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

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"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

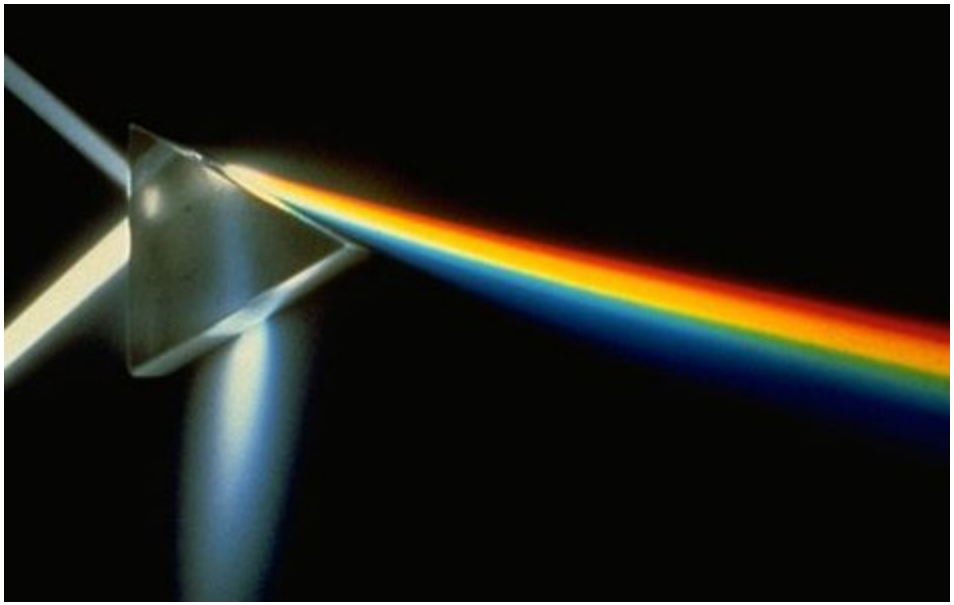
Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

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)

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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 are 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.

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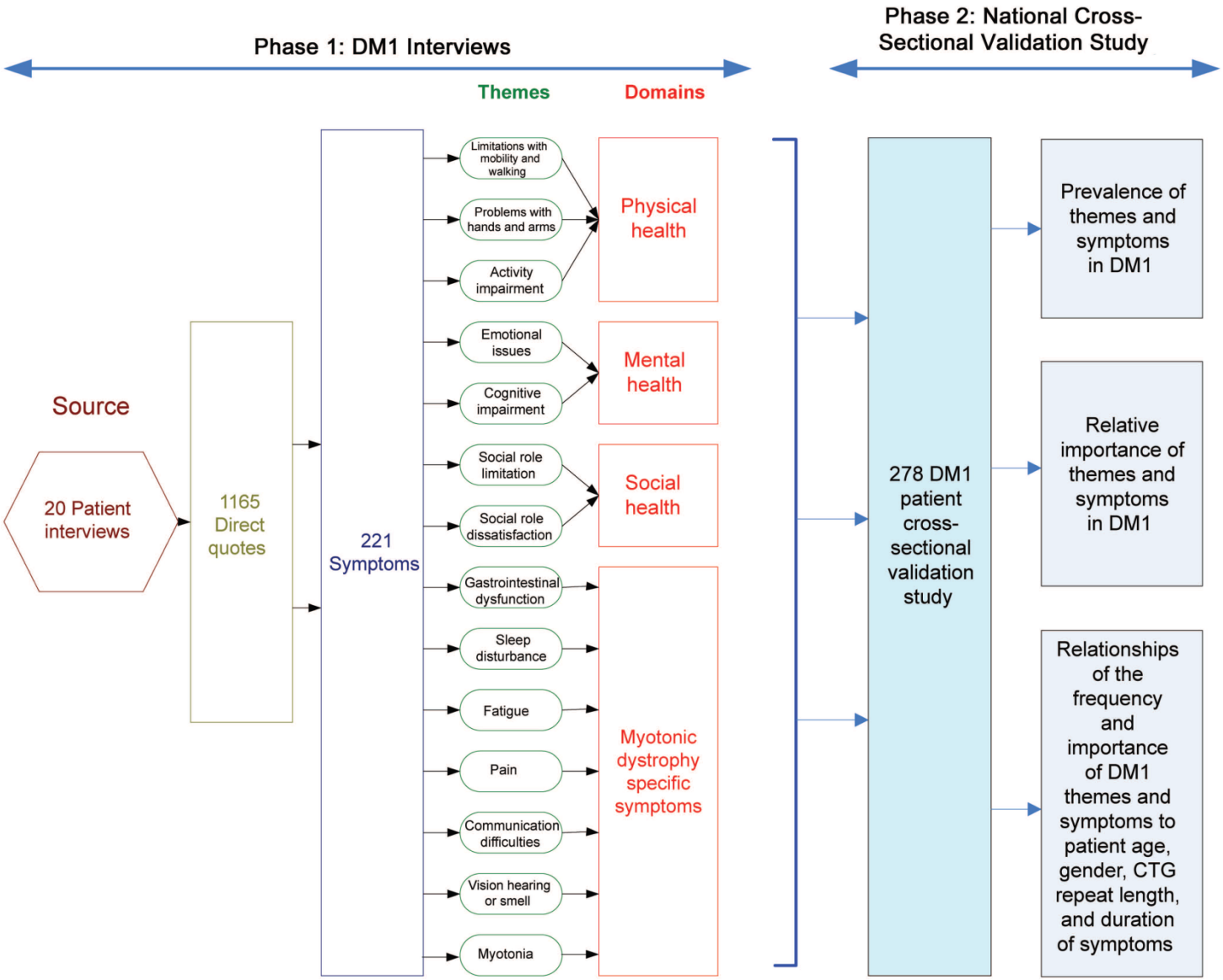

