

Review Article

Lessons Learned from the Population-Based Multiple Sclerosis Registries in the Developed Countries

Farkhondeh Asadi , Hassan Emami, Hamid Moghaddasi, Sara Ghalane

Shahid Beheshti University of Medical Sciences, School of Allied Medical Sciences, Tehran, Iran

Article Information

Received:2019-10-09

Revised:2019-11-02

Accepted:2019-11-03

Correspondence

Farkhondeh Asadi

Email: asadifar@sbmu.ac.ir

Cite this article as:

Asadi F, Emami H, Moghaddasi H, Ghalane S. Lessons Learned from the Population-Based Multiple Sclerosis Registries in the Developed Countries. Archives of Advances in Biosciences 2020:11(1)

Abstract

Context: The prevalence of Multiple Sclerosis (MS) in the world has grown and has attracted particular attention on the international level and governments, has considered prevention interventions and managing the symptoms of the disease to reduce the economic burden and has improved the quality of life of these patients necessary. One of the most important strategies in this field is MS population-based registry. Accordingly, this study was designed to identify the components of MS population-based registries within the developed countries.

Evidence Acquisition: The present study is a review article that was conducted in 2018. The population of the study consisted of MS population-based registry systems of developed countries such as USA, France, and Denmark. Based on the combination of related keywords, about 60 papers appropriately and after extraction, categorization and integration were formulated in the form of proper sequence for the purpose of the study.

Results: The main components of MS population-based registries in developed countries included registry goals, information resources, Minimum Data Sets (MDS), types of processes, types of reports, quality control measures, data transmission time limits, responsible for recording and collecting data, responsible organization and executor, data transmission method and the privacy practices

Conclusion: With regard to the results, it is suggested that the developing countries must consider creating an MS population-based registry as a national program due to their health system and the MS population-based registries structure in developed countries, so that they can adopt a suitable strategy for preventing and controlling the disease.

Keywords: Multiple Sclerosis (MS), Population-based registry, Registry

1. Context

Multiple sclerosis (MS) is one of the human's chronic neurological diseases; it is among one of the most common reported diseases, leading to disability in young adults, which appears by formation of multiple small and large plaques in the white matter of the brain and spinal cord [1-3].

Across the world, the prevalence of this disease has grown increasingly, and there

has been a special attention toward MS at the international level [4]. The prevalence of this disease among women is 1.77 compared with men [3] and the most prevalence are between the ages of 20 to 40 years [5, 6]. It has multiple complications such as visual problems, anal sphincter dysfunction, speech disorders, epilepsy, and depression [7-9]. Consequently, MS reduces the life expectancy up to between 8 to 10 years [7].

People with debilitating and chronic MS disease encounter many challenges such as physical, psychological, social and economic ones that limit their participation in health promotion activities and thus increase further complications, cause more limitations in their daily activities and also reduce their quality of life [10].

Therefore, MS imposes a lot of economic burden to patients, the society and the healthcare system [10]; therefore, the governments all over the world must pay attention to preventing of interventions and symptom management as to improve the patient's quality of life [11]. Achievement of prevention goals, screening and disease control programs in the healthcare system is possible through complete and timely data collections of MS. There are many strategies for disease prevention and control, among which one of the most important is the disease registry [12]. Registries could provide complete, accurate, and high-quality data [13] and have been established for different health problems and diseases with different purposes [14, 15], designed in two types, including hospital-based registries and population-based registries [16]. The population-based registry is an organized process for collecting, recording, retrieving, and using information from patients who have a particular disease and live in a specific geographical area [12, 17, 18]. The use of these registries in the healthcare systems has led to many improvements in various areas, including providing services and patient care [19]. The MS population-based registry is beneficial in terms of managing and controlling the symptoms of a large population with MS disease, monitoring the outbreak and prevalence of the disease, providing effective information on the safety and efficacy of MS treatment and drugs [20, 21], providing an important guidance to the decision making of both clinical and socioeconomic groups, and help to better understanding of the disease

process, quality of life, mortality, and complications of MS [22].

