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The Myotonic Dystrophy Health Index: Correlations with Clinical Tests and Patient Function

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Abstract

Introduction—The Myotonic Dystrophy Health Index (MDHI) is a disease-specific patient-reported outcome measure. Here we examine the associations between the MDHI and other measures of disease burden in a cohort of individuals with myotonic dystrophy type-1 (DM1).

Methods—We conducted a cross-sectional study of 70 patients with DM1. We examined the associations between MDHI total and subscale scores and scores from other clinical tests. Participants completed assessments of strength, myotonia, motor and respiratory function,

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The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Additional information regarding the MDHI is available at the *Neuromuscular Institute of Quality-of-Life Studies and Outcome Measure Development* website www.QOLINSTITUTE.com and MDHI licensing opportunities can be reviewed at: www.urmc.rochester.edu/techtransfer.

ambulation, and body composition. Participants also provided blood samples, underwent physician evaluations, and completed other patient-reported outcome measures.

Results—MDHI total and subscale scores were strongly associated with muscle strength, myotonia, motor function, and other clinical measures.

Conclusion—Patient-reported health status, as measured by the MDHI, is associated with alternative measures of clinical health. These results support the use of the MDHI as a valid tool to measure disease burden in DM1 patients.

Keywords

Myotonic Dystrophy Type-1; Patient-Reported Outcome Measure; Therapeutic Trial; Quality of Life; Patient-Relevant; Muscle Disease

INTRODUCTION

Myotonic dystrophy type-1 (DM1) is a dominantly inherited muscular dystrophy caused by a CTG repeat expansion in the *DMPK* gene on chromosome 19q13.3.^{1–3} In addition to muscle dysfunction, DM1 manifests with a wide variety of symptoms involving many organ systems.⁴

The Myotonic Dystrophy Health Index (MDHI) is a disease-specific, patient-reported outcome measure designed to measure patient-perceived disease burden. The MDHI was created using input from 278 DM1 patients and consists of 17 subscales that together measure overall patient disease burden and separately measure each of the most important symptomatic themes in this population.^{5, 6} These subscales are measures of mobility, upper extremity function, the ability to perform activities, fatigue, pain, gastrointestinal issues, vision, communication, sleep, emotional issues, cognitive impairment, social satisfaction, social performance, myotonia, breathing, swallowing, and hearing.

Disease-specific patient-reported outcomes that cover a broad range of symptom domains can be particularly useful in multisystem neurological diseases (e.g. DM1) that show non-uniform and variable progression of symptoms in different domains. Regulatory agencies, including the Food and Drug Administration (FDA), identify disease-specific patient-reported outcome measures as an acceptable and at times advised mechanism for measuring response to an intervention during clinical trials.⁷ Prior to use for drug labeling purposes, the FDA requests that the reliability, internal consistency, content validity, responsiveness to clinical change, and construct validity of a patient-reported outcome measure be demonstrated.^{7, 8} Convergent validity, the degree to which an outcome measure correlates with other outcome measures designed to measure similar concepts, is a key component of construct validity. Previous research has shown that the MDHI is reliable, representative of the most important areas of DM1 health, internally consistent, and able to differentiate between groups of patients with different severities of disease.⁶ The convergent validity of the MDHI has not previously been assessed.

Here we report the findings of the COMFORT study (Comparison of the Myotonic Dystrophy Health Index (MDHI) with Functional and Other Research Testing). Specifically,

we assess the MDHI by: 1) evaluating the baseline functional status of a large cohort of DM1 patients; and, 2) determining the relationships between MDHI scores and other outcome measures traditionally used in DM1 clinical trials.

METHODS

Eligibility Criteria

Participants: 1) were 18 years of age or older; 2) had a diagnosis of DM1 by clinical or genetic criteria;^{9, 10} 3) could complete a 6 minute walk test;^{11, 12} 4) had the decision-making capacity to provide informed consent to participate; and, 5) were enrollees in the Study of Pathogenesis and Progression in Dystrophia Myotonica (STOPP DM) study. STOPP DM is an ongoing DM1 natural history study that involves clinical study visits at baseline, 12 months, and 36 months. Exclusion criteria were: an onset of symptoms before age 10; treatment with anabolic steroids, growth hormone, IGF-1 or glucocorticoids within one year of enrollment; respiratory insufficiency; pregnancy; symptomatic liver or kidney disease; diabetes requiring insulin; untreated thyroid disease; major psychiatric illness; drug or alcohol abuse within 21 months; a history of bleeding diathesis; and a body mass index >30.

