Research Findings: Assessment of the Myotonic Dystrophy Research Landscape

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1. Executive Summary

The Myotonic Dystrophy Foundation (MDF) was founded in 2007 to improve the quality of life of people living with myotonic dystrophy and accelerate the search for therapies and a cure. Myotonic dystrophy (henceforth referred to as DM)[1] is a rare disease that affects every aspect of life for people living with the disease, their families, their providers, and others involved in their care. DM is an inherited disorder that can affect nearly every body system and appear at any age; it manifests differently in every person affected. Considered the most variable disease in medicine, there are currently no treatments or a cure.

In the spring of 2023, MDF engaged Third Plateau, a social impact strategy firm, to conduct a third-party assessment of the DM research landscape. The purpose of this assessment was to better understand:

1. Gaps and barriers to DM research (both type 1 and type 2) across the field;
2. Barriers to activating and maintaining high-functioning DM research sites and well-enrolled studies and trials; and
3. How MDF might better support progress in the field.

In February and March 2023, Third Plateau conducted 49 interviews and focus groups and administered a survey to capture additional perspectives from across the DM ecosystem, ultimately gathering input from 151 individuals across research and industry. Key takeaways from the assessment are outlined below and discussed at length in the report

Key Takeaways

1. Research: DM Priorities and Barriers
    a. There remain gaps in general understanding of the disease across the field, particularly for DM2. **Building a more comprehensive understanding of the disease alongside drug development is the top priority for research and industry. More specifically, both researchers and industry named identifying appropriate biomarkers for both DM1 and DM2 as a priority, and expanding genetic testing and diagnosis as a priority for DM2.**
    b. **MDF has a role to play in continuing to fuel the DM research pipeline and supporting the next generation of researchers and clinicians.** MDF's fellowship and grant programs have meaningfully contributed to the development and strength of a collaborative and committed bench of DM researchers. Yet, the future talent pipeline for DM remains a key concern among our sample.
    c. **There is an opportunity to support early stage research initiatives with pilot grants, or provide funding to cover gaps in larger institutional funding timelines. This will allow researcher teams and institutions to reduce barriers to launching new research programs and help attract larger-scale funding.** One opportunity discussed, primarily among researchers, was the challenge of accessing funding for new research initiatives and the toll and resource drain of ongoing funding uncertainty and grant seeking. Given MDF's credibility in the DM landscape, there may be a role to play in helping to seed new research and attract larger institutional funders.

[1] Note that we use "DM" throughout the report when speaking about myotonic dystrophy generally. In specific instances, we use "DM1" and "DM2" to distinguish between the two types of myotonic dystrophy.

2. DM Research Studies and Trials: Strengths and Opportunities
    a. Over the past decade, there has been significant growth in the development of active DM programs, studies, and trials. **However, the field has indicated that the Myotonic Dystrophy Clinical Research Network (DMCRN) and other active trial sites are not fully equipped to meet the near-term demand of the growth trajectory.** There is an opportunity to make critical investments in building the capacity of the DMCRN and/or other trial sites outside of the network.
    b. MDF is widely praised for its ability to bring together stakeholders across the DM ecosystem (patients and their families, physicians and specialists, researchers, industry partners) and its patient education programs. Respondents confirmed that it is **crucial that MDF continues to invest in patient education programs, particularly related to upcoming and current trials, enrollment, and preparation for participating in trials and studies.**
    c. While the DM research landscape is considered to be collaborative overall, **there is an opportunity to improve knowledge sharing and access to data across the ecosystem, both among researchers and industry.** MDF may have a role to play in promoting accountability and encouraging data publication and dissemination.

3. Other Opportunities to Support the Field
    a. Industry partners and researchers highlighted MDF's crucial role in advocating at the federal level with governing institutions, regulators, and policymakers, but expressed that **a more clearly defined agenda and increased transparency around advocacy efforts may help to accelerate progress in specific areas.**
    b. While MDF has a global presence and many international partnerships, some respondents suggested that MDF's viewpoint is still U.S.-centric. Industry partners and researchers alike noted that **there is an opportunity to better define the organization's international role and foster global collaboration to accelerate learning across the field.**

2. Introduction

2.1. Overview

Myotonic dystrophy (DM) is a rare disease that affects every aspect of life for patients, their families, their providers, and others involved in their care or concerned with their safety, health, and happiness. DM is an inherited disorder that can appear at any age and manifests differently in every person affected. There are currently no treatments or a cure.

The Myotonic Dystrophy Foundation (MDF) was founded in 2007 to improve the quality of life of people living with DM and accelerate the search for therapies and a cure. Over the past 16 years, MDF has become the largest DM-focused patient advocacy organization in the world, serving tens of thousands of individuals in the United States and across 121 countries. MDF's programs fund critical research, provide comprehensive resources and support to people living with DM and their families, and serve as a conduit to forge critical connections between patients, their care providers, research, and industry.

The mission of MDF is community, care, and a cure. MDF supports and connects the community of those affected by myotonic dystrophy, provides resources and advocates for care, and accelerates research toward treatments and a cure.

A year after launching a strategic plan in 2021, MDF continues to focus on providing support to its community, reducing barriers to accessing care, and pursuing research toward treatments and a cure.

In the spring of 2023, MDF engaged Third Plateau, a social impact strategy firm, to conduct a third-party assessment of the myotonic dystrophy research landscape. The purpose of this assessment was to better understand:

1. Gaps and barriers to myotonic dystrophy research (both type 1 and type 2) across the field;
2. Barriers to activating and maintaining high-functioning DM research sites and well-enrolled studies and trials; and
3. How the Foundation might better support progress in the field.

2.2. DM Landscape Assessment Background

The third prong of MDF's mission focuses on accelerating research toward treatments and a cure. MDF plays an important role in educating its community on current studies and clinical trials and engaging them as active partners in contributing to research through means such as participating in studies, joining registries, and responding to surveys.

Since 2009, MDF has provided pre- and post-doctoral research fellowships to support DM research and studies. Through this program, MDF aims to broaden the base of committed DM researchers to cultivate a robust and collaborative research community who will contribute to advancing DM research over the long term. To date, MDF has committed over $4 million in funding to support over 50 research fellows across five countries. Additionally, MDF provides grants to support scientific investigations that enhance quality of life for people living with DM and advance research aimed at finding therapies and a cure for the disease. MDF has offered a variety of funding opportunities for DM researchers and research efforts.

MDF also curates, and makes publicly available, resources important to the field in an effort to promote knowledge sharing and foster a collegial and connected network of researchers, practitioners, and drug developers. One such resource is the Myotonic Dystrophy Research Map, which is an interactive, visual database of the current DM research ecosystem, which compiles publicly available research on DM into a single database.[2]

In 2013, MDF awarded a grant to support the establishment of the first ever Myotonic Dystrophy Clinical Research Network (DMCRN) based on input from university researchers and industry partners. The creation of a clinical research network was a critical investment in DM research

[2] https://www.myotonic.org/myotonic-dystrophy-research-map

infrastructure to prepare for upcoming trials of potential treatments and lower the barriers to advancing DM science and research, both in the U.S. and globally. The goals of the DMCRN are threefold: 1) to develop research teams at each DMCRN member site who are dedicated to DM and have experience with research procedure, 2) to continue to develop knowledge on DM, as there is simply so much about the disease that is unknown; and 3) to collect additional data needed for clinical trials, such as outcome measures, disease progression, biomarkers, and endpoints. Ten years in, the network has contributed to the cultivation of a collaborative research environment and is engaged in a long-term natural history study to track the progression of DM in a large sample of patients over time.

The landscape assessment conducted by Third Plateau assesses the current strengths, needs, and barriers across the DM research ecosystem. The findings will inform how MDF and others in the space make future strategic investments and interventions to mitigate barriers and contribute to enabling conditions to accelerate research toward therapies and a cure.