Phase 1: DM1 Interviews
Phase 2: National Cross-Sectional Validation Study
Themes
Domains
Source
20 Patient interviews
1165 Direct quotes
221 Symptoms
Limitations with mobility and walking
Problems with hands and arms
Activity impairment
Emotional issues
Cognitive impairment
Social role limitation
Social role dissatisfaction
Gastrointestinal dysfunction
Sleep disturbance
Fatigue
Pain
Communication difficulties
Vision hearing or smell
Myotonia
Physical health
Mental health
Social health
Myotonic dystrophy specific symptoms
278 DM1 patient cross-sectional validation study
Prevalence of themes and symptoms in DM1
Relative importance of themes and symptoms in DM1
Relationships of the frequency and importance of DM1 themes and symptoms to patient age, gender, CTG repeat length, and duration of symptoms

Dropped Questions

Low Relevance to Population	60
Not Responsive to Therapeutic Intervention	31
Vague Wording	15
Redundant	6
Abrasive Question	5
Tied to Affluence	2
Vocabulary too Advanced	1

THE MYOTONIC DYSTROPHY HEALTH INDEX

(MDHI)

Date: Participant #:

6. How much does the following impact your life now?	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.) Inability to do things that you used to do						
b.) Self-conscious of muscle loss						
c.) Perceived burden to family members						
d.) Increased family stress						
e.) Dissatisfaction with social interactions						

7. How much does the following impact your life now?	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.) The reliance on family members						
b.) Decreased independence						
c.) Inability to care for family members						
d.) The avoidance of social situations						
e.) Impaired social interactions						
f.) Difficulty with relationships						

8. How much does the following impact your life now?	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.) Decreased energy						
b.) Impaired endurance						
c.) Tired muscles						

