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MOVR—NeuroMuscular ObserVational Research, a unified data hub for neuromuscular diseases

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Neuromuscular diseases (NMDs), an exceptionally diverse group of rare disorders, have recently become a focus of gene and antisense oligonucleotide therapies. The early results have been so astounding that it is now opportune to rethink research and clinical programs in NMDs. We urgently need greater numbers of patients to participate in clinical trials and better ways to track their clinical and genetic data to maximize the benefits of these therapies, ensure broad access, and support the fast and economic development of new drugs.

In spinal muscular atrophy (SMA, OMIM #25330/#253550/#253400/#271150), a severely disabling and often lethal inherited condition, treatment with an antisense oligonucleotide therapy (Spinraza® [nusinersin]) boosted levels of the missing survival motor neuron (SMN) protein, improved survival, and led to the accomplishment of motor milestones in the ENDEAR study group trial.[1] Gene therapy, under investigation for SMA, has shown promising results in a small phase 1 trial in which all treated patients were still alive at 20 months of age, an impressive departure from natural history.[2] Studies in other NMD phenotypes are following apace, with examples in Duchenne muscular dystrophy (DMD, OMIM #310200)[3,4] and a small trial in giant axonal neuropathy (OMIM #256850).[5] Importantly, the different therapeutic strategies utilized have the potential of "platform approaches"—a set of techniques that can be relatively easily adjusted to different disease alleles, different diseases' genes, or varying tissues. We may be at the beginning of an "age of therapies" in NMDs.

For this promise to be realized, however, we need a means to gather and link genetic information with other relevant patient data on a national level. The future of this field, we believe, rests on two key foundations: precise molecular genetic diagnosis (enabled by genetic discovery research) and personalized treatments (preceded by clinical trials). Most of our current knowledge had its genesis in genetic findings that yielded insights into NMD pathophysiology. Since the broad introduction of exome sequencing in late 2009, hundreds of novel NMD genes and broadened phenotype/genotype spectra have been identified.[6] Still, it is estimated that 40% of NMD patients carry yet unknown genetic defects.[7] Progress could be substantially enhanced by creating a rigorously managed, accessible, and unified national data registry for NMD patients. Ideally, patients with specific NMD phenotypes should be readily available for outreach, genetic testing should already have been performed, and carefully curated clinical data should be available to expedite rapid selection of optimal test groups. Without a national patient registry, researchers and industry will face bottlenecks in locating appropriate patients for trials and competing for a limited pool of rare NMD patients. The classic approach of patient registries combined with internet technologies, data sharing platforms, electronic medical records, and possibly the latest technologies such as artificial intelligence,[8] will be an ideal tool to combine research and clinical efforts, which often live in separate spaces.

The Muscular Dystrophy Association (MDA), the largest organization dedicated to research and care in NMDs, has begun a vital initiative to meet these needs. Convening with leaders in health data management, patient advocates, researchers, and a multidisciplinary Clinical Advisory Board, MDA has created a unified patient registry for NMDs, the MDA NeuroMuscular ObserVational Research (MOVR) data hub. Currently, more than 3000 patients with one of four diseases—amyotrophic lateral sclerosis (ALS), SMA, DMD, and Becker muscular dystrophy (BMD)—are represented in the registry. Included in its files are demographic data, diagnostic test results, standardized measures of muscle function and health status, other clinical metrics, and records of medical interventions drawn from more than 25 MDA Care Centers across the United States. Importantly, this registry matches medical data with individuals' genetic information, where available. The registry is updated during every MDA Care Center visit, providing crucial continuity and enabling longitudinal recording of symptoms.

Several participating sites have used the registry to monitor the effectiveness of certain interventions and to guide care decisions. For example, the team from Children's Hospital Colorado is monitoring the effectiveness of measuring

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vitamin D levels in patients with DMD, the effect of steroid use on growth parameters, and using pulmonary function test results to guide the decision to use assisted ventilation. Additionally, the registry data were used to observe that Hispanic/Latino patients at the Colorado site lost the ability to ambulate an average of 12 months earlier than non-Hispanic/Latino patients, which may be attributed to the lower prevalence of glucocorticosteroid use in Hispanic/Latino patients.[9] As the registry continues to accumulate longitudinal data, more insights will be forthcoming.