The existence of this type of registry facilitates the sampling methods in clinical trials across the country, and consequently reduces cost and time [23]. In addition, it has an effective role in improving the quality of healthcare [20, 21], and some useful information can be provided in terms of age, gender, and the geographical distribution of MS patients [24]. Therefore, considering the benefits and goals, designing population-based MS registry is of utmost importance.

Given the fact that the United States and European countries, including France, Denmark, and so forth have been pioneer in establishing the population-based MS registry, and have made a significant progress in developing this system, the present study aimed to introduce the instructions and experiences of the MS population registry in these developed countries for the use within developing countries.

2. Evidence Acquisition

In this review article, the population-based MS registries of the US, France and Denmark were reviewed. These countries were selected due to their leading role in the population-based registries. Related articles were extracted from databases including PubMed, Google Scholar, Springer, Science Direct and Wiley, with the following key keywords or a combination of them: multiple sclerosis; registry; population registry; multiple sclerosis population-based registry.

After a comprehensive search that was done based on the keywords, 110 articles were identified in 1998 to 2016. After the first review, 60 articles were considered based on the study objectives. To be included the articles in this review, studies were required to be related to the study purpose. The articles were carefully considered, and after extracting information, they were

categorized and integrated in the appropriate sequences to meet the needs of this study.

3. Results

There are different titles for the multiple sclerosis population-based registries in the developed countries. Most of the registries collect the main demographic data, the period of disease, disability, medication, hospitalization, and test results. They are, however, different in goals, content, data structure, data architecture, time, and the used resources [6, 25]. Each country's system, and state the systems similarities and differences in each country is described as follows.

3.1 The Multiple Sclerosis Population-Based Registry in the US

The US MS population-based registry is NARCOMS (The North American Research Committee on Multiple Sclerosis), which was created by the Consortium of Multiple Sclerosis Centers (CMSC) in 1993, for the purpose of developing patient-based MS registry and facilitating involvement of researchers from participating centers of MS treatment and research community [26, 27].

NARCOMS is a global registry system for research on MS, treatment and patient education [23]. The secret of NARCOMS' is its updated data which is obtained through collaborating and supporting of a number of organizations including the Multiple Sclerosis Consortium, the National Multiple Sclerosis Society (NMSS), the Paralyzed Veterans of America (PVA), and the Eastern Paralyzed Veteran's Association (EPVA) [5].

The registry data includes demographic and clinical data [26, 28]. Statistical analysis of the data was done by the official review committee of the registry, at the University of Alabama. The conducted results from this registry is usually published in scholarly journals and shared with

participants through NARCOMS quarterly journal [5].

Therefore, NARCOMS is one of the largest voluntary registry systems in the world, which provides extensive studies in the areas of MS research field [5].

3.2 EUREMS: European Registry for Multiple Sclerosis

The European MS registry is a central data source of various aspects of MS. The four key areas of this registry include epidemiology, the result of long-term treatment, healthcare issues and quality of life [29].

Currently, many European countries use the national registry of MS and other databases, including the Danish Multiple Sclerosis Registry (DMSR) and the European Database Multiple Scleroses (EDMUS).

3.3 The MS Database in France

EDMUS is a widespread clinical database at the French MS centers that has been available since 1992 [25]. The database is organized by the European Union and supported by the international associations. EDMUS provides a brief descriptive record for research purposes, as well as assessment, quality assurance, classification, and preserving confidentiality of the data [30]. The EDMUS registry developer, developed a software with the same name to collect data from medical centers and management of MS patient records. This is a web based registry software, that is accessible through internet, and its ability to send data to international registries make it easier to perform [29].

In fact, EDMUS is a descriptive registry with a necessary minimum data set, which is used for research purposes in clinical and laboratory data documents among patients with multiple sclerosis [25]. The data that entered the international registry through EDMUS are included in the 10 main categories [29].

In this system, many considerations have been taken to preserve confidentiality of the

data, and to access the software and files, with specific passwords defined for different levels [25]. It is worth mentioning that it can be shared on the network and used as a multi-user software. The data is also searchable based on different criteria in the database, and could be cleaned to detect or correct incomplete, inconsistent and incorrect data [31].

Therefore, EDMUS is a powerful database for registering MS patients in Europe with the aim of medical treatment and scientific research [25].

