Genetics, The Duchenne Registry And Your Family

Parent Project Muscular Dystrophy
JOIN THE FIGHT. END DUCHENNE.

Ann Martin, MS, CGC
February 2, 2019

Topics for Today:

1. Importance of genetics in Duchenne and Becker
2. Free genetic testing through Decode Duchenne
3. Connecting to research through The Duchenne Registry
4. Answer your questions!

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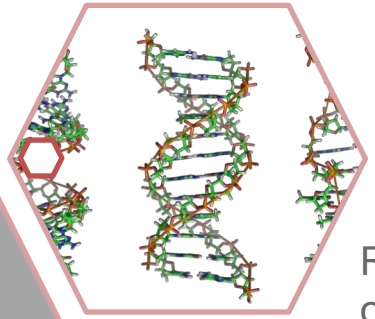
How genetics shapes the story…
And 3 reasons why testing is important

Genetic testing is the gold standard for diagnosis



Diagnosis

Results help other family members get testing

Family

Research

Mutation-specific therapies are in development

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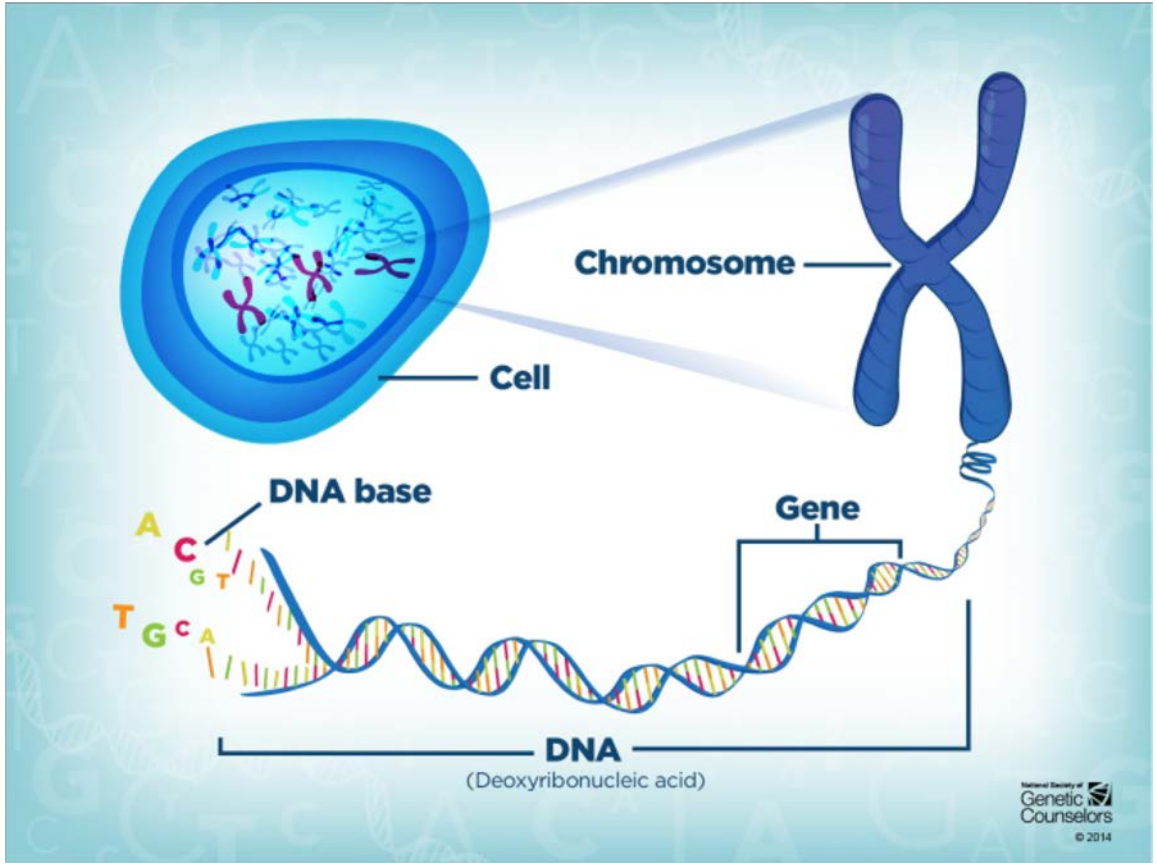
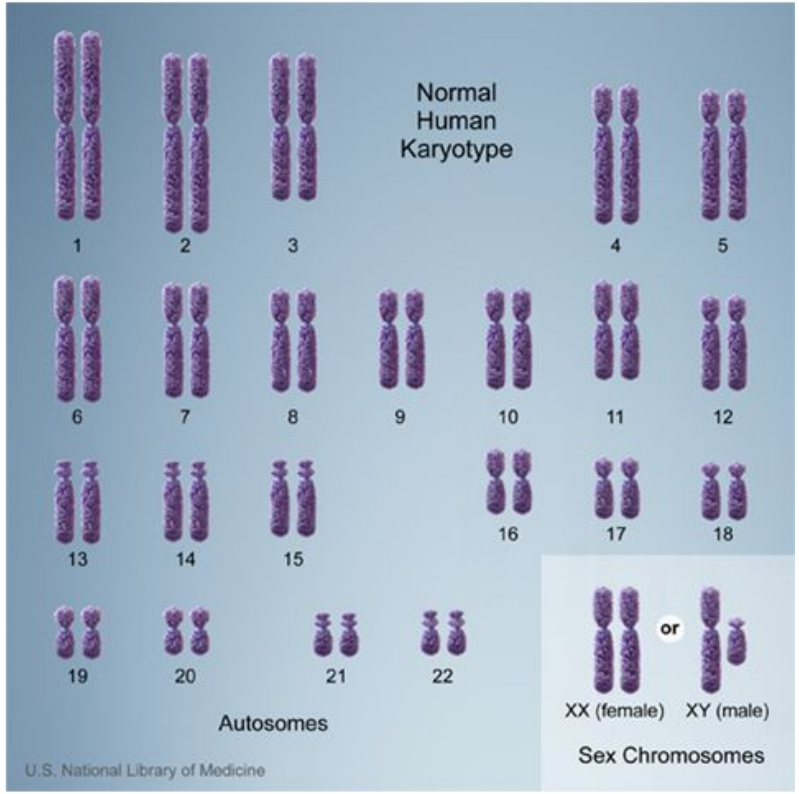
Genetics Review

