FIFTEEN YEAR REGISTRY REPORT

Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

ENDDUCHENNE.ORG

The Duchenne Registry

The Duchenne Registry is the largest, most comprehensive patient-reported registry for Duchenne and Becker muscular dystrophy worldwide. The Duchenne Registry began in 2007 with the goal of connecting and serving the needs of the Duchenne and Becker community, including patients and families, academic and industry researchers, and clinicians.

The Registry is now powered by **15 years of robust data** shared by patients and families with Duchenne and Becker as well as carrier females*. This report is a summary of data collected from nearly 5,500 individuals from October 2007 through October 2022.

The Registry has several Medical History surveys that together form the core of the data we collect. We ask registrants to complete all relevant surveys at the time of registration, and we request annual updates. The better the data we collect, the better the Registry, and the more we are able to learn about Duchenne, Becker, and female carriers. **The strength of the Registry really does depend on you, the registrants!**

15
Years of Data Collection

5,498
Total Registrants

125
Countries Represented

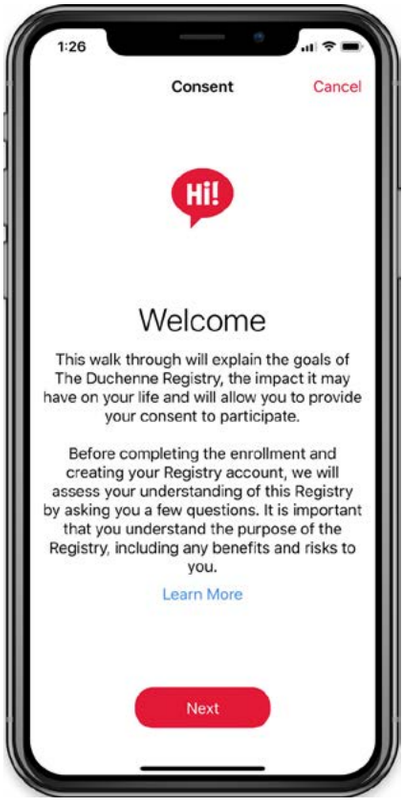
28,276
Surveys Completed

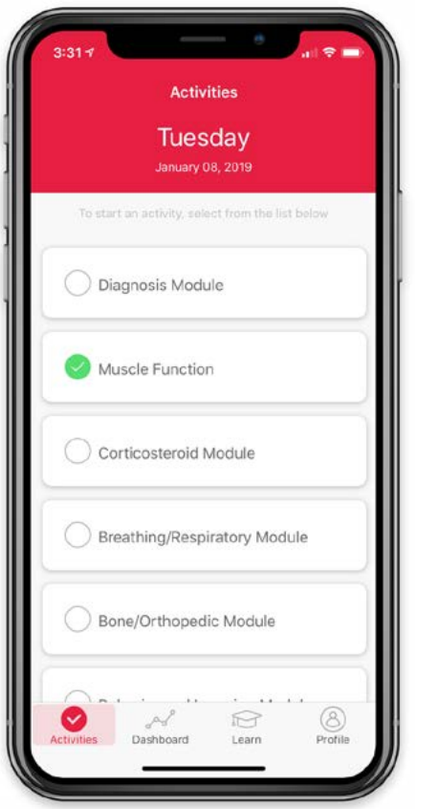
2,445
Genetic Test Reports

** Please note, throughout this report we will use male and female to refer to an individual's sex assigned at birth.*

Creating a User-Friendly Platform

In 2019, the Registry transitioned from a web platform to an app platform*, with the goal of increasing community engagement and providing families with a more user-friendly experience. We have found that registrants using the app are more likely than previous web users to complete all surveys, resulting in a more thorough understanding of those individuals. Registrants using the app were also more likely to submit genetic test reports. However, an app platform does have unique challenges and for this reason we are in the process of developing a parallel web platform to give each participant the option of choosing a preferred platform.





The Duchenne Registry is a program of PPMD, and PPMD is the sole guardian of the Registry and its material.

** The app was developed in partnership with THREAD Research, a company specializing in decentralized research platforms.*

"We have always believed in the importance of innovation and the power of patient data in the fight to end Duchenne," stated Pat Furlong, Founding President and CEO of PPMD. "We are excited to celebrate The Duchenne Registry's 15 Year Anniversary. This wonderful milestone is a reflection of the dedication of patients and families in this community, and their drive to advance research and treatments for Duchenne, Becker, and female carriers."

How the Data Has Been Used

The de-identified data in The Duchenne Registry has been used by researchers and industry sponsors to advance care and treatments for Duchenne and Becker. Over the past 15 years, **data has been exported and shared with researchers over 65 times**, including multiple exports to the TREAT-NMD International Neuromuscular Registry. To date, **13 publications** have used data from The Duchenne Registry. Numerous posters and presentations at scientific meetings have referenced the Registry data. Visit our website to learn more about our publications (**www.duchenneregistry.org/publications**) and posters (**www.duchenneregistry.org/poster-presentations**).

In the past 15 years, the Registry team has used the data to identify and connect individuals with Duchenne and Becker and female carriers to over **80 actively recruiting clinical trials** and nearly 100 non-interventional research studies.

82
Clinical Trials Recruited For

100
Research Studies Recruited For

26
Industry Partners

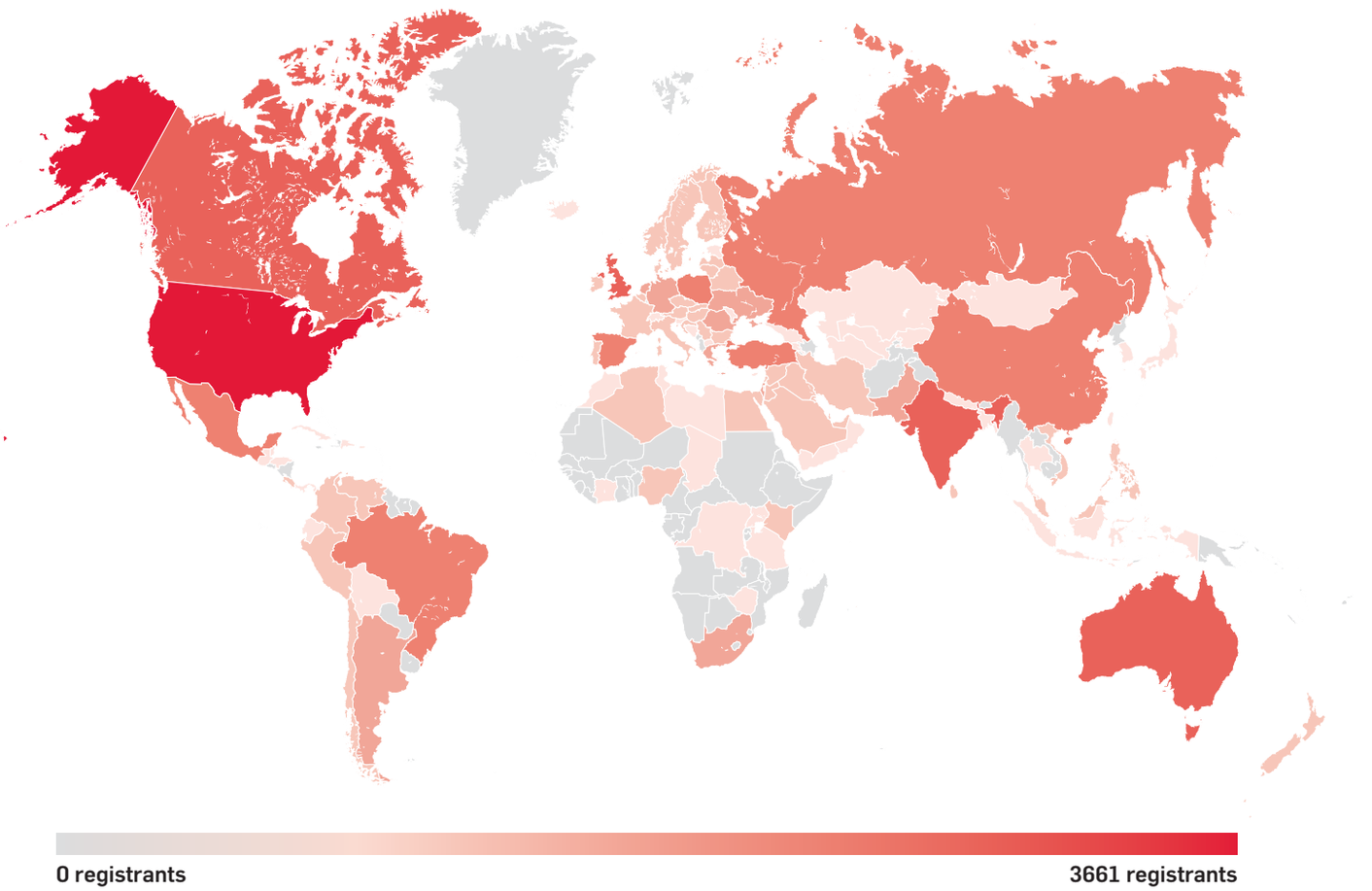
65
Times Data Has Been Shared

13
Publications Using Registry Data

About Duchenne and Becker Muscular Dystrophy Registrants

Demographics

Although two thirds of registrants in The Duchenne Registry live in the United States, the Registry has a diverse population from around the world with nearly 125 countries represented. As of the end of October 2022, the registry included a total of 5,498 registrants (including Duchenne, Becker, and carriers).

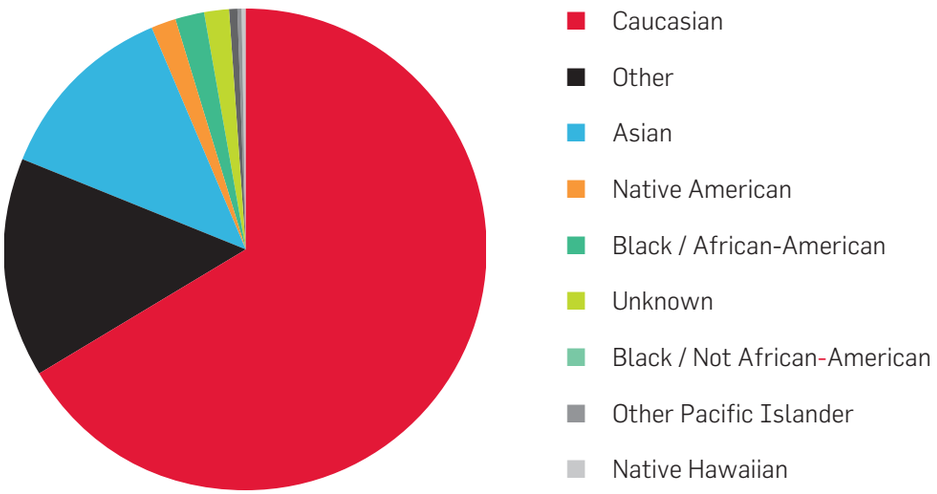


0 registrants **3661 registrants**

Top 5 Countries in The Duchenne Registry	
United States	3661 (67%)
India	327 (6%)
Australia	202 (4%)
Canada	188 (3%)
United Kingdom	141 (2%)

