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Medication adherence in patients with myotonic dystrophy and facioscapulohumeral muscular dystrophy

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Abstract
Myotonic dystrophy (DM) and facioscapulohumeral muscular dystrophy (FSHD) are the two most common adult muscular dystrophies and have progressive and often disabling manifestations. Higher levels of medication adherence lead to better health outcomes, especially important to patients with DM and FSHD because of their multisystem manifestations and complexity of care. However, medication adherence has not previously been studied in a large cohort of DM type 1 (DM1), DM type 2 (DM2), and FSHD patients. The purpose of our study was to survey medication adherence and disease manifestations in patients enrolled in the NIH-supported National DM and FSHD Registry. The study was completed by 110 DM1, 49 DM2, and 193 FSHD patients. Notable comorbidities were hypertension in FSHD (44 %) and DM2 (37 %), gastroesophageal reflux disease in DM1 (24 %) and DM2 (31 %) and arrhythmias (29 %) and thyroid disease (20 %) in DM1. Each group reported high levels of adherence based on regimen complexity, medication costs, health literacy, side effect profile, and their beliefs about treatment. Only dysphagia in DM1 was reported to significantly impact medication adherence. Approximately 35 % of study patients reported polypharmacy (taking 6 or more medications). Of the patients with polypharmacy, the DM1 cohort was significantly younger (mean 55.0 years) compared to DM2 (59.0 years) and FSHD (63.2 years), and had shorter disease duration (mean 26 years) compared to FSHD (26.8 years) and DM2 (34.8 years). Future research is needed to assess techniques to ease pill swallowing in DM1 and to monitor polypharmacy and potential drug interactions in DM and FSHD.

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Medication Adherence in Patients with Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy

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ABSTRACT

Myotonic dystrophy (DM) and facioscapulohumeral muscular dystrophy (FSHD) are the two most common adult muscular dystrophies and have progressive and often disabling manifestations. Higher levels of medication adherence lead to better health outcomes, especially important to patients with DM and FSHD because of their multisystem manifestations and complexity of care. However, medication adherence has not previously been studied in a large cohort of DM type 1 (DM1), DM type 2 (DM2), and FSHD patients. The purpose of our study was to survey medication adherence and disease manifestations in patients enrolled in the NIH supported National DM and FSHD Registry. The study was completed by 110 DM1, 49 DM2, and 193 FSHD patients. Notable comorbidities were hypertension in FSHD (44%) and DM2 (37%), gastroesophageal reflux disease in DM1 (24%) and DM2 (31%) and arrhythmias (29%) and thyroid disease (20%) in DM1. Each group reported high levels of adherence based on regimen complexity, medication costs, health literacy, side effect profile, and their beliefs about treatment. Only dysphagia in DM1 was reported to significantly impact medication adherence. Approximately 35% of study patients reported polypharmacy (taking 6 or more medications). Of the patients with polypharmacy, the DM1 cohort was significantly younger (mean=55.0 years) compared to DM2 (59.0 years) and FSHD (63.2 years) and had shorter disease duration (mean=26 years) compared to FSHD (26.8 years) and DM2 (34.8 years). Future research is needed to assess techniques to ease pill swallowing in DM1 and to monitor polypharmacy and potential drug interactions in DM and FSHD.

Keywords:

Myotonic dystrophy; facioscapulohumeral muscular dystrophy; muscular dystrophy; medication adherence

INTRODUCTION

Myotonic dystrophy (DM) and facioscapulohumeral muscular dystrophy (FSHD) are both autosomal dominant disorders and the most common adult-onset muscular dystrophies [1, 2]. Two subtypes of DM exist with different etiologies and similar, yet distinct clinical presentations. Myotonic dystrophy type 1 (DM1) is caused by an unstable CTG trinucleotide repeat within the *DMPK* gene on chromosome 19q13.3 [3-5] . Myotonic dystrophy type 2 (DM2) is caused by an unstable CCTG tetranucleotide repeat in intron 1 of the *CNBP (ZNF9)* gene on chromosome 3q21.3 [6]. DM1 affects 1 in 8,000 patients, whereas the prevalence of DM2 is not fully known. In some countries, DM2 may affect more patients than DM1 [7].

