Neuromuscular Disorders 51 (2025) 105368

Contents lists available at ScienceDirect

Neuromuscular Disorders

journal homepage: www.elsevier.com/locate/nmd

278th ENMC International Workshop: European standards for harmonization of myasthenia gravis registries and emerging digital solutions. 20th-21st September 2024, Hoofddorp, The Netherlands

Sabrina Sacconi [a,*], Fiammetta Vanoli [b], Frauke Stascheit [c], Elena Cortés-Vicente [d], Renato Mantegazza [b], Andreas Meisel [c], on behalf of the 278th ENMC Workshop participants

[a] Peripheral Nervous System & Muscle Department, Reference Center for Neuromuscular Disorders, Pasteur 2 Hospital, Nice University Hospital, Nice, France
[b] Neuroimmunology and Neuromuscular Diseases Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
[c] Department of Neurology with Experimental Neurologie, Neuroscience Clinical Research Center, Charité Universitätsmedizin Berlin, Charitéplatz 1, Berlin 10117, Germany
[d] Neuromuscular Diseases Unit, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

ARTICLE INFO

Keywords:
Myasthenia gravis
Registries
Digital solutions
ENMC workshop

ABSTRACT

The European Neuromuscular Centre workshop convened a diverse array of key stakeholders dedicated to the European standards for harmonization of national Myasthenia Gravis registries and emerging digital solutions. Participants included representatives from the pharmaceutical industry, patient advocacy organizations, clinicians with expertise in Myasthenia Gravis, and members of the European Reference Network for Rare Neuromuscular Diseases. This multidisciplinary composition, as well as preliminary activities, fostered robust discussions and facilitated the identification of shared objectives for future endeavors to allow collaboration at European level among national Myasthenia Gravis registries. Throughout the workshop sessions, relevant topics emerged, highlighting both the challenges and strengths towards harmonizing data on myasthenia gravis in national registries and improving outcomes for patients with myasthenia.

1. Introduction

The 278th ENMC International Workshop on "European standards for harmonization of myasthenia gravis registries and emerging digital solutions" took place the 20th and 21st of September 2024 as an hybrid meeting, with 34 participants, 29 on-site and five connected remotely, including patient representatives from five different countries: AFM Telethon Myasthenia Group, Asociación Miastenia de España (AMES), Belgian Association against Neuro-Muscular Diseases Myasthenia Group, Deutsche Myasthenie Gesellschaft and the Italian Association of Myasthenia Gravis). Additionally, EURORDIS, a European association working with over 74 countries, participated in this workshop. Representatives from four pharmaceutical companies: argenx, UCB Pharma, Alexion and Johnson & Johnson were allowed to attend remotely during the introduction and conclusion of the meeting.

Myasthenia Gravis (MG) is a rare and heterogeneous neuromuscular disease with a prevalence of approximately 200 *per* million and a mean incidence of 15.7 cases per million person-years that appears to be increasing [1,2]. The workshop focused exclusively on acquired MG, the most prevalent form [3]. Acquired MG is a prototypic B cell-mediated autoimmune disease characterized by muscle weakness and fatigability resulting from the production of autoantibodies (auto-Abs) targeting neuromuscular junction components such as the acetylcholine receptor (AChR), muscle-specific kinase receptor (MuSK), or the low-density lipoprotein receptor-related protein 4 (LRP4) [4].

Due to the rarity of MG, a multicenter and international approach is essential to collect real-world data, develop predictive biomarkers of disease progression and treatment response, and harmonize care quality and treatment availability across different European countries. Standard MG treatments include symptomatic drugs such as cholinesterase inhibitors, etiologic drugs such as steroids and non-steroidal immunosuppressants, and broad immunomodulatory therapies such as plasma exchange or intravenous immunoglobulins. Thymectomy is an option for selected anti-AchR patients [5]. However, most of these treatments lack rigorous randomized controlled trials, and may have significant side effects limiting their use in patients with comorbidities and/or may

* Corresponding author.
E-mail address: sacconi.s@chu-nice.fr (S. Sacconi).

https://doi.org/10.1016/j.nmd.2025.105368
Received 14 April 2025; Accepted 23 April 2025
Available online 18 May 2025

be insufficiently effective [6]. The range of therapeutic options for MG has expanded rapidly in recent years, offering new drugs such as anti-C5 inhibitors and neonatal Fc-receptor antagonists for treating "refractory" patients [7–9]. Several other innovative therapeutic strategies are in advanced phases of clinical testing [10].

The growing treatment options highlights the need for safe, preventive, and tailored personalized medicine (PM) strategies based on real-world data. These strategies should assess not only patient-specific effects (e.g., benefits versus side effects), but also the health economic impact of these highly effective but costly drugs. To address these challenges, MG patient registries and digital technologies have emerged worldwide to help overcome the inherent challenges of rare disease research by pooling data and achieving sufficient sample sizes for research purposes [11]. They contribute to clinical research and patient care by collecting high quality, longitudinal data and harmonizing clinical practices. Digital technologies can ease data collection and enhance real-world data knowledge, allowing for a more precise assessment of the disease's impact and therapy effects on patient's daily life.

Many countries worldwide have started implementing national MG registries and MG-specific digital solutions, but variability in data collection, management tools, governance models and funding may limit interoperability and data integration. Multiple stakeholders could benefit from these resources, but challenges such as a lack of coordination and harmonization, data sharing, ethical concerns, and sustainability may reduce efficiency, compromise data quality, and cause duplication of efforts.

The 278th ENMC workshop aimed to address these challenges by creating a network of stakeholders involved in MG patient registries and digital solutions. The goal was to establish European standards for harmonizing MG data collection and interoperability for future collaborations.

2. Preparatory pre-workshop activity

To facilitate the preparation of the workshop, the organizers and early-career experts (FV, FS) held four pre-workshops (Fig. 1). The first pre-workshop activity focused on developing a modified-Delphi process to establish which mandatory and optional data will be included in National European MG registries. A questionnaire including 100 items was submitted to 16 European MG experts: 11 neurologists, 4 neuropaediatricians and 1 physiotherapist. Three consecutive rounds were conducted, with consensus defined as at least 80 % agreement among panellists. Items that failed to reach consensus were rediscussed in the following rounds. A final consensus on data to be included has been reached and the result of this dataset will likely serve for data harmonization in future MG collaborations at the European level. Details on this activity are available on a dedicated paper [12]. The second pre-workshop activity was the creation of a surveys sent to 10 coordinators of national MG registries participating to the 278th ENMC Workshop, to obtain an overview of the European national MG registries. Detailed features of each registry are discussed and summarized in Fig. 2. The third pre-workshop activity was a preliminary discussion with pharma companies involved on MG drug development to identify their priorities regarding data collection and digital solutions. The fourth pre-workshop activity was a meeting with patient advocates to define priorities and unmet needs of MG patients that need to be addressed in MG registries and digital solutions.

2.1. Session 1: setting the scene: perspectives on registries and digital solutions for MG

In the last decades, interest in MG registries has grown, driven by the digital era's ability to collect and store large scale data in a systematic manner [13,14]. The availability of such data is a critical resource for epidemiological and clinical research, ultimately improving MG standard of care. The workshop opened with perspectives from key stakeholders of MG registries and digital solutions: patients, clinicians, regulators, and pharma companies.

2.1.1. Patient's perspective

An important goal of this meeting was to integrate and improve patient communication, given their unique perspective on MG that complements the healthcare professional's expertise. Matthieu Lusignan, one of the four patient advocates invited to the meeting, underlined that patients should be active partners in the design, development, and operation of MG registries. They should help defining the type of data collected and the registry's goals, ensuring that patients' real needs are addressed. To improve patient-centred care, MG registries should include different patient reported outcomes (PROs), as they reflect the patient's experiences with symptoms, treatments, and quality of life. PROs also enhance data accuracy and strengthen collaboration between patients and healthcare professionals. When participating to a disease registry, patients have two main concerns: data property and anonymity. It is crucial to provide patients with an exhaustive informed consent while ensuring confidentiality through ethical and legal standards, like general data protection regulation (GDPR). Moreover, financial sustainability requires a multi-source funding approach, combining public, private, and patient organization resources, with full transparency to maintain trust. Other key challenges for patients include unequal access to digital tools, legal and ethical differences across countries, and disparities in treatment availability.

