HHS Public Access

Author manuscript

Neuroepidemiology. Author manuscript; available in PMC 2024 January 09.

Published in final edited form as:

Neuroepidemiology. 2023 ; 57(2): 90–99. doi:10.1159/000528962.

Racial and ethnic differences in timing of diagnosis and clinical services received in Duchenne Muscular Dystrophy

Joshua Mann[1,*], **Yanan Zhang**[2], **Suzanne McDermott**[3], **Yinding Wang**[4,5], **Bo Cai**[2], **Kristin M. Conway**[6], **Pangaja Paramsothy**[5], **Julie Royer**[7], **Swamy Venkatesh**[8], **James F. Howard Jr.**[9], **Emma Ciafaloni**[10],

MD STAR*net*

[1]Department of Preventive Medicine, School of Medicine and John D. Bower School of Population Health, University of Mississippi Medical Center, Jackson, MS

[2]Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC

[3]Department of Environmental, Occupational, Geospatial Health Sciences, Graduate School of Public Health and Health Policy, City University of New York, New York, NY

[4]McKing Consulting Corporation, Atlanta, GA.

[5]Division of Birth Defects and Infant Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA

[6]Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, IA

[7]Health and Demographics Division, South Carolina Revenue and Fiscal Affairs Office, Columbia, SC

[8]Department of Neurology, University of South Carolina, Columbia, SC

[9]Department of Neurology, The University of North Carolina at Chapel Hill, Chapel Hill, NC

[*]Corresponding Author: Joshua R. Mann, Department of Preventive Medicine, School of Medicine and John D. Bower School of Population Health, University of Mississippi Medical Center, 1500 North State Street, Jackson, MS 39216, Tel: 601-815-8988 jmann4@umc.edu.

NOTE: Joshua Mann, Yanan Zhang, and Suzanne McDermott are all first authors, as they were equally responsible for the work described in this paper.

Author Contributions

Joshua Mann, Suzanne McDermott, and Bo Cai conceptualized the study and provided overall direction to analyses and writing. Yanan Zhang (primary analyst), Bo Cai, and Yinding Wang (secondary analyst) performed data analyses. Yanan Zhang, Joshua Mann, and Suzanne McDermott led the writing of the manuscript. Kristin M. Conway, Pangaja Paramsothy, Emma Ciafaloni, Julie Royer, Swamy Venkatesh, and James F. Howard, Jr. provided input and feedback on the background, study design, data analyses and interpretation, and provided editorial input during the writing of the paper.

The data analyzed were collected through the MD STAR*net*, a multi-state muscular dystrophy surveillance system operated with funding and direction from the Centers for Disease Control and Prevention.

Authors' conflicts of interest

None.

Statement on Ethics

All sites had Institutional Review Board approval or exemption: AZ (approved by University of Arizona, IRB 04-0203-02), CO (exempted by Colorado Department of Public Health & Environment), GA(approved by Centers for Disease Control and Prevention, IRB 4792.0), IA (approved by The University of Iowa, IRB 201408761), Piedmont region of NC (exempted by Research Triangle Institute), western New York (approved New York State Department of Health, IRB 03-062), SC (approved by South Carolina Department of Health & Environmental Control, IRB 15-001), and UT(approved by University of Utah, IRB 00077174).

[10]Department of Neurology, University of Rochester, Rochester, NY

Abstract

Introduction: Racial/ethnic differences in diagnostic and treatment services have been identified for a range of health conditions and outcomes. The current study aimed to analyze whether there are racial/ethnic differences in the timing of diagnostic testing and treatments for males with Duchenne Muscular Dystrophy (DMD).

Methods: Diagnostic and clinical data for male individuals with DMD born during 1990–2010 were analyzed from eight sites (Arizona, Colorado, Georgia, Iowa, Piedmont Region of North Carolina, western New York, South Carolina, Utah) of the Muscular Dystrophy Surveillance Tracking and Research Network (MD STAR*net*). Seven milestones related to diagnosis/treatment experiences were selected as outcomes. Times to each milestone were estimated and compared by four racial/ethnic groups using Kaplan-Meier estimation and Cox proportional hazard models. Times between initial evaluation or diagnostic testing and later milestones were also compared by race/ethnicity.

Results: We identified 682 males with definite or probable DMD of whom 61.7% were non-Hispanic White, 20.5% Hispanic, 10.6% other, and 7.2% non-Hispanic Black. Seven milestone events were studied (initial evaluation, first neurology/neuromuscular visit, diagnosis, corticosteroid treatment first offered, corticosteroid treatment started, first electrocardiogram or echocardiogram, and first pulmonary function testing). The first five milestone events occurred at an older age for non-Hispanic Black individuals compared to non-Hispanic White individuals. Time from diagnosis to first offering of corticosteroids and initiation of corticosteroid therapy was later for Hispanic individuals compared to non-Hispanic White individuals. When accounting for timing of initial evaluation/diagnosis, offering of corticosteroids continued to occur later, but first pulmonary testing occurred earlier, among Hispanic individuals compared to non-Hispanic Whites. No significant delays remained for non-Hispanic Black individuals after accounting for later initial evaluation/diagnosis.

Conclusion: We described racial/ethnic differences in ages at selected diagnostic and treatment milestones. The most notable differences were significant delays for five of seven milestones in non-Hispanic Black individuals, which appeared to be attributable to later initial evaluation/diagnosis. Findings for Hispanic individuals were less consistent. Efforts to address barriers to early evaluation and diagnosis for non-Hispanic Black children with DMD may promote more timely initiation of recommended disease monitoring and interventions.

Keywords

Duchenne muscular dystrophy; race; ethnicity; health services; disparities

Introduction

Duchenne Muscular Dystrophy (DMD) is an X-linked condition caused by a mutation in the *DMD* gene that interferes with dystrophin production. Typically, the symptoms of DMD are observed before age five years and there is gradual worsening of symptoms with loss of ambulation by about twelve years of age [1–3]. DMD is a complex disease that affects the

neuromuscular, cardiac, and pulmonary systems; neurocognitive and skeletal complications are also common. Early diagnosis is important for optimal treatment of primary muscle weakness and subsequent morbidities. A series of treatment guidelines have been published that outline the diagnostic process and multidisciplinary management of DMD, including initiation of corticosteroids and regular monitoring of pulmonary and cardiac function [4–8].

