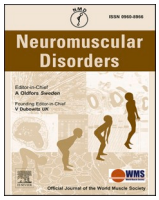
Neuromuscular Disorders 58 (2026) 106257

Contents lists available at ScienceDirect

Neuromuscular Disorders

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



287th ENMC international workshop: Harmonization and federated analysis of myotonic dystrophy registries to model heterogeneous disease trajectories. Hoofddorp, the Netherlands, 28–30 March 2025

Leandre A. la Fontaine [a,b,*,1], Daniël van As [c,d,1], Guillaume Bassez [e], Nicholas E. Johnson [f], Catharina G. Faber [a,b], Peter A.C.'t Hoen [c], on behalf of the 287th ENMC workshop participants

[a] Department of Neurology, Maastricht University Medical Center, Maastricht, the Netherlands
[b] Mental Health and Neuroscience Research Institute (MHeNS), Maastricht University, Maastricht, the Netherlands
[c] Department of Medical BioSciences, Radboud university medical center, Nijmegen, the Netherlands
[d] Department of Neurology, Donders Institute for Brain, Cognition, and Behaviour, Radboud university medical center, Nijmegen, the Netherlands
[e] Institute of Myology, French National Center for Scientific Research, Paris, France
[f] Department of Neurology, Richmond Commonwealth University, Richmond, USA

ARTICLE INFO

Keywords:
Myotonic dystrophy type 1 (DM1)
Patient registries
Fair data principles
Federated analysis
Disease trajectory modeling
Personalized medicine

ABSTRACT

The 287th ENMC International Workshop convened experts from ten countries to address the harmonization and federated analysis of Myotonic Dystrophy Type 1 (DM1) registries. With over 10,500 patients enrolled globally, registries remain fragmented, limiting their utility in modeling disease trajectories and supporting clinical trials. As new therapies enter advanced clinical testing, registries must evolve - not only to enable trial readiness but also to support downstream functions like pharmacovigilance. The workshop focused on four objectives: redefining a core dataset, enabling FAIRification of registries, establishing federated analysis infrastructure, and developing longitudinal modeling strategies. Key outcomes included a revised core set of clinical and patient reported outcome measures that is feasible to collect in a routine care setting, strategies for FAIR data integration, and governance models for federated analysis. Pragmatic and interpretable statistical approaches such as latent variable modeling and unsupervised clustering were discussed, with key prediction targets identified across motor, cardiac, and pulmonary domains. The workshop emphasized the need for sustainable funding, patient-centered design, and international collaboration.

Introduction

The 287th ENMC international Workshop on "Harmonization and federated analysis of myotonic dystrophy registries to model heterogeneous disease trajectories" took place from 28th to the 31st of March 2025. The workshop convened 22 participants from 10 countries - including medical doctors, researchers, and representatives from patient advocacy groups and pharmaceutical companies - to explore challenges and opportunities in patient registry-based data collection and analysis for Myotonic Dystrophy Type 1 (DM1).

Myotonic Dystrophy type 1 (DM1) is a multisystemic, heterogeneous, and progressive neuromuscular disorder characterized by progressive muscle weakness and myotonia. The global prevalence is estimated at 1 in 8000, with significantly higher rates in certain regions, such as 1 in 2100 in New York State [1,2]. DM1 has considerable variability in symptom severity and symptom occurrence [3]. Alongside locomotor degeneration, patients with DM1 experience multisystemic symptoms such as gastrointestinal, pulmonary and cardiac dysfunction [4–7]. However, the clinical variability of DM1 poses significant challenges for tracking disease trajectories and evaluating therapeutic efficacy, especially in the context of therapeutic trials.

Multiple DM1 patient registries have been established worldwide to address these core challenges associated with the disease. One of the primary goals is to better understand the heterogeneity and progression of the disease, thereby enabling more targeted clinical trials for individuals with shared disease characteristics. Registries also facilitate

* Corresponding author.
E-mail address: leandre.la.fontaine@mumc.nl (L.A. la Fontaine).
[1] These authors contributed equally to this paper. Early career researchers.

https://doi.org/10.1016/j.nmd.2025.106257
Received 21 October 2025; Accepted 23 October 2025
Available online 24 October 2025

rapid patient recruitment, as demonstrated in the largest DM1 trial to date (OPTIMISTIC), and may support pharmacovigilance, including post-marketing surveillance, in the future [8]. Although >10,500 adult DM1 patients are enrolled in 22 different patient registries, this is estimated to be <1 % of the global DM1 population when taking the prevalence into account [9]. Consequently, deriving meaningful insights requires pooled data from multiple registries, but fragmentation and inconsistent outcome measures used hinder interoperability and large-scale evaluation.

