Published in final edited form as:

J Pediatr. 2009 September ; 155(3): 380–385. doi:10.1016/j.jpeds.2009.02.007.

Delayed Diagnosis in Duchenne Muscular Dystrophy: Data from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STARnet)

Emma Cialfoni, MD, Deborah J. Fox, MPH, Shree Pandya, PT, MS, Christina P. Westfield, RN, BSN, Soman Puzhankara, MS, Paul A. Romitti, PhD, Katherine D. Mathews, MD, Timothy M. Miller, MD, Dennis J. Matthews, MD, Lisa A. Miller, MD, MSPH, Christopher Cunniff, MD, Charlotte M. Druschel, MD, MPH, and Richard T. Moxley, MD

Department of Neurology (E.C., S.P., R.M.), University of Rochester, Rochester, NY; New York State Department of Health (D.F., C.W., C.D.), Troy, NY; Department of Epidemiology (S.P., P.R.), University of Iowa, College of Public Health, Iowa City, IA; Department of Pediatrics (K.M.), University of Iowa Carver College of Medicine, Iowa City, IA; The Departments of Pediatrics and Neurology and the Steele Children's Research Center (T.M., C.C.), University of Arizona College of Medicine, Tucson, AZ; Department of Physical Medicine and Rehabilitation (D.M.), University of Colorado School of Medicine, The Children's Hospital, Denver, CO; and Colorado Department of Public Health and Environment (L.M.), Denver, CO

Abstract

Objective—To identify key factors for the delay in diagnosis of Duchenne muscular dystrophy (DMD) without known family history.

Study design—The cohort comes from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STARnet), a multistate, multiple-source, population-based surveillance system that identifies and gathers information on all cases of Duchenne and Becker muscular dystrophy born since 1982. We analyzed medical records of 453 Duchenne and Becker muscular dystrophy boys to document the time course and steps taken to reach a definitive diagnosis.

Results—Among 156 boys without known family history of DMD prior to birth, first signs or symptoms were noted at a mean age of 2.5 years. Concerns resulted in primary care provider evaluation of the child at a mean age of 3.6 years. Mean age at time of initial creatine kinase was 4.7 years. Mean age at definitive diagnosis of DMD was 4.9 years.

Conclusions—There is a delay of about 2.5 years between onset of DMD symptoms and the time of definitive diagnosis, unchanged over the previous 2 decades. This delay results in lost opportunities for timely genetic counseling and initiation of corticosteroid treatment. We recommend checking creatine kinase early in the evaluation of boys with unexplained developmental delay.

Reprint requests: Dr Emma Cialfoni, University of Rochester, 601 Elmwood Avenue, PO Box 673, Rochester, NY 14642. Emma_cialfoni@urmc.rochester.edu.

The authors declare no conflicts of interest.

Duchenne muscular dystrophy (DMD) is the most common muscular dystrophy in children, occurring in 1 of every 3500 male newborns.¹ DMD is an X-linked recessive disorder; approximately 30% of cases arise from spontaneous mutations in the dystrophin (*DMD*) gene.² DMD results from an absence of dystrophin, an essential transmembrane muscle protein in the dystrophin-glycoprotein complex.³ Signs and symptoms (SS) of DMD begin before 5 years of age, and there is progressive disability, with loss of ambulation in most individuals by 10 to 12 years of age.⁴ The clinical course of DMD is improved with corticosteroid therapy.^{5–9}

When there is no prior family history of DMD, the diagnosis should be suspected in boys who present with delayed development that include motor difficulties. Global developmental delay does not exclude the diagnosis of DMD as cognitive, behavioral and language abnormalities are found in about one third of cases.¹⁰ Creatine kinase (CK) level is a sensitive biochemical marker for early detection of DMD and is elevated 50- to 200-fold above normal in children with DMD. An elevated CK level localizes the problem to the muscle and usually results in a referral to a neurologist or neuromuscular specialist for definitive diagnosis, treatment, and genetic counseling.

Since the discovery of the *DMD* gene in 1987, significant progress has been made in genetic testing using DNA analysis for DMD, so that it is now possible to identify *DMD* mutations from blood specimens in over 95% of patients with DMD.¹¹ Several clinic-based studies spanning more than a decade show a mean age for diagnosis of DMD between 4 and 5 years.^{12–20}

The purpose of this population-based investigation was to describe the timeline in the diagnostic process among individuals without known family history of DMD, to identify reasons for delays in diagnosis, and to highlight clinical steps needed to shorten the time to diagnosis.

