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Quality assurance criteria of Multiple Sclerosis patient management in Hungary and Central-Eastern European countries

Ph.D. Thesis

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I.) Kokas Z, Sandi D, Fricska-Nagy Z, Füvesi J, Biernacki T, Köves Á, Fazekas F, Birkás AJ, Katona G, Kovács K, Milanovich D, Dobos E, Kapás I, Jakab G, Csépány T, Bense E, Mátyás K, Rum G, Szolnoki Z, Deme I, Jobbágy Z, Kriston D, Gerócs Z, Diószeghy P, Bors L, Varga A, Kerényi L, Molnár G, Kristóf P, Nagy ZÁ, Sátori M, Imre P, Péntek S, Klivényi P, Kincses ZT, Vécsei L, Bencsik K. Do Hungarian multiple sclerosis care units fulfil international criteria? *PLoS One*. 2022 Mar 3;17(3):e0264328. doi: 10.1371/journal.pone.0264328.

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I. Introduction

Multiple Sclerosis (MS) is an autoimmune, inflammatory, demyelinating, neurodegenerative disorder of the central nervous system (CNS). Besides its well-known physical disability causing nature and lifespan-shortening effect, it may also cause psychopathological symptoms and have a negative impact on quality of life. With continuous research of recent years, our knowledge on MS constantly evolved. The invention of imaging techniques made diagnostic processes accelerated with higher specificity and sensitivity. Now patients can be diagnosed when they experience their first neurological symptoms. Disease course classification also went through several transformations. Today, MS can be distinguished into two main categories: relapsing-remitting and progressive MS. Within these groups, according to disease activity or progression and therapeutic status individuals can be classified into further 4-4 subcategories. However, even though this can be considered sophisticated, due to the ever-evolving knowledge on the underlying patomechanism of MS and the ongoing paradigm shift regarding its dichotomy, future modifications are inevitable. Treatment options have also demonstrated a major expansion. The first disease modifying therapy (DMT), interferon-β was introduced almost 30 years ago. Nowadays, over 15 moderately and highly effective DMTs are available. With this therapeutic arsenal, all courses of the disease can be treated. Thus, today the clinicians' main objective is not only to preserve physical and cognitive abilities, but also to maintain quality of life. Considering the above-mentioned, it is not surprising that general practitioners and general neurologists cannot keep up with frequently evolving advancements in the field of MS. Nowadays, it is increasingly recognized that a multidisciplinary approach is necessary to ensure equal access to care and adequate treatment for people living with MS. In 2018 the international therapeutic guideline disclosed that DMTs should only be administered in specialized MS centres. Then, in 2019 the MS care unit criteria, describing the personnel and instrumental conditions of a multidisciplinary MS centre was published. However, there was limited information regarding the conditions of already existing MS centres and whether they fulfil international criteria.

II. Objectives

To assess whether MS centres in Hungary and in Central-Eastern European countries partaking in the Danube Symposium for Neurological Sciences (DSNS), fulfil international recommendation on MS care. To gather information on DMT and registry use in Hungary and internationally. To collect data on actual patient number receiving care in Hungary and internationally, and to compare to estimated patient number, to determine if equality in access to care is ensured.

III. Methods

Our assessments were conducted at the Department of Neurology University of Szeged, Albert Szent-Györgyi Health Centre, Szeged, Hungary.

Descriptive statistics were used to analyse data.

III.1. Do Hungarian multiple sclerosis care units fulfil international criteria?

A self-reported questionnaire surveying personnel and infrastructural criteria of MS care units, according to international recommendations, was assembled and sent to Hungarian MS centres. The questionnaire consisted of 3 main parts, of which the first focused on patient number.

The second portion surveyed 22 aspects of the MS care unit recommendation. While the third section assessed DMT and registry use. On DMT use additional National Health Insurance Fund (NHIF) data were also collected.

III.2. Real-world operation of multiple sclerosis centres in Central-Eastern European countries covering 107 million inhabitants

The questionnaire, used in the Hungarian study was translated to English and sent to further 8 DSNS member countries' MS centres. Moreover, one Danish and one German centre were asked to participate as reference centres. Regarding fulfilment of MSCU criteria, a definition of homogeneity and heterogeneity was created using quartile percentiles. Information on management of MS, DMT reimbursement and prevalence estimates were collected parallelly.

IV. Results

IV.1. Do Hungarian multiple sclerosis care units fulfil international criteria?

IV.1.a. Participation rate

In our survey 29/31 (94%) Hungarian MS centres participated, which is considered representative.