The hallmark manifestations of both DM1 and DM2 include cataracts, muscle weakness, myotonia, and multisystem manifestations [1, 8, 9]. The onset of DM1 manifestations often begin in the second and third decade of life and include myotonia and distal and facial weakness. Multi-system manifestations can include cardiac arrhythmias, insulin resistance, hypersomnia, gastrointestinal problems, and cognitive impairment that have variable ages of onset [1, 8, 9]. Based upon CTG repeat size and age of onset, DM1 is often classified into the following categories: congenital, childhood onset, adult or "classical" and minimal or late onset [8-11]. Patients with congenital DM1 present with severe weakness, dysphasia, cognitive deficits, and respiratory complications at birth [1, 8, 9, 11]. DM2 does not have a congenital form of the disease. Patients with DM2 typically have onset of symptoms in the fourth and fifth decade of life and have greater proximal weakness and often less muscle wasting compared to DM1 [12-14]. There are often delays in diagnosing patients with DM2 and DM1[15]. The multisystem manifestations of DM2 are understudied but are often less severe compared to DM1 [12].

The second most common adult muscular dystrophy is FSHD, affecting approximately 1 in 15,000 to 20,000 individuals [16-18]. Of FSHD cases, approximately 95% of patients have FSHD type 1 (FSHD1) and 5% of patients have FSHD type 2 (FSHD2) [2]. Recent evidence suggests that both FSHD types share a common pathophysiological pattern caused by an abnormal expression of the DUX4 gene on chromosome 4q35, most likely by a complex, toxic gain of function mechanism [19]. Studies suggest that both FSHD subtypes are clinically identical [2, 20]. Patients with FSHD present with a unique pattern of muscle weakness affecting the face, shoulders, and upper arms. Non-muscular symptoms are rare and may include retinal vascular changes (Coat's Syndrome) and hearing loss, especially in more severely affected patients [21, 22]. As the disease progresses, the distal anterior leg and hip-girdle muscles are also involved [2]. Studies indicate that approximately 20% of patients may require a wheelchair by their sixth decade [23, 24].

The broad manifestations of both DM and FSHD often have profound impact on quality of life due to a high frequency of pain, fatigue, limited mobility, and social and emotional complications [25-34]. The diseases also impact employment. One study indicated that nearly 20% of a large sample of FSHD patients (n=313) reported that their job was modified due to FSHD with an additional 16% of patients disabled due to FSHD [23]. The impact of the disease on employment is often even more severe in DM1 patients. A literature review on the multisystem manifestations and social concerns relevant to DM1 cites low education attainment, low employment, and the need for supplemental income/financial assistance as social features of

the disease [30]. In addition, DM1 often directly or indirectly causes a broad spectrum of cognitive manifestations, such as, visual spatial deficits, memory impairment, reduced executive function (trouble organizing & staying on task, reduced goal directed action), and apathy [1, 35-38].

Despite these broad, multisystem and social effects of both disorders, limited information is available about the most common pharmacological treatments used by patients and potential barriers to adherence. With the use of any medication, there exists a potential for poor adherence that ultimately results in poorer health outcomes [39, 40]. Moreover, research suggests that approximately 50% of patients with chronic disease do not take medications as prescribed [41]. Examples of barriers to adherence that patients may experience include regimen complexity, cost of medications, side effect profile, understanding the medications and disease states, and physical limitations. Patients with DM and FSHD may have larger barriers to adherence compared to the general population because of the chronic nature and progression of their manifestations, disease related comorbidities, dysphagia, reduced employment, and limited mobility [23, 25-34]. Studying the factors that affect adherence may facilitate the development and the refinement of clinical pharmacy services for DM and FSHD patients. Such information may also help guide the design of clinical trials in DM and FSHD to assess drug compliance, side effects, and the complexity of treatment regimens. To that end, this study was developed to assess the impact that DM and FSHD have on patients' adherence to medications.

METHODS

Participants

Participants for this study were recruited from the National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members based at the University of Rochester. The Registry has been funded by the National Institutes of Health (NIH) since 2001. Members of the National Registry are enrolled when the principal investigator or co-investigators have confirmed an enrollee's consent, reviewed their patient information form, and verified a diagnosis through medical record review and genetic or clinical/family history information [42].

Inclusion criteria for this study included enrollment in the National Registry, an age of 18 years or older, and a diagnosis of DM (DM1 and DM2) or FSHD. FSHD1 and FSHD2 were combined due to the lack of available genetic testing for FSHD2. Recruitment letters were mailed to all eligible members of the National Registry. Participants were given information about the study. If interested, they could either take the survey online or mail in a paper copy of the survey.

Participation in this study was voluntary and participants' responses were recorded anonymously. Both the St. John Fisher College Institutional Review Board and the Scientific Advisory Committee of the NIH National Registry approved the methodology and survey before it was distributed to participants.

