Myotonic Dystrophy Family Registry (MDFR)

Relationship between myotonic dystrophy type, disease severity, age of onset, and repeat length

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Introduction

Patient registries are databases designed to collect and organize information about populations defined by a specific disease or condition. They are invaluable tools for understanding the natural history of diseases, tracking patient outcomes, collating real-world evidence, identifying potential participants for research studies and clinical trials, and supporting the entire clinical trial process from pre- to post approval needs. Registries are especially crucial for rare diseases like myotonic dystrophy (DM), where gaps in knowledge persist, disease presentation is highly variable, and affected populations are often small, diverse, and geographically scattered.

To help overcome these barriers, the **Myotonic Dystrophy Family Registry** (MDFR) was launched in 2013. The MDFR is a patient-reported online database collecting information regarding the impact and scope of DM, from the perspective of patients and their families. Data gathered in the MDFR includes:

1. **Demographics**: contact information, diagnosis, and willingness to be contacted for trial opportunities.
2. **Symptoms**: motor function, cardiac, respiratory, GI, myotonia, fatigue, cataracts, pain, psychiatric/behavioral and malignancies.
3. **Quality of Life**: medical insurance coverage, employment, and disability impact on day-to-day living.

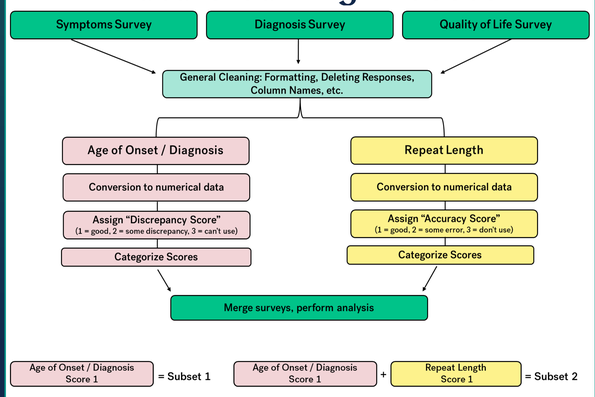
Objectives

Perform a rigorous analysis of MDFR data quality; describe demographics and test for possible relationships between disease type, disease severity, age of onset, and repeat length.

Methods

MDFR data entries gathered between February 2013 to July 2024 were compiled and analyzed. Following data cleaning, records were grouped into: **Subset 1:** participants with correctly reported diagnosis and matching age of symptom onset; **Subset 2:** participants with correctly reported diagnosis, matching age of symptom onset and a provided diagnostic test result with repeat length information.

Data Cleaning Process



Results

Table 1. Registry numbers by Subset grouping criteria

	Total N	CDM %	Juvenile DM1 %	Adult DM1 %	DM2 %
Subset 1	1680*	12.4	19.6	48.2	19.8
Subset 2	645**	21.5	5.1	64.8	8.6

*Represents 61 % of total Registry participants ** Represents 23.5 % of total Registry participants

Table 2. Demographics by Disease Sub-Type

	CDM	Juvenile DM1	Adult DM1	DM2
Current age (years)*	18.5 (9.3)	28.1 (9.0)	53.7 (12.4)	62.1 (12.8)
Male (%) Female (%)	54.2 45.8	46.5 53.5	43.1 56.9	36.5 63.5
Ethnicity – White (%)	85.6	93.0	92.0	93.8
Country USA (%)	86.4	81.2	81.7	92.7
Age of onset (years)*	Birth to 4 weeks**	8.1 (4.1)	33.9 (11.9)	35.5 (14.5)
First person in family given diagnosis (%)	58.5	25.4	42.5	56.3
BMI male BMI female*	18.3 ± (6.0) 18.5 ± (6.2)	20.3 (4.8) 21.6 (5.0)	25.8 (5.0) 24.6 (5.6)	26.4 (5.7) 26.7 (6.1)
Age at enrollment. M, F	9.8 (8.7) 11.2 (10.8)	22.2 (9.1) 19.4 (8.4)	49.6 (12.4) 45.8 (12.2)	57.1 (13.8) 56.4 (13.8)

Table 2: Subset 2, living participants. CDM n=118, Juvenile n=71, DM1 n=339, DM2 n=96.
* Results expressed as Mean (SD). ** 92.3% of responses. BMI at time of enrollment