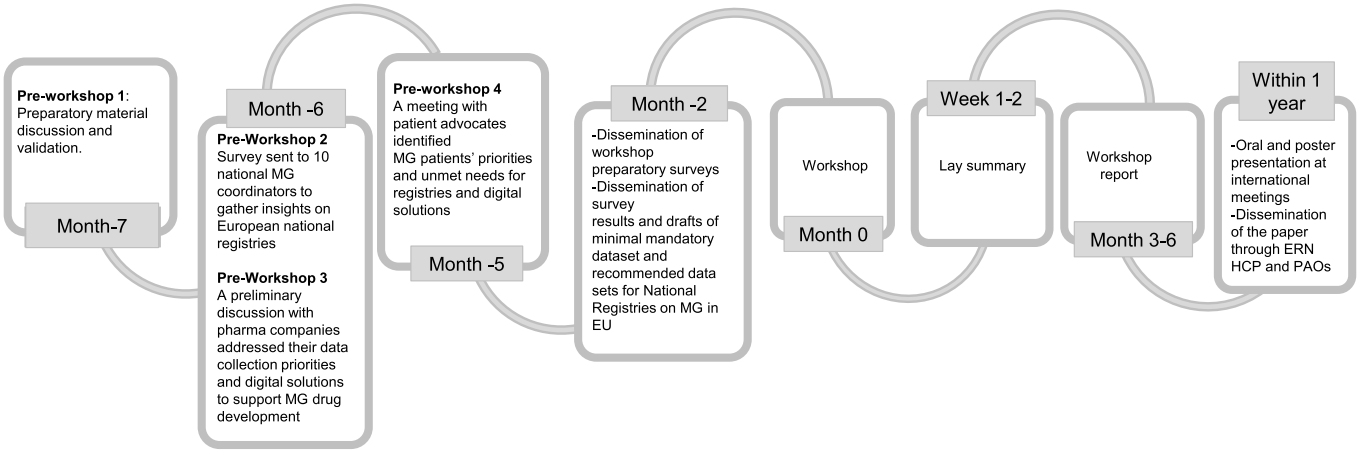

Fig. 1. Workflow of the 278th ENMC Workshop.

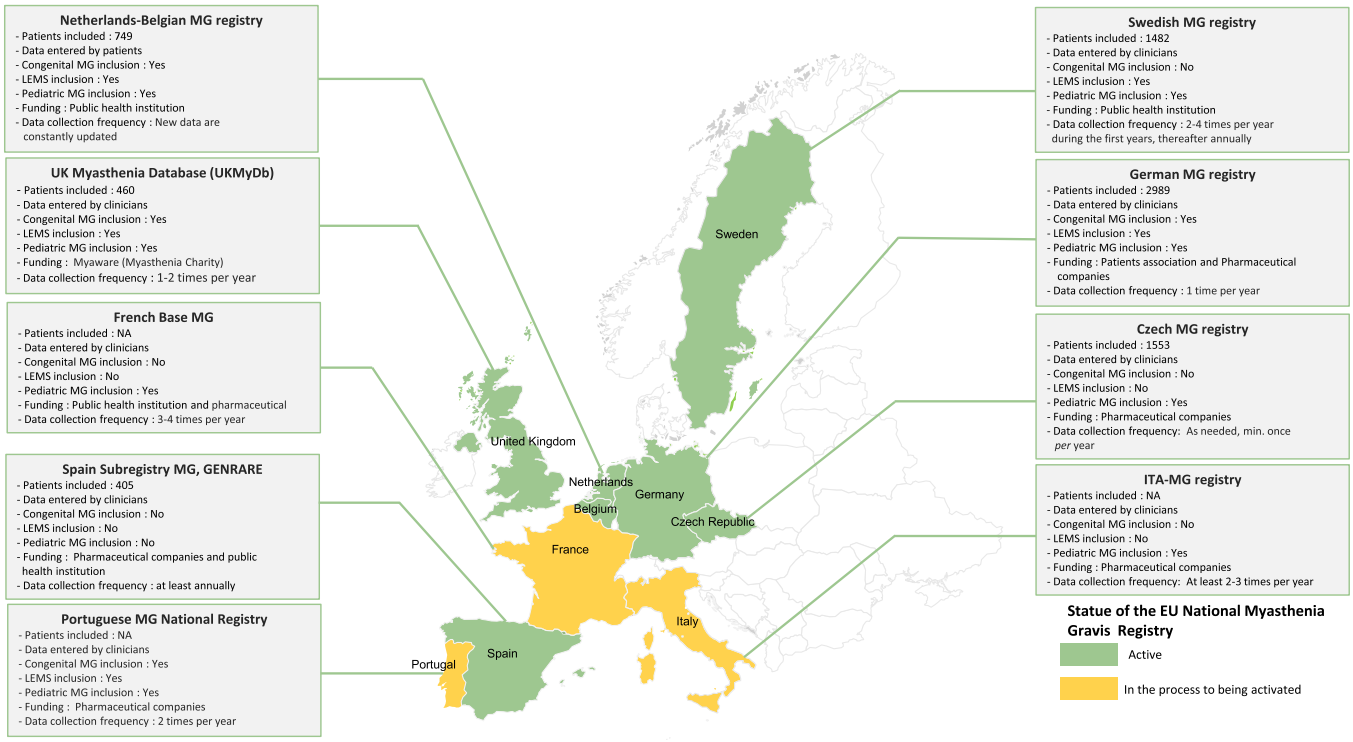

Fig. 2. Distribution and characteristics of national Myasthenia Gravis (MG) registries in Europe at the time of the ENMC workshop.
In green the already existing national MG registries, in yellow the registries that are in the process of being activated. The data are referred at the time of the survey and may not reflect the actual distribution of MG patients. (LEMS: Lambert-Eaton Myasthenic Syndrome).

2.1.2. Clinician's perspective

The clinician's perspective was addressed by Elena Cortés-Vicente, who defined what a registry is and why a national disease registry is important, especially for rare diseases where small sample sizes can limit the feasibility of research studies [15]. From the clinician's perspective, the ultimate goal of an MG registry is to develop and improve disease standard of care. To reach this goal, registries collect data from several studies including observational clinical studies (e.g. natural history studies), real-world outcome studies, epidemiological and pharmacovigilance studies. MG registries also offer a useful platform to identify possible candidates for clinical trials. Digital solutions use technology to enhance communication between doctors and patients, ultimately improving patient care and quality of life. Tools like electronic medical records or telemedicine have been used for years while mobile health apps and wearables are still in development. These tools may be very useful for both clinicians and patients, particularly in MG, a fluctuating disease that requires close monitoring to detect clinical worsening, exacerbations as well as record response to therapy and side effects in a real-life context.

2.1.3. Regulator's perspective

On behalf of the European Medicines Agency (EMA), Sabrina Sacconi discussed the regulator's perspective and the EMA rare diseases patient registry initiative. She highlighted the critical role of rare disease registries in regulatory frameworks, notably in Risk Management Plans (RMPs) for advanced therapies and orphan products. On this perspective, EMA had mandated registries for a growing number of authorized products, including MG, emphasizing the importance of long-term monitoring of product safety and efficacy. However, EMA recognizes that existing registries may face challenges, such as late initiations, low patient participation, data quality issues, and lack of interoperability. The EMA's initiative launched in 2015 aimed to address these challenges by enhancing the role of registries in benefit-risk evaluations, promoting better communication between regulators and registry holders, and differentiating between registry establishment and study performance to improve participation and outcomes. This initiative helped clarify the difference between registry as a comprehensive database to compare treatment outcomes or clinical data, and registry-based studies investigating specific research questions within a selected population. To help registry harmonization, the European Commission implemented the European Rare Disease Registry Infrastructure (ERDRI) platform, aiming to make registry data to be searchable and findable. Another initiative promoted by EMA is the European Directory of Registries (ERDRI.dor), which provide overviews of participating rare disease registries with their main characteristics and description [16]. Digital transformation in healthcare is increasingly necessary to address challenges such as an aging population and healthcare inequalities and is strongly advised by EMA. However, the success of digital health solutions hinges on establishing clear policies around data protection and effective interoperability among stakeholders. Indeed, mobile applications present advantages, like real-time tracking and enhanced patient communication, they also raise concerns about data privacy and usability. A successful app must prioritize user experience, regular updates, and engage effectively with users. Ultimately, the EMA perspective on the future of digital solutions for MG and other rare diseases focuses on patient empowerment through innovative technologies that foster better health outcomes and community engagement.

2.1.4. Pharma's perspective

Filip Callawaert (argenx) gave a presentation reflecting the aligned cross-industry views on the importance of current and future harmonized European MG registry practices. The following industry partners were involved: UCB pharma, Alexion, Johnson & Johnson and argenx.

For industry partners, patient registries are important tools in enhancing disease knowledge and characterization of rare diseases [17]. Improved consistency in MG registry practices across European countries, or harmonization at the European level, can help advance disease management, enhance treatment quality for patients, and improve the

usability of registries for research and development. MG registries can facilitate and support their research and development activities by ensuring uniform collection of information from rare patient populations [17]; enabling the initiation of research/product development [17,18] validating results from RCTs in real-world populations; collecting post-marketing surveillance data [17,18]; conducting registry-based studies [19]; forming a basis for consensus discussions; supporting regulatory or HTA discussions.

For industry partners, three main areas should be considered in view of European harmonization of MG registry practices. First, there is a need to establish consistent and functional registries at a national level as the basis for European collaboration. This will require the fostering of a 'culture of participation' but also suitable governance and structure/rules as part of data collection. The philosophy for national-level registries should be to create a 'tank' of national data with multiple centers contributing consistent and 'shareable' data. Second, experts, patients and industry should align on the strategy, the data collection and parameters in MG registries (either national or European level). Reinventing registry practice is not necessary, but alignment on the strategy for registry practice and key mandatory (and optional) data collection parameters is crucial, also considering how to minimize costs and maximize data 'shareability'. Lastly, harmonization across Europe is needed, but a single European registry might be difficult to immediately achieve, given the national-specific and regional regulations. A stepwise approach might be preferred and initially focus on identifying shared parameters/outcomes for collection and maintaining simplicity so that country-level data can be exported and shared. Finally, the industry partners gave their recommendations on important and mandatory items for registries to ensure impactful and consistent data capture in MG registries. Interestingly, there was a great correspondence between the mandatory and optional items proposed by pharmaceutical companies and those validated by MG experts in the modified Delphi process [12].