3. Methodology

To conduct the assessment, Third Plateau designed a mixed methods study that included targeted interviews, focus groups, and a survey of researchers, physicians, and industry professionals. Through this assessment, we sought to gather evidence to answer several key questions such as:

- What gaps and barriers exist in the field of myotonic dystrophy research?
- What investments will better enable researchers and industry to run clinical trials with a large and diverse enrolled patient population?
- What will enable existing and encourage prospective pharmaceutical partners to focus on myotonic dystrophy drug development?

Third Plateau conducted a third-party assessment of these and other questions to help inform MDF's future strategy and investments in the field. **151 individuals participated in this assessment across interviews, focus groups, and the survey. Our interview sampling targeted industry partners, principal investigators (PIs), and clinical coordinators, and our survey sampling targeted academic PIs and all-stage bench researchers. In total, 92 individuals from 39 institutions participated in 49 distinct interviews or focus groups, and 59 individuals participated in the survey.**

Approximately 130 individuals were invited to participate in interviews and focus groups, and over 150 individuals were invited to complete the survey. Of those invited to participate, our response rates were approximately 75% for the interviews and 30% for the survey. Participants who were invited to participate in the interview and survey include the following: MDF's current researchers, including past research grantees and fellows; MDF's Scientific Advisory Council (SAC) members; recommendations from SAC members active in the research space; DMCRN and other clinical study/trial site PIs and research coordinators (including all active/recruiting DM research sites on clinicaltrials.gov); biotech/pharma companies who have publicly announced

they have DM programs; companies in clinical trials; three companies with DM programs who have not been made public; and staff from companies/organizations who have ordered from MDF's iPSC cell line library, among others.

Table 1. Total Distribution of Interview and Survey Respondents

	Participant Type	Number		Percentage
Total Respondents	Number of industry respondents	Interview: 44 Survey: 8	**52**	34%
	Number of research respondents	Interview: 48 Survey: 51	**99**	66%
	Total	**151**		**100%**

Table 2. DMCRN Representation across Interview and Survey Respondents

	Participant Type	Number	Percentage of Researchers
DMCRN Respondents	Interview	**44**	92%
	Survey	**8**	16%
	Total number of sites represented	**17**	-

Table 3. Geographic Representation across Interview and Survey Respondents

	Participant Type	Number	Percentage
Geographic Representation (Non-US Participation)	Interview *(Canada, France, Germany, Netherlands, New Zealand, Spain, Switzerland, United Kingdom)*	13	14%
	Survey *(Canada, Costa Rica, France, Israel, Italy, Japan, Netherlands, Singapore, Spain, United Kingdom)*[3]	21	36%
	Total	34	**23%**

[3] Some survey respondents were anonymous, and locations were thus assumed based on the geographic coordinates provided as part of their survey response metadata.

3.1. Interviews and Focus Groups

Methodology

Interview and focus group participants opted in through direct outreach from MDF's CEO, Dr. Tanya Stevenson. No incentives were provided for participants. We used a purposive sampling method for interviews and focus groups that consisted of academic and scientific researchers, physicians, and industry professionals from a wide range of institutions in the United States and internationally. Participants signed up to engage in thirty-minute, one-on-one or small group interviews. We also conducted one hour-long focus group discussion for an institution with a larger team focused on myotonic dystrophy research.

Third Plateau developed the interview and focus group protocols and conducted all interviews and the focus group. Interviewees were categorized into two main groups based on their role and experience within the myotonic dystrophy research ecosystem. Separate protocols were developed to support effective analysis for these two groups: 1) researchers and physicians, and 2) industry researchers and partners. Third Plateau took extensive transcript-style notes of each interview and focus group conversation. No conversations were recorded.

One researcher then developed a code list and defined codes based on inductive and deductive coding methods for qualitative analysis. We used qualitative data analysis software (MaxQDA) to develop the thematic evidence and assess code frequency. The codebook can be found in Appendix D. We used thematic analysis and constant comparative techniques derived from grounded theory methods to analyze the data. Data was summarized and condensed until code indicated saturation. Where possible, direct quotes have been included in alignment with participatory research methodology.

Interview Sample

In total, 92 individuals from 39 institutions participated in 49 distinct interviews or focus groups. Our sampling prioritized industry partners and clinical researchers, given the significant anticipated number of upcoming trials and studies. A more detailed breakdown of participants, including countries represented, is included in the table below, and a list of participating institutions can be found in the Appendix A.

Table 4. Interview and Focus Group Participants

Respondent Category	Participant Type	Number	Percentage
Totals	**Number of interviews**	**49**	**-**
	Interviewees	**92**	**-**
Industry Respondents	*Number of industry interviews*	*24*	*49%*
	Number of industry interviewees	*44*	*48%*
	Number of small industry[4] interviews	7	29%
Research Respondents	*Number of research interviews*	*25*	*51%*
	Number of research interviewees	*48*	*52%*
	Number of DMCRN site interviews[5]	22	88%
	Number of DMCRN site interviewees	44	92%
	Number of clinical research interviewees	47	100%
	Number of non-clinical research interviewees	0	0%
Geographic Representation	Number of U.S. based interviewees	79	86%
	Number of non-U.S. based interviewees *(Canada, France, Germany, Netherlands, New Zealand, Spain, Switzerland, United Kingdom)*	13	14%

3.2. Survey

Methodology

In addition to conducting interviews and a focus group, Third Plateau ran a survey to gather input from a larger sample of the field. The survey was opt-in and was distributed to more than 150 individuals including researchers, physicians, and industry professionals, excluding those who had participated in interviews or focus groups. A greater number of academic and bench researchers were included in the survey to ensure that all areas of research were assessed.

[4] These are pharmaceutical and/or biotech companies that have a small amount of full-time staff and/or have early-stage DM programs.
[5] 16 of the 20 DMCRN sites participated in an interview; see Appendix B for a full list of DMCRN sites that participated in interviews and surveys.

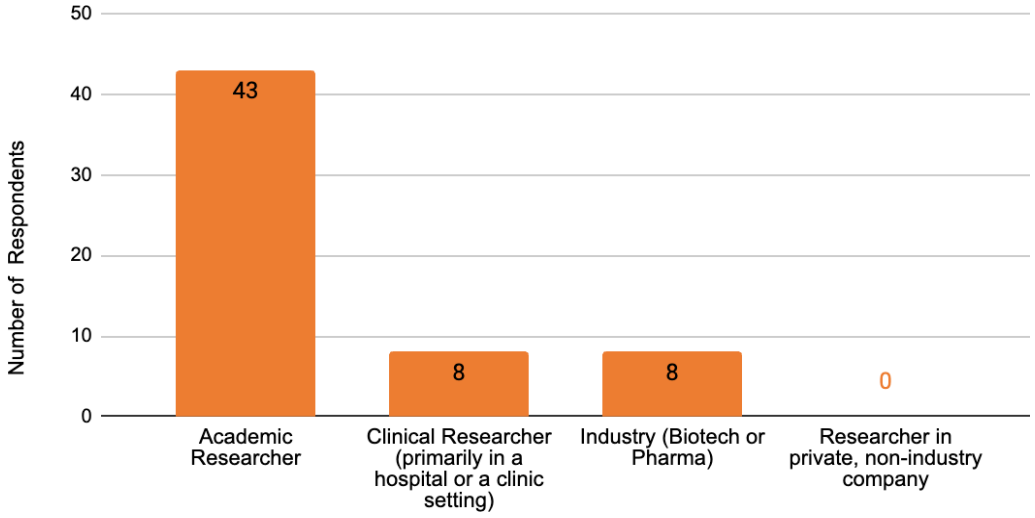
The survey was administered through Qualtrics using anonymous individual survey links and was open for approximately one month in March 2023. Respondents were not incentivized for their participation. The survey was developed after the majority of the interviews had been conducted; the survey questions were designed to supplement information gathered from the interviews. To aid in quantitative analysis and promote wide participation, the survey had a limited number of open response questions. For questions with multiple choice responses, the responses were developed based on responses from similar interview questions.