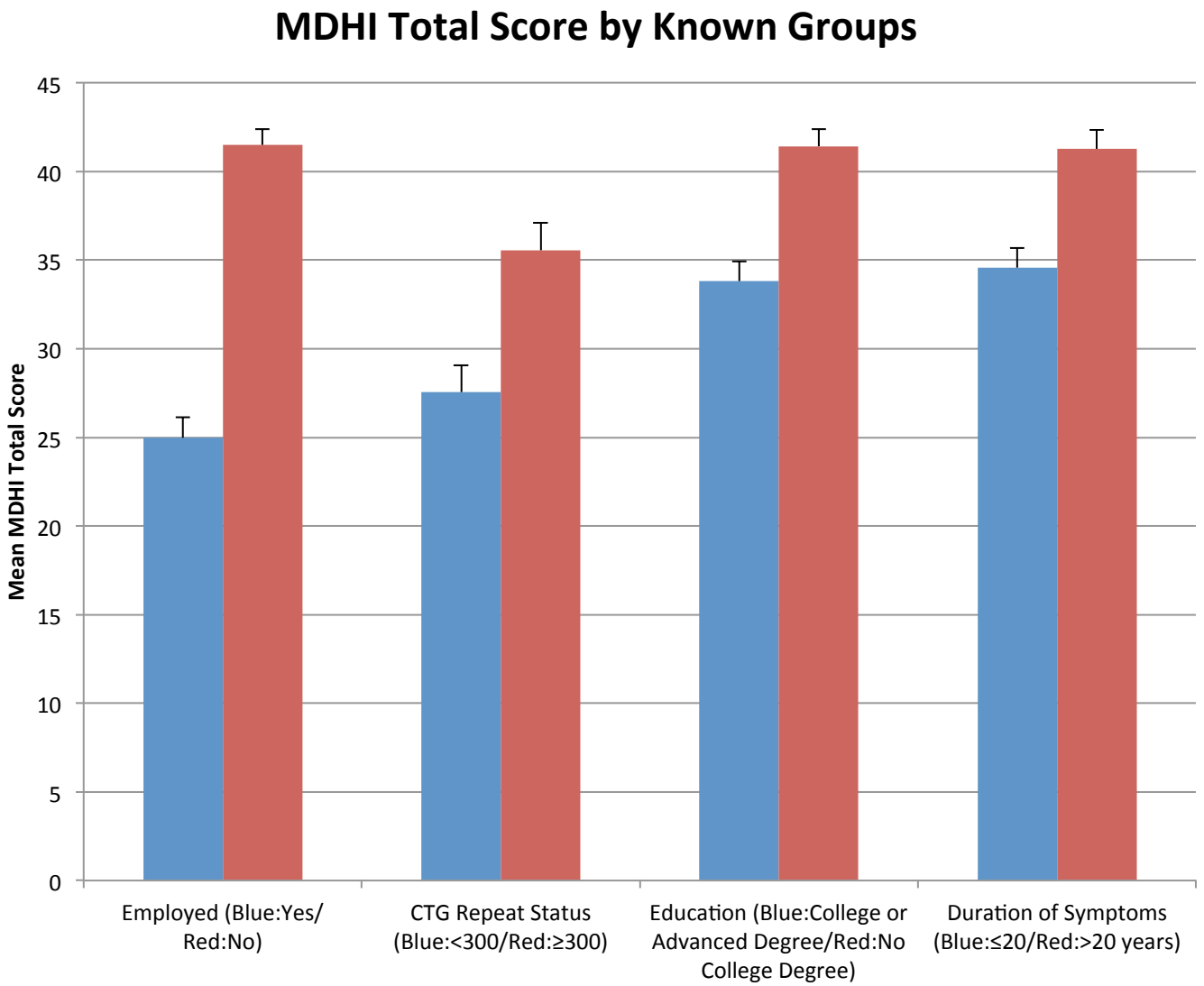
9. How much does the following impact your life now?	I don't experience this	I experience this but it does not affect my life	It affects my life a little	It affects my life moderately	It affects my life very much	It affects my life severely
a.) Back pain						
b.) Muscle stiffness						
c.) Leg pain						
d.) Limited activity from pain						
e.) Muscle cramping						
f.) Pain all over						
g.) Arm pain						

MDHI Question Distribution (17 Subscales)

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

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
Mean MDHI Total Score
45
40
35
30
25
20
15
10
5
0
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