2.2. Session 2: state of the art: MG patient registries

This session was chaired by Renato Mantegazza and Lutgarde Allard, a Belgian Association Against Neuro-Muscular Diseases (Myasthenia Group), focused on providing an overview of the existing or soon-to-be activated European MG registries. At the time of the Workshop, Europe had seven active MG registries and three registries in the process of activation presented in Fig. 2. In this session, juvenile MG, a rare form of autoimmune MG, was also separately discussed.

2.2.1. The Spanish MG registry

Elena Cortés-Vicente presented the MG Spanish registry, a neurologist-driven registry funded in 2010 with exclusively public funding by Isabel Illa as part of the NMD-ES project. The registry included adult patients with a confirmed diagnosis of MG with annual follow-up visits. Fifteen different hospitals participated to the registry enrolling about 1670 patients, which allowed the development and publishing of several studies [20–23]. Due to the need for long-term maintenance, in 2019 the registry was transferred to the Genetic and Low Prevalence Diseases Registry (GENRARE). GENRARE works as an umbrella for all rare disease registries in Spain, where each sub-registry works independently but shares the same protocol, patient information and informed consent. The MG sub-registry has a scientific committee driven by three neurologists and a patient representative and warrants specific data access and publication policies. All contributors have only access to their patients' data. If a national study is developed, a project protocol is submitted to the scientific committee, evaluated and approved before access to all data is granted. Pharma companies must follow the same process, but they will always receive reports of aggregated data. The software used is REDCap and funding is currently both public and private.

2.2.2. The German MG registry

Frauke Stascheit presented the German MG registry (MyaReg) which includes autoimmune MG, Lambert-Eaton Myasthenic Syndromes (LEMS), and Congenital Myasthenic Syndromes (CMS). MyaReg was created in 2019 by the German Myasthenia Gravis Foundation (DMG) supported by the German Institute of Quality and patients Safety (BQS) and funded by pharmaceutical companies. The DMG advisory board elects a user council who manages the register and coordinates requests for data use. The registry is based on a specific set of quality indicator and works using a web-based database (ASTHESIS®), provided by BQS, who is also responsible for administration and implementation of new data set as well as certification [24]. All certified integrated MG Centers in Germany participate in the registry, with about 3000 patients registered, including pediatric patients. The certification process depends on the full participation in the registry, based on the yearly published quality report with follow-up visits occurring annually. Moreover, together with the central Mya-Biobank, MyaReg will allow biomarker research in autoimmune MG [24] Data entry is currently only allowed to clinicians, however in the future patients could have the possibility to access their own data and fill out PROs.

2.2.3. The Netherlands/Belgian MG registry

Jan Verschuuren presented the Dutch/Belgian MG registry, which was created in 2015 after receiving the approval of the Dutch medical ethics review committee (METc). At the time of the 278th ENMC workshop, the Belgian registry was in the process of being activated. This registry is curated by the Leiden University Medical Center (LUMC), which is the only center entering data and host of the database software (CASTOR). It is entirely funded by public health institutions and research grants. The registry includes both adult and pediatric patients with autoimmune MG, LEMS or CMS. The main goal is to collect "basic data" from as many patients as possible using questionnaires. After consenting to participate, patients are provided with annual questionnaires to be filled on a dedicated website (paper version is also available for the elderly). These questionnaires cover symptoms, treatment effects and quality of life. Moreover, participants can grant permission to provide further data on their diagnosis and blood samples for future research on the relationship between hereditary factors and disease characteristics. They can also consent to being contacted in the future for additional data collection for specific research purposes or to participate in clinical trials if eligible. For informational and motivational purposes, participants receive a semi-annual newsletter via email, which shares results from the registry and provides information about other MG scientific research. The content of the newsletter is also published on the website of the myasthenia expertise center [25].

2.2.4. The Swedish MG registry

The Swedish MG registry was presented by Susanna Brauner. It is a national quality registry that belongs to the Swedish Neuro Registries, an umbrella organization for quality registries associated to neurological diseases, which in turn belongs to the public authority National Quality Registry, covering over 150 health registries. All neurology clinics, both in and outpatient clinics, are connected to the Swedish Neuro Registries and thereby also the MG registry. The MG registry was launched in 2011, based on a local registry with high coverage in Stockholm (83 % of prevalent patients according to the diagnosis registry) [26]. The MG registry has an appointed registry holder (Fredrik Piehl, Karolinska University Hospital, Stockholm) and a steering group with representatives from all university hospitals in Sweden as well as a patient representative. The steering group oversees the registry, approves applications to use data for research purposes and has also been involved in development of the latest national treatment guidelines from MG published in 2024 [27]. The main target groups of the registry are newly diagnosed MG patients and patients treated with immunosuppressants with only adult patients included. Participation in the registry is voluntary, and patients may withdraw at any time and may also choose

to contribute only their data for quality-of-care evaluation, as well as research purposes. Data recorded in the registry is divided between basic characteristics (age at onset and diagnosis, diagnostic workup and treating center) and longitudinally data (disease activity, quality-of-life, treatments, hospitalizations). An extensive validation and data update effort at all but one major clinic nationwide has been ongoing since 2021, ensuring accurate data. In 2024, 1767 patients were registered in the registry, of which 1482 were active. This mounts to >55 % total coverage of all MG patients in the country, and a larger proportion in the target group. The majority of patients are late-onset MG (47 %), followed by early onset MG (36 %) and thymoma associated MG (11 %). The registry runs on a webpage with limited authorized access.

2.2.5. The Czech MG registry

Stanislav Vohanka presented the Czech MG registry (MyReg). The MyReg was launched in 2015 among 15 Czech centers. It includes only autoimmune MG and contains the records of about 2400 MG patients of which 1553 are active [28]. Juvenile MG is included as well. The registry is the result of a joint collaboration among specialized Neuromuscular Centers and several other hospitals under the auspices of the Czech Neurological Society. Data are stored in a central server CLADE-IS (CLinicAl Data warEhousing – Information System) electronic database and are accessible via any internet browser. Secure data transmission is assured as well as data protection regulation. The database has five modules: (a) enrolment, (b) follow-up, (c) therapy, (d) pregnancy, and (e) end of monitoring. Data entry is entrusted to clinicians and each center has access only to their own data. However, access to all data is possible with permission from the other participating centers. The registry is supported by pharmaceutical companies.

2.2.6. The Italian MG registry

The Italian MG registry (ITA-MG) was presented by Carlo Antozzi. Although it was not active at the time of the workshop, it was launched the following month, in October 2024. The electronic case report form (eCRF) is based on the REDCap software, hosted at the IRCCS Neurological Institute Foundation of Milan and accessible via web for authorized users only. The eCRF includes one-entry epidemiological data (e.g. age, sex, ethnicity, disease classification, diagnostic procedures, thymectomy, comorbidities, side effects) as well as longitudinal data, which include the first and subsequent follow-up neurological visits (frequency is at treating physician discretion, but at least annually). The registry will include only autoimmune MG patients, both adult and juvenile. Each visit includes clinical evaluation with validated rating scales (e.g. QMG), PROs as well as treatment changes. An Opt-in approach is mandatory as well as the Ethics approval for each participating center. Particular attention has been paid to the pseudonymisation protocol, and to the identification of duplicates. Response options have been specified for each item of the eCRF to avoid variability, and ontology has been included for classification of comorbidities and side effects. A specific Data Protection Impact Assessment (DPIA) document has been drawn up. The registry is funded by pharmaceutical companies.

2.2.7. The French MG registry

Emmanuelle Salort Campana presented the French MG registry (BaseMG), which is in the process of being activated. It was created in 2023 under the guidance of the FILNEMUS network, the French network for rare neuromuscular diseases. The BaseMG is hosted by the French national rare disease database (BNDMR, Base nationale de Données maladies rares), which is a secure national database of health data implemented as part of the French National Plans for Rare Diseases (PNMR). This database aims to create a homogeneous collection of medical data on rare disease patients followed in French centers. It has been approved by the CNIL (French National Commission on Information Technology, Data Files and Civil Liberties). A minimum set of national rare disease data (SDM), shared by all stakeholders and all diseases, has been defined to allow a structured collection of high-quality data that can be used throughout France. BaseMG is hosted at the BNDMR using DoSpéra, a specialized rare disease file that allows the collection of specific elements dedicated to a particular pathology. It collects clinical information of both adult and juvenile patients with definite or probable MG who are followed at a reference center within the Filnemus network. The number of MG patients followed in all Filnemus reference centers is estimated to be 5000 with an enrolment target of 1000 patients per year for 4 years, starting in early 2025. Priority will be given to newly diagnosed patients and/or patients receiving an innovative treatment with early access (pre-marketing authorization or compassionate use). In the near future, long-term data chaining with French nationwide claims and hospitalization database (SNDS) will be possible. Patients must give non opposition to data collection, without signing a consent form. The registry is sponsored by the Hospital of Marseille and funded by several pharmaceutical companies.

