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Characterizing Enrollment in Observational Studies of Duchenne Muscular Dystrophy by Race and Ethnicity

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Abstract

Observational research benefits from inclusion of diverse cohorts. To characterize racial and ethnic diversity in observational and natural history research studies of Duchenne muscular dystrophy (DMD), highly cited and influential observational studies were identified. Fourteen United States-based articles were included. All studies cited >70% White participants with the majority having few racial minority participants. Enrollment of Black/African American individuals was particularly limited (<5% in all but one study), and Hispanic/Latino participants ranged from 3.3–26.5% of cohorts. These results suggest a need for effective strategies to recruit, enroll, and retain racially and ethnically diverse populations into observational research in DMD.

Keywords

Muscular dystrophies; Bibliometrics; Healthcare Disparities; Minority Health; Observational Studies

INTRODUCTION

Duchenne muscular dystrophy (DMD) is a life-limiting muscle wasting disorder that leads to progressive skeletal and cardiac muscle weakness (1). In the last decade, several natural history studies have been conducted in the United States (US) to better characterize disease progression in DMD. Additional studies have sought to characterize quality of life (QOL)

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Conflicts of Interest

Dr. Alison M Barnard has no conflicts of interest to report.

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and patient/caregiver preferences for potential therapies. The purposes of these observational research efforts are to inform clinical decision making, improve clinical trial design, develop better trial endpoints, understand what is meaningful to patients/caregivers, and quantify the impact of various factors on QOL (2–4).

In general, observational research studies such as these are at risk of selection bias because certain groups of people are more likely to volunteer to participate than others (5). For example, people from racial and ethnic minority groups in the US may be less likely to participate in research than White individuals for a number of reasons, including a distrust of medical research and a lack of access to information and resources (6–8). Little is known about the racial and ethnic make-up of the US DMD population, nor about the racial and ethnic makeup of individuals with DMD and caregivers who volunteer to participate in research. This problem is significant as a lack of racial and ethnic representation among study participants could lead to inaccurate evaluations of the true natural history of disease progression and erroneous conclusions regarding QOL and patient preference data. Therefore, the aim of this study was to examine the racial and ethnic composition of highly cited, contemporary, US-centric observational studies in DMD.

METHODS

A bibliometric analysis was conducted to identify the most highly cited observational and natural history studies involving individuals with DMD published within the last decade (Jan 2009 – May 2019) (9). We chose highly cited studies, defined as the ten articles with the highest total citation count, as they are likely the most influential observational studies informing decision-making. Because older articles tend to have higher total citation counts than newer articles, we also examined articles by citations/year. Any additional articles identified as one of the ten with the highest citations/year were included. Harzing's Publish or Perish software (Windows 4.17.2019 release) was used to query articles from Google Scholar (10). Search terms included combinations of the words Duchenne, race, ethnicity, Asian, Hispanic, Caucasian, and Black. Final queries were performed on 5/22/2019.

Results from the queries were reviewed by two independent reviewers (authors AMB, SLR) to identify the top ten articles by citations and citations/year. Included articles were required to meet the following criteria: 1) observational or natural history study design in a US-centric DMD population, 2) inclusion of sample size and race/ethnicity classifications, and 3) optional participation. To focus on individuals with DMD, manuscripts surveying caregivers regarding preferences or treatments for their child were included; however, manuscripts detailing caregiver burdens or other caregiver information were excluded. It was decided *a priori* to include qualifying Cooperative International Neuromuscular Research Group (CINRG) studies. Although this cohort is partly international, the initial cohort was comprised of nearly 150 individuals from the US (4)]. Retrospective studies, clinical trials, and interventional trials were excluded. Discrepancies within the final list were discussed and adjudicated by the two reviewers and coauthors.