Study Design

We recruited study participants through local and national referral and the National Registry of Myotonic Dystrophy Patients and Family Members (www.dystrophyregistry.org).¹³ All enrolled participants completed the MDHI, strength and function testing, laboratory testing, a supplementary battery of patient-reported outcome measures, and underwent a clinical assessment by a board certified neurologist. All strength and function evaluations were performed by a single trained evaluator (KE). All testing was performed on the same day that the MDHI was administered (with the exception of electromyography which was performed on the following day). Participants received testing in the following order: serum lab studies and dual-energy x-ray absorptiometry (DEXA), neurologist administered clinical assessments, strength and functional testing, and lastly the MDHI and all other patient-reported outcome measures. Patients also provided their age and stated if they were currently disabled from work.

Strength evaluations included manual muscle testing (MMT)^{14–18}, quantitative muscle testing (QMT)^{16, 19}, and grip strength measured using QMT and peak force during maximum voluntary dynamometer grip testing for myotonia.^{20, 21} Function testing included timed functional tests¹⁸ (time to go 30 feet, ascend 4 steps, descend 4 steps, stand from a chair, stand 10 times from a chair), the Purdue Pegboard test^{22, 23}, the Jebsen-Taylor hand function test²⁴, pinch grip strength (both palmar and lateral)^{16, 25}, forced vital capacities (FVC) (sitting and supine)¹⁶, and the six minute walk test.^{11, 12} A muscle impairment rating scale (MIRS)²⁶ was also completed for each participant.

We quantified strength assessed by MMT using four measures: 1) the average strength of 26 muscles (bilateral shoulder abductors, elbow flexors, elbow extensors, wrist flexors, wrist extensors, hip flexors, hip abductors, hip extensors, knee extensors, knee flexors, ankle dorsiflexors, ankle plantar flexors, plus neck extensor and neck flexors); 2) the average

strength of 30 muscles (the muscles listed above plus long and short finger flexors bilaterally); 3) the average strength of upper extremity muscles only (bilateral shoulder abductors, elbow flexors, wrist flexors, wrist extensors, and elbow extensors; and, 4) the average strength of lower extremity muscles only (bilateral hip flexors, hip extensors, hip abductors, knee flexors, knee extensors, ankle dorsiflexors, and ankle plantar flexors). We tested muscles in predefined positions including sitting, supine, prone, and side lying and each were graded using a modified Medical Research Council scale converted into numerical values (5 = 5, 5- = 4.67, 4+ = 4.33, etc.). MMT has been used as an outcome measure in natural history studies and therapeutic trials in individuals with muscular dystrophy for over 30 years. The validity, reliability, and sensitivity of the composite MMT score has been previously documented.^{18, 27-30}

Maximum Voluntary Isometric Contraction Testing of the limb muscles (QMT) was performed using the Quantitative Muscle Assessment system (Computer Source, Atlanta, GA). Results are expressed as “percent of predicted strength”, a percentage of the strength that would be predicted for a healthy person of the same age, gender, and height.²⁸ Testing included bilateral shoulder abduction, elbow flexion, elbow extension, knee flexion, knee extension, ankle dorsiflexion, and grip. A composite QMT score was computed as the average percent of predicted normal across all muscles tested. Composite QMT scores were also determined for lower extremity muscle groups (bilateral knee extension, knee flexion, and ankle dorsiflexion) and upper extremity muscle groups (bilateral shoulder abduction, elbow flexion, elbow extension, and hand grip). Grip strength was tested using a Jamar dynamometer and positioning recommended by the American Society of Hand Therapists.³¹ Grip strength was also determined with a dynamometer by measuring the peak force obtained during maximum voluntary isometric contraction.^{20, 21}

Many of the strength and functional measurement techniques selected for this study have been previously tested at our site using patients with myotonic dystrophy¹⁸, facioscapulohumeral muscular dystrophy¹⁶, and Duchenne muscular dystrophy.¹⁴