Survey Sample

All Respondents

Fifty-two individuals completed the survey, and an additional seven individuals partially completed the survey.[6] The respondents hold various roles in the myotonic dystrophy ecosystem across academic and clinical research, as well as industry (biotech or pharma) (Figure 1). Of them, 84% reported having an active DM program or project at their institution, with the majority focusing on DM1[7] (39), followed by CDM[8] (15), DM2[9] (14), and Juvenile onset[10] (10) (Figure 5). Two thirds of survey respondents with active DM programs or projects are running 1-3 studies at a time, with approximately a third of respondents running four or more studies. Survey respondents focus on a range of therapies and disease mechanisms, with most respondents focused on small molecule, gene therapy, and antisense oligonucleotides (ASOs).

Figure 1. Survey Respondent Role Types (n=59)



[6] The results shown in this report include responses from partial completions.
[7] Myotonic dystrophy type 1
[8] Congenital myotonic dystrophy
[9] Myotonic dystrophy type 2
[10] Juvenile/childhood onset myotonic dystrophy

Figure 2. Survey - DM Research Involvement[11] (n=51)

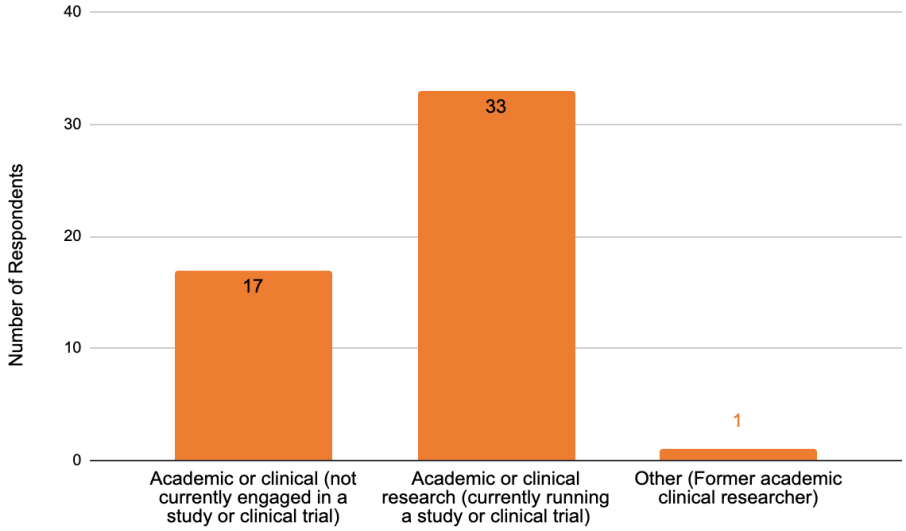


Table 5. Survey Respondent Roles in DM Ecosystem[12] (n=74, multiple select)

Which best describes your role?	Number	Percentage
Principal Investigator	32	43%
Scientist	9	12%
Lab Director	7	9%
Clinical Research Coordinator	6	8%
Doctoral/Medical Student	5	7%
Bench Researcher	3	4%
Vice President/Director	2	3%
Other[13]	2	3%
Physician	2	3%
Patient Advocacy	2	3%
Chief Executive Officer	1	1%
Chief Medical Officer	1	1%
Project Manager	1	1%
Clinical Research and Development	1	1%

[11] No respondents selected the following: Private facility researcher; not industry, not academic (currently running a study or clinical trial), Private facility research; not industry, not academic (not currently engaged in a study or clinical trial).
[12] No respondents selected the following roles: Chief Science Officer, Government Relations, Clinical Operations, or Public Affairs.
[13] "Other" responses were Research Fellow and Clinical Evaluator.

Figure 3. Survey Respondent Years of Experience in DM Research (n=59)

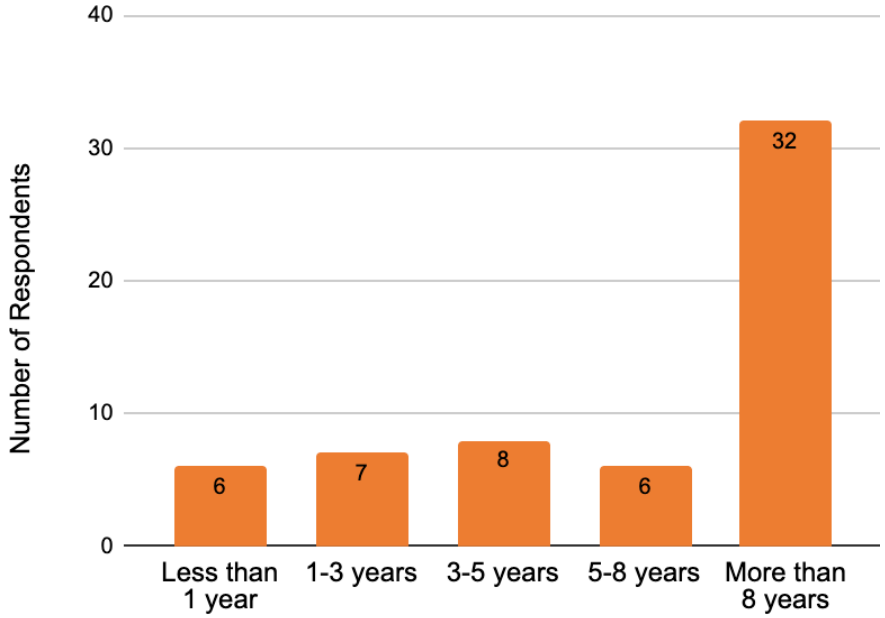


Table 6. Survey Respondent Areas of DM Research Focus[14] (n=58, multiple select)

Clinical Speciality Area for DM Research	Number
No clinical speciality area (68%)	40
Neurology	10
Genetics	9
Pediatrics	4
Psychology/ Psychiatry	3
Physical Therapy	2
Cardiology	1
Gastroenterology	1
Internal Medicine	1

[14] Of 58 respondents, 18 (32%) reported having a clinical specialty area, while 40 (68%) reported that they did not have a clinical speciality area. Of the 18 respondents with speciality areas, eight respondents selected multiple areas. No respondents selected the following specialty areas: Family Medicine, General Practitioner, Occupational Therapy, Ophthalmology/Optometry, Pain Management, Rheumatology, Social Work, or Speech Therapy.

Figure 4. Survey - Age (Years) of DM Programs or Projects (n=55)

