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Global Perspectives

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EUROPEAN DATABASE FOR MYASTHENIA GRAVIS: A MODEL FOR AN INTERNATIONAL DISEASE REGISTRY

International disease registries: Why are they needed? There has been a growing interest in establishing clinical registries or databases, especially for neurologic rare diseases (NRD). To set up these registries, the combined effort of professionals with different expertise is necessary to improve the overall clinical knowledge. In NRD, issues that need to be addressed are comprehension of the phenotypic expression, an expedited diagnosis, recognition of life-threatening conditions, therapeutic options, and drug side effects.

Furthermore, NRD may differ with regard to genetic background, epigenetic risk factors, or social habits in different geographic locations. Hence, local environmental factors such as occasional exposure to microorganisms/pollution/chemicals, diet, smoking, and socioeconomic conditions may directly or indirectly influence NRD.

Disease-specific registries should be mutually valuable to both patients and clinicians; selected information may be relevant for public health reporting, geographic surveys, and epidemiologic studies. These registries are crucial for clinical research (i.e., to evaluate patient outcomes), and are primarily based on clinical data collected in homogeneous populations. Registries are developed and implemented as a result of collaboration between clinicians and hospital information technology services. While electronic medical records track all patients, a disease-specific registry focuses on a subset of patients with a specific condition, and collects a well-defined set of items called common data elements (CDE); this will ensure quick retrieval of past and current information for single patients or permit cross-sectional queries in specified (sub) populations (e.g., patients with myasthenia gravis [MG] with follicular thymic hyperplasia and anti-MuSK antibodies).

Across Europe, these data are recorded in different languages and cannot be easily shared in an international setting; a codified system to retrieve information, which follows the clinical data harvest, is required. Such registries are generally defined as physician-driven but to increase their intrinsic value, they should be linked with patient-driven registries, developed and maintained by patient associations. With this goal in mind, the Myasthenia Gravis Foundation of America (MGFA) has just started a Myasthenia Gravis Patient Registry (MGPR), a database of persons with MG living in the United States. This database has been developed to boost research, improve treatment, and share patient information. The MGPR is managed and supervised by the MGFA Patient Registry Committee (www.myasthenia.org).

International disease registries: How to build them? During the past 3 years, the European Union Committee of Experts for Rare Diseases, Rare Diseases Europe, the National Organization for Rare Disorders, the Canadian Organization for Rare Disorders, and the Agency for Healthcare Research and Quality have released guidelines and recommendations regarding the development of disease registries.[1–3] The following definitions are taken from the guidelines (for complete information, refer to the original documents): "A patient registry is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and serves one or more predetermined scientific, clinical, or policy purposes. A registry database is a file (or files) derived from the registry."[1]

Most of the registries are population-based, as they refer to a geographically defined population and their aim is to register all cases in that population. Disease prevalence and incidence are defined on population-based studies. Alternatively, non-population-based registries rely on data collected in referring clinical centers for specific diseases and should be integrated by data from patients associations because the population coverage may not be comprehensive.[3]

The main features of a successful disease-specific registry are as follows: (1) registries need to be internationally interoperable, thus allowing data pooling to reach statistically significant numbers for clinical

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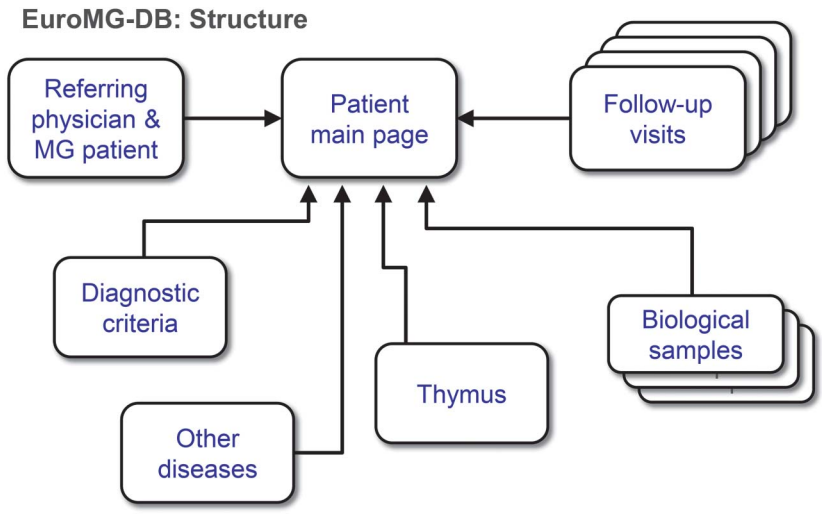
Figure 1 Schematic representation of the EuroMG-DB structure