IV.1.b. Personnel and instrumental background of MS care units

An MS nurse was employed by 26/29 centres, while 21/29 centres employed an administrator. Regarding spasticity (13/29), pain specialist (15/29), neuro-ophthalmologist (15/29), oto-neurologist (15/29), neuropsychologist (19/29), and speech therapist (21/29) greater shortcomings were reported. In total 3/29 centres fulfilled both minimum and recommended criteria, while further 7 care units provided all aspects of recommended criteria only.

IV.1.c. DMT use in MS care units

Low efficacy DMTs were used in all centres. However, only 20/29 care units ensured every highly effective DMT and only 15/29 centres provided every treatment option.

IV.1.d. Proportion of moderately and highly effective DMT use

NHIF data of December 2020 showed that 4 665 persons received MS specific treatment. Of these people 3131 (67.12%) used low efficacy DMT, of which 1 360 persons (43.44%) were injectable therapy users, and 1 771 patients (56.56%) were on oral agents. The rest, i.e. 1 534 people (32.88%) were on highly effective DMTs, of which 810 persons (52.80%) used oral medication, and 724 patients (47.20%) received infusions.

IV.1.e. Patient number receiving care in MS care units

In 27/29 facilities 7 213 people received MS specific care. In 8 centres 3 876 persons (53.74%) received care, (range 400-950/ centre), while 10 facilities cared for 2 483 people (34.42%) (range 196-348/ centre), and 9 hospitals cared for 854 individuals (11.84%) (range 40-150/ centre).

IV.2. Real-world operation of multiple sclerosis centres in Central-Eastern European countries covering 107 million inhabitants

IV.2.a Participation rate

From 9 DSNS countries, we received 101 questionnaires, plus 1-1 Danish and German reference surveys. In Austria (3/3), Romania (15/15) and Serbia (5/5) participation rate was 100%, while in Hungary, Slovakia, Slovenia, the Czech Republic, Croatia and Poland it reached 94% (29/31), 90% (9/10), 67% (2/3) and 60% (9/15), 50% (5/10), and 19% (24/129) respectively.

IV.2.b. Management of multiple sclerosis and disease-modifying therapy reimbursement in participating countries

Medical care of people with MS was pursued in specialized MS centres in all participating countries and every DMT was reimbursed by NHIFs. In Austria, the Czecz Republic, Denmark and Germany a well-defined centre system ensured medical care for people with MS.

IV.2.c. Multiple sclerosis care unit criteria

In Austria 3/3 centres fulfilled both the minimum and recommended criteria. In Croatia, 1/5 centre ensured both the minimum and recommended conditions, while 2/5 care units fulfilled only recommended criteria. In the Czech Republic 5/9 institutes fulfilled both minimum and recommended conditions, and 1/9 centre ensured only minimum criteria. In Hungary 3/29 hospitals fulfilled both minimum and recommended conditions, and 7/29 ensured only recommended criteria. In Poland 2/24 fulfilled both minimum and recommended conditions, 2/24 provided only minimum, while 5/25 facilities ensured only recommended criteria. In Romania 1/15 centre fulfilled only recommended criteria. In Serbia 1/5 fulfilled both minimum and recommended conditions, while 2/5 care units ensured only recommended criteria. In Slovakia 3/9 centres fulfilled only recommended criteria. In Slovenia

0/2 care units fulfilled every aspect of the minimum or the recommended conditions. In the 1-1 Danish and German reference centres both minimum and recommended criteria were fulfilled. Overall, in 4/9 DSNS countries most criteria were homogenously available. In the rest of the nations, care units provided more heterogenous availability of conditions. MS nurse, pharmacist, dietitian, neuroradiologist, laboratory, internal medicine specialist, psychiatry, and neurorehabilitation availability was quite homogenous. Whilst the availability of the rest of the criteria showed slight to high heterogeneity.

IV.2.d. DMT use

All DMTs were used in all Austrian, Slovenian and Slovakian care units. In Croatia, the Czech Republic and Serbia apart from 1-1 centre, all DMTs were provided. In Hungary and Poland 15/29 and 16/24 centres ensured every DMT respectively. In Romania DMT availability was heterogenous. The Danish and German reference centres provided all available DMTs.

IV.2.e. Patient number, prevalence estimates

In 99/101 respondent care units a total of 74 937 patients received care. When comparing reported and estimated patient number, only Austrian and Czech result were congruent, where registry use was mandatory. Whereas results in other countries were discrepant, which could be explained by low participation rates, and the lack of either mandatory registry use or up-to-date prevalence data.

