JAIN FOUNDATION | LGMD2B Dysferlinopathy Miyoshi

Clinical Outcome Study for Dysferlinopathy (COS)

Why do we call the disease Dysferlinopathy?

Dysferlinopathy means a disease that is caused by mutations in the dysferlin gene

Clinical diseases associate with mutations in dysferlin:

- **LGMD2B – weakness begins in the upper leg muscles**
- **Miyoshi Myopathy – weakness begin in the lower leg muscle**
- **Proximodistal – weakness begins in both the upper and lower legs**
- **DMAT – Distal Myopathy with anterior Tibial onset**

What is a Clinical Outcome?

Tests that measure disease progression that can be used in a clinical trial to determine whether or not a treatment is having any effect

What makes for a good clinical outcome?

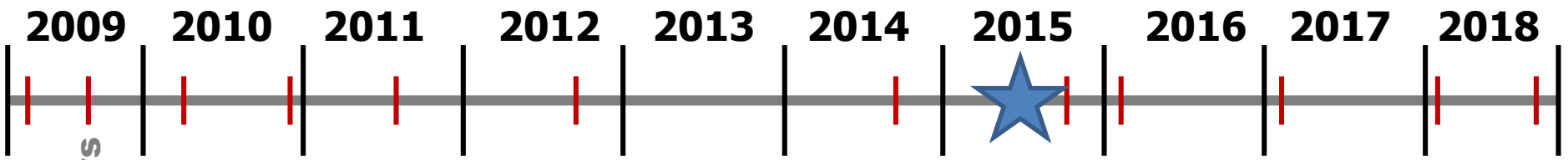
- **Can be consistently done the same way by different people**
- **When done multiple times, the variation in results is minimal**
- **Can measure a change in 6 m – 1 year**
- **Measures area affected in majority of individuals**

Why is a Clinical Outcome Study needed for Dysferlinopathy?

- Not much is known about the disease and how to measure it
- The clinical outcomes identified for other MD may not work the same way with all type of MD so the potential outcomes need to be tested in each type separately
- Having well defined clinical outcome measures for dysferlinopathy is essential for attracting the interest of the pharmaceutical industry to test their drugs on this disease