Methods

The study cohort of 156 patients with DMD without a family history of DMD comes from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STARnet) supported by the Centers for Disease Control and Prevention (CDC). MD STARnet identifies and gathers information on all cases of Duchenne and Becker muscular dystrophy (DBMD) born since 1982 and residing within Arizona, Colorado, Iowa, or Western New York State. The MD STARnet study population and surveillance methodology have been published previously.²¹

Data Collection

MD STARnet collects information from patient records from care providers in regional neuromuscular clinics, hospitals, outpatient clinics, death certificates, hospital discharge databases, and other medical sources. Records from these sources are reviewed, and relevant patient information is recorded by trained medical records abstractors using a computerized abstraction instrument. Abstracted information includes place of birth and residential history, growth data, symptoms, diagnostic tests (CK, muscle biopsy, DNA testing), data

documenting the effect of disease progression on musculoskeletal, pulmonary and cardiac systems, types of clinical treatment and management procedures, and changes in mobility and function over time.

Clinical, diagnostic, and family history information is then reviewed by a clinical review committee to classify the patients into one of the following case definitions: definite, probable, possible, asymptomatic, female, or not DBMD. For this study we included definite or probable cases of DMD without known family history of DMD prior to birth.²¹

To capture more detailed information pertinent to the early phases of the diagnostic process, a supplemental abstraction form was developed to record: (1) earliest SS; (2) SS that prompted evaluation; (3) identification of the individual who noticed the early SS; (4) identification of the care provider who evaluated the child and action taken as a result of the evaluation; (5) date of first CK test; and (6) date of definitive diagnosis. This form was completed by the clinician or medical abstractor from each MD STARnet site after thorough review of pertinent source records and of information already available in the database.

The clinicians, data managers, and clinical abstractors received standardized training to study purpose, definition of data elements, and best way to locate required information. Training sessions included practice in abstraction and review using several cases to improve interabstractor and intersite reliability.

Referral letters from pediatricians, initial history, and physical examination findings of specialists (neurologists, orthopedists, child neurologists, neuromuscular specialists, developmental pediatricians), parent intake forms, as well as physical, occupational, and speech pathology developmental assessments were used to determine the earliest SS and who noticed them, the date and type of care provider, and the date of first serum CK test. Information from these forms was entered into a computerized supplementary database for analysis.

Statistical Analysis

Univariate analyses were performed first to check for outliers and coding errors as well as to assess distributional properties of the data. General descriptive statistics were generated for all variables of interest. Simple linear regression was used to assess a potential change in age for the time of the first CK test and potential change in age of definitive diagnosis over the time period of the study. Data were analyzed and validated by investigators from 2 different MD STARnet sites using SAS version 9.1 (SAS Institute, Inc, Cary, North Carolina).

Results

Data abstracted from the medical records of 453 patients with either Duchenne or Becker muscular dystrophy (DBMD) were submitted for clinician review to assign case status. The final data set contains a cohort of 156 boys with a definite or probable Duchenne muscular dystrophy case definition and without a known family history of DMD prior to birth (Figure).

Because MD STARnet is a retrospective chart review, not all of the data elements were complete for all patients. For example, age at first SS was not available in 23 boys, and, for an additional 22 boys, the age of first SS could not be used for statistical analysis because SS were described as “always present” or “never could do.” In 29 of the 156 boys, data identifying specific diagnostic steps were missing: (1) the age of the patient when concerns were first communicated to a health specialist; (2) what action was taken as a result; (3) who was the first specialist to request a CK test; or (4) the date on which the patient had an evaluation by a neurologist or neuromuscular specialist. Those patients with missing data were excluded from some of the analyses.

Diagnostic Delay

The initial or first SS in our cohort of nonfamilial DMD were noted by parents or caregivers at a mean age of 2.5 years (Table I), with the first SS noted before 1.5 years of age in 28% of boys and before 3 years of age in 58% of the cohort. Table II displays the most frequent first SS noticed among these age groups.

Although the recognition of first SS of DMD occurred on average at age 2.5 years, there was an average delay of over 1 year before boys were brought to a health care provider for evaluation of the SS. The mean age at which concerns about the initial SS led to a clinical evaluation of the child was 3.6 years (Table I). Caregivers (either family members or another primary caregiver) were most often the first to identify the initial SS, followed by school personnel (Table III). For the majority of patients in the cohort, the health specialist first evaluating the child for initial concerns about SS of DMD was a pediatrician or family practitioner.

