

# Genetics, The Duchenne Registry And Your Family

**Parent** **Project** **Muscular** **Dystrophy**

JOIN THE FIGHT.  
END DUCHENNE.

*Ann Martin, MS, CGC*  
*Certified Genetic Counselor*

# Topics for Today:

1. Duchenne and Becker 101
2. Genetics and the importance of genetic testing
3. Connecting to research through The Duchenne Registry
4. Answer your questions!

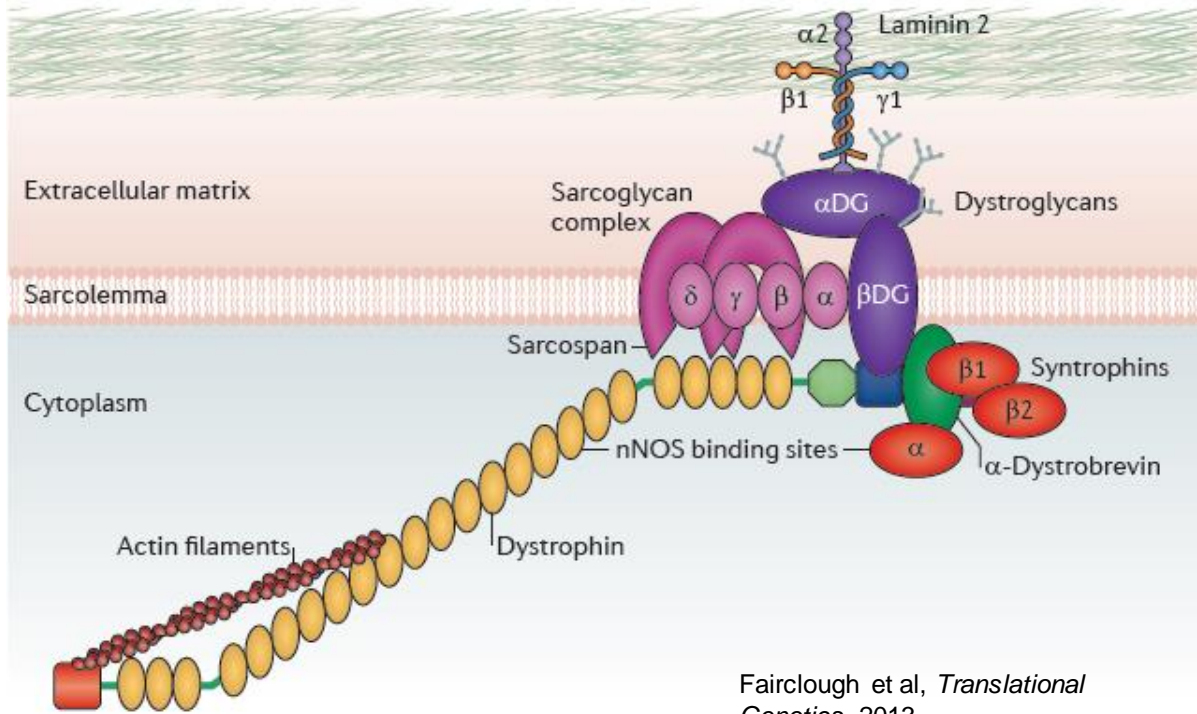


# What is Duchenne?

Duchenne and Becker muscular dystrophies are genetic conditions caused by problems with the gene that makes dystrophin (*DMD*). As a result, dystrophin is not made or is made incorrectly. Without dystrophin, muscles are not able to function or repair themselves properly.

**Parent** **JOIN THE FIGHT.**  
**Project** **END DUCHENNE.**  
**Muscular**  
**Dystrophy**

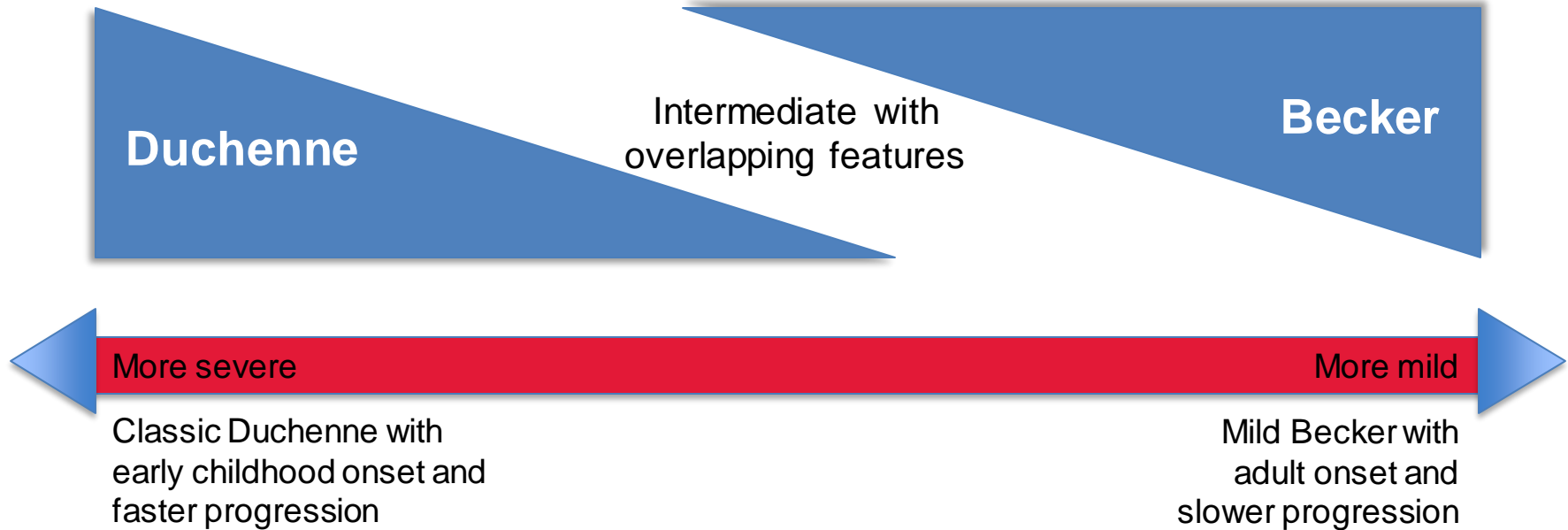
# Duchenne and Becker are dystrophinopathies



Fairclough et al, *Translational Genetics*, 2013



# The Spectrum of Dystrophinopathies

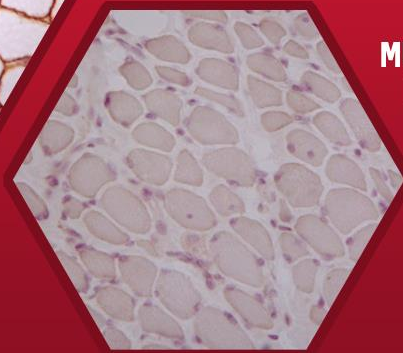


# DUCHENNE'S EFFECT ON MUSCLES

Without dystrophin, muscle cells are damaged, and, over time, are replaced with scar tissue and fat in a process called fibrosis.