Timeline of the Clinical Outcome Study

It took almost 4 years from idea to first patient recruited



Mar – JF determined need for COS

June – JF brought together world leaders

Apr – Development of COS started

Dec – COS protocol finalized

Jul – COS site set-up begins

Sept– First COS particpant recruited

Oct – Last COS particpant recruited

Nov –1st person to complete study

Jan – All 1 year visits completed

Jan – All 2 year visits completed

Jan – Last person to complete study

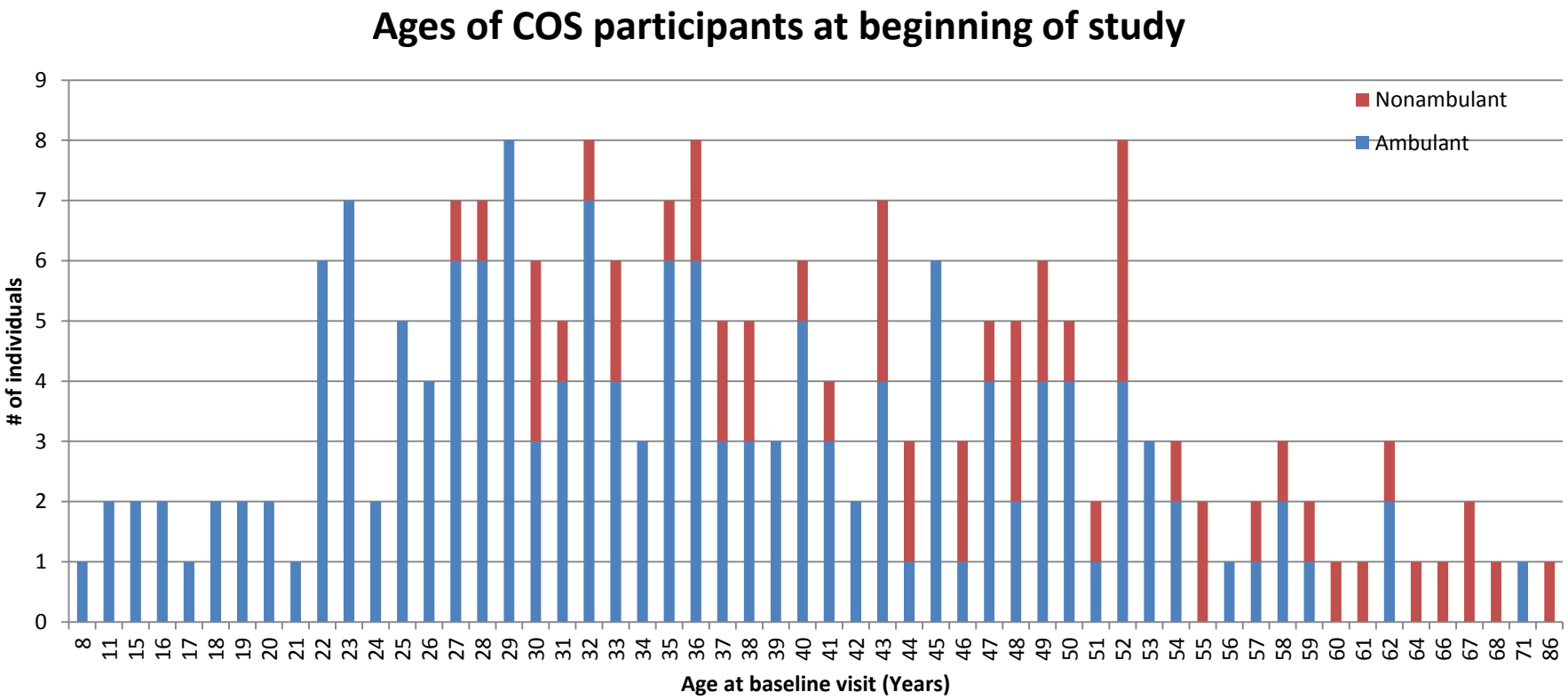
Dec – COS analysis complete

What is the purpose of COS?

