Neuromuscular Research Group (CINRG) using a central sonography protocol and 2 central readers. Forty-eight participants 8–18 years old with genetically confirmed Duchenne muscular dystrophy, Becker muscular dystrophy or limb girdle muscular dystrophy underwent electrocardiogram, echo and B-type natriuretic peptide testing. Notably, the echo quality was insufficient to read EF for 23 studies by one reader and for 5 studies by the other reader. In contrast, myocardial performance index (MPI) measured by Doppler could be read by both readers in 46 studies. Furthermore, the agreement of cardiac measures between the 2 independent readers and between one reader performing 2 different reads was greater for MPI than for EF. In 35% of studies, an abnormal MPI while EF remained normal suggested early cardiac dysfunction. This finding suggests that MPI may demonstrate increased sensitivity to detect cardiomyopathy when compared to EF. In subsequent analyses to explore echo measures of even greater sensitivity to detect cardiac dysfunction, speckle tracking was performed to measure longitudinal and circumferential strain. The results suggest that MPI and strain measures are sensitive and amenable to central reading for muscular dystrophy clinical trials.

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P.2.18
Bone mineral density and bone mineral content as measures of bone health in ambulatory boys with Duchenne Muscular Dystrophy

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Osteoporosis is a major problem in Duchenne Muscular Dystrophy (DMD) due to long term glucocorticoid (GC) therapy and impaired mobility. Dual-energy xray absorptiometry (DXA) assessment of bone health in DMD boys is challenging, as interpretation is affected by height, delayed bone maturation, puberty, and vertebral fractures. Accurate detection and intervention of osteoporosis are important for improving clinical care in DMD. To assess changes in bone mineral density (BMD) and bone mineral content (BMC) by functional status in ambulatory GC-treated DMD boys, Retrospective study of whole body (WB) and lumbar spine (LS) BMD and BMC by DXA in ambulatory GC-treated DMD boys, assessed from 2/2009 to 7/2012.

Bisphosphonate-treated boys were excluded. Age-adjusted z-scores (Z) and height-adjusted z-scores (HAZ) were derived using normal values. Generalized linear modeling was used to analyze changes in BMI and BMC by functional status (functional mobility score, FMS1, 2 or 3, by worsening status). 277 ambulant DMD boys were grouped by FMS (mean ages ±SD for FMS1, 2 and 3: 7.6 ± 2.2, 8.3 ± 2.6 and 11.2 ± 2.6 yrs). GC durations for FMS1, 2 and 3 were 2.7 ± 1.7, 2.9 ± 2.1 and 5.3 ± 2.6 yrs. For whole body, BMD-Z, BMC-HAZ, BMC-Z and BMC-HAZ all decreased with worsening FMS (p < 0.05 for FMS1 vs. FMS2). WB BMC was consistently lower than WB BMD for each FMS group. For spine, BMD-Z was similar between FMS groups, but BMC-Z was lower for FMS3 than FMS1 or FMS2 (p < 0.05). LS BMD-HAZ was surprisingly higher for FMS3 than the other groups, but LS BMC-HAZ remained similar between groups. WB bone indices worsened with declining mobility and increased GC duration. BMC was consistently lower than BMD, and spine BMC showed a relative decrease compared to BMD in weaker boys. Our study suggests that BMC may be a more sensitive indicator of bone health in DMD, and should be considered in conjunction with BMD as part of clinical care.

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P.2.19
Long term growth hormone therapy in Duchenne Muscular Dystrophy (DMD): A case report

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Long term glucocorticoid (GC) treatment compromises linear growth in DMD. Growth hormone (GH) therapy improves height, yet the impact on motor and cardiopulmonary function has not been studied in current DMD research. To report clinical outcomes in a DMD patient on long term GH for GC-induced linear growth failure. Retrospective review of motor, cardiac, and pulmonary outcomes pre- and post-GH therapy. Subject was a 19.6-year-old male with DMD, GC-induced linear growth failure, and GH deficiency (peak stimulated GH of 3.3 ng/mL, normal >10),
treated with daily GC for 9.9 y and GH for 6.3 y. GH treatment was associated with improved height growth (pre-GH height growth 1.25 cm per year compared to 4.3 cm per year on GH, reaching 151 cm at age 18.8 y). Motor function improved initially and stabilized after age 14.7 y, followed by a gradual decline; subject lost the ability to rise from the floor independently at age 16.2 y, to climb stairs unsupported at age 17.5 y, and to ambulate independently at age 18.8 y. Cardiac function remained stable after GC initiation (pre-GH, LVEF = 54.0%; post-GH, LVEF = 64.8%). Pulmonary function was also relatively unaffected by GH therapy (pre-GH, FVC = 1.4 L (72% of predicted), MIP = 64 cm H20, MEP = 64 cm H20, PCF = 200 L/min; post-GH, FVC = 2.3 L (82% of predicted), MIP = 76 cm H20, MEP = 76 cm H20, PCF = 300 L/min). Subject had no significant side effects of long term GH treatment. This single case report of a DMD patient with GC-induced growth failure improved with long term GH treatment suggests that GH did not adversely affect motor and cardiopulmonary function. Additional research on functional outcomes in GH-treated DMD patients is indicated.