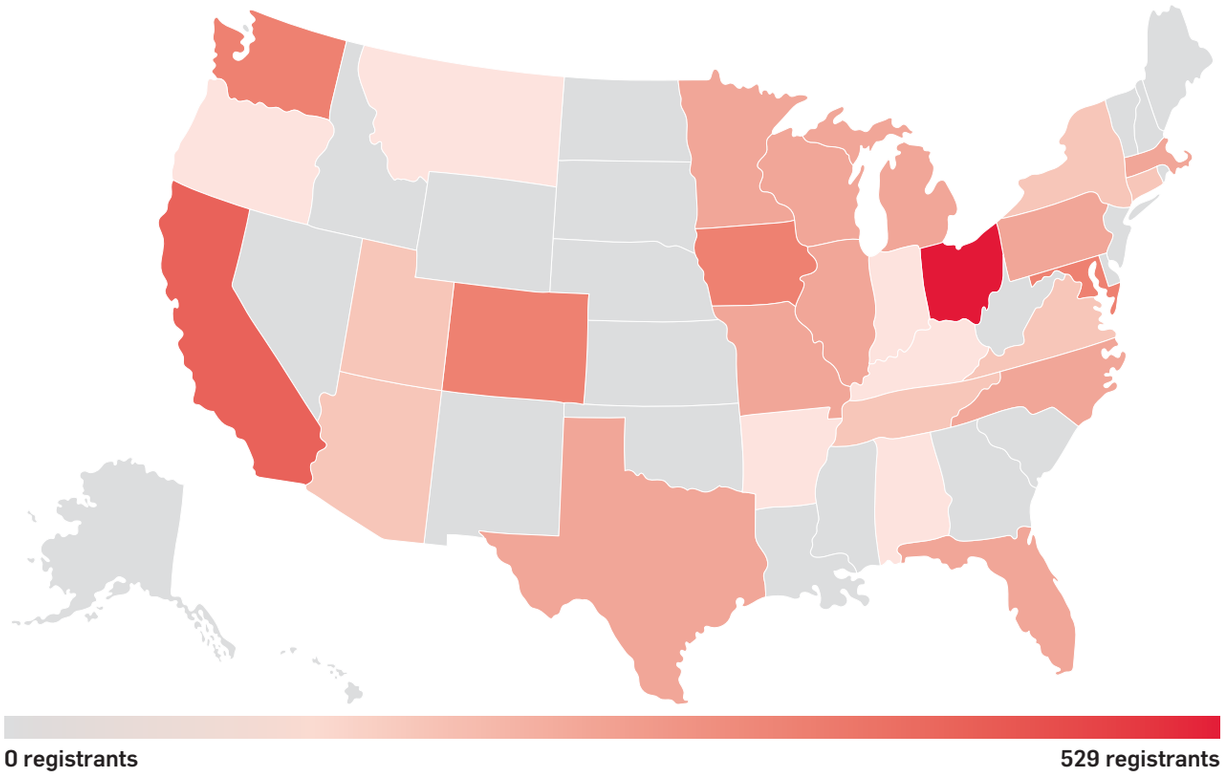
Registrants from all countries report a variety of race and ethnicities as seen in the chart below, but Caucasian is the most common race at 66%. Other was selected by 15% of registrants, Asian by 12%, Native American, Black/African-American, and Unknown by 2% each, and Black/Not African American, Other Pacific Islander, and Native Hawaiian by less than 1% each. 13% of the registrants are Latino/Hispanic, whereas 83% are Non-Latino/Hispanic, 3% are unsure, and 1% preferred not to respond to this question. Given the self-report nature of the Registry, these percentages are likely not representative of the total Duchenne and Becker population.

Race Reported by All Registrants



Registrants living in the United States are asked to provide the name of the clinic where they receive the majority of their neuromuscular care. The heat map below shows the states where registrants report receiving their care. The highest number of registrants report receiving their care in Ohio, where there are three PPMD Certified Duchenne Care Centers (CDCCs). The second highest state is California where there are five CDCCs. At the time of publication of this report, PPMD has 37 CDCCs across the United States.

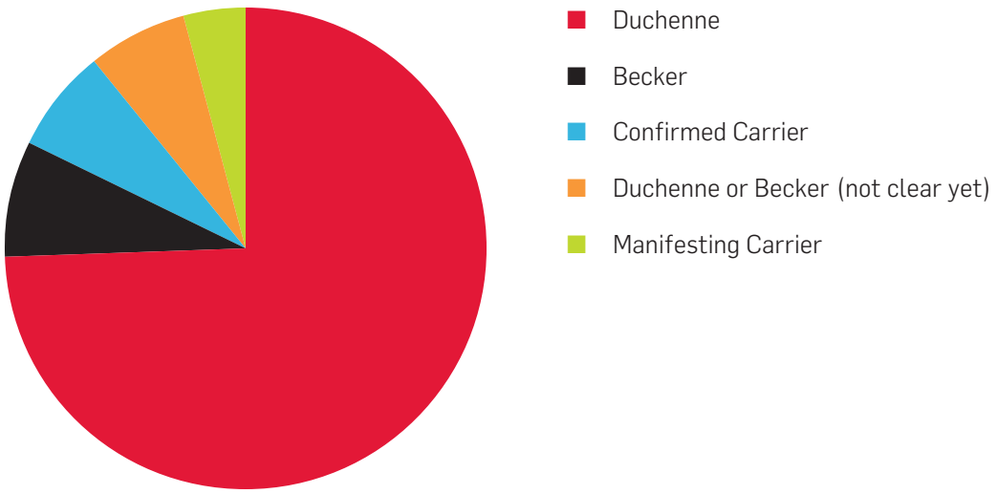
Where U.S. Registrants Are Receiving Care



Diagnosis

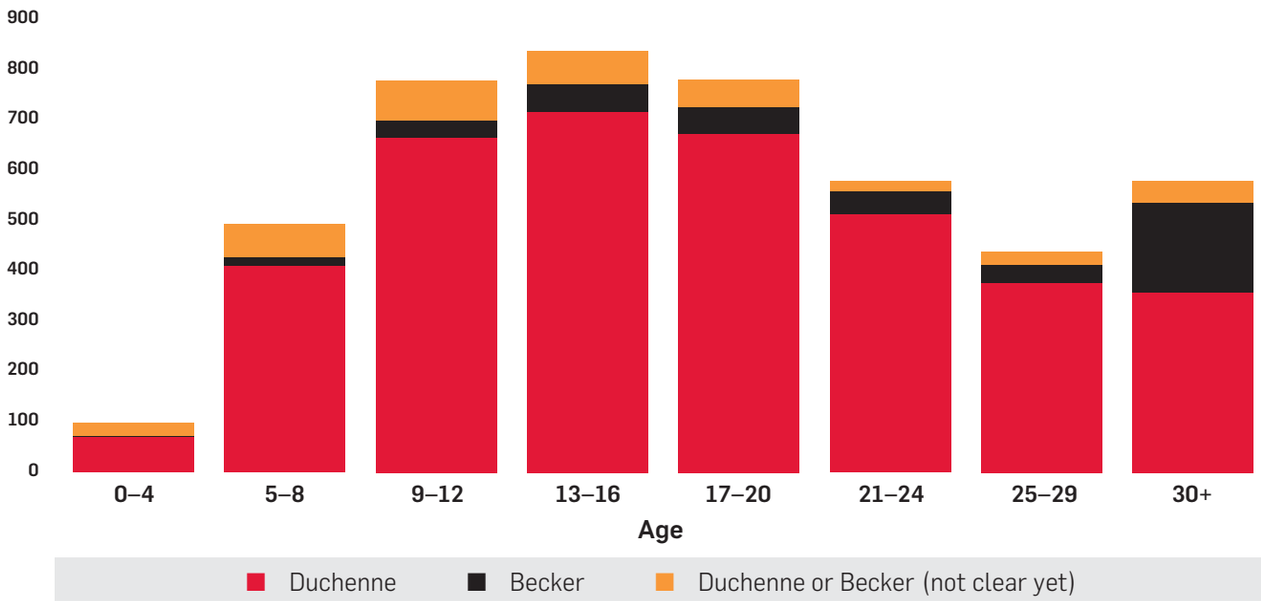
Registrants were asked about their diagnosis. Most registrants (4,102 people, or 75% of registrants) reported that they are individuals with Duchenne muscular dystrophy, while 429 (8%) reported they are individuals with Becker muscular dystrophy. 386 registrants (7%) were unclear if their diagnosis was Duchenne or Becker. Carriers were also invited to register, with 356 females (6%) identifying as confirmed carriers without symptoms, and 225 females (4%) identifying as manifesting carriers with symptoms. The percentage of Becker and carrier registrants was higher than reported in the Ten Year Registry Report, likely due to recent efforts to improve engagement within these communities. Please note, we will use the term **"dystrophinopathies"** throughout this report, and this term encompasses all diagnoses (Duchenne, Becker, and carriers) and reflects that these are a spectrum of conditions all caused by changes within the *DMD* (dystrophin) gene.

Diagnosis of All Registrants



The current age of registrants is shown in the bar graph below. The largest proportion (717) of Duchenne registrants are in the 13–16 year old age bracket. For Becker, the largest proportion (177) of registrants are in the 30 year old plus age bracket.

Current Age* of Duchenne and Becker Registrants

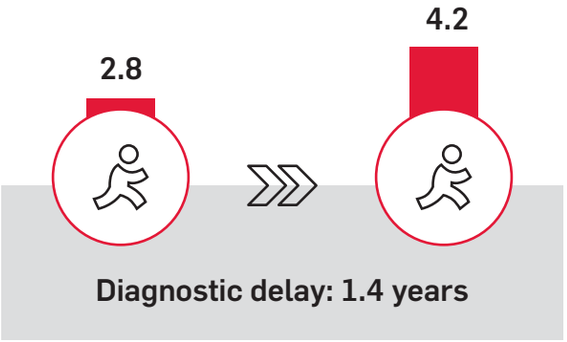


** Given the Registry is patient-reported, some individuals in the upper age groups could be deceased but not reported to us.*

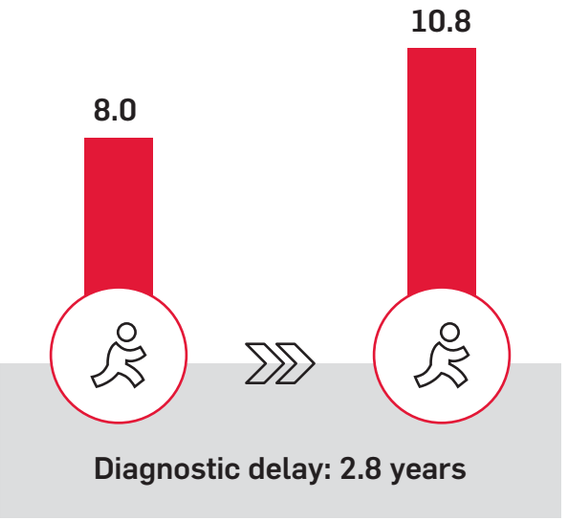
We asked registrants about the age in which they/their child first received their diagnosis. For all registrants in all countries, the average age for a Duchenne diagnosis was 4 years old, and for Becker muscular dystrophy was 11 years old. This includes registrants both with and without a family history of muscular dystrophy.

We also asked registrants the age in which symptoms were first noticed. The average age that Duchenne registrants first noticed symptoms was 2.8 years, which confirms a diagnostic delay of 1.4 years (16–17 months). The average age that Becker registrants first noticed symptoms was 8.0 years, which confirms a diagnostic delay of 2.8 years (33–34 months).

Average Age of Symptom Onset vs. First Diagnosed — Duchenne



Average Age of Symptom Onset vs. First Diagnosed — Becker



We also know that sociodemographic factors contribute to diagnostic delay. A study published in **Muscle & Nerve*** in 2019 by Kevin Counterman, DO and The Duchenne Registry team investigated whether a person's genotype (their genetic variant) and their sociodemographic factors (such as their race/ethnicity and where they live in the United States) could be influencing their age of diagnosis of Duchenne. The analysis revealed that the average age of diagnosis was significantly later for traditionally underserved populations (after adjusting for genotype and year of birth). Non-Caucasian registrants and registrants from high-poverty neighborhoods were older at diagnosis, and non-Caucasian registrants had significantly longer periods from symptom onset to diagnosis than Caucasian registrants.

** Counterman KJ, et al. Delays in diagnosis of Duchenne muscular dystrophy: An evaluation of genotypic and sociodemographic factors. Muscle & Nerve. 2019; 1–8. doi: 10.1002/mus.26720*

Family History

Registrants were asked questions regarding their family history in order to better understand the impact of dystrophinopathy within the family. When asked if they have any blood relatives (living or deceased) with a similar muscle disease, 23% indicated they do have affected blood relatives, 68% indicated they do not have similarly affected relatives, and 9% indicated they do not know.