3.4 The Population Registry of Multiple Sclerosis in Denmark

In Denmark, there are two population-based MS registries. The older one is the DMSR (the Danish Multiple Sclerosis Registry), an epidemiological registry for estimating MS incidence and prevalence, patients' survival, and identifying high-risk cases. This registry does not provide a systematic follow up for patients [32].

The DMSR was officially established in 1956, but data collection began from 1948. Initially, the American MS association was in charge of it, and later, the MS association of Denmark [20, 33].

The diagnostic criteria, until 1994, were based on Allison and Millar (a set of clinical criteria for the diagnosis of MS). From 1994, the diagnostic criteria were those of Poser, and McDowell criteria have been considered for diagnosis since 2005 [32, 34].

According to the regulations and rules of the data inspection office and in accordance with certain exceptions to the data security and privacy laws, there is no need for informed consent from the patient, provided that the data are stored in accordance with the confidentiality rules, and the data, with or without indicating the individual's identity can never be used for any other purposes of pure science [32].

Other Danish MS registry was Danish MS treatment registry that was established in 1996, sponsored and developed by the Danish safety association. In practice, this is a registry for following all MS patients who received health care services since 1996, and are followed every six months by neurological and reliable laboratory tests [32].

The data reported to the MS registry include primary clinical information and follow-up, recurrence of disease, disability status, MRI results, disease progression and side effects during treatment [32]. These data are stored on-line from all sites into a central database. The registry imports the collected data to the DMSR. The criteria for importing data are the same criteria for treatment (currently McDonald) that are evaluated by three neurologists [32, 34].

Finally, the reports from the research, such as the relationship between MS and genetics, the environment, age, sex, pregnancy complications, and other factors are presented for therapeutic analyses, identifying and controlling the high-risk cases, as well as identifying the prevalence rate by sex [32].

Based on the above-mentioned statements, the main components of the MS population-based registries in the United States, France and Denmark are shown in Table 1.

Table 1. the main components of the MS population register

Component/countries	Denmark	France	America
The registry goals	treatment and education of MS patients Medical research	treatment and education of MS patients Medical research	treatment and education of MS patients, Medical research
Data resources	Rehabilitation and neurological departments in hospitals, General practitioners, Central disability insurance court, Neurological centers, Doctors specializing in MS neurology, MS association	Hospital-based registries Medical centers MS association MS research centers	Patients' self-report data
Data elements	Demographic data (age, sex, place of living, etc.), and Clinical data (age of onset of symptoms, age of diagnosis, diagnostic criteria, information of the patient's family, injury or disability status, treatments, relapse date, disability status, MRI outcome and side effects during treatment)	Personal data, history, diagnosis, nervous events, irreversible disabilities, medical evaluations, paraclinical evaluations, treatments, summary, and chart	Demographic data (age, sex, race, etc.), and Clinical data (age of onset of symptoms, age of diagnosis, relapse date, etc.)
Types of data processing	Data processing using descriptive statistics such as mean and logistic regression to calculate odds ratio	Data processing using descriptive statistics Classification (encoding) data related to care and treatment and ECGPMS	Calculation of correlation coefficient (correlation evaluation and the relation between registry variables), Calculation of Bland-Altman plot (to analyze the agreement between two parameters, for example, comparing two clinical measures to evaluate care patterns)
Report types	The reports from the research, such as: prevalence rate, the relationship between MS and genetics, age, sex, and pregnancy complications, report of high-risk cases, prevalence rate among women, and men in the society	Providing reports based on the doctors need for medical analyses, such as: results of treatments, and a variety of disabilities in MS patients	The reports from the research, such as: prevalence rate, the relationship between MS and genetics, age of onset of symptoms, age of diagnosis
Data quality criteria	The entry of duplicate record is prevented by ID, and the data are evaluated by 3 neurologists	EDMUS software classified the data automatically, and the data is also searchable based on different criteria in the database, and could be cleaned to detect or correct incomplete, inconsistent and incorrect data	through the questionnaire and the NARCOMS form prevents the entry of unnecessary, incorrect, and inconsistent data
Follow-up patients	Through link to other registries, including Danish registry office, follow-up patients in the Danish MS registry is done via ID (Identification Number), Active and inactive follow-up	Active and inactive follow-up by neurologists	Communication and follow-up patients via email; for those who are not responsive to their emails through telephone number Active and inactive follow-up
The time interval for sending data	Every 6 months	At least once a year	Every 6 months
The responsible and executer organization	The Denmark MS association	A coordinated European action committee under the auspices of the European Union	With collaboration and support of CMSC, NMSS, PVA, EPVA
The person who is responsible for recording and collecting data in the registry	Neurologists	Neurologists	patients
Sending data method	Online and complete the questionnaire form	Online and complete the questionnaire form	Online and complete the questionnaire form
Confidentiality and privacy methods	Regulate data disclosure policies Assign unique identity to each patient, Assign password for providing information, Regulate data protection policies, Prohibition of using the data for other purposes	Regulate data disclosure policies Assign unique identity to each patient, Assign password for providing information	Regulate data disclosure policies Assign unique identity to each patient, Assign password for providing information