Figure 1. Global distribution of Registry participants

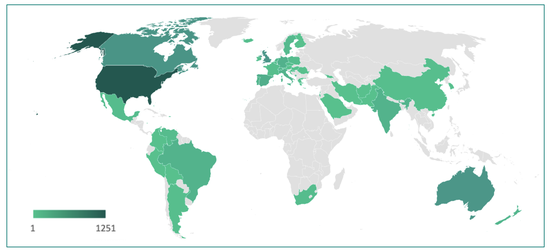
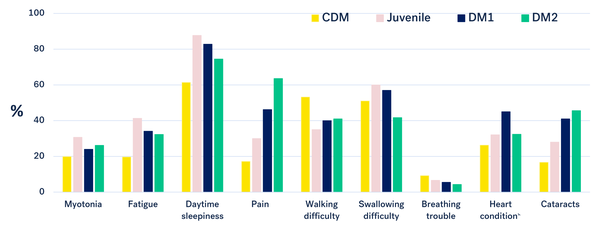


Figure 2. Symptom prevalence by disease type



Myotonia and Fatigue reported as "severe negative effect on normal daily activities". Pain: survey asked how much pain interfered with enjoyment of life, "very much" and "quite a bit" responses were combined. Difficulty walking: "yes, most or all the time" responses are shown. For all other symptoms/diagnoses, the "yes" responses are shown.

Table 3. Symptom as a function of age and repeat length

	DM1				DM2	
	Age (mean)		Repeat Length (mean)		Age (mean)	
Question	No	Yes	No	Yes	No	Yes
Do you have difficulty walking?	50.9	59.4	199.0	388.0	56.8	68.9
Does myotonia currently have a negative effect on your normal daily activities	57.2	55.4	217.3	416.4	67.8	60.9
Have you been diagnosed with a heart condition?	51.5	58.2	265.2	313.6	60.0	66.5
Have you had an operation to implant a device to control or normalize your heart rhythm?	52.7	61.7	278.8	331.7	61.8	65.4
Do you currently take any medication(s) to treat or protect your heart?	53.3	57.6	278.3	326.8	60.3	67.4
Do you have trouble breathing?	53.5	56.3	263.9	326.8	61.4	59.5
Do you have difficulty swallowing?	52.2	56.2	267.5	303.5	64.4	59.2
Do you have a tube for feeding	54.4	67.0	287.4	245.8	62.1	NA
Do you have trouble with your vision due to cataracts?	52.4	56.4	287.3	290.8	57.4	68.2
Have you had eye surgery for cataract removal?	49.7	59.6	314.8	248.2	56.2	68.5
Do you experience daytime sleepiness?	56.1	53.7	225.5	301.2	64.7	61.5
Does daytime sleepiness currently have a negative effect on your normal daily activities?	54.3	51.5	239.4	351.4	70.1	55.8
Does fatigue currently have a negative effect on your normal daily activities?	54.8	55.1	215.9	359.2	63.9	57.9
How much does pain interfere with your enjoyment of life?	53.0	52.6	229.9	418.2	62.3	58.9
Have you ever been diagnosed with a benign tumor?	52.6	54.9	287.3	302.2	60.0	64.9
Have you ever been diagnosed with any type of cancer?	52.7	58.3	293.7	246.0	60.5	67.12

Highlighted cell indicate significant difference between "No" and "Yes" groups, $p < 0.05$

Figure 3. Symptoms progression in adult DM1 and DM2

Summary

- Aggregate data show the prevalent symptom in DM1 and DM2, is daytime sleepiness (76.6% total respondents), followed by difficulty swallowing and difficulty walking. As many as 63.6% of DM2 patients experience high levels of pain
- Symptoms gradually increase with age, both in DM1 and DM2
- Higher repeat length numbers in DM1, correlate with more severe symptoms
- >2700 participants from >50 countries enrolled in the MDFR from March 2013 to July 2024
- 61% of total enrollees reported DM diagnosis and matching age of symptoms onset
- 23.5 % of total enrollees reported DM diagnosis, matching age of symptoms onset and provided diagnostic test result with repeat length information
- ~ 80% of participants are from United States
- On average, 45.7% of participants are the first in their families to receive a DM diagnosis

Conclusions

- The Myotonic Dystrophy Family Registry is an important tool to collect information on the impact and scope of myotonic dystrophy from the perspective of patients and their families
- Well curated data can be used to analyze and detect significant relationships between DM type, disease severity, age of onset, and repeat length
- Self-reported patient data requires stringent quality control to ensure high reliable dataset

Take home message

By participating in the Myotonic Dystrophy Family Registry, DM affected individuals can help:

- The community at large to learn more about the impact and scope of MD
- Speed up research by providing critically needed information to scientists
- Facilitate patient stratification and identification for clinical trials and studies

Learn more at
https://myotonicregistry.patientcrossroads.org/

Contact the Myotonic Dystrophy Family Registry Coordinator

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