P.34

MDA's MOVR Data Hub provides insights into adoption of approved therapies for neuromuscular disease

Elisabeth A Kilroy, PhD[1], Jessica Waits[1], Sharon Hesterlee, PhD[1]

[1] Muscular Dystrophy Association, 161 N. Clark, Suite 3550, Chicago, IL 60601

Abstract

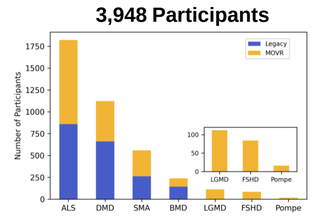
The field of neuromuscular disease (NMD) research is experiencing tremendous growth as a result of progress in both diagnostics and therapeutics. However, there continues to be a critical data shortage, as data regarding disease progression have not been captured systematically across NMDs nor in centralized, accessible databases. The **neuroMuscular ObserVational Research Data Hub (MOVR**) was created by the Muscular Dystrophy Association (MDA) to accelerate data collection, maximize drug development, and enhance the impact of new therapies. MOVR is powered by the MDA Care Center network, which consists of over 150 multidisciplinary care centers across the United States. Currently, 60 care centers have activated the MOVR Study Protocol and data from 3,948 participants and 12,376 encounters have been captured in MOVR. Preliminary analyses of MOVR Data have been performed to characterize the use FDA-approved therapies by participants living with spinal muscular atrophy (SMA), amyotrophic lateral sclerosis (ALS), or Duchenne muscular dystrophy (DMD). For participants living with SMA, the method of diagnosis (i.e., newborn screening, symptom onset) influences the type of therapy used and the age at which therapy is initiated. For participants living with ALS, over 75 percent of participants use an FDA-approved therapy, and these therapies are initiated on average less than 6 months after diagnosis. For participants living with DMD, the use of exon-skipping therapy is relatively limited among those participants who have mutations amenable to these therapies, with only 38 percent of participants receiving therapy. Future analyses will be performed to understand how these therapies may be impacting other core data elements captured by MOVR, including medication usage, multidisciplinary referral types, and functional measures. As the first data hub to aggregate clinical and genetic data across multiple NMDs, **MOVR continues to demonstrate its ability to transform the NMD space by serving as a powerful tool for clinical trial matching, clinical trial design and feasibility, and as a source for real-world data for pre- and post-approval submissions.**

MOVR as a Centralized Data Hub

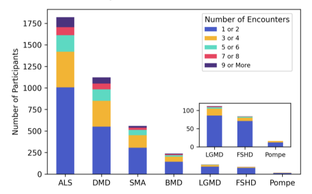
About 10 years ago, MDA recognized that there was a significant data shortage in the NMD space and started crafting strategic approaches to accelerate data collection and its use by researchers, clinicians, and drug developers. One strategy that was identified was to leverage the MDA Care Center Network as a source for efficiently capturing clinical data and growing a longitudinal dataset. Each year, over 90,000 medical visits are conducted and over 60,000 individuals living with NMDs receive expert care at these centers.

60 Active MOVR Sites

3,948 Participants



12,376 Encounters



Data elements captured by MOVR are functional and disease-specific outcome measures that have been identified by KOLs as important to understanding disease mechanisms, tracking disease progression, and implementing standards of care.

31

core data elements captured by the electronic Case Report Forms (eCRFs)

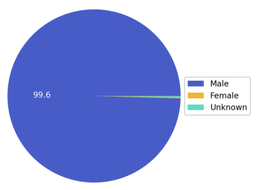
Demographics eCRF (During Enrollment)	Diagnosis eCRF* (During Enrollment)	Encounter eCRF* (During Clinical Visits)	Discontinuation eCRF (After End of Study)
Disease Type	Age at Diagnosis	Encounter Date	Date of Discontinuation
Enrollment Date	Age at Symptom Onset	Height	Reason for Discontinuation
Gender	Clinical Diagnosis	Weight	Date of Death
DOB	First Symptoms	Clinical Trial Participation	Cause of Death
Race	Family History	Surgeries	
Ethnicity	Genetic Testing Results	Hospitalizations	
Insurance		Medications	
Education		Pulmonary Devices	
Employment		Assistive Devices	
		Functional Testing	
		Pulmonary Tests	
		Referral Types	

* Diagnosis and Encounter eCRFs contain additional unique fields for each indication.

