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

2016 MDF Annual Conference

Chad Heatwole, MD, MS-CI

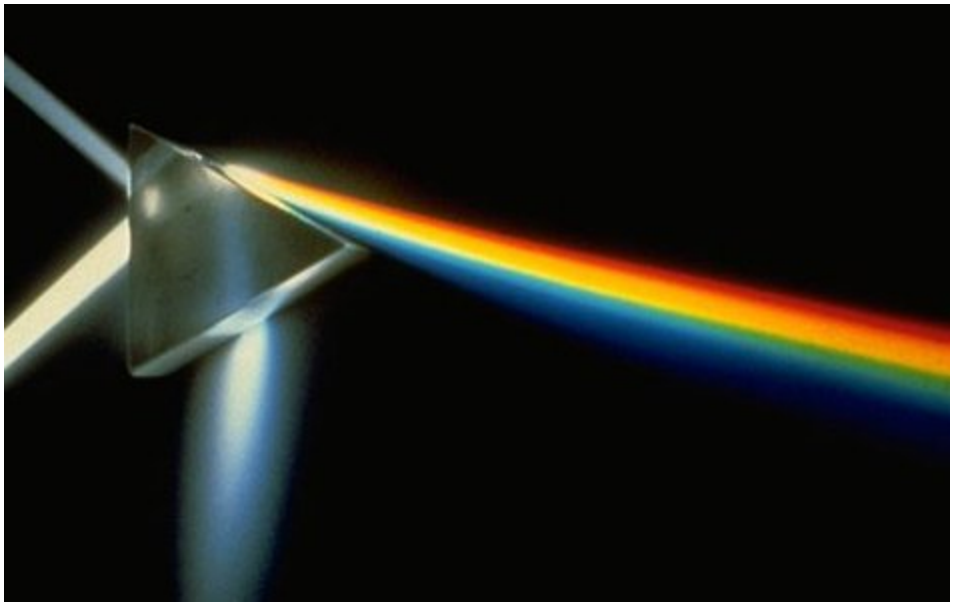
"Myotonic Dystrophy is perhaps the most variable of all human disorders."