Within the DM1 community, there is a growing recognition - and a sense of urgency - to optimize the collection of relevant disease information while simultaneously adopting FAIR (Findable, Accessible, Interoperable, and Reusable) principles to enhance interoperability. This urgency is particularly driven by significant progress in the development of disease-modifying therapies, with several therapeutic strategies now in advanced stages of clinical testing [10]. In response, this workshop focused on four key objectives: (1) define a core set of data elements in support of standardized data collection, (2) enable, and provide guidelines for FAIRifcation of patient registries, (3) to establish a federated analysis infrastructure and to (4) set up a longitudinal data analysis plan to facilitate individual disease trajectory modeling.

Workshop objectives

Defining a core set of data elements in support of standardized data collection

Previous workshops dedicated to defining core data elements and standardizing outcome measures for DM1 have established a crucial foundation for collaborative research and clinical trial enrolment [11–13]. A key set of outcome measures to be collected, referred to as the 'Naarden dataset', was established in 2009 and is currently adopted by the majority of all DM1 registries [9]. However, over time several limitations of the current Naarden dataset have become apparent, such as its reliance on yes/no questions, which make it unsuitable for tracking longitudinal disease progression, and its lack of instruments that can successfully capture the granularity of domain-specific (treatment) effects over time. Additionally, previous attempts that aimed to harmonize data elements failed to provide standard operating procedures (SOPs) for the selected outcomes.

It has become increasingly clear that registries serve different objectives, and the emergence of new therapies is actively reshaping the way registries should operate. There is now broad recognition that both pharmaceutical endpoints, which prioritize simple, robust and objective measures suitable for regulatory approval, and broader instruments that measure (patient-reported) quality of life (QoL), are necessary for comprehensive understanding of disease progression and treatment impact. QoL measures are crucial for evaluating the real-world effectiveness of pharmaceutical treatments, as improvements in clinical endpoints do not always translate to enhanced patient well-being. While muscular symptoms are often emphasized in clinical trials, patients consistently report non-muscular symptoms such as fatigue and gastrointestinal symptoms as burdensome in daily life. Furthermore, currently used endpoints often fail to correlate with real life functional improvements as experienced by patients, underscoring a gap between measurable change and meaningful change. A consensus was achieved that the selection and prioritization of outcome measures must therefore reflect both the clinicians' and patients' perspectives. For the patients' perspective, family members can play a crucial role in identifying which disease domains should be prioritized for data collection, as physicians and/or patients may have blind spots with regards to certain aspects of the disease.

In the growing landscape of clinical trials, the focus of patient registries must grow accordingly. While previous efforts focused on collecting information to identify patients for clinical trials and minimize the burden on patients and caregivers, this workshop came to the agreement that more comprehensive outcome measures should be collected. The emergence of new clinical trials necessitates not only the identification of trial-eligible cohorts but also supporting pharmacovigilance in a post-marketing surveillance setting.

In the preparatory work for the workshop, an inventory of registries was compiled detailing the number and subtypes of DM1 patients included (Fig. 1), as well as the outcome measures most frequently collected across these registries (Fig. 2; see Supplementary Table 1 for a more detailed overview of all collected outcome measures per registry). Together with the criteria outlined above, this inventory formed the foundation for discussions on which outcome measures should be prioritized in future data collection efforts. The results of this multidisciplinary dialogue are summarized in Table 1, which presents a proposed set of outcome measures to be adopted in the near future. Similar to the Naarden set of 2009, the list includes mandatory items to be collected by all registries. Especially for starting registries with potentially limited funding, it is advisable to strive for the complete set of mandatory items as soon as possible. The data elements listed in Table 1 are designed to align with EMA/FDA pharmacovigilance requirements, including post-marketing surveillance. Other outcome measures that are currently used in different DM registries, including the 6-minute walk test, 2-minute walk test, quantitative muscle testing (QMT), timed up and go (TUG), 9-Hole Peg Test (9HPT), Forced Vital Capacity in supine position, peak cough flow, and the Myotonic Dystrophy Health Index short form (MDHI-SF), were not included in the set of core data elements because they are less feasible to perform in a routine care setting given resource and time demands. Table 1 and its future modifications and specifications are available from Zenodo via this link: https://doi.org/10.5281/zenodo.17241361. This archive will be complemented with the exact definitions of the outcome measures, in human and computer-interpretable formats, and standard operating procedures (SOPs) describing the exact execution of the different tests.

All workshop participants recognized that it is important but currently difficult to assess symptoms of the gastrointestinal and the central nervous system (CNS), and that more research is needed to be able to include these outcomes in a set of core data elements. For the CNS, the utility of the CogState tool is currently evaluated in the END-DM1 study, but is unlikely to be used in a routine outpatient clinic setting. A dedicated ENMC workshop (#288 "Towards better diagnosing, understanding and treating gastrointestinal symptoms in myotonic dystrophy") took place in May 2025 [14]. We suggest to use the questionnaire resulting from this workshop.