4. Conclusion

The review of population-based MS registries in selected countries demonstrates that MS is considered as a significant national health status.

Henricksen, in a study entitled "Using the MS registry in epidemiological studies", introduced the role of Danish MS registry, and stated that using it in exploring the risk factors for MS outbreak and prevalence population-based MS registry is an effective tool for epidemiological studies of the disease [20]. In another study, entitled "Evaluation of usability and limitations of the Danish MS registry", done by Mason et.al, the importance of accuracy and precision of MS registry data sources was reviewed, due to its widespread use in research [35]. In 2015, Mayer et.al conducted a study entitled "Biobank and the Norwegian MS registry" to investigate MS risk factors. In this regard, he used MS registry and MS Bio-Bank for systematic collection of clinical and epidemiological data and biological samples [36].

The study of population-based MS registries in different countries, including the United States, France and Denmark, showed that these countries have designed their registries based on their healthcare system. Improving the quality of patient care, identifying the risk factors, monitoring the disease outbreak and prevalence and comprehensive guide to disease management are the most important goals of population-based MS registries within the selected countries. The NARCOMS registry is a patient-based registry, while the EDMUS and DMSR are physician-based registries.

The study of the data resources in France and Denmark showed that hospitals, neurological centers, general practitioners, neurologists and MS associations are the main data sources for the population-based MS registry across the most of the developed countries. In the United States, however, the population-based registry relies on patients' self-reported data.

Another feature of the registry is the minimum data set (MDS), which is used to monitor the disease outbreak and prevalence, develop educational programs, and assess high-risk areas. In fact, most of global advanced registries and data collection facilitate reaching to these goals. In the population-based registries of the selected countries, the data included demographic and clinical data.

The results of the study showed that in three selected countries, the reports are based on the need of physicians, other authorized individuals and organizations as to conduct medical analyses and to guide clinical and socio-economic groups.

In the United States, data quality control is carried out through the questionnaire by using the NARCOMS form, which prevents the entry of unnecessary, incorrect, and inconsistent data. The entry of duplicate record is prevented in France through the EDMUS software and in Denmark through link to other registries, including Danish registry office, and using the identification numbers. Patient follow-up was done in all three countries. In DMSR registry, the patients follow up data is not recorded with regard to this point, and the clinical follow up is impossible for all patients. In the reviewed countries, data are recorded based on the confidentiality rules. In the United States and France, collecting information from patients can be done through obtaining informed consent, but in Denmark, there is no need for informed consent, provided that the data is stored and retrieved in accordance with the confidentiality rules.

The study of population-based MS registry in progressed countries showed that this registry can be used as a useful tool for physicians to provide high-quality care, for patients to promote self-care, and for authorities to monitor the disease outbreak and prevalence. Therefore, developing countries, according to their healthcare system should consider establishing population-based MS registry as a national program, and through its implementation

and maintenance, adopt an appropriate strategy for controlling and preventing MS. In addition, the designing and developing of a registry needs providing appropriate infrastructure, equipment, deployment location, and appointing the MS registry executive officers. Considering these features would help developing countries to establish population-based MS registry, and also prevent possible problems.