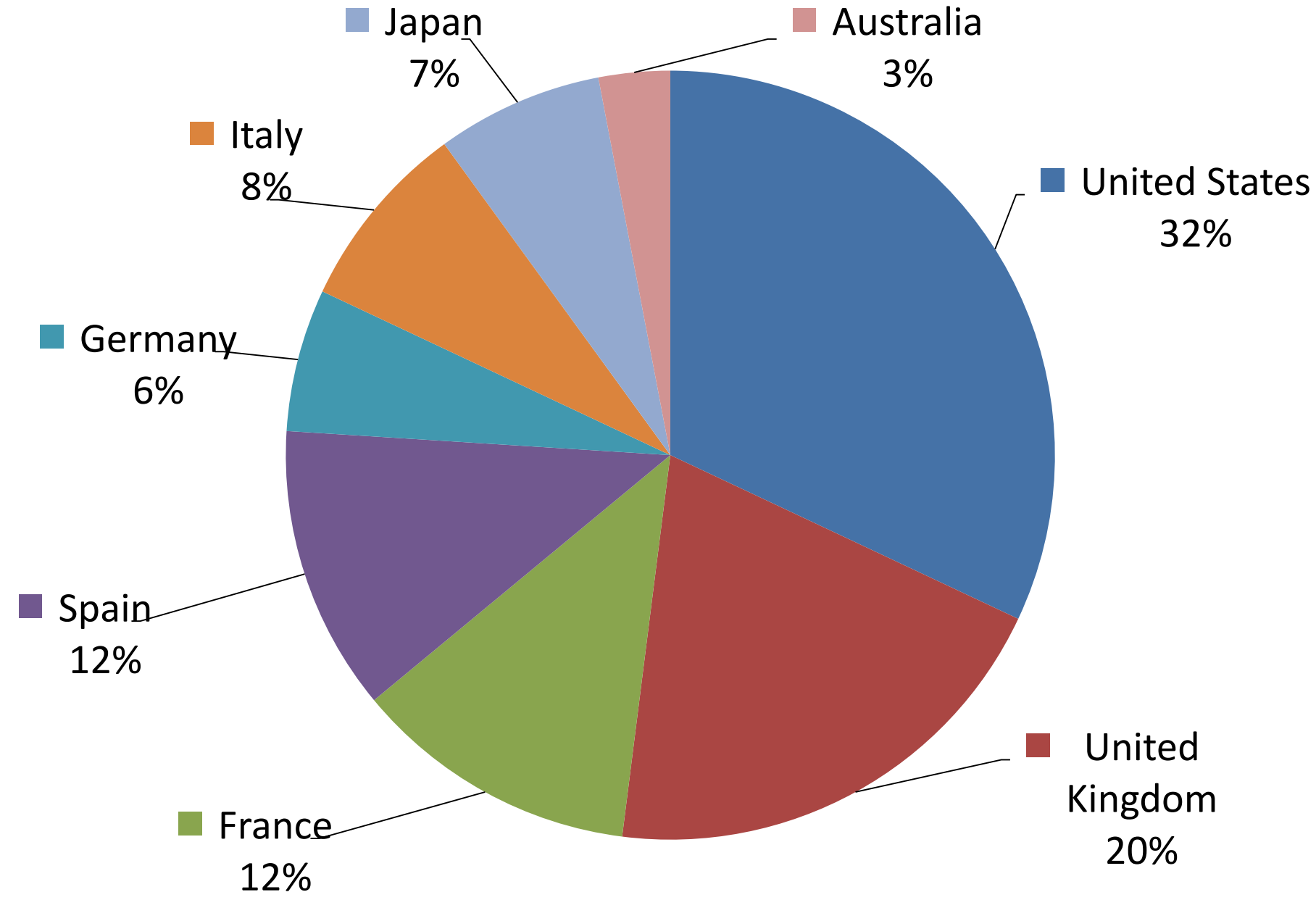
- To identify the best clinical outcomes for use in future clinical trials.
- To follow the normal course of the disease and see if it varies between individuals
- To identify a large group of genetically confirmed and clinically characterized dysferlinopathy patients
- To build an international network of clinical sites that are experts in dysferlinopathy
- To collect samples to use in additional experiments to better understand the disease

Who is in COS?

- 209 individuals genetically confirmed with dysferlinopathy
- Both ambulant (75%) and non-ambulant (25%)
- Males (48%) and females (52%)
- Ages: 8 to 86



Where are COS participants from?



What are we testing and why?

- **Visit schedule: 6 visits over 3 years**
  - Screening (100%)
  - Baseline (100%)
  - 6 months (96%)
  - 1 year (75%)
  - 2 year (12%)
  - 3 year (0%)