Advancements in digital tools - such as wearable technologies and mobile reporting - were acknowledged as promising avenues for capturing real-time, real-world, patient-relevant data. However, participants emphasized that additional research is required to evaluate their utility before they can be systematically integrated into patient registries. It was also noted that resource constraints and funding limitations restrict data completeness and threaten the long-term sustainability of data collection efforts. Moreover, while many research centers currently collect data on an annual basis, more frequent patient visits are likely warranted as new therapies become available, which may further increase the burden for data entry and hence the need for resources for sustained data collection.

The majority of current recommendations were observed to be based on expert opinions, with a systematic quantitative analysis of metrological properties using historical data still lacking. A discussion on composite scores - outcome measures that aim to capture multiple disease domains within a single instrument - yielded mixed reactions. Some participants viewed this approach as beneficial, particularly for clinical trial recruitment. In contrast, others cautioned that the clinical heterogeneity of the disease may dilute symptom representation or treatment effects when using such measures.

FAIRification of patient registries

The effort to make patient registries FAIR (Findable, Accessible, Interoperable and Reuseable) emerged from a growing recognition that

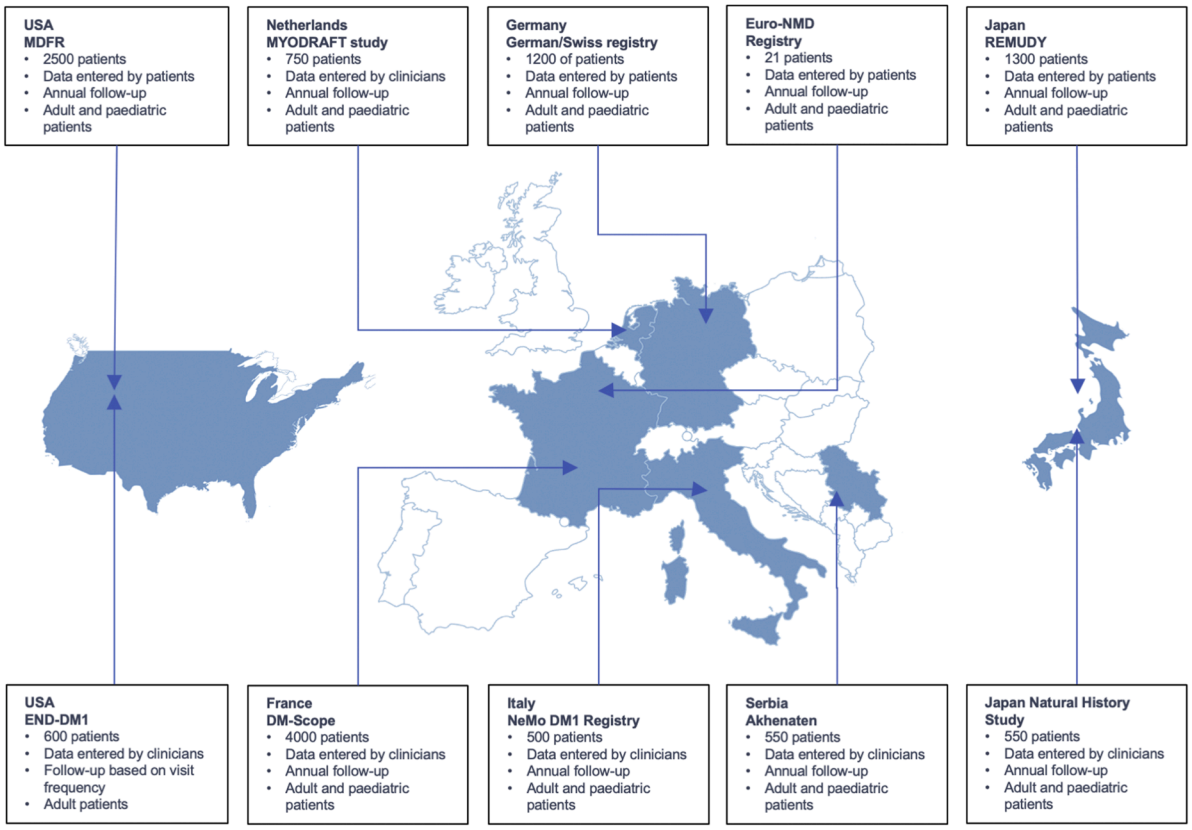


Fig. 1. Overview of DM1 Registries participating in this workshop. Except for the END-DM1 registry, where recordings are based on visit frequency, annual follow-ups are recorded. Note: The END-DM1 registry operates worldwide.