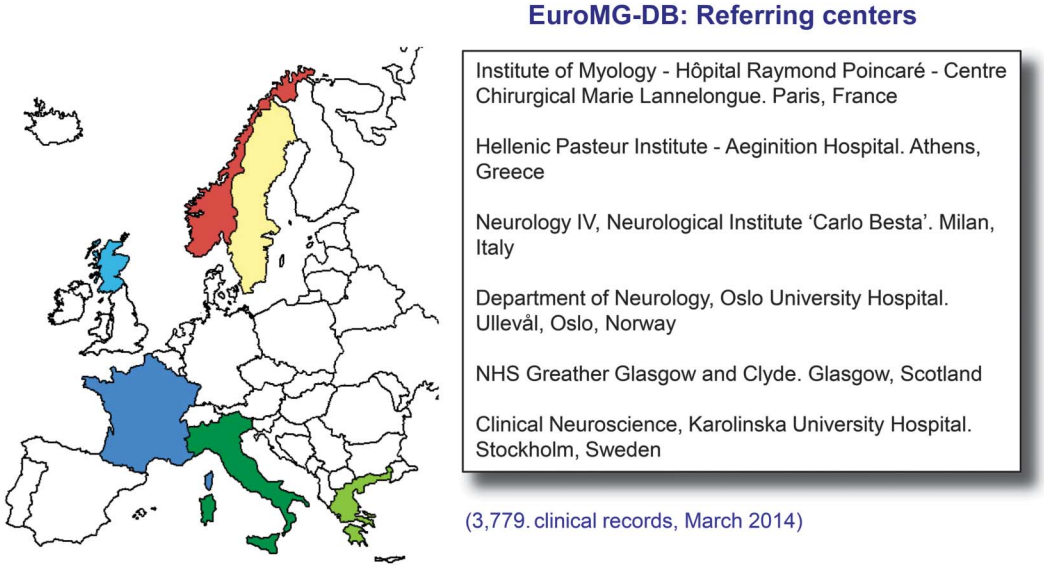


MG = myasthenia gravis.

research and public health purposes; (2) local/institutional databases should be built on a core of CDE because the multitude of database formats in use might create barriers to data sharing and would require extensive reformatting; (3) the minimum CDE should be defined by a scientific board, and possibly supported with a multilingual dictionary; and (4) CDE specific for the disease (or disease group) should be coded, and easily retrievable from medical records.

European database on MG. MG is a rare and heterogeneous neuromuscular disease leading to abnormal fatigability of various muscles; MG affects about 20 per 100,000 people worldwide and shows an increasing incidence. A European Network on MG, supported by EU funds (EuroMyasthenia Network, EU-2005105, DG SANCO, and Fight-MG project, HEALTH-F2-2010-242210), offers the best opportunity to establish a multidisciplinary team focused on this disease. The development of a database specific for patients with MG living in Europe (EuroMG-DB) was among the objectives. A working group defined the database structure along with the mandatory clinical and laboratory CDE that should be used to diagnose MG. The primary target was to collect clinical information for epidemiologic studies from 5,000 patients with MG. The secondary aims were to facilitate patient recruitment for research and clinical trials, to share information between MG Referring Centers, to ensure longitudinal assessments

Figure 2 European referring centers contributing to the EuroMG-DB



of patients, and to interact with a biological databank. The EuroMG-DB was built with a flexible structure for continued implementation (figure 1). Referring physicians are responsible for collecting patient data, in accordance with local ethical committees and national laws on personal data protection. The EuroMG-DB is accessible via an encrypted client–server protocol, allowing real-time data entry. Quality control of the data is assessed to guarantee reliability of the database itself. A routine evaluation is done by random examination of cases (performed by the database manager team), searching for possible discrepancies between collected (or missing) data. Any discrepancy is reported to the referring physician for a proper control between the data on the original documents and those loaded in the database.

Owing to the large amount of data, specific efforts have been made to ensure an almost real-time data analysis. Business intelligence (BI) programs are a powerful solution that can provide interactive analysis of the data, and allow the extraction of information from electronic databases. Data mining from the EuroMG-DB is then performed through a graphical interface to analyze correlations between data elements. BI software is a notable evolution from static reporting toward interactive visualization of data via dashboards.

Since its initial development, the EuroMG-DB anticipated most of the relevant features that are now considered to be mandatory in an international disease-specific registry. It should be considered as a shared platform, available to clinicians and researchers working on MG and developed to interact with local ongoing MG clinical records to collect information.

Recently, the Myasthenia Gravis Task Force of the MGFA stressed the importance of patient registries in improving knowledge on MG,[4] and the National Institute of Neurological Disorders and Stroke of the NIH recently completed a project to identify CDE for MG registries (www.commondataelements.ninds.nih.gov). In this regard, the analysis of data from 2 large MG registries, Duke University–Durham and Neurological Institute–Milan, provided preliminary demographic data on more than 2,300 patients with MG.[5]

Widening the use of the EuroMG-DB across Europe will enable us to obtain more accurate information about the MG population, highlighting local differences in disease manifestations and response to therapies, and improving clinical research to individualized MG treatment. The EuroMG-DB experience clearly indicated a way to collect homogeneous clinical data from different locations, fulfilling the expectations on the use of such registries. The EuroMG-DB has at its core some of the referring clinical and research centers for MG in western Europe (figure 2); in the long term, EuroMG-DB will collect information from the majority of patients with MG living in European countries, overcoming national barriers.

AUTHOR CONTRIBUTIONS

Dr. Baggi drafted and revised the manuscript. Dr. Mantegazza drafted and revised the manuscript.

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DISCLOSURE

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