We performed lean body mass measurements using DEXA.³²⁻³⁴ DEXA measurements included lean body mass in the total body, upper extremities only, and lower extremities only. Laboratory testing included creatine kinase (CK) levels.³⁵ Physiological assessments included electromyography (EMG) myotonia testing³⁶, and grip myotonia relaxation time.^{20, 21} During EMG myotonia testing, we observed 20 needle insertions at the tibialis anterior muscle and 20 insertions at the vastus lateralis muscle. We assigned one point for every insertion that was noted to have electrical myotonia (for a possible score ranging from 0-40). We assessed grip myotonia by recording the time interval between 90% and 5% peak hand grip force as measured by computerized hand grip myometry.^{20, 21}

Patient-reported outcome measures included: an upper extremity functional index³⁷, a lower extremity functional index³⁸, the SF-36³⁹, a myotonia visual analog score (VAS), a pain VAS, the Individualized Neuromuscular Quality of Life Questionnaire (INQoL)⁴⁰ (total score, weakness, locking, fatigue, pain, activities, independence, social, emotions, body image), and the Epworth Sleepiness Scale.⁴¹ For the myotonia and pain VAS, participants placed a mark on a line representing their myotonia or pain symptoms. The line was labeled

with a 0 (no symptoms) at one end and a 10 (severe symptoms) at the other end. The mark on the line was converted to a number (based on relative distance between 0 and 10).

Neurologists recorded the presence or absence of an affected voice, facial weakness, percussion myotonia at the thumb, grip myotonia, abnormal hearing, hearing aid use, and advanced grip myotonia (grip myotonia lasting greater than three seconds).

The University of Rochester Research Subjects Review Board approved all research activities. All study participants provided informed consent. Participants received their first inpatient evaluation between 4/4/11 and 11/13/12.

Statistical Analysis

Prior to conducting correlation analysis, two neuromuscular specialists (NJ, CH) hypothesized which assessments would be associated with each individual MDHI subscale score. The relationships between MDHI scores and continuous and ordinal outcome measures were quantified using Spearman rank correlations. When forming MDHI total and subscale scores, missing response data for any individual MDHI question were replaced with the mean response value for all other questions in the same subscale. Wilcoxon rank sum tests were used to compare the distributions of MDHI scores between known groups. The MDHI subscale with the highest level of correlation with each individual clinical test was determined.

RESULTS

Seventy DM1 patients participated in this study (Table 1). On average, participants completed 99.7% of the MDHI's questions. Sixty-eight of the 70 participants completed the MDHI without omitting any questions. There was no pattern apparent in terms of the questions that were omitted by the two participants.

The average MDHI score for the study participants was 24.4 representing a mildly-to-moderately affected DM1 sample⁶ (MDHI total scores range from 0 to 100 with a score of 100 representing the most severe disease burden). Participants had the highest scores in the following areas: fatigue (mean MDHI subscale score: 35.4), sleep (30.5), and mobility (30.3). Three participants reported no symptomatic disease burden via the MDHI. All three of these individuals had DM1 protomutations with CTG repeat lengths of 62, 80, and 84. All participants with CTG repeat lengths of 100 or greater reported symptomatic disease using the MDHI.

The MDHI total score was associated with patient-reported disability status ($p=0.0003$) as were 14/17 subscales. Table 2 provides the mean, standard deviation, floor effect (percentage of patients who reported the minimum level of disease burden), ceiling effect (percentage of patients who reported the maximum level of disease burden), and association with disability status for the MDHI total score and each of its 17 subscales. MDHI total scores were significantly associated ($p < 0.05$) with 54 (90%) of the 60 clinical tests performed. MDHI subscales were frequently associated with assessments hypothesized to measure similar concepts.

Associations with MDHI Total Score

We observed significant associations between the MDHI total score and all but one of the 22 strength and functional test scores. The Purdue Pegboard Test was the only functional measure that was not significantly associated with MDHI total score. Table 3 presents the correlations between the MDHI total score and strength and function tests.

The MDHI total score was significantly associated with all of the patient-reported outcome measures (Table 4). The MDHI total score was also significantly associated with DEXA measures of lean body mass and the presence of electromyographic myotonia, but not with CK levels or maximum voluntary isometric grip related myotonia (Table 5). MDHI total scores differed significantly between those with and without an affected voice, facial weakness, percussion myotonia, and grip myotonia (Table 6).