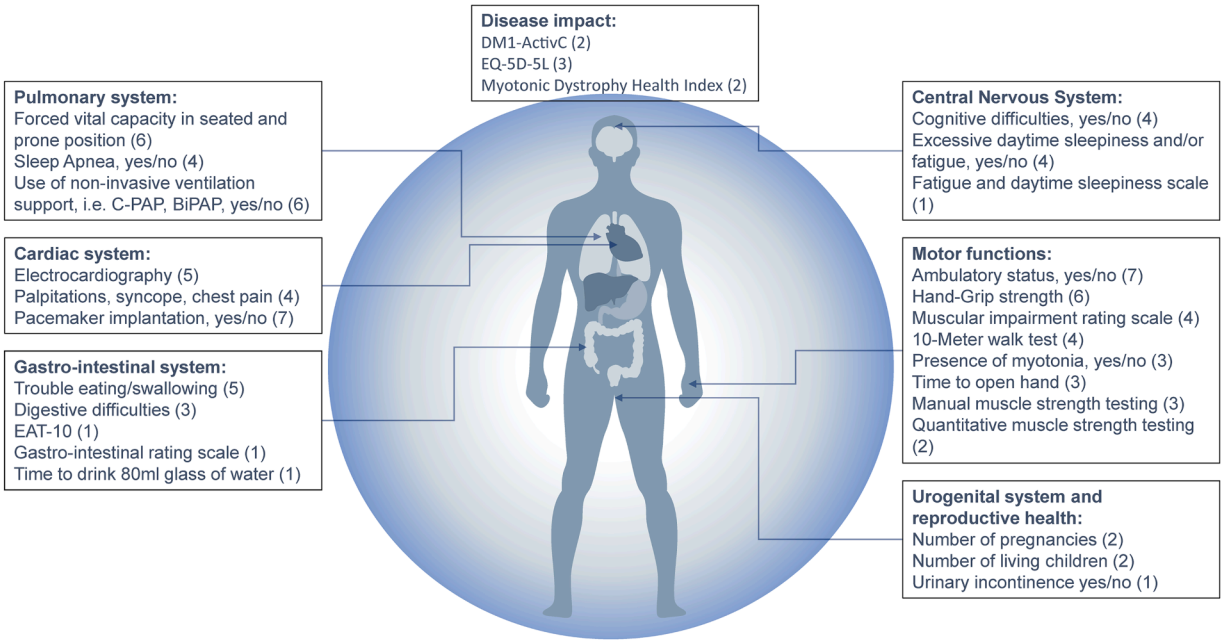


Fig. 2. Overview of outcome measures used in the ten participating registries. The numbers indicate the number of registries that use that outcome measure. Outcome measures that are infrequently used are not depicted in this figure.

current DM1 data remains largely underutilized and fragmented, limiting its potential for guiding therapeutic development and improving care. This underutilization arises from several challenges of classical meta-analysis frameworks, including legal barriers of data sharing, inconsistencies in outcome measures, variations in software infrastructure, and differences in how outcomes are recorded - such as units and language. FAIRification of data elements can help address these issues by promoting standardized metadata, harmonized terminologies, and machine-readable formats, thereby enabling more seamless data integration and reuse across studies and platforms.

Table 1
Proposed mandatory elements to be used in patient registries.

Disease domain	Mandatory items
General	- [n] Demographic details: name, date of birth, contact details - [n] Age at first symptom onset in years - Subtype: congenital, childhood, adult-onset, late-onset - [n] Genetic diagnosis: progenitor allele length and transmission (paternal or maternal) - [n] Medication usage: use of anti-myotonic drugs (e.g., mexiletine); yes/no, stimulant (e.g., modafinil) for daytime sleepiness; yes/no
Musculoskeletal	- [n] Ambulatory status; yes/no - Walking speed (10-meter walk run test; 10MWRT) - Global muscle strength (Manual muscle testing; 11 muscle pairs) - Global muscle impairment (Muscular Impairment Rating Scale; MIRS) - Handgrip strength (JAMAR dynamometer) - Lower limb performance test (Sit to stand test)
Myotonia	- [n] Myotonia present; yes/no - Hand opening time (HOT) in seconds
Cardiac	- [n] Symptoms: palpitations, syncope, orthopnea, dizziness; yes/no - [n] ECG (Holter): heartrate frequency, QRS interval, PR interval - [n] Cardiac device (ICD, pacemaker); yes/no
Pulmonary	- [n] Symptoms: morning headache, sleepiness during day, wake up not well rested, orthopnea, excessive night sweats, vivid dream; yes/no - [n] Use of (non-)invasive ventilation; yes/no - [n] Forced vital capacity (FVC) sitting - Number of pulmonary infections in the last year.
Gastro-intestinal	- Gastrointestinal Symptoms Questionnaire
Central nervous system*	- [n] Fatigue and daytime sleepiness (Fatigue and daytime sleepiness scale; FDSS)
Ophthalmologic	- [n] Cataract surgery; yes/no
Activity-participation level	- DM1-Activ[C]
For post-marketing purposes only (work in progress needs regulatory review)	- *Patient global impression of change (PGIC)* - *Systematically monitor and report new symptoms post-treatment using standard adverse event protocols.* - *Ensure compliance with EMA/FDA pharmacovigilance guidelines, including post-marketing surveillance and potentially increasing measurement frequency beyond annual assessments.*

[n] Mandatory or highly encouraged items in the 2009 Naarden dataset.
* At this point, no outcome measures could be identified for the cognitive domain.