We additionally inquired about the mothers of the registrants, and whether or not they have been determined to be a carrier of dystrophinopathy. The largest percentage of registrants responded they do not know if their mother is a confirmed carrier (36%). 30% reported that their mother is a confirmed carrier, and 25% reported their mother had negative genetic testing and is not a carrier. For 9% of registrants, their mother knows her carrier status due to family history, but it has not been confirmed with genetic testing. Looking at the number of responses indicating the mother's carrier status was unknown or unconfirmed, it appears there is still not full adherence to recommended carrier screening after a diagnosis. However, many mothers may undergo carrier testing after completion of this survey, which is only offered once.

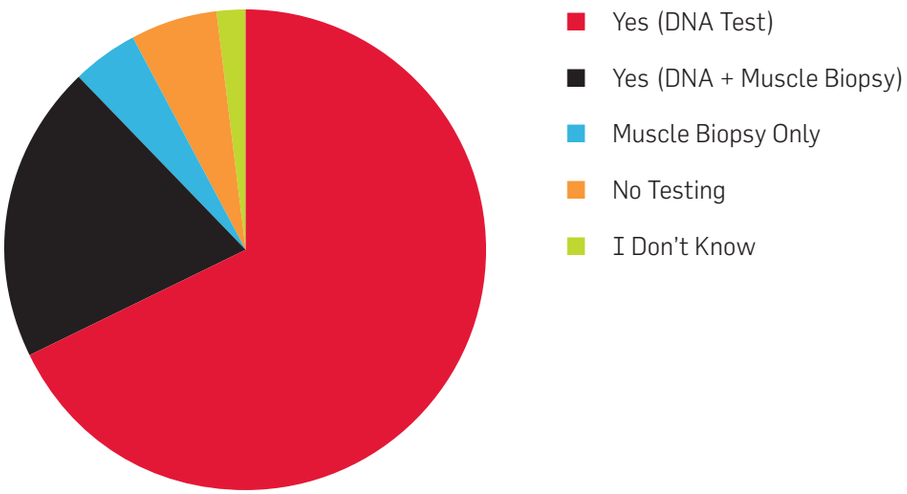
Is your mother a confirmed carrier?	
Genetic testing showed she is a carrier	885 (30%)
Genetic testing showed she is not a carrier	748 (25%)
I don't know	1069 (36%)
She knows she is a carrier based on family history but has not had genetic testing	278 (9%)

Genetic Information

Registrants in The Duchenne Registry are requested to send in a copy of their genetic test report. The Registry team reviews each of these reports and carefully enters the genetic variant for each registrant. This provides vital information that verifies the diagnosis that is self-reported by the registrant and helps answer important research questions.

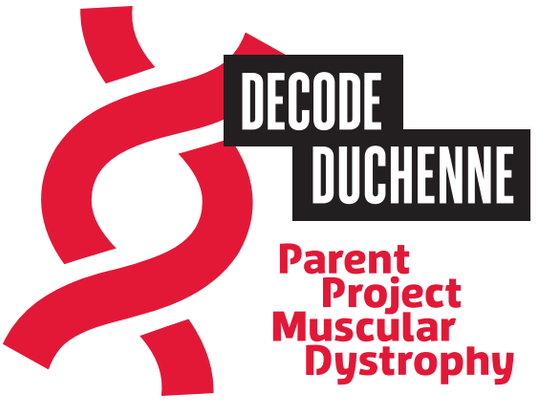
Registrants are asked to report how their diagnosis was made in order to help us understand how patients are being diagnosed, and how this has changed over the years. A great majority of patients (68%) were diagnosed via genetic testing alone. Additionally, 20% were diagnosed by a combination of genetic testing and muscle biopsy. Before the advent of genetic testing, diagnosis was made by a muscle biopsy documenting reduced dystrophin expression and muscle tissue damage. According to our data, only 4% of registrants were diagnosed by muscle biopsy alone.

Testing Performed to Confirm Diagnosis



The table below describes the categories of variants identified and their frequency after reviewing all the genetic test reports submitted to the Registry (n=2,445). Consistent with numbers recorded in our previous Ten Year Registry Report, deletions are the most common variant type reported (64%), followed by nonsense variants (12%) and duplications (11%).

Types of Genetic Variants in Registrants with Verified Results	
Deletion	1575 (64.4%)
Nonsense	296 (12.1%)
Duplication	275 (11.3%)
Deletion — Small mutation	116 (4.7%)
Splice site	98 (4.0%)
Duplication — Small mutation	43 (1.8%)
Missense	19 (0.8%)
Insertion	19 (0.8%)
Insertion / Deletion	3 (0.1%)



Since 2013, PPMD's genetic counselors have directed a free genetic testing program called **Decode Duchenne**. To date, the Decode Duchenne program has completed over 1,600 diagnostic tests and over 1,000 carrier tests. To qualify for testing, a patient should have a confirmed or suspected diagnosis of Duchenne or Becker, or be an asymptomatic relative of someone with a confirmed diagnosis. All testing is performed at Revvity Omics (formerly called PerkinElmer Genomics). The Decode Duchenne program is generously sponsored by our founding partner Sarepta Therapeutics, as well as PTC Therapeutics, Vertex Pharmaceuticals, and NS Pharma. Learn more at **parentprojectmd.org/decode**.

Review of all the genetic reports submitted to the Registry provided key information regarding potential treatment options. The Registry team identified 736 people with Duchenne* who have verified results demonstrating they may potentially benefit from treatments that cause **exon skipping** of exons 51, 53, 45, or 44. In the Registry, 12% of registrants are amenable to skipping exon 51; 8% of registrants are amenable to skipping exon 53; 9% of registrants are amenable to skipping exon 45; and 6% of registrants are amenable to skipping exon 44. These percentages are in line with the expected percentages that have been reported in the literature.

Exon Skipping Therapy	Total Duchenne* Registrants with Amenable Deletion	Expected Percentage**
Exon 51	256 (12%)	14%
Exon 53	168 (8%)	10%
Exon 45	189 (9%)	9%
Exon 44	123 (6%)	7%

** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*

*** Bladen CL, et al. The TREAT-NMD DMD Global Database: analysis of more than 7,000 Duchenne muscular dystrophy mutations. Human Mutation. 2015 Apr; 36(4):395–402. doi: 10.1002/humu.22758*

Approved Therapeutics

In the United States at the time of writing this report, we are fortunate to have five FDA-approved therapeutics for Duchenne. These include four exon skipping therapies and one corticosteroid therapy. Corticosteroids will be addressed in another section of this report.

We ask registrants to report if they are using one of the approved exon skipping therapies. This is a newer question in the Registry and has only been answered by approximately 16% of Duchenne* registrants living in the United States. Of those who answered this question, we determined how many are amenable and the percent amenable who are using the exon skipping therapy. The percent using therapy was highest for the exon 51 skip amenable group with 80% who are amenable reporting they are using EXONDYS 51 (eteplirsen). This makes sense since EXONDYS 51 was the first approved exon skipping therapeutic in 2016. For the exon 53 skip amenable group, 65% report using either VYONDYS 53 (golodirsen) or Viltepso (viltolarsen). For the exon 45 skip amenable group, 23% report using AMONDYS 45 (casimersen). Again, these percentages may be lower than the actual percentage using therapies given the low percentage of registrants who have answered this question.

Translarna (ataluren) is a nonsense variant readthrough therapy that is approved in several countries, including the European Union, Brazil, and Russia. It is not approved in the United States and is still considered an investigational drug. 12% of registrants have a nonsense variant in their *DMD* gene and could be eligible for nonsense variant readthrough therapy if approved in their country.

If you or a loved one need *DMD* genetic testing or have questions about your genetic variant or which variant-specific therapies you may be eligible for, please contact a PPMD genetic counselor at **coordinator@duchenneregistry.org**.

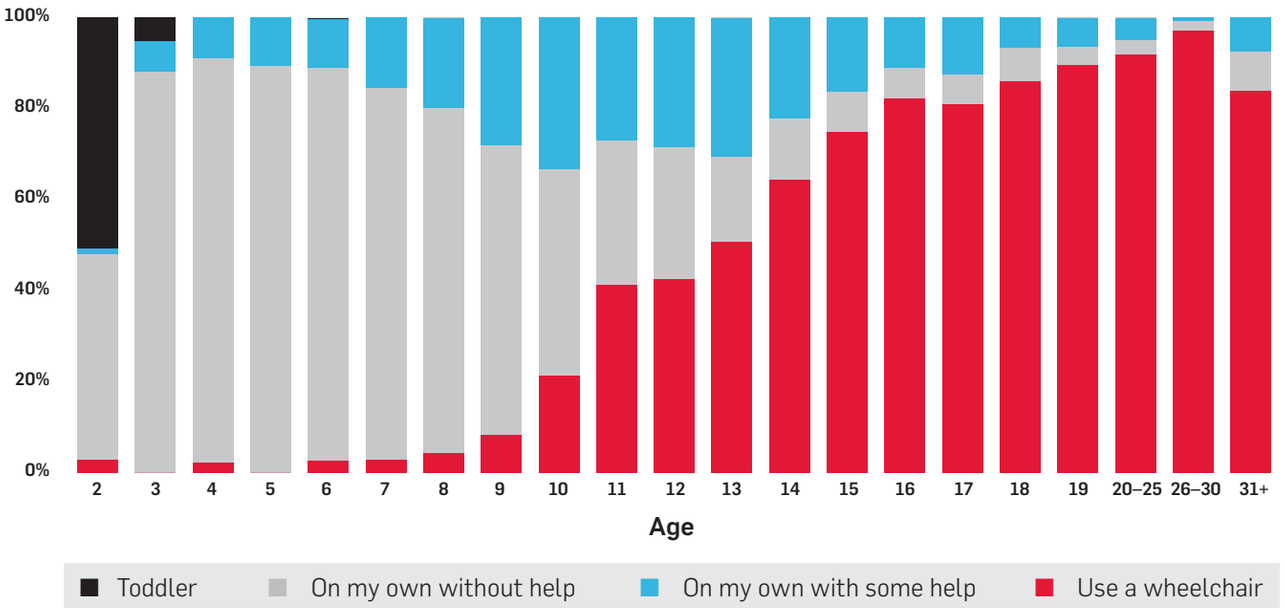
** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*

Muscle Function

Muscle Function is a key survey in the Registry that collects data about mobility and activities of daily living. We first asked registrants about their/their child's mobility.

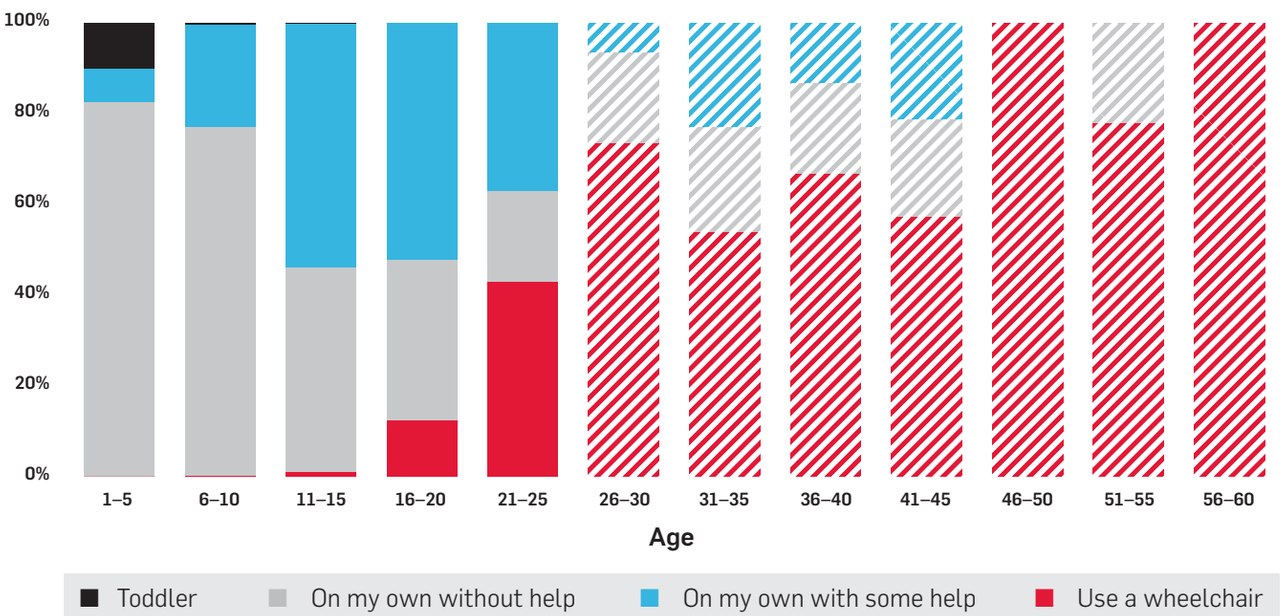
For registrants with Duchenne, we see that at young ages most children walk independently, with an increase of requiring assistance sometime in the late elementary years, transitioning to most registrants reporting using a wheelchair or mobility device full-time in their mid-teens.