The first evaluation by any health specialist included a serum CK test in only 35% of cases. For the entire cohort of nonfamilial patients with DMD, the mean age for obtaining first serum CK testing was 4.7 years of age, and the mean age these patients first had an evaluation by a neurologist or neuromuscular specialist was 4.6 years of age (Table I).

There was variation in the type of specialist who ordered the first serum CK, and there was variation between MD STARnet sites ($P = .009$) (Table III). Approximately 37% of the time a pediatrician or family practitioner ordered the first CK test. Once a referral to a neurologist or neuromuscular specialist was made, the patient almost always had a CK test performed. These CK test results had a pivotal role in establishing the diagnosis of DMD and helped to establish that the initial SS in the patient related to an underlying muscle disorder. Until the CK was obtained, the diagnosis of DMD was delayed in this cohort of nonfamilial cases.

To identify whether over the past 2 decades there has been a decrease in the age at which care providers have obtained the first CK in boys with nonfamilial DMD, we applied linear regression analysis of the ages when our cohort had their first CK over the time interval between 1982 and 2000. We did not find a significant change in mean age for obtaining the first measurement of serum CK in boys with no known family history of DMD ($P = .22$). The mean age for patients in our cohort at which a definitive diagnosis of DMD was established by DNA testing or muscle biopsy was 4.9 years. We found a nonsignificant trend

toward reduction in the age at which care providers have established a definitive diagnosis of DMD from 1982 to 2000 ($P = .055$).

Discussion

There continues to be a delay in recognition of the early signs and symptoms of DMD. This delay has not changed substantially over the past 20 years despite the availability of definitive molecular genetic testing and disease modifying treatments. The age of definitive diagnosis of DMD in our population-based study is 5 years, almost identical to that reported in small single clinic cohorts in the early 1980s and in the mid 1990s from the United States and Europe.^{12–20}

There is an average delay of 2.5 years between onset of symptoms and time of definitive diagnosis, and there is a delay of 1.1 years between onset of symptoms and the time at which these concerns result in an evaluation by a health care provider. Although this may be in part due to lack of awareness by parents, especially if they are first-time parents, frequently the first report of concerns triggers a referral to a care provider who cannot order CK screening test such as a physical, occupational, or speech therapist or a developmental stimulation program such as Early Intervention in NY State. The MD STARnet is currently conducting parents' interviews that include several questions regarding the "diagnostic odyssey" that will help to clarify the reasons for this portion of the diagnostic delay.

There is an additional delay of 1.1 years between the first clinical evaluation of SS of DMD and the time at which a care provider obtains a serum CK test. Our study is the first to identify where the delays occur. It also has the advantage of being a multistate, population-based cohort rather than a single clinic case review. One limitation of our study is that only 156 cases of the 453 could be included in the analysis.

Serum CK testing is an easy, sensitive, and inexpensive test that appears to be underutilized in patients that have early SS compatible with DMD. The first evaluation of children in our cohort presenting with motor or global developmental delay resulted in CK screening in only 35% of cases. In about 25% of children, referral was made to physical, occupational, or speech therapy or to a developmental stimulation program without any diagnostic testing. No referral or testing was made in an additional 6% of cases in our cohort.

There are compelling reasons to shorten the time to establish a definite diagnosis in DMD. Highly sensitive genetic testing is available to identify mutations responsible for DMD, and positive results allow timely genetic counseling, assessment of carrier status, and initiation of treatment with corticosteroids. In our cohort, 14 additional brothers and 1 maternal cousin with DMD were born into families before definitive diagnosis of DMD was made in the proband. Recognition of early signs and symptoms of DMD and its definitive diagnosis offers families an opportunity to use this information for reproductive planning. A definite diagnosis with documentation of the specific DNA mutation is also necessary for the patients to participate in new treatment trials currently underway.

Newborn screening has been advocated by some as the best solution for early detection of DMD.^{22–24} Screening during the newborn period or later in infancy to identify children

before onset of symptoms is currently undergoing investigation in 2 pilot studies in the United States. However, until newborn screening becomes established as an integral part of the search for patients with DMD, care providers must focus on improving their ability to make an early clinical diagnosis.