Associations with MDHI Subscales

Strength and Function Testing—With the exception of the Purdue Pegboard Test, each strength and function test was significantly associated with the majority of MDHI subscale scores (Supplemental Table 1a, 1b). Strength measured using MMT (26 muscles, upper extremity muscles, and lower extremity muscles) was significantly associated with all MDHI subscale scores while QMT (lower extremity % score), pinch grip, time to go 30 feet, time to ascend 4 steps, time to descend 4 steps, FVC while sitting, six minute walk distance, and MIRS were associated with all but one of the MDHI subscales.

The MDHI Mobility subscale had the strongest correlation with 12 of the 22 individual strength and function tests (Supplemental Table 1a, 1b). These tests included five of the MMT and QMT strength measurements, all of the timed mobility measurements (including the 6 minute walk test), and the MIRS. The MDHI Upper Extremity Function subscale had the strongest correlation with upper extremity MMT and QMT scores, grip strength, palmar pinch grip strength, Purdue Pegboard test score, and Jebsen-Taylor hand function score. The MDHI Activities subscale had the highest correlation with lateral pinch grip measurements, and both FVC measurements.

Patient-reported Outcome Measures—With the exception of two SF-36 mental health summary scores and the pain VAS, the patient-reported outcome measures were significantly associated with a majority of the MDHI subscale scores (Supplemental Table 2a, 2b).

The MDHI total score had the strongest correlation with several other patient-reported outcome measures. These included the: upper extremity functional index, SF-36 role-physical score, INQoL % score, and INQoL activities score. The MDHI Pain subscale had the highest correlation with SF-36 bodily pain, VAS pain assessments, and INQoL pain scores. The MDHI Sleep subscale had the highest correlation with the Epworth Sleepiness Scale. The MDHI Myotonia subscale had the highest correlation with the INQoL locking scale. The MDHI Fatigue subscale had the highest correlation with the SF-36 vitality score and the INQoL fatigue score. The MDHI Social Performance subscale had the highest correlation with SF-36 social function, while the MDHI Social Satisfaction subscale had the highest correlation with INQoL independence and INQoL social relationships. The MDHI

Emotional Issues subscale had the highest correlation with 4 measures including two SF-36 mental health scores, the SF-36 role-emotional score, and the INQoL emotions score. The MDHI Upper Extremity Function subscale had the highest correlation with the SF-36 general health and the myotonia VAS assessment while the MDHI Mobility subscale had the highest correlation with the lower extremity functional index and two SF-36 physical measures.

Laboratory Testing—Upper extremity lean body mass, lower extremity lean body mass, and electromyographic myotonia were significantly associated with the majority of MDHI subscales (Supplemental Table 3a, 3b). DEXA measures that included the entire body had weaker associations with the MDHI subscales and CK value had no significant association with any MDHI subscale. Grip myotonia after maximum voluntary isometric contraction was associated with the MDHI Mobility and MDHI Myotonia subscales without demonstrating an association with any other subscale.

The MDHI Mobility subscale had the highest correlation with electromyographic myotonia and DEXA upper extremity lean body mass. The MDHI Myotonia subscale had the highest correlation with voluntary grip myotonia. Surprisingly, the highest correlation with total lean body mass and lower extremity mass via DEXA was seen with the MDHI Vision subscale.

Neurologist Administered Clinical Assessments—The majority of MDHI subscale scores differed significantly between those with and without facial weakness, grip myotonia, and percussion myotonia (Supplemental Table 4a, 4b).

MDHI Hearing subscale scores were associated with both impaired hearing and hearing aid use. The MDHI Myotonia subscale score was most significantly associated with the presence of grip myotonia lasting more than 3 seconds. Interestingly, the presence of percussion myotonia was most strongly associated with the MDHI Pain and MDHI Fatigue subscales while grip myotonia had the strongest association with the MDHI Gastrointestinal subscale. The MDHI Communications subscale was most significantly associated with the presence of an affected voice. Facial weakness had the highest correlation with the MDHI Upper Extremity Function subscale, a scale that includes patient assessments of hand, arm, neck, and facial weakness.

DISCUSSION

The results of the COMFORT study provide further validation of the MDHI as a disease-specific, patient-reported outcome measure for DM1. The MDHI has a high level of convergent and construct validity as demonstrated by significant and widespread associations between MDHI scores and other clinical assessments. We found that multiple measures of physical function were correlated with both the motor and non-motor subscales of the MDHI. This finding may reflect shared pathophysiologic mechanisms or parallel progression of different organ systems in DM1.

