between the estimated and actual number of patients	The proportion of the participating centres / total number of centres
Austria	9 006 000 (https://www.worldometers.info/world-population/)	158.9 (Salhofer-Polanyi et al., 2017)	Based on ICD-10 codes, 2017 (Salhofer-Polanyi et al., 2017)	14 310	14 500	+190	3/3 (including one covering the entire Austrian MS Centre Network of 132 MS centres)
Croatia	4 105 000 (https://www.worldometers.info/world-population/)	143.8 (Benjak et al., 2018)	Based on three national patient registries and data from a non-governmental MS patient organization, 2018 (Benjak et al., 2018)	5 903 (6 160 according to the summary of 4 Croatian databases)	4 350	-1 553 (-1 810 according to the results of the summary of 4 Croatian databases)	5/10
Czech Republic	10 709 000 (https://www.worldometers.info/world-population/)	187 (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms)	As estimated by the Atlas of MS in 2020 (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms)	20 013 (17 485 Remus registry (https://www.czech-neuro.cz/content/uploads/2020/04/rs_odborna-2.0_final_pub_web-2.pdf))	12 400	-7 613 (-5 085 according to data reported in the Remus registry)	9/15
Hungary	9 660 000 (https://www.worldometers.info/world-population/)	101.8 (Kokas et al., 2022)	Based on regional registry data, 2020 (Kokas et al., 2022)	9 833	7 213	-2 620	29/31
Poland	37 846 000 (https://www.worldometers.info/world-population/)	109.1 (Kapica-Topczewska et al., 2018) (120 – Atlas of MS (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms))	Based on regional data, 2018 (Kapica-Topczewska et al., 2018)	41 289 (45 415 Atlas of MS (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms))	16 015	-25 274 (-29 400 according to Atlas of MS estimates)	24/140
Romania	19 237 000 (https://www.worldometers.info/world-population/)	53.6 (Cornea et al., 2015) (35 – Atlas of MS (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms))	Based on ICD-10 codes, using regional hospital data, data, 2015 (Cornea et al., 2015)	10 311 (6 732 Atlas of MS (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms))	5 255	-5 056 (-1 477 according to Atlas of MS estimates)	15/15
Serbia	8 737 000 (https://www.worldometers.info/world-population/)	136.8 (Pekmezovic et al., 2019)	Based on ECTRIMS online library data, 2019 (Pekmezovic et al., 2019)	11 952	6 570	-5 382	5/5
Slovakia	5 459 000 (https://www.worldometers.info/world-population/)	NA	NA	NA	4 834	not interpretable	9/10
Slovenia	2 078 000 (https://www.worldometers.info/world-population/)	151.9 (Peterlin et al., 2006)	Based on regional registry data, 2006 and Atlas of MS (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms , Peterlin et al., 2006)	3156	3 800	+643	2/3
Denmark		284 (Magyari et al., 2021)		17747 (most recent, not published data from the DMSR)	4 000		1/13

(continued on next page)

Table 4 (continued)

	Current population 2022	Prevalence /100 000 inhabitants	Methodology and date of the latest prevalence estimate	Number of patients according to prevalence estimate	Number of patients reported by centres	Difference between the estimated and actual number of patients	The proportion of the participating centres / total number of centres
	5 792 000 (https://www.worldometers.info/world-population/)		Based on the Danish Multiple Sclerosis Registry 2020 (Magyari et al., 2021)			not interpretable	
Germany	84 225 000 (https://www.worldometers.info/world-population/)	303 (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms , https://www.msregister.de/ms-register/veroeffentlichungen/berichte/)	Atlas of MS and GMSR 2020 (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms , https://www.msregister.de/ms-register/veroeffentlichungen/berichte/)	252 000 (GMSR (https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms , https://www.msregister.de/ms-register/veroeffentlichungen/berichte/))	2 000	not interpretable	1/187

Abbreviations: DMSR: Danish multiple sclerosis registry, ECTRIMS: European Committee for Treatment and Research, GMSR: German multiple sclerosis registry, MS: multiple sclerosis

also rarely administered. In the Danish and German centres all DMTs were available (eTable3).