In addition to studies identified in the search, self-reported racial/ethnic identity were determined for participants enrolled in ImagingDMD, a HIPAA-compliant and IRB-

approved natural history study of muscle magnetic resonance imaging biomarkers (NCT01484678). The US Food and Drug Administration (FDA) recommended categories for clinical trial reporting of race (White, Black/African American, Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and other/not reported) and ethnicity (Hispanic/Latino, not Hispanic/Latino) were utilized to report results (11). If studies utilized nonstandard categories, the categories of the original article were used with a note describing the deviation. For example, in several cases, Hispanic/Latino ethnicity was grouped with racial category rather than being reported separately.

RESULTS

In addition to ImagingDMD, 13 observational studies in DMD were identified from the search and identified as highly cited due to being in the top 10 most cited manuscripts or the top 10 manuscripts by citations/year, with seven articles overlapping (12–24). The manuscripts include seven natural history, three QOL, three patient preference, and one healthcare utilization studies. Sample sizes in the included studies ranged from 22 to 440 participants. Descriptions of all 14 studies are listed in Table 1.

The racial and ethnic composition of each study is described in Table 2. All study cohorts were comprised of >70% participants who identified as White/Caucasian (herein “White”), with 9/14 studies reporting ≥85% White participants. Black/African American (herein “Black”) participants were minimally represented with all but one study reporting cohorts of <5% (reported ranges: 1.0–8.3%). The numbers of American Indian/Alaska Native and Native Hawaiian/Pacific Islander participants were reported in 4/15 studies and were <4% in all cases. Hispanic/Latino (herein “Latino”) ethnicity was reported in 9/14 articles, and representation was highly variable, with reported ranges of 3.3–26.5% of cohorts.

DISCUSSION

The primary purpose of this study was to examine the US racial and ethnic composition of observational DMD studies deemed influential to the field. We found the majority of studies were comprised of participants who identified as White with limited participation of all other racial and ethnic groups. Census data from 2010 estimates that 72% of the US population identifies as White, 13% as Black, 5% as Asian, and 16% as Latino; however, the prevalence of DMD has been estimated to be lower in Black individuals and higher in Latino individuals compared to White individuals (25,26). The MD STARnet surveillance studies of Duchenne/Becker muscular dystrophy have found that within the surveillance network, 7.5% of individuals with DMD identified as Black, and 20.5% of individuals identified as Latino (26). Although these percentages cannot be assumed to be representative of the entire US population with DMD, in our review of highly cited observational literature, only one of the 14 studies had >7.5% Black participants, and only one had >20.5% Latino participants, indicating the potential for underrepresentation in nearly all studies.

The importance of racial diversity in medical research has been well recognized (27). For natural history studies in DMD specifically, surveillance data demonstrates that racial disparities and differences exist, warranting inclusion of diverse cohorts in observational

studies. For example, Black and Latino individuals are first evaluated in the diagnostic process nearly one year after White individuals, and age at DNA testing is nearly two years older (28). This finding was recently corroborated by a Duchenne Registry study in which White individuals were diagnosed nearly 9 months earlier than individuals of other racial and ethnic backgrounds (29). Black and Latino individuals are also less likely to be treated with corticosteroids than individuals who are White, and Black individuals with DMD initiate steroid treatment at an older age [28]. In a study in South Carolina, Black individuals with muscular dystrophy had lower overall health care utilization even when controlling for socioeconomic status [29]. Finally, racial and ethnic differences in milestone events such as age at loss of ambulation, development of cardiomyopathy or heart failure, and death are well-described [13,30].

Genetic differences could also affect the natural history of disease. Polymorphisms in *SPP1* and *LTBP4*, which have been linked to older age at loss of ambulation, occur with different frequencies in individuals of diverse racial or ethnic backgrounds, and within the CINRG cohort, the modifying effects of *LTBP4* could only be validated in a Caucasian subgroup analysis [13,31,32]. For QOL and patient preference studies, it is possible that cultural and/or socioeconomic differences lead to differences between racial/ethnic groups. A recent needs assessment of the MD STARnet cohort demonstrated differences in needs and unmet needs between minority and non-minority caregivers of individuals with DMD [33]. Without specific efforts to include racial and ethnic minority populations in observational trials, it appears unlikely the true natural history of the disease is being appropriately captured in these groups.