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

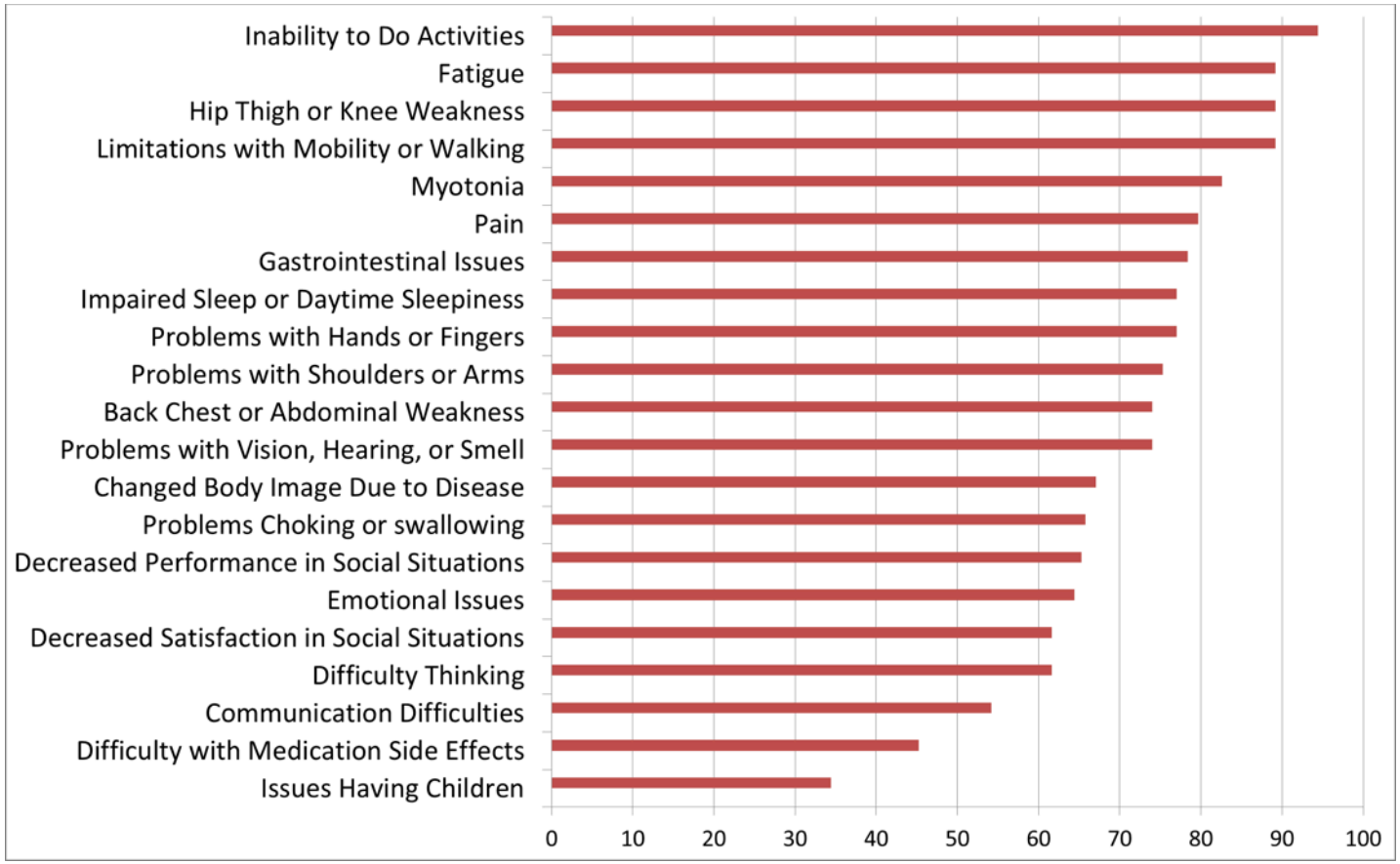
Directions: Please check the box that applies to you for each item.						
9. How much does the following impact your life?	I don't experience this	I experience this but it does not affect my life	It affects my life a little	It affects my life moderately	It affects my life very much	It affects my life severely
a.) Limitations with mobility or walking						
b.) Problems with hands or fingers						
c.) Emotional issues						
d.) Difficulty thinking						
e.) Decreased satisfaction in social situations						
f.) Decreased performance in social situations						
g.) Inability to do activities						
h) Fatigue						
i.) Pain						
j.) Problems eating						
k.) Communication difficulties						
l.) Problems with shoulders or arms						
m.) Back, chest, or abdomen weakness						
n.) Changed body image due to disease						
o.) Problems with physical health						

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%)

Table 1. Clinical and Demographic Information of Phase II Myotonic Dystrophy Type-2 Respondents from the National Registry	
Characteristic	
No. of patients studied	**74**
Sex, no. (%)	
Male	**26 (35.1)**
Female	**48 (64.9)**
Age in years	
Mean (SD)	**57.0(12.0)**
Range	**27-82**
Responded by paper survey, no. (%)	**74 (100.0)**
Race, no. (%)	
White	**73 (98.7)**
Other	**1 (1.4)**
Stated that they had a genetic test for DM2, no. (%)	
Yes	**67 (90.5)**
No	**5 (6.8)**
Omitted †	**2 (2.7)**
States represented	**31**
Hispanic or Latino, no. (%)	**1(1.4)**
Reported age when symptoms first started	
Mean, (SD)	**36.2(13.4)**
Employed, no. (%)	**33(44.6)**
Level of education completed, no. (%)	
Master's or doctorate	**24 (32.4)**
College	**27 (36.5)**
Technical degree	**6 (8.1)**
High school	**15 (20.3)**
Grade school	**1 (1.4)**
Omitted †	**1 (1.4)**
† Number of times the question was left unanswered by study participants	