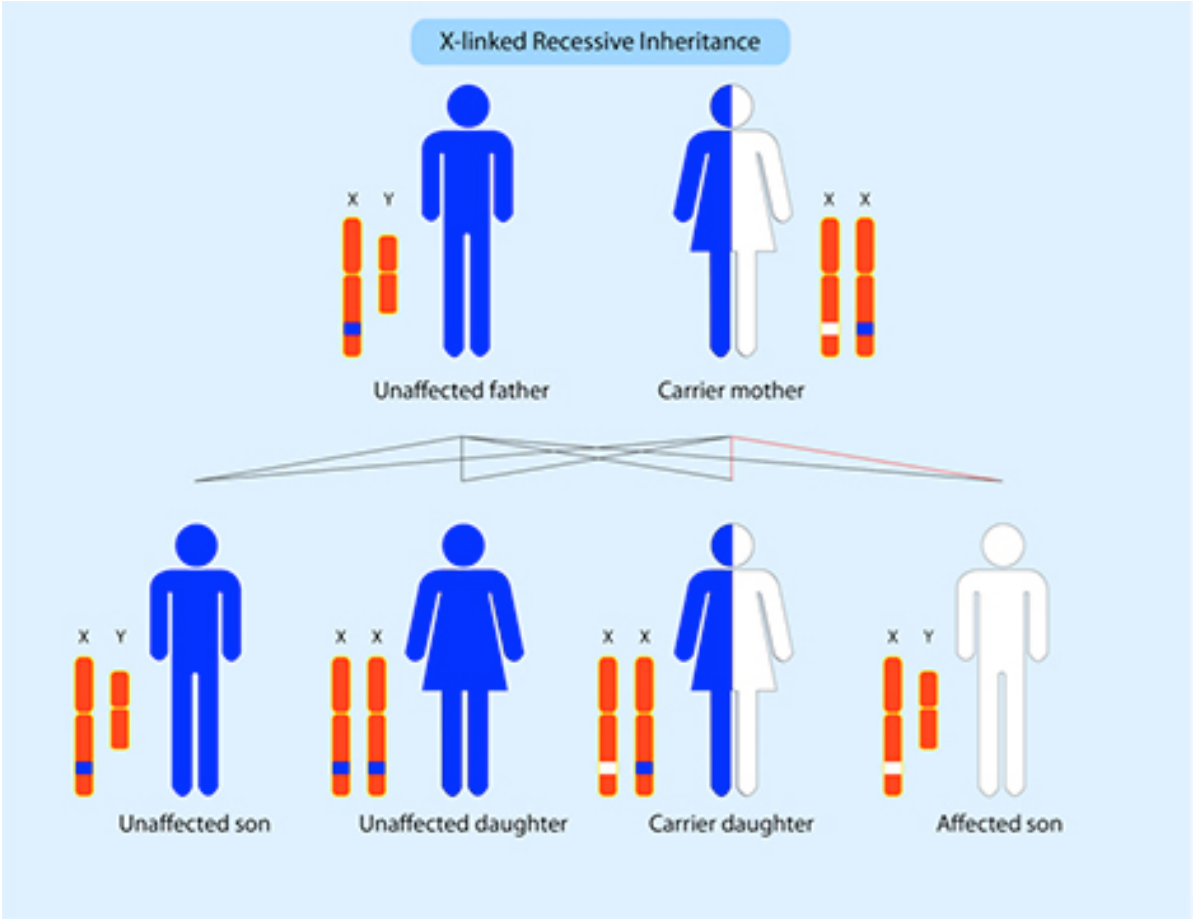


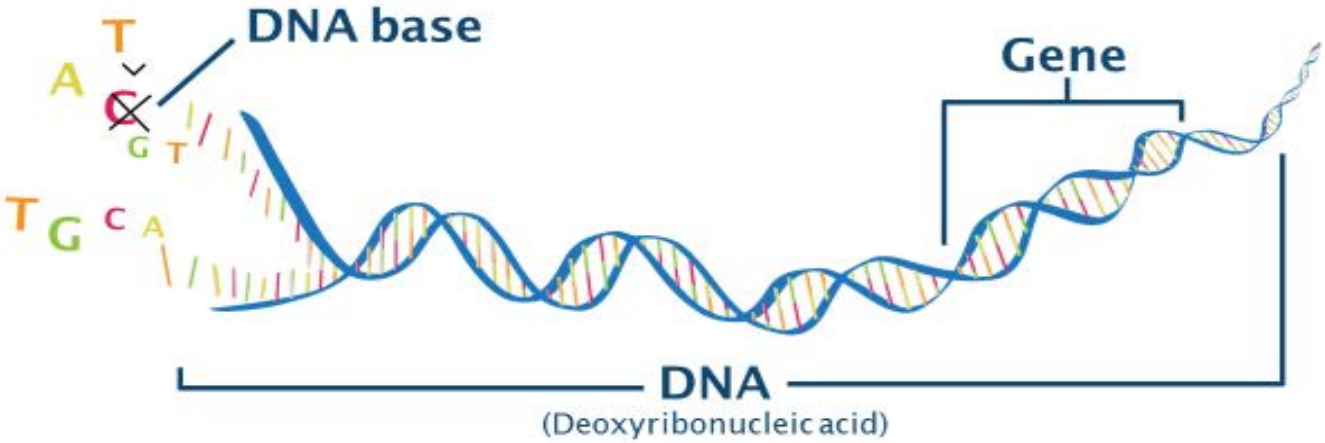
Normal Human Karyotype

- The chromosomes in a human karyotype are arranged in **homologous pairs.**
- The first **22** pairs of chromosomes are called **autosomes.**
- The **23rd** pair of chromosomes are known as the **sex chromosomes**.