The limited diversity found in observational studies is likely recapitulated in clinical trials. US trials of edasolonexent and eteplirsen had 100% and 98.6% White cohorts, respectively [34,35]. Similarly, phase three international trials of ataluren and idebenone, which presented results to the US FDA, had <1% Black and 1.5% Latino participants, respectively [36,37]. Natural history data from another international ataluren trial has been utilized extensively in clinical trial planning and natural history comparisons in the US and informed the top two most cited articles in our search, but these studies had <2% Black and <3% Latino participants [38,39]. It can be argued that inclusion of more diverse cohorts into clinical trials may increase clinical heterogeneity and reduce the ability to detect treatment effects. This may be true; however, reducing racial disparities in standards of care and developing novel solutions to address cohort heterogeneity are more sustainable options than exclusion of potential participants. When clinical trials lack racial diversity, the investigational therapeutic is not being evaluated in a cohort that is representative of the entire population. In life-limiting disorders such as DMD, reduced minority participation in clinical trials may unintentionally limit minority access to novel therapeutics.

We do not underestimate the herculean efforts required to recruit large samples in any of the cited studies. We also recognize the challenges of recruiting diverse populations into observational studies in rare diseases such as DMD. Our hope is that this evidence of reduced participation from minority groups will lead to further discussion among academics, healthcare providers, advocacy organizations, the DMD community, and clinical trial sponsors regarding inclusion, participation, and retention of representative cohorts. Cues can

be taken from successful efforts in other populations to improve cohort diversity [40–43]. In investigational studies, obtaining better representation from diverse individuals leads to the best chances of maximizing impact on the entire DMD community.

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References

1. Birnkrant DJ, Bushby K, Bann CM, Apkon SD, Blackwell A, Brumbaugh D, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol. 2018 3;17(3):251–67. [PubMed: 29395989]
2. Straub V, Balabanov P, Bushby K, Ensini M, Goemans N, De Luca A, et al. Stakeholder cooperation to overcome challenges in orphan medicine development: the example of Duchenne muscular dystrophy. Lancet Neurol. 2016;15(8):882–90. [PubMed: 27302365]
3. Mayer OH, Aliverti A, Meier T. Breathe Duchenne: what natural history studies tell us about the progression of pulmonary morbidity in Duchenne muscular dystrophy. Neuromuscul Disord. 2018 11;28(11):910–3. [PubMed: 30266222]
4. McDonald CM, Henricson EK, Abresch RT, Han JJ, Escolar DM, Florence JM, et al. The Cooperative International Neuromuscular Research Group Duchenne Natural History Study — A longitudinal investigation in the era of glucocorticoid therapy: design of protocol and the methods used. Muscle Nerve. 2013 7;48(1):32–54. [PubMed: 23677550]
5. Tripepi G, Jager KJ, Dekker FW, Zoccali C. Selection bias and information bias in clinical research. Nephron Clin Pract. 2010;115(2):c94–99. [PubMed: 20407272]
6. Webb FJ, Khubchandani J, Striley CW, Cottler LB. Black-White differences in willingness to participate and perceptions about health research: results from the population-based HealthStreet Study. J Immigr Minor Health. 2019;21(2):299–305. [PubMed: 29603088]
7. Shavers VL, Lynch CF, Burmeister LF. Racial differences in factors that influence the willingness to participate in medical research studies. Ann Epidemiol. 2002 5;12(4):248–56. [PubMed: 11988413]
8. Wendler D, Kington R, Madans J, Van Wye G, Christ-Schmidt H, Pratt LA, et al. Are racial and ethnic minorities less willing to participate in health research? PLoS Med. 2006 2;3(2):e19. [PubMed: 16318411]
9. Narin F, Hamilton KS. Bibliometric performance measures. Scientometrics. 1996 7 1;36(3):293–310.
10. Jacsó P Calculating the h-index and other bibliometric and scientometric indicators from Google Scholar with the Publish or Perish software. Online Inf Rev [Internet]. 2009 11 27 [cited 2019 Aug 17]; Available from: https://www.emerald.com/insight/content/doi/10.1108/14684520911011070/full/html
11. U.S. Food and Drug Administration. Collection of race and ethnicity data in clinical trials: guidance for industry and food and drug administration staff. Silver Spring, MD; 2016.
12. Arias R, Andrews J, Pandya S, Pettit K, Trout C, Apkon S, et al. Palliative care services in families of males with Duchenne muscular dystrophy. Muscle Nerve. 2011 7;44(1):93–101. [PubMed: 21674523]
13. Bello L, Kesari A, Gordish-Dressman H, Cnaan A, Morgenroth LP, Punetha J, et al. Genetic modifiers of ambulation in the CINRG Duchenne Natural History Study. Ann Neurol. 2015 1;77(4):684–96. [PubMed: 25641372]
14. Chung J, Smith AL, Hughes SC, Niizawa G, Abdel-Hamid HZ, Naylor EW, et al. Twenty-year follow-up of newborn screening for patients with muscular dystrophy. Muscle Nerve. 2016 4;53(4):570–8. [PubMed: 26260293]