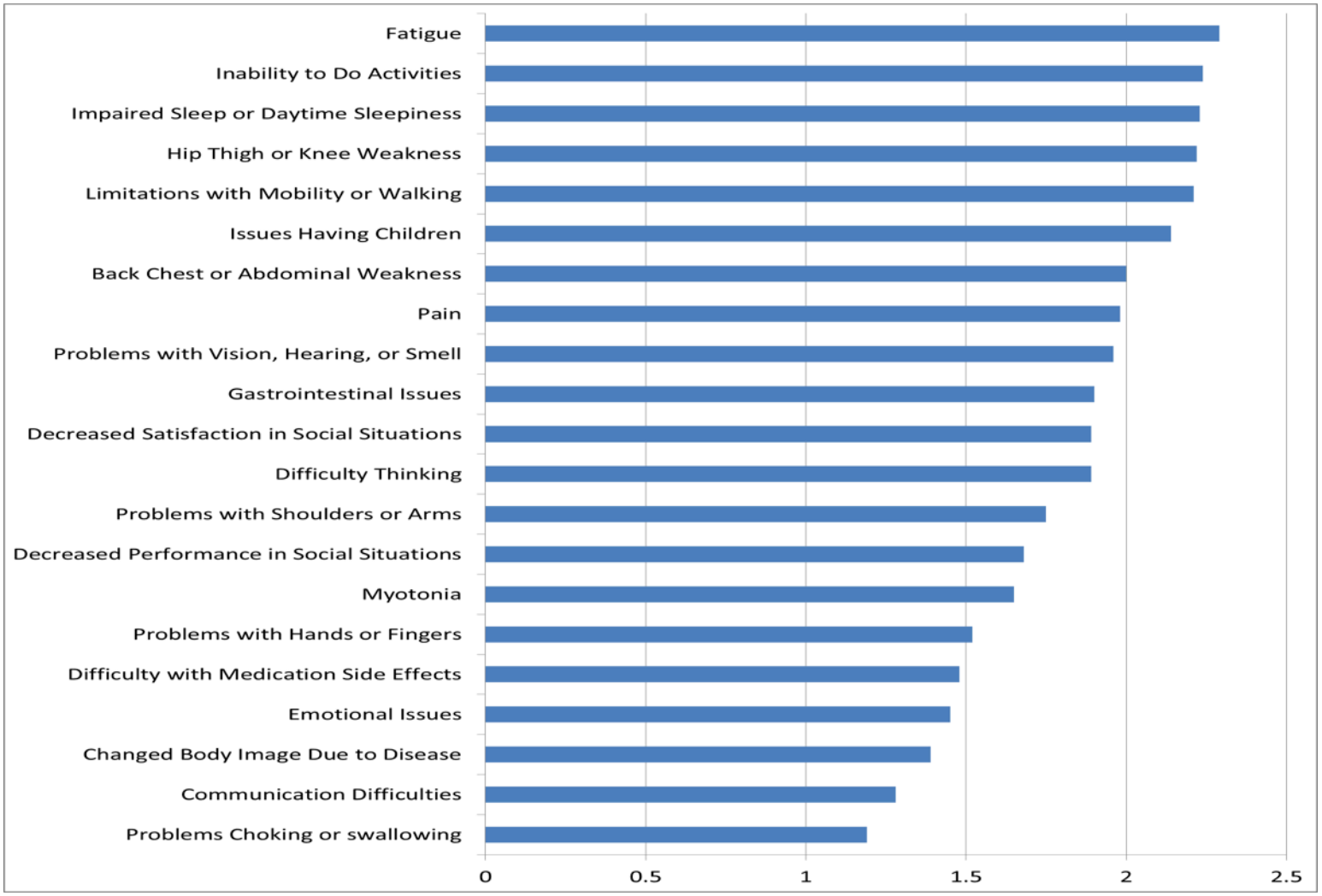
Prevalence of Symptomatic Themes



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

