REAL-DMD: Baseline Findings From an Electronic Observer-Reported Outcome (ObsRO) Survey of Long-Term, Real-World Experiences of Patients With Duchenne Muscular Dystrophy (DMD)

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Introduction

- Duchenne muscular dystrophy (DMD) is a rare, debilitating neuromuscular disease leading to muscle weakness and functional decline that primarily affects young males[1,2]
- DMD is usually diagnosed in early childhood.[3] Over time, lower extremity functioning becomes increasingly strenuous, leading to loss of independent ambulation; serious orthopedic, respiratory, and cardiac complications; and ultimately, premature death[1,4]
- Due to DMD's early onset and progressive nature, caregivers play a crucial role in assessing and relaying information about patients' health, including their clinical status and functional ability

Objectives

Real-world data on functional ability and experiences, from a patient perspective, are lacking. REAL-DMD, a prospective, longitudinal cohort study involving caregivers of ambulatory DMD patients, aims to fill this evidence gap by generating real-world data on caregiver-reported patient function and experiences. The objectives of this analysis were to:

- Describe baseline characteristics and functional ability of patients included in REAL-DMD
- Explore differences in baseline functional ability by age groups

Methods

Study Population

Caregivers in the US were recruited through two patient advocacy groups (Parent Project Muscular Dystrophy and the Akari Foundation)

Inclusion Criteria

- Aged ≥18 years at the time of the study enrollment
- Resident of the US and able to read English or Spanish
- Primary caregiver (not for hire) for at least 6 months of a patient:
  - With a caregiver-reported diagnosis of DMD
  - Ambulatory
  - Consent to participate

Exclusion Criteria

- Professional paid caregiver
- The patient is currently enrolled in a DMD clinical trial or has been treated with PF-06939926 (fordadistrogene movaparvovec) or SGT-001

Data Collection

- Caregivers reported on patient's demographics, clinical characteristics, treatments, and functionality through a web-based survey (**Tables 1** and **S1** [*Click QR code to see* **S1**])
- Data were collected at baseline and will be collected every 6 months thereafter, for a minimum of 5 years

Statistical Analysis

- Patients were stratified by age at enrollment (≤7 years old; 8–12 years old; ≥13 years old)
- Continuous variables were summarized as mean, standard deviation (SD), and median, whereas categorical variables were summarized as frequency count and percentage
- Unadjusted statistical comparisons between subgroups tested the hypothesis that outcomes for all subgroups are equal. Analysis of variance (ANOVA) was used for continuous variables, and chi-squared/Fisher's exact tests for categorical variables

Results

Patient Characteristics (Table 1)

- Overall, 123 caregivers provided the experience of 137 patients
- The mean age (SD) of patients was 9.6 (4.7) years. Mean (SD) time since diagnosis was 5.7 (4.7) years
- Majority of patients had large deletions of one or more exons
- Most patients were treated with corticosteroids alone (67.2%), and 19.0% of patients were treated with dystrophin replacement therapies

Functional Ability

- Mean raw scores (MRS) were significantly different between age groups for Patient-Reported Outcomes Measurement Information System Parent Proxy (PROMIS PP) Mobility (P<0.001) and PROMIS PP Fatigue (P=0.002) (**Table 2**), with older age groups experiencing greater impairments in mobility and level of fatigue. PROMIS PP Upper Extremity MRS were similar across age groups (P=0.642)
- Almost all (94.2%) patients had moderate or severe limitations in mobility, with a higher proportion of patients in the ≥13 years age group within these categories of severity (P<0.001) (**Figure 1**)
- Almost all (94.9%) patients had moderate or severe limitations in upper extremity function, with the proportion of patients within these categories being similar across age groups (P= 0.7) (**Figure 2**)
- More than half (66.4%) of the patients had moderate to severe fatigue, with a higher proportion of patients in the ≥13 years age group within these categories of severity (P<0.001) (**Figure 3**)
- Despite being ambulatory at the time of enrollment, only 13.1% of patients were able to rise from floor and able to climb 4 steps of stairs without supports (**Figure 4**). Older patients had, in general, lower functional ability than younger patients (P<0.05)
- Caregiver-rated severity of patients' symptoms, physical ability, and overall health was moderate to very severe in most patients (*Click QR code to see* **Table S2**). Severity of patients was higher in older patients (P<0.05)

