Update on Myotonic Dystrophy Type-2 Research
(University of Rochester)

2016 MDF Annual Conference
Chad Heatwole, MD, MS-CI
“Myotonic Dystrophy is perhaps the most variable of all human disorders.”

Peter S. Harper, PhD
Professor of Human Genetics
Cardiff, United Kingdom
Important First Question:

- What symptoms and issues have the greatest impact on myotonic dystrophy type-2 (DM2) patients’ lives?
Patient Reported Impact of Symptoms for Myotonic Dystrophy Type-2 (PRISM-2)
Patient-Reported Impact of Symptoms in Myotonic Dystrophy Type 2 (PRISM-2)

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ABSTRACT

Objective: To determine the frequency and relative importance of the most life-affecting symptoms in myotonic dystrophy type 2 (DM2) and to identify the factors that have the strongest association with these symptoms.

Methods: We conducted a cross-sectional study of adult patients with DM2 from a National Registry of DM2 Patients to assess the prevalence and relative importance of 310 symptoms and 21 symptomatic themes. Participant responses were compared by age categories, sex, educational attainment, employment status, and duration of symptoms.

Results: The symptomatic themes with the highest prevalence in DM2 were the inability to do activities (94.4%), limitations with mobility or walking (89.2%), hip, thigh, or knee weakness (89.2%), fatigue (89.2%), and myotonia (82.6%). Participants identified the inability to do activities and fatigue as the symptomatic themes that have the greatest overall effect on their lives. Unemployment, a longer duration of symptoms, and less education were associated with a higher average prevalence of all symptomatic themes ($p < 0.01$). Unemployment, a longer duration of symptoms, sex, and increased age were associated with a higher average effect of all symptomatic themes among patients with DM2 ($p < 0.01$).

Conclusions: The lives of patients with DM2 are affected by a variety of symptoms. These symptoms have different levels of significance and prevalence in this population and vary across DM2 subgroups in different demographic categories. Neurology® 2015;85:2136-2146
The Goldberg Nathan Foundation for Myotonic Dystrophy Type-2 Research at the University of Rochester
Specific Aim

- To use direct patient input to identify the symptoms that are **most common** to adult myotonic dystrophy type-2 patients.
- To use direct patient input to identify the symptoms that are **most important** to adult myotonic dystrophy type-2 patients.
Phase 1:

- 15 DM2 patients were interviewed and were asked what aspects of DM2 have the highest impact on their lives
Results

- 943 direct quotes were coded
- 310 potential high-impact DM1 symptoms were identified
- 21 major symptomatic themes
Symptomatic Themes

- Myotonia
- Activity limitation
- Limitations with mobility or walking
- Impaired sleep or daytime sleepiness
- Problems with shoulders or arms
- Back, chest, or abdominal weakness
- Problems with choking and swallowing
- Decreased satisfaction in social situations
- Difficulty thinking
- Difficulty with medication side effects
- Pain
- Hip, thigh, or knee weakness
- Gastrointestinal issues
- Problems with hands or fingers
- Problems with vision, hearing, or smell
- Impaired body image
- Decreased performance in social situations
- Emotional issues
- Communication difficulties
- Issues having children
Phase 2: Cross Sectional Validation Study

- All eligible DM2 registry patients were sent questions (in survey form) regarding 310 specific symptoms and 21 major themes of health identified through phase 1.
- For each symptom participants answered if they had the symptom (and if so how much impact it had on their life).
- Participants also provided their gender, age, time since symptoms started, employment status, and education level.
Participants

- 21 or older
- DM2 Members of the National Registry of DM and FSHD Patients and Family Members
Directions: Please check the box that applies to you for each item.