Current Ambulation of Duchenne Registrants



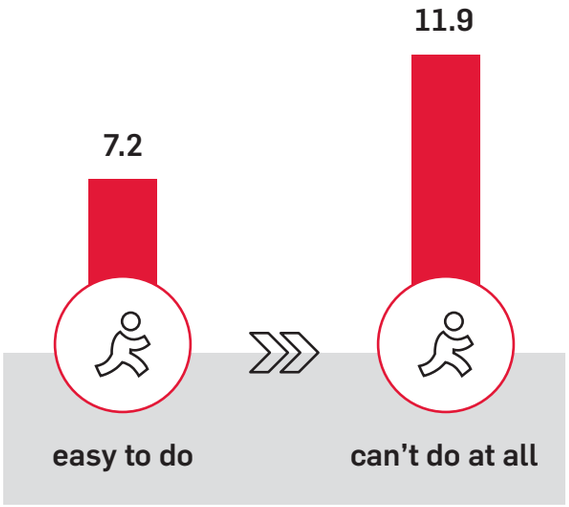
For registrants with Becker, this transition is later, with most registrants reporting full-time wheelchair or mobility device use after age 25. There are fewer registrants with Becker, and Becker can be a more variable condition. *The hashing shown here and throughout the report means there were fewer than 25 people in that category.* In this case, there were fewer than 25 people in each of the age categories after age 25. When the numbers are small as they are in this graph, it can be difficult to identify trends we would see with a larger group.

Current Ambulation of Becker Registrants

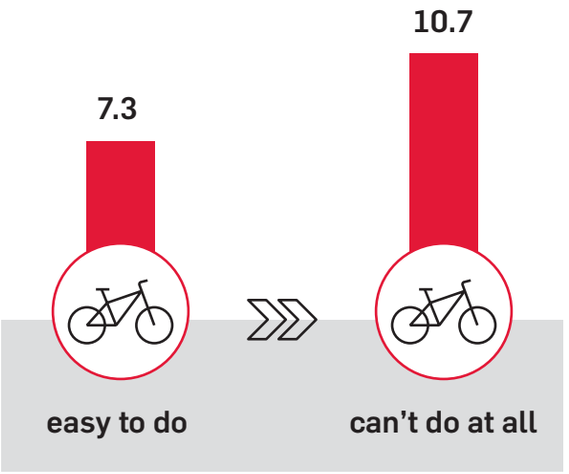


The Muscle Function survey contains a section of the Pediatric Outcomes Data Collection Instrument (PODCI), to help us understand more specifically how mobility and activities of daily living are affected in dystrophinopathies. In these questions, registrants rate how easy or difficult it is to do activities such as climbing stairs, walking one block, running, or using a fork or a spoon. In registrants with Duchenne who are ambulatory, we see that the average age of children who rate running short distances as “easy” is 7.2 years, while the average age of not being able to run short distances is 11.9 years. Similarly, riding a bicycle or tricycle is reported on average as “easy” at age 7.3 years and “can’t do at all” at age 10.7 years.

Duchenne Registrants Average Age — Difficulty Running Short Distances

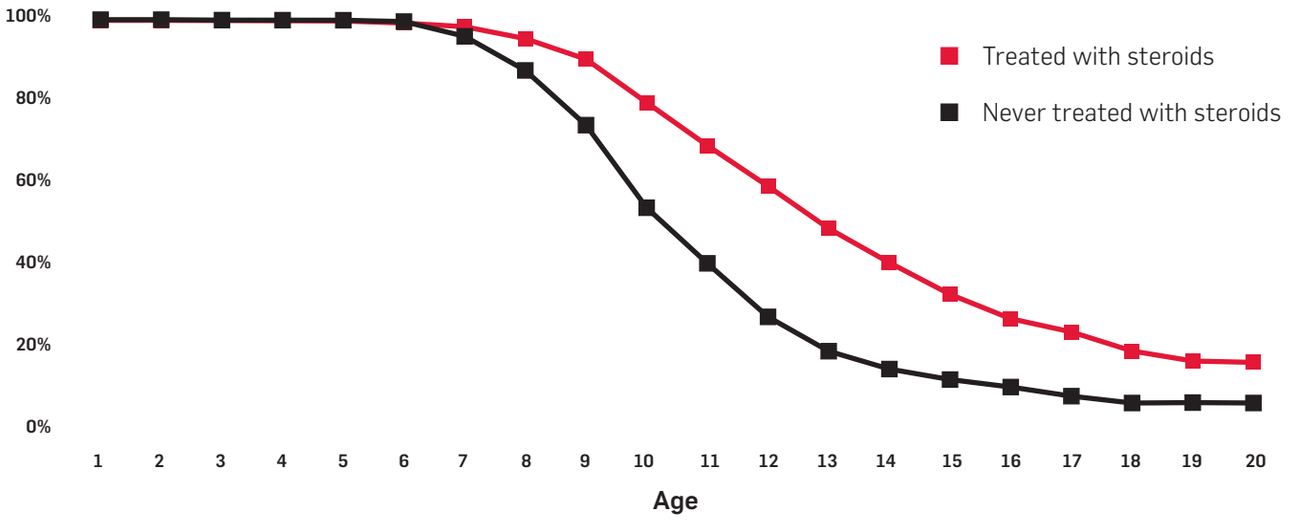


Duchenne Registrants Average Age — Difficulty Riding a Bicycle / Tricycle



We used the Registry data to look at the relationship between taking corticosteroids, specifically what kind of corticosteroid a person took, and time to full-time wheelchair use. We see the expected corticosteroid benefit in the Registry: those who used corticosteroids, either currently or in the past, are older when they need to start using a mobility device like a wheelchair full-time.

Percentage of Ambulatory Duchenne Registrants Based on Corticosteroid Use

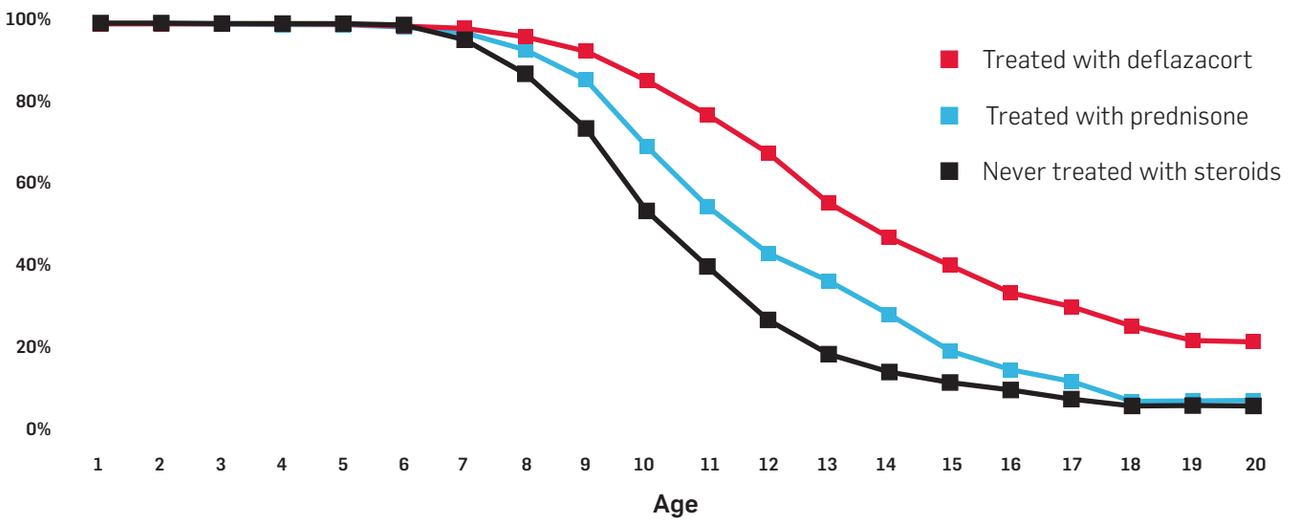


When we look at the type of corticosteroid, taking deflazacort (Emflaza) is associated with needing a wheelchair full-time at a later age than taking prednisone. Registrants taking prednisone report needing a wheelchair full-time at a later age than registrants who have never used corticosteroids. Both of these differences are **highly statistically significant** (p-values less than 0.001).

Statistical significance refers to the claim that a result from data generated by testing is not likely to occur randomly or by chance, but is instead likely to be attributable to a specific cause. A p-value less than 0.05 is usually considered statistically significant and a p-value less than 0.001 is considered highly statistically significant.

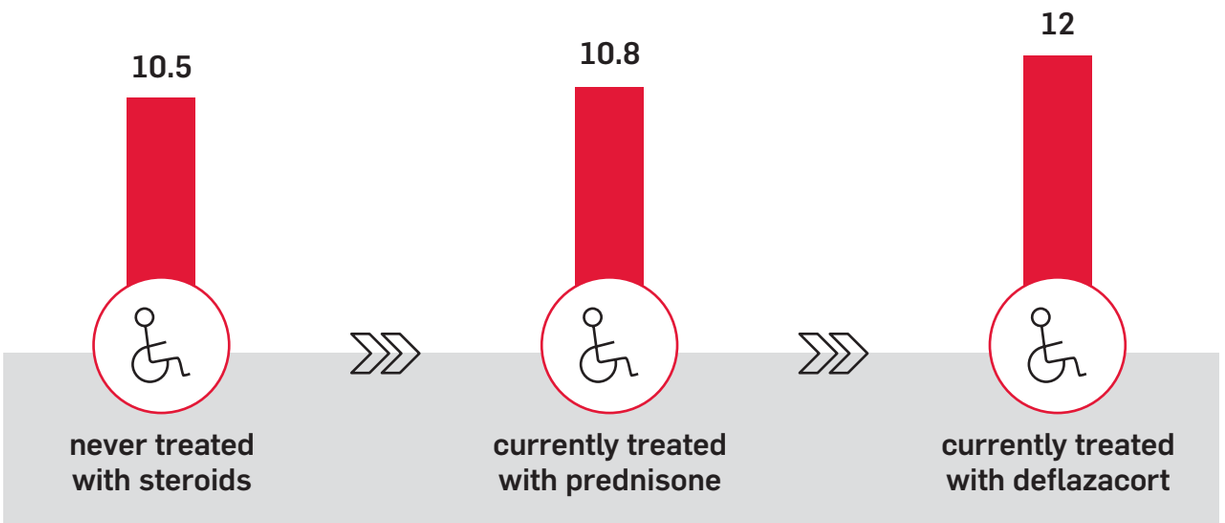
This data clearly demonstrates that registrants using deflazacort maintain ambulation longer than registrants using prednisone or no corticosteroids.

Percentage of Ambulatory Duchenne Registrants Based on Type of Corticosteroid



We asked registrants who use a mobility device or wheelchair full-time at what age they needed full-time mobility assistance. Registrants who never used corticosteroids reported needing full-time wheelchair assistance at an average age of 10.5 years. Registrants who are currently taking prednisone reported needing full-time wheelchair assistance at an average age of 10.8 years, and registrants who are currently taking Emflaza reported needing full-time wheelchair assistance at an average age of 12 years.

