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Secondary conditions among males with Duchenne or Becker muscular dystrophy

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Abstract

Duchenne and Becker muscular dystrophy are X-linked neuromuscular disorders characterized by progressive muscle degeneration. Despite the involvement of multiple systems, secondary conditions among affected males have not been comprehensively described. Two hundred and nine caregivers of affected males (aged 3–31 years) identified by the Muscular Dystrophy Surveillance, Tracking, and Research Network completed a mailed survey that included questions about secondary conditions impacting multiple body functions. The five most commonly reported

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Author Contributions

RL contributed to study conception and design, analyzed and interpreted the data, and drafted the manuscript. NS contributed to study conception and design, data acquisition, and data interpretation. KCC, CC, and JO contributed to data acquisition and interpretation. KJ contributed to data analysis. DF, EC, and CW contributed to data acquisition. PP contributed to the study design, data analysis, and data interpretation. All authors critically revised the manuscript and approved the final version.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Declaration of Conflicting Interests

The authors declare that there are no conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

Each site received institutional review board (IRB) approval for the caregiver survey (University of Arizona IRB-1, protocol #05-0426-01; Colorado Department of Public Health and Environment IRB, protocol #2006001; Georgia Department of Public Health IRB, protocol #090805; Centers for Disease Control and Prevention IRB-A, protocol #4792; University of Iowa IRB-1, protocol #200509724; New York State Department of Health, protocol# 03-062).

conditions in males with Duchenne were cognitive deficits (38.4%), constipation (31.7%), anxiety (29.3%), depression (27.4%), and obesity (19.5%). Higher frequencies of anxiety, depression, and kidney stones, were found among non-ambulatory males compared to ambulatory males. Attention deficit hyperactivity disorder was more common in ambulatory than non-ambulatory males. These data support clinical care recommendations for monitoring of patients with Duchenne or Becker muscular dystrophy by a multidisciplinary team to prevent and treat conditions that may be secondary to the diagnosis.

Keywords

Duchenne; Becker; muscular dystrophy; secondary conditions; co-morbidities

Introduction

Duchenne and Becker muscular dystrophies are the most common pediatric inherited muscular dystrophies[1, 2]. The most prominent feature is progressive muscle degeneration that leads to loss of ambulation, as well as primary multisystem complications involving the heart, skeletal and respiratory systems[3]. Multidisciplinary care is recommended for clinical management of Duchenne and Becker muscular dystrophies, and such care typically includes monitoring and treatment of complications, including oral corticosteroids to maintain muscle strength[3–5].

Though focus on primary complications is important for diagnosis and clinical management of Duchenne and Becker muscular dystrophies, secondary complications may also develop and amplify the severity of disease[4, 5]. These complications, commonly referred to as secondary conditions, include additional physical or mental problems that are related to the underlying disease[6]. Previous studies have typically focused on a single or few conditions that could be considered secondary to a diagnosis of Duchenne muscular dystrophy[7–25]. Collectively, these studies suggest a higher than expected occurrence of conditions affecting cognition, behavior, gastrointestinal, and genitourinary functioning.

In this study, we surveyed caregivers of males with Duchenne or Becker muscular dystrophies identified through the population-based Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STAR*net*) about the presence of secondary conditions affecting multiple body systems. The objectives of this study are to report the frequencies of a broader range of secondary conditions than previously reported by phenotype of Duchenne or Becker muscular dystrophy, and to evaluate whether frequencies of these conditions differ by ambulation status.

Methods

MD STAR*net* is a population-based surveillance system established in 2002 by the Centers for Disease Control and Prevention to determine the prevalence of Duchenne and Becker muscular dystrophies and track clinical practices and health outcomes[26]. Beginning in 2004, MD STAR*net* retrospectively identified and longitudinally followed individuals who were born since January 1, 1982, diagnosed by December 31, 2011, and resided in four US sites:

Arizona, Colorado, Iowa, and western New York State. In 2005 and 2008, Georgia and Hawaii, respectively, joined the network. MD STAR*net* used medical record data and pertinent state (e.g. state vital records, hospital discharge and emergency room visits) and national data (e.g. national death index) to describe the care and outcomes of these individuals. Annual follow-up abstraction was attempted for at least one year for ascertained individuals. Individuals identified before September 2011 were followed through December 2011, and those identified between September 2011 and December 2011 were followed through December 2012. A committee of clinical experts reviewed clinical and laboratory data to assign each individual a case definition designation (definite, probable, possible, asymptomatic, affected female, or not Duchenne or Becker muscular dystrophy). The data used for assigning the case definition included clinical symptoms, age at onset of symptoms, diagnostic testing (i.e. creatine kinase value, *DMD* mutation analysis, muscle biopsy results, and family history[24]. Full descriptions of MD STAR*net* surveillance methods and case definitions have been published previously[26, 27].