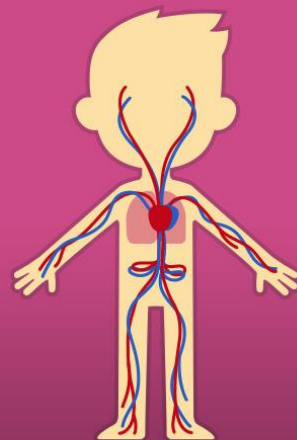


**HEALTHY MUSCLE TISSUE**

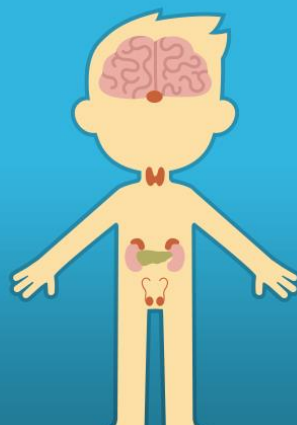
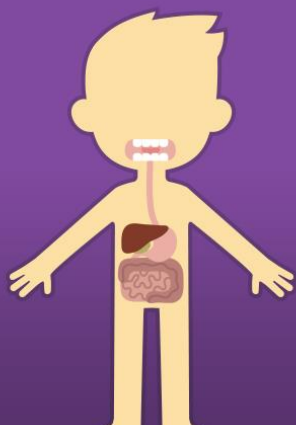
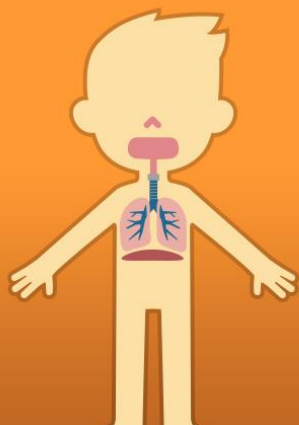