Average Age of Full-Time Mobility Assistance for Duchenne Registrants*

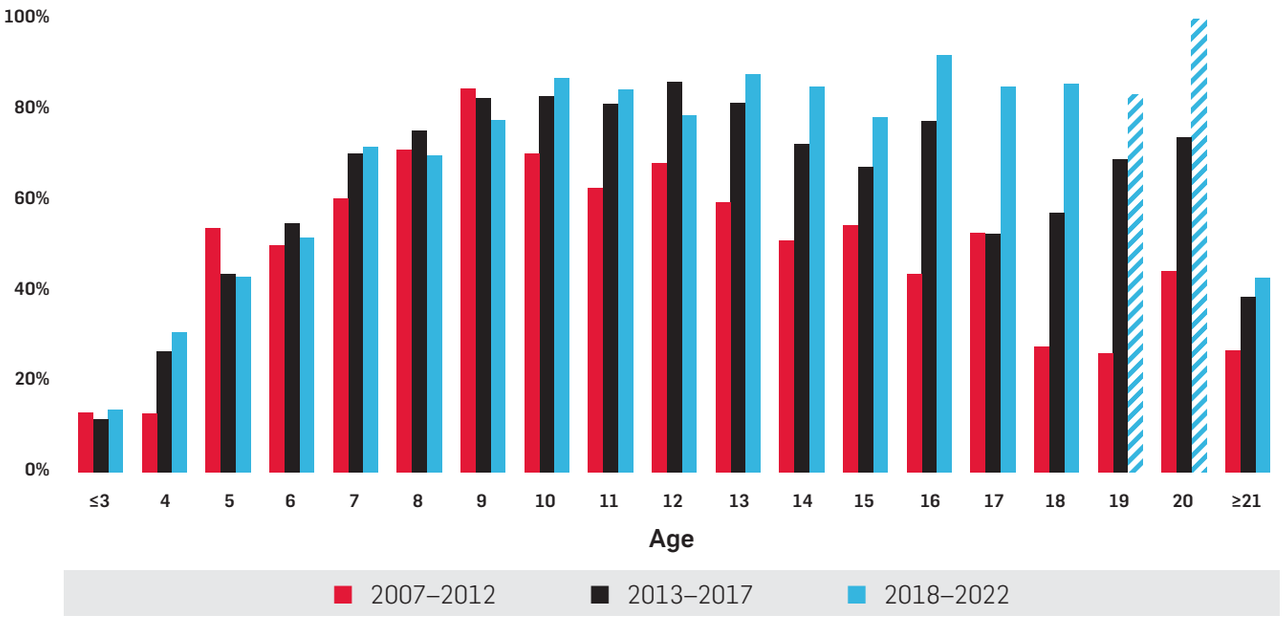


** Please note that because this question is only answered by non-ambulatory registrants, it does not take into account people who do not need mobility assistance. Consequently, the average ages are not the same as the ages shown in the curves on the previous page.*

Corticosteroids

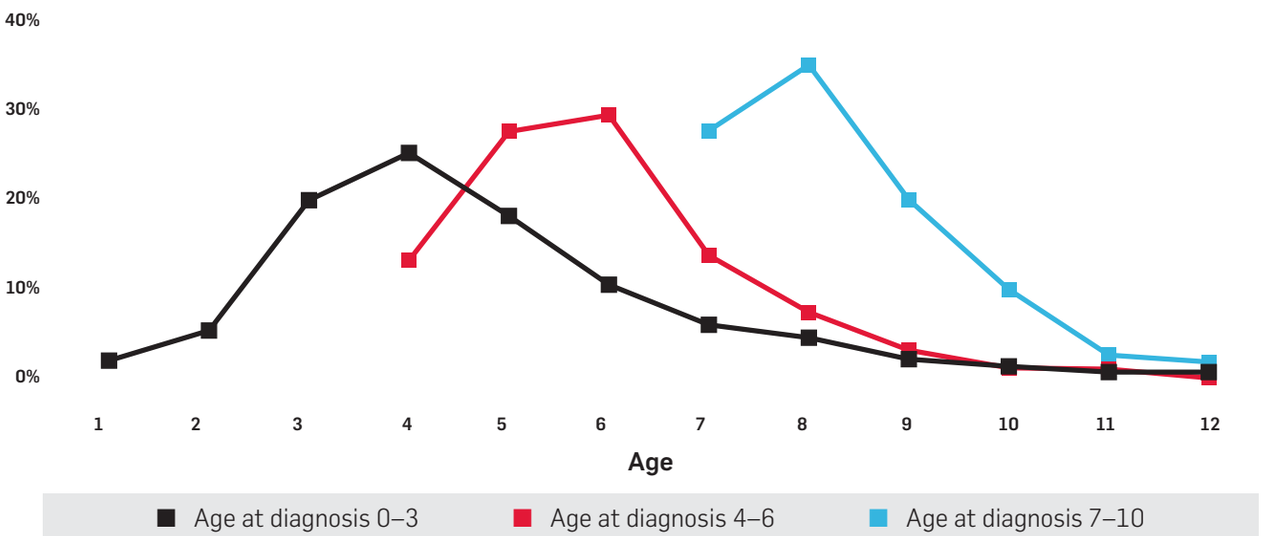
Corticosteroids are considered standard of care in Duchenne and used to reduce inflammation in damaged muscles. The recommendations regarding when to start corticosteroids and the importance of continuing corticosteroids have changed as the **Duchenne Care Considerations*** have been updated. We compared the use of corticosteroids over the last 15 years in people with Duchenne. As we have learned more about the immediate and long-term benefits of corticosteroid use, we have seen an increase in use over time, with the increase being most noticeable for registrants in their teens.

Duchenne Registrants Using Corticosteroids by Age and Time Period



We also ask registrants about when they started corticosteroids. The average age of initiating corticosteroids in children with Duchenne is 5.9 years. Children with Duchenne who are diagnosed at a younger age are more likely to initiate corticosteroids at a younger age. Children who are diagnosed at ages 0–3 are most likely to start before age 4, while children diagnosed at ages 4–6 are most likely to start corticosteroids around ages 5 or 6.

Duchenne Registrants Initiating Corticosteroids based on Age at Diagnosis

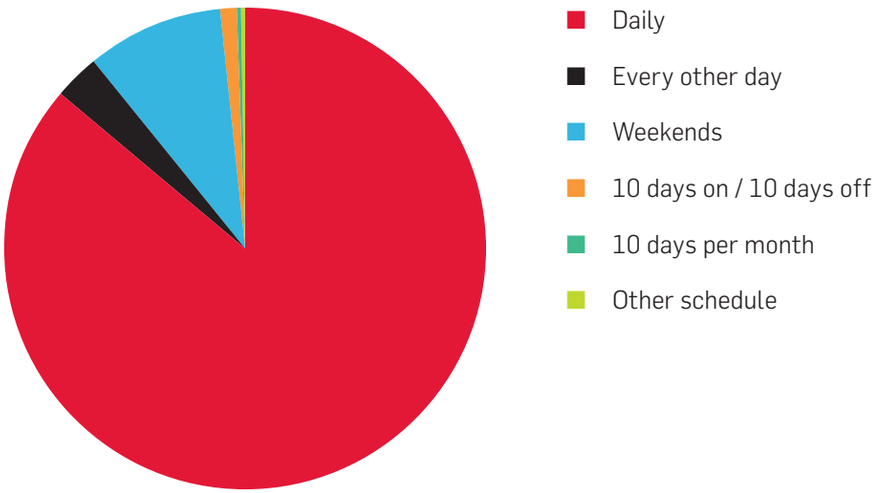


** https://www.parentprojectmd.org/care/care-guidelines*

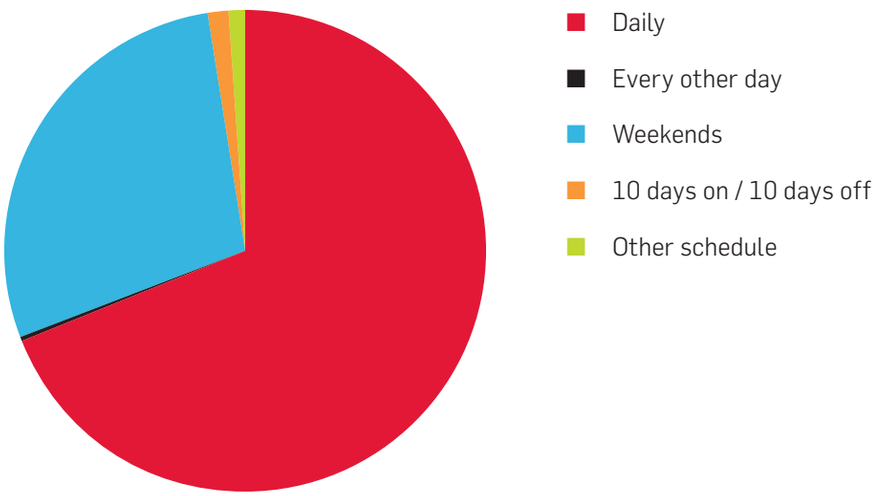
The hashing shown in the chart above means there were fewer than 25 people in that category.

We ask registrants with Duchenne about the schedule that they use for steroid dosing. Most registrants in the United States report taking corticosteroids daily (83%). However, if we look at changes over time, we notice an increase in the percentage of registrants using weekend (also called twice-weekly) dosing, with registrants who were born more recently (during or after 2010) being more likely to use a weekend dosing schedule than those who were born before 2010 (28% versus 9%).

Corticosteroid Schedule — Born Before 2010 (U.S. Only)



Corticosteroid Schedule — Born 2010 and After (U.S. Only)



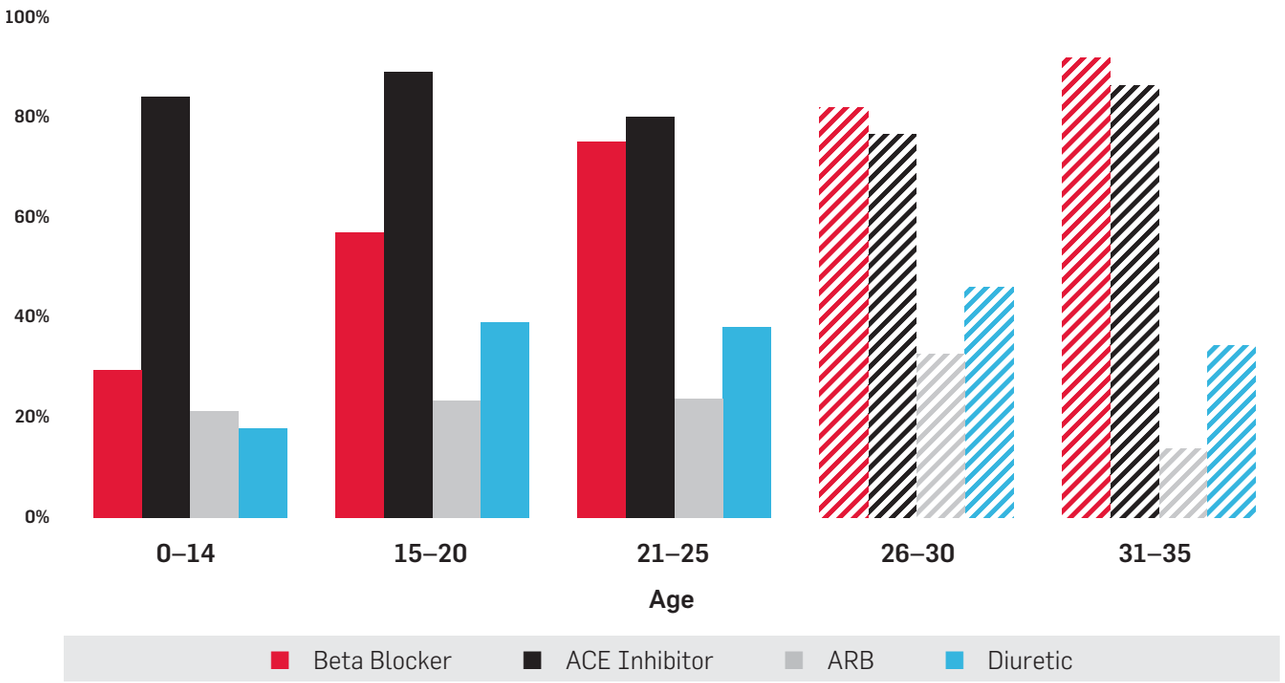
PPMD led a study* to understand the perspectives of parents and people with Duchenne on the side effects and benefits of corticosteroids by interviewing a small group and asking a larger group to complete a survey. A range of side effects including risk of fractures, unwanted weight gain, and diabetes were considered important and common. However, most people using corticosteroids and parents indicated that they felt the benefits — including breathing, heart function, arm strength, slowing progression of weakness, and getting around — outweighed the side effects. Overall, most participants in the study were satisfied with the use of corticosteroids.