15. Davis SE, Hynan LS, Limbers CA, Andersen CM, Greene MC, Varni JW, et al. The PedsQL in pediatric patients with Duchenne muscular dystrophy: feasibility, reliability, and validity of the Pediatric Quality of Life Inventory Neuromuscular Module and Generic Core Scales. J Clin Neuromuscul Dis. 2010 3;11(3):97–109. [PubMed: 20215981]
16. Donders J, Taneja C. Neurobehavioral characteristics of children with Duchenne muscular dystrophy. Child Neuropsychol. 2009 5;15(3):295–304. [PubMed: 19160150]
17. Fee RJ, Hinton VJ. Resilience in children diagnosed with a chronic neuromuscular disorder. J Dev Behav Pediatr. 2011 11;32(9):644–50. [PubMed: 22008789]
18. Hollin IL, Peay HL, Bridges JFP. Caregiver preferences for emerging Duchenne muscular dystrophy treatments: a comparison of best-worst scaling and conjoint analysis. Patient. 2015 2;8(1):19–27. [PubMed: 25523316]
19. Hollin IL, Peay HL, Apkon SD, Bridges JFP. Patient-centered benefit-risk assessment in Duchenne muscular dystrophy. Muscle Nerve. 2017;55(5):626–34. [PubMed: 27649378]
20. Mayer OH, Finkel RS, Rummey C, Benton MJ, Glanzman AM, Flickinger J, et al. Characterization of pulmonary function in Duchenne muscular dystrophy. Pediatr Pulmonol. 2015 5;50(5):487–94. [PubMed: 25755201]
21. McDonald CM, Henricson EK, Abresch RT, Duong T, Joyce NC, Hu F, et al. Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study. The Lancet. 2017;391(11019):451–61.
22. McDonald CM, Gordish-Dressman H, Henricson EK, Duong T, Joyce NC, Jhawar S, et al. Longitudinal pulmonary function testing outcome measures in Duchenne muscular dystrophy: Long-term natural history with and without glucocorticoids. Neuromuscul Disord. 2018 11;28(11):897–909. [PubMed: 30336970]
23. Peay HL, Hollin I, Fischer R, Bridges JFP. A community-engaged approach to quantifying caregiver preferences for the benefits and risks of emerging therapies for Duchenne muscular dystrophy. Clin Ther. 2014 5;36(5):624–37. [PubMed: 24852596]
24. Uzark K, King E, Cripe L, Spicer R, Sage J, Kinnett K, et al. Health-related quality of life in children and adolescents with Duchenne muscular dystrophy. Pediatrics. 2012 12;130(6):e1559–1566. [PubMed: 23129083]
25. Humes KR, Jones NA, Ramirez RR. Overview of race and Hispanic origin: 2010 [Internet]. 2011 [cited 2019 Nov 9]. Available from: https://www.census.gov/library/publications/2011/dec/c2010br-02.html
26. Romitti PA, Zhu Y, Puzhankara S, James KA, Nabukera SK, Zamba GKD, et al. Prevalence of Duchenne and Becker muscular dystrophies in the United States. Pediatrics. 2015 3;135(3):513–21. [PubMed: 25687144]
27. Oh SS, Galanter J, Thakur N, Pino-Yanes M, Barcelo NE, White MJ, et al. Diversity in clinical and biomedical research: A promise yet to be fulfilled. PLOS Med. 2015 12 15;12(12):e1001918. [PubMed: 26671224]
28. Holtzer C, Meaney FJ, Andrews J, Ciafaloni E, Fox DJ, James KA, et al. Disparities in the diagnostic process of Duchenne and Becker muscular dystrophy. Genet Med Off J Am Coll Med Genet. 2011 11;13(11):942–7.
29. Counterman KJ, Furlong P, Wang RT, Martin AS. Delays in diagnosis of Duchenne muscular dystrophy: An evaluation of genotypic and sociodemographic factors. Muscle Nerve. 2019 10 1;
30. Fox DJ, Kumar A, West NA, DiRienzo AG, James KA, Oleszek J, et al. Trends with corticosteroid use in males with Duchenne muscular dystrophy born 1982–2001. J Child Neurol. 2015 1;30(1):21–6. [PubMed: 24682290]
31. Ozturk OD, McDermott S, Mann JR, Hardin JW, Royer JA, Ouyang L. Disparities in health care utilization by race among teenagers and young adults with muscular dystrophy. Med Care. 2014 10;52(10 Suppl 3):S32–39.
32. Kenneson A, Vatave A, Finkel R. Widening gap in age at muscular dystrophy–associated death between blacks and whites, 1986–2005. Neurology. 2010 9 14;75(11):982–9. [PubMed: 20837966]