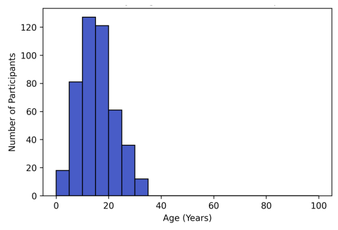
Approved Therapy Use in DMD Participants

Demographics of MOVR Participants with DMD

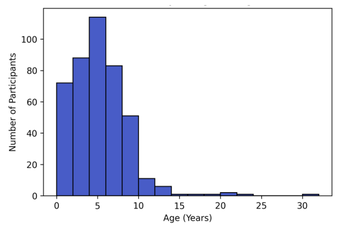
99.6%
of DMD participants are male



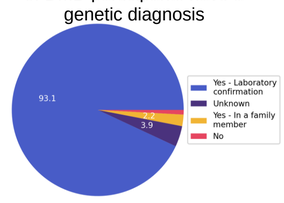
15.2 ± 6.7 years
average age of active DMD participants



5.2 ± 3.6 years
average age at diagnosis



93.1%
of DMD participants have a genetic diagnosis



DMD Therapeutic Approval Timeline

There are **4 exon-skipping therapies** approved by the FDA for individuals living with DMD.

2016
Exondys 51
(eteplirsen)
Sarepta
Mutations amenable to exon 51 skipping

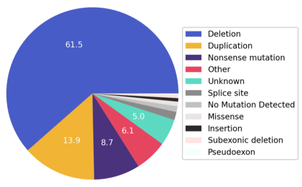
2019
Vyondys 53
(golodirsen)
Sarepta
Mutations amenable to exon 53 skipping

2020
Viltepso
(viltolarsen)
NS Pharma
Mutations amenable to exon 53 skipping

2021
Amondys 45
(casimersen)
Sarepta
Mutations amenable to exon 45 skipping

Therapy Use in MOVR Participants with DMD

61.5%
of DMD participants have a genetic deletion



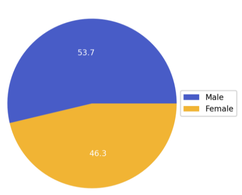
38.3%
of DMD participants harboring mutations amenable to exon-skipping are on therapy

	Amondys 45	Exondys 51	Vyondys 53	Viltepso
Amenable Mutation				
No Therapy	32 (84%)	13 (23%)	23 (77%)	27 (90%)
Therapy	6 (16%)	38 (68%)	7 (23%)	3 (10%)
No Mutation Information				
No Therapy	0	5 (9%)	0	0

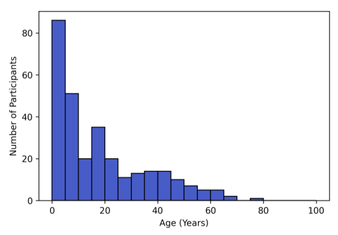
Approved Therapy Use in SMA Participants

Demographics of MOVR Participants with SMA

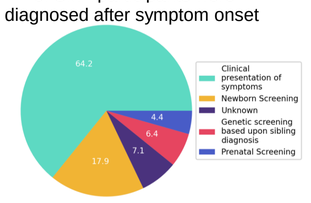
53.7%
of SMA participants are male



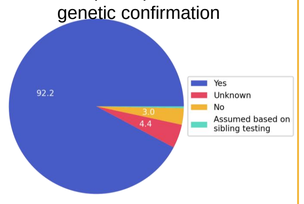
17.9 ± 17.3 years
average age of active SMA participants



64.2%
of SMA participants were diagnosed after symptom onset



92.2%
of SMA participants have a genetic confirmation



SMA Therapeutic Approval Timeline

There are **3 therapies** approved by the FDA for individuals living with SMA.