** Fischer R, et al. A Mixed-Method Study Exploring Patient-Experienced and Caregiver-Reported Benefits and Side Effects of Corticosteroid Use in Duchenne Muscular Dystrophy. Journal of Neuromuscular Diseases. 2023; 10(4):593-613. doi: 10.3233/JND-221617*

Cardiac

The heart is a muscle too and it plays a vital role in the health of all individuals but especially those with dystrophinopathy. For that reason we have a survey specific to cardiac concerns within the Registry. We asked registrants several questions about their use of heart medications. The most commonly used classes of heart medications for Duchenne* registrants include ACE inhibitors (88%), beta blockers (57%), diuretics (33%), and angiotensin receptor blockers (ARBs) (25%). The graph below shows the percentage of Duchenne* registrants in different age groups who report currently taking each of the four most common classes of heart medications.

Duchenne* Current Heart Medication Use by Age



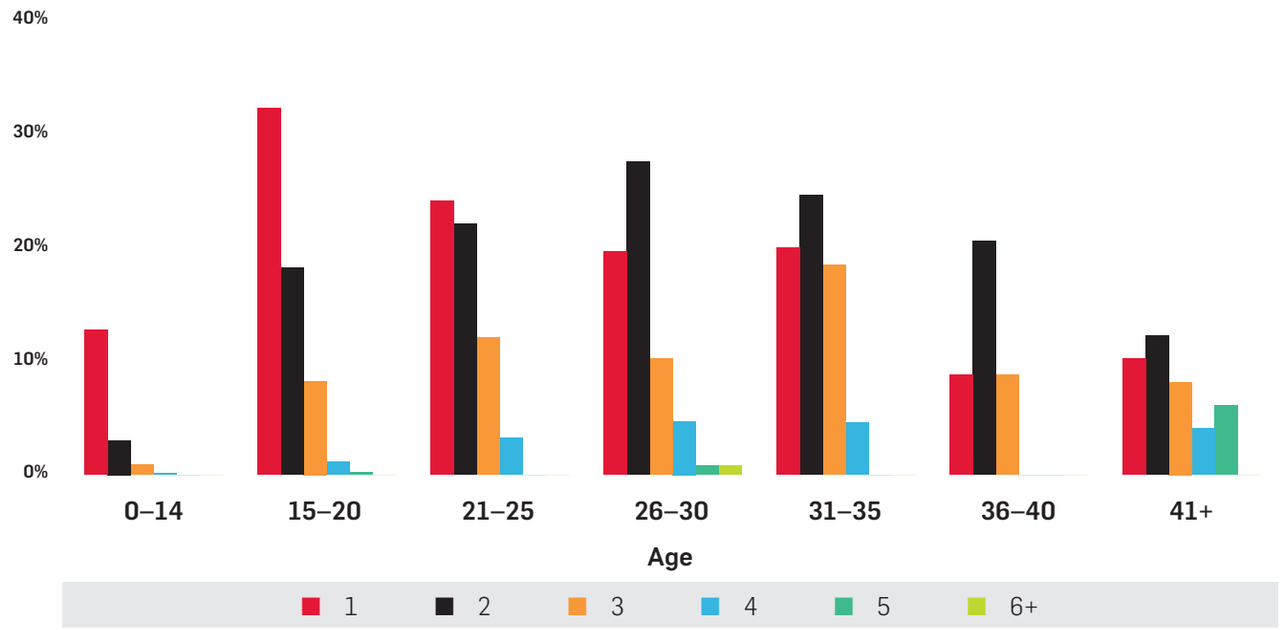
The table below shows the average age that the four most common classes of heart medications were started for Duchenne* registrants born on or after the year 2000.

Medication Class	Average Age Started
Beta Blockers	10.4
ACE Inhibitors	9.3
ARB	9.5
Diuretics	11.1

** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*
The hashing shown in the chart above means there were fewer than 25 people in that category.

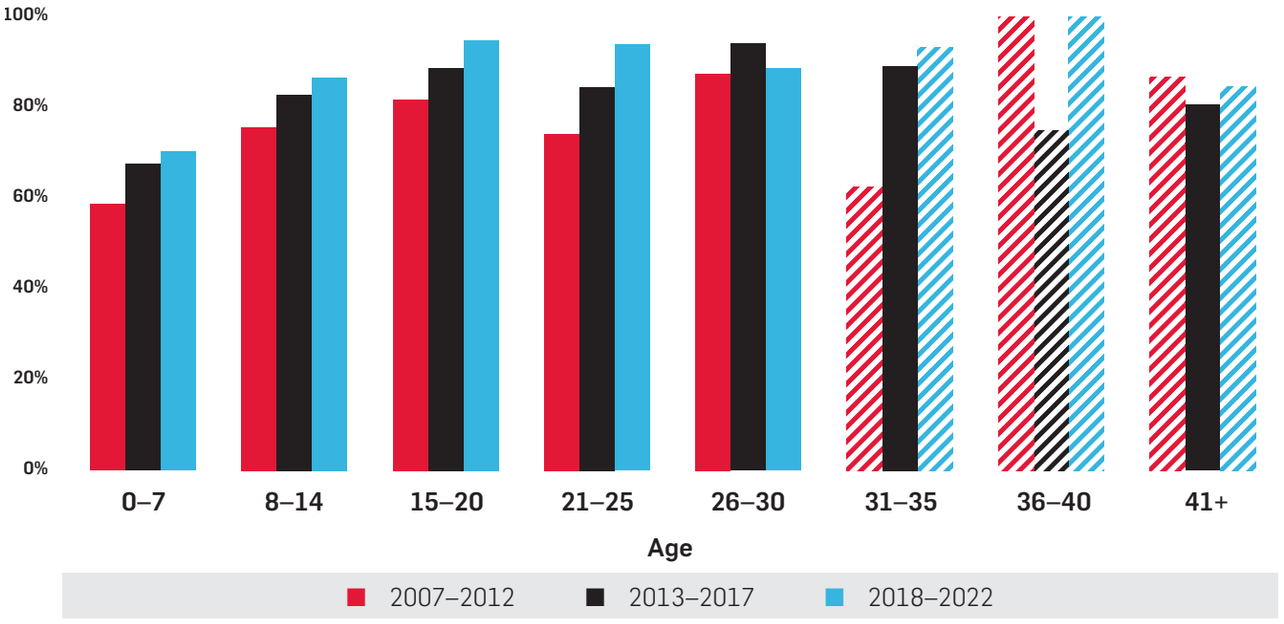
We also evaluated the total number of heart medications used by Duchenne* registrants in different age groups. In the graph below, the percentage of Duchenne registrants using two, three, four or more heart medications did increase with increasing age, except in the oldest age groups (36–40 and 41+) which each had a smaller total number of registrants who completed this survey (less than 50).

Total Number of Current Heart Medications by Age



We asked registrants to report if they have had an echocardiogram or cardiac MRI. For Duchenne* registrants across all countries, the majority of ages showed an increase in the use of echocardiogram over the past 15 years. The highest percentage of echocardiogram use was in the most recent five years (2018–2022), with the lowest percentage in the initial five years (2007–2012). The increase was **statistically significant** for the 0–7, 8–14, and 15–20 year old age groups (p-values less than 0.05).

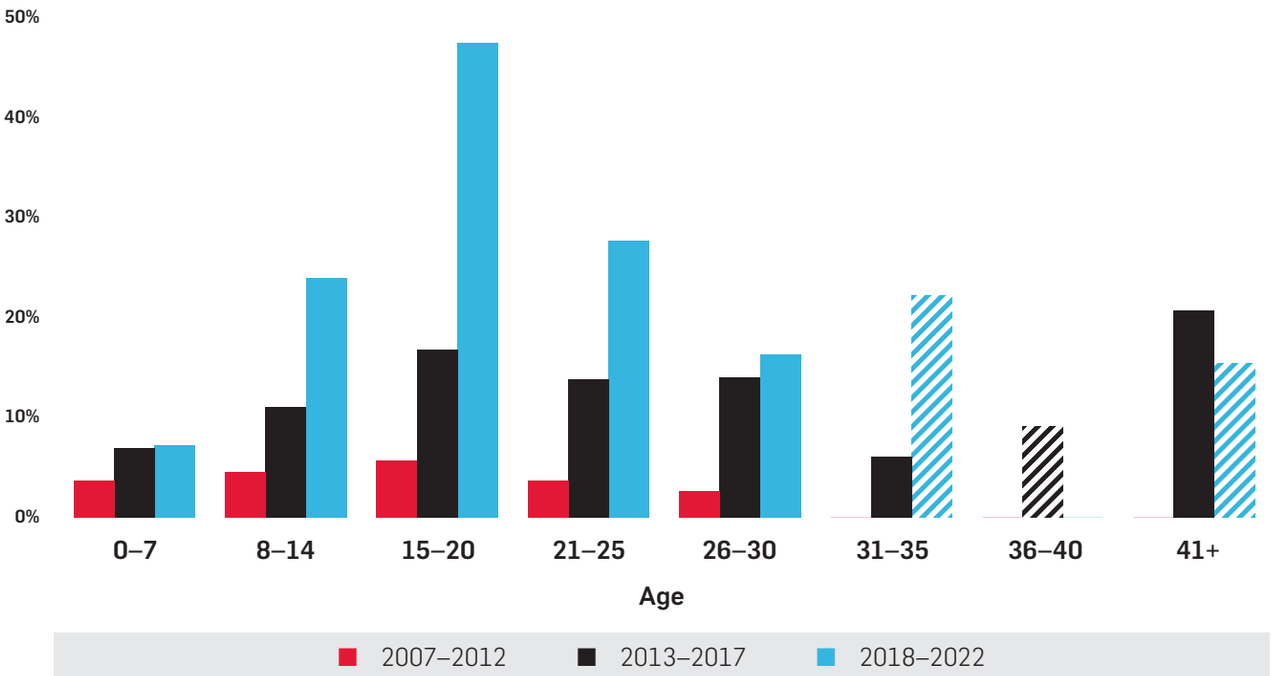
Duchenne* Registrants Who Had an Echocardiogram by Age and Time Period



** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*
The hashing shown in the chart above means there were fewer than 25 people in that category.

The use of cardiac MRI has also increased over the past 15 years. Cardiac MRI is becoming more routine for Duchenne and Becker at many clinics across the country. The graph below illustrates the increase in the use of cardiac MRI for Duchenne* registrants in the past 15 years. The published **Duchenne Care Considerations**** (last updated in 2018) have likely had an impact on increasing cardiac surveillance and improving the overall standard of care for Duchenne individuals.

Duchenne* Registrants Who Had a Cardiac MRI by Age and Time Period



We asked registrants about whether or not they have an implanted cardiac device. Examples of such devices include an ICD (implantable cardioverter defibrillator), an AICD (automatic implantable cardioverter defibrillator), and an LVAD (left ventricular assist device). Out of 811 registrants who answered this question, only 12 (1.5%) responded that they have an implanted device. The use of implanted devices did increase with age, from 0% in the 0–14 year olds to 6% in 26–30 year olds and up to 19% in the 41+ year olds.

** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*

*** https://www.parentprojectmd.org/care/care-guidelines*

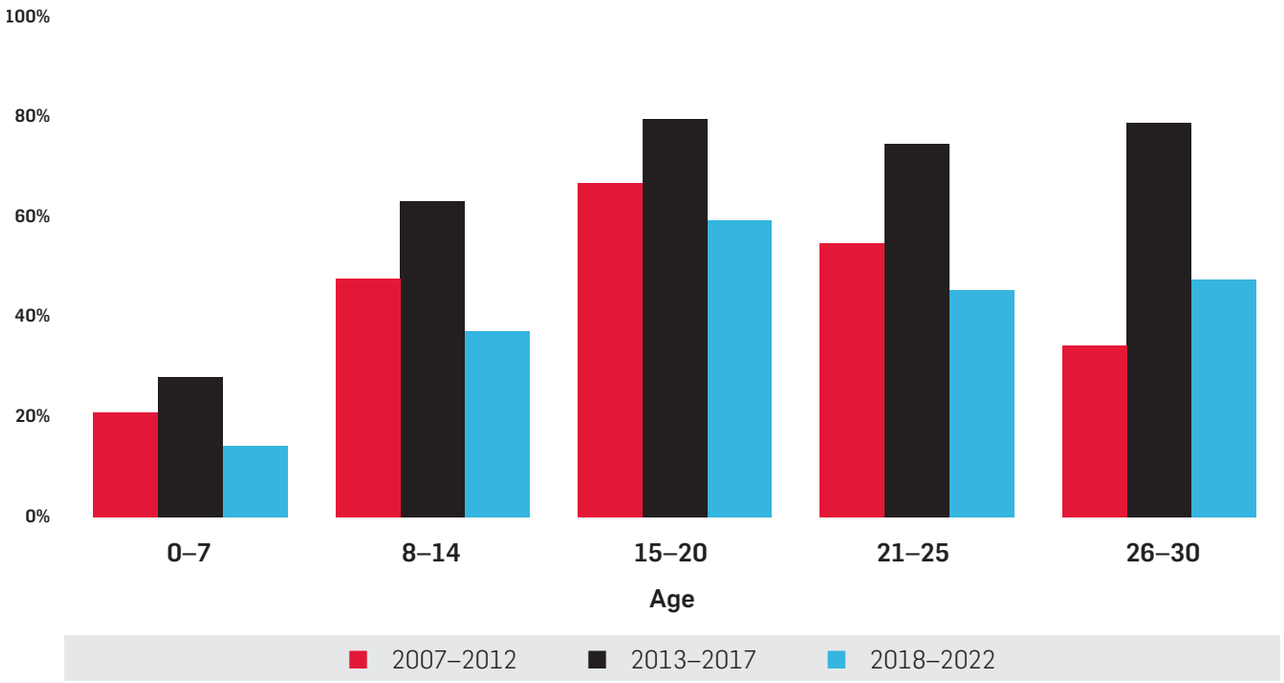
The hashing shown in the chart above means there were fewer than 25 people in that category.

Respiratory

We asked registrants about their breathing and lungs, specifically about testing of their lung function through pulmonary function tests (PFTs).

For Duchenne* registrants, we compared how many registrants reported having lung function tests in each of the time periods. In general, we see an increase from 2007–2012 to 2013–2017, but then a decrease in the most recent time period 2018–2022. This may be because many clinics paused doing pulmonary function testing during the COVID-19 pandemic.

Duchenne* Registrants Who Had a Pulmonary Function Test by Age and Time Period



We also ask registrants if they have ever used breathing devices such as cough assist, BiPAP, CPAP and ventilator. In registrants with Duchenne* over age 10 at the time of survey completion, 14% report using cough assist, 27% report using BiPAP, 4% report using CPAP, 2% report using non-invasive ventilation all the time, and less than 1% report using a ventilator with tracheostomy all the time.

** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*

Bone

The Duchenne Registry includes a Bone survey to help gather information on incidence of orthopedic issues such as fractures and scoliosis, since these are known to occur in Duchenne. For registrants with Duchenne age 12 years and older, we wanted to know if they reported a diagnosis of scoliosis, and how that related to their corticosteroid use. A majority of registrants currently using corticosteroids reported no scoliosis (63%). Comparatively, for both the never used and the previously used groups, a larger percent of those registrants report having scoliosis (73% and 74%, respectively). **Based on our survey responses, we determined that non-corticosteroid users are 4 times more likely to develop scoliosis than those who currently use corticosteroids.**

	Currently Using Corticosteroids	Never Used Corticosteroids	Used and Discontinued
Scoliosis	233 (38%)	211 (73%)	183 (74%)
No Scoliosis	388 (62%)	78 (27%)	63 (26%)

Additionally, we explored which registrants required scoliosis surgery, and how that related to both their corticosteroid use and their age cohort. Of registrants with scoliosis born before the year 2000, 28% required corrective scoliosis surgery. Within that age cohort, 16% used corticosteroids and needed surgery. However, if we exclude individuals who used and discontinued corticosteroids, the percentage needing scoliosis surgery drops to 5%. Within the younger age cohorts, a vast majority of registrants have not yet needed corrective scoliosis surgery (98% born 2000–2010, 99% born after 2010).

We asked registrants about their use of bisphosphonates for bone health. In our Ten Year Registry Report, only 11% of registrants reported taking these medications, but now data shows that 21% of registrants have taken these medications. It appears that individuals of older age cohorts report higher rates of bisphosphonate use compared to their younger counterparts.

	Bisphosphonate	No Bisphosphonate
Born Before 2000	78 (32%)	166 (68%)
Born 2000–2010	153 (29%)	384 (72%)
Born After 2010	51 (9%)	542 (91%)

Behavior and Learning

An increased chance for developmental, cognitive, learning, and behavioral difficulties has been documented in people with Duchenne and Becker. Many researchers think this occurs because forms of the dystrophin protein (isoforms) are present in the brain. The dystrophin isoforms expressed in the brain include Dp427p, Dp140 and Dp71. Therefore, when dystrophin is missing or altered in individuals with Duchenne or Becker, the brain cells may not function as efficiently as they should. However, not every child with Duchenne or Becker is going to have behavioral or learning challenges.

Several studies have confirmed an association between where an individual's variant is located within the *DMD* gene and the presence of behavioral and/or learning concerns. A **recent publication led by Drs. Kevin Counterman and Yaacov Anziska** used data from The Duchenne Registry and found that *DMD* variants disrupting expression of the Dp140 and Dp71 isoforms were associated with a higher likelihood of reported behavioral and learning concerns. In other words, they found an increasing prevalence of learning and behavioral concerns the further a patient's variant is towards the end of the *DMD* gene. These associations have been reported in prior studies but all these studies have been performed using much smaller sample sizes or single centers. **Utilizing data from The Duchenne Registry provided a much larger and diverse cohort and greater statistical power than previous studies.**

Within the Registry, we have a survey focused on Behavior and Learning. We asked registrants about the existence of any behavioral or emotional disorders. For all Duchenne** registrants, one third (33%) reported a diagnosis of a behavioral or emotional disorder.

Behavioral / Emotional Diagnosis	Percentage of Duchenne** Registrants
None	67%
Attention Deficit Hyperactivity Disorder (ADHD)	10%
Asperger* **	9%
Anxiety	7%
Obsessive Compulsive Disorder (OCD)	7%
Autism Spectrum Disorder (ASD)* **	7%
Attention Deficit Disorder (ADD)	6%
Pervasive Developmental Disorder (PDD)	4%
Sensory Processing Disorder	4%
Depression	4%
Oppositional Defiant Disorder (ODD)	2%
Other	2%

Totals are greater than 100% because individuals could choose more than one diagnosis.

** Counterman KJ, et al. Associations Between Self-Reported Behavioral and Learning Concerns and DMD Isoforms in Duchenne Muscular Dystrophy. Journal of Neuromuscular Diseases. 2022; 9(6):757–764. doi: 10.3233/JND-220821*

*** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*

**** We have since combined the Asperger and Autism response options into one Autism Spectrum Disorder (ASD) option.*

Registrants can report if they are using counseling and/or medication for any of their behavioral or emotional concerns. For all the Duchenne* registrants who responded to this question, almost 30% reported using counseling, medications, or a combination of the two (11% reported using counseling alone, 10% reported using medications alone, and 8% reported using a combination of counseling and medications). Given the importance of mental health for all individuals with dystrophinopathies, PPMD hosted a specialty care conference in November 2021 that was focused on dystrophinopathies and the brain. A **summary publication can be found here**.**

We also asked registrants about the existence of any cognitive or learning disorders. For all Duchenne* registrants, over half (54%) reported a diagnosis of a cognitive disorder, learning disability or developmental delay. The most commonly reported diagnoses were speech/expressive language delay (21%), learning disability / type unspecified (12%), and learning disability in math / dyscalculia (10%). For Duchenne and Becker registrants living in the United States, 57% report using an Individualized Educational Plan (IEP) or 504 Plan for assistance in school. PPMD has several **Classroom Resources***** available to assist parents and teachers of children from early childhood through the teenage years and into adulthood.

Learning / Cognitive Diagnosis	Percentage of Duchenne* Registrants
None	82%
Speech / Expressive language delay (problems explaining and describing things)	21%
Learning disability (but I am not sure what type)	12%
Learning disability in math (dyscalculia)	10%
Learning disability in reading (dyslexia)	9%
Receptive language delay (problems with language comprehension/understanding)	8%
Global developmental delay	8%
Writing disability (dysgraphia)	8%
Short term memory problems	7%
Verbal apraxia / dyspraxia (motor speech disorder, cannot correctly pronounce words)	6%
Auditory processing deficits	4%
Dyslexia	3%
Intellectual disability (mild, moderate, or severe)	2%
Visual processing deficits	2%

Totals are greater than 100% because individuals could choose more than one diagnosis.

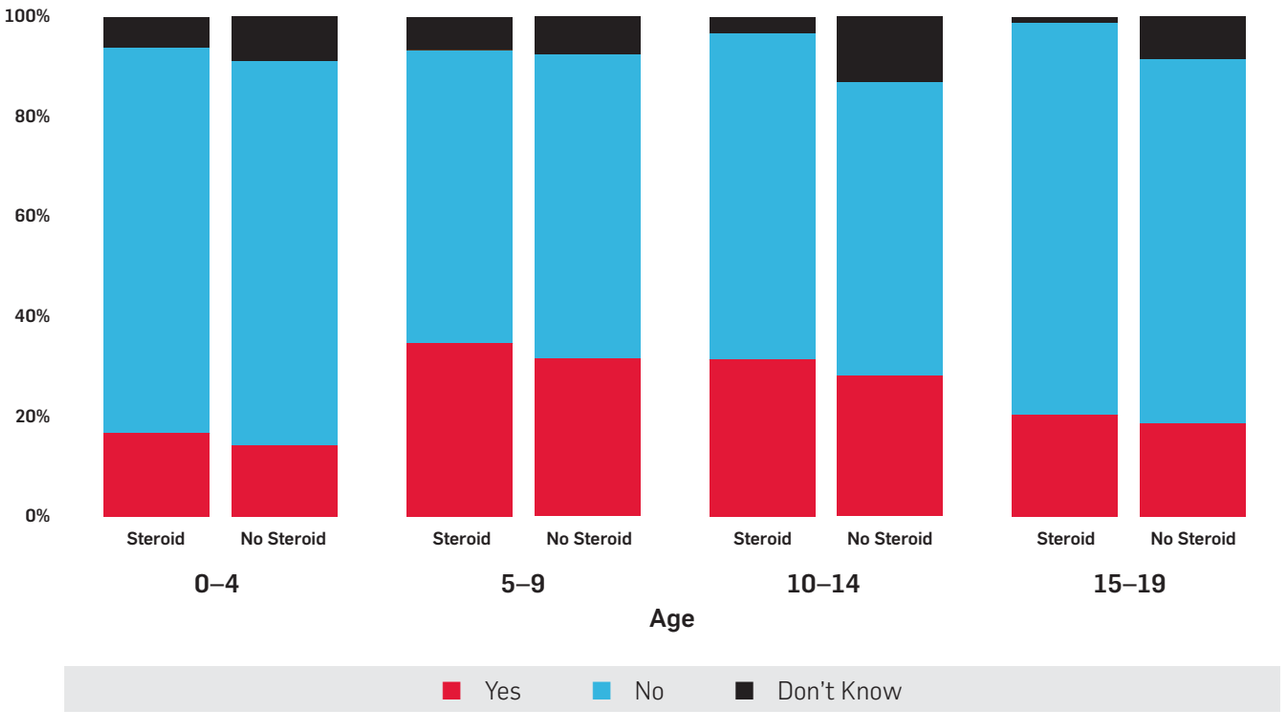
** Duchenne refers to registrants who selected either "Duchenne" or "Unclear if Duchenne or Becker" as diagnosis.*

*** Colvin MK, et al. Dystrophinopathy and the brain: A Parent Project Muscular Dystrophy (PPMD) meeting report November 11-12, 2021, New York City, NY. Neuromuscular Disorders. 2022 Dec; 32(11-12):935-944. doi: 10.1016/j.nmd.2022.10.002*

**** https://www.parentprojectmd.org/care/for-families/classroom-resources-for-teaching-about-duchenne*

The graph below shows four different age groups and the percent who reported behavioral concerns and/or diagnosis, separated by corticosteroid users (current or previous) and those who never used. Registrants using corticosteroids in the 10–14 year old age group had a statistically significant increased rate of reporting behavioral concerns and/or diagnosis compared to those individuals who never used corticosteroids. Registrants using corticosteroids in the other age groups (0–4, 5–9, 15–19) did not have a statistically significant increased rate of reported behavioral concerns and/or diagnosis. Even the registrants who never used corticosteroids had behavioral disorders, so we know that multiple factors (not just corticosteroid use) contribute to the development of behavioral issues.