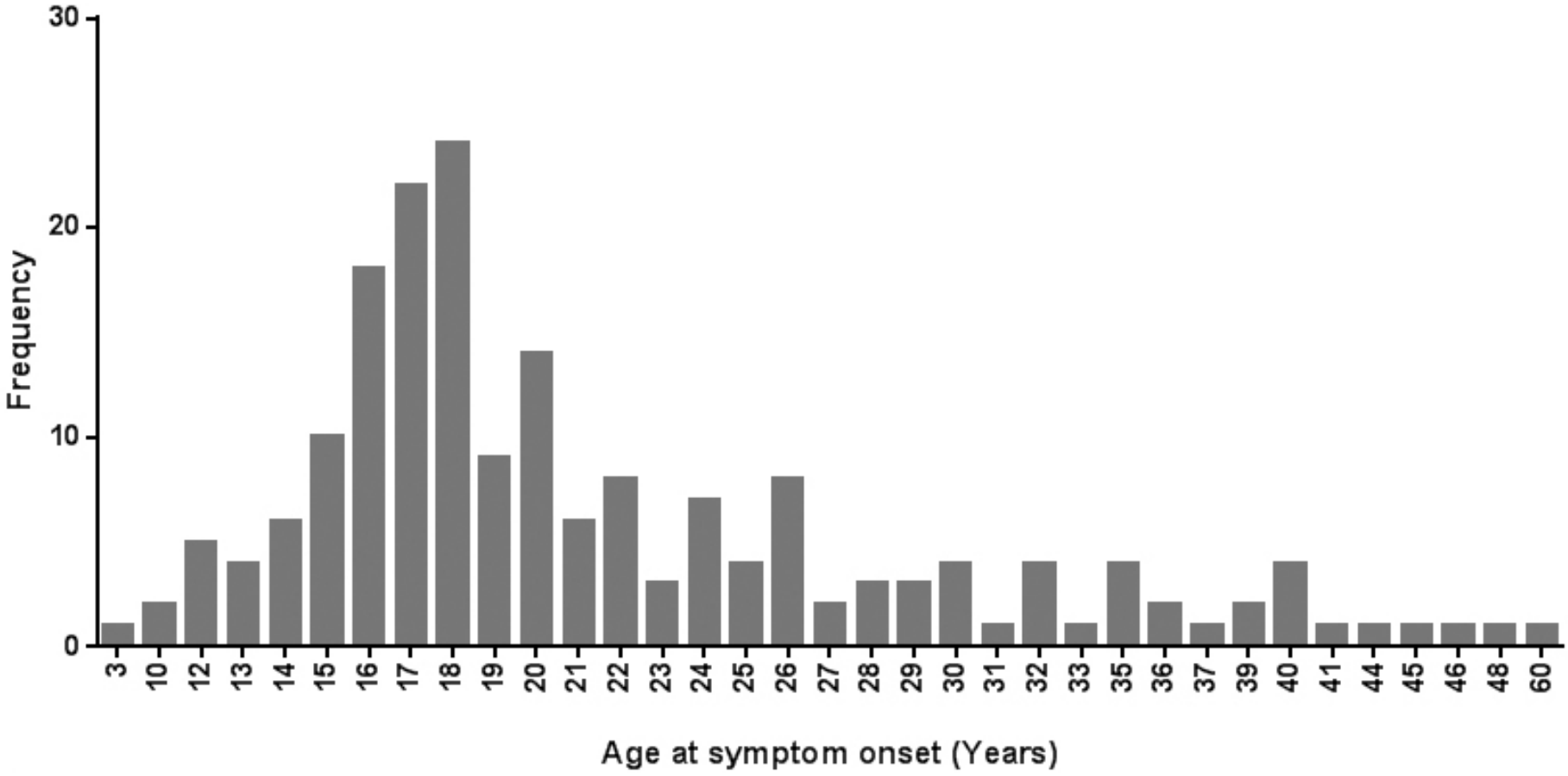
- **Evaluations**
  - Physiotherapy (muscle strength, timed evaluations, functional tests)
  - Quality of life questionnaire
  - Physical exam
  - Respiratory function
  - Cardiac studies
  - Blood tests
  - MRI/MRS imaging
  - Biobank samples

What are we learning?