Survey Design

The survey was created using Qualtrics® software and contained 40 questions on demographics, basic medication information, medication adherence factors, comorbidities, and quality of life. The survey was designed so that participants were able to skip or not to respond to any question that they chose.

Demographics and disease specific questions

All participants were asked basic demographic questions, including gender identity, race, ethnicity, year of birth, employment status, and education level. Patients completed a question to rate their general health on a five point scale: excellent (1), very good (2), good (3), fair (4), and poor (5). Higher scores indicated poorer health. Demographic information about participants' disease was also gathered by asking for muscular dystrophy diagnosis, size of DNA deletion/repeat (if applicable), and age of symptomatic onset. Because of the clinical heterogeneity of patients with DM1 [8], we categorized our DM1 cohort into the following groups [8-11]

- congenital (age of onset at birth and CTG expansion of greater than 1,000 repeats;
- childhood (age of onset between 1 and 10 years old or CTG expansion between 101-999);
- adult or "classical" (age of onset between 11-40 or CTG expansion between 101-999);
- mild/late onset (age of onset greater than 41 years old or CTG expansion between 51-100); and
- Indeterminable (conflicting data between age of onset and CTG expansion size; example an age of onset reported over age 50 years old and repeat size above 600).

An additional question in all patients inquired about the most burdensome manifestations of the disease. The question was open-ended and phrased as: "If you could pick one problem of DM or FSHD that could be helped by a new treatment, what would it be?" This question was asked to broadly assess disease manifestations that may impact the patients the most and influence clinical care (e.g., pain management and assistive devices) or future experimental therapies. We coded the patient reported symptoms into categories related to strength, function, and multi-system manifestations (fatigue, gastrointestinal, pain, balance, etc.).

Basic Medication Information

Participants were asked general questions about their medications, including the number of medications taken daily, how they are taken, knowledge of the indication for their medications, and the most difficult medication to take. In this section, questions were also asked to assess participants' beliefs and habits related to their medications. Additionally, comorbidities of participants were gathered by asking a question about concomitant medical conditions and treatments received (phrased: "select the following conditions that you have been diagnosed with or received treatment for"). Participants could select from a checklist of medical conditions or provide their response in free text.

Medication Adherence

Medication adherence was assessed by asking questions about medication administration and assessing potential barriers of medication use: forgetting to take medications, choosing not to take medications, difficulty taking medications, cost, and side effects. To understand the impact that side effects may have on medication adherence, several questions were asked about current

side effects, previous severe side effects, and whether participants were counseled on these side effects.

Statistical Analysis

We performed all statistical analyses using IBM SPSS Statistics 22. We used descriptive statistics to summarize demographics, disease burden, and comorbidities. We compared all three disease groups using ANOVA for continuous variables (and post hoc Tukey, as appropriate); for categorical variables, Pearson chi square were performed and separate comparisons between each group were also performed for those with overall significant p-values. To compare the different types of muscular dystrophy with medication use, regimens, and barriers to adherence, we used X^2 and student-t test in assessing these relationships. Data were analyzed through manual compilation based on comorbidity categories. Comorbid conditions reported were grouped by a single researcher with follow-up review by two additional researchers. Data are reported as means ± standard deviations or percentages. Significance was set at $\alpha = 0.05$

RESULTS

Survey Response Rate and Demographics

The survey was mailed to 1,516 eligible members of the National Registry. The survey and consent were completed by 366 patients (response rate of 24.1%). Nineteen of these participants mailed in surveys completed by hand, while the rest were electronically completed and collected. All surveys were completed between January and July 2014.

The mean age of the participants was 55.5 years (SD = 13.7; range = 20-90). The majority of participants identified as male (53.4%), white (98.3%), and non-Hispanic (97.4%). The full list of participant demographics is listed in Table 1.

Patients with DM1 were categorized into the following categories: congenital (1%; n=1/110); childhood (2.8%; n=3/110; adult onset or "classical" (73.4%; n=80/110); mild or late onset (15.6% (n=17/110), and indeterminable (7.3%; n=8/110). The majority of patients with DM2 reported their onset of symptoms in their third to fifth decade (64.6%). No patients reported onset of symptom in their sixth decade. The majority of FSHD patients (61.7%) reported onset of symptoms before 20 years old as typically seen in FSHD [2].