9. How much does the following impact your life?

<table>
<thead>
<tr>
<th></th>
<th>I don’t experience this</th>
<th>I experience this but it does not affect my life</th>
<th>It affects my life a little</th>
<th>It affects my life moderately</th>
<th>It affects my life very much</th>
<th>It affects my life severely</th>
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DM2 Results:

- 74 DM1 patients participated (62% response rate)
- 31 states represented
- White, Black, Asian, American Indian/Alaska Native, and Latino Americans were represented
- In total patients replied to over 12,713/13,008 questions (97.7%)
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<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients studied</th>
<th>Sex, no. (%)</th>
<th>Age in years</th>
<th>Responded by paper survey, no. (%)</th>
<th>Race, no. (%)</th>
<th>Stated that they had a genetic test for DM2, no. (%)</th>
<th>Employed, no. (%)</th>
<th>Level of education completed, no. (%)</th>
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<td>Age in years Mean (SD) 57.0(12.0)</td>
<td>74 (100.0)</td>
<td>White 73 (98.7)</td>
<td>Yes 67 (90.5)</td>
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<td>Master's or doctorate 24 (32.4)</td>
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<td>Other 1 (1.4)</td>
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† Number of times the question was left unanswered by study participants
Prevalence of Symptomatic Themes

- Inability to Do Activities
- Fatigue
- Hip Thigh or Knee Weakness
- Limitations with Mobility or Walking
- Myotonia
- Pain
- Gastrointestinal Issues
- Impaired Sleep or Daytime Sleepiness
- Problems with Hands or Fingers
- Problems with Shoulders or Arms
- Back Chest or Abdominal Weakness
- Problems with Vision, Hearing, or Smell
- Changed Body Image Due to Disease
- Problems Choking or swallowing
- Decreased Performance in Social Situations
- Emotional Issues
- Decreased Satisfaction in Social Situations
- Difficulty Thinking
- Communication Difficulties
- Difficulty with Medication Side Effects
- Issues Having Children
The Themes that have the Greatest Impact on Patients

- 0: No impact
- 1: Impacts one’s life a little
- 2: Affects one’s life moderately
- 3: Affects one’s life very much
- 4: Affects one’s life severely
Relative Impact of Symptomatic Themes

- Fatigue
- Inability to Do Activities
- Impaired Sleep or Daytime Sleepiness
- Hip Thigh or Knee Weakness
- Limitations with Mobility or Walking
- Issues Having Children
- Back Chest or Abdominal Weakness
- Pain
- Problems with Vision, Hearing, or Smell
- Gastrointestinal Issues
- Decreased Satisfaction in Social Situations
- Difficulty Thinking
- Problems with Shoulders or Arms
- Decreased Performance in Social Situations
- Myotonia
- Problems with Hands or Fingers
- Difficulty with Medication Side Effects
- Emotional Issues
- Changed Body Image Due to Disease
- Communication Difficulties
- Problems Choking or swallowing
Most Prevalent DM2 Symptoms

- Difficulty getting up from the floor or ground (100%)
- Leg weakness (100%)
- Difficulty squatting down (100%)
- Difficulty walking up hills or inclines (100%)
- Difficulty rising from a seated position (97.4%)
- Impaired walking (97.4%)
- Difficulty with stairs (97.4%)
- The inability to run (97.4%)
- Difficulty with balance (97.3%)
- Difficulty with rough ground (97.2%)
Prevalence of Cognitive Symptoms in DM2

- Trouble finding the right word
- Decreased ability to think fast
- Memory deficits
- Decreased motivation
- Problems concentrating
- Requirement for increased planning
- Not able to focus
- Disorganization
- Cognitive fatigue
- Reduced decision making abilities
- Difficulty with comprehension
- Problems reading
- Confusion
- Being in a dream like state
- Difficulty with math
- Learning difficulties
- Inability to keep appointments
- Visual spatial difficulties
DM2 Subgroup Analysis (Prevalence)

- No difference based on gender
- Participants older than 60 had a higher prevalence of pain ($p = 0.04$)
- Participants who had a college degree had problems with their shoulders and arms less frequently than those without a college degree ($p = 0.03$).
- Participants with a longer duration of symptoms were more likely to report fatigue ($p < 0.01$), limitations with mobility or walking ($p = 0.02$), or problems with shoulders or arms ($p = 0.04$).
Figure 2: Prevalence of Symptomatic Themes by Employment Status