IV.2.f. Registry use

National registry use was mandatory in Austria, the Czech Republic, Denmark and Germany, while it was voluntary in Poland, Romania and Slovakia. In Croatia, Hungary, Slovenia, and Serbia a national registry was not available, yet some centres recorded data in regional or international registries on a voluntary basis.

V. Discussion and Conclusion

V.1. Do Hungarian multiple sclerosis care units fulfil international criteria?

Recently, the standardization of MS care became a topic of conversation. Since the publication of the MS care unit criteria there was no study that examined the real-world operation of already existing MS centres, thus we focused on this aspect. Firstly, we discovered that in Hungary only 3 centres ensured both minimum and recommended criteria, and 7 care units fulfilled recommended conditions only, suggesting there is room for improvement. Most commonly unfulfilled criteria were spasticity and pain specialist, neuro-ophthalmologist and oto-neurologist. To provide these specialties, it would be reasonable to assign regional, fully equipped centres ensuring consultation for facilities with less fortunate background. Or since greater centres are more equipped, it might be sensible to merge smaller units into larger ones. Secondly regarding DMT use, we found that even though in Hungary MS specific treatments are funded by the NHIF, only half of the care units provided the entire spectrum of therapies. Mainly highly effective infusions were not ensured. Since infusion therapies might pose a higher risk of serious adverse events, smaller, less-developed centres might not be able to address them properly, explaining this phenomenon. NHIF data also proved that only two-thirds of Hungarian patients received DMTs, of which two thirds used low-efficacy therapies, and one-third was on highly effective treatment. Compared to international literature on proportional distribution of disease activity, this implies that one-third of Hungarian patients might not receive adequate treatment. Thirdly, regarding patient number we discovered that in 27 centres 7 213 individuals receive medical care. This number falls 2 500 people short when compared prevalence estimates. One explanation might be late or inadequate diagnosis of progressive disease course, which might be amended by education of general practitioners and neighbouring specialties. Also, progressive patients experiencing spasticity, incontinence and chronic pain, with higher level of disability might not attend doctors' appointments, as lot of centres lack personnel background to adequately treat these symptoms. In conclusion our survey suggests, that to provide equality in access to care, and to ensure adequate treatment for people with MS, over half of the Hungarian MS centres should improve personnel circumstances and DMT availability. To reach these goals, well-developed patient pathways and a centre system with regular quality control ensured by consistent registry use are also necessary.

V.2. Real-world operation of multiple sclerosis centres in Central-Eastern European countries covering 107 million inhabitants

After the Hungarian MSCU assessment, we aimed to extend our survey to a larger region to gain a more comprehensive overview on MS care. Firstly, we discovered that MS care in DSNS member countries takes place in specialized care units with MS neurologists and MS nurses in charge. Yet, due to diverse financial and health care backgrounds, and different institutional circumstances disparities were discovered both on an international and a national level. Regarding minimum criteria, the availability of neuropsychologists, administrators, speech therapists, pain, spasticity and continence specialists showed slight to high heterogeneity, while the rest of the conditions were homogenously fulfilled in over half of the countries. As proposed in the MSCU recommendation, with further education, MS specialists and MS nurses could provide the role of a pain, spasticity or incontinence specialist, thus resolving equality in access to care. Concerning recommended conditions, slight to high heterogeneity was discovered in the availability of microbiology, electrophysiology, ophthalmology, surgeon, neurosurgeon, obstetrician-gynaecologist, neuro-ophthalmologist and an oto-neurologist. To concur this issue, similarly to the Austrian, Czech, Danish and German example, foundation of a referral centre network should be considered. Secondly, regarding DMT use we found that MS specific treatment was reimbursed in all countries. However, only in two-thirds of the nations did most centres provide the entire spectrum of DMTs, which might be attributed to missing personnel and instrumental criteria of care units. Thirdly, regrading patient number and registry use we discovered that only in countries where registry use was mandatory, was reported patient number comparable with prevalence estimates.

In conclusion our results reinforce the need for adaptation of the international MS care unit criteria considering economic and health care differences among countries. An MS centre system similar to the Austrian and Czech examples, where institutions with less fortunate background closely collaborate with more developed centres, enabling consultation with the rarest specialties, might amend MS management. Furthermore, in order to sufficiently improve MS care, MS specialists, Health Insurance Funds and Ministry of Health Institute should closely cooperate, and regular, registry-based quality control should be ensured.