Racial/ethnic differences in diagnosis, treatment, and outcomes are well known for a range of health conditions and outcomes, but few studies have evaluated whether such differences exist among individuals diagnosed with DMD [9]. The National Survey of Children's Health asked parents about their children's experiences with racial or ethnic discrimination in 2011–2012 [10] and in 2016–2017 [11]. Significantly higher proportions of parents of non-Hispanic Black children reported discrimination (approximately 9% in the two study periods) as compared to less than 1.5% by parents of non-Hispanic White children. In addition, when parents reported that children experienced discrimination, they had twice the odds of unmet healthcare needs, compared to children who did not experience discrimination [11]. A review of racial, ethnic and socioeconomic differences in pediatric critical care in the United States identified differences in care by race/ethnicity and by socioeconomic status [12]. Using administrative databases to identify teenagers and young adults with muscular dystrophy (MD), Ozturk et al. reported differences by race with fewer visits to primary care and specialist providers and physical/occupational therapists and higher rates of emergency department visits and hospitalizations among Black individuals as compared to White individuals even though the same insurance benefits were available [13]. Similarly, two studies by the US population-based Muscular Dystrophy Surveillance, Tracking and Research Network (MD STAR*net*) have found racial differences in times of evaluation and diagnosis for individuals diagnosed of Duchenne-Becker MD (DBMD). Holtzer et al 's paper [14] analyzed samples born during 1982–2001. Older ages at initial evaluation, creatine kinase (CK) measurement, and DNA testing were found in non-Hispanic Black and Hispanic combined. Thomas et al 's paper [15] used individuals born during 2000–2015 and without a documented family history. Compared to non-Hispanic White individuals, non-Hispanic Blacks were found have older ages in initial evaluation, CK testing, first neurology/ neuromuscular visit, and DNA/ muscle biopsy testing; Hispanics have older ages in CK and DNA/ muscle biopsy testing. Another MD STAR*net* study showed significantly less corticosteroid use by Hispanic and non-Hispanic Black individuals when compared to their non-Hispanic White counterparts [16]. Using MD STAR*net* data from a structured interview with 34 primary caregivers of young men with DMD, racial/ethnic differences in the receipt of services were not found, although it was noted that, overall, potentially beneficial health care services were frequently not utilized [17].

The previous MD STAR*net* studies focus on one or more aspects of the health services received by patients (e.g., diagnosis, steroids treatment, or health service utilization). Our study aimed to conduct a full evaluation of potential racial/ethnic differences by using seven important milestone events. We included cases from the extended study period of 1982 – 2015, so that the increased sample size allows us to study non-Hispanic Black and Hispanic independently. In addition to comparing the timing of diagnostic and treatment milestones by race/ethnicity, we also examined times from initial evaluation (age when concerns about neurological symptoms/developmental delays prompted initial evaluation) or

diagnostic testing to later milestones to evaluate racial/ethnic differences in the provision of services once diagnosed. The goal of this analysis was to evaluate whether racial/ethnic differences in later experiences were accounted for (fully, partially, or not at all) by delays in early/diagnostic milestones. Finally, we examined the possibility of changes in racial/ethnic differences over time since the study period spans approximately 3 decades.

Methods

Study Population and Data Sources

MD STAR*net* is a multisite population-based surveillance system funded by the Centers for Disease Control and Prevention that identifies and follows individuals diagnosed with DBMD. The surveillance methodology has been described previously [18–22]. Briefly, data collection was initiated in 2004 at 4 sites (Arizona [AZ], Colorado [CO], Iowa [IA], and 12 counties in Western New York [wNY]); two additional sites were added in 2006 (Georgia [GA], Hawaii [HI]). Medical record abstraction was completed for residents of an MD STAR*net* site who were born on or after and had a health encounter during January 1, 1982 through December 31, 2011 (December 31, 2012 for those identified in 2011). In 2014, MD STAR*net* was comprised of 6 sites (CO, IA, 31 counties in North Carolina's Piedmont region [NC], 21 counties in wNY, South Carolina [SC], Utah/Nevada [UT/NV]). Medical record abstraction was completed for those born on or after January 1, 2000 through December 31, 2015 who were residents of a site and had a health encounter during this time. When combining data from the two cohorts of data collection, we retained data for the most recent data collection period for any individual in both cohorts (those born on or after January 1, 2000 in CO, IA, or wNY). The overall study period is from January 1, 1982, to December 31, 2015.

The MD STAR*net* case identification and data abstraction approach have been described in detail previously [18, 19, 23]. In short, cases were screened for cohort eligibility (resident of MD STAR*net* site, eligible cohort birth date, and diagnosis prior to cohort end date) using International Classification of Diseases, Ninth Revision ICD-9 (ICD-9-CM) code 359.1 and International Classification of Diseases, Tenth Revision (ICD-10) code G71.0, from neuromuscular clinics, private practices, and hospitals. Administrative data sources were also used to determine eligibility, though availability varied across participating sites. These administrative data sources could include birth defects surveillance programs, health system administrative data, hospital discharge summaries, Medicaid claims, and birth and death certificates.

Medical record abstraction was conducted for cases screened to be eligible to confirm the diagnosis of DBMD and to collect longitudinal clinical care and outcome information. Abstraction was conducted by trained abstractors for demographic characteristics, medical history (including clinical signs and symptoms), diagnostic information, clinical care, outcomes and milestones, and family history. Cases were reviewed by a committee of neuromuscular clinical experts and were assigned a case status (definite, probable, possible, asymptomatic, manifesting carrier/affected female, or not affected).

Inclusion/Exclusion Criteria

We included males diagnosed with DMD who were assigned a definite or probable case status (shown in Supplemental Table 1, Fig. 1). Due to incomplete case ascertainment or truncated data collection, cases from HI and NV were excluded. We excluded males born before January 1, 1990, due to differences in health services in the earlier years; males born after December 31, 2010 were also excluded because they had not reached 5 years of age during the surveillance period. Younger brother(s) from multiple-affected families were excluded as their diagnosis timeline and treatment choices could have been impacted by the older sibling's experience. DMD phenotype (Duchenne, Becker, affected female, termination, inconclusive) was determined post-hoc using an analytic algorithm developed by MD STAR*net* researchers (Supplemental Table 2) [24]. There were 100 cases who were classified as Becker or unclassified phenotype, which were excluded from the main analysis.

Outcomes

Abstractors recorded the date or age (accurate to month) if date was missing when the medical record indicated a child was evaluated or referred for a concern about development. Clinical data included complete dates (month, day, year) of neuromuscular or neurology visits and corticosteroid treatment, and partial dates (month, year) for ages at diagnostic testing (muscle biopsy or DNA testing), electrocardiogram or echocardiogram, and pulmonary function testing. Missing month was imputed as 7 and missing day was imputed as 15. We calculated the ages for the following clinical milestones: (1) initial evaluation, (2) first neurology/ neuromuscular specialist visit, (3) earliest diagnostic confirmation by genetic testing or muscle biopsy, (4) first ECG or echocardiogram, (5) first offering of corticosteroid treatment, (6) initiation of corticosteroid treatment, and (7) first pulmonary function test (PFT). Typically children at least five years old are able to cooperate with PFT procedures [25]. Based on input from clinician experts on the research team, we excluded PFTs collected before 4 years of age, from analysis.