Survey Collection

The Family Quality of Life Survey was developed by MD STAR*net* investigators and inquired about issues such as family quality of life, social support and stress, spirituality, and the affected male's current functioning and secondary conditions. The questions were primarily multiple choice style responses, but some write-in responses were included. The survey asked caregivers to report if their child's doctor or healthcare provider ever informed them that their child had/has each of 29 conditions. The timing of these conditions included any time up to the point of survey completion. Investigators modeled questions about lower extremity function after the Vignos Lower Extremity Scale in which the caregiver chooses the option that best describes their child's level of lower extremity physical functioning[28]. Responses about the affected male's secondary conditions and lower extremity function, and caregiver and affected male demographics (e.g. date of birth, date of survey completion) were used for this cross-sectional study.

Sample and Methods

Investigators identified eligible caregivers using MD STAR*net* surveillance data and recruited participants from six MD STAR*net* sites (Arizona, Colorado, Georgia, Hawaii, Iowa, and western New York State). Two participants from Hawaii were excluded from analyses due to an abbreviated recruitment protocol. Caregivers of living males with definite or probable Duchenne or Becker muscular dystrophy were eligible. The sample included 460 caregivers defined (in priority order) as birth mother, birth father, and legal guardian. Only one caregiver was selected per household and, among those with multiple affected children, the caregiver was asked to complete the survey for the oldest affected male in the household if still living (Figure 1). If the oldest affected male was not living, the caregiver was asked to complete the survey for the next oldest sibling. For the majority of caregivers (n= 457), the eligible child was the first-born affected male. Caregivers were excluded from recruitment if they refused further contact following previous recruitment, were not currently the primary caregiver (e.g. individuals who did not have a designated primary caregiver or did not live with the caregiver), could not be located during prior recruitment efforts, or were identified after recruitment was initiated. Participants completed surveys

between April 2011 and February 2012. The protocol and consent for the caregiver survey varied by site. Overall, eligible caregivers were invited to complete the survey and could refuse participation or opt out at any time. In most sites, consent was implied if the caregiver completed and returned the survey, but written consent was required in Colorado. The survey was available in English and Spanish and compensation was provided. Each site received institutional review board approval for the Family Quality of Life Survey.

Statistical analyses

Two secondary conditions, developmental delay affecting learning and mental retardation/intellectual disability, were combined into one cognition category called cognitive deficits. Ambulation ceased was defined for survey participants using caregiver responses to the Vignos scale items and included males who could not walk with assistance, used a wheelchair, or were confined to bed[28]. Additional survey data incorporated in analyses included responses about date of survey completion and dates of birth for caregivers and affected males.

To evaluate differences between participants and non-participants, the survey data was supplemented with surveillance data about sociodemographics, ambulation status, and Duchenne or Becker muscular dystrophy phenotype. Sociodemographic information included: MD STAR*net* site, affected male date of birth, race/ethnicity, caregiver relationship to the affected male, and neighborhood percent below poverty. Neighborhood percent poverty, defined as the percentage of residents in the census tract with household incomes below the federal poverty line, was calculated by combining residential information as of the most recent clinical visit with U.S. census tract data from The Public Health Disparities Geocoding Project Monograph created by the Harvard School of Public Health[29]. Individual race/ethnicity was determined from medical and vital records (non-Hispanic white, Hispanic, non-Hispanic Black, Other, Unknown). Age of affected males was grouped into four categories (3–10, 11–15, 16–20, 21–31 years of age). Ambulation status (i.e. ambulatory versus non-ambulatory) was differentiated by whether an age for ambulation cessation was recorded in the surveillance dataset. Affected males were categorized as having a Duchenne phenotype if the following criteria were met: 1) ambulation ceased before 12 years of age or 16 years of age, when prior to cessation, any steroid use or continuous steroid use of at least 24 months was ascertainable, respectively; OR 2) observation of an out-of-frame *DMD* mutation consistent with a Duchenne phenotype or a Western blot showing less than or equal to 5% dystrophin; OR 3) onset of symptoms occurred before 5 years of age. Affected males were categorized as having a Becker phenotype if the following criteria were met: 1) ambulation ceased after 16 years of age, regardless of steroid use; OR 2) observation of an in-frame *DMD* mutation consistent with a Becker phenotype or a Western blot showing less than or equal to 20% dystrophin; OR 3) onset of symptoms occurred after 10 years of age. Those individuals for whom a Duchenne or Becker phenotype could not be determined were assigned an Indeterminate phenotype.

Missing information was limited to at most 4 observations for all variables – with the exception of neighborhood percent poverty (52 missing). We excluded individuals with missing observations, where appropriate. We included the 52 individuals with missing

values for neighborhood percent poverty as ‘unknown’. For analyses describing the frequencies of secondary conditions, responses of caregivers about males assigned the Indeterminate phenotype were excluded (n=17). We used t-tests to compare mean values for continuous variables and chi-square or Fisher exact tests to compare categorical variables. We conducted all statistical analyses using SAS version 9.3 (SAS Institute, Cary NC), and statistical significance was defined by a p-value < 0.05.