Given the nonspecific presentation of early DMD, the relatively high frequency of cognitive and language impairment along with motor delay, and the low cost of the test, we strongly advocate the addition of CK test to standard evaluation of any boy presenting with developmental delay by pediatricians and family practitioners who usually see these children first. Others have made similar recommendations.¹⁸ We believe this is a serious omission in the current version of the American Academy of Neurology Practice Parameter for the evaluation of a child with developmental delay.²⁵

We also support the ongoing effort by all organizations involved in the care of children with DMD, such as the Centers for Disease Control and Prevention, American Academy of Pediatrics, the American Academy of Family Physicians, the Muscular Dystrophy Association, and Parent Project Muscular Dystrophy, to develop and disseminate new educational tools that will assist care providers in recognizing early symptoms and signs of DMD.

Acknowledgments

Supported by the Centers for Disease Control and Prevention Cooperative Agreement (5U01DD000187).

We are grateful to the families who participated in this study. We acknowledge the efforts of the following personnel without whom this work would not have been feasible: Rebeca Arias, April Bryant, April Breen, Shawnell Damon, Patricia Ennis, Carrie Fall, Katy Fox, Brad McDowell, Pratyay Rath, Tricia Steen, and Cynthia Vogel for record abstraction; Susan Apkon, Zoe Powis, and Carrie Stephan for abstract review; Amy Alman, Jennifer Andrews, Florence Foo, Katherine James, Russ Roberge, Tanner Wenzel, and Jiji Kantamnen for data management; Valerie Cwik and F. John Meaney for study design; and April Montgomery for project coordination.

Glossary

CK	Creatine kinase
DBMD	Duchenne and Becker muscular dystrophy
DMD	Duchenne muscular dystrophy
MD STARnet	Muscular Dystrophy Surveillance, Tracking, and Research Network
SS	Signs or symptoms

References

1. Emery AE. Population frequencies of inherited neuromuscular diseases: a world survey. *Neuromuscul Disord.* 1991; 1:19–29. [PubMed: 1822774]
2. Emery, AE. *Duchenne Muscular Dystrophy*. 2. New York: Oxford University Press; 1987.
3. Koenig M, Hoffman EP, Bertelson CJ, Monaco AP, Feener C, Kunkel LM. Complete cloning of the Duchenne muscular dystrophy (DMD) cDNA and preliminary genomic organization of the DMD gene in normal and affected individuals. *Cell.* 1987; 50:509–17. [PubMed: 3607877]

