Capturing What Patients Already Know: The Development and Use of the Myotonic Dystrophy Health Index (MDHI)

9/12/14
The Myotonic Dystrophy Foundation Annual Conference
Beyond Biology – Important DM Research Projects
Chad Heatwole, MD, MS-CI
"Not everything that counts can be counted, and not everything that can be counted counts."
What is a Patient Reported Outcome Measure?

- A validated outcome measure designed to evaluate one or several aspects of patient health
- Responses are provided directly by patients without required interpretation or administration by other individuals
- Can measure the severity of a specific symptom, sign, functionality, or overall state of disease
- Can be disease-specific or generic
The Need for Patient Reported Outcome Measures

- Provides a unique window by patients into the effects of a disease and treatment effectiveness
- Therapies should be shown to have “patient-relevance” during clinical trials
- The FDA has identified this as an acceptable mechanism for supporting labeling claims
Guidance for Industry
Patient-Reported Outcome Measures:
Use in Medical Product Development
to Support Labeling Claims

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2009
Clinical/Medical
The use of a PROM is advised when measuring a concept best known by the patient or best measured from the patient’s perspective. (FDA)
Patient Reported Impact of Symptoms for Myotonic Dystrophy Type-1 (PRISM-1)
Patient-reported impact of symptoms in myotonic dystrophy type 1 (PRISM-1)

ABSTRACT

Objective: To determine the most critical symptoms in a national myotonic dystrophy type 1 (DM1) population and to identify the modifying factors that have the greatest effect on the severity of these symptoms.

Methods: We performed a cross-sectional study of 278 adult patients with DM1 from the national registry of patients with DM1 between April and August 2010. We assessed the prevalence and relative significance of 221 critical DM1 symptoms and 14 disease themes. These symptoms and themes were chosen for evaluation based on prior interviews with patients with DM1. Responses were categorized by age, CTG repeat length, gender, and duration of symptoms.

Results: Participants with DM1 provided symptom rating survey responses to address the relative frequency and importance of each DM1 symptom. The symptomatic themes with the highest prevalence in DM1 were problems with hands or arms (93.5%), fatigue (90.8%), myotonia (90.3%), and impaired sleep or daytime sleepiness (87.9%). Participants identified fatigue and limitations in mobility as the symptomatic themes that have the greatest effect on their lives. We found an association between age and the average prevalence of all themes (p < 0.01) and between CTG repeat length and the average effect of all symptomatic themes on participant lives (p < 0.01).

Conclusions: There is a wide range of symptoms that significantly affect the lives of patients with DM1. These symptoms, some previously underrecognized, have varying levels of importance in the DM1 population and are nonlinearly dependent on patient age and CTG repeat length. Neurology® 2012;79:1-1

GLOSSARY

DM1 = myotonic dystrophy type 1; FDA = Food and Drug Administration; FSHD = facioscapulohumeral muscular dystrophy; PRISM-1 = Patient Reported Impact of Symptoms in Myotonic Dystrophy Type 1.
# Dropped Questions

<table>
<thead>
<tr>
<th>Reason</th>
<th>Count</th>
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<tbody>
<tr>
<td>Low Relevance to Population</td>
<td>60</td>
</tr>
<tr>
<td>Not Responsive to Therapeutic Intervention</td>
<td>31</td>
</tr>
<tr>
<td>Vague Wording</td>
<td>15</td>
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<tr>
<td>Redundant</td>
<td>6</td>
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<tr>
<td>Abrasive Question</td>
<td>5</td>
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<tr>
<td>Tied to Affluence</td>
<td>2</td>
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<tr>
<td>Vocabulary too Advanced</td>
<td>1</td>
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</tbody>
</table>
### THE MYOTONIC DYSTROPHY HEALTH INDEX (MDHI)