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P.2.20
Prioritizing the worries of parents of children with Duchenne muscular dystrophy using best-worst scaling
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Duchenne muscular dystrophy (DMD) is a rare, progressive disorder with significant emotional and care-related burden on caregivers. Affected individuals typically lose ambulation at 8–12 years and die in the third decade. We identified and prioritized the most significant DMD-related parental worries.

Based on input from parent advisors and previous research, we identified 16 DMD-related parental worries – child-related and parent/family worries. Best-worst scaling (BWS) was used to prioritize worries in a survey of parents of children with DMD in the U.S. Participants were recruited from advocacy organizations, the DuchenneConnect Registry, and snowball recruiting. Parents responded to 16 BWS choice tasks consisting of subsets of 6 possible worries generated from a Youden design. Parents assessed the most and least significant worries over the past 7 days, which were given the value of +1 and −1 respectively. Across the sample, the average score was then estimated for each possible worry.

119 parents of children with DMD completed the survey. The mean age of the affected child was 12.1 (SD 6.4). The worry rated as the most significant was “My child getting weaker” (utility score 0.637), followed by “Getting the right care for my child over time” (0.254) and “My child missing out on new treatments” (0.245). Of the top 8 worries, only one was parent-directed, “Managing my uncertainty about my child’s future” (0.127) and only one included family effects, “Affording care my child needs within the family budget” (0.065). The worry least prioritized was “Having time for myself” (−0.557).

Parents prioritized worries about the health and care of their child, which collectively scored higher than factors relating to their own and their family wellbeing. Interventions to improve family wellbeing, even if focused on parental psychosocial status, should address worries about illness progression and treatment access.

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DISTAL MYOPATHIES

P.3.1
GNE myopathy functional activity scale (GNEM-FAS): Development of a disease-specific instrument for measuring function and independence

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GNE myopathy or hereditary inclusion body myopathy (HIBM) is an autosomal recessive myopathy presenting with distal leg weakness in early adulthood. Progressive weakness results in greater dependence and disability over time. A disease-specific measure of functional activity is needed to better understand the burden of illness, inform the design of clinical studies and optimize care. After clinical interview of patients, a 25-item questionnaire was validated to assess ability and independence in three domains: mobility, upper extremity (UE) use and self-care. Each item was rated from 0 to 4 with higher scores representing better function. Total scores range from 0 to 100; subscale scores range from 0 to 40 for Mobility, 0–32 for UE and 0–28 for Self-Care. The GNE Myopathy Functional Activity Scale (GNEM-FAS) was administered to 47 ambulatory subjects enrolled in a Phase 2 study of extended release sialic acid. Physical therapists completed the GNEM-FAS based on clinical observation and subject interview. Scores were compared to performance on volitional measures of strength and function, as well as scores on the Inclusion Body Myositis Functional Rating Scale (IBMFRS), a validated instrument for myositis. The mean GNEM-FAS total score was 69 out of 100 (23–94). Mobility subscores averaged 50%, UE, 81% and Self-Care, 82% of the maximum possible. Higher Mobility scores were associated with greater lower extremity strength (r = 0.83) and longer 6MWT distances (r = 0.83). A moderate association was seen between the UE domain scores and UE strength (r = 0.66). Self-care domain scores and the stair climb time were negatively related (r = −0.68). There was a strong correlation between GNEM-FAS total scores and IBMFRS scores (r = 0.94).

Mobility was limited more than UE or self-care function in this cohort of ambulatory subjects with GNE myopathy. Repeat administration in treated and untreated patients with varying degrees of severity is underway to further validate the instrument.

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P.3.2
Characterization of strength and function in adults with inclusion body myopathy (HIBM)/GNE myopathy

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Mobility was limited more than UE or self-care function in this cohort of ambulatory subjects with GNE myopathy. Repeat administration in treated and untreated patients with varying degrees of severity is underway to further validate the instrument.

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