Exposure

Race/ethnicity was collected from medical records or linkages to birth certificate data, where available. Racial/ethnic groups were reclassified as non-Hispanic White, non-Hispanic Black, Hispanic and, because of small sample sizes, Other (includes Asian or Hawaiian or Pacific Islander, Native American or American Indian or Alaska Native, Multiple, Other, and Unknown).

Confounders and Other Variables

Parental age at the child's birth was obtained from medical records and birth certificates; age from the medical record was used if discrepant. Since the maternal and paternal ages are highly linear correlated, we used the average of both parents' ages. If one parent's age was missing, the other parent's age was used as the parental age at birth. Maternal and paternal education were collected from birth certificate data. If maternal education was missing, paternal education level was used, if available. Parental education was categorized into 5 levels: less than high school, high school graduate or GED, some college or 2-year degree, bachelor's degree or higher, and missing/unknown. Family history of DMD was defined as

Yes, No and Unknown. Cohort eligibility was used to indicate the birth cohort from which data were used. MD STAR*net* site was also included (AZ, CO, IA, GA, SC, NC, wNY, and UT).

Statistical Analysis

Frequencies and proportions were used to describe the distributions of categorical variables; means and standard deviations were used for continuous variables. The age in years when 50% (25%, 75%) of individuals had each milestone was estimated using Kaplan-Meier (KM) estimator. The log-rank test was used to compare survival distribution of each milestone by racial/ethnic groups.

Cox proportional hazards (PH) models were used to estimate adjusted hazard ratios (aHR)s and 95% confidence intervals (CI)s after controlling for parental age at child's birth, parental education, family history, birth year, cohort eligibility and MD STAR*net* site. Site was treated as a random effect so that the impact of site on the outcomes can be adjusted and the hazard ratios can be generalized to the DMD population across the combined eight state area [26]. Age at each milestone was used as the survival time; the last medical provider visit was used for those who did not experience the milestone. To evaluate changes over time, interactions between birth year and race/ethnicity were also tested. When examining time between milestones, Cox PH models were fitted using the time from initial evaluation or diagnosis to each remaining milestone. The PH assumption was assessed by the Schoenfeld residuals. If the assumption was violated, a time-dependent Cox model using linear time function was fitted. To assess any potential bias resulting from classification of clinical case status and phenotype, a sensitivity analysis was done by including only definite cases who met at least two phenotype criteria. Statistical analyses were conducted using SAS statistical software 9.4 (SAS Institute Inc). All tests were two-tailed, and type I error probability was set at 0.05.

Results

We identified 682 males diagnosed with DMD. The racial/ethnic distribution was mostly non-Hispanic White followed by Hispanic, non-Hispanic Black, and Other races/ethnicities (shown in Table 1). On average, males were evaluated for DMD prior to 4 years old and diagnosed by age 5 (Fig. 2); subsequent treatments and evaluations occurred 2–3 years following diagnosis.

KM analyses demonstrated variation by race/ethnicity for reaching all milestones except first ECG/echocardiogram and PFT (Table 2). Age at initial evaluation was latest for non-Hispanic Black males (6.0 years), followed by Hispanic and non-Hispanic White males (3.7 years), and those of Other race/ethnicity (4.1 years). The delay in the other outcomes depended on the delay in initial evaluation. For example, the later initial evaluation (6.0 years for non-Hispanic Black vs. 3.7 years for non-Hispanic White) led to the older age at first neurology visit (7.0 years for non-Hispanic Black vs. 4.7 years for non-Hispanic White). The time intervals between initial evaluation and age at first neurology visit, are one year for both racial/ethnic groups.

Results from PH modeling showed Hispanic males were older at first offering and initiation of corticosteroid treatment as compared to non-Hispanic White males. Additionally, non-Hispanic Black males were older at initial evaluation, consultation with a neurology/neuromuscular specialist, confirmatory diagnosis, and first offering and initiation of treatment with corticosteroids as compared to non-Hispanic White males (Table 3). For the time when corticosteroid was initially offered, the proportional hazard assumption was violated, and thus a time dependent Cox PH model was fitted. Figure 3 illustrated how the racial/ethnic differences changed with time. The decreased hazard ratio indicated at an earlier age, non-Hispanic Black and Hispanic individuals have slight differences in receiving the first corticosteroid, compared to non-Hispanic Whites. But the delay becomes more pronounced as age increased.

PH modeling of time from initial evaluation to the first neurology/neuromuscular visit or confirmatory diagnostic testing showed no differences by race/ethnicity (Table 4). Modeling of time from diagnosis to subsequent milestones showed Hispanic males experienced a longer time between diagnosis to first offering of corticosteroids, but a shorter time to first PFT, as compared to non-Hispanic White males.

Interactions between birth year and race/ethnicity were insignificant for all milestones: earliest concern ($p=0.74$), first neurology/neuromuscular visit ($p=0.96$), diagnosis ($p=0.99$), first ECG or echocardiogram ($p=0.27$), corticosteroid treatment first offered ($p=0.38$), corticosteroid started ($p=0.09$), and first PFT ($p=0.42$).

Restricting analyses to 595 males classified as definite DMD and who had at least two criteria for assigning DMD phenotype suggested no substantive bias due to phenotypic misclassification. (Supplemental Tables 3, 4).

Discussion

We identified racial/ethnic differences for diagnostic milestones and offering of corticosteroids among males with confirmed DMD that persisted over the period of birth years covered by the study. However, examination of times from initial evaluation or confirmatory diagnosis and the remaining milestones suggested no delays for subsequent milestones for non-Hispanic Black individuals, and only in first offering of corticosteroid treatment in Hispanics. Based on these findings, racial/ethnic differences in the timing of initial evaluation and confirmatory diagnosis may lead to delays in service provision. The 2.3-year difference in initial evaluation among non-Hispanic Black males compared to both non-Hispanic White and Hispanic males is notable and represents a potential target for intervention to ameliorate delays in receipt of recommended services. Our surveillance data do not allow further assessment of underlying reasons in late recognition of neurological symptoms/developmental delays that would lead to seeking care, specifically for DMD. That said, it is important to consider the difference in the context of the drivers of health differences in the United States as a whole.