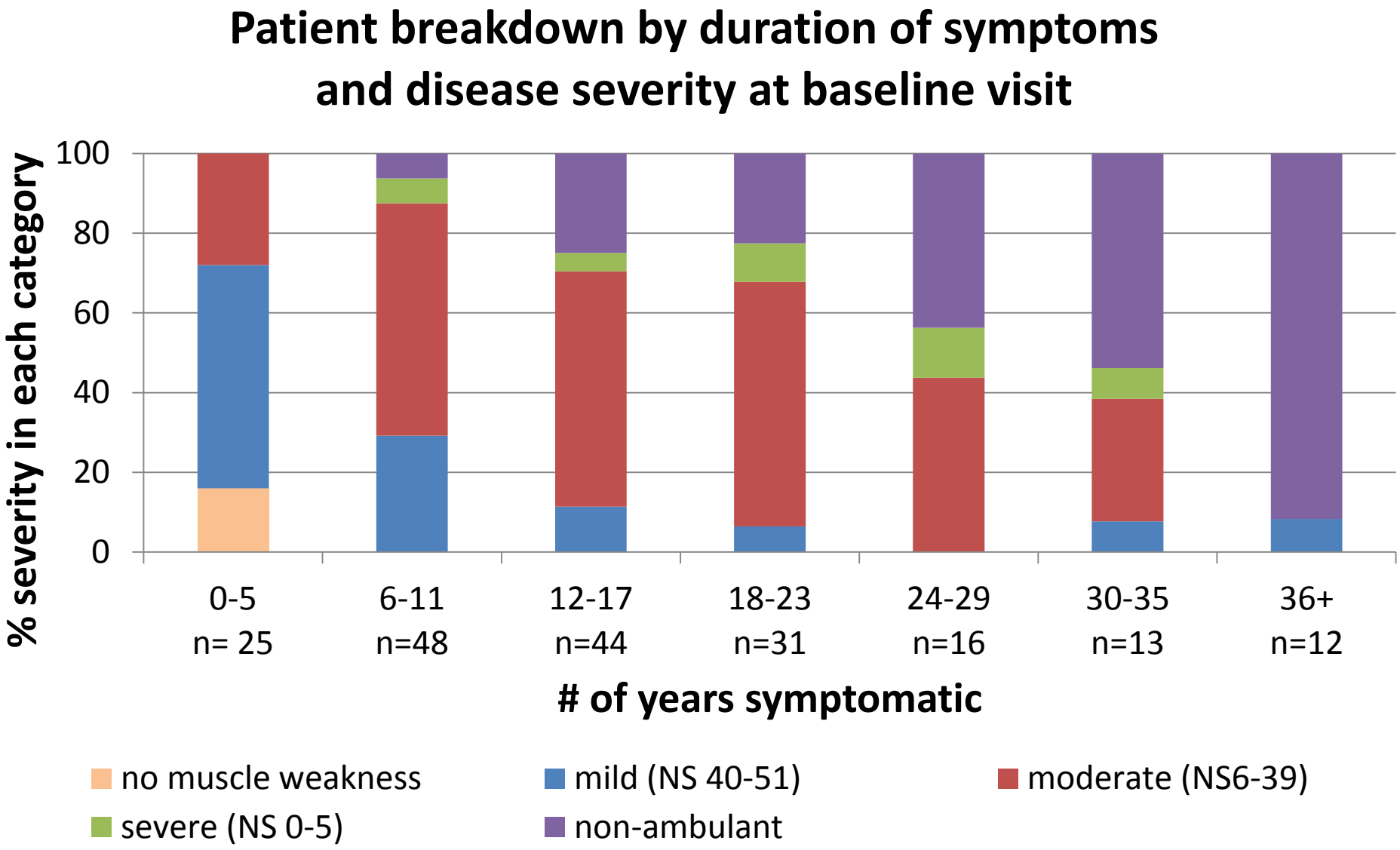
- **3 publications are already scheduled for 2015**
  - **Baseline paper – describing who is in the study and what we see initially**
  - **Physio analysis – describes how good the physio testing is at measuring dysferlinopathy and what changes need to be made**
  - **1 year progression – describing how the disease progresses over this time period and what tests appear to be able to measure a change**

- **Learnings so far…**
  - **MRI/MRS showing early changes and may be a good sensitive measure**
  - **Modifications are needed to the physio assessments to make them better at evaluating dysferlinopathy**
  - **Seeing some indication of possible respiratory issues so modifying evaluations to more accurately assess**
  - **Seeing differences in dysferlinopathy patients (onset, progression rate)**

Onset of muscle weakness



Disease progression variation



What are the next steps?

- Every COS participant completes all 6 visits and continues to stay involved beyond last COS visit
- Continue analyzing COS data as it becomes available
- Use collected biobank samples for additional research
- Use COS data to entice interest from industry
- Use COS data to inform design of future clinical trials
- Continue to identify individuals with dysferlinopathy
- Spread awareness of dysferlinopathy and the need for involvement of all of us in the development of a therapy

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