2.2.8. The Norway MG data collection

Nils E. Gilhus talked about data collection in the Norwegian MG population as there is no specific MG registry in Norway. However, there is an increasing demand for specific disease registries within neurology, built on the same principles as the highly successful Norwegian Multiple Sclerosis (MS) Registry, funded by government [29]. Despite the absence of a specific registry, ongoing efforts to collect chart information about all MG patients recorded and treated in Norwegian hospitals may help establish and promote an independent MG registry. Currently, health information regarding Norwegian MG patients is collected in several mandatory national registries, with the most important being the Norwegian Patient Registry, which records all specialist healthcare consultations, including hospital and outpatient care. Other relevant registers are the Norwegian Prescription Registry, the Norwegian Birth Registry, and the Norwegian Cause of Death Registry. MG patients are easily identified among the registries using the ICD-10 diagnostic code for MG (G70.0). Another strategy used to identify MG patient is the search for repeated pyridostigmine prescriptions in the prescription registry [30]. Data from several registries can be linked and exported into one file using a personal eleven-digit code number unique for each person in Norway. Through Statistics Norway, health information from the registries can be linked to level of education, annual income, cohabitation, and other social markers. These health registries have provided MG-specific information on epidemiology, use of MG-related and unrelated drugs, comorbidity, pregnancy and childbirth, death rates, and health economics [31,32]. However, they lack detailed information about MG subgroups, disease severity, antibody status, and therapeutic response.

2.2.9. The Portuguese MG registry

Ernestina Santos presented the project of Portuguese MG registry. The base of this national registry will be an epidemiological and clinical study performed between 2013 and 2015 in the Northern Region of Portugal. It was a hospital databased study completed with information from primary care prescriptions of pyridostigmine as a source for identifying patients. This study provided epidemiological information on the Portuguese MG population such as prevalence (111,7 per million) and incidence (6.3 per year per million), with highest incidence observed in males with very late onset MG [33]. This study is being expanded nationally as a registry to collect clinical data and evaluate if there is a uniform standard of care across centers. The registry will include 37 hospitals divided into three geographical regions, with three principal investigators and three study coordinators, also facilitating the contact with smaller hospitals treating MG patients. Only adult patients with confirmed diagnosis of autoimmune MG will be enrolled. The registry will be hospital based and will use REDCap as software for data entry hosted in Hospital Santo Antonio, Porto. Ethical approval still needs to be obtained for all participating hospitals. By June 2025, the initial epidemiological and clinical data should be finished and updated at least twice a year. The registry is funded by a pharmaceutical

company.

2.2.10. The UK MG registry

Mohammad Ashragi presented the UK MG database (UKMyDb), which includes autoimmune MG, Lambert-Eaton myasthenic syndrome (LEMS) and congenital myasthenia gravis (CMG) in both adults and juveniles. The creation of the UKMyDb was funded by the myasthenia charity Myaware and is sponsored by Oxford University. It uses REDCap, with the data stored on the University of Oxford computers. A steering committee of MG, LEMS and CMS specialists from across the UK meets regularly to advise on the database. National ethical approval was obtained in January 2024, and first local approval was given in June 2023, with data entry beginning in July 2023 at Oxford University Hospitals. All patients provide written consent to be included and to be contacted about future research. Data entry is performed by patient's clinical team, with no patient-led data entry and is updated one to two times a year. The collected data is divided into Tiers 1, 2 and 3. Tier 1 includes basic information such as demographics and diagnosis, while Tiers 2 and 3 include comprehensive clinical data such as antibody/genetic status, thymic status, comorbidities, symptoms/signs, outcome scores and treatments for newly diagnosed and historic patients respectively. This allows sites with limited resources to contribute data for epidemiological studies, while sites with greater capacity can provide more detail for more specific research. At the time of the workshop 14 sites across England, Wales and Scotland were participating to the registry with 460 patients included, with numbers growing rapidly. To avoid duplicated data, a health number is used for pseudonymization. Access to the data is available to UK researchers at no charge. In the future, the database aims to expand to include more sites across the UK, with a focus on increasing the inclusion of paediatric patients.

2.2.11. Juvenile MG

Adela Della Marina introduced the topic of autoimmune juvenile MG (JMG), which is defined by onset of symptoms before the age of 18 years. It is a very rare form of autoimmune MG, accounting for about 10 % of adult MG and has the peculiarity that, particularly in prepubertal patients, the clinical presentation and course of JMG can differ from that of adults. Indeed, pre-pubertal JMG present more often pure ocular symptoms with milder course of the disease [34–36]. This subgroup may be more often seronegative and in the absence of specific antibodies, especially in infants and very young children, the important differential diagnosis is with CMS.

There are no randomized, control studies for the immunosuppression in this patient population. Therapy and patient-care recommendations are mostly based on retrospective data collections and generally follow the same indications as for adults [37,38]. However, in children's treatments and their side effects have a greater impact than in adults, especially with long-term steroid use, affecting behavior, growth, weight, height and bone.

Standardized scores (QMG, MG-ADL) are used in adults for clinical evaluation and therapeutic decisions. However, they require good patient cooperation therefore in children under ten years of age it will best use a modified form adapted to younger children. In older children (>10 years of age), experience from practice demonstrate the feasibility of these scales, however no studies have been conducted to verify their applicability in JMG. It is encouraging to note that an open-label study of eculizumab in JMG met statistical significance in primary and all secondary efficacy end points [39], and a few other medications are currently in the open label trial phase (efgartigimod (NCT05374590, NCT06203457), ravulizumab (NCT05644561), rozanolixizumab (NCT06540144), zilucoplan (NCT06055959).

2.2.12. National registry survey discussion

During the discussion, data of the survey conducted on existing or soon to be launched registries were commented. Overall, the survey (Fig. 2) showed that for all existing European registries, except for The Netherlands-Belgian MG registry, clinicians are responsible for data entry. Most registries enter data annually and monitor it at least once a year. Eight registries have servers connected to internet hosted by a hospital or institutional server. In half of the registries data can be retrieved by their identifier using a standardized, open, and universally accessible protocol. In all registries, a data access policy and a data access committee are either in place or planned to be established. 9 over 10 registries already have a consent form in place, while the French registry data collection is based on the principle of "non opposition form". Patients have access to their own data in only three registries: the Czech MyReg registry, the Swedish MG registry, and the UK Myasthenia Database. This is an aspect that should be improved, considering that patients are among the main stakeholders of registries.

Funding is always a critical aspect, and the survey results reveal that about one-third-of the registries were funded by public health institutions or charities (the Netherland/Belgian Myasthenia Gravis Registry, the UKMyDb, the Swedish MG registry), the Spanish Subregistry MG GENRARE has both public and private funding, while all the other registries are funded by pharmaceutical companies. Most of the MG registries are actively seeking additional funding options to ensure their sustainability. Finally, the survey demonstrated that no registry is registered in the European Directory of Registries Infrastructure (www.ERDRI.dor), highlighting an important issue in communication of national initiatives on MG at the European community.

In total, at the time of ENMC workshop data on 7518 MG patients were already available through the active European registries and the number is growing every day. The percentage of mandatory and optional data defined by the second pre-worshop activity [12] included in different registry is reported in Fig. 3. Globally, there is 89 ± 0,15 % agreement on mandatory items among different registries, while for optional items the agreement is 67± 0,18 %. These percentages can be further improved to ensure the possibility of future collaborations.

The final part of the discussion was focused on Juvenile MG (JMG). Experts recommended including JMG patients in national MG registries, given their similar pathophysiology and therapeutic recommendations to adults. This would allow to collect precious information on this rare MG subgroup, improving the knowledge on their clinical features and response to therapies, crucial for optimal therapies. Accordingly, the mandatory and optional data established by the modified Delphi process [12] must be adapted to this group's requirement: collection of metric data like weight and height, information on educational options (kindergarten, school), a partial assessment of the QMG score (list of items performed), and the use of pediatric PROs and quality of life measures.

2.3. Session 3: state of the art: MG digital solutions for data collection

This session, chaired by Sabrina Sacconi, focused on the rapid advancements in digital technologies within the field of neuromuscular diseases. These innovations not only promise to enhance patient care but also aim to alleviate the burden of data collection, thereby enriching our understanding of real-world data.