**MUSCLE TISSUE WITH  
DUCHENNE MUSCULAR DYSTROPHY**

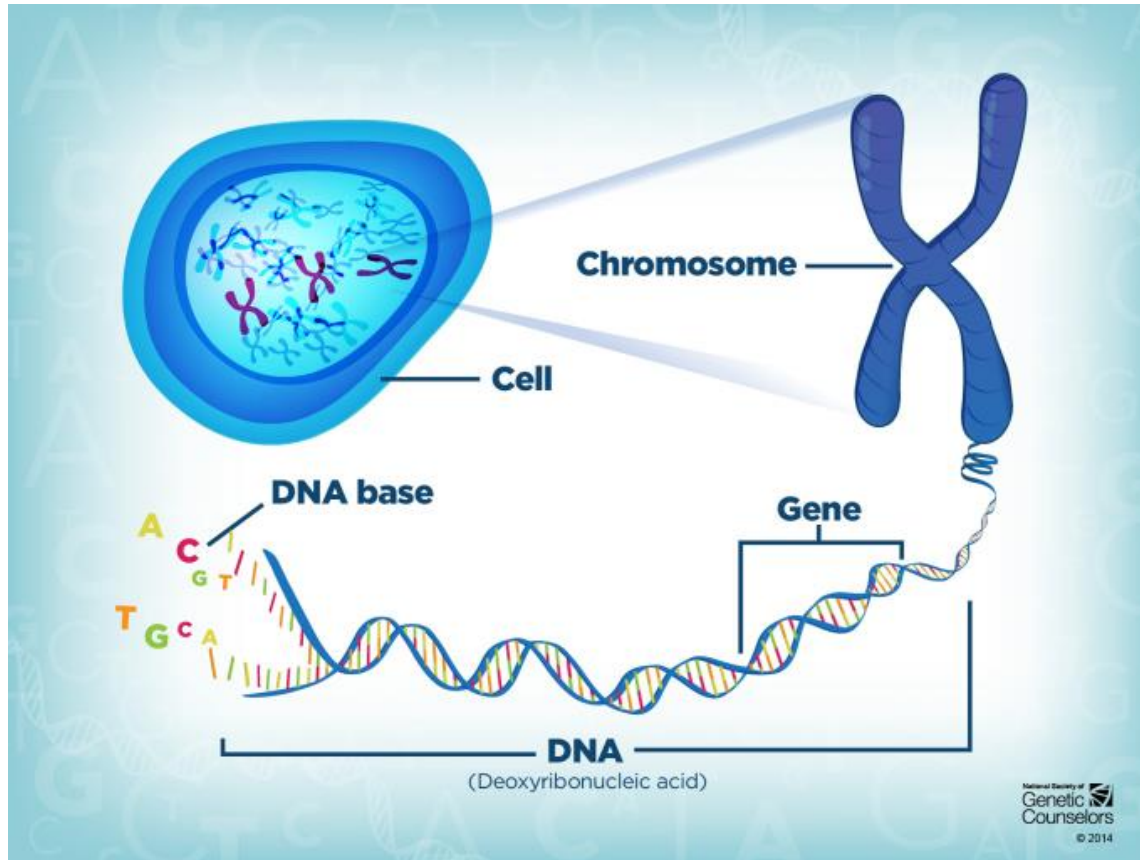




**DUCHENNE IS NOT JUST A DISEASE OF THE MUSCLES.  
IT AFFECTS EVERY SYSTEM IN THE HUMAN BODY.**

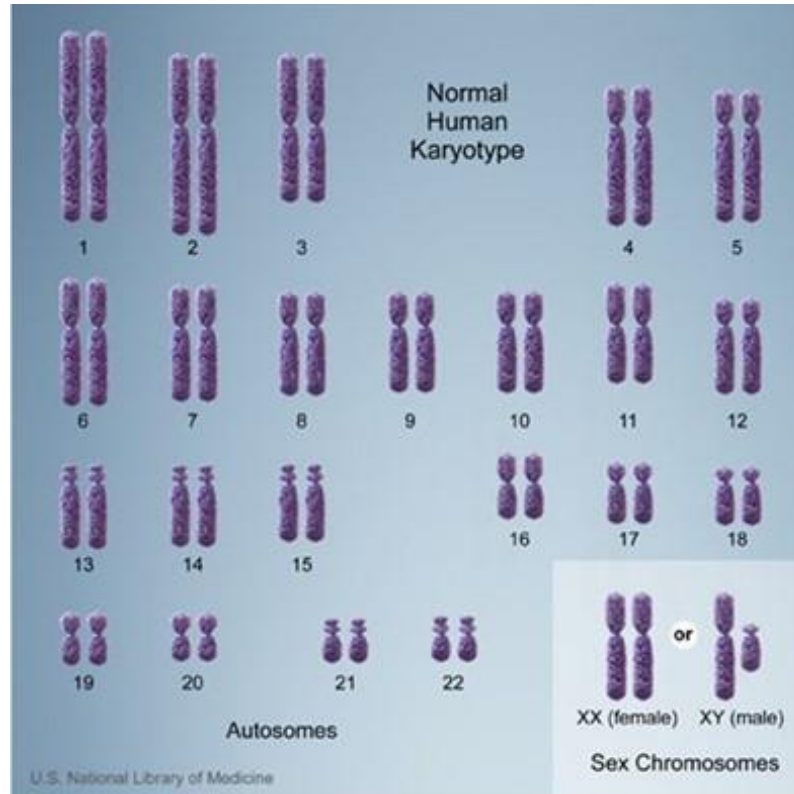


# Genetics Review



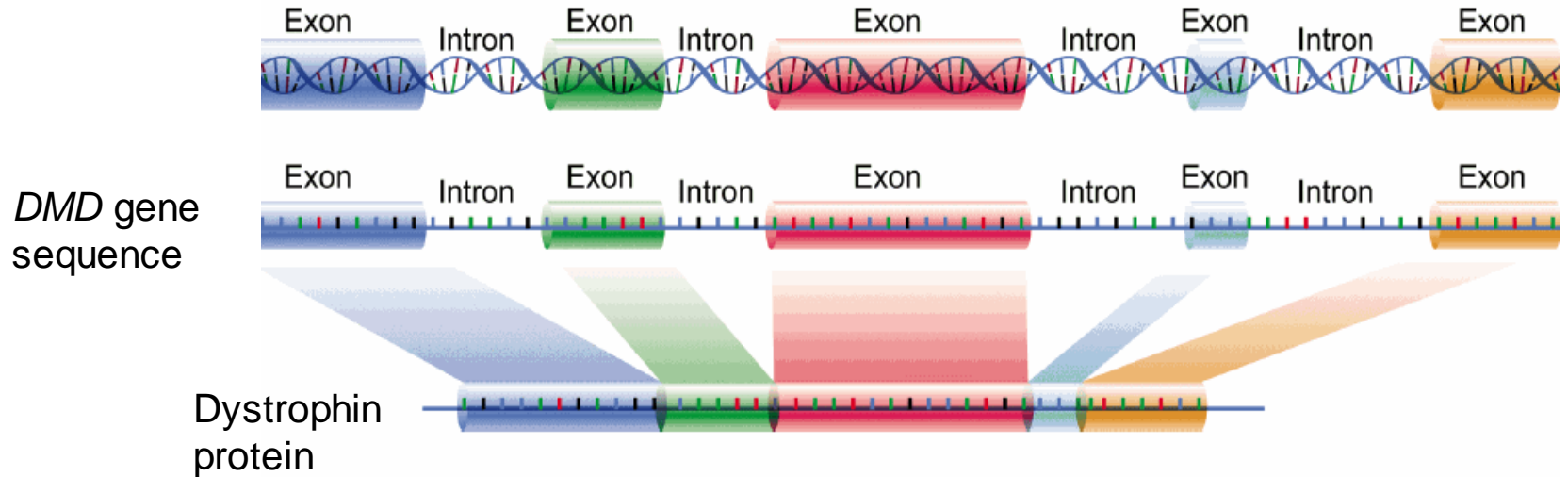


# Typical Human Karyotype

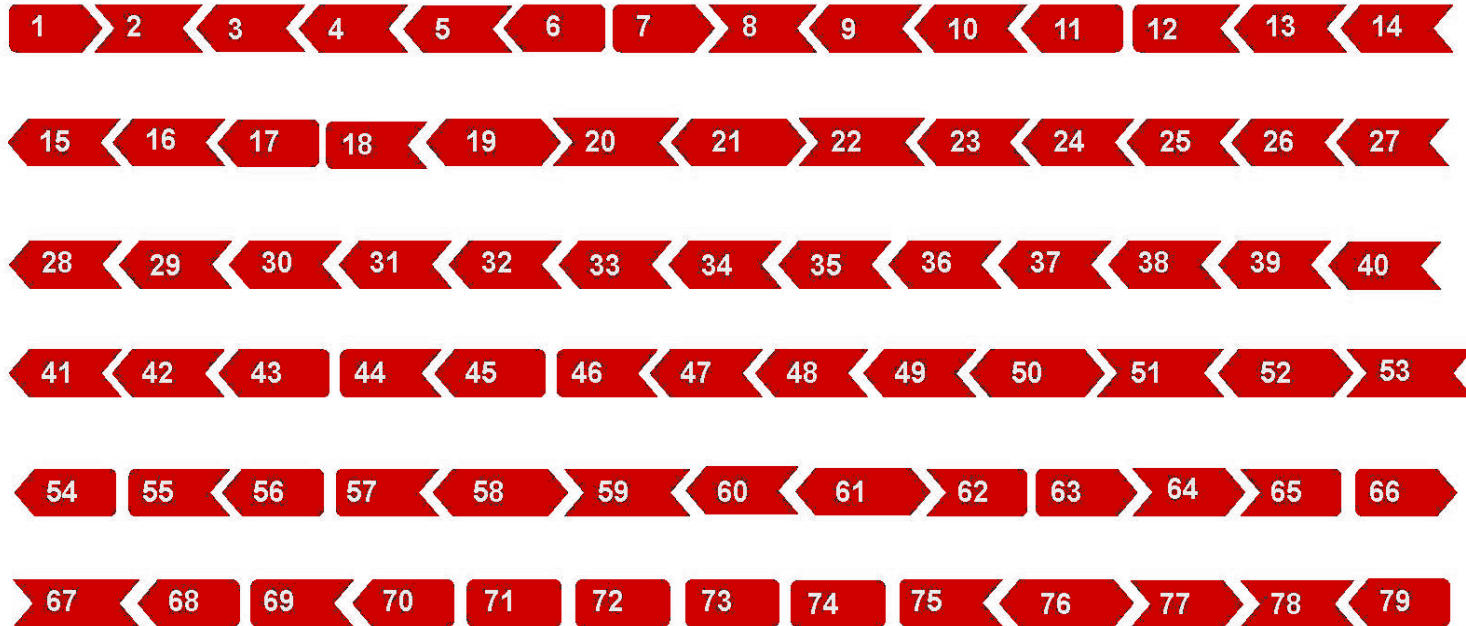


# Background: the *DMD* gene

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




# *DMD* Gene Exons



# Types of Changes in the *DMD* gene

- More than 4000 unique genetic changes (*aka* mutations, variants)
- Fall into categories



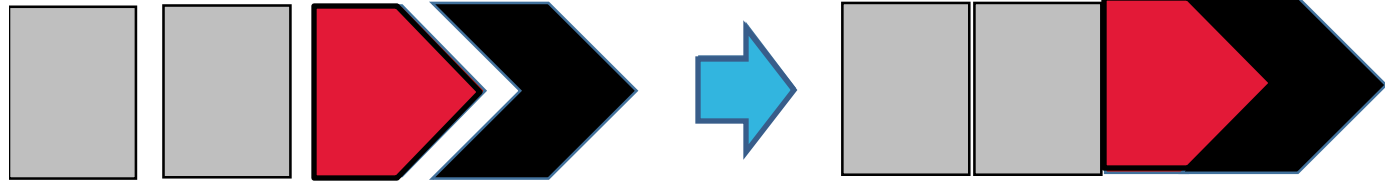
Type of Change	% of Duchenne cases	% of Becker cases
Large deletions	60-70%	80-85%
Large duplications	10%	5-10%
Point mutations and other small changes	15-30%	10-15%