Acknowledgment

The present study was part of the MSc thesis done by Sara Ghalaneh and was supported by Shahid Beheshti University of Medical Sciences.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Studney DR, Lubin FD, Marcucci L. MS COSTAR: A PC based medical information system to support and pool data among multiple sclerosis clinics. In Proceedings of the Annual Symposium on Computer Application in Medical Care 1989 Nov 8 (p. 943). American Medical Informatics Association.
2. Fox CM, Bensa S, Bray I, Zajicek JP. The epidemiology of multiple sclerosis in Devon: a comparison of the new and old classification criteria. *Journal of Neurology, Neurosurgery & Psychiatry*. 2004 Jan 1;75(1):56-60.
3. Motamed M, Fereshte Nejad SM, Panah K. The comparison of sex hormones and interferon's impacts on the number of relapses and the progression of disability in relapsing-remitting multiple sclerosis (RRMS). *Razi Journal of Medical Sciences*. 2007 Nov 15;14(56):157-64.
4. Browne P, Chandraratna D, Angood C, Tremlett H, Baker C, Taylor BV, Thompson AJ. Atlas of multiple sclerosis 2013: a growing global problem with widespread inequity. *Neurology*. 2014 Sep 9;83(11):1022-4.
5. Marrie RA. The influence of comorbid diseases and health behaviors on clinical characteristics, disability at diagnosis, and disability progression in multiple sclerosis (Doctoral dissertation, Case Western Reserve University).
6. Pugliatti M, Eskic D, Mikolcić T, Pitschnau-Michel D, Myhr KM, Sastre-Garriga J, et al. Assess, compare and enhance the status of Persons with Multiple Sclerosis (MS) in Europe: a European Register for MS. *Acta Neurologica Scandinavica*. 2012 Dec;126:24-30.
7. Weinshenker BG, Bass B, Rice GP, Noseworthy J, Carriere W, Baskerville J, Ebers GC. The natural history of multiple sclerosis: a geographically based study: I. Clinical course and disability. *Brain*. 1989 Feb 1;112(1):133-46.
8. Fry DK, Huang M, Rodda BJ. Core muscle strength and endurance measures in ambulatory persons with multiple sclerosis: validity and reliability. *International Journal of Rehabilitation Research*. 2015 Sep 1;38(3):206-12.
9. Reding MJ, LaRocca N, Madonna M. Acute-hospital care versus rehabilitation hospitalization for management of nonemergent complications in multiple sclerosis. *Journal of Neurologic Rehabilitation*. 1987 Mar;1(1):13-7.
10. Noroozi F. Mediating role of cognitive-emotional ordering strategies in relation to attachment styles and quality of life in patients with multiple sclerosis. *SSU_Journals*. 2018 Aug 15;26(5):410-25.
11. Haresabadi M, Karimi Monaghi H, Froghipor M, Mazlom SR. Quality of life in patients with multiple sclerosis referring to Ghaem hospital, Mashhad in 2009. *Journal of North Khorasan University of Medical Sciences*. 2011 Mar 15;2(4):7-12.
12. Metzger J. Using computerized registries in chronic disease care. *California HealthCare Foundation*; 2004.
13. Asadi F, Paydar S. Presenting an evaluation model of the trauma registry software. *International journal of medical informatics*. 2018 Apr 1;112:99-103.
14. Samadbeik M, Garavand A, Saremian M, Baraei Z, Adeli M. Readiness of Patients with Chronic Diseases to Use Health Information Technology: An Experience of a Developing Country. *Shiraz E-Medical Journal*. 2018 Oct;19(10).
15. Garavand A, Samadbeik M, Kafashi M, Abhari S. The identification and classification of deployment challenges related to electronic health records: A review article. *Shiraz E-Medical Journal*. 2016 Feb 1;17(2).