Most Burdensome Problem

Regardless of disease group, muscle weakness was the most common problem that patients reported that they wanted helped by a new treatment (Table 2). In total, 84% of FSHD patients reported that they would choose a muscle-related problem to be helped by new treatments, specifically muscle weakness (48.5%), mobility (21.1%) and muscle loss (14.4%). DM1 patients reported more non-muscle-related problems than FSHD patients (Table 2). For example, DM1 patients reported wanting a new treatment to help fatigue (14.3%) versus DM2 (2.0%) and FSHD (1.5%). More DM2 patients (14.3%) reported pain as an important problem to treat which was twice the number of patients with DM1 and FSHD reports of pain.

Comorbidities

Chronic comorbid conditions reported by patients are listed in Table 3. The two most frequently reported comorbidities for DM1 were depression (29.1% versus 22.9% in the general population) [43] and arrhythmias (29.1% in DM1 versus 20.4% in DM2 and 7.8% in FSHD). Normative data suggest that approximately 2-9% in the general population has atrial fibrillation [44], which has been reported to be the most common type of tachyarrhythmia in DM1 patients [45]. The most frequent comorbidity in FSHD was hypertension (44%) which was also higher compared to adults in the US (32.5%) according to published reports from the Centers for Disease Control [46].

Hypertension was more prevalent in FSHD compared to DM1 or DM2. Also, a larger percentage of participants with FSHD reported having arthritis and osteoporosis or osteopenia than participants with DM1 or DM2. Participants with DM1 reported having more cardiac arrhythmias than participants with FSHD or DM2. Of the three disease groups, depression, thyroid disorders, and heart disease were more common in DM1, whereas gastroesophageal reflux disease (GERD) and diabetes were more common in DM2.

Number of Medications, Age, and Employment

Table 4a lists the number of medications and mean ages of participants with FSHD, DM1 and DM2. The mean age at the time of taking this survey was lower for participants who reported taking five or fewer medications than participants who reported taking six or more medications (23.7 years versus. 29.2 years, $p<0.001$). Additionally, those who took six or more medications were more likely to be unemployed compared to those who took fewer medications (73.8% versus. 52.4%, $p<0.001$). When analyses were conducted for each subgroup separately, findings were similar within the FSHD group, but no such significant findings occurred in the DM1 or DM2 groups. However, the mean age of DM1 patients taking six or more medications was significantly lower than FSHD patients taking six or more medications (Table 4b; 55.0 years old versus 63.1 years old, $p<0.001$). Correspondingly, the duration of disease in patients taking six or more medications was significantly lower in DM1 patients compared to FSHD patients (26.0 years versus 36.7 years, $p<0.001$). Patients with DM1 were less likely to be employed compared to patients with FSHD, regardless of number medications being taken.

Barriers to adherence and medication regimens

Table 5 reports the barriers to adherence and medication regimens, comparing each of the three muscular dystrophy types. Of all participants, 64.9% reported taking five or fewer medications daily and 35.1% took six or more medications daily. Most participants (92.3%) reported that the cost of medications did not interfere with taking them as prescribed and 93.0% had insurance to help cover medication costs.

Of all participants, 53.4% reported no side effects from their medications. Of those who did report experiencing side effects, 43.3% (n=71/164) reported that side effects made them stop taking their medications (data not shown). Specifically, those with DM1were less likely to report that side effects impacted their adherence to medications, compared to those with the FSHD or DM2 (37.4% in DM1 vs. 51.3% in FSHD and 60.5% in DM2, $p=0.020$). Difficulty swallowing whole tablets or capsules was reported by 19.8% of all participants. More DM1

participants reported having difficulty with or being unable to swallow whole tablets or capsules (33.3% compared to 20.9% in DM2 and 10.9% in FSHD; $p<0.020$).

Participants reported having a good understanding of their disease manifestations and medications with no significant differences between sub-groups (Supplemental Table 6). All participants reported that they knew the prescribed indications for all or some of their medications (data not shown). When taking medications, 82.2% of participants reported taking their medications as directed all of the time and 84.5% of participants agreed that taking their medications as directed is important to them. The majority of participants disagreed or strongly disagreed that their medications impacted their social lives (81.6%) or their work lives (82.4%). When asked if their medications made them feel better, 71.6% of participants agreed or strongly agreed. 67.7% of participants responded that they have not forgotten to take a dose of their medications in the past two weeks.