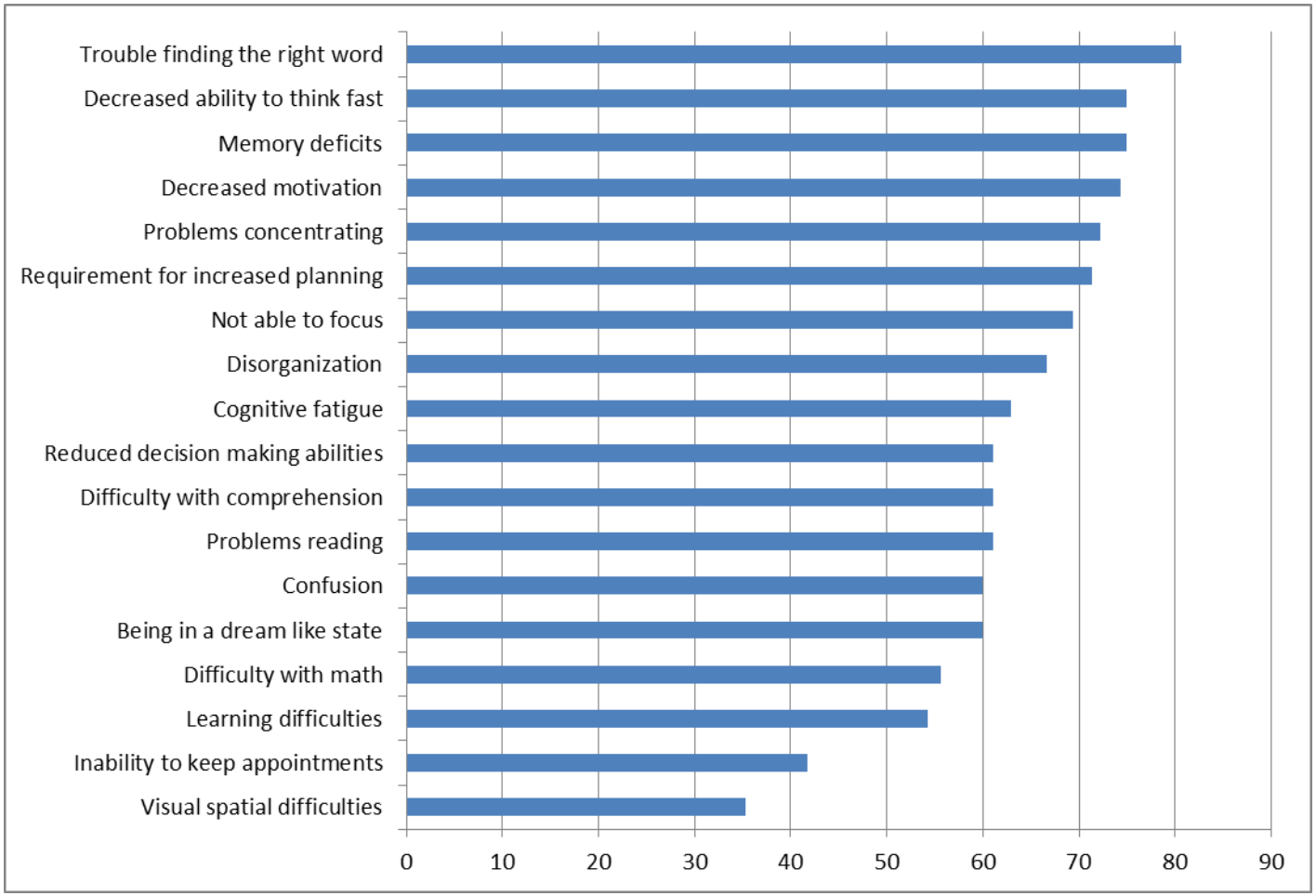
Relative Impact of Symptomatic Themes



Most Prevalent DM2 Symptoms (310)