The MDHI was well tolerated by our study participants who completed the instrument without detailed instruction and left few items blank (0.3%). This is what would be expected

for a disease-specific patient-reported outcome measure that includes questions that are highly relevant and well understood by a target population.

Researchers have traditionally used clinician-administered functional tests to gauge the effects of a potential treatment. More recently, disease-specific patient-reported outcome measures have been utilized as secondary and sometimes primary outcome measures in clinical trials.⁴² Patient-reported outcome measures that are highly capable of highlighting the patient's point of view and measuring relevant clinical changes during clinical trials are desirable.^{7, 43, 44} Disease-specific outcome measures have been hypothesized to be highly relevant, and responsive to clinical change.^{45–47} Our data help interpret the clinical meaning behind differences in MDHI total or subscale scores by correlating these scores to those observed using other clinical metrics. As expected, participants' assessments of their functional status (as determined by MDHI scores) were associated with traditional outcome measures designed to measure similar clinical concepts. Future longitudinal studies are needed to determine which outcome measures are the most sensitive for detecting disease progression or therapeutic response.

Several strength and function tests were associated with patient reported health. Six minute walk distance, MMT scores, time to descend or ascend 4 steps, and pinch grip strength were not only associated with MDHI subscales related to physical health, but also with those related to emotional state, social satisfaction, and social performance. Similarly, FVC (sitting) was associated with a patient's perception of their breathing (MDHI Breathing), their ability to do activities (MDHI Activities), and 14 additional MDHI subscales. These associations and others highlight possible interconnections between the physical and respiratory health of DM1 patients and the social and emotional burden of the disease.

Some associations were unexpected. For example, we did not predict that MDHI Sleep subscale score would be related to muscle strength, that MDHI Fatigue score would be related to electromyographic and percussion myotonia, that gastrointestinal issues would be related to grip myotonia, or that vision would be related to lean body mass. While these associations may be a function of overall disease severity, it is also possible that more direct physiological connections exist between specific entities. Of course, it is also possible that some of the observed associations were spurious due to the many associations examined (multiple statistical testing). Additional research is needed to further investigate the possible physiological relationships between the multiple and varied symptoms of DM1.

It is currently not known which muscles are best suited for serial evaluation when assessing "strength" in patients with myotonic dystrophy. To this end we compared MDHI scores to strength assessments obtained using common techniques (e.g. MMT and QMT) assessing different muscle groups (e.g. those muscles representing the upper or lower extremities). Additional research is needed to determine which method (and specific muscle profile) provides the optimal mechanism to formally measure change in strength in DM1.

We recognize several limitations with our study. First, our study represents a very specific DM1 patient cohort. The sample did not include individuals who were non-ambulatory, or had congenital onset or juvenile onset DM1. The DM1 participants in this study were a

“healthier” DM1 sample than would be expected from the general DM1 population. Some participants had minimal CTG repeat length expansions. Other potential participants were excluded due to severe or comorbid disease. The eligibility criterion requiring the ability to walk six minutes also restricted our sample. It is important to acknowledge the potential for impaired cognition in DM1. Our study population was well educated. Many participants had college degrees. While formal cognitive testing was not performed, it is suspected that our study attracted patients with fewer or less severe cognitive symptoms. In addition to formal cognitive testing, our study did not assess gastrointestinal physiology, sleep physiology, audiology, or vision. This supplemental testing would have augmented the evaluation of several of the MDHI subscales. Another limitation relates to the absence of a true “gold standard” test for multiple concepts measured by the MDHI subscales. We recognize that currently there are no universally accepted measures for concepts such as myotonic dystrophy pain, cognitive impairment, or social dissatisfaction.