Results

Participants

Of the 460 eligible caregivers, 209 completed the survey, 170 refused, and 81 could not be located (Figure 1). Males for whom the surveys were completed were aged 3 to 31 years. Using the American Association for Public Opinion Research rate calculator[30], we estimated an overall response rate of 50.8%, a refusal rate of 28.7%, and a contact rate of 81.0%. Using the same calculator, we estimated the cooperation rate for each MD STAR*net* site: 75.3% for Arizona, 45.0% for Colorado, 53.8% for Georgia, 81.8% for Iowa, and 82.4% for western New York.

Table 1 summarizes differences between participants and non-participants based on surveillance data through 2011. Most surveys (95.2%) were completed by biological parents; 91.4% by females (data not shown). Participants were more likely to be caring for non-Hispanic white males (71.8%) than non-participants (57.0%). The majority (80.0%) of eligible caregivers did not live in a poverty area (i.e. census tracts with poverty rates of 20 percent or more) (data not shown). For this reason, we stratified eligible participants by the median neighborhood percent poverty value (7.5%). Participants were more likely to have a known neighborhood percent poverty value and live in a geographical area where less than 7.5% of its residents had a household income below the federal poverty line than non-participants. Participant caregivers were more likely to be caring for older males compared to non-participants (data not shown). The mean age of males cared for by non-participants was 16 years while the mean age of males cared for by participants was 17 years (p=0.04). Participation by caregivers was not associated with phenotype or ambulation status of affected males.

Descriptive analyses

Of the 209 males whose caregiver completed the survey, there were 164 with the Duchenne phenotype, 28 with the Becker phenotype, and 17 with an Indeterminate phenotype. Frequencies of secondary conditions in males with Duchenne or Becker phenotypes are listed in Table 2. Responses of caregivers of affected males for whom a phenotype could not be determined were excluded. In this study, the five most commonly reported secondary conditions for males with the Duchenne phenotype were cognitive deficits (38.4%), anxiety problems (29.3%), depression (27.4%), constipation (31.7%), and obesity (19.5%) (Table 2). Among males with the Becker phenotype, the most frequently reported conditions were cognitive deficits (35.7%), depression (28.6%), attention deficit hyperactivity disorder (32.1%), constipation (21.4%), and trouble holding urine (21.4%).

Bivariate analyses

Table 3 shows associations between reported secondary conditions and ambulation status of affected males with the Duchenne phenotype. Caregivers of ambulatory males were likely to report attention deficit hyperactivity disorder compared to those of non-ambulatory males ($p < 0.01$). Conversely, caregivers of non-ambulatory males were more likely to report anxiety ($p=0.02$), depression ($p < 0.01$), and kidney stones ($p=0.02$), compared to caregivers of ambulatory males. Although not statistically significant, a higher percentage of caregivers of non-ambulatory males versus those of ambulatory males reported high blood pressure ($p = 0.07$), whereas a higher percentage of caregivers of ambulatory males reported asthma compared to caregivers of non-ambulatory males ($p = 0.06$).

Discussion

In this population-based, cross-sectional study, we described the frequencies of a broad range of mental and physical conditions among individuals diagnosed with Duchenne or Becker muscular dystrophy and compared frequencies of these conditions by ambulation status among males with the Duchenne phenotype. Caregivers of males with Duchenne or Becker phenotypes reported secondary conditions affecting cognition, behavior, obesity, gastrointestinal, and genitourinary functioning. We did not formally compare differences in the frequencies of secondary conditions by phenotype due to small cell counts among those with the Becker phenotype. Significant differences in frequencies of selected conditions were found by ambulation status for males with the Duchenne phenotype with higher frequencies for anxiety, depression, and kidney stones among non-ambulatory males, and a higher frequency of attention deficit/hyperactivity disorder among ambulatory males.

Males with Duchenne muscular dystrophy are frequently reported to have an average IQ below that of the general population[7, 12, 17–20, 31–34]. In this study, caregivers were asked to report if their child had been diagnosed with cognitive issues that included developmental delay affecting learning and mental retardation/intellectual disability. Among those with the Duchenne phenotype, 38.4% of caregivers reported at least one of the two cognitive issues. When considering the full spectrum of cognitive issues, our estimate falls within the range of studies reporting on cognitive function among males with Duchenne muscular dystrophy[7, 12, 17–20, 31, 32].