- 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%)

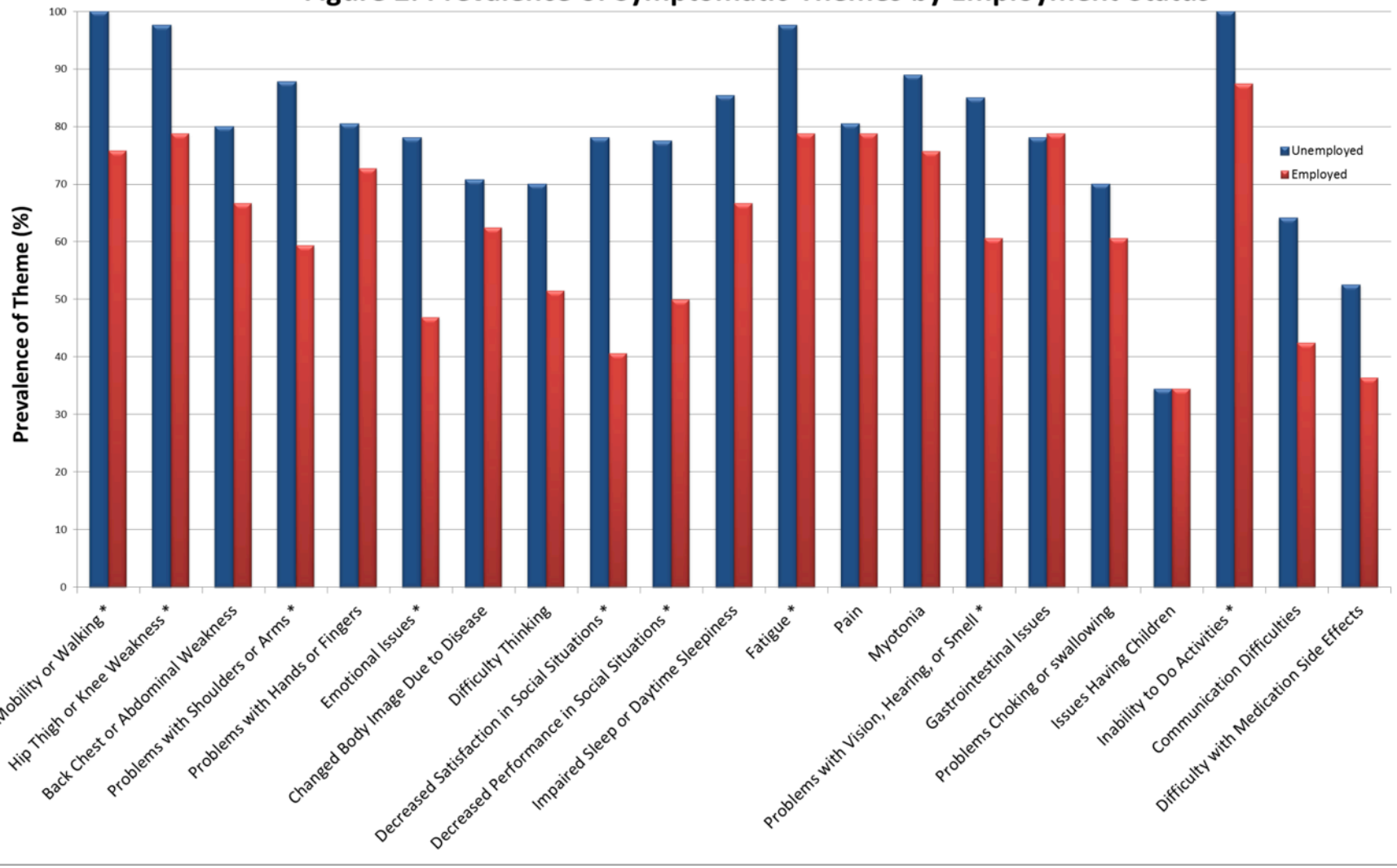
Prevalence of Cognitive Symptoms in DM2



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)