33. Flanigan KM, Ceco E, Lamar K-M, Kaminoh Y, Dunn DM, Mendell JR, et al. LTBP4 genotype predicts age of ambulatory loss in Duchenne muscular dystrophy. Ann Neurol. 2013 4 1;73(4):481–8. [PubMed: 23440719]
34. Pegoraro E, Hoffman EP, Piva L, Gavassini BF, Cagnin S, Ermani M, et al. SPP1 genotype is a determinant of disease severity in Duchenne muscular dystrophy. Neurology. 2011;76(3):219–226. [PubMed: 21178099]
35. Conway KM, Eichinger K, Trout C, Romitti PA, Mathews KD, Pandya SK, et al. Needs management in families affected by childhood-onset dystrophinopathies. SAGE Open Med. 2019;7:2050312119834470. [PubMed: 30854202]
36. Finanger E, Vandenborne K, Finkel RS, Lee Sweeney H, Tennekoon G, Yum S, et al. Phase 1 study of Edasalonexent (CAT-1004), an oral NF-κB inhibitor, in pediatric patients with Duchenne muscular dystrophy. J Neuromuscul Dis. 2019;6(1):43–54. [PubMed: 30452422]
37. Khan N, Eliopoulos H, Han L, Kinane TB, Lowes LP, Mendell JR, et al. Eteplirsen Treatment Attenuates Respiratory Decline in Ambulatory and Non-Ambulatory Patients with Duchenne Muscular Dystrophy. J Neuromuscul Dis. 2019 3 7;6(2):213–25. [PubMed: 30856119]
38. Buyse GM, Voit T, Schara U, Straathof CSM, D'Angelo MG, Bernert G, et al. Efficacy of idebenone on respiratory function in patients with Duchenne muscular dystrophy not using glucocorticoids (DELOS): a double-blind randomised placebo-controlled phase 3 trial. The Lancet. 2015 5 8;385(9979):1748–57.
39. McDonald CM, Campbell C, Torricelli RE, Finkel RS, Flanigan KM, Goemans N, et al. Ataluren in patients with nonsense mutation Duchenne muscular dystrophy (ACT DMD): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2017 23;390(10101):1489–98. [PubMed: 28728956]
40. McDonald CM, Henricson EK, Abresch RT, Florence J, Eagle M, Gappmaier E, et al. The 6-minute walk test and other clinical endpoints in Duchenne muscular dystrophy: reliability, concurrent validity, and minimal clinically important differences from a multicenter study. Muscle Nerve. 2013;48(3):357–368. [PubMed: 23674289]
41. McDonald CM, Henricson EK, Abresch RT, Florence JM, Eagle M, Gappmaier E, et al. The 6-minute walk test and other endpoints in Duchenne muscular dystrophy: longitudinal natural history observations over 48 weeks from a multicenter study. Muscle Nerve. 2013 9;48(3):343–56. [PubMed: 23681930]
42. Ratto AB, Anthony BJ, Pugliese C, Mendez R, Safer-Lichtenstein J, Dudley KM, et al. Lessons learned: Engaging culturally diverse families in neurodevelopmental disorders intervention research. Autism Int J Res Pract. 2017 7;21(5):622–34.
43. Ejiogu N, Norbeck JH, Mason MA, Cromwell BC, Zonderman AB, Evans MK. Recruitment and retention strategies for minority or poor clinical research participants: lessons from the Healthy Aging in Neighborhoods of Diversity across the Life Span study. The Gerontologist. 2011 6;51 Suppl 1:S33–45. [PubMed: 21565817]
44. Bonevski B, Randell M, Paul C, Chapman K, Twyman L, Bryant J, et al. Reaching the hard-to-reach: a systematic review of strategies for improving health and medical research with socially disadvantaged groups. BMC Med Res Methodol. 2014 3 25;14:42. [PubMed: 24669751]
45. Hilton CL, Fitzgerald RT, Jackson KM, Maxim RA, Bosworth CC, Shattuck PT, et al. Brief report: Under-representation of African Americans in autism genetic research: a rationale for inclusion of subjects representing diverse family structures. J Autism Dev Disord. 2010 5;40(5):633–9. [PubMed: 19936905]