2.3.1. MyaLink

Andreas Meisel presented the MG app Myalink. The Myalink app closes a gap in patient care. Vital parameters are monitored using spirometers and wearables and patients document their symptoms using standardized questionnaires (PROM) [40]. Myalink is special, because it offers a direct communication tool, which is very important for the patients. It allows the treating specialist to assess the course of the disease remotely and to contact the patient and, if necessary, adjust the therapy at an early stage. The long periods between appointments with specialists are therefore no longer a black box and myasthenia crises can be prevented. A proof-of-concept study has been performed with 45 patients; the adherence was by nearly 90 %. Patients had about 10 contacts per month to physicians [41] A roll out to other MG centers of

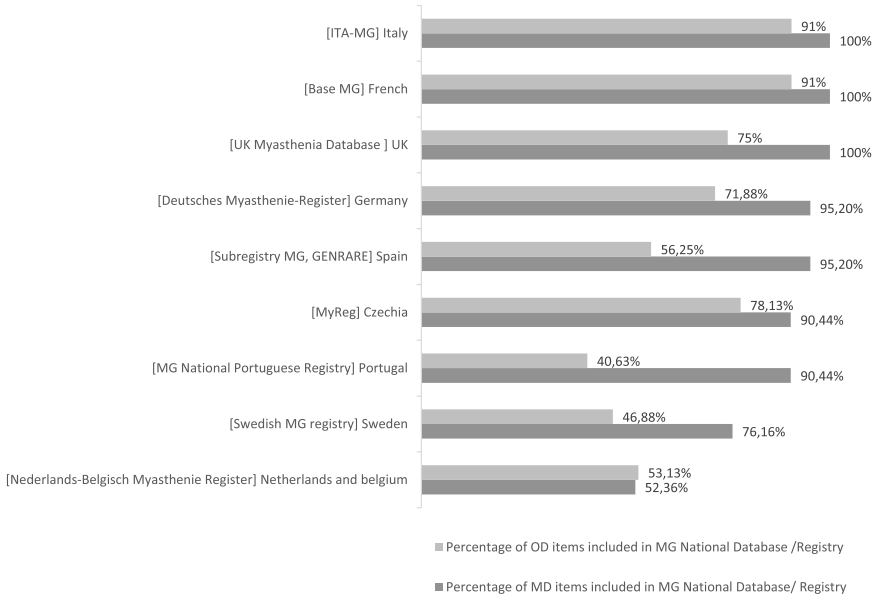

Fig. 3. Survey results on percentage of mandatory and optional items present in Myasthenia Gravis (MG) registries and data bases.

excellence in Germany is planned. Moreover, data from Myalink is planned to be added to the database of the German myasthenia gravis registry.

2.3.2. *MyRealWorld MG*

Fiammetta Vanoli presented study results of MyRealWorld [42]. It was a study on the burden of disease from a patient perspective together with the Italian patient organization, funded by argenx. The study started in October 2021 and ended 2024 showing that despite current treatment, patients still experience moderate burden and impairment to quality of life; patients were reached globally, and results were periodically shared to MG patient community.

2.3.3. *ME&MG™*

Pascal Laforêt presented ME&MG™, a Software as a Medical Device (SaMD) developed by Ad Scientiam—a French ISO-13,485 certified MedTech company—in collaboration with experts, patients, and patient associations currently undergoing validation [43]. The ME&MG™ is a tool designed for unsupervised digital self-assessment of muscle weakness, fatigability, and disability in MG patients. Using their smartphones, patients can collect objective digital biomarkers related to key MG symptoms (ptosis, dysarthria, respiratory capacity, upper and lower limb weakness) as well as complete e-questionnaires on quality of life, daily activities, pain, sleep, and mood disorders (e.g., MG-QOL-15r, MG-ADL, Pain Likert Scale, ISI, PHQ8). The results are then communicated in real-time to clinicians *via* a dedicated secured web portal. DOMYA (NCT: 05,564,936) is an international, prospective, low-intervention study currently enrolling participants in 21 US and French sites, to validate the clinical performance and safety of ME&MG™ [44]. This study aims to recruit 94 adults with generalized MG (gMG) and positive for anti-acetylcholine receptor antibodies, along with healthy volunteers. The study will last a total of 21 months, including a 9-month enrollment phase and a 12-month follow-up period. The primary objectives are to validate the accuracy, reliability, and reproducibility of the unsupervised self-assessment of symptoms at home using ME&MGTM compared to standard in-clinic testing (Quantitative MG score (QMG)). Secondary objectives include evaluating the safety, usability, and user satisfaction of ME&MG™. The anticipated outcomes of this study include the validation of an innovative device for the real-world monitoring of MG patients, paving the way for the registration of ME&MGTM as a medical device in both Europe and the United States. This milestone will enable the widespread availability of the tool to clinicians and patients, marking a significant advancement in the integration of digital biomarkers into the care and research of MG. Additionally, a complementary study evaluating real-world user experience and long-term adherence is ongoing in the USA and Canada (NCT05566964), with over 200 MG patients already enrolled [45].

2.3.4. *LumiiMG*

Sabrina Sacconi presented the HumaMG platform, which is an innovative digital solution aimed at improving the management of Myasthenia Gravis, a condition where 50 % of patients report a low quality of life. The platform provides remote data capture for symptoms, medication adherence tracking, and educational resources, classified as Software-as-a-Medical Device (SaMD). Future developments include AI algorithms for objective symptom measurement, thus enhancing clinician notifications and patient engagement through personalized feedback. A recent usability study indicated high satisfaction rates among users, although navigation challenges were noted, pointing to the need for continued enhancements.

2.4. *Session 4: challenges and opportunities for European countries registries and emerging digital solutions harmonization*

This session was chaired by Andreas Meisel and focused on the ethical, legal, and economic challenges of data sharing within the European countries, particularly regarding rare neuromuscular disorders (NMDs).

2.5. *Discussing the ERN-NMD initiative of a comprehensive EU registry on all NMD's*

Teresinha Evangelista presented the ERN EURO—NMD registry, which aims to unify data collection and improve care for individuals with rare neuromuscular diseases (NMDs) across Europe. As the first EU-wide patient registry for NMDs, it collects longitudinal clinical data to harmonize clinical practices, enhance patient care, and support research and policymaking. The initiative has faced challenges, particularly in European data sharing due to varying legal and regulatory frameworks across countries.

While GDPR provides a broad legal structure, national regulations differ, complicating data ownership, consent management, and ethical

approvals. To comply, the registry adopts customized, country-specific consent approaches and legal adaptations to meet local standards.

The registry uses centralized and decentralized data collection models. In the centralized model, patient data is entered directly, requiring patient consent and strict data-sharing agreements. The decentralized (hub-based) model is also in development to enables existing national registries to interoperate with EURO—NMDHub while keeping their databases, to perform joint data analysis without data transfer. A Data Sharing Agreement (DSA) in place among the 82 healthcare providers belonging to the ERN EURO—NMD. It defines the legal basis for data processing, outlining participant rights, security measures, data transfer policies, and storage conditions. The governance of the registry is overseen by a Steering Committee (SC), which provides strategic direction and oversight. The SC includes representatives from healthcare providers, patient organizations, and scientific experts from the EURO—NMD consortium.

2.6. Ethical and legal aspects: challenges toward a responsible European data sharing

Lorenzo Maggi talked about ethical and legal aspects: challenges toward a responsible European data sharing. Key challenges are mainly due to different legal and ethical frameworks across European countries, with need of local adaptations, because European member states interpret and implement GDPR differently and compliance must align with requirements from multiple national Data Protection Authorities. Moreover, definition of data ownership and governance structures may be very challenging considering that national rules in this regard vary, complicating cross-border data movement, and disputes over data ownership and usage rights when data crosses borders. Lastly, varying national laws and ethical requirements necessitate tailored, country-specific consent approaches. He presented as example the EURO—NMD registry. Eight guiding principles of this registry guarantee that its usefulness matches its legal and ethical high standards: 1) transparency; 2) accountability; 3) follow the rule of law; 4) integrity; 5) participation and inclusiveness; 6) impartiality and independence; 7) effectiveness, efficiency and responsiveness; 8) reflexivity and continuous quality improvement [46]. A Data Sharing Agreement is necessary for participating in the EURO—NMD Registry, requiring the signature of a hospital legal representative and ethics or regulatory approvals. Responsibilities and liabilities for GDPR compliance are shared among the Parties, which are EURO—NMD Registry Consortium and health care practitioners (HCPs) participating in the Registry (data providers). Participation in the EURO—NMD Registry adheres to a shared governance model defined by the Data Access Policy. Access to data is controlled by the Data Access Committee (DAC). Healthcare providers may have access to their own patients' data and to all registry data at an aggregated level; access to pseudonymized data requires DAC approval.

2.7. FAIR principles to ensure interoperability and facilitate federated analysis across registries

Peter-Bram't Hoen talked about the FAIR principles to ensure interoperability and facilitate federated analysis across neuromuscular disease registries, more specifically European national MG registries. The survey revealed a reasonable overlap in the data elements collected (Fig. 3), but the European national MG registries refer to these elements in different ways and different languages. Ontologies (hierarchical vocabularies) to standardize are hardly used. This makes it hard to assess which fields in the different registries map to the same data elements. The default approach to tackle this problem is to bring all individual registries data in a centralized European database. Several arguments suggest this may not be the best approach as it may lead to double work. For example, MG patients are not only registered in dedicated MG registries but should also be registered in national rare disease registries, and the EURO—NMD registry from the ERN for Neuromuscular Disorders [46]. A new centralized registry may be difficult to sustain, given that existing databases are difficult to sustain and mostly dependent on project funding [47]. Synchronization issues between the existing registry and the centralized registry may arise [48]. Governance on the data may be difficult to arrange as the governance of the individual registries may prevail [49]. Jurisdictions in some European countries may prevent sharing of data across borders. He presented, as possible solution, the EURO—NMD registry hub [46] in which queries or algorithms would travel to the data instead of data travelling to the algorithm. A prerequisite for the success of this project is that national MG registries will become FAIR. This means that data elements will be mapped to common ontologies and that (meta)data will be exposed in a secure manner through an interoperability layer like a FAIR Data Point (47). To join, MG registries will need to start using common ontologies, have their content transformed into machine readable formats such as the Resource Descriptive Framework (RDF), and deploy a few technical components to receive approved, safe and privacy-preserving queries and analysis algorithms.