Within every racial/ethnic group, there is expected individual level variation in social risk and protective factors. However, the focus of most of the literature is on between group

differences related to the social determinants of health [27]. Specific factors that may impact propensity to seek care and ability to access care include racial/ethnic differences in health literacy [28], language and communication challenges [29, 30], geographic factors and barriers related to travel [31, 32], and insurance coverage [33]. When racial/ethnic minority families seek and access health care, challenges in navigating the health care system and obtaining appropriate health care services remain. Limitations in cultural competence of health care providers have been documented, and greater cultural competence has been associated with higher levels of patient satisfaction [34]. On the other hand, while efforts are being made to increase physician cultural competence via education, more research will help inform the effectiveness of such efforts [35, 36]. Evidence is limited on social factors specifically for children with DMD. However, it seems reasonable to hypothesize that similar barriers to accessing early and appropriate health care may exist for non-Hispanic Black and Hispanic families of young males with DMD. Barriers to obtaining health care may lead to delayed, reduced frequency, or reduced quality of interactions between a young child with DMD and the health care system. In turn, such experiences would likely reduce the number of opportunities for a parent to report signs of delayed development, or for a health care provider to detect potential developmental delays that should be addressed.

Another possible explanation for the delay in initial evaluation among non-Hispanic Black males could be differences in gene frequency or gene expression. DMD prevalence has been shown to vary across racial/ethnic groups in the United States [20, 22]. Further, there are genetic modifiers known to modulate the DMD phenotype [37, 38], and there may be others still undiscovered. It is not known whether such genetic modifiers differ by race/ethnicity and identifying such genetic/phenotype differences by race/ethnicity in the United States is challenging given the small number of affected individuals in some racial/ethnic groups. However, such research may be important and has the potential to more fully explain observed differences in the health care experience of DMD.

A major strength of this population-based study is that the information used in the analyses was directly abstracted from health records of individuals with confirmed DMD, from a range of geographic locations and with a variety of racial/ethnic backgrounds. The most significant limitation of this study is the small sample size. Although the sample size increased compared to previous MD STAR*net* studies, it is still not large enough, particularly for non-Hispanic Black individuals to conduct additional analyses. This reduced the statistical power to detect differences in the timing of the milestones assessed. Despite the small sample size for non-Hispanic Black individuals, significant differences were found for the timing of many of the clinical milestones assessed suggesting sufficient power to detect certain differences.

A second limitation of the study is that individual-level indicators of social economic factors such as family income, and community-level indicators such as rurality could impact the diagnostic or treatment time. Since care of DMD extends over the lifetime of the patient, reliably evaluating the role of community-level characteristics on care received is not possible in MD STAR*net* due to the lack of historical address information. Another limitation is that some health care encounters may be missed since the surveillance did not include all sites of medical care. For example, if a boy with DMD received most of

his care from a primary care provider, his early data may not be captured until he visits a neuromuscular clinic where surveillance is conducted. Besides, we do not have access to qualitative data about the perceptions and knowledge of parents of boys with DMD. We cannot assess the quality of primary care received in early childhood, and we did not have information about whether guidance or education about developmental milestones differed by race/ethnicity for the parents of the children in this study. Information about these factors would likely be helpful in identifying the optimal approaches for intervening to improve earlier identification of children from racial and ethnic minority groups, who have DMD. Additional studies could identify the reason(s) for later recognition of developmental delays and, ultimately, develop effective approaches for remedying the differences.

Conclusion

Racial/ethnic differences were identified in the timing of clinical milestones experienced by non-Hispanic Black and Hispanic individuals with DMD, compared to non-Hispanic White individuals. Non-Hispanic Black individuals were older at each of the seven milestones assessed, with the differences being statistically significant for five milestones. Findings were less consistent for Hispanic individuals, with statistically significant delays only for offer and initiation of corticosteroid therapy. For non-Hispanic Black individuals, older age at initial evaluation and at diagnosis with DMD could impact timing of future milestones. Our findings could inform the development of targeted interventions that promote earlier evaluation and diagnostic confirmation of DMD, especially for non-Hispanic Black individuals, which may allow for timely initiation of recommended disease monitoring and interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement

The authors would like to acknowledge the entire MD STAR*net* team involved in the surveillance program. We would also like to thank each of the surveillance sites for access to the data for this study. The authors would like to thank Intermountain Healthcare for its role in the collection of and access to the data at one of the surveillance sites.

Funding Sources

This publication was supported by the Cooperative Agreement Nos. DD000187, DD000189, DD000190, DD000191, DD001126, DD001119, DD001123, DD001116, DD001117, DD001108, DD001120, DD001054, DD001244, and DD001245 funded by the Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Diseases Control and Prevention.

Data Availability Statement

Due to privacy concerns, data from the MD STAR*net* are not publicly available. Researchers interested in MD STAR*net* may contact MD STAR*net* at MDSTARnet@cdc.gov.

References

1. Yiu EM, Kornberg AJ. Duchenne muscular dystrophy. Journal of paediatrics and child health. 2015;51(8):759–64. [PubMed: 25752877]
2. Mah JK, Korngut L, Fiest KM, Dykeman J, Day LJ, Pringsheim T, et al. A systematic review and meta-analysis on the epidemiology of the muscular dystrophies. Canadian Journal of Neurological Sciences. 2016;43(1):163–77.
3. Mercuri E, Bönnemann CG, Muntoni F. Muscular dystrophies. The Lancet. 2019;394(10213):2025–38.
4. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. The Lancet Neurology. 2010;9(1):77–93. [PubMed: 19945913]
5. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. The Lancet Neurology. 2010;9(2):177–89. [PubMed: 19945914]
6. Birnkrant DJ, Bushby K, Bann CM, Alman BA, Apkon SD, Blackwell A, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. The Lancet Neurology. 2018;17(4):347–61. [PubMed: 29395990]
7. 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. The Lancet Neurology. 2018;17(3):251–67. [PubMed: 29395989]
8. Birnkrant DJ, Bushby K, Bann CM, Apkon SD, Blackwell A, Colvin MK, et al. Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan. The Lancet Neurology. 2018;17(5):445–55. [PubMed: 29398641]
9. Cheng TL, Emmanuel MA, Levy DJ, Jenkins RR. Child health disparities: what can a clinician do? Pediatrics. 2015;136(5):961–68. [PubMed: 26459644]
10. Montes G. US children with special health care needs and ethnic discrimination: results from multivariate modeling. World Journal of Pediatrics. 2019;15(2):182–89. [PubMed: 30591989]
11. Liu SY, Pabayo R, Muennig P. Perceived Discrimination and Increased Odds of Unmet Medical Needs Among US Children. International Journal of Health Services. 2021;51(3):364–70. [PubMed: 33709808]
12. Mitchell HK, Reddy A, Perry MA, Gathers C-A, Fowler JC, Yehya N. Racial, ethnic, and socioeconomic disparities in paediatric critical care in the USA. The Lancet Child & Adolescent Health. 2021.
13. 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;52(10 Suppl 3):S32–S39.
14. 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. Genetics in medicine : official journal of the American College of Medical Genetics. 2011 Nov;13(11):942–7. [PubMed: 21836521]
15. Thomas S, Conway KM. Time to diagnosis of Duchenne muscular dystrophy remains unchanged: Findings from the Muscular Dystrophy Surveillance, Tracking, and Research Network, 2000–2015. 2022 Aug;66(2):193–97.
16. Fox DJ, Kumar A, West NA, DiRienzo AG, James KA, Oleszek J. Trends with corticosteroid use in males with Duchenne muscular dystrophy born 1982–2001. Journal of child neurology. 2015 Jan;30(1):21–6. [PubMed: 24682290]
17. Andrews JG, Davis MF, Meaney FJ. Correlates of care for young men with Duchenne and Becker muscular dystrophy. Muscle & nerve. 2014;49(1):21–25. [PubMed: 23558904]
18. Miller LA, Romitti PA, Cunniff C, Druschel C, Mathews KD, Meaney FJ, et al. The muscular dystrophy surveillance tracking and research network (MD STARnet): Surveillance methodology.