X-linked Recessive Inheritance





The gray cat ran down the hall.

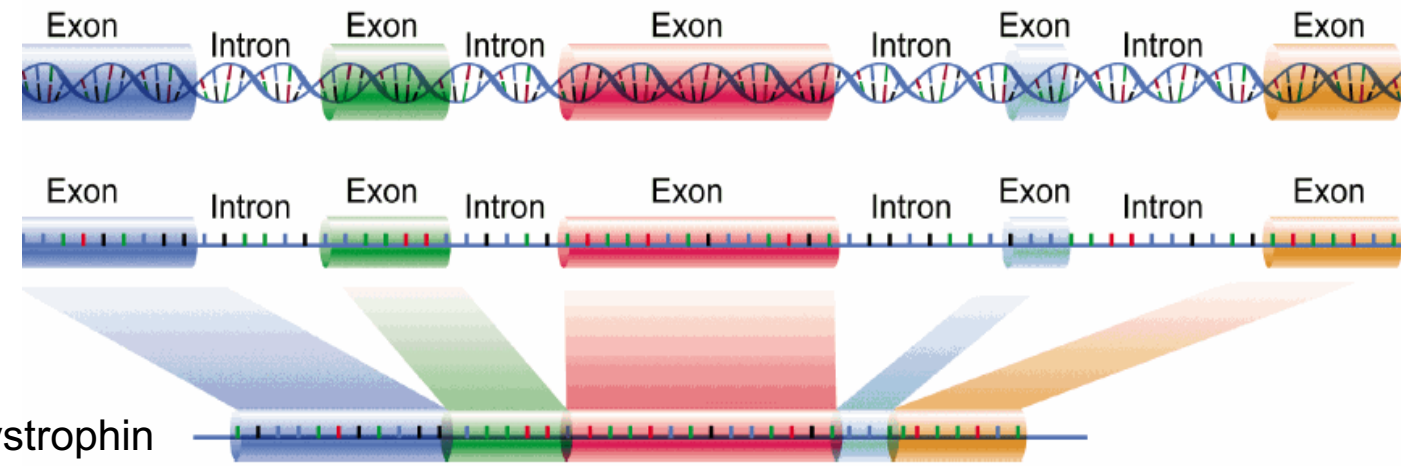
The gray cat ran down the ball.

Changes in DNA might change the way a gene works.

National Society of Genetic Counselors
©2014

Background: the *DMD* gene

The DMD gene has 79 exons…
but what is an exon?



DMD gene sequence

Dystrophin protein

Types of Changes in the *DMD* gene

- More than 4000 unique genetic changes
- Fall into categories

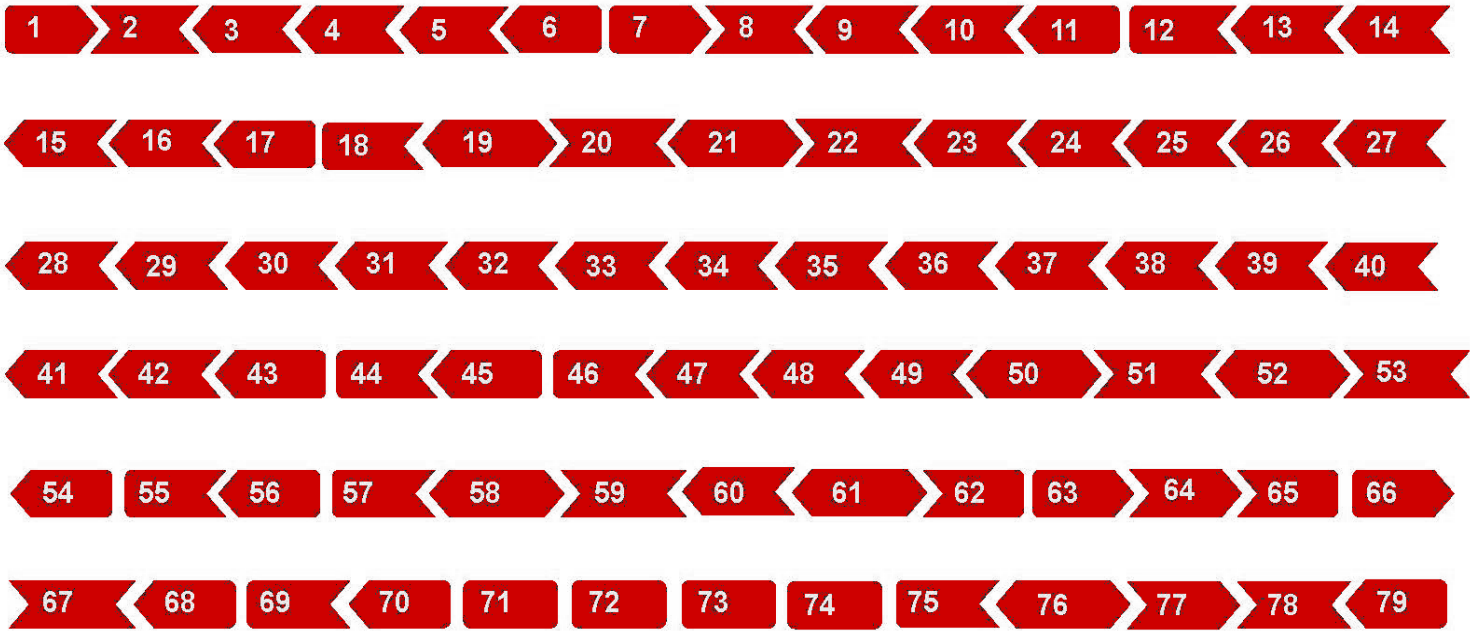
Type of Change	% of Duchenne cases	% of Becker cases
Large deletions	60-70%	80-85%
Large duplications	10%	5-10%
Point mutations and other small changes	15-30%	10-15%