Note: Consult the doi for the most up to date version of this table: https://doi.org/10.5281/zenodo.17241361.

Pre-workshop FAIRification efforts laid the foundation for the discussions that followed during the workshop. First, the Clinical And Registry Entries (CARE) Semantic Model (CARE-SM) was selected as semantic data model, because CARE-SM was developed within the European Joint Programme on Rare Diseases (EJP-RD) for the modelling of data concerning rare disease patients and because it is continued to be used and developed in its successor program, the European Rare Diseases Research Alliance (ERDERA) [15]. Second, each data element within a registry must be cross-referenced to a common ontology term. Preferably, this is a term from an existing ontology, like the SNOMED-CT ontology, with a unique identifier, such as http://purl.bioontology.org/ontology/SNOMEDCT/1144649008 for the 6 Min Walk Test. Alternatively, a new ontology term needs to be created. For this, we created a neuromuscular domain ontology: https://github.com/World-Duchenne-Organization/nmd-domain. These steps facilitate adoption of consistent data representations across diverse registries and therefore contributes to data harmonization.

Initial FAIRifcation efforts have focused on aligning data from functional motor assessments, using existing ontologies and standard operating procedures to guide the mapping. These efforts will be expanded to additional domains in the foreseen post-workshop efforts, supported by governance structures that balance global coordination with local implementation.

The EURO—NMD Registry Hub exemplifies how FAIRification can be effectively implemented through a centralized infrastructure. Acting as a central coordination point, the Hub connects multiple disease-specific registries - such as the EURO—NMD registry and DM-Scope for DM1 - into a cohesive network. Within this framework, Key Performance Indicators (KPIs) are used to align and interlink data elements across registries, ensuring that data is analysed consistently and meaningfully. A critical aspect of this network is the clear definition of data ownership, which governs who controls access, how the data can be used, and ensures ethical data management throughout the process.

Practical implementation of these FAIRification efforts require dedicated funding. Lack of funding, along with the absence of dedicated and specialized teams, has been the main bottleneck in previous registry FAIRification efforts in DM1. Examples from FAIRification projects focused on Duchenne Muscular Dystrophy highlighted the value of dedicated funding, which enables greater autonomy and strategic control over data management approaches [16]. Considering the critical role of registries in the post-marketing setting (e.g. assess surveillance of new drugs or establish effectiveness in clinical practice), the role of the pharma industry in co-funding registry infrastructure and/or FAIRification efforts was discussed; funding models should be built having broad stakeholder involvement to ensure data quality and sustainability while ensuring transparency and neutrality. The SMARtCARE registry for SMA patients, which is currently supported by the industry, serves as an example of how such funding models can be successfully implemented [17].

Another key aspect of successful FAIRification is ensuring the ongoing security, adaptability, and privacy of the data infrastructure. Continuous monitoring of IT security is essential to protect the integrity and confidentiality of sensitive patient data. In parallel, teams must be equipped with the resources and readiness to update data pipelines in response to evolving FAIR standards and technological advancements. Additionally, there is an increasing need for a standardized pseudonymization service, which can safeguard patient identities while still enabling meaningful and compliant data analysis across registries.

Federated analysis infrastructure in DM1

Federated analysis is a method that enables collaborative data analysis across multiple patient registries without requiring data to be centralized. Instead of transferring sensitive data to a single location, the data visiting approach allows algorithms to "visit" each data source, perform computations locally, and return only aggregated or anonymized results. This preserves data privacy, maintains institutional control over data, and supports compliance with regulations like GDPR - while still enabling meaningful cross-site research and insights.

Application of this framework necessitates all registries to be FAIR in order to ensure seamless data integration, interoperability across systems, and consistent analysis that supports collaborative research and informed decision-making. For federated analysis to function effectively, several components must be in place. First, the technical infrastructure must support secure and standardized querying, including the use of common data models (CDMs) to ensure that data from different registries can be interpreted uniformly. Second, semantic interoperability is essential, requiring agreed-upon ontologies and precise mapping of clinical concepts across databases. Third, robust governance structures must define who can issue queries, how results can be used, and how data use agreements are maintained and enforced. To ensure fair

and ethical oversight, these governance structures should be inclusive and multidisciplinary. Patients and/or patient representatives must be involved as primary stakeholders in decisions about data usage. Legal and ethical experts should ensure compliance with relevant regulations, while physicians and researchers contribute essential medical and scientific expertise. To maintain neutrality and prevent conflicts of interest, the governance of the project should ideally be overseen by an independent organization. In practice, a research question ('query') is sent to a registry hub like the EURO—NMD registry hub, where a multidisciplinary governance structure critically reviews whether or not the research question is appropriate [18]. Subsequently, each registry that is associated with the registry hub can also individually decide whether or not to allow the inclusion of their data for the analysis, thereby ultimately remaining in control of how their data is used. While this workflow ensures maximum data security, it was noted that it can be labor-intensive - particularly when numerous independent or follow-up queries are submitted within a short timeframe. Introducing a pre-approved set of standardized queries could help reduce this burden by streamlining the process and minimizing repetitive manual review. Furthermore, it was noted that this approach opens avenues for registries with limited resources to participate in international research efforts.