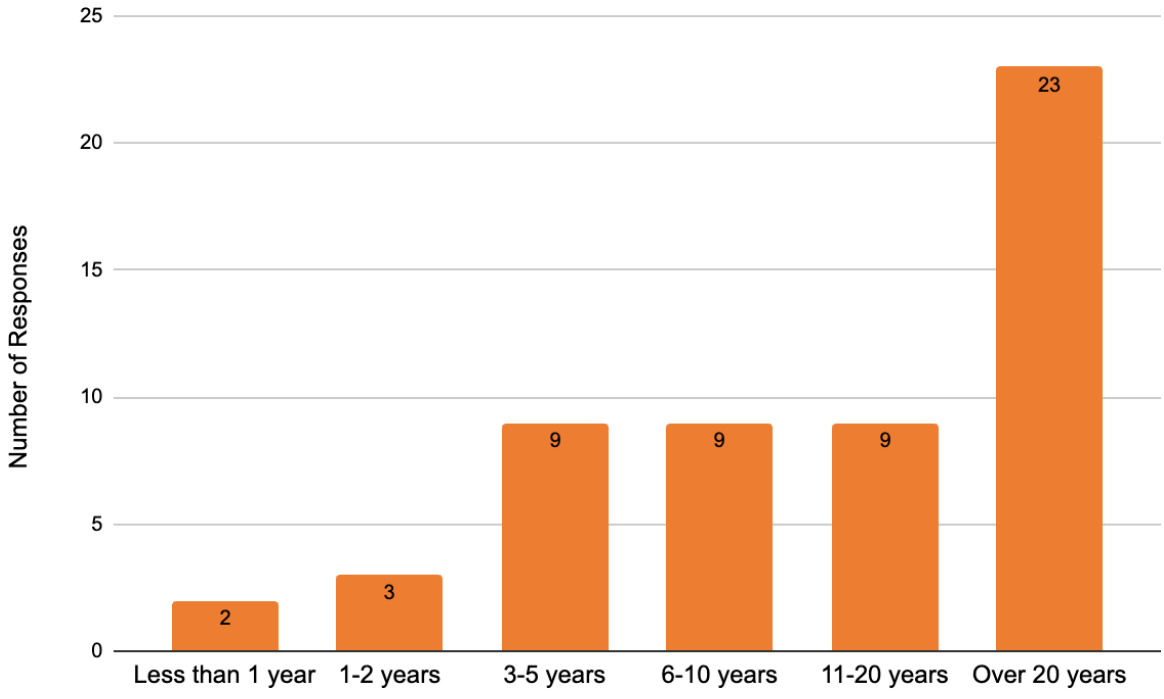
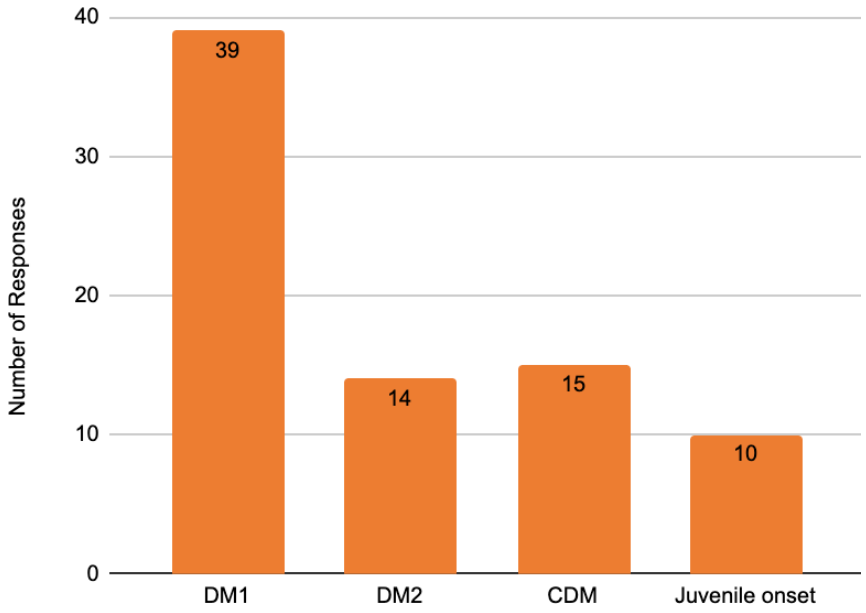


Figure 5. Survey - Active DM Programs or Projects (n=42, multiple select)



Industry Representation of Survey Sample

Respondents working in industry (biotech or pharma) were less represented among the survey sample, with nine total respondents. Of them, only one reported that they are currently sponsoring a study or trial, and four reported that they plan to launch a trial within the next one to two years.

Table 7. Survey - DM Program Current Stage of Development (n=8, multiple select)

Stage of Development	Number	Percentage
Exploratory	2	22%
Preclinical	6	67%
Clinical	1	11%
Review	0	0%
Other	0	0%

3.3. Limitations

While this study provides valuable insights into the myotonic dystrophy field, there are several limitations that should be considered. One potential limitation is the sample size, particularly for the survey portion of the study. While the survey was distributed to over 150 individuals, only 52 individuals completed the survey, with an additional seven partial completions. This relatively small sample size may not be fully representative of findings to the broader myotonic dystrophy research community.

Additionally, the study relied on a purposive sampling method for selecting interview and focus group participants. While this approach allows for targeted recruitment of individuals with relevant experience and expertise, it may introduce bias into the sample and limit the representation of diverse perspectives within the myotonic dystrophy research ecosystem. Furthermore, while the interview and focus groups had nearly equal representation from research and industry, the survey sample was dominated by individuals with academic or clinical research roles (51), with fewer respondents working in industry (8). This more limited representation of industry professionals in the survey may impact how representative survey findings are related to industry perspectives on myotonic dystrophy research and development (see Tables 1 and 4 and Figure 1 for survey and focus group sizes for industry professionals).

Finally, the scope of our research did not include an estimate of the size of the field at large, and therefore we are not able to confirm the representativeness of our sample.

4. Findings

The findings are discussed across three categories: 1) research concerned with knowledge acquisition and discovery, 2) research related to trial and study sites, and 3) the Myotonic Dystrophy Foundation's strengths and opportunities.

4.1. Research Priorities and Barriers

4.1.a Variability and Multisystemic Nature of Myotonic Dystrophy

Across most interviews, both industry and researchers highlighted the variability and multisystemic nature of myotonic dystrophy, with a total of 30 coded mentions, including multiple mentions for individual respondents. Variability was coded 20 times across industry partners, versus 10 for researchers, suggesting that this poses particular challenges from a treatment perspective. The heterogeneity of the disease impacts the systems that are affected, the symptoms that patients experience, and the outcomes to be measured. Diagnosis can occur at any point in a patient's life with a range of varying symptoms. Furthermore, the outcome measures can vary among patients, which makes it difficult to run controlled studies and develop meaningful endpoints to be approved by regulators. All of this in turn impacts how treatments are developed.

> *[The] multisystemic nature of DM means that it is quite heterogeneous… [there are] patients who are born with it young, all the way through people who are mildly symptomatic and may go decades without diagnosis… [I]dentifying priorities is really a challenge…. How do you measure [treatment] benefits in a heterogeneous population? At this point in time, those endpoints don't exist from a regulatory and reimbursement perspective. (Industry)*

The multisystemic nature of myotonic dystrophy poses challenges for treatment development, as researchers and industry alike decide whether to focus on particular symptoms or various symptoms to lesser degrees. Consequently, a one-size-fits-all approach to treatment may fail to capture the heterogeneity of disease progression and symptoms.

> *The impact of DM1 on each person is different, even within a family…. [There are] some individuals with some symptoms but not others…..[This] makes it so one size doesn't fit all. (Research)*

> *This is a condition that affects multiple organ systems so you either need a treatment that is capable of targeting all the organ systems or you need to be comfortable with developing [a] treatment that only addresses a narrow portion of the condition. (Industry)*

In order to address the multisystemic nature of the disease, some respondents highlighted the importance of multidisciplinary clinician and researcher teams trained across multiple areas.