4. Dubowitz, V. Muscle Disorders in Childhood. 2. Philadelphia: WB Saunders; 1995. Muscular dystrophies.
5. Brooke MH, Fenichel GM, Griggs RC, Mendell JR, Moxley RT 3rd, Miller JP, et al. Clinical investigation of Duchenne muscular dystrophy: interesting results in a trial of prednisone. *Arch Neurol.* 1987; 44:812–7. [PubMed: 3632393]
6. Mendell JR, Moxley RT 3rd, Griggs RC, Brooke MH, Fenichel GM, Miller JP, et al. Randomized, double-blind six-month trial of prednisone in Duchenne's muscular dystrophy. *N Engl J Med.* 1989; 320:1592–7. [PubMed: 2657428]
7. Griggs RC, Moxley RT 3rd, Mendell JR, Fenichel GM, Brooke MH, Pestronk A, et al. Prednisone in Duchenne dystrophy: a randomized, controlled trial defining the time course and dose response: Clinical Investigation of Duchenne Dystrophy Group. *Arch Neurol.* 1991; 48:383–8. [PubMed: 2012511]
8. Fenichel GM, Florence JM, Pestronk A, Mendell JR, Moxley RT 3rd, Griggs RC, et al. Long-term benefit from prednisone therapy in Duchenne muscular dystrophy. *Neurology.* 1991; 41:1874–7. [PubMed: 1745340]
9. Fenichel GM, Mendell JR, Moxley RT 3rd, Griggs RC, Brooke MH, Miller JP, et al. A comparison of daily and alternate-day prednisone therapy in the treatment of Duchenne muscular dystrophy. *Arch Neurol.* 1991; 48:575–9. [PubMed: 2039377]
10. Cyrulnik SE, Fee RJ, De Vivo DC, Goldstein E, Hinton VJ. Delayed developmental language milestones in children with Duchenne's muscular dystrophy. *J Pediatr.* 2007; 150:474–8. [PubMed: 17452219]
11. Flanigan KM, von Niederhausern A, Dunn DM, Alder J, Mendell JR, Weiss RB. Rapid direct sequence analysis of the dystrophin gene. *Am J Hum Genet.* 2003; 72:931–9. [PubMed: 12632325]
12. Crisp DE, Ziter FA, Bray PF. Diagnostic delay in Duchenne's muscular dystrophy. *JAMA.* 1982; 247:478–80. [PubMed: 7054550]
13. Green JM, Murton FE. Diagnosis of Duchenne muscular dystrophy: parents' experiences and satisfaction. *Child Care Health Dev.* 1996; 22:113–28. [PubMed: 8820016]
14. Parsons EP, Clarke AJ, Bradley DM. Developmental progress in Duchenne muscular dystrophy: lessons for earlier detection. *Eur J Paediatr Neurol.* 2004; 8:145–53. [PubMed: 15120686]
15. O'Brien T, Sibert JR, Harper PS. Implications of diagnostic delay in Duchenne muscular dystrophy. *Br Med J (Clin Res Ed).* 1983; 287:1106–7.
16. Bushby KM, Hill A, Steele JG. Failure of early diagnosis in symptomatic Duchenne muscular dystrophy. *Lancet.* 1999; 353:557–8. [PubMed: 10028989]
17. Zalaudek I, Bonelli RM, Koltringer P, Reisecker F, Wagner K. Early diagnosis in Duchenne muscular dystrophy. *Lancet.* 1999; 353:1975.
18. Mohamed K, Appleton R, Nicolaides P. Delayed diagnosis of Duchenne muscular dystrophy. *Eur J Paediatr Neurol.* 2000; 4:219–23. [PubMed: 11030068]
19. Smith RA, Sibert JR, Wallace SJ, Harper PS. Early diagnosis and secondary prevention of Duchenne muscular dystrophy. *Arch Dis Child.* 1989; 64:787–90. [PubMed: 2476078]
20. Marshall PD, Galasko CS. No improvement in delay in diagnosis of Duchenne muscular dystrophy. *Lancet.* 1995; 345:590–1.
21. 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 Res A Clin Mol Teratol.* 2006; 76:793–7. [PubMed: 17036307]
22. Kemper AR, Wake MA. Duchenne muscular dystrophy: issues in expanding newborn screening. *Curr Opin Pediatr.* 2007; 19:700–4. [PubMed: 18025940]
23. Ross LF. Screening for conditions that do not meet the Wilson and Jungner criteria: the case of Duchenne muscular dystrophy. *Am J Med Genet A.* 2006; 140:914–22. [PubMed: 16528755]
24. Acharya K, Ackerman PD, Ross LF. Pediatricians' attitudes toward expanding newborn screening. *Pediatrics.* 2005; 116:e476–84. [PubMed: 16199673]
25. Shevell M, Ashwal S, Donley D, Flint J, Gingold M, Hirtz D, et al. Practice parameter: evaluation of the child with global developmental delay: report of the quality standards subcommittee of the

American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2003; 60:367–80. [PubMed: 12578916]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure.

Flow diagram of the selection process of patients with Duchenne dystrophy without a family history from the initial pool population of patients with Duchenne/Becker.

Table I

Timeline of diagnostic steps for patients with Duchenne dystrophy without family history of dystrophy (N = 156).

Measure	n	Mean years of age $\pm$ SD	Range, years of age
Earliest sign or symptom noted	111	2.5 $\pm$ 1.4	0.2–6.1
First evaluation by health specialist	127	3.6 $\pm$ 1.7	0.2–8.0
First neurology/neuromuscular visit	131	4.6 $\pm$ 1.7	0.3–8.6
First CK test	151	4.7 $\pm$ 1.7	0.3–8.6
Age at definitive diagnosis	154	4.9 $\pm$ 1.7	0.3–8.8

Table II

Percentage of signs and symptoms first reported to care providers by patients with Duchenne dystrophy without family history of dystrophy (n = 111).

Finding	Age when first signs or symptoms are noted (y)			
	<1.5	1.5 and <3	3 and <5	5
All cases	27.9	29.7	37.8	4.5
Motor or mobility-related				
Abnormal gait	9.7	12.1	11.9	20.0
Frequently falling/clumsy	6.5	15.2	33.3	20.0
Gross motor delay	58.1	48.5	38.1	40.0
Inability to keep up with peers in motor	0	12.1	26.2	80.0
Activities				
Loss of motor skills	0	0	4.8	0
Muscle hypotonia	16.1	0	7.1	0
Muscle pain	3.2	6.1	11.9	0
Muscle weakness	32.3	6.1	40.5	80.0
Toe-walking	0	6.1	7.1	0
Trouble walking or running	19.4	54.6	38.1	40.0
Trouble climbing	6.5	24.2	31.0	40.0
Trouble rising or getting up	12.9	21.2	23.8	20.0
Nonmotor				
Speech delay or articulation difficulties	9.7	18.2	16.7	20.0
Behavioral issues	0	0	4.8	0
Calf hypertrophy	0	6.1	7.1	0
Cognitive delay	0	0	7.1	0
Failure to thrive/poor weight gain	16.1	0	4.8	0
Other	16.1	9.1	2.4	20.0

The most prevalent SS in each age group are shown in **bold** type.