2.8. Economical aspects: sustainability and funding strategies

Frederico Spandonaro talked about sustainability and funding for a European registry. He pointed out that MG treatment has reached a turning point thanks to the efficacy of new therapies, however, the innovation has also led to a solution of continuity in treatment costs. The price of the new therapies (sometimes over times the previous standard of care) is justified by their innovativeness, but also by the fact that MG is a rare disease. Elaborations from the administrative databases of the Italian NHS demonstrated that the cost of patients who experience exacerbations (presumably those most likely to be eligible for new therapies) is more than double (+107 %) than that of stable patients, mostly due to the incidence of hospitalization costs) [47]. Lastly, in view of the fact that MG is a rare disease, the considerations of equity linked to access should prevail over those of efficiency (cost-effectiveness) also because the budget impact of innovative therapies is limited by the rarity of eligible patients (considered around 5 % of total MG population). He also discussed that informed decisions require deeper knowledge into several factors, such as the savings from upcoming biosimilar molecules: the persistence of the effects of therapies and their real consumption in clinical practice, especially with personalized administration schedules. Another gap in knowledge is the consideration of how the efficacy aspects of molecules on the quality-of-life side, particularly their impact on the psychological aspects that concern patients. These considerations highlight the need for developing registries to collect the deficient information, generating evidence to support a correct and sustainable use of innovation, which is a condition for overcoming access barriers deriving from the limited resources available.

2.9. Session 5: conclusion and future perspectives

This session was chaired by Anja Hoffmeister and focused on summarizing the upcoming actions needed to reach future harmonization of National Myasthenia Gravis (MG) registries across Europe to allow future collaborations. The main goal of a European registry initiative is to improve the quality of care for patients with myasthenic syndromes. The sharing of high quality, aggregated, and harmonized data between national registries could greatly assist in driving regulatory decisions and ensuring more equitable management of MG patients across Europe. However, several challenges remain. First, meaningful large-scale, high-quality data sets on the long-term care of these patients from national registries are a prerequisite. These data sets, based on a large number of EU patients, will enable innovative projects, including epidemiological research, health services research and non-randomized analyses to assess the benefits of therapies. Currently, there are 10 registries including almost 7000 patients with myasthenic syndromes assessing data once-twice a year.

Workshop participants outlined key principles for developing a European MG registry. Foremost, the patient perspective must be integrated. This involves active participation of patient representatives in developing the core dataset, including personal assessments of disease burden. Additionally, patient representatives should be involved in planning analyses, interpreting and communicating results and solving data protection and transfer problems, including possible commercial use of the data. Furthermore, registry results are to be made available to patients in a way that is understandable to laypersons. Patients are to be enabled to enter their own data (e.g. via an app-based module for high-frequency PROM) and to access their own data (e.g. for benchmarking purposes).

Secondly, a European registry should be based on a robust infrastructure and a harmonized core data set. The database should be built on web-based, preferably open-access platforms (RedCap) according to the FAIR principles. The data set must contain key data elements defining mandatory and optional data sets, which have been defined by a modified Delphi procedure-based expert consensus on collectable data. Digital solutions like MG apps may encourage patient participation in registries and simplify data entry. The principles of the EMA Patient Registry Initiative should be considered. Furthermore, national registries should be registered, e.g. in the ERDRI to increase the visibility.

Thirdly, a European registry must be built on a strong governance structure. A Steering or Data Use Committee should be responsible for managing the registry together with patient organizations or patient advisory boards. Furthermore, the governance structure should define the mode as well as responsible persons for interacting with any EU-wide registry or data-sharing initiative on myasthenic syndromes. In doing so, the principles of representation of the interests of patients and those who make the registry possible through their work must be taken into account.

The fourth principle requires measures to ensure financial sustainability. To this end, multiple funding sources should be used, sustainable and ethical operating models should be employed, and maintaining transparency around funding sources. The role of pharmaceutical companies must be defined. An owner of the registry must be identified. Ideally, the registry should be owned by a MG patient organization, ensuring long-term commitment to its goals and the long-term viability of the registry.

For the success of a European registry, data entry must be as complete and convenient as possible. Moreover, patient participation and research opportunities are often the best motivator for success.

In conclusion, this workshop helped to strengthen a "taking and giving" culture within the network of the national registries, so that we can learn from each other to better reach our goals in order to optimize MG patient care.

3. Discussion and workshop deliverables

The ENMC workshop convened a diverse array of key stakeholders dedicated to the European standards for harmonization of MG registries and emerging digital solutions. Participants included representatives from the pharmaceutical industry, patient advocacy organizations, clinicians with expertise in MG, and members of the ERN—NMD alongside representatives from the EMA. This multidisciplinary composition fostered robust discussions and facilitated the identification of shared objectives for future endeavors. Throughout the workshop sessions, relevant topics emerged, highlighting both the challenges and strengths towards harmonizing data on MG in national registries and improving outcomes for patients with myasthenia.

From the patients' perspective, their active involvement in the design and functioning of MG registries is crucial. According to representatives of patient associations, it is essential to include patient-reported outcomes (PRO) to accurately reflect the lived experiences of individuals with MG. Concerns have been raised regarding data ownership, anonymity, and the ethical standards surrounding data management. Furthermore, there is an urgent need for equitable access to digital tools across different regions.

National registries for various diseases, particularly for rare conditions like MG, serve as platforms for observational studies and pharmacovigilance, significantly contributing to the enhancement of patient care standards. Digital solutions, including telemedicine and mobile health applications, have been discussed as essential tools for improving communication between patients and clinicians, as well as for monitoring disease progression [50]. The regulatory perspectives of the EMA have highlighted the crucial role of registries in risk management and product evaluation for orphan drugs. The EMA's initiatives aim to address challenges related to data quality, patient participation, and interoperability among existing registries [19].

In the realm of digital solutions, innovative tools such as Myalink, ME&MG™, and LumiiMG were showcased, demonstrating advancements in remote monitoring and patient engagement. These technologies aim to empower patients through real-time data collection while enhancing clinicians' access to comprehensive patient information.

The workshop concluded with a discussion of the ethical, legal, and economic challenges of data sharing within the Europe, especially concerning rare diseases. The discussions underscored the necessity of a robust governance framework, financial sustainability, and patient involvement in registry initiatives. Ultimately, the workshop fostered a spirit of collaboration among participants, emphasizing the importance of integrating diverse stakeholder perspectives to optimize care for MG patients across Europe.

Funding

The workshop was funded by the ENMC organization and supported by Alexion, Argenx, Johnson & Johnson Medicine, Roche and UCB.

278th ENMC Workshop participants

Prof. Andreas Meisel (Department of Neurology, Charité - Universitätsmedizin Berlin, 10,117, Berlin, Germany).

Prof. Ernestina Santos (Neurology Department, Centro Hospitalar Universitário de Santo António, Porto; Unit for Multidisciplinary Research in Biomedicine, Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal).

Prof. Jan Verschuuren (Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands).

Prof. Nils Erik Gilhus (Department of Clinical Medicine, University of Bergen, Bergen, Norway).

Prof. Pascal Laforêt (Nord/Est/Île-de-France Neuromuscular Reference Center, FHU PHENIX, AP-HP, Raymond-Poincaré Hospital, Department of Neurology, Garches, France).

Prof. Peter-Bram Hoen (Radboud University Medical Center, Nijmegen, Netherlands).

Prof. Sabrina Sacconi (Peripheral Nervous System & Muscle Department, Reference Center for Neuromuscular Disorders, Pasteur 2 Hospital, Nice University Hospital, Nice, France).

Dr. Adela Della Marina (Department of Pediatric Neurology, Centre for Neuromuscular Disorders, C-TNBS, University Duisburg-Essen, Essen, Germany).

Dr. Carlo Antozzi (Neuroimmunology and Neuromuscular Diseases Unit, Immunotherapy and Apheresis Departmental Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy).

Dr. Elena Cortes Vicente (Neuromuscular Diseases Unit, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain).

Dr. Emmanuelle Salort Campana (Referral Centre for Neuromuscular Diseases and ALS, Hospital La Timone, Aix-Marseille University, Marseille, France).

Dr. Fiammenta Vanoli (Neuroimmunology and Neuromuscular Diseases Unit, Immunotherapy and Apheresis Departmental Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy).

Dr. Frauke Stascheit (Department of Neurology, Charité - Universitätsmedizin Berlin, 10,117, Berlin, Germany).

Dr. Lorenzo Maggi (Neuroimmunology and Neuromuscular Diseases Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy).

Dr. Mohammad Ashragi (Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK).