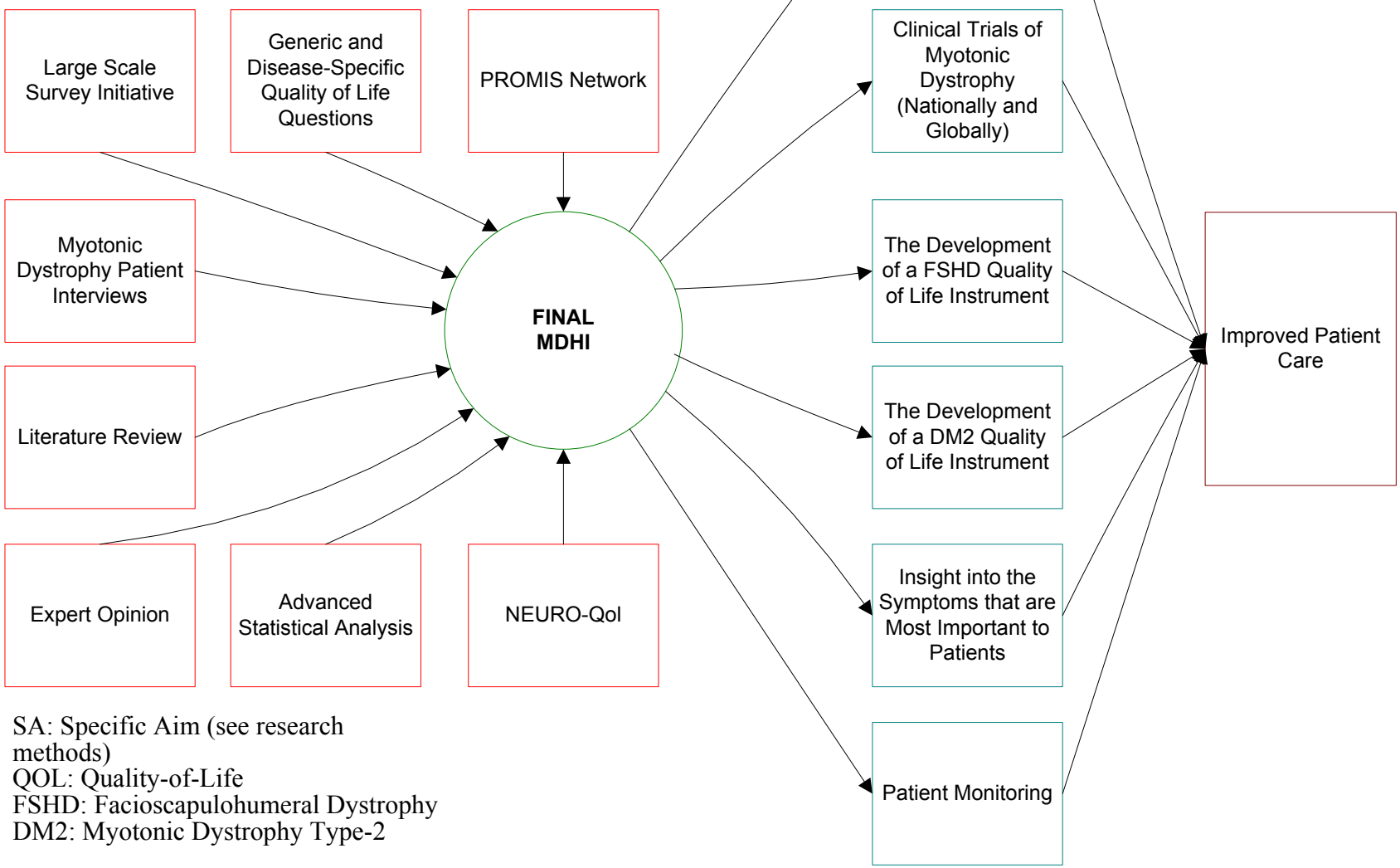
Use of the MDHI

- 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)



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

Thank You

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MYOTONIC DYSTROPHY FOUNDATION

Connecting people with researchers

MDA Muscular Dystrophy Association

SEN. PAUL D. WELLSTONE MD COOPERATIVE RESEARCH CENTER

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES National Institutes of Health

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

THE GREAT SEAL OF THE STATE OF NEW YORK EXCELSIOR

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

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