First medical evaluation for concern about signs and symptoms for patients with Duchenne dystrophy without family history of dystrophy.

Table III

Measure	AZ n (%)	CO n (%)	IA n (%)	NY n (%)	Total n (%)
Individual who initiated a medical investigation for the concerns					
Family or primary caregiver	14 (51.9)	20 (71.4)	22 (68.8)	18 (45.0)	74 (58.3)
Child's physician	3 (11.1)	4 (14.3)	3 (9.4)	5 (12.5)	15 (11.8)
School (teacher, RN, PT, PE)	3 (11.1)	1 (3.6)	3 (9.4)	14 (35.0)	21 (16.5)
Other	2 (7.4)	2 (7.1)	2 (6.3)	1 (2.5)	7 (5.5)
Unknown	5 (18.5)	1 (3.6)	2 (6.3)	2 (5.0)	10 (7.9)
Health provider evaluating the child for the first concerns					
Pediatrician or family practitioner	8 (29.6)	23 (82.1)	24 (75.0)	26 (65.0)	81 (63.8)
Neurologist or neuromuscular specialist	8 (29.6)	1 (3.6)	1 (3.1)	2 (5.0)	12 (9.4)
Developmental pediatrician	1 (3.7)	0	0	1 (2.5)	2 (1.6)
Orthopedist	1 (3.7)	0	1 (3.1)	1 (2.5)	3 (2.4)
Emergency room/urgent care physician	1 (3.7)	1 (3.6)	0	0	2 (1.6)
Speech therapist	0	0	0	6 (15.0)	6 (4.7)
Physical or occupational therapist	1 (3.7)	0	2 (6.3)	4 (10.0)	7 (5.5)
Other	3 (11.1)	2 (7.2)	3 (9.4)	0	8 (6.3)
Unknown	4 (14.8)	1 (3.6)	1 (3.1)	0	6 (4.7)
Type of referral or action taken as a result of the first evaluation					
Ordered a CK test	14 (51.9)	10 (35.7)	11 (34.4)	9 (22.5)	44 (34.6)
Referred to neurologist or neuromuscular specialist	4 (14.8)	7 (25.0)	5 (15.6)	5 (12.5)	21 (16.5)
Referred to pediatrician	0	0	4 (12.5)	1 (2.5)	5 (3.9)
Referred to developmental pediatrician	0	0	0	3 (7.5)	3 (2.4)
Referred to orthopedist or rehabilitation medicine	1 (3.7)	3 (10.7)	3 (9.4)	3 (7.5)	10 (7.9)
Referral to PT/OT/speech therapy	3 (11.1)	5 (17.9)	3 (9.4)	9 (22.5)	20 (15.7)
Referral to developmental stimulation program (eg, early intervention)	0	0	3 (9.4)	4 (10.0)	7 (5.5)
Follow-up in less than 6 mo	1 (3.7)	0	0	0	1 (0.8)
No action or referral	2 (7.4)	1 (3.6)	2 (6.3)	1 (2.5)	6 (4.7)
Other	2 (7.4)	2 (7.1)	1 (3.1)	3 (7.5)	8 (6.3)
Unknown	0	0	0	2 (5.0)	2 (1.6)

Measure	AZ n (%)	CO n (%)	IA n (%)	NY n (%)	Total n (%)
First health provider to request CK test *					
Pediatrician or family practitioner	4 (14.8)	10 (35.7)	18 (56.3)	15 (37.5)	47 (37.0)
Neurologist or neuromuscular specialist	18 (66.7)	8 (28.6)	9 (28.1)	14 (35.0)	49 (38.6)
Other healthcare specialist					
Developmental pediatrician	0	0	0	5 (12.5)	5 (3.9)
Orthopedist	1 (3.7)	1 (3.6)	2 (6.3)	2 (5.0)	6 (4.7)
Emergency room or urgent care physician	1 (3.7)	1 (3.6)	0	0	2 (1.6)
Other or unknown	3 (11.1)	8 (28.6)	3 (9.4)	4 (10.0)	18 (14.2)

* $\chi^2 = 17.1$, degrees of freedom = 6, $P = .009$.