3.5. Patient number, prevalence estimates

Regarding number of pwMS, 99/101 centres from DSNS countries provided information. In these 99 centres 74 937 pwMS were receiving care. Additionally, a further 4 000 and 2 000 pwMS were reported from the Danish and German centres, respectively. In the countries where the participation rate was low, the difference between the “number of patients according to prevalence estimates” and the “number of patients reported by centres” was substantial. Thus, it should only be compared with caution. However, despite this shortcoming, this method still estimates the proportion of patients receiving adequate care and further reinforces the need for national registries. According to the measures described above only Austrian, and Czech data were congruent, where a national registry was available and regular data recording was mandatory. While in other countries, because of the lack, irregular or voluntary use of national registries, the lack of recent prevalence estimates, or low participation rate, results were discrepant. In Slovakia, where no MS prevalence data is available, no calculations were implemented. Furthermore, since only one-one German and Danish centres participated in the survey as reference, the “difference between estimated and actual number of patients” calculation was not implemented, since considering the lack of representativity, this measure would have not been interpretable (Table 4) (Kokas et al., 2022, Benjak et al., 2018, Salhofer-Polanyi et al., 2017, <https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms>, Kapica-Topczewska et al., 2018, Cornea et al., 2015, Pekmezovic et al., 2019).

3.6. Registry use

In Austria, the Czech Republic and Denmark, patient data recording in national MS or MS treatment registries was mandatory. Accordingly, all participating centres reported an up-to-date data entry (https://www.oegn.at/wp-content/uploads/2015/07/%C3%96GN-Kriterien_MSZentrum_18Februar2014.pdf, https://nfmimpuls.cz/images/docs/remus_zaverecne-zpravy/aj_zaverecna_zprava_2020_12_souhrnna_web.pdf, Magyari et al., 2021, Salhofer-Polanyi et al., 2017). In Germany, data entry was only mandatory for centres participating in the DMSG registry, covering a significant proportion but not the total population of pwMS. In most of the remaining DSNS countries, a national registry was not available, and data recording in regional or international registries was miscellaneous among centres. In Croatia, Hungary, Slovenia, and Serbia, 3/5, 7/29, 1/2, and 1/5 centres reported registry use, respectively. In Poland, Romania and Slovakia, a national registry was available, however, in these countries data entry was voluntary. Accordingly, 20/24, 11/15, and 4/9 centres reported voluntary participation in data recording, respectively (Berger et al., 2018, https://www.braincouncil.eu/wp-content/uploads/2020/06/ROMANIA_DEF_EBC_pp_03122019.pdf).

4. Discussion

In this nonconventional epidemiological survey, we investigated the real-world operation of MS centres in Central-Eastern European countries.

Our results reveal that the management of MS in DSNS member countries is pursued in centres by MS neurologists and specially trained MS nurses. Nevertheless, notable differences were established between countries according to distinct financial environments and health care systems. Moreover, within-country differences were observed corresponding to diverse institutional circumstances (university, county hospital, general hospital, or outpatient unit), though, the pattern of fulfilled and unfulfilled criteria was reasonably similar. Concerning minimum criteria, MS nurses, pharmacists, dietitians, were