# Types of Genetic Variants

The old dog ran too far.	Original
The old ____ ran too far.	Deletion
The old dog <b>dog</b> ran too far.	Duplication
The old.	Nonsense
The old dog ran too <b>fat</b> .	Missense
The old dog ran too <b>way</b> far.	Insertion

# Reading Frame Rule: What is supposed to happen.

Exons

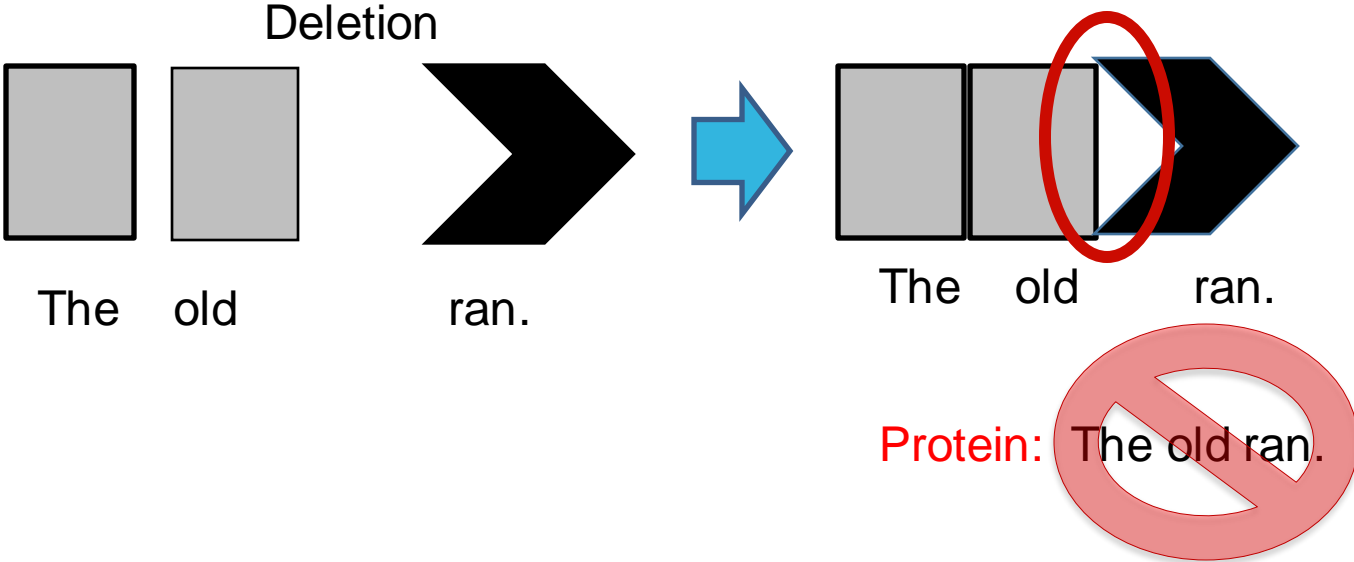


The old dog ran.

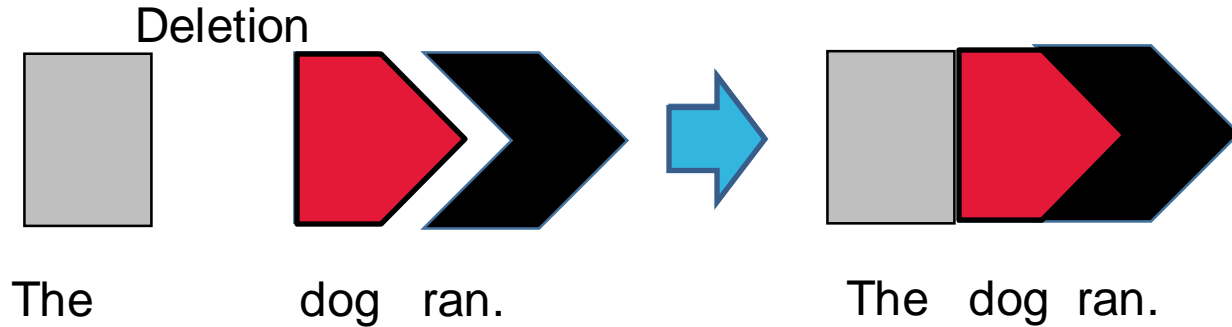
The old dog ran.