Table 1 *Baseline Patient Demographics and Clinical Characteristics*

	All Patients (N=137)
Age at enrollment (years)	
Mean ± SD [median]	9.6 ± 4.7 [9.0]
Time since DMD diagnosis (years)	
Mean ± SD [median]	5.7 ± 4.7 [4.7]
Race, n (%)	
White	121 (88.3)
Asian	14 (10.2)
Other	12 (8.8)
Age groups, n (%)	
≤7 years	50 (36.5)
8–12 years	50 (36.5)
≥13 years	37 (27.0)
Comorbidities,[a] n (%)	
Anxiety	49 (35.8)
Learning disabilities	46 (33.6)
Attention-deficit/hyperactivity disorder	39 (28.5)
Behavioral disorders	38 (27.7)
Constipation	38 (27.7)
History of falls	37 (27.0)
Stunted growth	37 (27.0)
Fatigue	23 (16.8)
Autism	22 (16.1)
Obsessive–compulsive disorder	20 (14.6)
Compression fractures	19 (13.9)
Osteoporosis	18 (13.1)
Obesity	13 (9.5)
Cataract	12 (8.8)
Bone fractures	11 (8.0)
Depression	8 (5.8)
Scoliosis	8 (5.8)
Type of mutation, n (%)	
Large deletions	73 (53.3)
Point mutations/small changes	31 (22.6)
Large duplications	23 (16.8)
Treatment history, n (%)	
Steroids (corticosteroids)	114 (83.2)
Steroids alone	92 (67.2)
Steroids + other	22 (16.1)
Eteplirsen	10 (7.3)
Casimersen	9 (6.6)
Delandistrogene moxeparvovec-rokl	6 (4.4)
Viltolarsen	1 (0.7)
Golodirsen	1 (0.7)
None of the above	19 (13.9)

[a]Comorbidities with a prevalence of at least 5% in all patients are shown. DMD=Duchenne muscular dystrophy.

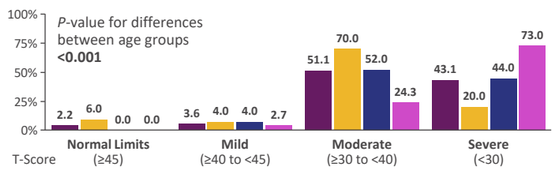
Table 2 *PROMIS PP Mean Raw Scores*

	All Patients (N=137)	≤7 (N=50)	8–12 (N=50)	≥13 (N=37)	*P*-value
PROMIS PP Mobility (mean ± SD)	3.3 ± 0.9	3.7 ± 0.7	3.4 ± 0.8	2.8 ± 0.9	<0.001
PROMIS PP Upper Extremity (mean ± SD)	3.1 ± 1.1	3.1 ± 1.2	3.1 ± 1.0	3.3 ± 1.1	0.642
PROMIS PP Fatigue (mean ± SD)	2.6 ± 0.9	2.3 ± 0.7	2.8 ± 0.9	2.9 ± 0.9	0.002

PROMIS PP=Patient-Reported Outcomes Measurement Information System Parent Proxy.