> *When patients are at the site, they feel like they don't have a lot of support within other areas of practice from clinicians and specialists.… Areas of research are multidisciplinary, [including] care arrangement, occupational therapy, communication strategies through families and within healthcare systems, physical therapy, aspects of nutrition, endocrinology. Because it's such a multisystems disorder, there are as many research priorities as there are impacts. (Research)*

4.1.b Barriers to Research and Treatment Development

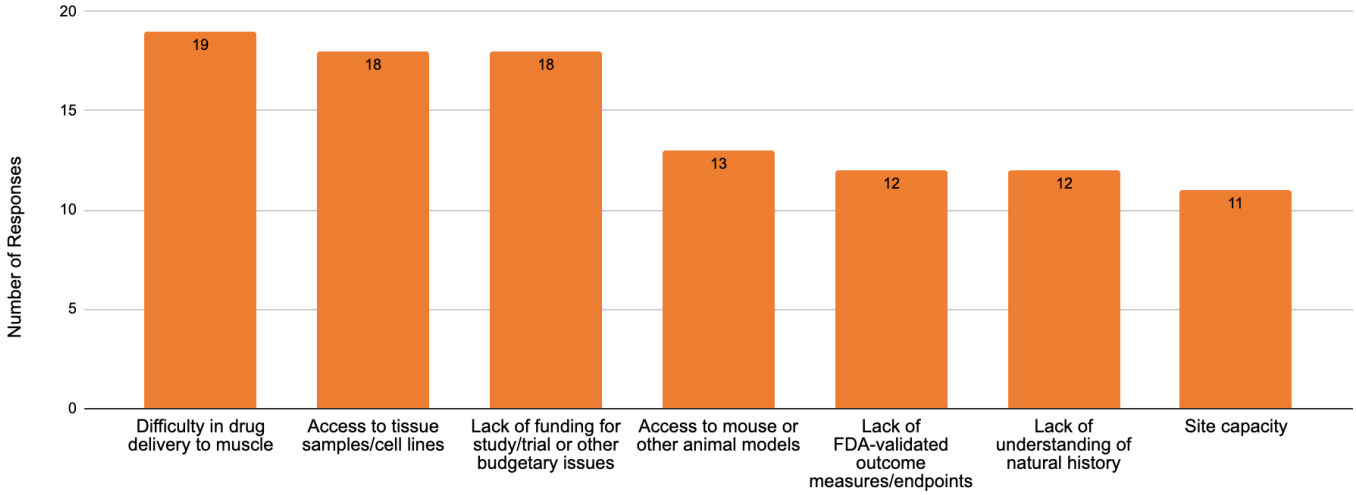
Both interviewees and survey respondents were asked about the most common barriers to myotonic dystrophy research and treatment development. Interviewees responded with a range of barriers, which are described below. Top barriers based on mentions in interview coding are:

- Natural history (32)
- Logistical challenges and demands of studies and trials (29)
- Biomarkers (21)
- Endpoints (17)
- Patient education (15)
- Outcome measures (15)
- Patient apathy and cognitive challenges (12)

Survey respondents were asked to choose from a list of 22 options.[15] The top survey responses are shown below,[16] and several of these are described in greater detail in the following section based on interview responses. Barriers related to research studies and trials, particularly funding and site capacity, are discussed later in the report. **Lack of understanding of natural history and lack of clear endpoints and outcome measures were the top shared barriers across both interviews and the survey.**

[15] These 22 options were created based on information gathered from the interviews. Respondents could also select "Other" and add additional barriers not included on the initial list.
[16] The complete list of responses can be found in Appendix C.

Figure 6. Survey - Top Barriers to DM Research (n=50, multiple select)

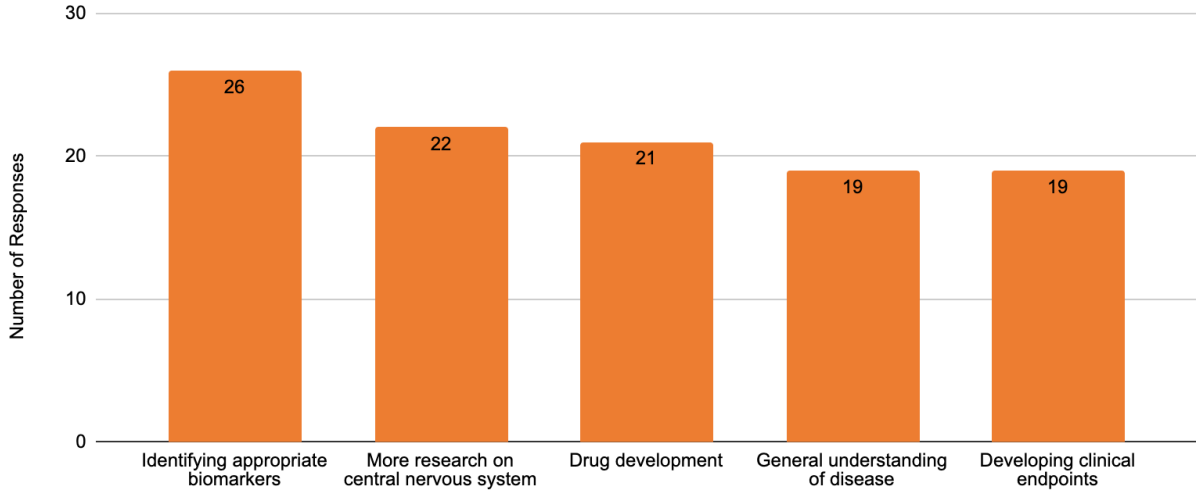


DM1 research priorities

Figure 7 below shows the top priorities for DM1 research, according to 53 survey respondents.[17] These priorities were shared among interview respondents as well. Some of these top priorities are described in greater detail in the following sections.

While not discussed in greater detail below, survey respondents listed "more research on the central nervous system" as the second highest priority for DM1, and CNS was coded ten times across interviews. Understanding the impact of myotonic dystrophy on the central nervous system is particularly important given the cognitive impacts of the disease and the complications this poses for patient recruitment and study retention.

Figure 7. Survey - Top Priorities for DM1 Research (n=53, multiple select)



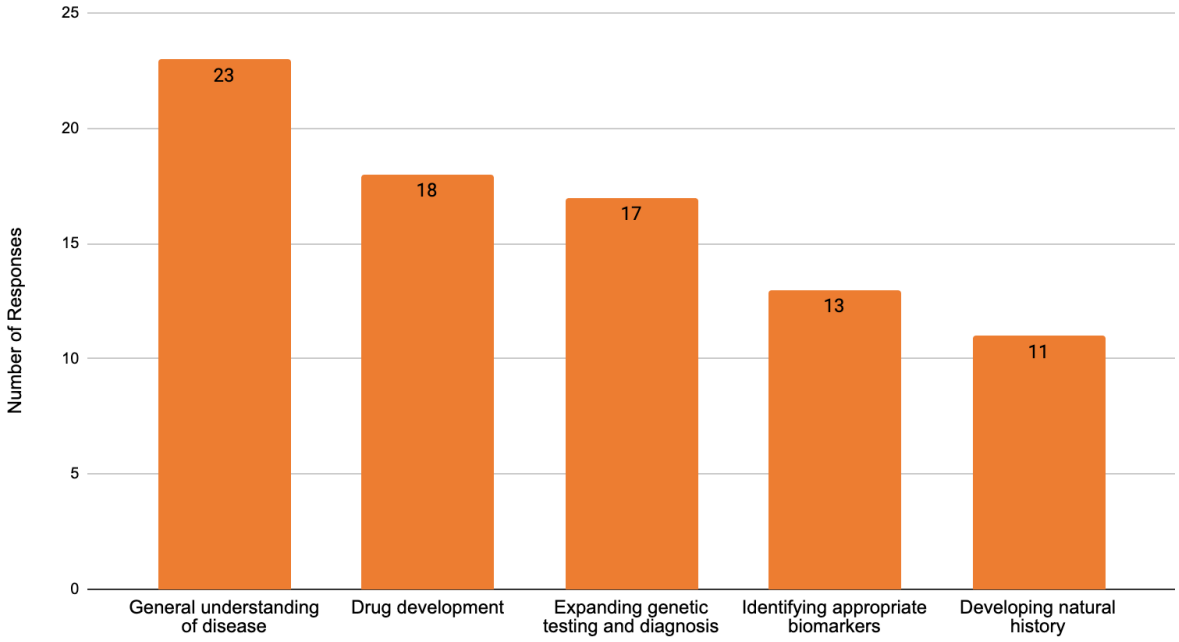
[17] The complete list of responses can be found in Annex C.

Additional DM1 priorities that were mentioned in interviews include symptom management, such as excessive daytime sleepiness (mentioned by four industry partners and five researchers) and fatigue (mentioned by three industry partners and two researchers), as well as helping patients maintain independence and physical abilities more generally.