**Protein:** The old dog ran.

# Reading Frame: Out-of-Frame - Duchenne



# Reading Frame: In-Frame - Becker

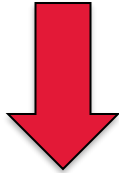


**Protein:** The dog ran.

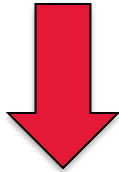


# Does my variant predict the severity?

Out of frame



No dystrophin



**Duchenne**

In frame



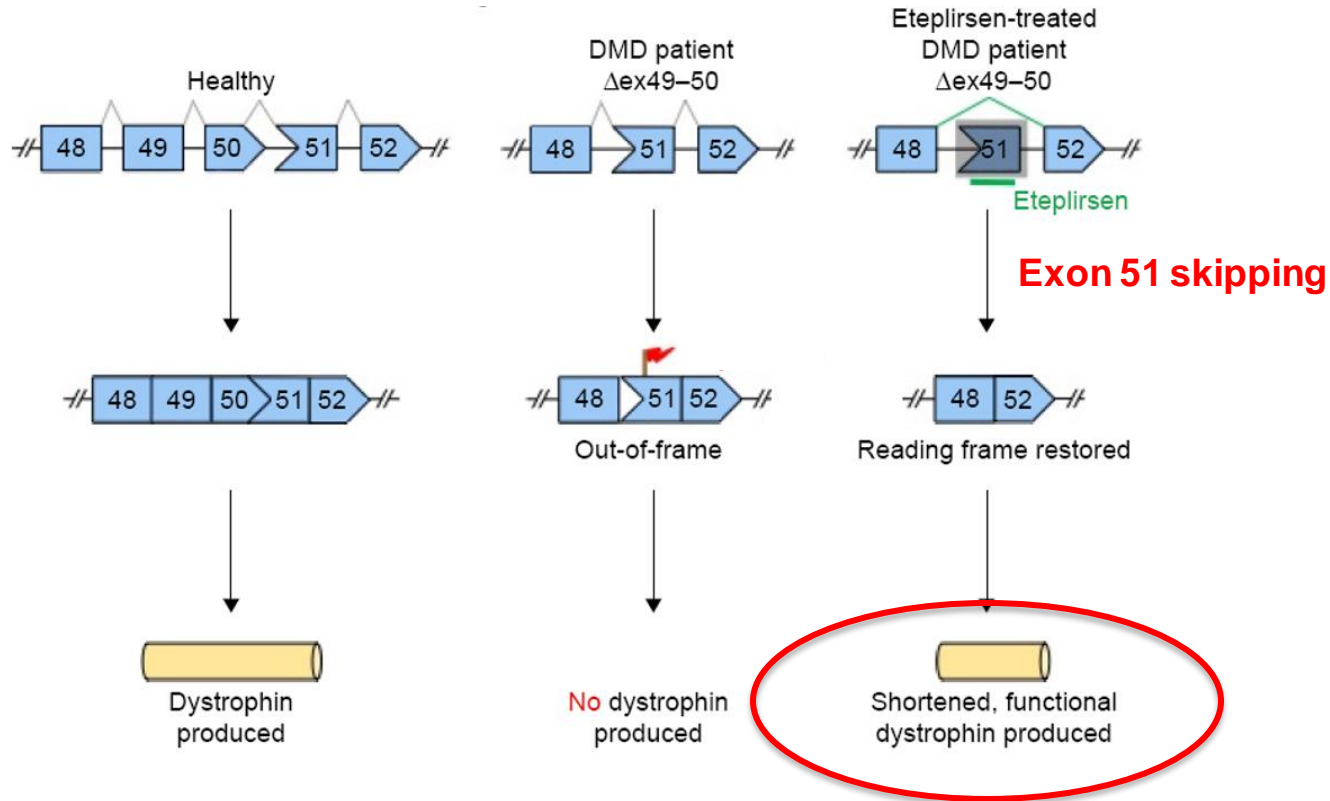
Partially functional dystrophin



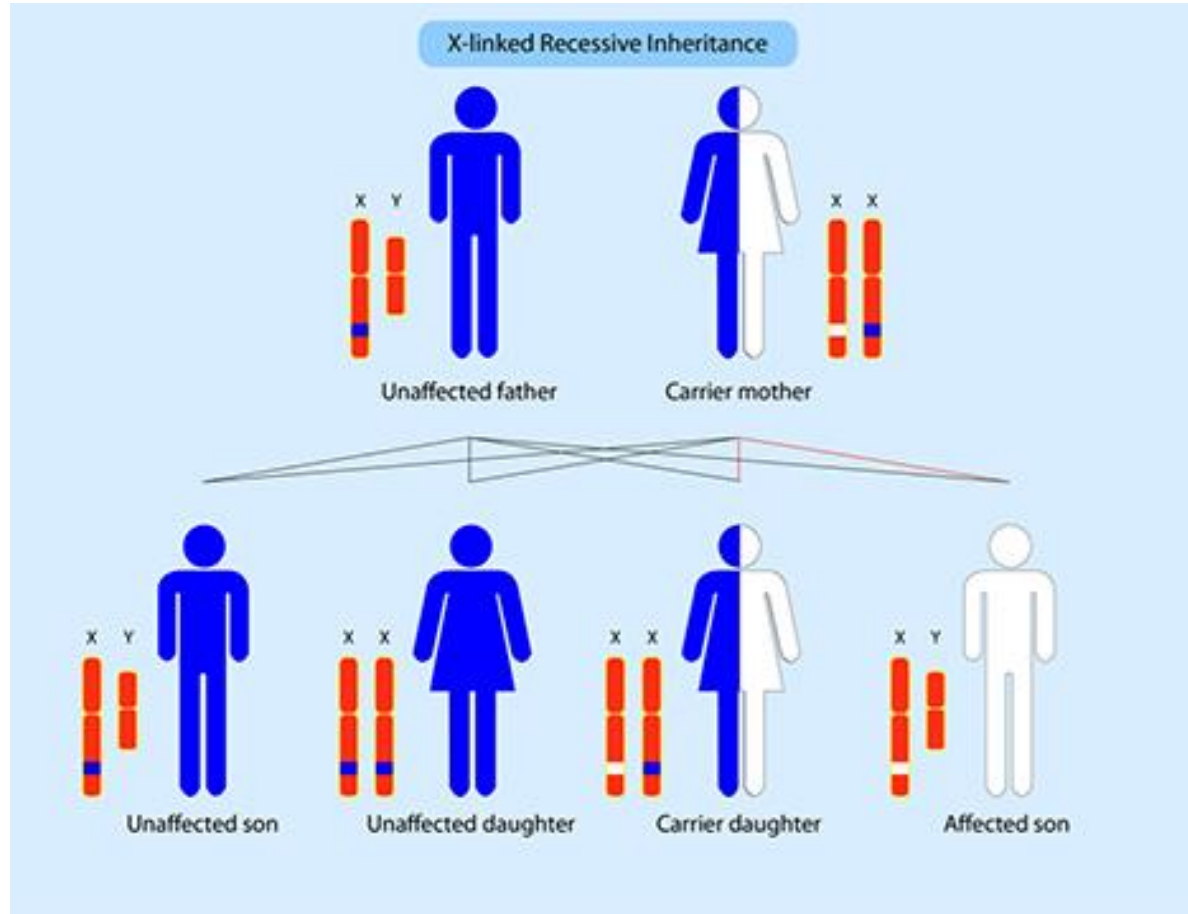
**Becker**

*Important – There are many exceptions to the reading frame rule!*

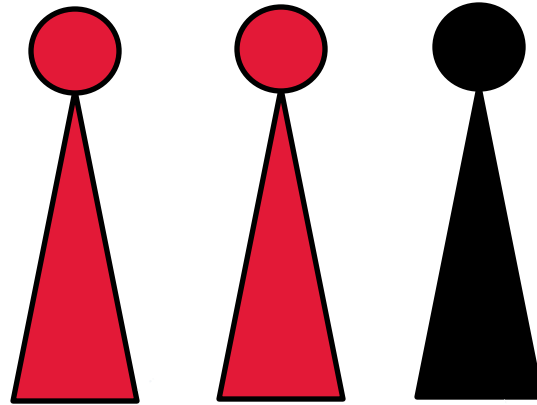
# Exon skipping therapies are based on the reading frame rule:



# X-linked Inheritance



If I don't have any family history of Duchenne, what are the chances that I'm a carrier?