Types of Genetic Mutations

The gray cat ran down the hall.	**Original**
The gray cat ran down the ball.	**Missense**
The gray green cat ran down the hall.	**Insertion**
The gray ____ ran down the hall.	**Deletion**
The gray cat cat ran down the hall.	**Duplication**
The gray.	**Nonsense**

Large deletions and duplications

- One or more exons are missing or repeated



Out-of-frame vs. In-frame

- Letters in the DNA sequence must stay in groups of three:

AAC ATG CGG TAC

- Example sentence: THE OLD DOG RAN TOO FAR

Out-of-frame deletion:

THE OLD DOG RAN TOO FAR

THL DDO GRA NTO OFA R

Duchenne

In-frame deletion:

THE OLD **DOG** RAN TOO FAR

THE OLD RAN TOO FAR

Becker

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Why is the type of genetic variant so important?

1. Helps to confirm the **diagnosis**
2. Essential for coordinating testing of **family** members
3. Critical for mutation-specific **research and approved therapies**…new strategies target the specific DNA variant

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Mutation-Specific Therapies

- **For Nonsense Mutations:**
  - Nonsense mutation read-through
    - PTC Therapeutics (Translarna®)
- **For Deletions**
  - Exon skipping
    - Sarepta Therapeutics (exon 51: Exondys 51®; exon 45: SRP-4045; exon 53: SRP-4053)
    - NS Pharma (exon 53: NS-065/NCNP-01)
    - Wave Life Sciences (exon 51: WVE-210201)

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DECODE DUCHENNE

Free genetic testing and counseling for Duchenne and Becker muscular dystrophy

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SAREPTA THERAPEUTICS

PTC THERAPEUTICS

DECODE DUCHENNE

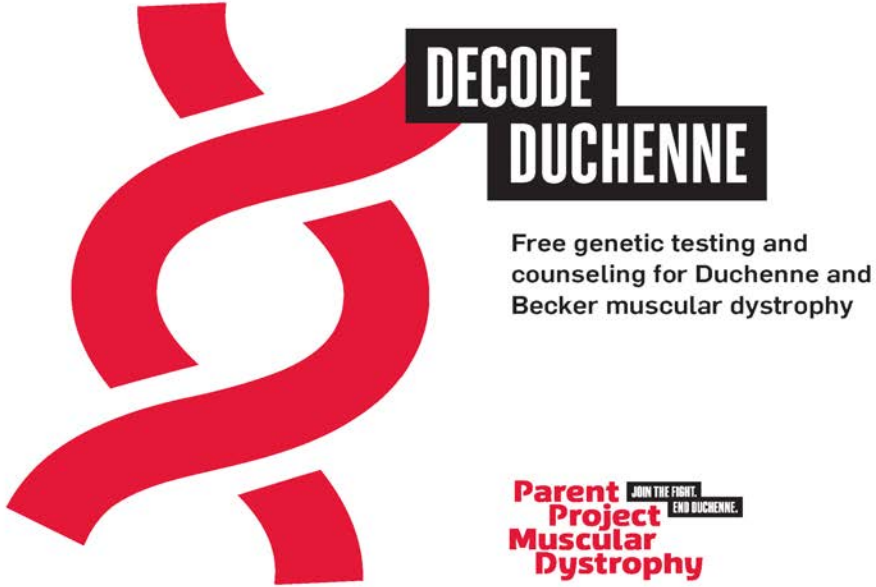
Criteria for Free Testing:

- ☑ Male with a confirmed or suspected diagnosis of Duchenne or Becker,
  OR
  Female with a relative with Duchenne or Becker with a known mutation
- ☑ Never had genetic testing OR previous genetic testing has not confirmed a mutation
- ☑ Any financial barrier
- ☑ Legal resident of US or Canada

All testing performed at:

PerkinElmer For the Better | PerkinElmer Genetics

Over 1,100 participants to date in the Decode Duchenne program!



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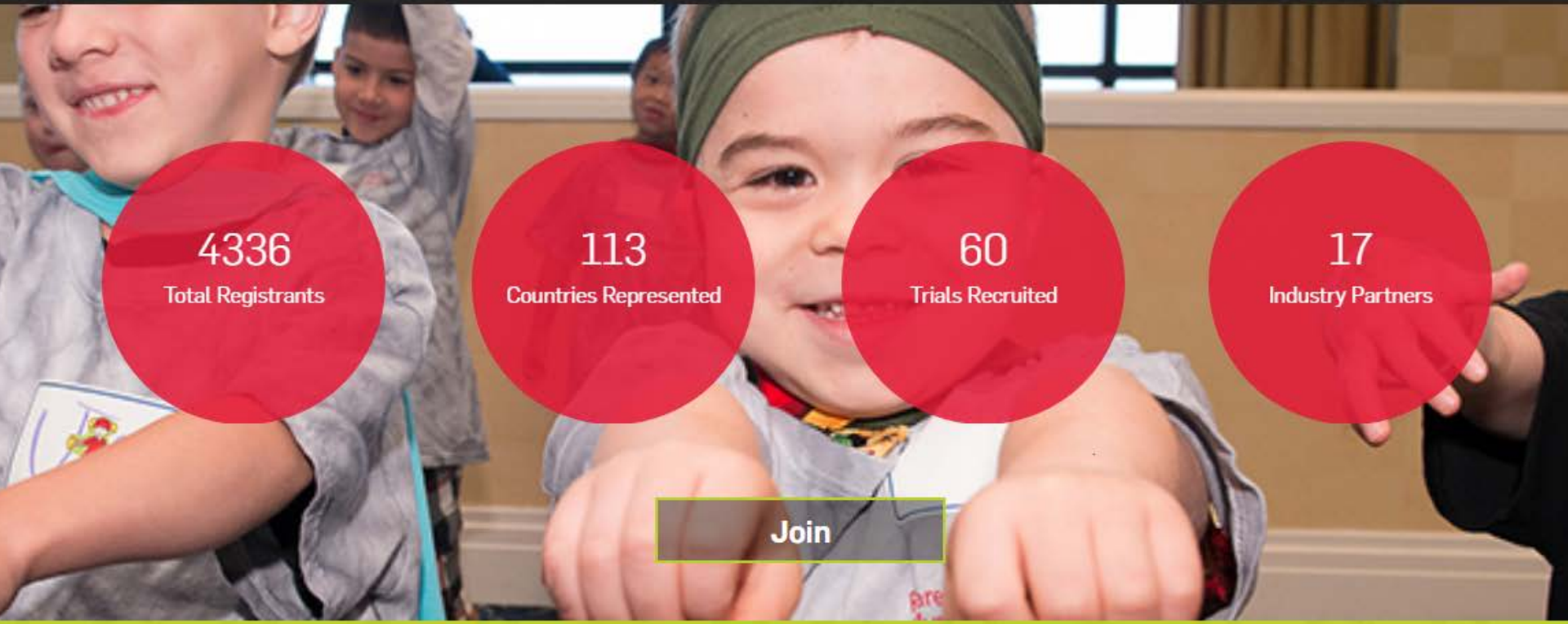
THE DUCHENNE REGISTRY