Our findings represent another step in the validation process and development of a disease-specific patient-reported outcome measure for DM1. The MDHI provides clinicians and researchers with an option to assess a DM1 patient’s perception of their health in 17 different areas. Our results suggest that the concepts measured by MDHI subscales correlate well with conventional measures of patient strength and function. The responsiveness of the MDHI to DM1 disease progression and therapeutic intervention has not yet been determined but is being currently studied. These ongoing studies will be helpful to define the responsiveness of the MDHI and each of its individual subscales.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

MDHI	The Myotonic Dystrophy Type-1 Health Index
DM1	Myotonic dystrophy type-1
FDA	United States Food and Drug Administration
COMFORT Study	Comparison of the Myotonic Dystrophy Health Index (MDHI) with Functional and Other Research Testing
STOPP DM	Study of Pathogenesis and Progression in Dystrophia Myotonica

MMT	Manual Muscle Testing
QMT	Quantitative muscle testing
FVC	Forced vital capacities
MIRS	muscle impairment rating scale
DEXA	Dual-energy x-ray absorptiometry
EMG	Electromyography
CK	creatine kinase
VAS	Visual analog scale

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Table 1

Participant Characteristics

Number of Patients Studied	70
Sex, no. (%)	
Women	47 (67.1)
Age in years	
Mean, (SD)	47.9 (12.5)
Range	19 to 69
Years Since Diagnosis	
Mean, (SD)	11.4 (8.4)
Range	0.1 to 40.4
Years of Education	
Mean, (SD)	15.7 (2.9)
Range	11 to 25
Genetically Tested for DM1, no., (%)	58 (82.9)
Number of CTG repeat, mean, (SD)	532.7 (397.9)
No. of patients who report being on disability (%)	17 (24.3)

Table 2

Descriptive Statistics for the MDHI

MDHI Subscales	Number of Questions	Mean Score	Standard Deviation	Floor Effect % (lowest score) [†]	Ceiling Effect % (highest score) [‡]	Mean Score for ND Patients (N=53)	Mean Score for D Patients (N=17)	Association with Disability Status (P-value)
a.) Mobility	13	30.31	29.46	25.71	1.43	22.54	54.54	<0.01
b.) Upper Extremity Function	11	27.06	25.45	20.00	0.00	22.34	41.76	<0.01
c.) Ability to do Activities	14	29.62	26.40	18.57	0.00	22.51	51.78	<0.01
d.) Fatigue	4	35.37	31.04	25.71	2.86	27.88	58.72	<0.01
e.) Pain	8 [*]	20.33	23.00	25.71	0.00	14.59	38.24	<0.01
f.) Gastrointestinal Issues	6	22.00	23.77	27.14	2.86	20.32	27.26	0.11
g.) Vision	4	22.86	26.51	30.00	1.43	18.04	37.87	0.05
h.) Communication	7	14.34	19.15	32.86	0.00	10.10	27.55	<0.01
i.) Sleep	4	30.45	29.14	27.14	2.86	25.01	47.41	<0.01
j.) Emotional Issues	12	18.17	22.33	27.14	0.00	13.22	33.62	<0.01
k.) Cognitive Impairment	9	18.03	23.45	30.00	1.43	13.11	33.36	<0.01
l.) Social Satisfaction	6	25.91	25.46	30.00	0.00	19.23	46.73	<0.01
m.) Social Performance	7	17.98	26.24	44.29	0.00	10.17	42.28	<0.01
n.) Myotonia	4	26.62	25.30	27.14	0.00	22.85	38.37	0.06
o.) Breathing	1	12.86	26.15	74.29	4.29	7.08	30.88	<0.01
p.) Swallowing	3	15.44	22.06	54.29	0.00	13.19	22.46	0.27
q.) Hearing	1	8.21	20.29	81.43	1.43	7.08	13.24	0.49
Total MDHI	114	24.40	20.04	4.29 [§]	0.0	18.91	41.49	<0.01

^{*} Initially this bank had 9 questions. One question (foot pain) was ultimately dropped from the final MDHI due to a low test-retest reliability

[†] Percentage of patients who had no disease burden in the stated theme (measured as a score of 0)

[‡] Percentage of patients who had the maximum level of disease burden in the stated theme (measured as a score of 100)

[§] No participants with a CTG repeat length greater than 100 had a total MDHI score of 0