Birth Defects Research Part A: Clinical and Molecular Teratology. 2006;76(11):793–97. [PubMed: 17036307]

19. Mathews KD, Cunniff C, Kantamneni JR, Ciafaloni E, Miller T, Matthews D, et al. Muscular Dystrophy Surveillance Tracking and Research Network (MD STARnet): case definition in surveillance for childhood-onset Duchenne/Becker muscular dystrophy. Journal of child neurology. 2010;25(9):1098–102. [PubMed: 20817884]
20. Romitti PA, Zhu Y, Puzhankara S, James KA, Nabukera SK, Zamba GK, et al. Prevalence of Duchenne and Becker muscular dystrophies in the United States. Pediatrics. 2015;135(3):513–21. [PubMed: 25687144]
21. Sahay KM, Smith T, Conway KM, Romitti PA, Lamb MM, Andrews J, et al. A Review of MD STAR net's Research Contributions to Pediatric-Onset Dystrophinopathy in the United States; 2002–2017. Journal of child neurology. 2019;34(1):44–53. [PubMed: 30345857]
22. Zhang Y, Mann JR, James KA, McDermott S, Conway KM, Paramsothy P, et al. Duchenne and Becker Muscular Dystrophies' Prevalence in MD STARnet Surveillance Sites: An Examination of Racial and Ethnic Differences. Neuroepidemiology. 2021;55(1):47–55. [PubMed: 33477152]
23. Do TN, Street N, Donnelly J, Adams MM, Cunniff C, Fox DJ, et al. Muscular Dystrophy Surveillance, Tracking, and Research Network pilot: Population-based surveillance of major muscular dystrophies at four US sites, 2007–2011. Birth defects research. 2018;110(19):1404–11. [PubMed: 30070776]
24. Andrews JG, Lamb M, Conway K, Street N, Westfield C, Ciafaloni E, et al. Differentiation of Pediatric-Onset Duchenne and Becker Muscular Dystrophy Subphenotypes Using the Muscular Dystrophy Surveillance Tracking and Research Network (MD STARnet). J Neuromuscul Dis. 2021 Nov 6.
25. Johnson JD, Theurer WM. A stepwise approach to the interpretation of pulmonary function tests. American family physician. 2014;89(5):359–66. [PubMed: 24695507]
26. Yamaguchi T, Ohashi Y, Matsuyama Y. Proportional hazards models with random effects to examine centre effects in multicentre cancer clinical trials. Statistical Methods in Medical Research. 2002;11(3):221–36. [PubMed: 12094756]
27. Hill L, Artiga S, Haldar S.[Internet]. Key Facts on Health and Health Care by Race and Ethnicity [cited 2022 Apr 12]. Available from: https://www.kff.org/report-section/key-facts-on-health-and-health-care-by-race-and-ethnicity-social-determinants-of-health/.
28. Villagra VG, Bhuva B, Coman E, Smith DO, Fifield J. Health insurance literacy: disparities by race, ethnicity, and language preference. Am J Manag Care. 2019;25(3):e71–e75. [PubMed: 30875174]
29. Timmins CL. The impact of language barriers on the health care of Latinos in the United States: a review of the literature and guidelines for practice. Journal of midwifery & women's health. 2002;47(2):80–96.
30. Adebayo CT, Walker K, Hawkins M, Olukotun O, Shaw L, Sahlstein Parcell E, et al. Race and Blackness: A thematic review of communication challenges confronting the Black community within the US health care system. Journal of Transcultural Nursing. 2020;31(4):397–405. [PubMed: 31762404]
31. Basu J. Severity of illness, race, and choice of local versus distant hospitals among the elderly. Journal of Health Care for the Poor and Underserved. 2005;16(2):391–405. [PubMed: 15937400]
32. Erwin PC, Fitzhugh EC, Brown KC, Looney S, Forde T. Health disparities in rural areas: the interaction of race, socioeconomic status, and geography. Journal of health care for the poor and underserved. 2010;21(3):931–45. [PubMed: 20693736]
33. Rhoades JA. STATISTICAL BRIEF# 437: Health Insurance Status of Young Adults Ages 19–25, 2012.
34. Paez KA, Allen JK, Beach MC, Carson KA, Cooper LA. Physician cultural competence and patient ratings of the patient-physician relationship. Journal of General Internal Medicine. 2009;24(4):495–98. [PubMed: 19194767]
35. Horvat L, Horey D, Romios P, Kis-Rigo J. Cultural competence education for health professionals. Cochrane database of systematic reviews. 2014 (5).

36. Mainous A, Xie Z, Yadav S, Williams M, Blue A, Hong Y-R. Physician Cultural Competency Training and Impact on Behavior: Evidence From the 2016 National Ambulatory Medical Care Survey. Family Medicine. 2020;52(8):562–69. [PubMed: 32931004]

37. Barp A, Bello L, Politano L, Melacini P, Calore C, Polo A, et al. Genetic modifiers of Duchenne muscular dystrophy and dilated cardiomyopathy. PloS one. 2015;10(10):e0141240. [PubMed: 26513582]

38. Vo AH, McNally EM. Modifier genes and their effect on Duchenne muscular dystrophy. Current opinion in neurology. 2015;28(5):528. [PubMed: 26263473]