Login: Username Password Login

Forgot login?

HOME ABOUT REPORTS JOIN

OUR IMPACT


4336
Total Registrants
113
Countries Represented
60
Trials Recruited
17
Industry Partners
Join

TEN YEAR REGISTRY REPORT

Parent Project Muscular Dystrophy

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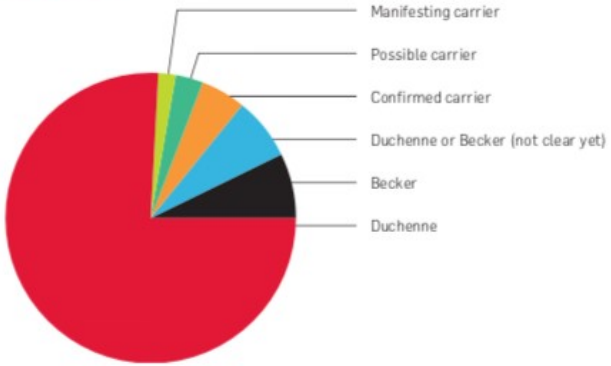
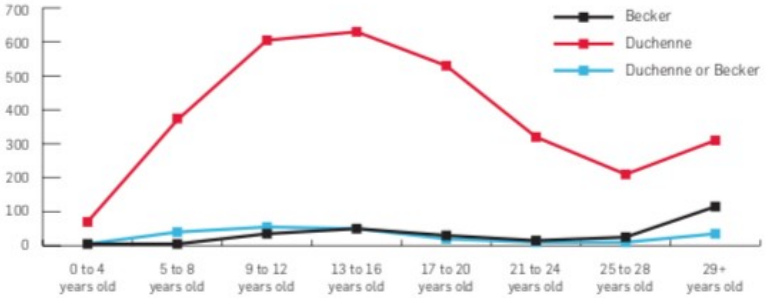
ENDDUCHENNE.ORG

Diagnosis



Registry participants were asked about their diagnosis. Most registrants (3054 people, or 76% of registrants) self-reported that they are individuals with Duchenne muscular dystrophy, while 306 (7% of registrants) reported they are individuals with Becker muscular dystrophy. Carriers were also invited to register, with 155 women (5% of registrants) identifying as confirmed carriers without symptoms, 87 women (2%) identifying as manifesting carriers with symptoms, and 103 women (3%) identifying themselves as possible carriers.

Age By Diagnosis



Goal of Duchenne Registry

- To educate and connect the entire Duchenne and Becker community:
  - Individuals with Duchenne and Becker
  - Families and caregivers
  - Healthcare providers
  - Researchers
  - Industry

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What We Do

The Duchenne Registry

Education

Website, newsletters, email blasts, social media

Recruitment

Recruited for 8 clinical trials & 8 research studies in 2018

Genetic Testing

Decode Duchenne genetic testing program

Advance Research

Exported data to 5 industries in 2018

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THE DUCHENNE REGISTRY

www.DuchenneRegistry.org

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Welcome back, Bruce!

Your newest survey, the Corticosteroid Module is now available. Take it today and view the Survey Data to see how others have responded.

CHAT STATUS

Offline

Health Surveys (3 of 12 Complete)

INCOMPLETE SURVEYS

Bone/Orthopedic Module — START SURVEY ›

A moderate length survey covering spinal X-rays, scoliosis, bone fractures, ...

Behavior & Learning Module — START SURVEY ›

A moderate length survey covering any diagnosed behavior or learning problems ...

Clinical Trials & Registry Participation Module — START SURVEY ›

A moderate length survey about your participation in any research studies, ...