Several studies have also focused on behavior problems among males with Duchenne muscular dystrophy[7, 8, 11–13, 15, 16, 18, 19, 21]. In this study, the percentage of caregivers reporting attention deficit hyperactivity disorder (14.0%), obsessive compulsive disorder (11.0%), or autism spectrum disorder (6.7%) was slightly higher than that reported (11.7%, 4.8%, and 3.1%, respectively) by caregivers in a larger study by Hendriksen et al. (n=351)[21]. Similar to this study, Caspers Conway et al. found attention deficit hyperactivity disorder in 18.0% of affected males in MD STAR*net* using medical record abstraction data (n=765)[11]. In this study, the percentage of males with caregiver-reported depression (27.4%) and behavioral/conduct issues (12.2%) differed from those found by Caspers Conway et al., which had lower rates of depression (17.0%) , but higher rates of behavior problems (26.0%)[11]. The observed differences are likely a result of data collection methods, attributes of the study population including average age, and condition definitions. Of note, the

aforementioned behavior problems were more prevalent in this study population than that reported for general pediatric and adolescent populations[35–40].

Small clinic-based studies have identified co-occurrence of gastrointestinal and nutritional issues in the Duchenne population[10, 22, 41]. It has been suggested that some of these problems may be related to reduced gastric motility[7, 10]. A clinic-based study of 118 patients with Duchenne muscular dystrophy by Pane et al. described percentages of their patients with weight above 2 standard deviations (3.4%), gastroesophageal reflux needing treatment (4.2%), and constipation needing treatment (36.4%)[10]. In the current report, the gastrointestinal and nutritional issues reported most often by caregivers were obesity (19.5%), gastroesophageal reflux/heartburn (17.7%), and constipation (31.7%). Jaffe et al. reported a similar percentage of heartburn (16.3%) to our study in their 55 patients with Duchenne muscular dystrophy[22]. The frequency of constipation is slightly higher than that of the general pediatric population[42, 43]. However, it is difficult to compare data across studies because clinical definitions may vary[42–46].

In this study, higher frequencies of anxiety, depression, and kidney stones were found among non-ambulatory males when compared to ambulatory males with the Duchenne phenotype. The findings of higher frequencies of anxiety and depression among those who are no longer able to independently ambulate may be due to increased disease awareness facilitated by age-related cognitive development or by emergent symptoms of muscle weakness and wasting as disease progresses[47]. The finding of a higher frequency of kidney stones in non-ambulatory males with Duchenne muscular dystrophy is consistent with findings from a study that used MD STAR*net* surveillance data as well as other clinic-based studies[14, 23–25].

A higher frequency of attention deficit hyperactivity disorder was reported for ambulatory males compared to non-ambulatory males with the Duchenne phenotype. These findings contradict the statistically non-significant association with ambulation status found by Caspers Conway et al., which used MD STAR*net* surveillance data and statistical methods that took into account age at last clinic visit, as well as those of Pane et al. who completed formal clinical assessments at the time of determining ambulation status[11, 12]. Thus, one potential confounding factor to the observed difference in this paper may be recall bias due to the age of the affected male at survey completion. Attention deficit hyperactivity disorder is a childhood disorder and DSM-IV diagnostic criteria requires onset before the age of 7 years. Less time from diagnosis to survey completion may have contributed to better recall of the diagnosis among caregivers of younger, ambulatory children compared to caregivers of older, non-ambulatory males.

Limitations of this study include generalizability of study results to the larger patient population, which is common of observational studies that rely on subject report. In this study, participants were more likely than non-participants to be non-Hispanic White and live in census tracts with less than median percent poverty. In addition, the survey was cross-sectional and did not collect the date when a secondary condition was first diagnosed, which prohibited analyses of factors where time ordering was clinically important (e.g., corticosteroid use preceding onset of behavior problems) Because of the variability in age of the individuals at the time of survey recruitment, caregiver reports may be influenced by

recall bias depending on the time elapsed between a secondary condition diagnosis and survey participation. Results are also based on caregiver report which could result in under or over-reporting of secondary conditions. The small sample size of some conditions introduced statistical uncertainty and limited the power of certain conclusions. Finally, this study used available clinical data abstracted from medical records to determine Duchenne or Becker phenotypes. This resulted in 17 cases being assigned an Indeterminate phenotype and exclusion from analyses further reducing our sample size.

Conclusion

According to caregiver reports, males with Duchenne or Becker phenotypes were reported to have lifetime diagnoses of conditions affecting cognition, behavior, gastrointestinal, and genitourinary functioning. These data support clinical care recommendations for careful monitoring of patients with Duchenne or Becker muscular dystrophy by a multidisciplinary care team to identify conditions that may be secondary to the diagnosis. Longitudinal follow-up of disease progression and the emergence of these conditions would help identify potential etiology and aid in their prevention and/or treatment.