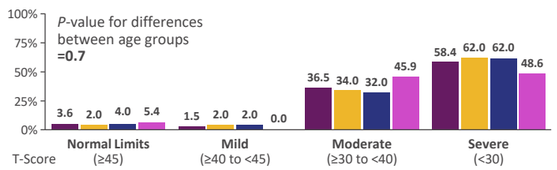
All Patients ≤7 years old 8 to 12 years old ≥13 years old

Figure 1 *PROMIS PP Mobility T-Score Distribution of Patients With DMD*



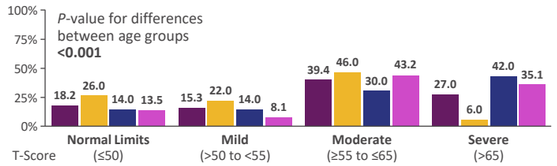
DMD=Duchenne muscular dystrophy; PROMIS PP=Patient-Reported Outcomes Measurement Information System Parent Proxy.

Figure 2 *PROMIS PP Upper Extremity T-Score Distribution of Patients With DMD*



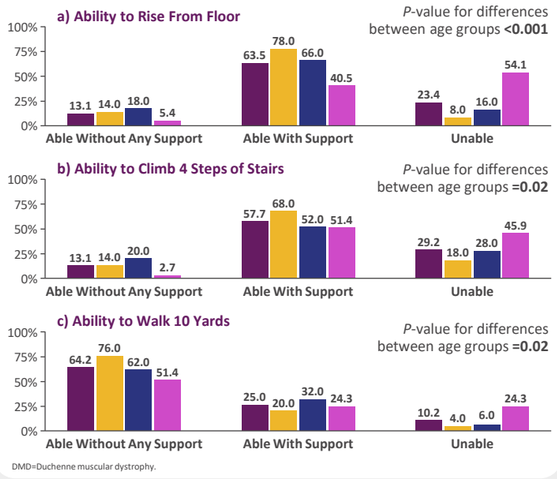
DMD=Duchenne muscular dystrophy; PROMIS PP=Patient-Reported Outcomes Measurement Information System Parent Proxy.

Figure 3 *PROMIS PP Fatigue T-Score Distribution of Patients With DMD*



DMD=Duchenne muscular dystrophy; PROMIS PP=Patient-Reported Outcomes Measurement Information System Parent Proxy.

Figure 4 *Functional Ability of Patients With DMD*



DMD=Duchenne muscular dystrophy.

Key Findings

Real-DMD baseline data provide insights into real-world characteristics and functional ability of ambulatory patients with DMD

Conclusions

The majority of the surveyed caregivers reported on patients who experienced moderate to severe mobility and upper extremity functioning impairments, and had moderate to severe fatigue

Moderate to severe impairments to mobility and fatigue were significantly more common among children ≥13 years old. However, findings also suggest that moderate impairments in mobility were common in ages ≤7 years old

Difficulties in ability to rise from floor and ability to climb 4 steps was significantly different across ages groups, with a higher proportion of patients in the older age groups experiencing difficulties. There is a high proportion of younger children (≤7 years) that are also experiencing difficulties in ability to rise from floor and climb 4 steps without assistance contrarily to the ability to walk 10 yards, which is an ability known to be lost as DMD progresses

Longitudinal follow-up from this study will further inform functional changes to improve the current understanding of DMD by depicting the trajectory of functionality of patients over time

Acknowledgments & Disclosures

Acknowledgments: Study was sponsored and funded by Sarepta Therapeutics, Inc.

Disclosures: SP, KLG, and **IFA** are employees of Sarepta Therapeutics, Inc., and may own stock/options in the company. **MY, ET, BM,** and **FY** are employees of Analysis Group, Inc., which received funding from Sarepta Therapeutics, Inc., to support this research.

References

1. Duan D, et al. *Nat Rev Dis Primers*. 2021;7:13. **2**. Crisafulli S, et al. *Orphanet J Rare Dis*. 2020;15:141. **3**. Ciafaloni E, et al. *J Pediatr*. 2009;155:380-5. **4**. Mercuri E, et al. *Lancet*. 2019;394:2025-38. **5**. Scott E, et a. *Physiother Res Int*. 2012;17:101-9.