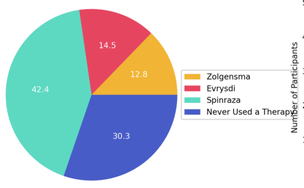
2016
Spinraza
(nusinersen)
Biogen
Antisense oligonucleotide that selectively binds and targets RNA to regulate SMN protein production

2019
Zolgensma
(onasemnogene abeparvovec-xioi)
Novartis
Gene therapy that introduces a fully functional copy of the human SMN gene

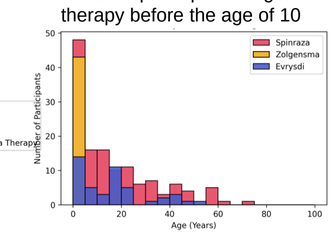
2020
Evrysdi
(risdiplam)
Genentech
SMN2-splicing modifier that increases the production of full-length SMN protein

Therapy Use in MOVR Participants with SMA

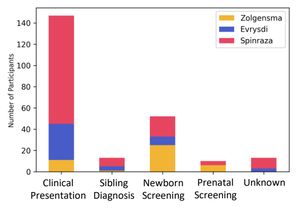
69.7%
of SMA participants have used an FDA-approved therapy



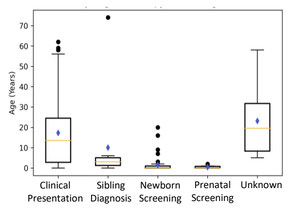
57.0%
of SMA participants begin therapy before the age of 10



60.1%
of SMA participants have received Spinraza



SMA participants diagnosed via **prenatal screening start therapy sooner**



Therapy Start Age (Years)

	Zolgensma	Evrysdi	Spinraza
count	43.00	46.00	134.00
mean	0.58	15.93	15.77
std	0.73	14.13	17.10

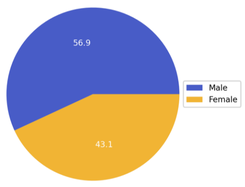
Therapy Start Age (Years)

	Clinical Presentation	Sibling Diagnosis	Newborn Screening	Prenatal Screening	Unknown
count	140	10	51	10	12
mean	17.24	10.00	1.49	0.40	23.08
std	15.87	22.57	3.80	0.70	17.65

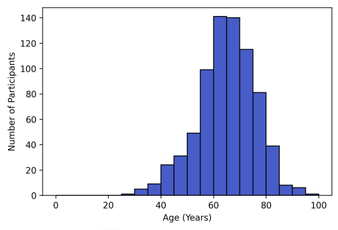
Approved Therapy Use in ALS Participants

Demographics of MOVR Participants with ALS

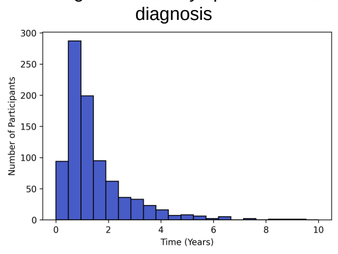
56.9%
of ALS participants are male



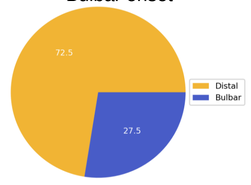
64.5 ± 10.9 years
average age of active ALS participants



1.5 ± 1.3 years
average time from symptom onset to diagnosis



72.5%
of ALS participants had non-Bulbar onset



ALS Therapeutic Approval Timeline

There are **5 therapies** approved by the FDA for individuals living with ALS.