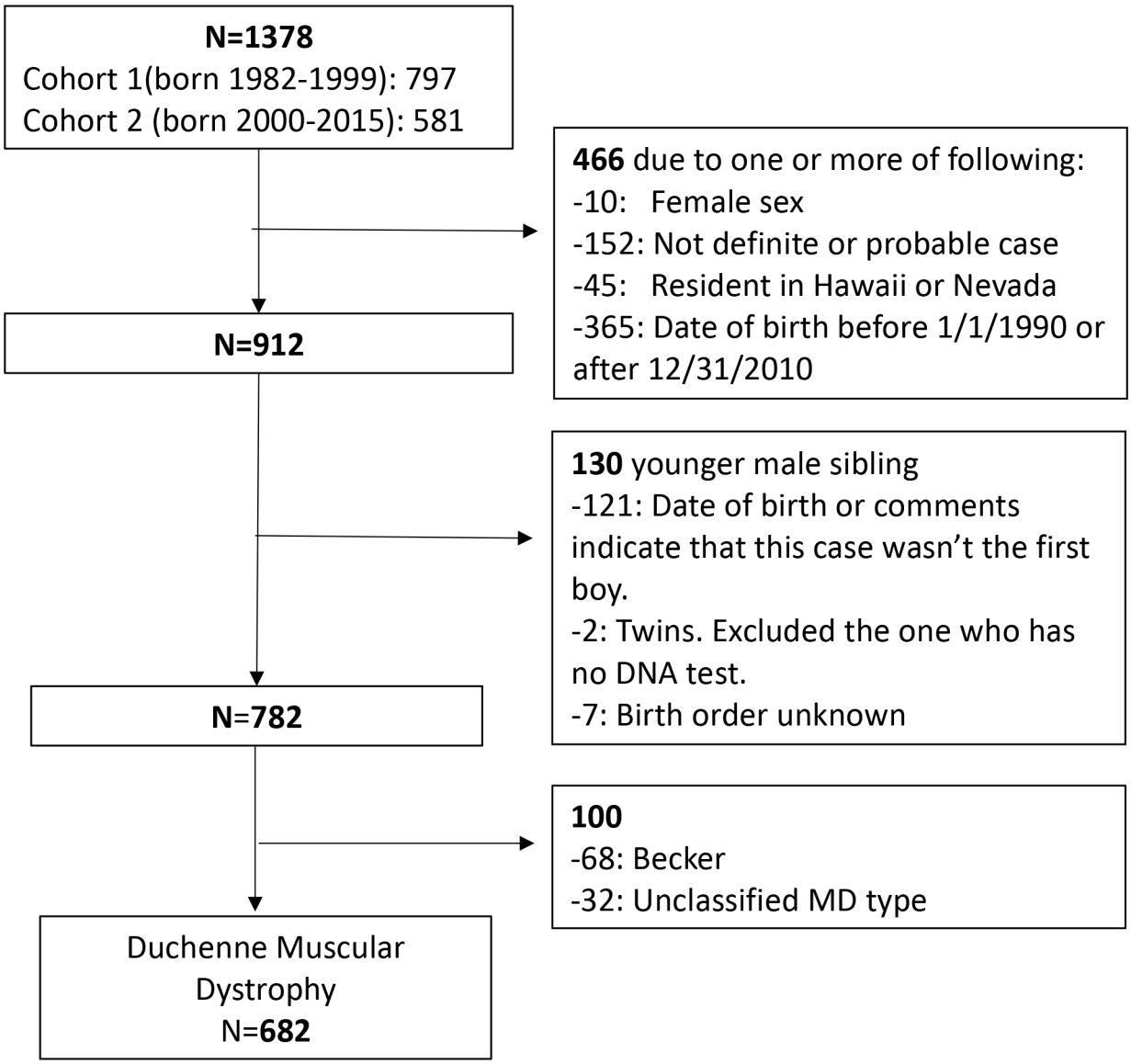

Fig. 1.

Flow chart of study eligibility from eight Muscular Dystrophy Surveillance, Tracking, and Research network (MD STAR*net*) sites.

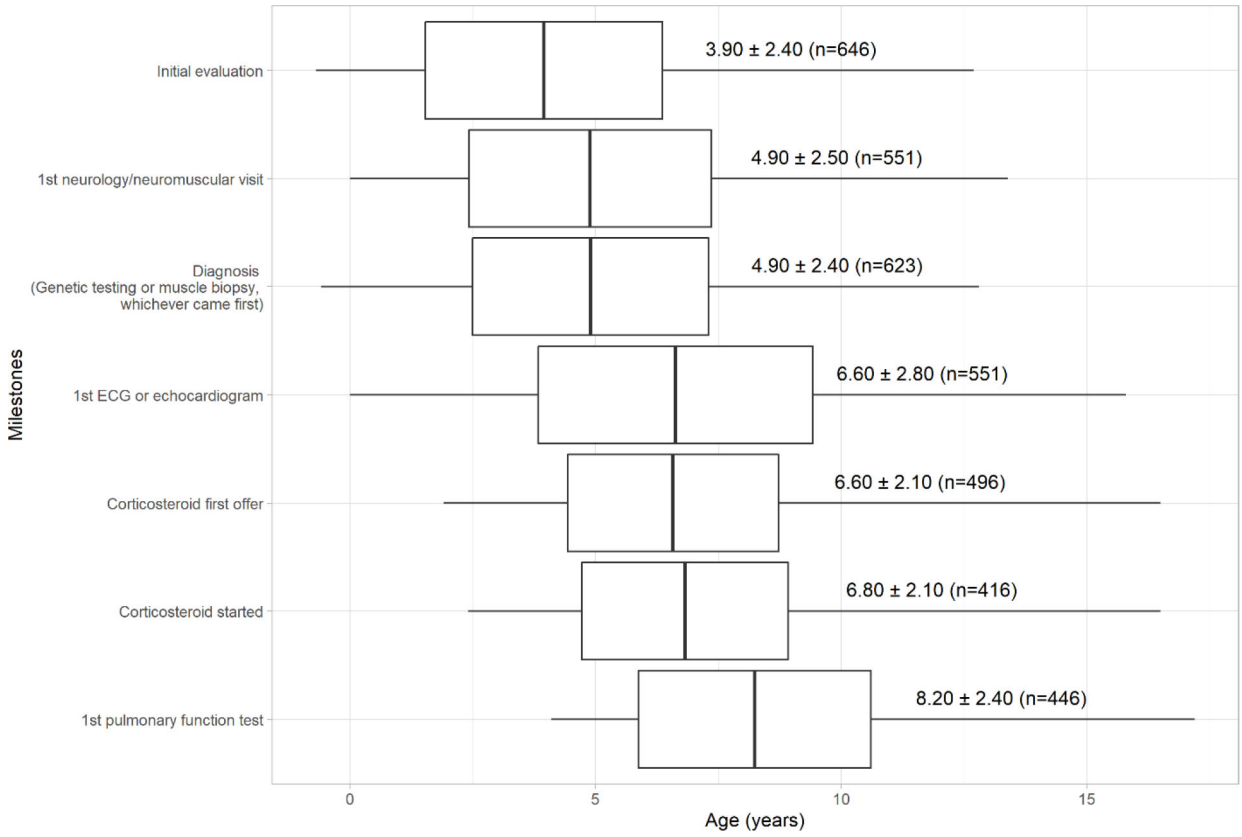

Fig. 2.