DISCUSSION

This is one of the first studies on medication adherence in FSHD and DM. Results indicate that in this patient sample, disease manifestations do not significantly impact patients' ability to adhere to their medications. Our study sample consisted of mild to moderately affected patients based on age, duration of disease, self-reported health, and comorbidities. The ages of onset in our cohorts compare to previous research in DM1, DM2, FSHD [1, 2, 47]. The majority of patients self-reported their general health as good (40.3%) with a normal distribution of self-reported health ranging from excellent (2%) to poor (5%). We further classified DM1 patients according to broad subtypes. 79% of our DM1 sample was classified as adult onset or "classical" DM. There are a few limitations of these common DM1 classifications, such as: a.) broad variability of disease manifestations [1]; b.) lack of strict correlations between disease manifestations and CTG expansions that range from 100-999 [8] and c.) difficulty to determine the age of onset of DM symptoms in teens and young adults and whether the symptoms were patient-reported or queried by a physician. Our data are limited by: a.) self-reported CTG repeat size; and b.) we did not ask the patient to distinguish between the onset of muscle related or multi-systemic manifestations.

Another limitation is that we did not inquire about cognitive effects of our cohorts, most pertinent to patients with DM1. Given the often variable cognitive effects in DM1, particular apathy and memory impairment in more severely affected patients [35-37], the data from our DM1 cohort may under-estimate barriers to medication adherence. Future studies are needed to: a.) develop consensus on the most appropriate neuropsychological tests to use for patients with DM1; b.) assess other disease factors that may influence cognition (e.g., sleep apnea, endocrine disturbances, hypersomnia); and c.) ask family members about potential cognitive affects in the patient. Such cognitive assessments will provide even greater details on adherence to medications from the perspective of the DM1 patient and family members.

A third limitation is that our study patients may not be representative of the entire DM and FSHD populations in the United States or the world. Participants from registries may have milder disease, be more eager to participate in research, and may be more knowledgeable about their manifestations than the overall DM an FSHD populations. Additional studies are needed to

compare populations across other registries and amongst patients with an even broader range of disease severities.

Given the multisystem effects of these three diseases, especially DM1 and DM2, we inquired about which disease manifestations patients wanted helped by a new treatment. Most participants reported muscle weakness as the most burdensome problem of their disease in need of treatment. Mobility was reported as a greater problem in FSHD than in DM1 or DM2. This observation may be attributed to the FSHD patients in our study population having a longer disease duration compared to the surveyed DM patients. Participants with DM1 reported that fatigue, balance, cardiac, gastrointestinal, psychiatric, and respiratory components of their disease were more in need of a new therapy than participants with FSHD or DM2. These multisystem manifestations may also have been exacerbated by muscle weakness, which had a higher response rate in the DM cohorts. It may be beneficial for future studies to separate secondary problems of DM and FSHD from muscle-related complications to adequately identify the most significant problems to patients. This information may help guide the clinical care of patients, including use of assistive devices and exercise, and may facilitate the development of future therapies to focus on improvements in mobility and other, skeletal muscle components of the disease.

One key example of the need for more effective treatment of skeletal muscle weakness relates to facial weakness. Although our results suggest that in our select patient population there are limited barriers to adherence, dysphagia was noted to be a barrier for DM1 patients. This finding corresponds to previous research which has shown that dysphagia is a common problem in DM1, but not FSHD or DM2 [12, 48]. Because many medications are only available as oral tablets or capsules, DM1 patients may find it difficult to swallow their medications and this may impact their ability to be adherent. Given the higher percentage of DM1 patients reporting difficulty swallowing compared to FSHD or DM2 patients, alternate dosage forms besides tablets and capsules may be preferred by these patients. Patients with DM1 should also be counselled on techniques to on how to make swallowing pills easier, such as the “lean forward” and “pop bottle” techniques [49].

A frequent hindrance to medication adherence in the general population is polypharmacy, which is defined as patient taking five or more prescriptions or alternatively as the use of more medications than necessary [50]. Whereas not a main focus on this paper, our data suggest polypharmacy in our participants. 35.1% of participants reported that they took six or more medications (prescription and over the counter (OTC)), and 9.0% reported they took 11 or more medications (data not shown). In other chronic diseases, higher regimen complexity is associated with poorer adherence [51]. Another limitation of this study is that we did not distinguish between the numbers of prescription versus OTC medications. Therefore, a direct comparison with data from general populations is not possible. However, one recent study suggests that 35.8% of older adults reported concurrent use of at least five prescription medications (n= 2351; average age = 71.4 years old) [52]. Their data also indicate that 37.9% of adults reported the use of OTC medications. It appears as though our respondents were reporting a comparable level of polypharmacy (regardless of either prescription or OTC) at a younger age compared to this one study.