Insurance Module — START SURVEY ›

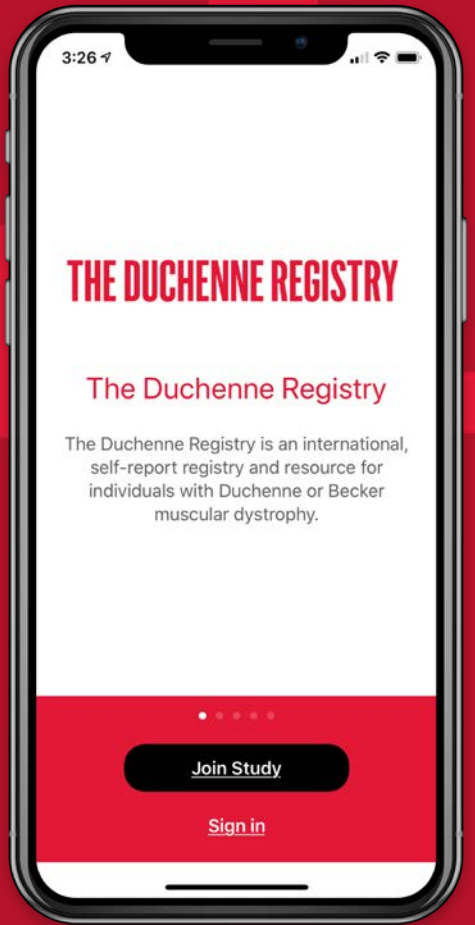
Medical Records

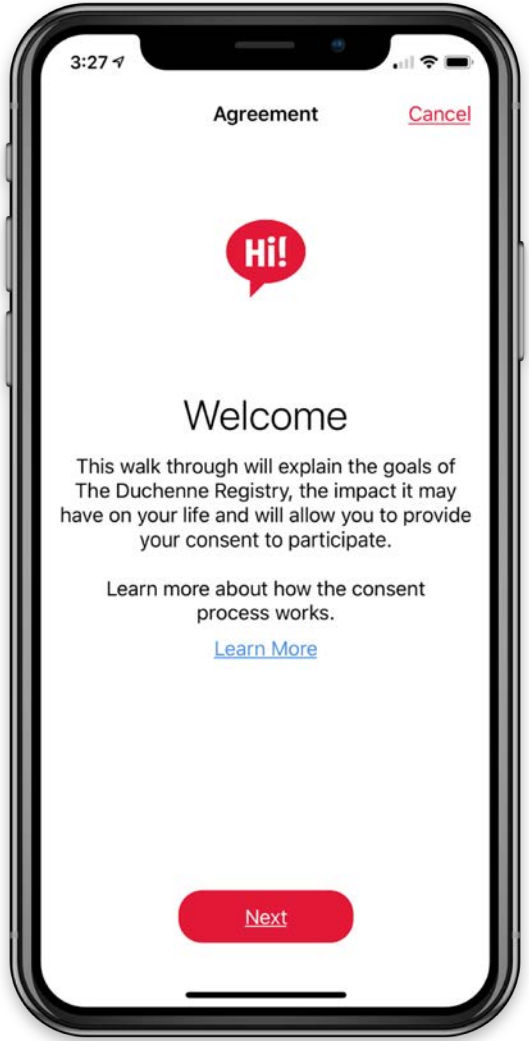
Upload relevant medical records to share more detailed data while protecting your privacy.

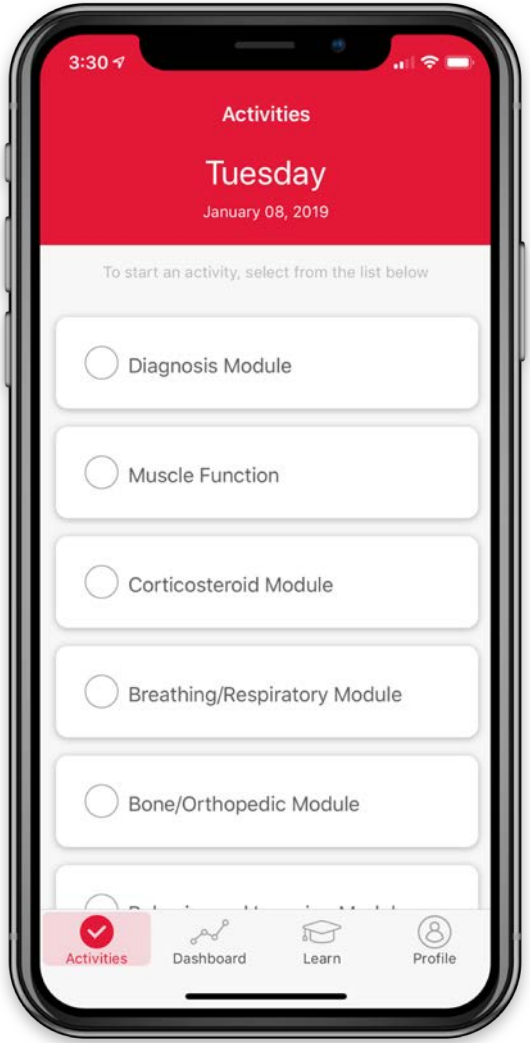
ADD MEDICAL RECORDS

Medications

NEW Registry App Launching in 2019!




3:27
Agreement
Cancel
Hi!
Welcome
This walk through will explain the goals of The Duchenne Registry, the impact it may have on your life and will will allow you to provide your consent to participate.
Learn more about how the consent process works.
Learn More
Next


3:30
Activities
Tuesday
January 08, 2019
To start an activity, select from the list below
Diagnosis Module
Muscle Function
Corticosteroid Module
Breathing/Respiratory Module
Bone/Orthopedic Module
Activities
Dashboard
Learn
Profile

3:30

Cancel

Muscle Function

By "you" in this survey we mean the person being registered; the person with Duchenne or Becker, or the carrier of Duchenne or Becker.