Table 1:

Most Highly Cited Observational Studies in DMD that Include Race/Demographics (2009–2019)

Article	Study Type	Cohort	Study Description and Outcomes
ImagingDMD NCT01484678	NH	Primarily nationally recruited cohort of boys and adolescents with DMD. Participants were compensated $20.	Natural history study of muscle magnetic resonance biomarkers.
Arias 2011(12)	SU	Caregivers recruited via neuromuscular clinics in the MD STARnet network and MDA/PPMD announcements. Participants were compensated $20.	Survey study of palliative care services utilized by individuals with DMD.
Bello 2015(13)	NH	Cooperative International Neuromuscular Research Group Duchenne Natural History Study cohort.	*LTBP4* and *SPP1* polymorphisms examined for differences in age at loss of ambulation.
Chung 2015(14)	QOL	Subset of individuals with DMD or BMD (born between 1986–1996) followed at Pittsburgh MDA clinics and their parents.	Survey assessments of quality of life and attitudes regarding newborn screening.
Davis 2010(15)	QOL	Recruited 8–18 year olds from the Neuromuscular Disease Clinic at Children's Medical Center of Dallas.	Administered the PedsQL at baseline and 2–6 weeks later to determine feasibility, reliability, and validity.
Donders 2009(16)	NH	6–16 year olds with DMD recruited from a regional neuromuscular clinic and siblings were included if applicable. Participants were compensated $25.	Administered tests of neuropsychological function and behavior.
Fee 2011(17)	NH	Individuals with DMD recruited from four MDA clinics and information distributed by MDA.	Administered the Child Behavior Checklist as a proxy for resilience.
Hollin 2015(18)	PP	Caregivers were recruited through PPMD and DuchenneConnect.	Compared best-worst scaling assessment of benefit and risk preferences for therapies to conjoint analysis of therapy acceptance
Hollin 2017(19)	PP	Individuals with DMD, BMD, IMD, and caregivers recruited at the annual PPMD conference and through email to Duchenne Registry participants.	Best-worst scaling survey used to assess benefits, risks, and preferences for therapies for pulmonary health.
Mayer 2015(20)	NH	Individuals with DMD recruited from the neuromuscular clinic at the Children's Hospital of Philadelphia.	Cross sectional study of pulmonary function in 5–24 year olds.
McDonald 2018 A(21)	NH	Cooperative International Neuromuscular Research Group Duchenne Natural History Study cohort.	Compared function, survival, and QOL in steroid treated and untreated individuals.
McDonald 2018 B(22)	NH	Cooperative International Neuromuscular Research Group Duchenne Natural History Study cohort.	Assessed pulmonary function over a period of up to 10 years.
Peay 2014(23)	PP	Caregivers were recruited using social media, newsletters, PPMD emails, and DuchenneConnect.	Best-worst scaling survey used to assess benefit and risk preferences for therapies.
Uzark 2012(24)	QOL	Recruited 6–18yos and their parents from the Comprehensive Neuromuscular Care Center at Cincinnati Children's Hospital and the annual PPMD conference.	PedsQL assessed in 203 families.