Dr. Renato Mantegazza (Neuroimmunology and Neuromuscular Diseases Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy).

Dr. Stanislav Vohanka (Department of Neurology, Faculty of Medicine, University Hospital Brno, Masaryk University, Brno, Czechia).

Dr. Susanna Brauner (Department of Neurology, Karolinska University Hospital, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden).

Dr. Terenshina Evangelista (Department of Neuropathology, Sorbonne University, Reference Center for Muscle Diseases Paris-Est, Myology Institute, APHP, Pitié-Salpêtrière Hospital, 75,013 Paris, France).

Dr. Frederico Spandonaro (C.R.E.A. Sanità (Centre for Applied Economic Research in Healthcare, Rome, Italy).

Anja Hoffmeister (Deutsche Myasthenie Gesellschaft, Germany).

Charlotte Gary (Johnson & Johnson).

Cheryl Hudson (UCB Pharma).

Filip Callawaert (argenx, Ghent, Belgium).

JT Tibung (Alexion, AstraZeneca Rare Disease).

Ludgarde Allard (Myasthenia Group, Belgian Association against Neuro-Muscular Diseases, Belgium).

Matthieu Lusignan (Myasthenia Group, AFM Telethon, France).

Raqual Pardo (Asociación Miastenia de España, Spain).

Disclaimer

The opinions presented in this article are solely those of the authors and should not be interpreted or cited as representing the views of the agencies or organizations with which the authors are associated.

CRediT authorship contribution statement

Sabrina Sacconi: Writing – original draft, Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing. **Fiammetta Vanoli:** Writing – review & editing. **Frauke Stascheit:** Writing – review & editing. **Elena Cortés-Vicente:** Conceptualization, Methodology, Validation, Writing – review & editing. **Renato Mantegazza:** Writing – review & editing, Conceptualization, Methodology, Validation. **Andreas Meisel:** Conceptualization, Methodology, Validation, Writing – review & editing.

Declaration of competing interest

Sabrina Sacconi is a speaker who has collaborated with Sanofi, LFB, Biogen, Alnylam, Dyne Therapeutics, Lupin, UCB Pharma, argenx, Alexion, Fulcrum Therapeutics, and Takeda. She has also received funding for scientific projects from Sanofi, Biogen, Roche, Pfizer, Lupin, UCB Pharma, and Huma.

Andreas Meisel is an advisor, consultant, speaker, and/or investigator and has received research grants (paid to his institution) and honoraria from Alexion AstraZeneca Rare Disease, argenx, Axunio, Grifols, Hormosan, Immunovant, Janssen, Merck, Novartis, Octapharma, Regeneron, Sanofi and UCB. He served as chairman of the medical advisory board of the German Myasthenia Gravis Society.

Elena Cortés-Vicente received public speaking honoraria and compensation for advisory boards and/or consultations fees from UCB, argenx, Alexion, Janssen and Lundbeck.

Renato Mantegazza has received funding for Travel, Meeting attendance or Advisory Board participation from Alexion, argenx, Biomarin, Catalyst, SANOFI, Regeneron, Merck and UCB.

Frauke Stascheit received travel/accommodation/meeting expenses from Alexion Pharmaceuticals and argenx, received speaking honoraria and honoraria for attendance at advisory boards from

Alexion Pharmaceuticals, argenx and UCB pharma. She received research grants from Alexion Pharmaceuticals and Octapharma and grants for administrative support for the German myasthenia gravis registry from the German Myasthenia gravis Society e.V.

Fiammetta Vanoli received compensation for travel, meeting attendance, consultation and speaking by Alexion Pharmaceuticals, UCB Pharma, argenx, and Biogen.

Acknowledgments

The workshops and next generation programme are made possible thanks to the financial support of the European Neuromuscular Centre (ENMC) and its Full Partners: Association Française contre les Myopathies (France), Deutsche Gesellschaft für Muskelkranke (Germany), Muscular Dystrophy Campaign (UK), Muskelsvindfonden (Denmark), Prinses Beatrix Spierfonds (The Netherlands), Schweizerische Stiftung für die Erforschung der Muskelkrankheiten (Switzerland), Spierziekten Nederland (The Netherlands), Telethon Foundation (Italy). In addition, we would like to thank the Associated Partners: Österreichische Muskelforschung (Austria), SMA Europe, TREAT-NMD, World Duchenne Organisation, World Muscle Society (WMS), and the members of the ENMC Company Forum: Amicus Therapeutics, Dyne Therapeutics, Lupin Neuroscience, Novartis, Roche, Sanofi, Santhera and Sarepta. We would like to express our sincere gratitude to the patient associations for their active contributions: AFM Telethon (Myasthenia Group), Deutsche Myasthenie Gesellschaft, EURORDIS, the Italian Association of Myasthenia Gravis, Asociación Miastenia de España (AMES), and the Belgian Association Against Neuro-Muscular Diseases (Myasthenia Group). Their valuable input and unwavering support have been instrumental throughout this research. We would like to thank Abderhmane Slioui and Laura Bouchareychas for their contributions to the writing of this manuscript. Additionally, we extend our appreciation to the pharmaceutical companies—Alexion Pharmaceuticals, argenx, Johnson & Johnson, and UCB Pharma—for their participation in this important discussion.

References

[1] Carr AS, Cardwell CR, McCarron PO, McConville J. A systematic review of population based epidemiological studies in Myasthenia Gravis. BMC Neurol 2010; 10:46. https://doi.org/10.1186/1471-2377-10-46.

[2] Phillips LH. The epidemiology of myasthenia gravis. Ann N Y Acad Sci 2003;998: 407–12. https://doi.org/10.1196/annals.1254.053.

[3] Gilhus NE, Tzartos S, Evoli A, Palace J, Burns TM, Verschuuren JJGM. Myasthenia gravis. Nat Rev Dis Primer 2019;5:30. https://doi.org/10.1038/s41572-019-0079-y.

[4] Meriggioli MN, Sanders DB. Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity. Lancet Neurol 2009;8:475–90. https://doi.org/10.1016/S1474-4422(09)70063-8.

[5] Alhaidar MK, Abumurad S, Soliven B, Rezania K. Current treatment of Myasthenia Gravis. J Clin Med 2022;11:1597. https://doi.org/10.3390/jcm11061597.

[6] Sanders DB, Wolfe GI, Benatar M, Evoli A, Gilhus NE, Illa I, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology 2016;87:419–25. https://doi.org/10.1212/WNL.0000000000002790.

[7] Vu T, Meisel A, Mantegazza R, Annane D, Katsuno M, Aguzzi R, et al. Terminal complement inhibitor Ravulizumab in generalized Myasthenia Gravis. NEJM Evid 2022;1. https://doi.org/10.1056/EVIDoa2100066. EVIDoa2100066.

[8] Howard JF, Bril V, Vu T, Karam C, Peric S, Margania T, et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. Lancet Neurol 2021;20:526–36. https://doi.org/10.1016/S1474-4422(21)00159-9.

[9] Antozzi C, Vu T, Ramchandren S, Nowak RJ, Farmakidis C, Bril V, et al. Safety and efficacy of nipocalimab in adults with generalised myasthenia gravis (Vivacity-MG3): a phase 3, randomised, double-blind, placebo-controlled study. Lancet Neurol 2025;24:105–16. https://doi.org/10.1016/S1474-4422(24)00498-8.

[10] Iorio R. Myasthenia gravis: the changing treatment landscape in the era of molecular therapies. Nat Rev Neurol 2024;20:84–98. https://doi.org/10.1038/s41582-023-00916-w.