Next

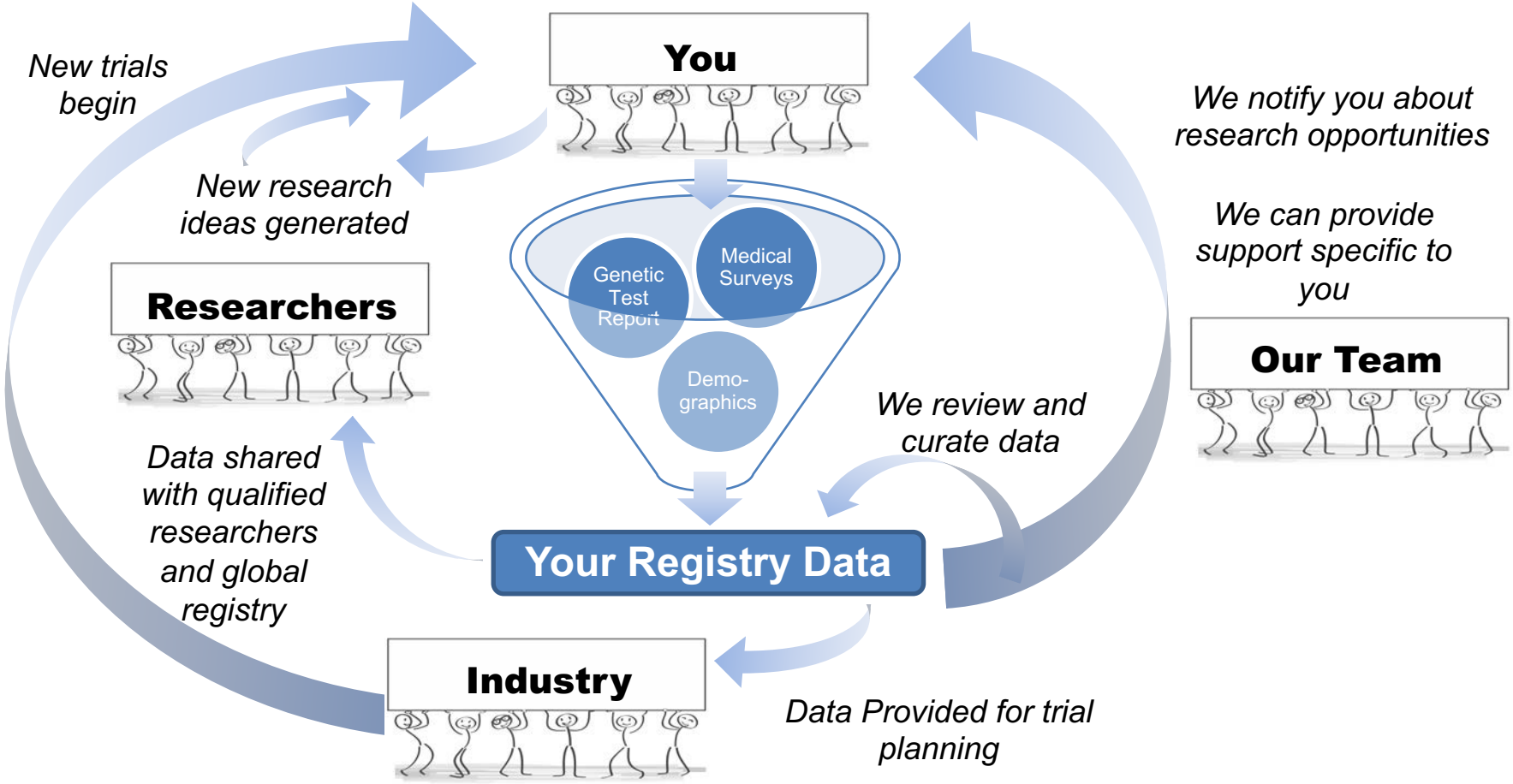
3:30

Cancel

How do you or your child (the person with Duchenne or Becker) usually get around? Please choose one answer below.

- I usually or always walk on my own without help or mobility devices.
- I can get around on my own but I sometimes need help from a mobility device.
- I use a wheelchair or other mobility device and rarely or never walk.
- My child is an infant/toddler and has not yet taken his/her first steps.

The Duchenne Registry: Working Together to Advance Research



Your Data at Work

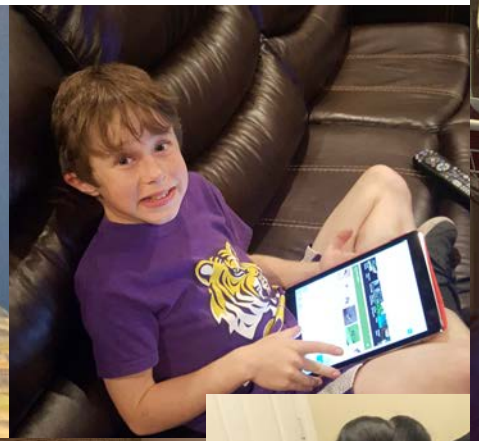
Your de-identified data is shared with:

- TREAT-NMD Global Duchenne Registry
- Duchenne Regulatory Science Consortium

Your Data Makes a Difference
Register Today!

www.duchenneregistry.org

You Could Win an iPad!