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References

1. Romitti PA, Zhu Y, Puzhankara S, et al. Prevalence of Duchenne and Becker muscular dystrophies in the United States. Pediatrics. 2015; 135(3):513–21. [PubMed: 25687144]
2. Emery AE. Population frequencies of inherited neuromuscular diseases--a world survey. Neuromuscul Disord. 1991; 1(1):19–29. [PubMed: 1822774]
3. Sussman M. Duchenne muscular dystrophy. J Am Acad Orthop Surg. 2002; 10(2):138–51. [PubMed: 11929208]
4. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. Lancet Neurol. 2010; 9(2):177–89. [PubMed: 19945914]
5. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol. 2010; 9(1):77–93. [PubMed: 19945913]
6. Pope AM. Preventing secondary conditions. Ment Retard. 1992; 30(6):347–54. [PubMed: 1474911]
7. Pane M, Lombardo ME, Alfieri P, et al. Attention deficit hyperactivity disorder and cognitive function in Duchenne muscular dystrophy: phenotype-genotype correlation. J Pediatr. 2012; 161(4): 705–9. e1. [PubMed: 22560791]
8. Wu JY, Kuban KC, Allred E, et al. Association of Duchenne muscular dystrophy with autism spectrum disorder. J Child Neurol. 2005; 20(10):790–5. [PubMed: 16417872]
9. Melo M, Vieira AH, Passos-Bueno MR, Zaty M. Association of schizophrenia and Duchenne muscular dystrophy. Br J Psychiatry. 1993; 162:711–2.

10. Pane M, Vasta I, Messina S, et al. Feeding problems and weight gain in Duchenne muscular dystrophy. Eur J Paediatr Neurol. 2006; 10(5–6):231–6. [PubMed: 17045498]
11. Caspers Conway K, Mathews KD, Paramsothy P, et al. Neurobehavioral Concerns Among Males with Dystrophinopathy Using Population-Based Surveillance Data from the Muscular Dystrophy Surveillance, Tracking, and Research Network. J Dev Behav Pediatr. 2015; 36(6):455–63. [PubMed: 26020585]
12. Banihani R, Smile S, Yoon G, et al. Cognitive and Neurobehavioral Profile in Boys With Duchenne Muscular Dystrophy. J Child Neurol. 2015; 30(11):1472–82. [PubMed: 25660133]
13. Hinton VJ, Cyrulnik SE, Fee RJ, et al. Association of autistic spectrum disorders with dystrophinopathies. Pediatr Neurol. 2009; 41(5):339–46. [PubMed: 19818935]
14. Zhu Y, Romitti PA, Caspers Conway KM, et al. Genitourinary health in a population-based cohort of males with Duchenne and Becker Muscular dystrophies. Muscle Nerve. 2015; 52(1):22–7. [PubMed: 25297835]
15. Pangalila RF, van den Bos GA, Bartels B, et al. Prevalence of fatigue, pain, and affective disorders in adults with duchenne muscular dystrophy and their associations with quality of life. Arch Phys Med Rehabil. 2015; 96(7):1242–7. [PubMed: 25731937]
16. Darke J, Bushby K, Le Couteur A, McConachie H. Survey of behaviour problems in children with neuromuscular diseases. Eur J Paediatr Neurol. 2006; 10(3):129–34. [PubMed: 16766215]
17. Pane M, Messina S, Bruno C, et al. Duchenne muscular dystrophy and epilepsy. Neuromuscul Disord. 2013; 23(4):313–5. [PubMed: 23465656]
18. Sarrazin E, von der Hagen M, Schara U, et al. Growth and psychomotor development of patients with Duchenne muscular dystrophy. Eur J Paediatr Neurol. 2014; 18(1):38–44. [PubMed: 24100172]
19. Ricotti V, Mandy WP, Scoto M, et al. Neurodevelopmental, emotional, and behavioural problems in Duchenne muscular dystrophy in relation to underlying dystrophin gene mutations. Dev Med Child Neurol. 2016; 58(1):77–84. [PubMed: 26365034]
20. Wingeier K, Giger E, Strozzi S, et al. Neuropsychological impairments and the impact of dystrophin mutations on general cognitive functioning of patients with Duchenne muscular dystrophy. J Clin Neurosci. 2011; 18(1):90–5. [PubMed: 21109441]
21. Hendriksen JG, Vles JS. Neuropsychiatric disorders in males with duchenne muscular dystrophy: frequency rate of attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder, and obsessive--compulsive disorder. J Child Neurol. 2008; 23(5):477–81. [PubMed: 18354150]
22. Jaffe KM, McDonald CM, Ingman E, Haas J. Symptoms of upper gastrointestinal dysfunction in Duchenne muscular dystrophy: case-control study. Arch Phys Med Rehabil. 1990; 71(10):742–4. [PubMed: 2403280]
23. Askeland EJ, Arlen AM, Erickson BA, et al. Urological manifestations of Duchenne muscular dystrophy. J Urol. 2013; 190:1523–1528. [PubMed: 23357214]
24. Singh M, Jacobs IB, Spirnak JP. Nephrolithiasis in patients with Duchenne muscular dystrophy. Urology. 2007; 70:643–645. [PubMed: 17707891]
25. Shumyatcher Y, Shah TA, Noritz GH, et al. Symptomatic nephrolithiasis in prolonged survivors of Duchenne muscular dystrophy. Neuromuscul Disord. 2008; 18:561–564. [PubMed: 18579382]
26. Miller LA, Romitti PA, Cunniff C, et al. The Muscular Dystrophy Surveillance Tracking and Research Network (MD STARnet): surveillance methodology. Birth Defects Res A Clin Mol Teratol. 2006; 76(11):793–7. [PubMed: 17036307]
27. Mathews KD, Cunniff C, Kantamneni JR, et al. Muscular Dystrophy Surveillance Tracking and Research Network (MD STARnet): case definition in surveillance for childhood-onset Duchenne/Becker muscular dystrophy. J Child Neurol. 2010; 25(9):1098–102. [PubMed: 20817884]
28. Vignos PJ Jr, Archibald KC. Maintenance of ambulation in childhood muscular dystrophy. J Chronic Dis. 1960; 12:273–90. [PubMed: 13842210]
29. Krieger, N. U.S. Census tract poverty data. 2000.
30. The American Association for Public Opinion Research. Standard Definitions: Final Dispositions of Case Codes and Outcome Rates for Surveys. 6th. AAPOR; 2009.