DM2 research priorities

Figure 8 below shows the top priorities for DM2 research, according to 35 survey respondents.[18] **Shared top priorities across DM1 and DM2 for survey respondents included a general understanding of disease, drug development, and identifying appropriate biomarkers. Expanding genetic testing and diagnosis ranks third for DM2, while it ranked seventh for DM1, reflecting a greater need for testing and diagnosis for DM2**.

Figure 8. Survey - Top Priorities for DM2 Research (n=35, multiple select)



The top priority, "general understanding of disease," reflects the general lack of understanding of DM2 across the field, as well as many industry partners and researchers' limited experience working on DM2. Across interviews, one industry member and six researchers spoke to the need for a greater understanding of DM2. A key theme expressed in the interviews was a need for more unique research on DM2, as respondents mentioned that much of the research base for DM2 comes from part of a DM1 study. While this was also a top priority for DM1, its higher ranking for DM2 reflects a greater need for general understanding of DM2.

[18] In addition to the 35 respondents, 14 respondents selected "N/A (haven't worked on DM2)" and four respondents did not answer this question. The complete list of responses can be found in Annex C.

More published data on DM2, particularly natural history data, is also needed to better understand the disease and inform trial design. To address the lack of DM2 research, one researcher suggested that MDF earmark funding specifically for DM2 so that researchers are not competing with DM1 studies for funding. However, one industry partner noted in an interview that while MDF funds DM2 natural history studies, the data is not being published.[19]

> *That is a number one priority–academics need to put data into the public domain, otherwise companies cannot design trials, cannot determine feasibility, cannot determine endpoints. (Industry)*

The lack of unique research on and understanding of DM2 in turn contributes to feelings of exclusion or being overlooked among DM2 patients, as described by some researchers. Since DM2 symptoms are often milder than DM1 and/or later onset, patients with DM2 may not receive the same level of care and support.

> *DM2 [patients] often feel a little marginalized because there are fewer of them and the research isn't as advanced as it is in DM1. Making sure that they have their own space and know that they're not forgotten or peripheral would be good. There's a feeling of 'why do we have to wait for DM1 to get a treatment for DM2 to have a trial.' (Research)*

> *DM2 is milder and later onset, but patients feel left out–[this is] oftentimes what happens when you're on the milder end of spectrum. Patients are suffering and hoping that efforts in DM1 lead to some efforts & success stories in DM2…they're also looking for their children who are probably going to have this disease. [DM2] patients are later in life so are not necessarily expecting a treatment for themselves, but they're looking at the next generation. (Research)*

While identifying and recruiting patients with DM2 can be harder due to the smaller patient population, one researcher who works primarily on DM2 noted that working with DM2 patients does not involve the same challenges as DM1 patients with regards to patient apathy and cognitive challenges. DM2 patients may be easier to enroll in studies than DM1 patients because of the nature of disease and impact on cognitive functioning.

> *I think that the challenge of DM1 study is patient compliance. [MDF] should invest more in DM2 because it's the opposite; patients are much more engaged and compliant and would actually follow through. The cognitive issues are unique to DM1. (Research)*

[19] See the section on natural history below for additional comments about natural history data publication and sharing, both for DM1 and DM2.

One researcher mentioned that they "have a very motivated DM2 community that would love to participate, but we don't have anything to offer them," demonstrating the community's eagerness to participate in DM2 studies.

Drug Delivery

Because of the variability and multisystemic nature of myotonic dystrophy, effective drug delivery is a priority for industry partners and researchers alike. While drug delivery was listed as a top priority for survey respondents, it was mentioned considerably less among interview respondents, with approximately ten coded mentions, all but one of which came from industry partners. The heterogeneity of the disease and the systems it impacts requires drug treatments that can effectively target and treat multiple systems and symptoms. This often forces treatment to either focus on a single system or symptom or focus on more wide reaching treatment, while sacrificing specificity in targeting specific systems or symptoms.

> *"Treating system-wide defects (CNS, muscular, cardio) would be a game changer for patients. Being able to take a pill instead of going in for monthly infusions would be a huge benefit for patients. (Industry)*

Respondents also spoke to the difficulty of crossing the blood brain barrier and of targeting drug delivery to muscle. Developing a pill instead of an injectable is one potential solution to this problem. However, one researcher also noted that it's essential to understand patients' needs at this stage, as swallowing a pill may be difficult for many patients.

As one industry partner expressed, it's critical to be engaging with patients during drug development to understand what symptoms they hope to treat. **Given the variability of the disease and the varying impacts it has on patients, there is no one-size-fits-all approach to treatment development and drug delivery. MDF can support industry partners and patients alike by incorporating patients' voices in this process and ensuring that drug development and delivery aligns with patients' needs.**

> *"It's hard to know how much to target one of these areas over another. Knowing what kind of relief patients want from each of their symptoms is very critical to know. (Industry)*

Biobank

Access to tissue samples and cell lines was listed as the second priority for survey respondents, and similar themes were coded approximately ten times across interviews. Across both groups of respondents, the need for biopsies and a biobank to improve research was a common theme. **Lack of biosamples is a barrier to improving disease understanding and treatment options, as evidenced by both industry and research respondents.**

Researchers also acknowledged the sensitivity of collecting biosamples and autopsies. Collecting biopsies can also be a barrier to research participation because some patients are averse to needles/biopsies.

> *Many patients want to come to clinical trials, but for all of these new things, you need to have muscle tissue biopsies, and many patients don't like this or needle biopsies. This is a hurdle on the recruitment side for clinical trials if you put in a lot of muscle biopsies. (Research)*

Supporting biopsy collection and biobank efforts was also flagged in several interviews as an area for MDF support, either through advocacy or through funding.

> *For research, it's really challenging for academics and companies to get ahold of DM1 patient cells to do research on. It would be phenomenal if MDF could establish something like a biobank of biopsy samples from volunteer patients that could be shared with the research community. Right now we're going through private companies who are trying to solicit DM1 patients to have a biopsy so then [these companies] can sell these biopsies for for-profit companies to research. Having a biobank would be an add for the research community. (Industry)*

Endpoints and Outcome Measures

The lack of clear, validated endpoints came up frequently as a priority for drug development, as shown in Figure 6 above. This was echoed by 17 coded mentions across interviews, with the majority of mentions coming from industry respondents. Since validated endpoints are necessary for regulatory approval, it is essential to have clear endpoints for trial design. Across interviews, it was clear that MDF can continue to play an important role in helping industry members and researchers alike to develop meaningful endpoints. More detail on how MDF can support the development of meaningful endpoints and outcome measures, with an eye to engaging regulators, is discussed below.

> *Some therapies aren't getting accepted because they aren't looking at the right endpoints. MDF's role is huge to [create a] clear path to approval and bridge the gap between companies and patients on the ground who suffer from DM1. (Industry)*

Similarly, respondents mentioned a need for universal outcome measures, rather than specific measures that require highly technical or expensive equipment and measurement. Outcome measures were coded 15 times across interviews, with slightly more mentions from researchers than industry partners. Some sites expressed that acquiring expensive, highly technical equipment is a significant barrier; thus outcome measures that rely on such equipment may preclude these sites' participation. Additionally, researchers noted that outcome measurements

cannot be too onerous, otherwise patients will not be willing to participate. This is discussed further below.

Some respondents suggested that MDF can be particularly useful in translating patients' needs and symptoms into endpoints and outcomes, and making sure that the endpoints and outcomes being measured in trials are meaningful and make sense to patients.