2/3 or ~70% of boys with Duchenne have a mother who is a carrier

1/3 or ~30% of mothers are NOT carriers

# Why is it important to know if I'm a carrier?

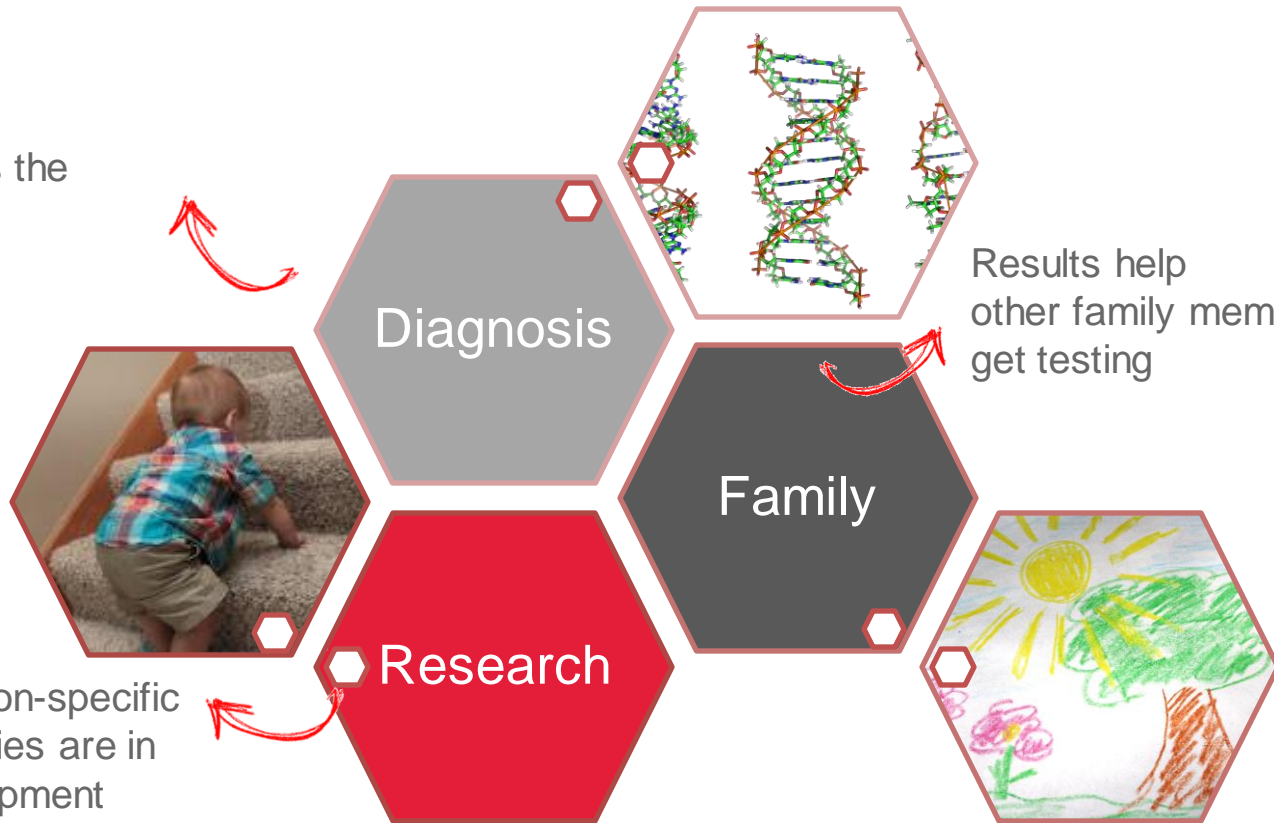
For your own health

For family planning

For your relatives

# *Genetic testing is also important for understanding which therapies and/or trials may benefit your child...*

Genetic testing is the gold standard for diagnosis



Results help other family members get testing

Mutation-specific therapies are in development

# Genetic Approaches to Therapies

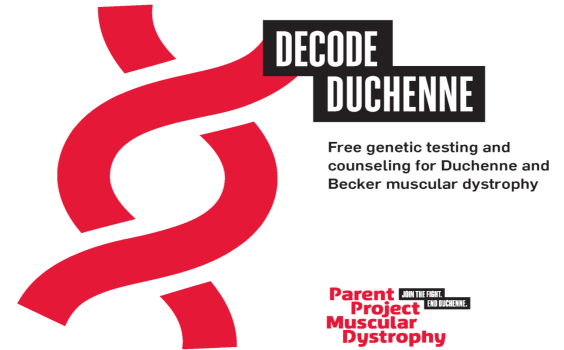
- **For Nonsense Variants:**  
Nonsense read-through
  - PTC Therapeutics (Translarna™)
- **For Deletions:**  
Exon skipping
  - Sarepta (exon 51: Exondys 51™)
  - Sarepta (exon 53: Vyondys 53™)
  - NS Pharma (exon 53: Viltepso™)
  - Sarepta (exon 45: Amondys 45™)
- **Gene Therapy**



# Roles of PPMD Genetic Counselors



**THE  
DUCHENNE  
REGISTRY**



**PP  
MD**





# DECODE DUCHENNE

Free genetic testing and  
counseling for Duchenne and  
Becker muscular dystrophy

**Parent Project  
Muscular  
Dystrophy** JOIN THE FIGHT.  
END DUCHENNE.



# DECODE DUCHENNE

## Criteria for

### Free Testing:

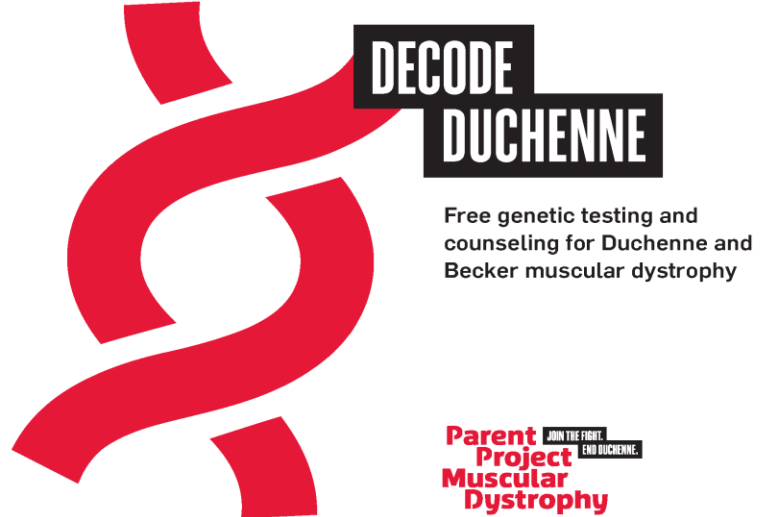
- ☑ Male with a confirmed or suspected diagnosis of Duchenne or Becker,  
**OR**  
*Female with a relative with Duchenne or Becker*
- ☑ Never had genetic testing OR previous genetic testing has not confirmed a variant
- ☑ Legal resident of US or Canada

### All testing performed at:



# Over 2,000 patients tested through the Decode Duchenne program!

- 1,500+ diagnostic testing
- 700+ carrier testing



# DuchenneRegistry.org

Parent  
Project  
Muscular  
Dystrophy

THE DUCHENNE REGISTRY

ABOUT

REPORTS

Join

A photograph of a woman with long dark hair kissing a young child on the cheek. The child is smiling and looking towards the camera. They are outdoors in a grassy area with buildings in the background.

**THE STRENGTH OF  
THE REGISTRY IS YOU**

Your data is critical in the fight to end Duchenne.