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https://www.sareptacongresshub.com/ISPOR2024/ispor2024/realdmd

International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Annual Meeting; May 5–8, 2024; Atlanta, GA

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Methods (cont)

Table S1 *Key Survey Elements*

Caregiver-Reported Outcome	Description
PROMIS® Parent Proxy Item Bank v2.0 – **Mobility**	• Contains 23 items assessing physical mobility over the past 7 days. Each item is rated on a 5-point response scale • Raw summed scores are translated into a T-score for each respondent. A higher T-score represents higher/better levels of mobility
PROMIS® Parent Proxy Item Bank v2.0 – **Upper Extremity** – Short Form 8a	• Contains 8 items assessing physical functioning of the upper extremities over the past 7 days. Each item is rated on a 5-point response scale • Raw summed scores are translated into a T-score for each respondent. A higher T-score represents higher/better levels of upper extremity functioning
PROMIS® Parent Proxy Short Form v2.0 – **Fatigue** 10a	• Contains 10 items assessing fatigue over the past 7 days. Each item is rated on a 5-point response scale • Raw summed scores are translated into a T-score for each respondent. A higher T-score represents worse or more fatigue
Caregiver Global Impression of Severity for DMD (CaGI-S)	• The CaGI-S includes 4 separate questions that ask about the severity level of the child's 1) observable symptoms, 2) physical ability, 3) ability to perform daily activities, and 4) overall health at the time • Each item is rated on a 5-point response scale from "very mild impact/impairment" to "very severe impact/impairment"
Questions adapted from North Star Ambulatory Assessment (NSAA)[5]: • Ability to rise from floor • Ability to climb 4 steps of stairs • Ability to walk 10 yards	• Three questions from the NSAA were adapted to be answered by caregivers on the patient's ability to rise from floor, climb 4 steps of stairs, and walk 10 yards • Each item was rated on a 3-point response scale, composed of i) being able to perform the task independently/without difficulty, ii) being able to perform the task, but with needed assistance or difficulties, iii) being unable to perform the task

DMD=Duchenne muscular dystrophy; PROMIS=Patient-Reported Outcomes Measurement Information System.

Ambulatory Definitions

1. He walks all day. He may or may not use a wheelchair or scooter for long distances on special occasions (on vacation, at an amusement park or the zoo)
2. He uses a wheelchair or scooter for some time of the day on most days of the week throughout the year, but he can regularly walk down the hall in your home with or without assistance

Results (cont)

Table S2 *Caregiver Impression of Severity of Patients With DMD[a,b]*

	All Patients (N=137)	Age Subgroups (Years) ≤7 (N=50)	8–12 (N=50)	≥13 (N=37)	*P*-value
Severity of patient's observable DMD symptoms	2.6 ± 0.9 [3.0]	2.2 ± 0.8 [2.0]	2.7 ± 0.8 [3.0]	3.1 ± 0.8 [3.0]	<0.001
Severity of impairment in patient's physical ability	2.7 ± 0.9 [3.0]	2.2 ± 0.9 [2.0]	2.9 ± 0.8 [3.0]	3.1 ± 0.9 [3.0]	<0.001
Patient's ability to perform daily activities	2.5 ± 1.0 [2.0]	2.2 ± 0.9 [2.0]	2.5 ± 0.9 [2.5]	2.8 ± 1.1 [3.0]	0.013
Patient's overall health	2.6 ± 0.9 [3.0]	2.3 ± 0.9 [2.0]	2.7 ± 0.8 [3.0]	2.8 ± 1.0 [3.0]	0.011

[a]Data are presented as mean ± SD [median]. [b]Each item is rated on a 5-point response scale: 1 = very mild impact/impairment, 2 = mild impact/impairment, 3 = moderate impact/impairment, 4 = severe impact/impairment, 5 = very severe impact/impairment. DMD=Duchenne muscular dystrophy.

References

1. Duan D, et al. *Nat Rev Dis Primers*. 2021;7:13.
2. Crisafulli S, et al. *Orphanet J Rare Dis*. 2020;15:141.
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