* Signifies P < 0.05
DM2 vs DM1

- pain (DM2: 79.7%; DM1: 74.0%)
- inability to do activities (DM2: 94.4%; DM1: 84.6%)
- difficulty thinking (DM2: 61.6%; DM1: 55.2%)
- limitations with mobility or walking (DM2: 89.2%; DM1: 85.0%)
Key Points from PRISM-2

- There are many issues and symptoms that have a varying level of impact on DM2 patients’ lives
- The most frequently occurring (or described) issue is not always the one that is most important to patients
- Pain is an important symptom that progresses with DM2 age
- Employment status is highly associated with disease burden in DM2
Utility of PRISM-2

- May help physicians better identify and address areas of importance to patients
- Provides an estimate of expected progression of disease in DM1
- Provides base information for the creation of a custom designed instrument to measure patient-relevant outcomes during upcoming clinical trials (MDHI2)
Teaching Video NeuroImages: Trapezius myotonia percussion sign in myotonic dystrophy type 2
Nicholas E. Johnson and Chad R. Heatwole
Neurology 2013;80:e251
DOI 10.1212/WNL.0b013e318296e905
A New Clinical Sign for DM2
Ongoing Research
Study of Pathogenesis and Progression in DM (ST OPP DM)

- Studying 40 patients with DM2
- Patients evaluated at baseline, 1 year, and 3 year in Rochester, NY
- Evaluating strength, muscle function, myotonia, EKG, patient reported disease burden, muscle mass, laboratory data, genetic biomarkers
- Muscle biopsy, EMG
Purpose

- Learn more about how myotonic dystrophy type-2 changes over time
- Develop clinical trial infrastructure in preparation for therapeutic trials
- Identify factors that modify disease
Contact Information

- Jeanne Dekdebrun, Elizabeth Luebbe (Vending Area)
- 585-276-4611
- Jeanne_Dekdebrun@urmc.rochester.edu
National Registry for Myotonic Dystrophy & Facioscapulohumeral Dystrophy
National Registry for Myotonic Dystrophy & Facioscapulohumeral Dystrophy

- Registry designed to study patients with DM1, DM2, and FSHD patients over time
- 203 verified DM2 patients (1152 DM1 patients)
- In existence for 16 years
- Utilized as a mechanism to contact patients for potential involvement in clinical trials
- Medical records are reviewed prior to inclusion in the registry
Contact Information

- dystrophy_registry@urmc.rochester.edu
- Jim Hilbert/ Liz Luebbe
- 1-888-925-4302
- Vending Area
- Clinicaltrials.gov (NCT00082108)
Join the Myotonic Dystrophy Family Registry today - help us better understand and improve the lives of the people and families living with DM.

**BENEFIT:**

- You will learn about clinical trials for which you or your affected family member(s) may be eligible.
- You can see graphs and charts of the anonymous data, any time you want, by simply logging into and searching the Registry’s anonymous (de-identified) data.

www.myotonicregistry.org
Thank You

Nicholas Johnson, MD
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Robert Holloway, MD, MPH
Charles Thornton, MD
Robert Griggs, MD
James Hilbert, MS
Tracy Forrester
Liz Luebbe
Nuran Dilek
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Rita Bode, Ph.D. (PROMIS Network)
David Victorson, Ph.D. (NeuroQol Network)
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Giovanni Meola, MD (Milan, Italy)
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Anné-Berit Ekstroem, MD, PhD (Queen Silvia Children’s Hospital, Sweden)

The Goldberg Nathan Foundation for Myotonic Dystrophy Type-2 Research

MD Cooperative Research Center
National Institutes of Health
U.S. Department of Health and Human Services

The Neuromuscular Institute of Quality-of-Life Studies and Outcome Measure Development

National Institutes of Health, Department of Health and Human Services