1995
Rilutek
(riluzole)
Sanofi
Inhibits glutamate release

2011
Nuedexta
Avanir Pharmaceuticals
Treatment of pseudobulbar affect

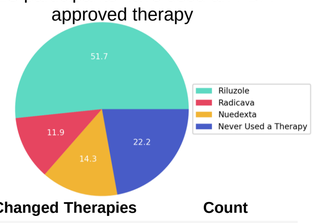
2017
Radicava
(edaravone)
Mitsubishi Tanabe Pharma America
Prevent accumulation of reactive oxygen species

2018
Tiglutik
(thickened riluzole)
ITF Pharma
Inhibits glutamate release

2019
Exservan
(riluzole oral film)
Mitsubishi Tanabe Pharma America
Inhibits glutamate release

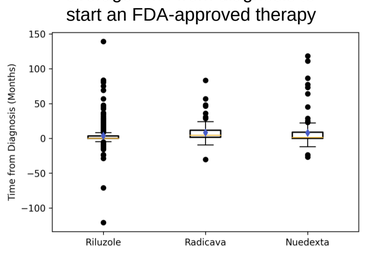
Therapy Use in MOVR Participants with ALS

77.8%
of ALS participants have used an FDA-approved therapy

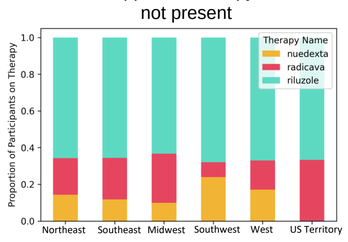


Changed Therapies	Count
No	689 (71.5%)
Yes	274 (28.5%)

5.2 ± 15.6 months
average time from diagnosis to start an FDA-approved therapy



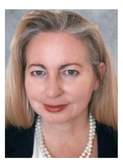
Regional Differences
in FDA-approved therapy use are not present



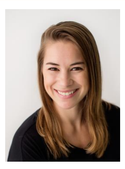
Conclusions

The MOVR Data Hub is experiencing tremendous growth in the number of participants enrolled in this observational study as well as in the number of longitudinal clinical encounters. Standardization of data elements across the 7 indications provides MOVR with the ability to examine the same outcome measures across time. For these analyses, we examined the use of FDA-approved therapies in MOVR Participants living with DMD, SMA, and ALS. The majority of ALS and SMA participants are receiving (or have received) an FDA-approved therapy but relatively few DMD participants have received a therapy. Building these two cohorts (therapy vs therapy-naïve) provides an opportunity to explore how therapies impact disease progression as well as standard of care practices. The MOVR Data Hub is a valuable tool for monitoring longitudinal response to therapies and could serve as an excellent source for real-world efficacy data for future regulatory submissions.

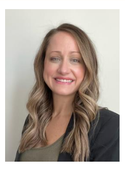
Contact the MOVR Team



Sharon Hesterlee, PhD
EVP & Chief Research Officer
shesterlee@mdausa.org



Elisabeth Kilroy, PhD
MOVR Data Analytics
ekilroy@mdausa.org



Jessica Waits
MOVR Clinical Operations
jwaits@mdausa.org

For access to MOVR Data, please email MDAMOVR@mdausa.org

Acknowledgements
This study was conducted using data from the Muscular Dystrophy Association's neuroMuscular ObserVational Research (MOVR) Data Hub. MOVR is operated through participating MDA Care Centers with the support of participants, MOVR Site PIs, coordinators, and staff. The authors would also like to thank members of the MOVR Research Advisory Committee, including James Berry, Barry Byrne, John Day, Rod Howell, Monkol Lek, Nicholas Maragakis, and Sabrina Paganoni, for sharing their expertise in neuromuscular diseases, the original MDA team members who spear-headed the development of the MOVR eCRFs, including Grace Pavlath, Lianna Orlando, Amanda Hayden-Phillips, and Laura Hagerty, and Tracy Blumenfeld for her contributions in launching MOVR. Finally, the authors would like to thank the teams at IQVIA and DNAnexus.