31. Cotton S, Voudouris NJ, Greenwood KM. Intelligence and Duchenne muscular dystrophy: full-scale, verbal, and performance intelligence quotients. Dev Med Child Neurol. 2001; 43(7):497–501. [PubMed: 11463183]
32. Allen JE, Rodgin DW. Mental retardation in association with progressive dystrophy. Am J Dis Child. 1960; 100:208–11. [PubMed: 13792750]
33. Nardes F, Araujo AP, Ribeiro MG. Mental retardation in Duchenne muscular dystrophy. J Pediatr (Rio J). 2012; 88(1):6–16. [PubMed: 22344614]
34. Maulik PK, Mascarenhas MN, Mathers CD, et al. Prevalence of intellectual disability: a meta-analysis of population-based studies. Res Dev Disabil. 2011; 32(2):419–36. [PubMed: 21236634]
35. Merikangas KR, Nakamura EF, Kessler RC. Epidemiology of mental disorders in children and adolescents. Dialogues Clin Neurosci. 2009; 11(1):7–20. [PubMed: 19432384]
36. Boyle CA, Boulet S, Schieve LA, et al. Trends in the prevalence of developmental disabilities in US children, 1997–2008. Pediatrics. 2011; 127(6):1034–42. [PubMed: 21606152]
37. Visser SN, Danielson ML, Bitsko RH, et al. Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003–2011. J Am Acad Child Adolesc Psychiatry. 2014; 53(1):34–46. e2. [PubMed: 24342384]
38. Kessler RC, Avenevoli S, Costello EJ, et al. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement. Arch Gen Psychiatry. 2012; 69(4):372–80. [PubMed: 22147808]
39. Froehlich TE, Lanphear BP, Epstein JN, et al. Prevalence, recognition, and treatment of attention-deficit/hyperactivity disorder in a national sample of US children. Arch Pediatr Adolesc Med. 2007; 161(9):857–64. [PubMed: 17768285]
40. Christensen DL, Baio J, Braun KV, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012. MMWR Surveill Summ. 2016; 65(3):1–23.
41. Davis J, Samuels E, Mullins L. Nutrition Considerations in Duchenne Muscular Dystrophy. Nutr Clin Pract. 2015; 30(4):511–21. [PubMed: 25977513]
42. Loening-Baucke V. Prevalence rates for constipation and faecal and urinary incontinence. Arch Dis Child. 2007; 92(6):486–9. [PubMed: 16857698]
43. Mugie SM, Benninga MA, Di Lorenzo C. Epidemiology of constipation in children and adults: a systematic review. Best Pract Res Clin Gastroenterol. 2011; 25(1):3–18. [PubMed: 21382575]
44. Gunasekaran TS, Dahlberg M, Ramesh P, Namachivayam G. Prevalence and associated features of gastroesophageal reflux symptoms in a Caucasian-predominant adolescent school population. Dig Dis Sci. 2008; 53(9):2373–9. [PubMed: 18204971]
45. Sherman PM, Hassall E, Fagundes-Neto U, et al. A global, evidence-based consensus on the definition of gastroesophageal reflux disease in the pediatric population. Am J Gastroenterol. 2009; 104(5):1278–95. quiz 96. [PubMed: 19352345]
46. Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptoms of gastroesophageal reflux during childhood: a pediatric practice-based survey. Pediatric Practice Research Group. Arch Pediatr Adolesc Med. 2000; 154(2):150–4. [PubMed: 10665601]
47. Bray P, Bundy AC, Ryan MM, et al. Health-related quality of life in boys with Duchenne muscular dystrophy: agreement between parents and their sons. J Child Neurol. 2010; 25(10):1188–94. [PubMed: 20179004]