NH = natural history, SU = service utilization, MDA = Muscular Dystrophy Association, PPMD = Parent Project Muscular Dystrophy, QOL = quality of life, BMD = Becker muscular dystrophy, PP = patient preference, IMD = intermediate muscular dystrophy

Table 2:

Racial and Ethnic Composition of Highly Cited Observational Studies in DMD

Article	Study size (N)	White	Black/ African American	American Indian or Alaska Native	Asian (including South Asian)	Native Hawaiian or Pacific Islander	Other/ Unknown	Hispanic/ Latino
ImagingDMD NCT01484678	182	164 90.1%	3 1.6%	2 1.1%	10 5.5%	1 0.5%	2/0 1.1/0%	17 9.3%
Arias 2011(12)	34	25 73.5%	-	-	-	-	-	9[a] 26.5%
Bello 2015(13)	340	248 72.9%	6 1.8%	-	55 16.2%	-	13/0 3.8/0%	41[a] 12.1%
Chung 2015(14)	40[b]	37 92.5%	-	-	3 7.5%	-	-	-
Davis 2010(15)	44	37 84.1%	2 4.5%	-	-	-	2/3 4.5/6.8%	7 15.9%
Donders 2009(16)	22[c]	21 95%	-	-	-	-	-	-
Fee 2011(17)	165[d]	- 89%	- 4%	-	- 3%	-	-	-[a] 4%
Hollin 2015(18)	119	109 91.6%	-	-	-	-	-	-
Hollin 2017(19)	133[e]	119 89.5%	6 4.5%	5 3.8%	3 2.2%	-	2/0 1.5/0%	10 7.5%
Mayer 2015(20)	60	51 85.0%	5 8.3%	-	2 3.3%	-	-	2[a] 3.3%
McDonald 2018 A(21)	440	315 71.6%	6 1.4%	-	77 17.5%	3 0.7%	29/10 6.6/2.3%	51 11.6%
McDonald 2018 B(22)	397	285 71.8%	6 1.5%	-	69 17.4%	3 0.8%	28/6 7.1/1.5%	50 12.6%
Peay 2014(23)	119	109 91.6%	-	-	-	-	-	-
Uzark 2012(24)	203[f]	183 90.1%	2 1.0%	-	3 1.5%	-	8/7 3.9/3.4%	-

Percents may not sum to 100 due to rounding.

[a] Ethnicity was reported in combination with race, rather than as a separate category.

[b] n=15 individuals with dystrophinopathy (DMD=14, BMD=1) and n=25 parents (DMD=22, BMD=3).

[c] In addition to the 22 individuals with DMD, the study included 18 unaffected siblings (94% White).

[d] Only percentages were reported, precluding reporting of exact sample sizes.

[e] Participants were allowed to choose more than one racial category; thus, numbers do not sum to 133 and percentages do not sum to 100%. N=51 participants with dystrophinopathy (DMD=42, BMD=9). N=82 caregivers (DMD=72, BMD=8, intermediate muscular dystrophy=2).

[f] N=117 individuals with DMD, and N=200 parents, representing 203 families. Results describe family units. Asian and Pacific Islander categories grouped by author.