#### 6. How much does the following impact your life now?

<table>
<thead>
<tr>
<th>Item</th>
<th>1. Don't experience it</th>
<th>2. Experience that but it doesn't affect my life</th>
<th>3. It affects my life a little</th>
<th>4. It affects my life moderately</th>
<th>5. It affects my life very much</th>
<th>6. It affects my life severely</th>
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</thead>
<tbody>
<tr>
<td>a) Inability to do things that you used to do</td>
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<tr>
<td>b) Self-consciousness of muscle loss</td>
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<td>c) Prolonged burden to family members</td>
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<tr>
<td>d) Increased family stress</td>
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<tr>
<td>e) Disatisfaction with social interactions</td>
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</tbody>
</table>

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</thead>
<tbody>
<tr>
<td>a) The reliance on family members</td>
<td></td>
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<td>b) Decreased independence</td>
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<td>c) Inability to care for family members</td>
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<td>d) The avoidance of social situations</td>
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<td>e) Impaired social interactions</td>
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<td>f) Difficulty with relationships</td>
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</thead>
<tbody>
<tr>
<td>a) Decreased energy</td>
<td></td>
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<td>b) Impaired endurance</td>
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<td>c) Tired muscles</td>
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<th>5. It affects my life very much</th>
<th>6. It affects my life severely</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Back pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>b) Muscle stiffness</td>
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<tr>
<td>c) Leg pain</td>
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<tr>
<td>d) Limited activity from pain</td>
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<tr>
<td>e) Muscle cramping</td>
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<tr>
<td>f) Pain all over</td>
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<td>g) Arm pain</td>
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</tbody>
</table>

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Date: ____________________

Participant #: ________
# MDHI Question Distribution

(17 Subscales)

<table>
<thead>
<tr>
<th>DM1 Specific Subscales</th>
<th>Number of Questions in Subscale (total= 114)</th>
<th>Internal consistency (Cronbach’s alpha)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.) Limitations with your mobility or walking</td>
<td>13</td>
<td>0.977</td>
</tr>
<tr>
<td>b.) Problems with your hands or arms</td>
<td>11</td>
<td>0.941</td>
</tr>
<tr>
<td>c.) Inability to do activities</td>
<td>14</td>
<td>0.949</td>
</tr>
<tr>
<td>d.) Fatigue</td>
<td>4</td>
<td>0.940</td>
</tr>
<tr>
<td>e.) Pain</td>
<td>8</td>
<td>0.933</td>
</tr>
<tr>
<td>f.) Gastrointestinal issues</td>
<td>6</td>
<td>0.849</td>
</tr>
<tr>
<td>g.) Problems with your vision</td>
<td>4</td>
<td>0.816</td>
</tr>
<tr>
<td>h.) Communication difficulties</td>
<td>7</td>
<td>0.889</td>
</tr>
<tr>
<td>i.) Impaired sleep or daytime sleepiness</td>
<td>4</td>
<td>0.837</td>
</tr>
<tr>
<td>j.) Emotional issues</td>
<td>12</td>
<td>0.933</td>
</tr>
<tr>
<td>k.) Difficulty thinking</td>
<td>9</td>
<td>0.910</td>
</tr>
<tr>
<td>l.) Decreased satisfaction in social situations</td>
<td>6</td>
<td>0.854</td>
</tr>
<tr>
<td>m.) Decreased performance in social situations</td>
<td>7</td>
<td>0.903</td>
</tr>
<tr>
<td>n.) Myotonia</td>
<td>4</td>
<td>0.874</td>
</tr>
<tr>
<td>o.) Breathing difficulties</td>
<td>1</td>
<td>n/a</td>
</tr>
<tr>
<td>p.) Choking or swallowing issues</td>
<td>3</td>
<td>0.758</td>
</tr>
<tr>
<td>q.) Hearing difficulties</td>
<td>1</td>
<td>n/a</td>
</tr>
</tbody>
</table>
Validation of the Myotonic Dystrophy Health Index

- Factor Analysis
- Test-retest reliability
- Known groups testing
- Concurrent validity
- Responsiveness testing
- Beta Testing with patients
MDHI Total Score by Known Groups