MDHI: Myotonic Dystrophy Health Index

ND patients: patients who report that they are not disabled

D patients: patients who report that they are disabled

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Table 3

Correlations Between Strength and MDHI Total Score

TEST		r	P-value
Manual Muscle Testing (MMT)	Average of 30 muscles	−0.69	<0.0001
MMT	Average of 26 muscles	−0.72	<0.0001
MMT	Upper Extremity Muscles Only	−0.63	<0.0001
MMT	Lower Extremity Muscles Only	−0.72	<0.0001
Quantitative Muscle Testing (QMT)	% of Predicted Normal	−0.56	<0.0001
QMT	Upper Extremity	−0.55	<0.0001
QMT	Lower extremity	−0.57	<0.0001
Grip Strength (QMT)	Right Hand	−0.63	<0.0001
Grip Strength (Maximum Voluntary Isometric Contraction of Grip with a Dynamometer)	Peak Force	−0.64	<0.0001
Time To Go 30 Feet	Seconds	0.63	<0.0001
Time To Ascend 4 Steps	Seconds	0.62	<0.0001
Time To Descend 4 Steps	Seconds	0.61	<0.0001
Time To Stand From Chair	Seconds	0.45	<0.0001
Time To Stand 10 x From Chair	Seconds	0.46	0.0001
Purdue Pegboard Test	Total Score	−0.18	0.1493
Jebsen-Taylor Hand Function	Total Score	0.35	0.0029
Pinch Grip	Right Palmar	−0.68	<0.0001
Pinch Grip	Right Lateral	−0.65	<0.0001
Forced Vital Capacity (FVC) Sitting	% Predicted	−0.44	<0.0001
FVC Supine	% Predicted	−0.41	0.0004
Six Minute Walk Test	Meters	−0.69	<0.0001
Muscle Impairment Rating Score (MIRS)	1 to 5	0.61	<0.0001

Table 4

Correlations Between Patient-Reported Outcome Measures and MDHI Total Score

TEST	r	P-value
Upper Extremity Functional Index	−0.83	<0.0001
Lower Extremity Functional Index	−0.88	<0.0001
SF-36 (Physical Health) Summary Measure	−0.82	<0.0001
SF-36 (Mental Health) Summary Measure	−0.25	0.0355
SF-36 Physical Functioning	−0.81	<0.0001
SF-36 Role- Physical	−0.75	<0.0001
SF-36 Bodily Pain	−0.65	<0.0001
SF-36 General Health	−0.64	<0.0001
SF-36 Vitality	−0.72	<0.0001
SF-36 Social Functioning	−0.55	<0.0001
SF-36 Role- Emotional	−0.44	0.0001
SF-36 Mental Health	−0.36	0.0023
Epworth Sleepiness Scale	0.36	0.0024
Myotonia VAS	0.40	0.0014
Right Pain VAS	0.63	0.0202
INQoL% score	0.73	<0.0001
INQoL weakness	0.79	<0.0001
INQoL locking	0.47	<0.0001
INQoL fatigue	0.79	<0.0001
INQoL pain	0.64	<0.0001
INQoL activities	0.83	<0.0001
INQoL independence	0.75	<0.0001
INQoL social relationships	0.73	<0.0001
INQoL emotions	0.69	<0.0001
INQoL body image	0.70	<0.0001

Table 5

Correlations Between Laboratory Test Results and MDHI Total Score

LABORATORY TEST		r	P-value
DEXA *	Total Lean Body Mass (LBM)	−0.35	0.0028
	Upper Extremity LBM	−0.45	<0.0001
	Lower Extremity LBM	−0.35	0.0028
CK †		0.02	0.9109
Electromyography Myotonia	Number of times myotonia observed at 40 locations	0.61	0.002
Voluntary Grip myotonia	Time between 90% to 5% peak hand grip force	0.22	0.0697

* Dual-energy x-ray absorptiometry

† Creatine kinase

Table 6

Associations Between Physician Assessments and MDHI Total Score

CLINICAL ASSESSMENT	Number of Participants With the Clinical Finding	Number of Participants Without the Clinical Finding	Mean MDHI Total Score In Those With the Clinical Finding	Mean MDHI Total Score In Those Without the Clinical Finding	P-value
Grip myotonia	51	19	28.17	14.26	0.0013
Grip greater than 3 seconds (right hand)	32	33	25.82	22.31	0.2938
Percussion myotonia	62	6	26.70	0.4949	0.0002
Voice affected	37	32	29.36	17.88	0.0229
Facial weakness	61	9	26.77	8.34	0.0037
Hearing normal	61	8	25.24	20.96	0.6664
Hearing aid *	5	24	20.39	24.58	0.9081

* Hearing aid data not collected in initial participants