In the current study, participants with FSHD and DM1 who took more medications (six or more medications) were found to have a higher average age than those who took fewer medications (five or fewer medications). DM1 patients on six or more medications have a shorter disease duration than FSHD patients. Additionally, participants with DM1 are taking more medications at a younger age than participants with FSHD. This age disparity between FSHD and DM1 has similarly been observed with the age of disability onset. Disability often occurs by age 30-50 in DM1 and does not frequently occur in FSHD [12, 53]. Disability as well as the more complex, multisystem manifestations may contribute to participants with DM1 taking more medications at an earlier age compared to FSHD.

With both FSHD and DM1, the majority of participants who took six or more medications were unemployed. In addition, for respondents taking five or fewer medications, more DM1 participants were unemployed compared to FSHD participants. The higher percentage of DM1 patients who take fewer medications and were unemployed may be explained by increased cognitive manifestations and often more frequent disability in DM1 patients compared to FSHD and DM2. Despite high levels of unemployment in all disease groups, a large majority of participants identified that medication costs did not interfere with taking their medications as prescribed and that they had sufficient insurance to cover medication costs. Generally, higher co-payments and medication costs are associated with lower levels of adherence in patients with chronic conditions [45]. In our study, it can be inferred that the FSHD and DM cohorts had a high degree of health literacy and do not have many barriers to overcome in order to remain adherent to their medications. However, given the patient-reported impact of muscle weakness, muscle and mobility loss, it is apparent that DM and FSHD patients still have significant challenges that may require consultations on physical therapy, exercise, orthotics, and other mobility devices. Limitations or barriers to such access or therapies may contribute to the high levels of polypharmacy seen in our sample.

The community pharmacist may play an important role to counsel patients taking multiple medications and to encourage physical therapy, exercise, and use of orthotics especially as disease manifestations progress. Previous research has demonstrated the impact of community pharmacists in educating about and managing medications in patients who require polypharmacy [54], but studies have not been completed yet in the muscular dystrophy population. Such studies are needed. Lastly, a thorough analysis of the specific medications that DM and FSHD patients in the National Registry take will illuminate common potential adverse reactions and potential drug interactions that need to be discussed amongst pharmacists, primary care doctors, neurologists, and patients.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

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Table 1. Demographic information of study participants				
	All Participants	FSHD (n=193)	DM1 (n=110)	DM2 (n=49)
	Mean (SD)			
Age (years)	55.5 (13.7)	57.5 (13.6)	51.0 (13.4)	58.0 (12.2)
Age at symptom onset (years)_	25.8 (15.5)	22.6 (15.0)	27.9 (14.9)	34.3 (15.2)
*Duration of Disease (years)	29.7 (15.9)	35.0 (15.7)	23.0 (11.8)	23.4 (17.1)
	N (%)			
Gender identity Male Female Not reported	 187 (53.4) 163 (46.6)	 108 (56.0) 85 (44.0)	 52 (47.3) 57 (51.8) 1 (0.9)	 27 (56.3) 21 (43.8)
Race White Black Asian Other	 346 (98.3) 1 (0.28) 2 (0.57) 3 (0.85)	 189 (97.9) 1 (0.5) 2 (1.0) 1 (0.5)	 109 (99.1) 0 (0.0) 0 (0.0) 1 (0.9)	 48 (98.0) 0 (0.0) 0 (0.0) 1 (2.0)
Ethnicity Hispanic Non-Hispanic	 9 (2.6) 334 (97.4)	 5 (2.6) 185 (97.4)	 3 (2.8) 105 (97.2)	 1 (2.2) 44 (97.8)
Education level Some high school High school graduate Some college College graduate Graduate/professional Not reported	 6 (1.7) 39 (11.1) 68 (19.4) 116 (33.0) 122 (34.8)	 1 (0.5) 21 (10.9) 30 (15.5) 63 (32.6) 78 (40.4)	 4 (3.6) 13 (11.8) 27 (24.6) 44 (40.0) 21 (19.1) 1 (0.9)	 1 (2.0) 5 (10.2) 11 (22.5) 9 (18.4) 23 (46.9)
Self-reported health Excellent Very good Good Fair Poor	 6 (2.0) 78 (26.2) 120 (40.3) 79 (26.5) 15 (5.0)	 4 (2.6) 41 (26.5) 65 (41.9) 36 (23.2) 9 (5.8)	 1 (1.0) 21 (21.0) 39 (39.0) 34 (34.0) 5 (5.0)	 1 (2.3) 16 (37.2) 16 (37.2) 9 (20.9) 1 (2.3)
* Employed Yes No	 139 (39.6) 212 (60.4)	 90 (46.9) 102 (53.1)	 27 (24.5) 83 (75.5)	 22 (44.9) 27 (55.1)