- Employed (Blue: Yes/Red: No)
- CTG Repeat Status (Blue:<300/Red:≥300)
- Education (Blue: College or Advanced Degree/Red: No College Degree)
- Duration of Symptoms (Blue: ≤20/Red: >20 years)
COMFORT Study

- Comparison of MDHI with functional and other research testing (COMFORT)
- A cross-sectional study of 70 DM1 patients comparing MDHI scores to 22 functional tests, six laboratory tests, 25 generic patient reported outcome assessments, and seven physician assessments
- Completed as part of our Wellstone initiative
Use of the MDHI

- FDA funded randomized double-blinded drug labeling trial of Mexiletine for DM1
- Three NIH DM1 longitudinal studies
- European Optimistic Trial
- University of Utah DM1 pregnancy study
- University of Iowa
- Planned for additional therapeutic and non-therapeutic studies
Future Directions

- MDHI Online/ MDHI App
- Translation to other languages
- Use in MDA clinics
The Development and Use of the Myotonic Dystrophy Health-Related Quality of Life and Function Instrument (MDHI)

- Large Scale Survey Initiative
- Generic and Disease-Specific Quality of Life Questions
- PROMIS Network
- Myotonic Dystrophy Patient Interviews
- Literature Review
- Expert Opinion
- Advanced Statistical Analysis
- NEURO-QoL

Clinical Trials of Myotonic Dystrophy at The University of Rochester
Clinical Trials of Myotonic Dystrophy (Nationally and Globally)
The Development of a FSHD Quality of Life Instrument
The Development of a DM2 Quality of Life Instrument
Insight into the Symptoms that are Most Important to Patients
Patient Monitoring

Improved Patient Care

SA: Specific Aim (see research methods)
QOL: Quality-of-Life
FSHD: Facioscapulohumeral Dystrophy
DM2: Myotonic Dystrophy Type-2
Thank You

Nicholas Johnson, MD
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Robert Griggs, MD
James Hilbert, MS
Tracy Forrester
Liz Luebbe
Bill Martens, BA
Mike McDermott, Ph.D
Nancy Chin, Ph.D.
Eileen Eastwood
Jeanne Dekdebrun
David Herrmann, M.B.B.Ch.
Shree Pandya, PT, MS
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Cindy Gibson, NP
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Nan Rothrock, Ph.D (Northwestern, IL)
Rita Bode, Ph.D. (PROMIS Network)
David Victorson, Ph.D. (NeuroQol Network)
Ora Prilleltensky, Ed.D. (University of Miami)
John Day, M.D., Ph.D. (Stanford, California)
John Kisel, M.D. (The Ohio State, Ohio)
Kevin Flanigan, M.D. (Nationwide Children’s, Ohio)
Kenneth Fischbeck, M.D. (NIH)
Tatiana Foroud, Ph.D. (Indiana University, Indiana)
Giovanni Meola, MD (Milan, Italy)
Baziel Van Engelen, MD, Ph.D. (Nijmegen, Netherlands)
Benedikt Schoser, MD (Munich, Germany)
Silvere van de Maarel, Ph.D. (University of Leiden)
Richard Lemmers, Ph.D. (University of Leiden)
Michael Rose, M.D. (Kings College, United Kingdom)
Craig Campbell, M.D. (University of Western Ontario, Canada)
Anne-Berit Ekstroem, MD, PhD (Queen Silvia Children’s Hospital, Sweden)
Final MDHI

- 114 questions
- Measure total health and 17 areas of DM1 subhealth
- Average time to completion: 19 minutes
- Scored to prioritize the items of greatest importance to the DM1 population
- Content Validity: Assured
- Construct Validity: Assured
- Face Validity: Assured
- Reliability: Assured
- Responsiveness: Estimated using known groups analysis (being tested in longitudinal trial)
- Patient Burden: Low
- Concurrent Validity: Assured
Figure 1: The Test-Retest Reliability of the MDHI

ICC = 0.95