> *Trying to understand what is clinically meaningful for a patient and translating from an outcome measure to what it means in a person… is extremely meaningful for patients. It's extremely powerful when patients can talk to the FDA and explain what an X point change on a scale actually means for [them]. (Industry)*

Additionally, one researcher noted that outcomes must be translatable to other languages as well for greater inclusion. For instance, patients who speak Spanish or Mandarin were unable to participate because there were no translated patient outcome measures for them to complete. This is particularly important in ensuring that a more diverse population is included in myotonic dystrophy research.

Natural History

A lack of understanding of natural history was cited as a key barrier to DM research by survey respondents (Figure 6). This was echoed by interviewees as well, with 32 coded mentions– approximately one third from industry partners and two thirds from researchers. **Many industry partners and researchers highlighted that patient eagerness for treatments often comes at the expense of participation in natural history studies, due to exclusion criteria, which can prevent patients from participating in multiple trials or studies simultaneously.**

To address the lesser demand for natural history participation, many respondents highlighted the importance of educating patients around the value of natural history studies. Patients must understand that natural history studies lead to a better understanding of the disease as it helps to understand biomarkers and outcomes. In turn, this improves the likelihood of successful treatment development.

> *With DM, [there is] more of a therapeutic misconception. [Patients] want to be involved in trials if it is going to make their disease better. We want people to be in trials that lead to a better understanding [of the disease], whether or not it leads to direct improvement. (Research)*

> *Over time the population has become more amenable to participating in natural history studies. Initially when they heard it wasn't a drug/treatment trial, they weren't interested. There has probably been more education*

> *over the years about how important it is to participate in natural history studies. (Research)*

Industry partners stressed the importance of natural history data to inform therapeutic design. **Respondents across both groups also expressed eagerness for results from the END-DM1 study and optimism that the study will help guide future research and therapeutic development.** The need for natural history data was particularly salient for DM2, which is widely agreed to be less understood than DM1, as elaborated upon above.

> *When you go into designing a new therapeutic, there isn't a backdrop of well-known natural history of these individuals, so you don't know what the natural course of the disease is…. There's no interaction with patient groups such as MDF to know what patients hope to get out [of trials]. All that information is largely lacking, and it's challenging to find that information out. [We] often have to try and produce that data. (Industry)*

Collaboration and Data Sharing

In general, respondents spoke of collaborative environments where knowledge and best practices passed freely between research and clinical sites. The DMCRN and MDF were particularly praised for facilitating this collaboration and flow of information. Some respondents did note that improved collaboration and information and data sharing between industry and researchers would help to improve treatment development. One industry partner spoke about difficulties establishing connections with a clinical site due to slow communication and NDAs. Another industry partner suggested that organizing more drug developers' roundtables would help further collaboration between industry and research.

4.2. Research Studies and Trials: Strengths and Opportunities

4.2.a. Trial Site Capacity

A common theme across many interviews was limited capacity at research and clinical sites, and this was corroborated by survey responses. This was cited 11 times by survey respondents (see Figure 6 above), as well as by nine industry partners and at least ten researchers across interviews. There was a general sense of resource constraint across research sites, particularly with regards to staffing. Some capacity issues are tied to funding constraints, which are discussed below. Respondents mentioned the need for more trained evaluators and specialists, as well as a need for better training for coordinators. Smaller sites, as well as some sites outside of the U.S., appear to face greater capacity challenges than larger sites in the U.S. This makes it harder for these sites to run multiple studies or trials simultaneously.

Staffing challenges are partly due to the rarity of myotonic dystrophy; because it is a relatively rare disease, there are not as many researchers and clinicians working in the field.

> *No one knows about DM, so the opportunities to train up people and opportunities for people to gain familiarity with people with myotonic dystrophy is something we have to work quite hard at. (Research)*

From an industry perspective, low-capacity research sites can be an inhibitor to running sufficient trials for regulatory approval.

> *Sites were going to be challenged before COVID-19. Now we have sites that are dealing with 25 concurrent studies at a time. There are not enough PIs, not enough CRCs, physical therapists, beds, days in the week to be able to process all the studies that are currently underway. For companies coming after [sites], it's going to be a disaster because there's not going to be enough capacity in the system to deliver on potential therapy studies that are coming. (Industry)*

Current capacity strain is in part due to the COVID-19 pandemic, which had significant impacts on medical capacity across the board. Three years after the start of the pandemic, this is still a major issue, as capacity strains related to COVID-19 were coded at least ten times across interviews. The pandemic has also led to higher rates of burnout and turnover among coordinators and medical professionals. Several respondents spoke to the impacts that COVID-19 had on site capacity, as well as the ability to recruit and enroll patients.

> *Post-pandemic, research staff are spread pretty thin; some places laid off staff during COVID-19 and have seen a lot of personnel turnover since; people are juggling so many things and don't have enough time to do it. (Research)*

> *What happened during COVID-19 to halt clinical research has been really significant, [and we're] still seeing the ripple impacts of that…. Major academic research centers aren't running clinical trials because health care workers were overwhelmed, they need to take care of sick people at their hospital, [and there has been] enormous turnover in clinical trial coordinators and [there are] sites that don't have clinical staff for months or years on end. While the trial can be up and running and have an active physician, clinics are still understaffed. (Industry)*

4.2.b. Patient Education and Enrollment

Across interviews, both industry partners and researchers noted that patients are eager for therapies and thus are willing and eager to be involved in trials. The potential for treatment can be an important motivating factor that keeps patients enrolled and actively participating in trials.

> *[The] potential promise of treatments… piques patients' interests. In the old days, patients would show up to appointments but sometimes they wouldn't because they weren't sure how important it was [or they] would reschedule. Now patients are more motivated to come because they think there might be an update, a new treatment, [or] a new trial they can enroll in. (Research)*

While this is beneficial for treatment development, participation in drug trials often happens at the expense of participation in natural history studies, as mentioned above. More education needs to be done among patients on the importance of participating in natural history studies, in addition to treatment studies.

Ensuring that patients are properly informed about studies and clinical trials is a key factor to ensuring study and trial success, according to many industry partners and researchers. **Patient education was coded approximately 15 times across interviews, with a nearly even split in mentions between industry partners and researchers. An important component of patient education is preparing patients for study and trial visits and helping patients manage expectations.**

> *Working with patients to ensure they're feeling less anxiety about participation and travel and having comprehensive plans to help prepare them for visits [is important]. (Industry)*

> *[MDF can continue] explaining to people the process of development/phases and keep on reminding people how long it takes, worst scenarios, and be more honest with patients about timelines. (Industry)*

Relatedly, making sure that patients understand the importance of natural history studies would support recruitment efforts for these studies. **Across all types of studies and trials, helping patients understand the importance of the research and their participation is important in ensuring patient follow-through.**

Additional patient education is also necessary to demystify and clear up misconceptions about other research and treatment areas, such as gene therapy.

Several respondents identified expanding genetic testing as an effective way to increase enrollment, as well as general awareness and treatment of myotonic dystrophy. Furthermore, underdiagnosis/misdiagnosis because of lack of education of medical professionals can lead to delayed treatment for patients.

4.2.c. Patient Support at Study and Trial Sites

While researchers and clinicians have strong theoretical understandings of myotonic dystrophy, they may lack a more thorough understanding of the day-to-day challenges facing the myotonic dystrophy community and the reality of living with the disease. Educating researchers and clinicians on these challenges, and how to better design studies and trials to support patients, will help strengthen these sites and their studies and trials. Industry partners identified this as an important role for MDF to fill, in that MDF can help communicate patients' needs to industry partners and help determine how best to address these needs.