Timeline map of ages (standard deviations) at seven selected milestones for males with Duchenne muscular dystrophy, the Muscular Dystrophy Surveillance, Tracking, and Research network (MD STAR*net*), N=682. The hinge represents the mean age; the lower and upper hinges are one standard deviation from the mean; the upper and lower whisker goes from minimum to maximum age. The initial evaluation age and genetic testing could be less than zero due to prenatal testing based on positive family history. Individuals who did not experience the milestone or those who experienced the milestone but the age was not available are excluded from the estimates.

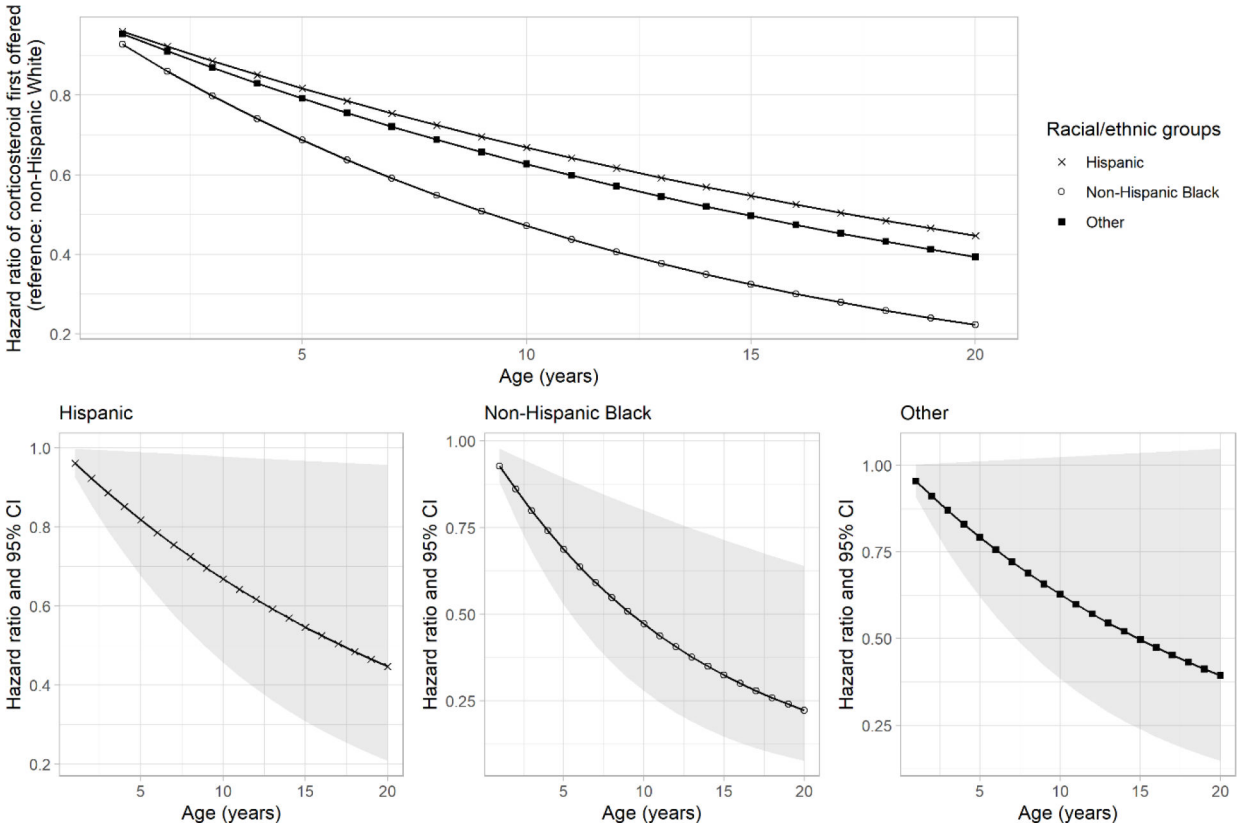

Fig. 3.

Plot of time-dependent adjusted hazard ratios estimated from time-dependent Cox Proportional Hazards modeling for age at first offering of corticosteroids by race/ethnicity among males with Duchenne muscular dystrophy, Muscular Dystrophy Surveillance, Tracking, and Research network (MD STAR*net*), N=554. The reference group is non-Hispanic White. Adjusted hazard ratios for non-Hispanic Black and Hispanic were statistically significant (type I error = 0.05). Age in years at each milestone was used as the survival time; the last medical provider visit was used for those who did not experience the milestone. Individuals who experienced the milestone but the age at the milestone was unavailable were excluded. Hazard ratio below 1 indicates a delay for a specific milestone.

Table 1.

Characteristics of males with definite or probable Duchenne muscular dystrophy, the Muscular Dystrophy Surveillance, Tracking, and Research network (MD STAR*net*), N=682

Characteristics		**N**	**%**
Case status	Definite	661	96.9
	Probable	21	3.1
Race/ethnicity	Hispanic	140	20.5
	Non-Hispanic Black	49	7.2
	Non-Hispanic White	421	61.7
	Other [a]	72	10.6
Parental education level [b]	Less than high school	121	17.74
	High school graduate or GED	136	19.9
	Some college or 2-year degree	127	18.6
	Bachelor's degree or higher	89	13.05
	Missing/Unknown	209	30.7
Birth Cohort	Jan 1, 1990–Dec 31, 2010 (Cohort 1)	376	55.1
	Jan 1, 2000–Dec 31, 2010 (Cohort 2)	306	44.9
Family history	Yes	177	26.0
	No	438	64.2
	Unknown	67	9.8
MD STAR*net* Site	Arizona	114	16.7
	Colorado	125	18.3
	Georgia	141	20.7
	Iowa	77	11.3
	Piedmont region of North Carolina	57	8.4
	western New York	73	10.7
	South Carolina	46	6.7
	Utah	49	7.2
Birth year	1990–1994	129	18.9
	1995–1999	156	22.9
	2000–2004	213	31.2
	2005–2010	184	27.0
Parent's average age at child's birth (years) [c]	(mean ± standard deviations)	608	27.7 ± 5.8
Age at the last visit in records (years)	(mean ± standard deviations)	682	11.8 ± 4.3

Note.

[a] Other race/ethnicity includes: Asian or Hawaiian or Pacific Islander, Native American or American Indian or Alaska Native, Multiple, Other, or Unknown.

[b] Parental education level is defined based on the maternal education level. Missing values for maternal education are replaced by paternal education level, if available.

[c] If missing a parent's age, the age of the available parent was used.