A discussion emerged on whether participating in this federated analysis framework would require new patient consent documents. While federated analysis - particularly through the data visiting approach - can enhance GDPR compliance by avoiding the transfer of personal data, the need for new consent depends on the original scope of consent provided by patients. If the intended use within the federated framework falls outside the original consent terms, updated or additional consent may be necessary. Researchers of the Radboud university medical center have developed updated consent forms, including videos that explain these concepts in 5 different languages. It was noted that going forward it was deemed useful to generally adopt federated analysis approaches in patient consent documents.

Longitudinal data analyses plan to facilitate individual disease trajectory modeling

Building on the progress achieved through the harmonization of datasets and the implementation of a federated infrastructure, the next phase in advancing our understanding of DM1 should focus on the application of statistical methodologies capable of informing both patients and caregivers. Ultimately, these analyses are important for more targeted clinical trials of DM1 patient subgroups with shared disease characteristics, improved patient counselling, and pharmacovigilance, including post-marketing surveillance.

For many diseases including DM1, statistics is considered to be the weakest link in personalized medicine, as often only old and/or simple analyses are applied to complex datasets. While artificial intelligence, including deep neural networks, is increasingly gaining traction, it was noted that their 'black box' structure poses significant threats to data privacy. If the generated neural network is of sufficient size, patient data could be hidden within complex combinations of nodes and edges, making it vulnerable to unintended memorization and potential re-identification through model inversion or extraction attacks. Instead, alternative solutions have been discussed such as factor analysis and (Bayesian based) latent variable modeling.

Individual outcome measures often show high variability across repeated assessments. Although stricter SOPs - driven partly by clinical trial standards - are being adopted, some variance remains due to uncontrollable factors like daily fluctuations in patient condition, fatigue, or environment. As an alternative, domain-specific latent variables were proposed. Using tools like factor analysis, domain scores can be derived from multiple related outcomes, offering more robust and interpretable results. These scores also enable retrospective comparisons across registries with differing measures. However, accurate estimates of domain scores require multiple inputs per domain and was therefore currently only deemed feasible for the motor function domain, highlighting the need for standardized and longitudinal data collection in other disease domains.

One of the workshop sessions focused on identifying priority events for developing statistical prediction frameworks in DM1. While predicting the latent construct of 'motor function' was deemed valuable, changes in ambulatory function were also highlighted as highly relevant for patients. Key cardiac and pulmonary targets included time to major cardiac event (such as AV block), forced vital capacity (FVC), and time to ventilation support. However, predicting cardiac issues in DM1 remains particularly challenging; no clear predictive relationships have been identified to date. The discussion emphasized that cardiologists should be aware of the variability in PR interval changes in DM1 patients, and that such fluctuations should not automatically lead to exclusion from clinical trials. Myotonia was represented by the time to open the hand (HOT). CNS and GI domains were noted as not feasible to predict due to insufficient data. However, the outcomes of two additional 2025 ENMC workshops need to be considered here. Measures of activity, participation and quality of life - such as DM1-Activ-c, MDHI, and caregiver input - were also highlighted as important, though complex to model.

A key goal is the identification of patient subgroups with shared disease characteristics. It was argued that the highest chance for success lies in the application of unsupervised machine learning based algorithms. This approach overcomes the limitations of hypothesis-driven subgroup analysis by enabling the discovery of meaningful clusters without predefined disease modifiers. Identifying such subgroups allows for targeted interventions and directly informs clinical trial design. By recognizing homogeneous groups with similar disease trajectories, inclusion criteria can be refined to improve trial efficiency and relevance.

To maximize clinical relevance, modeling should start with a pragmatic approach that aligns with clinical practice rather than overcomplicating analyses. Well-established statistical frameworks should be prioritized. Ultimately, all modeling efforts should prioritize what is most relevant to patients, ensuring that the outcomes are meaningful and applicable in real-world clinical settings.

Conclusions

The workshop marked a pivotal step toward unifying global efforts in DM1 registry development and analysis. Participants reached consensus on updating the core dataset to better reflect both clinical and patient-reported outcomes, ensuring relevance for future therapeutic trials and post-marketing surveillance. The adoption of FAIR principles and federated analysis frameworks was recognized as essential for enabling secure, interoperable, and ethically governed data sharing. Emphasis was placed on pragmatic statistical modeling approaches that prioritize patient relevance and clinical applicability. While challenges remain - particularly in funding, data standardization, and integration of underrepresented domains such as CNS and gastrointestinal symptoms - the workshop laid a strong foundation for collaborative, patient-centered research. Continued international coordination and stakeholder engagement will be critical to realizing the full potential of DM1 registries in advancing care and accelerating therapeutic development.