Join/Login >

# Our Impact

**5500+**

Registrations  
since launch

**115+**

Countries  
Represented

**15YRS**

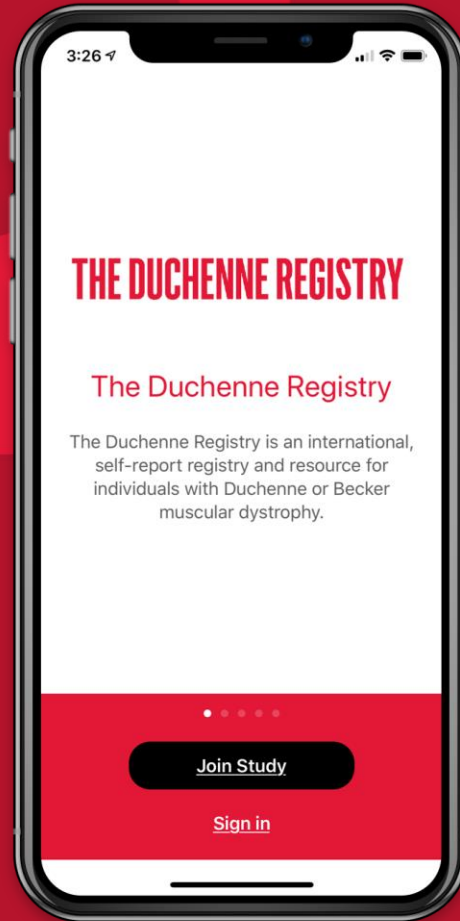
of Longitudinal  
Data

**100+**

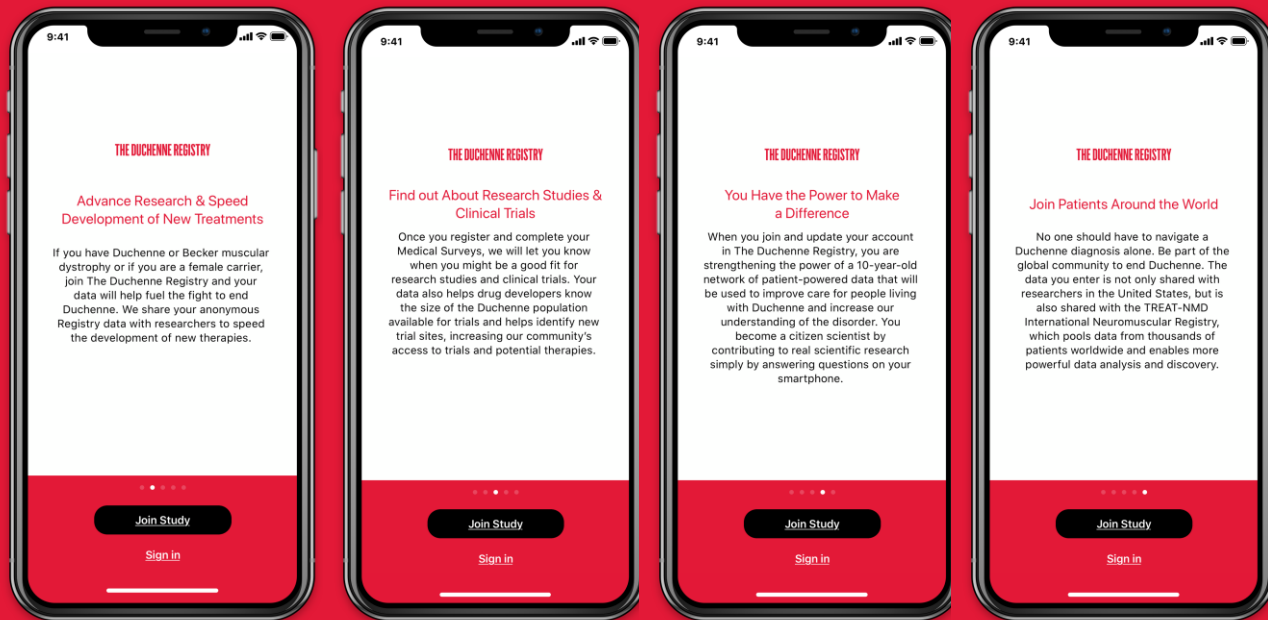
Trials & Studies  
Recruited



# The Duchenne Registry App



# The Duchenne Registry App



**Welcome Screens-  
Click Join Study!**

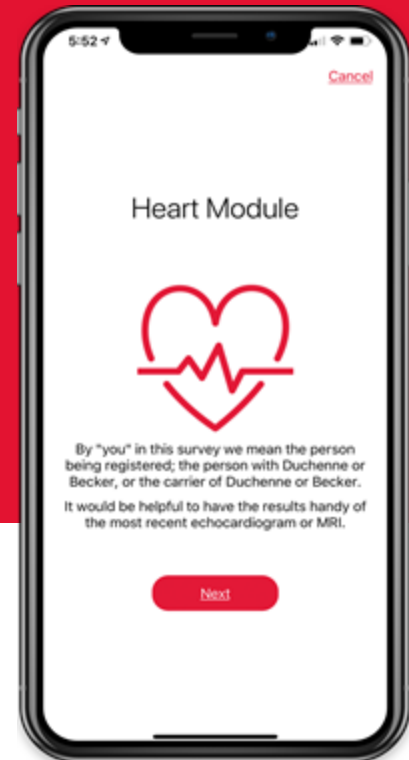
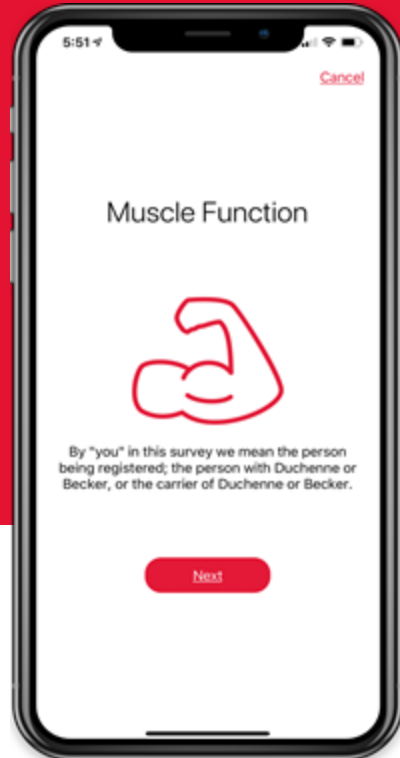
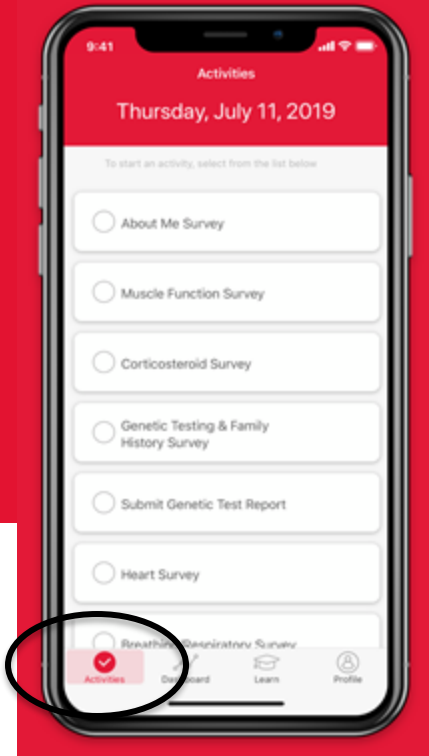
# The Duchenne Registry App