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Research > Clinical Trials

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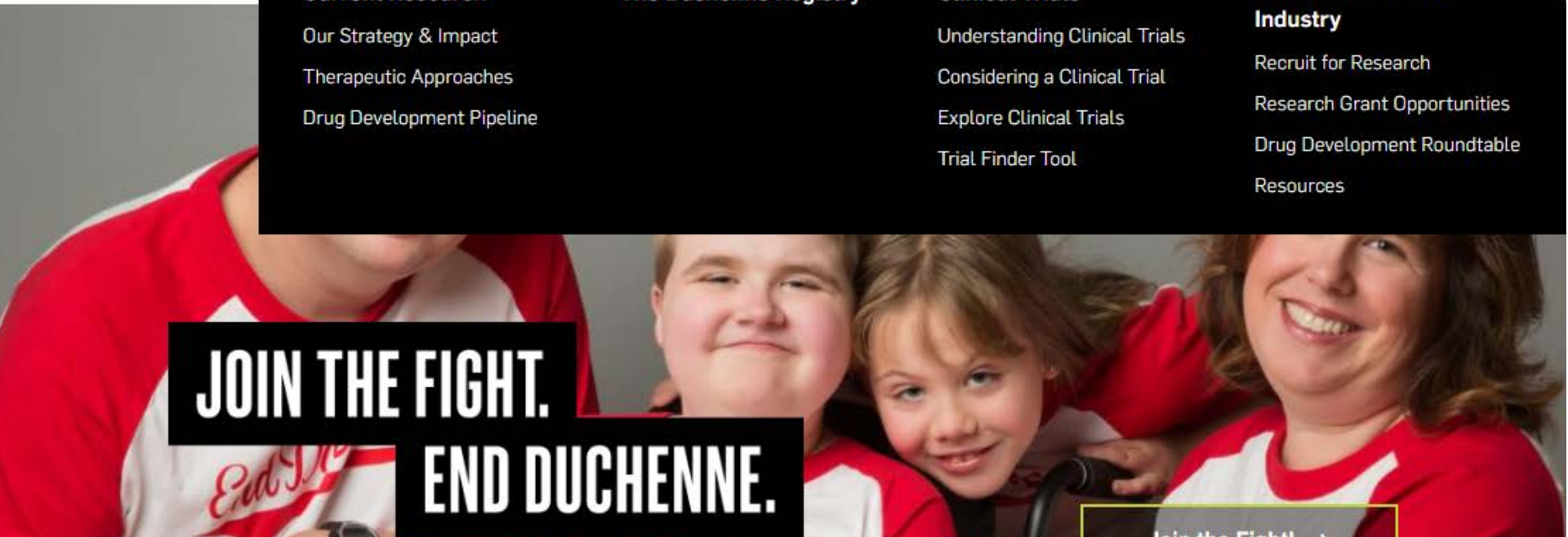
ABOUT DUCHENNE | CARE | ADVOCACY | RESEARCH | GET INVOLVED | Duchenne Registry | Donate

Current Research
- Our Strategy & Impact
- Therapeutic Approaches
- Drug Development Pipeline

The Duchenne Registry

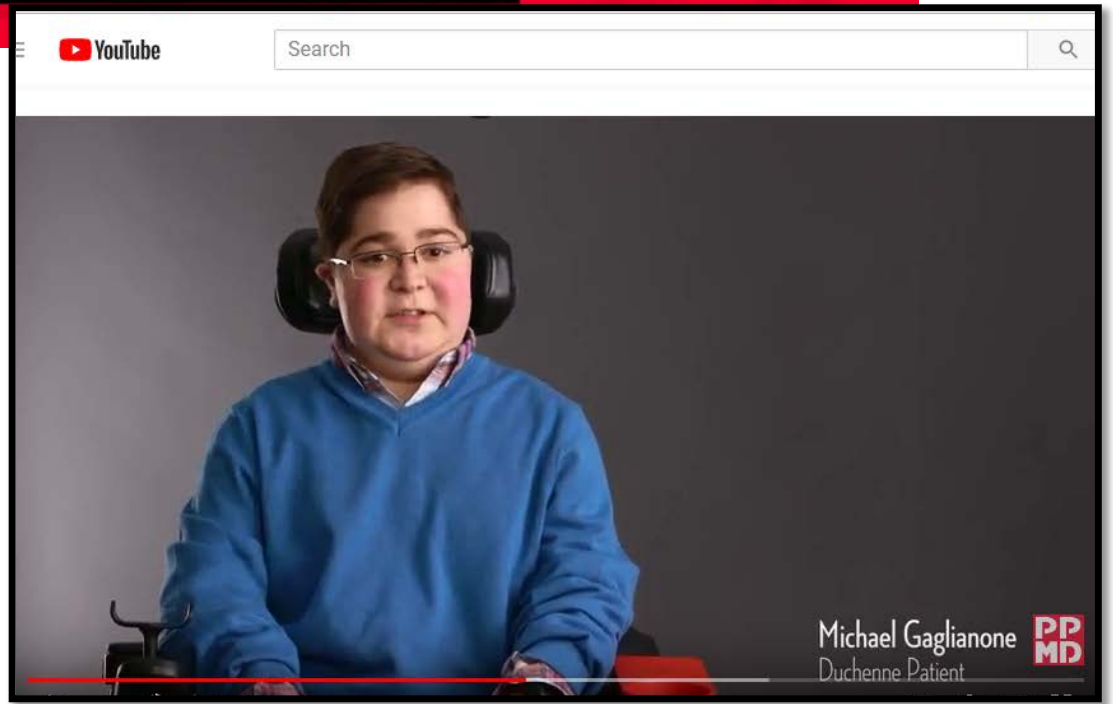
Clinical Trials
- Understanding Clinical Trials
- Considering a Clinical Trial
- Explore Clinical Trials
- Trial Finder Tool

For Researchers & Industry
- Recruit for Research
- Research Grant Opportunities
- Drug Development Roundtable
- Resources



UNDERSTANDING CLINICAL TRIALS

CLINICAL TRIAL VIDEO LIBRARY



CLINICAL TRIALS

CONSIDERING A CLINICAL TRIAL

MAKING THE RIGHT CHOICE ABOUT CLINICAL TRIALS

A Guide for Adults with Duchenne and Becker Muscular Dystrophy

Parent Project Muscular Dystrophy
LEADING THE FIGHT TO END DUCHENNE

RTI INTERNATIONAL

CLINICAL TRIALS

EXPLORE CLINICAL TRIALS

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ABOUT DUCHENNE | CARE | ADVOCACY | RESEARCH | GET INVOLVED | Duchenne Registry

Preclinical | **Enrolling** | Ongoing | Female Carriers

The following trials are currently actively recruiting. Click any title to go to the study's FAQ page (when available).

Search:

Study	Therapeutic Approach	Industry/ Institution	Age (years)	Ambulation Status	Mutation Specific	Steroid Use	Location
Assessment of Cardiopulmonary Function	Observational	University of Florida	5-15	Either	No	No	United States
Ataluren	Stop Codon Readthrough	PTC	5+	Ambulatory	Yes - Nonsense mutation	Currently using	United States + Other
Cardiac MRI Biomarkers	Observational	NIH	7-21	Either	No	No specific requirement	United States

Thank you!

Please visit us at the Registry table!

coordinator@duchenneregistry.org

888-520-8675