homogeneously available, and the availability of a neuropsychologist was slightly heterogeneous among countries. On the other hand, the availability of an administrator, speech therapist, pain, continence, and spasticity specialist showed high heterogeneity, suggesting a persistent shortage of these specialties both nationally and internationally. While administrators are valuable in precise patient documentation and data recording in registries, taking of a load of MS specialists' shoulders, its availability might be solved by increasing the budget for human resources and hiring new employees. On the other hand resolving the availability of the latter four specialties are more complicated, yet are of particular importance, since these are essential in the management of people with a progressive disease course. Even though (active) PPMS and SPMS can be treated with DMTs that are available free of charge in the surveyed countries, the role of symptomatic treatment in the adequate management of progressive MS, especially in case of people with more advanced disease, is essential. Therefore, ensuring the availability of these professions is non-negotiable. As stated in the MSCU criteria, MS neurologists and MS nurses with appropriate training might sufficiently maintain the obligations of a pain, continence, and spasticity specialist, thus ensuring proper training can be a feasible solution to alleviate this issue (Soelberg Sorensen et al., 2019). Regarding recommended criteria a neuroradiologist, laboratory, internal medicine specialist, psychiatry and neurorehabilitation were homogeneously available, the availability of microbiology, electrophysiology, ophthalmology, surgeon, neurosurgeon, and obstetrician-gynaecologist was slightly heterogeneous. The availability of a neuro-ophthalmologist and an oto-neurologist showed high heterogeneity, also representing a persistent shortcoming nationally and internationally. A solution to this problem might be the establishment of a referral centre system, with close cooperation between centres; thus, in case of consultation with the specialties mentioned above is needed, pwMS can be referred to more highly specialized centres. The latter approach has been applied during the development of the Austrian and Czech MS centre systems (Soelberg Sorensen et al., 2019, https://www.oegn.at/wp-content/uploads/2015/07/%C3%96GN_Kriterien_MSZentrum_18Februar2014.pdf, https://nfimpuls.cz/images/docs/remus_zaverecne-zpravy/aj_zaverecna_zprava_2020_12_souhrnna_web.pdf). To obtain centre status, institutions need to fulfil predetermined requirements regarding instrumental, personnel, and professional background to adequately diagnose and treat pwMS according to the latest international guidelines. Moreover, regular quality control ensures that requirements remain fulfilled. Management of MS in these centres usually takes place in an ambulatory setting. However, inpatient care is guaranteed if needed. In case of unfulfilled conditions, close collaboration with nearby highly specialized centres is ensured to manage all MS-related necessities. Furthermore, MS neurologists and nurses regularly participate in training and centre meetings to remain up-to-date in the field of MS, and MS centre status is renewed at predetermined intervals. A similar approach is employed by the Danish and fostered by the German health care systems (Magyari et al., 2021, <https://www.dmsg.de/service/kli-niken-und-praxen/dmsg-ausgezeichnete-zentren>). In Germany the registry and MS centre qualification certificate is provided by the German MS Society. In Denmark MS specialists, the Ministry of Health Institutes (MoHIs), and HIFs work in close collaboration to create conditions to sufficiently provide multidisciplinary care for pwMS. Additionally, regular data entry and analysis of national MS and/or MS treatment registries enable quality control and further understanding and improvement of MS care. Therefore, these approaches can be considered exemplary for other countries.

Regarding DMT use, all DMTs were reimbursed, and most centres from 6/9 DSNS member countries, and the Danish and German reference centres ensured all therapeutic options. However, in Hungary, Poland, and Romania, a smaller proportion of centres were providing all DMTs. In Hungary approximately half of the centres used all available therapies, which might be explained by the fact that according to the MSCU criteria, the instrumental and personnel background to administer

HEDMTs and treat potential adverse events adequately, was not ensured in almost 2/3 of the centres (Kokas et al., 2022). In Romania, besides potential gaps concerning personnel and instrumental background, cladribine was not used at all at the time of data acquisition, as it was not yet approved by the Romanian National Agency of Medicines and Medical Devices. Furthermore, dimethyl-fumarate was rarely provided because of the limited experience with it, and alemtuzumab was also not widely administered. In Poland, 16/24 centres ensured all available DMTs, which might be attributable to the fact that only specialized MS centres provide full spectrum of DMTs within a state-funded treatment programme. In contrast, general MS centres offer first-line therapies solely, indicating that rather specialized than general MS centres partook in our assessment. Furthermore, while there was previously a time limit for treating MS with HEDMTs, this limitation has been abolished, thus, DMTs are currently prescribed according to their summary of product characteristics (Berger et al., 2018, Kapica-Topczewska et al., 2020). Nonetheless, strict regulations regarding switching first-line treatment to second-line options still exist, possibly restricting wider usage of HEDMTs (Kapica-Topczewska et al., 2020). Ultimately, as DMT reimbursement was provided in all participating countries, the inequalities among centres in DMT availability suggest that the next step in providing equality in access to adequate treatment and appropriate management of MS may lie in improving institutional and personnel background.