Note: Some participants skipped these questions, so the N for these responses do not include the full sample (n=352)

** $p<0.05$ (p-value is based on comparison of all three illness types using ANOVA for continuous variables and Pearson chi square for categorical variables)*

Table 2. Disease manifestations that study patients would like helped by a new treatment			
	FSHD (n=193)	DM1 (n=110)	DM2 (n=49)
	N (%)		
Muscle weakness	94 (48.5)	49 (43.8)	27 (55.1)
Mobility	41 (21.1)	11 (9.8)	1 (2.0)
Muscle loss	28 (14.4)	1 (0.9)	4 (8.2)
Disease progression	28 (14.4)	4 (3.6)	3 (6.1)
Pain	13 (6.7)	7 (6.3)	7 (14.3)
Fatigue	3 (1.5)	16 (14.3)	1 (2.0)
Balance	3 (1.5)	7 (6.3)	0 (0)
Cardiac	1 (0.5)	7 (6.3)	2 (4.1)
Gastrointestinal	1 (0.5)	6 (5.4)	1 (2.0)
Psychiatric	0 (0)	4 (3.6)	2 (4.1)
Respiratory/speech	2 (1.0)	3 (2.7)	0 (0)

Table 3. Comorbidities				
Condition	All Participants (n=352)	FSHD (n=193)	DM1 (n=110)	DM2 (n=49)
Number of comorbidities, Mean (SD)	2.20 (1.3)	2.24 (1.3)	2.04 (1.2)	2.29 (1.4)
	N (%)			
Hypertension	110 (31.3)	85 (44.0)	7 (6.4)	18 (36.7)
Depression	98 (27.8)	55 (28.5)	32 (29.1)	11 (22.4)
GERD	76 (21.6)	35 (18.1)	26 (23.6)	15 (30.6)
Arthritis	76 (21.6)	57 (29.5)	11 (10.0)	8 (16.3)
Arrhythmia	57 (16.2)	15 (7.8)	32 (29.1)	10 (20.4)
Thyroid disease	54 (15.3)	26 (13.5)	22 (20.0)	6 (12.2)
Osteoporosis/osteopenia	40 (11.4)	28 (14.5)	8 (7.3)	4 (8.2)
Diabetes	39 (11.1)	24 (12.4)	4 (3.6)	11 (22.4)
Heart disease	28 (8.0)	11 (5.7)	13 (11.8)	4 (8.2)

Table 4a. Number of Medications, Age, Age at Diagnosis, and Employment Status								
	All		**FSHD**		**DM1**		**DM2**	
	0-5 meds (n=226)	≥ 6 meds (n=122)	0-5 meds (n=130)	≥ 6 meds (n=61)	0-5 meds (n=70)	≥ 6 meds (n=38)	0-5 meds (n=26)	≥ 6 meds (n=23)
	Mean (SD)							
Mean Age; (years)	53.2 (13.4)**	59.8 (13.3)**	54.8 (13.4)**	63.2 (12.7)**	48.7 (13.6)*	55.0 (12.6)*	57.2 (10.5)	59 (14.1)
Mean Age at Diagnosis (years)	23.7 (14.7)**	29.2 (16.4)**	20.4 (13.4)*	26.8 (17.1)*	26.5 (14.9)	29.9 (15.0)	33.9 (14.8)	34.8 (16.1)
Disease Duration (years)	29.2 (15.0)	31.0 (17.5)	34.4 (14.6)	36.7 (18.1)	21.5 (10.4)	26.0 (13.6)	23.3 (17.3)	23.5 (17.3)
	N (%)							
Employed								
Yes	107 (47.6)**	32 (26.2)**	75 (58.1)**	15 (24.6)**	19 (27.1)	8 (21.1)	13 (50.0)	9 (39.1)
No	118 (52.4)**	90 (73.8)**	54 (41.9)**	46 (75.4)**	51 (72.9)	30 (78.9)	13 (50.0)	14 (60.9)

Note: Some participants skipped these questions, so the N for these responses do not include the full sample (n=352)
***Indicates significant findings (p<0.001)*
**Indicates significant findings (p<0.05)*