The image displays two sequential screens of the 'Consent' form on a smartphone. The left screen, titled 'Consent', contains the following text: 'By providing your name and signature, you confirm that you read the information contained herein and that you wish to take part in this research study.' Below this text are two input fields labeled 'First Name' and 'Last Name'. A 'Next' button is located at the bottom of the screen. The right screen, also titled 'Consent', contains the text: 'Signature' followed by 'By providing your name and signature, you confirm that you read the information contained herein and that you wish to take part in this research study.' Below this is the instruction: 'Please sign using your finger on the line below.' A handwritten signature is visible on a horizontal line. A 'Clear' button is positioned below the signature line, and a red 'Done' button is at the bottom of the screen.

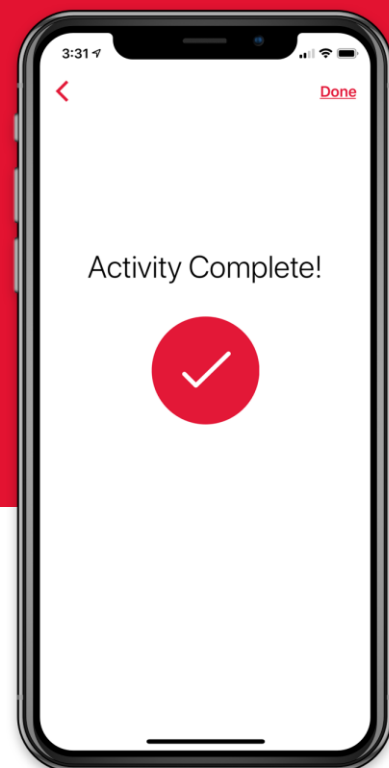
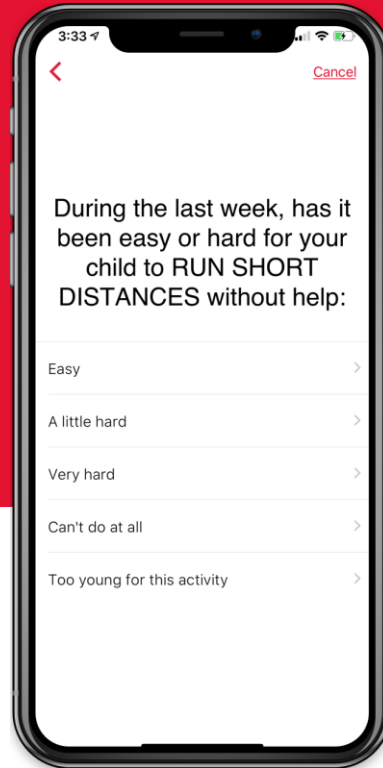
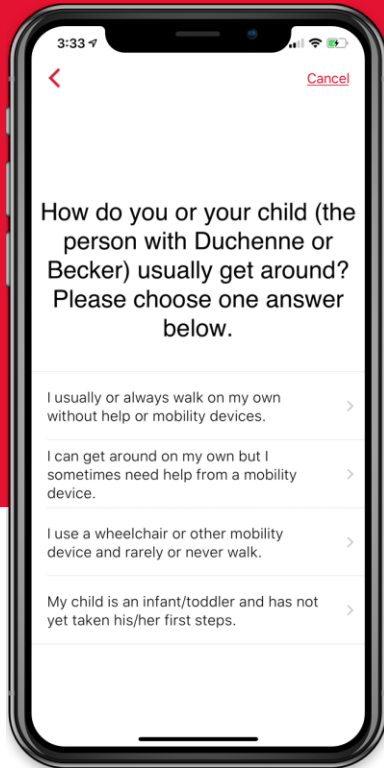
**E-Signature  
Consent Form**



# The Duchenne Registry App



# The Duchenne Registry App



# Why YOU should join the Registry

1. Be a citizen scientist
2. Get specific information on clinical trials and drug approvals
3. Better understanding of EVERYONE with Duchenne/Becker/Carriers



**Activation Code**  
needed to join!

You must first  
pre-register on our website.

Go to [www.DuchenneRegistry.org](http://www.DuchenneRegistry.org)

Click “**JOIN**”

Enter your email under Pre-Registration

Invitation email will come from  
[no-reply@threadresearch.com](mailto:no-reply@threadresearch.com), which  
will contain link & activation code.

#### Already Participating?

If you are an existing Duchenne Registry participant, your account will automatically be transferred over to the new Duchenne Registry Mobile App, powered by THREAD (the vendor working with The Duchenne Registry & PPMMD). You DO NOT need to pre-register below; you will receive an email invitation with a link to download the new mobile app. The email will include your Activation Code, which you will use to register within the app. Once you receive the email, please install and launch the app on your iPhone or Android phone. Tap “Join the Study” to begin the registration process. If you have any questions, do not receive your email invitation, misplace your Activation Code or need assistance in any way, please contact us at: [coordinator@duchenneregistry.org](mailto:coordinator@duchenneregistry.org) or 1-888-520-8675.

#### Joining for the First Time?

If you are joining The Duchenne Registry for the first time, there are 3 simple steps to begin your participation:

1. Complete the pre-registration form below.
2. You will receive an email invitation with a link to download The Duchenne Registry Mobile App. The email will also include your Activation Code, which you will use to register within the app
3. Install and launch the app on your iPhone or Android phone. Tap “Join the Study” to begin registration process.

\*If you are registering for more than one participant, you will need to repeat the above steps with a unique email address for each participant.

#### Pre-Registration (New Registry Participants only):

Email \*

Enter email

Confirm Email \*

Enter email

#### Please read the agreement below.

If you would like to continue with the registration process, you will need to agree to the following:

- Give your personal and contact information to THREAD™ (the vendor working with PPMMD of this study who created this website).
- Allow THREAD™ to confirm your identity by answering questions about yourself.
- Allow THREAD™ to use and share your personal and contact information (such as your name, date of birth, email address, phone number, and home address) with PPMMD.
- The website's Privacy Policy and Terms of Use.
- Allow THREAD™ to store your personal and contact information for a minimum of 7 years. After that time your information will be destroyed.
- You can change your mind and stop at any time during this initial screening process. If you change your mind contact the Duchenne Registry Coordinator at 1-888-520-8675.
- By clicking the agreement button below, I understand and agree to continue in the screening process and authorize the use of my personal information as stated above.

I agree to continue in the screening process

**Questions?**

**Reach out to Ann, Niki, Kayla**

**[coordinator@duchenneregistry.org](mailto:coordinator@duchenneregistry.org)**

**888-520-8675**