MDA is now embarking on the next phase of the MOVR Data Hub, expanding the number of diseases covered and doubling the collection of data from 25 to 50 separate sites. Through a partnership with IQVIA™, a leading global provider of information, innovative technology solutions and contract research services focused on using data and science to help healthcare stakeholders find better solutions for their patients, the MOVR data hub will be able to meet the ambitious goal of managing and integrating data from various sources.

Importantly, MDA has stated a commitment to work with other existing patient registries, and to share insights and infrastructure knowledge to advance technology currently being developed. MDA's investment in the platform and infrastructure will allow the integration with other existing registry efforts, and the addition of new registries with lower up-front costs. MDA does not, and will not, collect any fee from patients or participating sites. Rather, participating Care Centers receive support from MDA to carry out data entry. We anticipate support from the public and private sources to help offset the cost of the platform. De-identified data can be used for natural history studies, postmarketing surveillance, or regulatory filings—all of which serve the NMD community. As financial support for MOVR grows, we will be able to expand the diseases covered and add sites, which will allow more patients to be able to participate.

The MOVR data hub will provide extensive genetic testing for patients. By collecting both genetic and clinical information, the data hub can identify correlations between genotypes and phenotypes and expand into genetic modifier and risk gene studies for Mendelian disorders. This will further improve the pace and scope of gene and allele discovery and support a collaborative spirit. Interested industry partners will benefit from specific access permissions that enhance clinical trials, identify eligible patients for precision medicine trials, and allow for deeper correlations of genetic signatures with the natural history of diseases.

The MOVR data hub provides patients with the strongest levels of privacy protection now available. Just as controlled clinical trials require, an independent Institutional Review Board (IRB) protects the rights and welfare of participants involved in the registry and ensures all research conducted is held to the highest ethical standards. State-of-the-art security measures protect patient privacy, yet also provide for dynamic aggregation of data for research purposes and the ability for researchers to reach out to clinicians about trials and advances that may benefit individual patients of theirs.

To reach its full potential, however, the MOVR data hub needs several forms of support from the clinical community. The first step is awareness. Each one of us can spread the word. Everyone who treats or helps patients with these diseases should know of the MOVR data hub and its value, as well as its potential. Clinicians can participate by contributing data by referring patients to a participating Care Center. Researchers can also use the data to facilitate their own research by submitting a data access request, which outlines the proposed questions to be addressed and why these questions are important. This has not only scientific value, but will provide valuable educational opportunities, such as virtual grand rounds, hands on variant evaluation, and interdisciplinary evaluation of patients.

Secondly, by alerting patients to the data hub and encouraging enrollment, clinicians can help ensure that the data hub remains comprehensive, complete, and reflective of the full range of NMDs. This also means many patients who cannot be treated today can be made "trial ready," able to be informed the moment new treatments begin recruiting subjects. Finally, by publicly rallying behind this data hub initiative, clinicians can build confidence and trust in its outputs.

The challenges we are facing require substantial ongoing investments and coordinated efforts, and data hub designers must navigate a complex network of medical, legal, and political interests. The potential for improved patient care and cost savings, however, is immense. Given our recent successes in finding therapies and the current keen interest in NMD treatments within academia and industry, the time to act is now.

Medicine rarely has transformative moments in which longstanding barriers give way, knowledge multiplies, and substantive therapies begin to replace purely supportive care. Genetic and therapeutic advances have begun such a transformation in neuromuscular medicine. The MOVR data hub will help sustain this momentum toward our goal of freeing patients from these devastating illnesses. To find a participating MDA Care Center or to request access to de-identified data for use in your research, please visit https://www.mda.org/services/neuromuscular-disease-registry or e-mail mdaregistry@mdausa.org.

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DISCLOSURE

The authors declare no conflicts of interest.

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