Neurology®

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 (STOPP 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

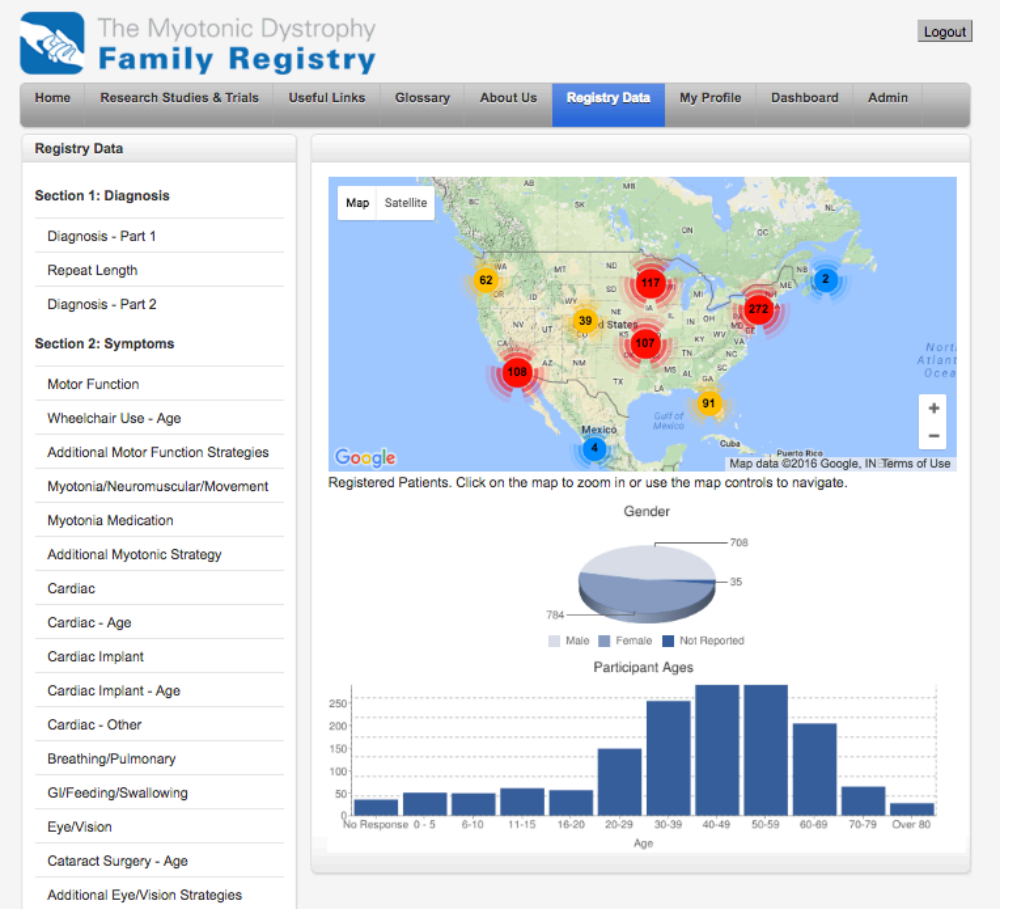
- dystrophy_registry@urmc.rochester.edu
- Jim Hilbert/ Liz Luebbe
- 1-888-925-4302
- Vending Area
- Clinicaltrials.gov (NCT00082108)

The Myotonic Dystrophy
Family Registry

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

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MYOTONIC DYSTROPHY FOUNDATION

Connecting people with researchers

MDA Muscular Dystrophy Association

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cure SMA

FIELDS FSHD & Neuromuscular Research CENTER

University of Rochester Medical Center

LUMC Leiden University Medical Center

NIAMS National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institutes of Health, Department of Health and Human Services

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