Table 4b. Stratified Analyses based on Number of Medications				
	0-5 Meds		**≥ 6 meds**	
	DM1 (n=70)	**FSHD (n=130)**	**DM1 (n=38)**	**FSHD (n=61)**
	Mean (SD)		Mean (SD)	
Mean Age (years)	48.7 (13.6)**	54.8 (13.7)**	55.0 (12.6)**	63.1 (12.7)**
Mean Age at Diagnosis (years)	26.5 (14.9)**	20.4 (13.4)**	29.9 (15.0)	26.8 (17.1)
Duration of Disease (years)	21.5 (10.4)**	34.4 (14.6)**	26.0 (13.6)**	36.7 (18.1)**
	N (%)		N (%)	
Employed				
Yes	19 (27.1)**	75 (58.1)**	8 (21.1)	15 (24.6)
No	51 (72.9)**	54 (41.9)**	30 (78.9)	46 (75.4)

Note: Some participants skipped these questions, so the N for these responses do not include the full sample (n=352)
*** indicates significant findings (p<0.010)*

Table 5. Medication Regimen Factors (pill burden, regimen complexity, side effects, etc.) and physical limitations that influence adherence to medications.				
	All Participants	FSHD (n=193)	DM1 (n=110)	DM2 (n=49)
	N (%)			
Number of daily medications				
No. of medications taken daily 0 - 5 ≥ 6	 226 (64.9) 122 (35.1)	 130 (68.1) 61 (31.9)	 70 (64.8) 38 (35.2)	 26 (53.1) 23 (46.9)
Medication costs				
Costs interfere Yes No	 23 (7.7) 276 (92.3)	 11 (7.1) 145 (92.9)	 7 (7.0) 93 (93.0)	 5 (11.6) 38 (88.4)
Insurance helps cover costs Yes No / no insurance	 267 (93) 20 (7.0)	 143 (92.9) 11 (7.1)	 86 (92.5) 7 (7.5)	 38 (95.0) 2 (5.0)
Side effects				
Currently experiencing side effects At least one reported No side effects	 164 (46.6) 188 (53.4)	 101 (52.3) 92 (47.7)	 39 (35.5) 71 (64.5)	 24 (49.0) 25 (51.0)
Stopped taking medications due to side effects Yes No	 143 (48.0) 155 (52.0)	 80 (51.3) 76 (48.7)	 37 (37.4) 62 (62.6)	 26 (60.5) 17 (39.5)
Physical limitations				
Able to swallow whole tablets/capsules Yes **No / Yes, but with difficulty ****	 239 (80.2) 59 (19.8)	 139 (89.1) 17 (10.9)	 66 (66.7) 33 (33.3)	 34 (79.1) 9 (20.9)

Note: Some participants skipped questions, so the N for some responses do not include the full sample (n=352)
*** Indicates significant difference (p<0.001) for the overall comparison between the 3 groups. In further analyses comparing these groups separately, patients with DM1 had more swallowing difficulty compared to FSHD and DM2 (p<0.001).*

Supplemental Table 6. Patient Characteristics (beliefs, literacy, etc.) that often hinder medication adherence.				
	All Participants	FSHD (n=193)	DM1 (n=110)	DM2 (n=49)
	N (%)			
Health literacy				
Taking medications as prescribed All of the time Some / None of the time	 273 (82.2) 59 (17.8)	 154 (84.2) 29 (15.8)	 85 (81.7) 19 (18.3)	 34 (75.6) 11 (24.4)
Taking medications as prescribed is important to me Agree Neutral / Do not agree	 250 (84.5) 46 (15.5)	 133 (86.9) 20 (13.1)	 83 (83.0) 17 (17.0)	 34 (79.1) 9 (20.9)
Medication beliefs				
Interferes with social life Agree Neutral / Do not agree	 54 (18.4) 240 (81.6)	 26 (17.1) 126 (82.9)	 22 (22.2) 77 (77.8)	 6 (14.0) 37 (86.0)
Interferes with work life Agree Neutral / Do not agree	 51 (17.6) 239 (82.4)	 26 (17.4) 123 (82.6)	 21 (21.4) 77 (78.6)	 4 (9.3) 39 (90.7)
Makes me feel better Agree Neutral / Do not agree	 212 (71.6) 84 (28.4)	 109 (70.8) 45 (29.2)	 71 (71.7) 28 (28.3)	 32 (74.4) 11 (25.6)
Forgetfulness				
Forgotten over past two weeks Yes No	 97 (32.3) 203 (67.7)	 46 (29.3) 111 (70.7)	 33 (33.0) 67 (67.0)	 18 (41.9) 25 (58.1)

Note: Some participants skipped these questions, so the N for these responses do not include the full sample (n=352)