Table 2.

Milestone ages (50% [25%, 75%]) from Kaplan-Meier estimation for males with definite or probable Duchenne muscular dystrophy, the Muscular Dystrophy Surveillance, Tracking, and Research network (MD STAR*net*) (n=682)

Outcomes	Total n (% Censored)[a]	Hispanic	non-Hispanic Black	non-Hispanic White	Other	Log-Rank test ($\chi^2\left(df=3\right)$)
Initial evaluation	642 (0%)	3.7 (2.0, 5.8)	6.0 (3.0, 7.2)	3.7 (2.0, 5.4)	4.1 (2.1, 6.2)	23.02, p<0.001
1st neurology/ neuromuscular visit	551 (0%)	5.2 (3.4, 7.0)	7.0 (5.6, 8.7)	4.7 (2.8, 6.1)	5.5 (3.8, 7.3)	32.74, p<0.001
Diagnosis	625 (1.6%)	5.1 (3.6, 6.8)	7.1 (5.7, 8.6)	4.8 (3.2, 6.3)	5.4 (3.6, 6.9)	16.54, p<0.001
1st ECG or echocardiogram	603 (8.6%)	7.1 (5.7, 9.1)	8.6 (6.8, 9.5)	6.4 (4.7, 8.4)	7.1 (5.9, 8.9)	6.43, p=0.092
Corticosteroid first offered	617 (19.6%)	7.7 (6.3, 9.8)	9.2 (7.4, 11.3)	6.5 (5.0, 8.1)	7.5 (5.4, 9.4)	37.14, p<0.001
Corticosteroid started	637 (34.7%)	8.1 (6.6, NC)	11.1 (8.2, NC)	7.3 (5.7, 10.1)	8.7 (6.9, 14.5)	26.32, p<0.001
1st pulmonary function testing	621 (28.2%)	8.4 (6.8, 10.6)	10.3 (8.6, 11.5)	8.6 (7.0, 10.8)	8.8 (6.6, 10.8)	3.80, p=0.284

Note. df=degree of freedom. NC = not calculated.

Age in years at each milestone was used as the survival time; the last medical provider visit was used for those who did not experience the milestone. Individuals who had prenatal initial evaluation or prenatal 1st neurology/ neuromuscular visit or who experienced the milestone but the age at the milestone was unavailable were excluded.

[a]Racial specific sample sizes and percentage of censoring were reported in Supplement Table 5.

Table 3.

Adjusted hazard ratios for age at each milestone, in males with definite or probable Duchenne muscular dystrophy, the Muscular Dystrophy Surveillance, Tracking, and Research network (MD STAR*net*)

Outcomes	Total (% Censored)[a]	non-Hispanic White	Hispanic aHR (95% CI)	non-Hispanic Black aHR (95% CI)	Other aHR (95% CI)
Initial evaluation	578 (0.0%)	1.00 (Reference group)	1.00 (0.78, 1.28)	**0.50 (0.34, 0.72)**	0.75 (0.54, 1.03)
1st neurology/ neuromuscular visit	506 (0.0%)		0.89 (0.68, 1.17)	**0.50 (0.35, 0.71)**	0.72 (0.50, 1.04)
Diagnosis	561 (1.8%)		0.98 (0.76, 1.25)	**0.49 (0.35, 0.70)**	0.76 (0.56, 1.05)
1st ECG or echocardiogram	552 (9.1%)		0.99 (0.77, 1.28)	0.78 (0.54, 1.12)	0.82 (0.59, 1.14)
Corticosteroid first offered [b]	554 (18.4%)		**0.75 (0.58, 0.98)**	**0.59 (0.41, 0.85)**	0.72 (0.51, 1.02)
Corticosteroid started	573 (34.6%)		**0.71 (0.53, 0.96)**	**0.51 (0.32, 0.82)**	**0.66 (0.45, 0.98)**
1st pulmonary function testing	561 (27.8%)		1.16 (0.87, 1.55)	0.78 (0.52, 1.17)	0.95 (0.66, 1.35)

Note. aHR=adjusted hazard ratio. CI=confidence interval.

The outcome is the survival time to each milestone. Model adjusted for parent's average age at child's birth, parental education, family history, birth year, cohort eligibility, and site. aHR below 1 indicates a delay for a specific milestone.

[a]Due to missing covariates, the sample sizes in Table 3 are reduced compared to the sample sizes in Table 2. Racial specific sample sizes and percentage of censoring was reported in Supplement Table 5.

[b]For age at first offering of corticosteroids, the proportional hazard assumption was violated, and a time-dependent Cox proportional hazard model was fit. (see Fig. 3). The aHR in this table are the aHRs estimated at 7 years old, which is the average age at corticosteroid first offered in our data.

Table 4.

Adjusted hazard ratios of time between two milestones, in males with definite or probable Duchenne muscular dystrophy, the Muscular Dystrophy Surveillance, Tracking, and Research network (MD STAR*net*)

Time interval from event A to B	Total (% Censored)[a]	non-Hispanic White	Hispanic aHR (95% CI)	non-Hispanic Black aHR (95% CI)	Other aHR (95% CI)
Initial evaluation -> 1st neurology/neuromuscular visit	463 (0.0%)	1.00 (Reference group)	0.86 (0.65, 1.14)	0.88 (0.60, 1.29)	0.86 (0.59, 1.24)
Initial evaluation -> Diagnosis	508 (1.8%)		0.91 (0.70, 1.18)	0.87 (0.60, 1.26)	0.93 (0.67, 1.31)
Diagnosis -> 1st ECG or echocardiogram	464 (9.1%)		1.18 (0.89, 1.55)	1.32 (0.88, 1.98)	1.08 (0.75, 1.56)
Diagnosis -> Corticosteroid first offered	486 (18.1%)		0.73 (0.55, 0.98)	0.80 (0.51, 1.25)	1.03 (0.71, 1.48)
Diagnosis -> Corticosteroid started	506 (33.6%)		0.80 (0.58, 1.10)	0.76 (0.45, 1.27)	0.95 (0.64, 1.40)
Diagnosis -> 1st pulmonary function testing	506 (27.3%)		1.38 (1.02, 1.87)	1.41 (0.91, 2.20)	1.44 (1.00, 2.07)

Note. aHR=adjusted hazard ratio. CI=confidence interval.

The outcome is the time interval from initial evaluation or diagnosis and subsequent milestones. Model adjusted for parent's average age at child's birth, parental education, family history, birth year, cohort eligibility, and site. aHR below 1 indicates a delay for a specific milestone.

[a]Due to missing values on outcomes and covariates, the sample sizes in Table 4 are reduced compared to the sample sizes in Tables 2 and 3. Racial specific sample sizes and percentage of censoring was reported in Supplement Table 5.