Workshop Participants

D. van As, Radboud university medical center, Nijmegen, The Netherlands

Prof. Dr. G. Bassez, Institute of Myology, French National Center for Scientific Research, Paris, France

Prof. Dr. C.G. Faber, Maastricht University Medical Center, Maastricht, The Netherlands

L.A. la Fontaine, Maastricht University Medical Center, Maastricht, The Netherlands

Prof. Dr. C. Gagnon, Université de Sherbrooke, Sherbrooke, Canada

A. Geille, Euro-DyMA, Paris, France

Dr. A. Guerra, Avidity Biosciences, Zug, Switzerland

Prof. Dr. P.A.C. 't Hoen, Radboud university medical center, Nijmegen, The Netherlands

Prof. Dr. N.E. Johnson, Virginia Commonwealth University, United States

Dr. C. Jonkers, European Medicine Agency, Amsterdam, The Netherlands

Prof. Dr. A.C.C. Coolen, Radboud University Nijmegen, The Netherlands

N. Lalout, Radboud university medical center, Nijmegen, The Netherlands

Prof. Dr. I.S.J. Merkies, Curaçao Medical Center, Willemstad, Curaçao

Dr. A. Novack, Dyne Therapeutics, Boston, United States

Dr. S. Olmos, Myotonic Dystrophy Foundation, Oakland, United States

Dr. S. Peric, University of Belgrade, Belgrade, Serbia

Dr. A. Rohrwaser, Myotonic Dystrophy Foundation, Oakland, United States

Prof. Dr. V.A. Sansone, NeMo Center, Milan, Italy

Prof. Dr. B. Schoser, Friedrich-Baur Institute, Munich, Germany

Dr. R. Thompson, Children's Hospital of Eastern Ontario, Ottawa, Canada

E. Vroom, World Duchenne Organization, Veenendaal, The Netherlands

Dr. M. Wilkinson, Universidad Politécnica de Madrid, Madrid, Spain.

CRediT authorship contribution statement

Leandre la Fontaine: Writing – original draft, Conceptualization, Investigation, Resources, Data Curation, Visualization, Project Administration. **Daniël van As:** Writing – original draft, Conceptualization, Investigation, Resources, Data Curation, Project Administration. **Guillaume Bassez:** Writing – Review & Editing, Conceptualization, Supervision, Funding acquisition. **Nicholas Johnson:** Writing – Review & Editing, Conceptualization, Supervision, Funding acquisition. **Catharina Faber:** Writing – Review & Editing, Conceptualization, Supervision, Funding acquisition. **Peter 't Hoen:** Writing – Review & Editing, Conceptualization, Supervision, Funding acquisition.

Declaration of competing interest

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Microsoft Copilot in order to summarize workshop notes and aid in writing the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

D. van As reports no conflicts of interest.

L.A. la Fontaine reports no conflicts of interest.

P.A.C. 't Hoen reports no conflicts of interest.

G. Bassez has received grant funding from AFM Telethon. He has consulted with Arthexbiotech, Dyne, Avidity, Jahnsen Cilag, Novartis, and Vertex Pharmaceuticals.

Acknowledgments

The workshops and next generation program 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 and in-kind contributions: Euro-Dyma, Myotonic Dystrophy Foundation. Finally, we extended our gratitude to the pharmaceutical companies for their presence and financial support: Dyne Therapeutics and Avidity Biosciences.

Prof. C.G. Faber reports grants from European Union's Horizon 2020 research and innovation programme Marie Sklodowska-Curie grant for PAIN—Net, Molecule-to-man pain network (grant no. 721,841), Steering committees/advisory board for studies in small fibre neuropathy of Biogen/Convergence, Vertex, Lilly and OliPass, outside the submitted work and grants from Prinses Beatrix Spierfonds for the Myodraft national registry in Myotonic Dystrophy type 1.

Prof. N.E. Johnson reports funding from NINDS (R01NS104010, U01NS124974) and the FDA (7R01FD006071). He receives royalties from the CCMDHI and the CMTHI. He receives research funds from Novartis, Takeda, PepGen, Sanofi Genzyme, Dyne, Vertex Pharmaceuticals, Fulcrum Therapeutics, AskBio, ML Bio, and Sarepta. He has provided consultation for Arthex, Angle Therapeutics, Juvena, Rgenta, PepGen, AMO Pharma, Takeda, Design, Dyne, AskBio, Avidity, and Vertex Pharmaceuticals. He has equity in Repeat RNA Therapuetics, Angle Therapeutics, Evolyra Therapeutics, and Juvena Therapeutics.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.nmd.2025.106257.