16. Asadi F, Mirshekarlou SJ, Rahimi F. A Comparative Study of the National Infertility Registry System and The Proposed Model for Iran. *Crescent Journal of Medical and Biological Sciences*.;5(4).
17. Lana-Peixoto MA, Talim LE, Faria-Campos AC, Campos SV, Rocha CF, Hanke LA, Talim N, Batista PH, Araujo CR, Kleinpaul R. Nmo-dbr: the brazilian neuromyelitis optica database system. *Arquivos de neuro-psiquiatria*. 2011 Aug;69(4):687-92.
18. Ajami S, Ahmadi G, Etemadifar M. The role of information system in multiple sclerosis management. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*. 2014 Dec;19(12):1175.
19. Moghaddasi H, Asadi F, Rabiei R, Rahimi F, Shahbodaghi R. Presenting an Evaluation Model for the Cancer Registry Software. *Acta Informatica Medica*. 2017 Dec;25(4):267.
20. Koch- Henriksen N, Stenager E, Laursen B. The use of epidemiological multiple sclerosis registers in research: the Danish MS Registry. *Acta Neurologica Scandinavica*. 2012 Dec;126:7-12.
21. Flachenecker P, Stuke K, Elias W, Freidel M, Haas J, Pitschnau-Michel D, et.al. Multiple sclerosis registry in Germany: results of the extension phase 2005/2006. *Deutsches Ärzteblatt International*. 2008 Feb;105(7):113.
22. Hurwitz BJ. Analysis of current multiple sclerosis registries. *Neurology*. 2011 Jan 4;76(1 Supplement 1):S7-13.
23. Vollmer TL, Ni W, Stanton S, Hadjimichael O. The NARCOMS patient registry: a resource for investigators. *International Journal of MS Care*. 1999 Sep;1(1):28-34.
24. Hillert J, Stawiarz L. The Swedish MS registry—clinical support tool and scientific resource. *Acta Neurologica Scandinavica*. 2015 Jul;132:11-9.
25. European Database for multiple sclerosis, EDMUS project. 2013, Cited [10/6/2018]. available at: www.edmus.org/en/proj/index.html
26. Nickerson M, Marrie RA. The multiple sclerosis relapse experience: patient-reported outcomes from the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry. *BMC neurology*. 2013 Dec;13(1):119.
27. Barrow Neurological Institute.North American Research Committee on Multiple Sclerosis(NARCOMS) Project [online]. 2015, Cited [17/5/2019]. Available from: http://www.thebarrow.org/research/Alzheimers_Disease/205498.
28. Warner J, Johnston M, Korngut L, Jette N, Pringsheim T. Common data elements for neurological registries. *Canadian Journal of Neurological Sciences*. 2013 Jul;40(S2):S62-3.
29. European Database for multiple sclerosis, EDMUS entry forms. 2015 France European database for Multiple Sclerosis. 2015, Cited [17/5/2019]. Available at:www.edmus.org/en/proj/index.html.
30. Flachenecker P, Khil L, Bergmann S, Kowalewski M, Pascu I, Pérez-Miralles F, Sastre-Garriga J, Zwingers T. Development and pilot phase of a European MS register. *Journal of neurology*. 2010 Oct 1;257(10):1620-7.
31. Stenager EN, Stenager E, Koch-Henriksen N, Brønnum-Hansen H, Hyllested K, Jensen K, et.al. Suicide and multiple sclerosis: an epidemiological investigation. *Journal of Neurology, Neurosurgery & Psychiatry*. 1992 Jul 1;55(7):542-5.
32. Koch- Henriksen N, Magyari M, Laursen B. Registers of multiple sclerosis in Denmark. *Acta Neurologica Scandinavica*. 2015 Jul;132:4-10.
33. Koch-Henriksen N. The Danish multiple sclerosis registry: a 50-year follow-up. *Multiple Sclerosis Journal*. 1999 Aug;5(4):293-6.
34. Brønnum-Hansen H, Koch-Henriksen N, Stenager E. The Danish multiple sclerosis registry. *Scandinavian journal of public health*. 2011 Jul;39(7_suppl):62-4.
35. Mason K, Thygesen LC, Stenager E, Brønnum- Hansen H, Koch- Henriksen N. Evaluating the use and limitations of the Danish National Patient Register in register- based research using an example of multiple sclerosis. *Acta neurologica Scandinavica*. 2012 Mar;125(3):213-7.
36. Harbo HF, Utsi E, Lorentzen ÅR, Kampman MT, Celius EG, Myhr KM, Lie BA, Mellgren SI, Thorsby E. Low frequency of the disease- associated DRB1* 15- DQB1* 06 haplotype may contribute to the low prevalence of multiple sclerosis in Sami. *Tissue antigens*. 2007 Apr;69(4):299-304.