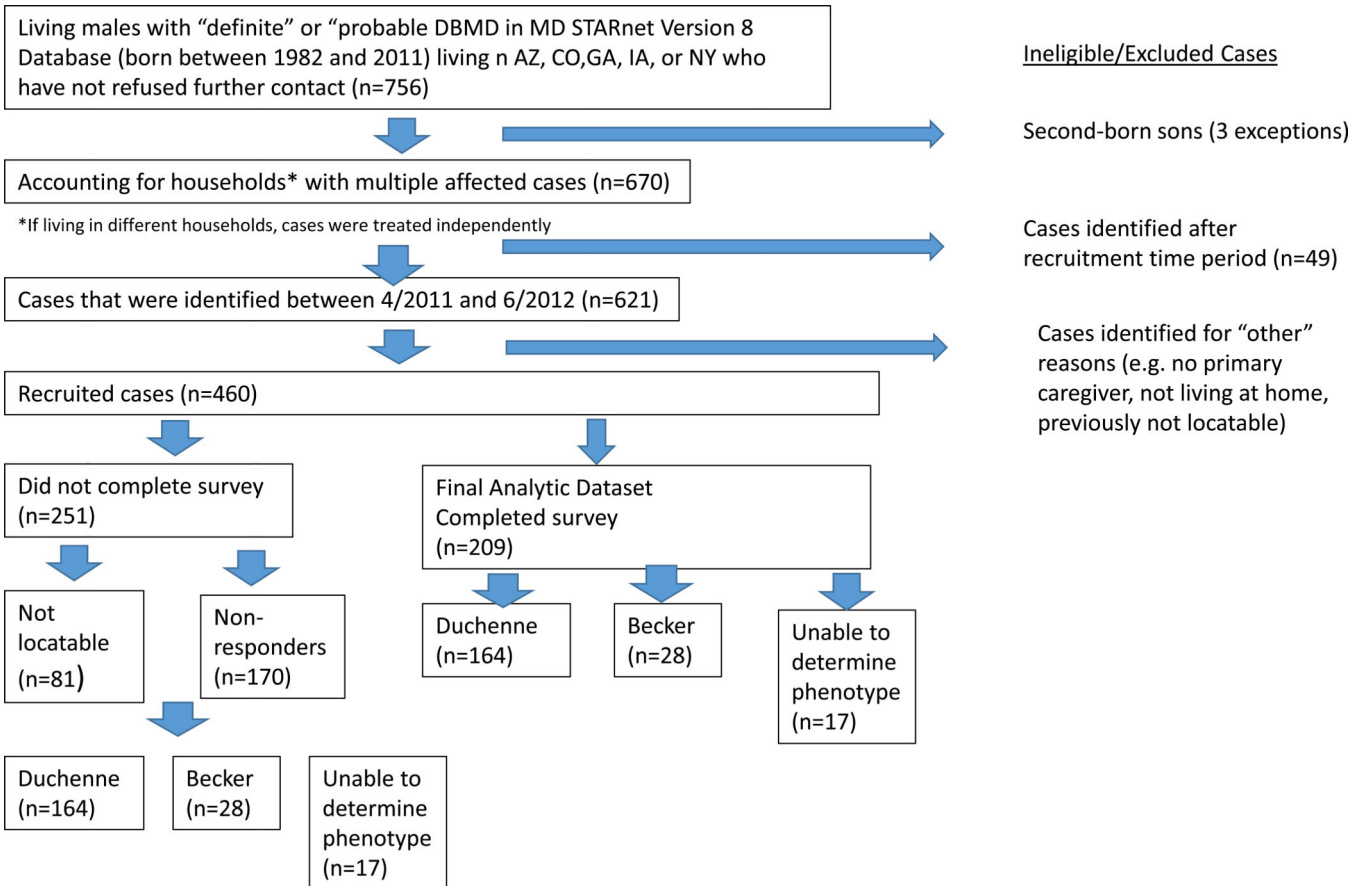

Figure 1.
Eligibility for the Family Quality of Life Survey

Table 1

Comparison of eligible caregivers who did and did not complete the survey.

Characteristic	Participants N= 209 n (%)	Non-participants N= 251 n (%)	P value*
Caregiver relationship			0.09
Biological parent	199 (95.2)	229 (91.2)	
Other	10 (4.8)	22 (8.8)	
Neighborhood Percent Poverty†			0.04
<7.5%	106 (50.7)	102 (40.6)	
≥7.5%	86 (41.2)	114 (45.4)	
Unknown	17 (8.1)	35 (13.9)	
Affected male race/ethnicity			<0.01
Non-Hispanic White	150 (71.8)	143 (57.0)	
Hispanic	30 (14.4)	59 (23.5)	
Non-Hispanic Black	12 (5.7)	17 (6.8)	
Other‡	4 (1.9)	18 (7.2)	
Unknown	13 (6.2)	14 (5.6)	
Phenotype			0.12
Duchenne	164 (78.5)	212 (84.5)	
Becker	28 (13.4)	29 (11.6)	
Indeterminate	17 (8.1)	10 (4.0)	
Age of affected male, years			
3–10	37 (17.7)	58 (23.1)	0.07
11–15	46 (22.0)	73 (29.1)	
16–20	62 (29.7)	57 (22.7)	
21–31	64 (30.6)	63 (25.1)	
Affected male ambulation status			0.47
Ambulatory	92 (44.0)	119 (47.4)	
Non-Ambulatory	117 (56.0)	132 (52.6)	

*χ^2 test

†The percentage of residents in the participant's census tract whose household income is below the federal poverty level.

