State of inclusion of patient-centered endpoints in Duchenne Muscular Dystrophy (DMD) clinical trials

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Introduction

- There are 4 types of Clinical Outcome Assessments (COAs):
  - Clinician-Reported Outcome (ClinRO) Measures
  - Performance Outcome (PerfRO/PerfO) Measures
  - Patient-Reported Outcome (PRO) Measures
  - Observer-Reported Outcome (ObsRO) Measures
- Duchenne Muscular Dystrophy (DMD) is a rare, progressive, neuromuscular disease characterized by loss of ambulation occurring in late adolescence
- DMD clinical trials generally focus on improving muscular function measured with ClinROs and/or PerfROs, such as the North Star Ambulatory Assessment (NSAA) or 6 Minute Walk Test (6MWT)
- A challenge for interpreting scores on functional tests is the scores are not in a meaningful metric that is easily translated into changes in concepts meaningful to patients
- Recent qualitative studies with DMD participants and their caregivers have found that concepts distal to muscular function (e.g., ability to perform activities of daily living, fatigue, difficulty keeping up with peers) are important to both ambulatory and non-ambulatory patients (Brown et al 2023; Schwartz et al 2023)

Objectives

- Examine the inclusion of COAs in DMD clinical trials and whether they capture concepts important to patients identified in qualitative studies

Methods

- ClinicialTrials.gov was searched for DMD clinical studies:
  - Types: Interventional, Natural history/ Observational, Behavioral/Psychosocial
  - Dates: January 1, 2019 through October 21, 2024

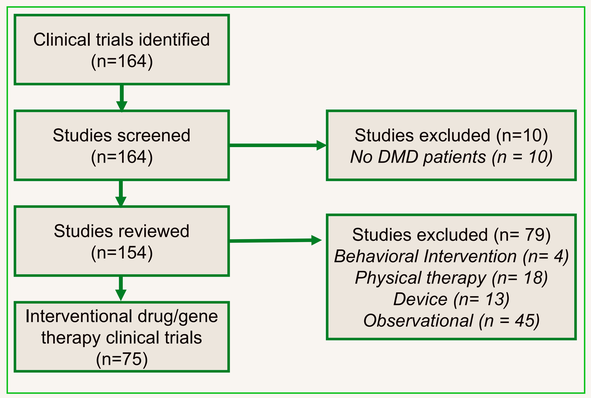

Figure 1. Flow diagram of the clinical trials review process

Search Results

- Initial search returned 164 clinical trials
  - 10 studies were excluded because the study populations included patients with muscular dystrophies other than DMD
  - Of the 154 DMD studies reviewed, 75 (48.7%) were drug/gene therapy clinical trials **(Figure 1)**
- Of the 75 trials reviewed **(Figure 2)**:
  - 33 studies included both ambulatory and non-ambulatory participants
  - 32 studies were limited to ambulatory participants
  - 7 studies focused on non-ambulatory participants
  - 3 studies included infant and toddler participants who were pre-ambulatory (too young to walk) or early ambulatory

Key Findings

- Of the 75 DMD trials reviewed, only 5 incorporated PRO measure
  - 3 studies measured overall quality of life using generic measures
  - 2 studies assessed self-reported mobility
- PerfRO assessments and ClinRO measures were used more frequently than PRO measures as primary or secondary endpoint measures, a trend which did not change over the past 5 years **(Figure 3)**
- Ambulation and muscular function were the most common primary and secondary endpoints in DMD trials **(Table 1)**

COA	Primary Endpoint Measure	Secondary Endpoint Measure	Overall
NSAA	7	25	32
10MWT	4	21	25
PUL	0	15	25
TTR/ TTS	5	14	19
6MWT	1	13	14
4 Stair Climb	0	10	10

Abbrev: NSAA = North Star Ambulatory Assessment, 10MWT = 10 Meter Walk Test, PUL = Performance of Upper Limb, TTR/TTS = Time-To-Rise/Time-To-Stand, 6MWT = 6 Minute Walk Test

Table 1. Most Commonly Used COAs in DMD Interventional Trials

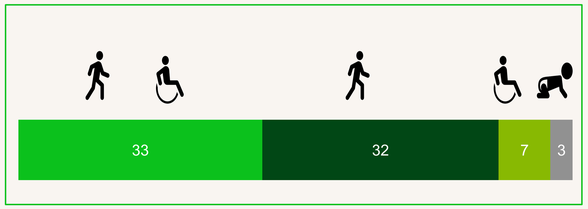

Figure 2. Number of Clinical Trials by Participant Type

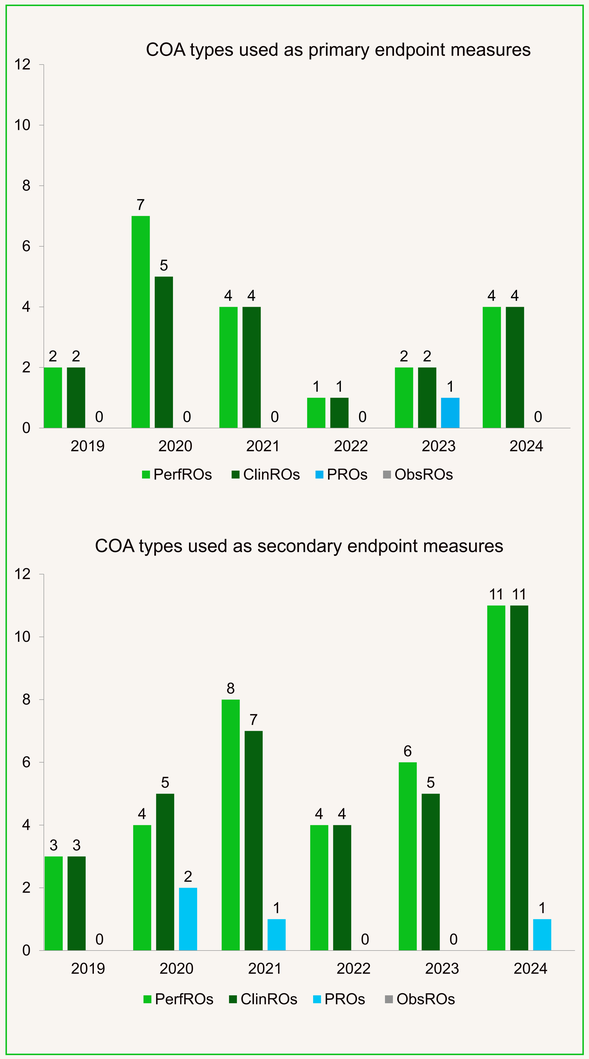

Figure 3. Number of COAs by type used as primary endpoints or secondary endpoints by year

Discussion

- Even with the FDA PFDD guidance series, few DMD interventional trials in the past 5 years have used COAs that measure concepts important to patients and their caregivers as identified in qualitative studies
- To better incorporate the patient experience and understand how changes in muscular function translate to meaningful changes in patients' daily lives, patient-centered endpoints should be incorporated into outcome measures and guided by results from qualitative studies in DMD patients
- Most endpoints in DMD clinical trials focus on changes in muscular function measured with PerfRO assessments and ClinRO measures, but more work is needed to understand the meaningfulness of assessments and measures of change for patients' daily lives
- Consideration should be given to the inclusion of clinical trial embedded interviews to provide insight into the patient experience and perceptions of meaningful change
- These data are important for the calibration of scores from muscular function against the real lives of patients with DMD (Sechrest et al 1996)

References

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