Behavioral Concerns in Duchenne Based on Corticosteroid Use and Age



Therapy Services

Therapy services such as physical therapy, speech therapy, and occupational therapy are an important part of care for people with Duchenne and Becker. We developed a new survey within the Registry to understand what therapies people are using, when they use them, and how helpful they feel those therapies are. Overall, 84% of registrants who had received therapy services felt that at least one therapy service had been helpful for them/their child, with physical therapy, occupational therapy, and speech therapy most often reported as helpful.

Pain

Pain has a major impact on quality of life and is under-studied in Duchenne, Becker and carriers. In the Registry, we ask about pain over the last 7 days, but we ask differently depending on whether the registrant is an adult or a child. The adult version of the survey asks about *how much* pain interferes with enjoyment of life and daily activities, while the child version asks about *how often* pain affects enjoyment of life and daily activities. All questions in the Pain Survey were taken from the PROMIS Pain Interference patient-reported outcome measure.

In adult registrants, the reported effect of pain varied depending on the person's diagnosis and what aspect of their life was covered in the question. Overall, adults with Becker were more likely to report that pain "quite a bit" or "very much" affected their enjoyment of life, day to day activities, and tasks away from home. If we look at all of the pain questions combined, on average about half of adults with Duchenne (50%) reported that pain affected their lives not at all, while 42% of adults with Becker report the same.

Pain in Adult Registrants

In the past 7 days, how much did pain interfere with:	Duchenne		Becker	
	Affected quite a bit or very much	Affected not at all or a little bit	Affected quite a bit or very much	Affected not at all or a little bit
Enjoyment of life	16%	68%	22%	59%
Ability to concentrate	9%	77%	7%	78%
Day to day activities	12%	73%	18%	60%
Tasks away from home	13%	72%	21%	68%

In children with Duchenne, most registrants reported that pain "never" or "almost never" affected their enjoyment, learning or feelings. There was a higher percentage of children with Becker who reported experiencing difficulties when they had pain, with having fun most frequently affected. Because the questions and possible answer responses are different for children versus adults, it is not possible to compare responses over time.

Pain in Pediatric Registrants

In the past 7 days, when I had pain:	Duchenne		Becker	
	Often or almost always	Never or almost never	Often or almost always	Never or almost never
I felt angry	7%	65%	18%	62%
I had trouble sleeping	7%	71%	11%	67%
I had a hard time getting along with others	10%	71%	21%	61%
Had a hard time having fun	12%	61%	28%	49%

Clinical Trial and Research Experience

In the past 5 years, 31% of all Duchenne and Becker registrants in the United States reported either currently or previously participating in a clinical trial, meaning a study that is designed to see if an experimental therapy or treatment works. This is a significant increase over the 19% reported in the Ten Year Registry Report. If we separate Duchenne and Becker, **33% of Duchenne registrants in the United States reported either currently or previously participating in a clinical trial, and 12% for Becker**.

The increase in clinical trial participation is remarkable given the COVID-19 pandemic and fewer trials being available in 2020. However, we recognize that the Registry population is skewed towards registrants who are interested in research and trial participation and likely does not reflect the overall Duchenne and Becker population in the United States.

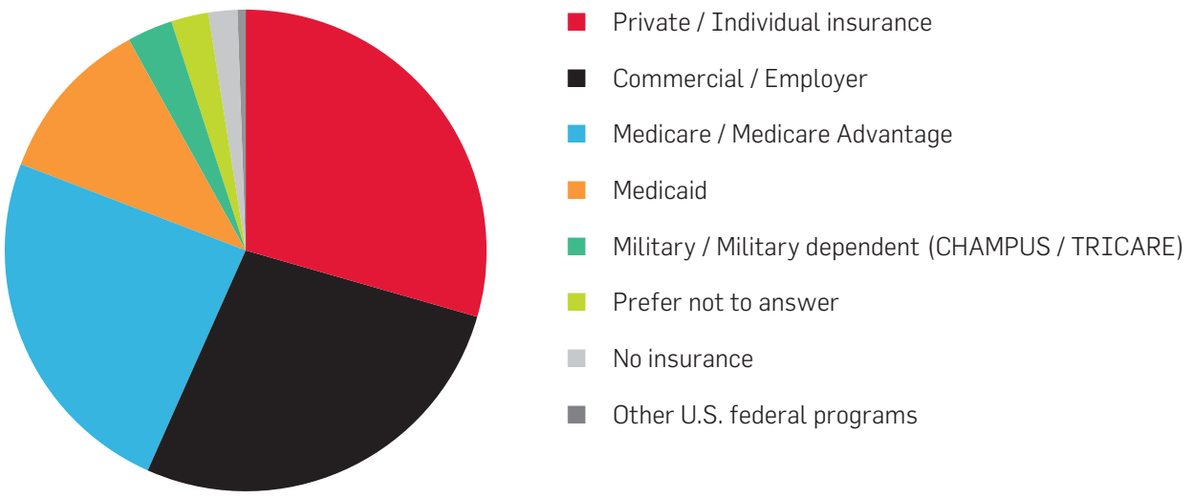
We also asked registrants about their participation in Duchenne or Becker research activities other than clinical trials. This would include participation in activities such as natural history and observational studies, survey studies and interview studies. In the past 5 years, 22% of all Duchenne and Becker registrants in the United States reported either currently or previously participating in a research activity other than a trial. This is similar to the 21% reported in the Ten Year Registry Report. If we separate Duchenne and Becker, 23% of Duchenne registrants in the United States reported either currently or previously participating in a research study, and 14% for Becker.

Insurance

In order to understand registrants' insurance usage and access issues, we asked them what type of insurance they utilize, and which services (if any) they have had difficulty with obtaining insurance coverage.

We analyzed all Duchenne registrants living in the United States and found that the greatest number (30%) report having private/individual insurance, closely followed by those with commercial/employer insurance (27%) or Medicare/Medicare Advantage (24%). Fewer registrants reported having Medicaid (11%) and military/military dependent insurance (3%). Of those who completed the survey, 2% reported they have no insurance.

Insurance Types for Duchenne Registrants (U.S. Only)



In the United States, the most frequently reported services that registrants had difficulty obtaining coverage for include medical devices/equipment, genetic testing, and medications. Other reported services that were difficult to obtain coverage for include specialty care, personal care attendants/nursing care, mental health counseling, operations/procedures, and respite care.

For families living in the United States who are experiencing difficulty obtaining coverage for care services, staff at PPMD are available to talk with families and provide recommendations. Visit **PPMD for You** to learn more (www.parentprojectmd.org/care/for-families/ppmd-for-you-schedule-a-one-to-one-meeting).

Female Carriers

The Duchenne Registry has always collected data on females who are carriers. However, we have seen a recent increase in the number of carriers participating in the Registry. In the web version of the Registry (before 2019), 10% of registrants reported being carriers. Currently, 18% of registrants active in the app version of the Registry identify as carriers. This increase is likely a result of initiatives within PPMD to increase outreach to carriers and to better understand the effects of being a carrier on a person's health. We especially want to understand aspects of health not previously studied, which led to the development of the Female Carrier survey (launched August 2022) to ask about reproductive health in carriers.

Carriers are asked to report if they are a confirmed carrier who does not currently have symptoms or if they are a manifesting carrier who is having symptoms. Responses to many of the surveys varied greatly based on whether registrants had symptoms or not.

Carriers are also asked to complete the same surveys used to collect data on people with Duchenne and Becker, including the Muscle Function survey. Of interest, 94% of asymptomatic carriers report walking independently all or most of time, versus 74% of the manifesting carriers.

A much higher percentage of manifesting carriers reported that pain "very much" or "quite a bit" affected their enjoyment of life and their daily activities, versus carriers with no symptoms. Recreation was reported to be most affected in the manifesting carriers, while ability to concentrate was most affected in the asymptomatic carriers. Of all registrants who completed the pain survey, asymptomatic carriers were most likely to report that pain affected their daily life and enjoyment of life "not at all", with an average of 67% of carriers reporting no effects of pain.

Pain in Carriers

In the past 7 days, how much did pain interfere with:	Carrier with no symptoms		Manifesting carrier	
	Affected quite a bit or very much	Affected not at all or a little bit	Affected quite a bit or very much	Affected not at all or a little bit
Enjoyment of life	2%	84%	40%	46%
Ability to concentrate	5%	92%	27%	49%
Day to day activities	3%	89%	34%	46%
Recreation	4%	85%	42%	43%
Tasks away from home	4%	87%	38%	51%

Cardiac screening is recommended for all adult carriers given the increased risk of cardiac complications such as dilated cardiomyopathy. In the last five years, 219 carriers completed the Heart Survey, and of those, 76% reported having an echocardiogram and 19% reported having a cardiac MRI. We hope to see these percentages increase in the future as knowledge surrounding cardiac screening for carriers expands. When asked about cardiac medication use, 28% of carriers reported taking cardiac medications, with beta blockers and ACE inhibitors being the most frequently used.

For the past several years, PPMD has been focused on raising awareness and increasing knowledge about carrier health issues.

2016

Provided support for a large carrier natural history study at Nationwide Children's Hospital which focused on the muscle, cardiac and mental health issues experienced by some carriers.

2018

Added free carrier testing to the Decode Duchenne genetic testing program.

2019

Convened a Manifesting Carrier Pre-Conference prior to the start of the Annual Conference, to initiate dialogue that would ultimately lead to improved clinical care for all females with dystrophinopathy.

2021

Published a resource for carriers entitled **Duchenne Muscular Dystrophy Carriers: Your Questions Answered**.** This comprehensive booklet is available in English and Spanish.

2022

Supported the development and launch of the first-ever **Duchenne and Becker Carrier Clinic at Penn Medicine*** in Philadelphia. We are hopeful this multidisciplinary clinic will serve as a model for other clinics in the country.

** https://www.pennmedicine.org/for-patients-and-visitors/find-a-program-or-service/heart-and-vascular/inherited-heart-disease/duchenne-and-becker-carrier-clinic*

*** https://www.parentprojectmd.org/care/for-carriers/download-duchenne-carriers-your-questions-answered*

Conclusion and Acknowledgements

We would like to thank all the families in our community who have participated in The Duchenne Registry and contributed data over the past 15 years. We are grateful for every person who registered and entered data — we sincerely appreciate your time and dedication! We would also like to thank Kevin Counterman, DO and Prometheus Research (an IQVIA company) for their work on the statistical analyses and graphics for the 15 Year Registry Report.

We strongly encourage your continued participation in The Duchenne Registry. We have several upgrades coming in 2023, including the integration of electronic health records from multiple hospitals across the country, the launch of the Registry app in Spanish, and a new web portal for users who prefer using a web interface over an app.

Continue to advance research and speed the development of new therapies by participating in The Duchenne Registry.

You have the power to make a difference!

Parent Project Muscular Dystrophy

JOIN THE FIGHT.
END DUCHENNE.

1012 14th Street NW, Suite 500
Washington, DC 20005
800.714.5437

ENDDUCHENNE.ORG