Doubtlessly, to sufficiently improve MS care, besides cooperation between MS specialists, HIFs, and MoHIs, adequate quality control is also essential to provide accurate data regarding the patient number and disease characteristics, including disease course, therapy adherence, and therapeutic effectiveness. This issue can be resolved by the establishment and regular use of national MS and/or MS treatment registries to monitor quality indicators (Magyari et al., 2021). The need for adequate data entry into national registries was also supported by our results. In total 74 937 pwMS received MS-specific care in 101 MS centres from nine DSNS member countries. However, when comparing patient numbers reported in our survey to patient numbers according to prevalence estimates country by country, only Austrian and Czech data were comparable (https://www.czech-neuro.cz/content/uploads/2020/04/rs_odborna-2.0_final_pub_web-2.pdf, Salhofer-Polanyi et al., 2017, <https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms>). Even though 40% of Czech centres did not participate in our survey, these centres supposedly are accountable for the observed difference between patient numbers reported by centres and patient numbers according to prevalence estimates. In Croatia, Poland and Romania, where some sort of databases were available, results were somewhat comparable. Nevertheless, the prevalence of MS might have changed in these countries since the latest prevalence estimates (Benjak et al., 2018, Cornea et al., 2015, Kapica-Topczewska et al., 2018). In Slovenia, prevalence estimates can be considered outdated as well. Thus, even though patient numbers reported by centres and patient numbers according to prevalence estimates might seem commensurable, the reliability of this comparison is questionable (Peterlin et al., 2006). Whereas in Slovakia, no prevalence estimates were available. In Hungary, two prevalence studies with distinct methodologies were conducted in the past two years, resulting in significantly different prevalence estimates (Kokas et al., 2022). These examples further underline the importance of the using an up-to-date registry, both from a financial quality control and an epidemiological point of view.

There are strengths of this survey. Ours is the first international study assessing the operation of MS centres covering a large region with so far limited information regarding MS care. These baseline data show current advantages and shortcomings in different countries' MS care systems. We identified several factors that should and could be improved and have shown possible examples to follow in order to achieve better care. By dissecting these data, MS care systems, MoHIs and neurologist of participating countries or even worldwide might consider adopting or adapting to some of the above detailed schemes. Furthermore, this

assessment can be considered a baseline for future surveys inspecting MS care. By reproducing this assessment in subsequent times by employing the same participants, we can determine whether and what advancements were implemented. Moreover, further countries located in other regions might also find the method of this investigation helpful in assessing the real-world operation of MS centres.

Undoubtedly, however, this study has limitations as well. The use of self-report questionnaires might have possibly resulted in reporting bias; however, this bias may have been reduced by the comprehensive research regarding each country's health care background. Moreover, because of the longevity of data acquisition, some data reported in the questionnaires might have become somewhat outdated.

5. Conclusion

In conclusion, it is in the MS specialists' and pwMS' best interests to remodel MS care in line with each country's economic and health care system. Instrumental and personnel background to diagnose and treat MS should be available in any country's MS centres, with 100% price subsidy for DMTs to ensure equality in access to treatment. However, the term "multiple sclerosis care unit" can be interpreted as a separate organizational unit, a separate entity, implying that a centre should fulfil the minimum and recommended criteria independently. However, it might also be interpreted that even though a centre is independent of the general neurology department, it is physically embedded in the institution with various departments available. Thus, neighbouring specialties are accessible if needed, ensuring adequate multidisciplinary care. The former approach might be difficult for many centres to fulfil. The latter, on the other hand, as the Austrian and Czech examples represent, might be a feasible solution for adequate MS care. As detailed in this paper, in these countries diagnostic, therapeutic and personnel conditions are completely ensured, just like in other Western-European countries' health care systems, thus are great examples to follow. Nevertheless, to accomplish similar conditions and truly amend the quality of MS care, close cooperation between MS specialists, Health Insurance Funds and Ministry of Health Institutes and regular quality control using national registries are fundamental.

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Data availability statement

All relevant data are included in the paper and its supporting information.

CRediT authorship contribution statement

Zsófia Kokas: Methodology, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Visualization. **Anett Járdánházy:** Methodology, Investigation, Resources, Data curation, Writing – original draft. **Dániel Sandi:** Resources, Data curation, Writing – original draft. **Tamás Biernacki:** Resources, Data curation, Writing – original draft. **Zsanett Friczka-Nagy:** Resources, Writing – review & editing. **Judit Füvesi:** Resources, Writing – review & editing. **Halina Bartosik-Psujek:** Resources, Writing – review & editing. **Vanja Basic Kes:** Resources, Writing – review & editing. **Thomas Berger:** Resources, Writing – review & editing. **Achim Berthele:** Resources, Writing – review & editing. **Jelena Drulovic:** Resources, Writing – review & editing. **Bernhard Hemmer:** Resources, Writing – review & editing. **Dana Horakova:** Resources, Writing – review & editing. **Alenka Horvat Ledinek:** Resources, Writing – review & editing. **Eva Kubala Havrdova:** Resources, Writing – review & editing. **Melinda Magyari:** Resources, Writing – review & editing. **Konrad Rejdak:**

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The authors declare that no conflicting interests exist.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.msard.2022.104406](https://doi.org/10.1016/j.msard.2022.104406).

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