‡Asian or Hawaiian or Pacific Islander and Native American or American Indian or Alaska Native

Notes: There is slight variation in denominator values due to the removal of missing responses

Table 2

Frequencies of caregiver reported secondary conditions in affected males by Duchenne and Becker phenotypes

Secondary Conditions	Duchenne Muscular Dystrophy N=164 n (%)	Becker Muscular Dystrophy N=28 n (%)
Cognitive deficits	63 (38.4)	10 (35.7)
Anxiety problems	48 (29.3)	5 (17.9)
Depression	45 (27.4)	8 (28.6)
Attention deficit disorder/attention deficit hyperactivity disorder	23 (14.0)	9 (32.1)
Behavioral/Conduct problems	20 (12.2)	4 (14.3)
Obsessive-compulsive disorder	18 (11.0)	1 (3.6)
Autism spectrum disorder	11 (6.7)	1 (3.6)
Personality disorder	4 (2.4)	1 (3.6)
Psychiatric disorder	1 (0.6)	0 (0)
Constipation	52 (31.7)	6 (21.4)
Obesity	32 (19.5)	4 (14.3)
Gastroesophageal reflux disease/heartburn	29 (17.7)	3 (10.7)
Failure to thrive/trouble gaining weight	18 (11.0)	0 (0)
Inflammatory bowel disease/Crohn's/ulcerative colitis	4 (2.4)	0 (0)
Gallstones	2 (1.2)	0 (0)
Diabetes	1 (0.6)	0 (0)
Trouble holding urine	21 (12.8)	6 (21.4)
Trouble urinating	15 (9.2)	1 (3.6)
Kidney stones	13 (7.9)	1 (3.6)
High blood pressure	21 (12.8)	1 (3.6)
Asthma	17 (10.4)	2 (7.1)
Cataracts	12 (7.3)	5 (17.9)
Migraines	12 (7.3)	2 (7.1)
Seizures/epilepsy	5 (3.1)	2 (7.1)
Deep vein thrombosis/blood clots in legs	4 (2.4)	0 (0)
Pseudotumor cerebri	3 (1.8)	0 (0)
Cerebral palsy	2 (1.2)	0 (0)
Cancer	1 (0.6)	0 (0)

Notes: Caregivers could report more than one condition; there is slight variation in denominators due to missing responses

Table 3

Comparisons of secondary conditions among males with Duchenne muscular dystrophy by ambulation status (n=164)

Secondary Conditions	Ambulatory* (N= 45) n (%)	Non-ambulatory† (N= 119) n (%)	p-value‡
Cognitive Deficits	19 (42.2)	44 (37.0)	0.54
Anxiety problems	7 (15.6)	41 (34.5)	0.02
Depression	4 (8.9)	41 (34.5)	<0.01
Attention deficit disorder/attention deficit hyperactivity disorder	12 (26.7)	11 (9.2)	<0.01
Behavioral/Conduct problems	8 (17.8)	12 (10.1)	0.18
Obsessive-compulsive disorder	3 (6.7)	15 (12.6)	0.40
Autism spectrum disorder	5 (11.1	6 (5.0)	0.18
Constipation	15 (33.3)	37 (31.1)	0.78
Obesity	6 (13.3)	26 (21.9)	0.22
Gastroesophageal reflux disease/heartburn	4 (8.9)	25 (21.0)	0.11
Failure to thrive/trouble gaining weight	4 (8.9)	14 (11.8)	0.78
Trouble holding urine	8 (17.8)	13 (10.9)	0.24
Trouble urinating	1 (2.2)	14 (11.8)	0.07
Kidney stones	0 (0)	13 (10.9)	0.02
High blood pressure	2 (4.4)	19 (16.0)	0.07
Asthma	8 (17.8)	9 (7.6)	0.06
Cataracts	2 (8.4)	10 (8.4)	0.51
Migraines	4 (8.9)	8 (6.7)	0.74

Notes: Participants could report more than one condition across categories; conditions that had ≤5 observations for the total sample are not reported here; there is slight variation in denominators due to missing responses

*At a minimum, ability to walk with assistance or long-leg braces

†At a maximum, can stand with long-leg braces, but cannot walk even with assistance

‡χ^2 or Fisher's exact test if the expected cell was <5 observations.