References

[1] Harper PS. Myotonic dystrophy. 3rd ed. London: Saunders; 2001.

[2] Johnson NE, Butterfield RJ, Mayne K, Newcomb T, Imburgia C, Dunn D, et al. Population-based prevalence of myotonic dystrophy type 1 using genetic analysis of statewide blood screening program. Neurology 2021;96:e1045–53. https://doi.org/10.1212/wnl.0000000000011425.

[3] Wenninger S, Montagnese F, Schoser B. Core clinical phenotypes in myotonic dystrophies. Front Neurol 2018;9:303. https://doi.org/10.3389/fneur.2018.00303.

[4] Bellini M, Biagi S, Stasi C, Costa F, Mumolo MG, Ricchiuti A, Marchi S. Gastrointestinal manifestations in myotonic muscular dystrophy. World J Gastroenterol 2006;12:1821–8. https://doi.org/10.3748/wjg.v12.i12.1821.

[5] Fragola PV, Luzi M, Calo L, Antonini G, Borzi M, Frongillo D, Cannata D. Cardiac involvement in myotonic dystrophy. Am J Cardiol 1994;74:1070–2.

[6] Griggs RC, Davis RJ, Anderson DC, Dove JT. Cardiac conduction in myotonic dystrophy. Am J Med 1975;59:37–42.

[7] Hawkins AM, Hawkins CL, Abdul Razak K, Khoo TK, Tran K, Jackson RV. Respiratory dysfunction in myotonic dystrophy type 1: a systematic review. Neuromuscul Disord 2019;29:198–212. https://doi.org/10.1016/j.nmd.2018.12.002.

[8] Okkersen K, Jimenez-Moreno C, Wenninger S, Daidj F, Glennon J, Cumming S, et al. Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. Lancet Neurol 2018;17:671–80. https://doi.org/10.1016/s1474-4422(18)30203-5.

[9] Wood L, Bassez G, Bleyenheuft C, Campbell C, Cossette L, Jimenez-Moreno AC, et al. Correction to: eight years after an international workshop on myotonic dystrophy patient registries: case study of a global collaboration for a rare disease. Orphanet J Rare Dis 2019;14:199. https://doi.org/10.1186/s13023-019-1157-7.

[10] Pascual-Gilabert M, Artero R, López-Castel A. The myotonic dystrophy type 1 drug development pipeline: 2022 edition. Drug Discov Today 2023;28:103489. https://doi.org/10.1016/j.drudis.2023.103489.

[11] Thompson R, Schoser B, Monckton DG, Blonsky K, Lochmüller H. Patient registries and trial readiness in myotonic dystrophy–TREAT-NMD/Marigold International Workshop Report. Neuromuscul Disord 2009;19:860–6. https://doi.org/10.1016/j.nmd.2009.08.009.

[12] van Engelen BG, Eymard B, Wilcox D. 123rd ENMC International Workshop: management and therapy in myotonic dystrophy, 6-8 February 2004, Naarden, The Netherlands. Neuromuscul Disord 2005;15:389–94. https://doi.org/10.1016/j.nmd.2005.02.001.

[13] Wood L, Bassez G, van Engelen B, Lochmüller H, Schoser B. 222nd ENMC International Workshop:: myotonic dystrophy, developing a European consortium for care and therapy, Naarden, The Netherlands. 1-2 July 2016 Neuromuscul Disord 2018;28:463–9. https://doi.org/10.1016/j.nmd.2018.02.003.

[14] Scholten S, Peterson JAM, Orriëns LB, Pastorelli L, Meola G, Schoser B, Braakman HMH. 288th ENMC workshop participants. 288th ENMC International Workshop. Towards better diagnosing, understanding and treating gastrointestinal symptoms in myotonic dystrophy: extended insights and practical recommendations. 16-18 May 2025, Hoofddorp, the Netherlands. Neuromuscul Disord 2025:106250. https://doi.org/10.1016/j.nmd.2025.106250.

[15] Alarcón-Moreno P, Wilkinson MD. Take CARE of your patient data. Clinical and registry entries (CARE) semantic model. In: Proceedings of the 15th International SWAT4HCLS Conference Semantic Web Applications and Tools For Health Care and Life Science; 2024.

[16] van Lin N, Paliouras G, Vroom E, t Hoen PAC, Roos M. How patient organizations can drive FAIR data efforts to facilitate research and health care: a report of the virtual second International Meeting on Duchenne Data Sharing, March 3, 2021. J Neuromuscul Dis 2021;8:1097–108. https://doi.org/10.3233/jnd-210721.

[17] Pechmann A, König K, Bernert G, Schachtrup K, Schara U, Schorling D, et al. SMArtCARE - A platform to collect real-life outcome data of patients with spinal muscular atrophy. Orphanet J Rare Dis 2019;14:18. https://doi.org/10.1186/s13023-019-0998-4.

[18] 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.