[11] Forrest CB, Bartek RJ, Rubinstein Y, Groft SC. The case for a global rare-diseases registry. Lancet Lond Engl 2011;377:1057–9. https://doi.org/10.1016/S0140-6736(10)60680-0.
[12] Slioui A, Tammam G, Vanoli F, Marina AD, Vohanka S, Gilhus NE, et al. Toward European harmonization of national myasthenia gravis registries: modified Delphi procedure-based expert consensus on collectable data. Orphanet J Rare Dis 2025; 20:115. https://doi.org/10.1186/s13023-024-03520-3.
[13] Stausberg J, Harkener S, Semler SC. Recent trends in patient registries for health services research. Methods Inf Med 2021;60:e1–8. https://doi.org/10.1055/s-0041-1724104.
[14] Irgens LM. The origin of registry-based medical research and care. Acta Neurol Scand Suppl 2012:4–6. https://doi.org/10.1111/ane.12021.
[15] Baggi F, Mantegazza R, Antozzi C, Sanders D. Patient registries: useful tools for clinical research in myasthenia gravis. Ann N Y Acad Sci 2012;1274:107–13. https://doi.org/10.1111/j.1749-6632.2012.06771.x.
[16] ERDRI.dor 2025 https://eu-rd-platform.jrc.ec.europa.eu/erdridor/ (accessed March 4, 2025).
[17] Boulanger V, Schlemmer M, Rossov S, Seebald A, Gavin P. Establishing patient registries for rare diseases: rationale and challenges. Pharm Med 2020;34:185–90. https://doi.org/10.1007/s40290-020-00332-1.
[18] Gliklich RE, Dreyer NA. Registries for evaluating patient outcomes: A user's guide. 2nd ed. Rockville (MD): Agency for Healthcare Research and Quality (US); 2010.
[19] Guideline on registry-based studies - scientific guideline | European Medicines Agency (EMA) 2021. https://www.ema.europa.eu/en/guideline-registry-based-studies-scientific-guideline (accessed December 11, 2024).
[20] Ramos-Fransi A, Rojas-García R, Segovia S, Márquez-Infante C, Pardo J, Coll-Cantí J, et al. Myasthenia gravis: descriptive analysis of life-threatening events in a recent nationwide registry. Eur J Neurol 2015;22:1056–61. https://doi.org/10.1111/ene.12703.
[21] Cortés-Vicente E, Álvarez-Velasco R, Segovia S, Paradas C, Casasnovas C, Guerrero-Sola A, et al. Clinical and therapeutic features of myasthenia gravis in adults based on age at onset. Neurology 2020;94:e1171–80. https://doi.org/10.1212/WNL.0000000000008903.
[22] Álvarez-Velasco R, Gutiérrez-Gutiérrez G, Trujillo JC, Martínez E, Segovia S, Arribas-Velasco M, et al. Clinical characteristics and outcomes of thymoma-associated myasthenia gravis. Eur J Neurol 2021;28:2083–91. https://doi.org/10.1111/ene.14820.
[23] Cortés-Vicente E, Álvarez-Velasco R, Pla-Junca F, Rojas-Garcia R, Paradas C, Sevilla T, et al. Drug-refractory myasthenia gravis: clinical characteristics, treatments, and outcome. Ann Clin Transl Neurol 2022;9:122–31. https://doi.org/10.1002/acn3.51492.
[24] Myasthenie Register. Dtsch Myasthenie Ges EV n.d. https://dmg.online/myasthenie-register/ (accessed March 4, 2025).
[25] Leiden L.A. 2 2333 Z. Nederlands-Belgisch Myasthenie Register. myasthenieën 2018. https://mgexpertisecentrum.nl/research/nederlands-belgisch-myasthenie-register/ (accessed March 4, 2025).
[26] Fang F, Sveinsson O, Thormar G, Granqvist M, Askling J, Lundberg IE, et al. The autoimmune spectrum of myasthenia gravis: a Swedish population-based study. J Intern Med 2015;277:594–604. https://doi.org/10.1111/joim.12310.
[27] Swedish Neuromuscular Association. Myastenia Gravis (MG), Svenskt konsensusprogram 2024:23.
[28] Registr MyReg: Úvod 2025 https://myreg.registry.cz/index.php (accessed March 4, 2025).
[29] Willumsen JS, Grytten N, Aarseth J, Myklebust TÅ, Myhr KM, Midgard R. Mortality and cause of death in multiple sclerosis in western Norway 1950-2021: a registry-based linkage study. J Neurol Neurosurg Psychiatry 2022;93:1154–61. https://doi.org/10.1136/jnnp-2022-329169.
[30] Andersen JB, Engeland A, Owe JF, Gilhus NE. Myasthenia gravis requiring pyridostigmine treatment in a national population cohort. Eur J Neurol 2010;17:1445–50. https://doi.org/10.1111/j.1468-1331.2010.03089.x.
[31] Engebretsen I, Gilhus NE, Kristiansen IS, Sæther EM, Lindberg-Schager I, Arneberg F, et al. The epidemiology and societal costs of myasthenia gravis in Norway: a non-interventional study using national registry data. Eur J Neurol 2024;31:e16233. https://doi.org/10.1111/ene.16233.
[32] Andersen JB, Heldal AT, Engeland A, Gilhus NE. Myasthenia gravis epidemiology in a national cohort; combining multiple disease registries. Acta Neurol Scand Suppl 2014:26–31. https://doi.org/10.1111/ane.12233.
[33] Santos E, Coutinho E, Moreira I, Silva AM, Lopes D, Costa H, et al. Epidemiology of myasthenia gravis in Northern Portugal: frequency estimates and clinical epidemiological distribution of cases. Muscle Nerve 2016;54:413–21. https://doi.org/10.1002/mus.25068.
[34] Evoli A, Batocchi AP, Bartoccioni E, Lino MM, Minisci C, Tonali P. Juvenile myasthenia gravis with prepubertal onset. Neuromuscul Disord NMD 1998;8:561–7. https://doi.org/10.1016/s0960-8966(98)00077-7.
[35] VanderPluym J, Vajsar J, Jacob FD, Mah JK, Grenier D, Kolski H. Clinical characteristics of pediatric myasthenia: a surveillance study. Pediatrics 2013;132:e939–44. https://doi.org/10.1542/peds.2013-0814.
[36] Heckmann JM, Europa TA, Soni AJ, Nel M. The epidemiology and phenotypes of ocular manifestations in childhood and juvenile myasthenia gravis: a review. Front Neurol 2022;13:834212. https://doi.org/10.3389/fneur.2022.834212.
[37] Ionita CM, Acsadi G. Management of juvenile myasthenia gravis. Pediatr Neurol 2013;48:95–104. https://doi.org/10.1016/j.pediatrneurol.2012.07.008.
[38] Munot P, Robb SA, Niks EH, Palace J, ENMC workshop study group. Corrigendum to "workshop report: 242nd ENMC international workshop: diagnosis and management of juvenile myasthenia gravis, Hoofddorp, The Netherlands, 1-3 March 2019" [Neuromuscular Disorders 30 (2020) 254-264]. Neuromuscul Disord NMD 2021;31:264. https://doi.org/10.1016/j.nmd.2021.02.003.
[39] Brandsema JF, Ginsberg M, Hoshino H, Mimaki M, Nagata S, Rao VK, et al. Eculizumab in adolescent patients with refractory generalized Myasthenia Gravis: a phase 3, open-label, multicenter study. Pediatr Neurol 2024;156:198–207. https://doi.org/10.1016/j.pediatrneurol.2024.04.020.
[40] Stein M, Meisel A, Mönch M, Narayanaswami P, Sun H, Herdick M, et al. The telemedical platform MyaLink for remote monitoring in myasthenia gravis - rationale and protocol for a proof of concept study. J Neuromuscul Dis 2024: 22143602241296310. https://doi.org/10.1177/22143602241296314.
[41] Stein M, Stegherr R, Narayanaswami P, Legg D, Herdick M, Meisel A, et al. App- and wearable-based remote monitoring for patients with Myasthenia Gravis and its specialists: feasibility and usability study. JMIR Form Res 2025;9:e58266. https://doi.org/10.2196/58266.
[42] Berrih-Aknin S, Palace J, Meisel A, Claeys KG, Muppidi S, Saccà F, et al. Patient-reported impact of myasthenia gravis in the real world: findings from a digital observational survey-based study (MyRealWorld MG). BMJ Open 2023;13:e068104. https://doi.org/10.1136/bmjopen-2022-068104.
[43] Berling E., Orlikowski D., Nicolas G., Prigent H., N'Dah Sekou G., Carment L., et al. 2025 ME&MG, novel digital device for patients with generalized Myasthenia gravis: a first step towards validation (P1-11.016) 04092024;102.
[44] The ME&MG Digital Solution for autonomous assessment of Myasthenia Gravis. CtvVeevaCom 2025 https://ctv.veeva.com/study/the-me-mg-digital-solution-for-autonomous-assessment-of-myasthenia-gravis (accessed March 12, 2025).
[45] Descriptive analysis of real-world data collected with ME&MGopen 2025 https://inclinicaltrials.com/myasthenia-gravis/NCT05566964/ (accessed March 12, 2025).
[46] Atalaia A, Wandrei D, Lalout N, Thompson R, Tassoni A, 't Hoen PAC, et al. EURO-NMD registry: federated FAIR infrastructure, innovative technologies and concepts of a patient-centred registry for rare neuromuscular disorders. Orphanet J Rare Dis 2024;19:66. https://doi.org/10.1186/s13023-024-03059-3.
[47] Antonini G, Habetswallner F, Inghilleri M, Mantegazza R, Rodolico C, Saccà F, et al. Real world study on prevalence, treatment and economic burden of myasthenia gravis in Italy. Heliyon 2023;9:e16367. https://doi.org/10.1016/j.heliyon.2023.e16367.
[48] Dos Santos Vieira B, Bernabé CH, Zhang S, Abaza H, Benis N, Cámara A, et al. Towards FAIRification of sensitive and fragmented rare disease patient data: challenges and solutions in European reference network registries. Orphanet J Rare Dis 2022;17:436. https://doi.org/10.1186/s13023-022-02558-5.
[49] Groenen KHJ, Jacobsen A, Kersloot MG, Dos Santos Vieira B, van Enckevort E, Kaliyaperumal R, et al. The de novo FAIRification process of a registry for vascular anomalies. Orphanet J Rare Dis 2021;16:376. https://doi.org/10.1186/s13023-021-02004-y.
[50] Mumtaz H, Riaz MH, Wajid H, Saqib M, Zeeshan MH, Khan SE, et al. Current challenges and potential solutions to the use of digital health technologies in evidence generation: a narrative review. Front Digit Health 2023;5:1203945. https://doi.org/10.3389/fdgth.2023.1203945.