> *Engagement with the patient advocacy community has made us realize that we needed to put in place more education for how the sites would need to behave to conduct clinical trials properly. (Industry)*

> *[The best way to understand patients' challenges] short of going to their houses and observing them is engaging with a partner that understands that on many different levels (e.g., we need a van to come pick us up from doctor's visits). All these different layers that we don't understand immediately, MDF opens the door on. It's important for [our company] to understand all that as we design studies because studies won't be relevant without a window into these patients' lives. (Industry)*

One key area for improvement, as expressed across many interviews, is addressing the logistical challenges and burdens of study and trial participation. This was a key priority across interviews, with approximately 30 coded mentions, a third of which came from industry partners and two thirds of which came from researchers. Many studies or trials require patients to complete full-day or multi-day visits. Due to the nature of the disease and its symptoms, many patients can be too tired or physically unwell to travel to sites. Furthermore, patients often have to travel great distances to research sites, and the extended visits frequently require overnight stays, meals, and other related expenses, which often are not covered (or not covered entirely) by the study or trial. This provides a financial and logistical burden to patients and caregivers, in addition to the physical and cognitive toll of traveling to study sites and participating in the trials.

For many patients and their caregivers, the intensity of these visits and the associated logistical burdens can inhibit trial participation, even when they would otherwise be motivated to participate.

> *Most studies do not budget for [overnight stays] or will only reimburse up to a certain amount. The same thing with transportation–[patients] may be able to get a driver but it would go way over budget… When participants don't have extra funds or are on disability, they need to have funds to fully*

> *reimburse them. They don't need incentives because they are motivated personally, but the cost is high. (Research)*

Further exacerbating this is the fact that caregivers oftentimes face the same physical and cognitive challenges as patients. This can particularly impact child and adolescent studies. At the same time, however, this can boost enrollment efforts as multiple family members can participate during a site visit. Mentions of caregivers were coded over 15 times across interviews, including both the critical role of caregivers as well as the challenges facing many caregivers who are themselves affected by DM.

Potential ways to ameliorate these barriers and increase participation include paying for parking, providing meals, covering transportation costs, and putting patients up in a hotel for the study duration. Additionally, more remote visits where possible can help reduce these challenges.

Extensive patient visits can also have a negative effect on the quality of the research. One researcher noted that the time required to complete extensive questionnaires and measure certain outcomes can exhaust patients and lead to lower quality results.

> *Sometimes [studies] overdo it with too many questionnaires, or repetitive questionnaires that are boring for patients, so the first time [patients will] do it correctly, but then you see quality fading. (Research)*

Interestingly, travel and related logistics are not a universal issue. One researcher based in Europe noted that since families live close together and cities are well connected, these logistical challenges are not as significant of a hurdle.

4.2.d. Patient Apathy and Other Challenges

Many respondents across both groups expressed that patient apathy is a significant hurdle to recruitment and study and trial success. In interviews, five industry partners and seven researchers spoke specifically to patient apathy. The intensive nature of site visits and participation exacerbates this apathy. This apathy manifests in no-shows and lack of follow-through on clinical recommendations. Cognitive challenges may also cause patients to miss appointments. To counteract this, sites must be proactive and aggressive in their outreach and reminder strategies. Such strategies include multiple reminders using various outreach methods, relying on caregivers to ensure participation and follow-up, and scheduling visits later in the day to accommodate sleep schedules. Dedicated recruitment staff who are familiar with patients was also a strategy mentioned by one researcher.

> *Apathy is such a key feature of myotonic dystrophy. Patients are really interested, but nailing down a day and time for them to come in is more challenging. We need to keep on top of patients and remind them a lot more than you do for other patients. (Research)*

4.2.e. International Inclusion and Patient Diversity

The following section details comments from interview and survey respondents about promoting international inclusion and increasing patient diversity.[20] Mentions of international inclusion were coded over 30 times across interviews, with a nearly even split between industry partners and researchers. Given that over a third of survey respondents are based outside of the United States, feedback about international inclusion was particularly prevalent in survey responses.

While many interview respondents commended efforts at expanding the global reach of the DMCRN, there is still room for greater international inclusion, according to both interview and survey respondents. Expanding the global footprint of the DMCRN is important to ensure standardization across countries, both in terms of clinical trial standards and outcome measures. Some European researchers noted that collaboration is made difficult by different clinical standards and tools, patient registries, and regulatory processes between countries.

One researcher also noted that supporting research and registry development in low-income countries would help ensure that more countries outside of the U.S. and Europe are included in the DM studies and trials. In both interviews and surveys, some respondents noted that MDF's patient registry is not of use because it is U.S.-centric (below). As the registry is indeed inclusive of many countries, perhaps MDF can improve their communication around the registry's international inclusion.

Several interview respondents also addressed the need for increased patient diversity in trials and research studies. One researcher noted that different racial and ethnic communities are more likely to experience certain health occurrences, such as strokes, so it's important for advocacy organizations to have this in mind when working with these communities.

> *In regards to the African American community, it is very helpful to work with an organization that will focus on minorities around neuromuscular diseases. [For example], strokes hit [the African American] demographic hard. If it happens, having the awareness of where to go and who to call to get treatment in real time early on is always a good thing. (Research)*

As mentioned earlier, ensuring that outcome measures have validated translations into other languages (e.g., Spanish and Mandarin) can also help include a more diverse patient population as well.

Gender diversity also came up as an area for research to focus on, as DM can have varied impacts across gender. One researcher noted that studies do not pay enough attention to females with DM1, who may have different experiences than males.

[20] While many of these comments about diversifying patient enrollment and furthering international inclusion were expressed by individuals and do not represent the majority of interview and survey respondents, we believe these opinions are still important to highlight given that our sampling strategies are not representative and did not seek to include racial, ethnic, and gender diversity.

4.2.f. Research Funding Needs for Trial Success

Both industry partners and researchers mentioned funding constraints as major barriers to study and trial success.[21] In interviews, comments about funding for trials and clinical sites were coded over 30 times,[22] with the vast majority of comments coming from researchers. For smaller biotech and pharmaceutical companies, high start-up costs, combined with the long timelines for clinical trials, makes it hard to participate in trials. One industry partner shared that many small companies who want to develop trials do not have the money, and the larger companies with funding may not be as interested.

> *There are either small companies with the will but without the money, or there are big companies with the money without the will. (Industry)*

For researchers, relying on grant funding for their studies and trials is a significant barrier to a smooth operation. One U.K. based researcher mentioned having to stop a trial due to a lack of funding, despite having plenty of patients enrolled. As one researcher described, the short timeline of grants, compared to the extended timelines for approval and trials, make it so they "are living from hand to mouth." As noted above, some research sites also mentioned lacking funding for research coordinators and other critical staff.

Several researchers mentioned that pilot grants would be particularly helpful in getting research off the ground, which they can then leverage to apply for larger grants. One researcher referred to this aptly as a "startup barrier."

> *For grants, you need pilot data that you need to generate without any resources. I have been able to get pilot grants but it is very time consuming and slows down the process. (Research)*

> *It is a vast amount of effort to get a new study up and running. Often we are tied up in a 'Catch 22;' until we do a certain amount of work, we are unable to get contracts signed, until we get contracts signed, we can't get money for a study, until we get money for a study, then we can't hire anyone. (Research)*

[21] For data on survey respondents' current sources of funding, see Appendix C. Uniform data was not collected from interview respondents on funding sources.
[22] Funding is also discussed below in relation to MDF's potential areas for support, with approximately 45 coded mentions. There is some overlap between comments about funding for trials and clinical sites and comments about MDF funding support.

4.2.g. Myotonic Dystrophy Clinical Research Network (DMCRN)

All 20 DMCRN sites were invited to participate in an interview, with 16 sites (80%) participating. One additional site that did not participate in an interview completed the survey, bringing DMCRN participation in this assessment to 17 sites.

Interview and survey respondents shared a range of experiences working with the DCMRN, expressing both strengths of the network and opportunities for improvement. Of 52 survey respondents, 58% said that they are familiar with the DMCRN and 42% reported that they are not familiar with the DMCRN. Of those who are familiar with or members of the DMCRN, they pointed to access to patient networks and databases and access to natural history data as top reasons for why they use or will consider using the network.

Current Strengths of the DMCRN

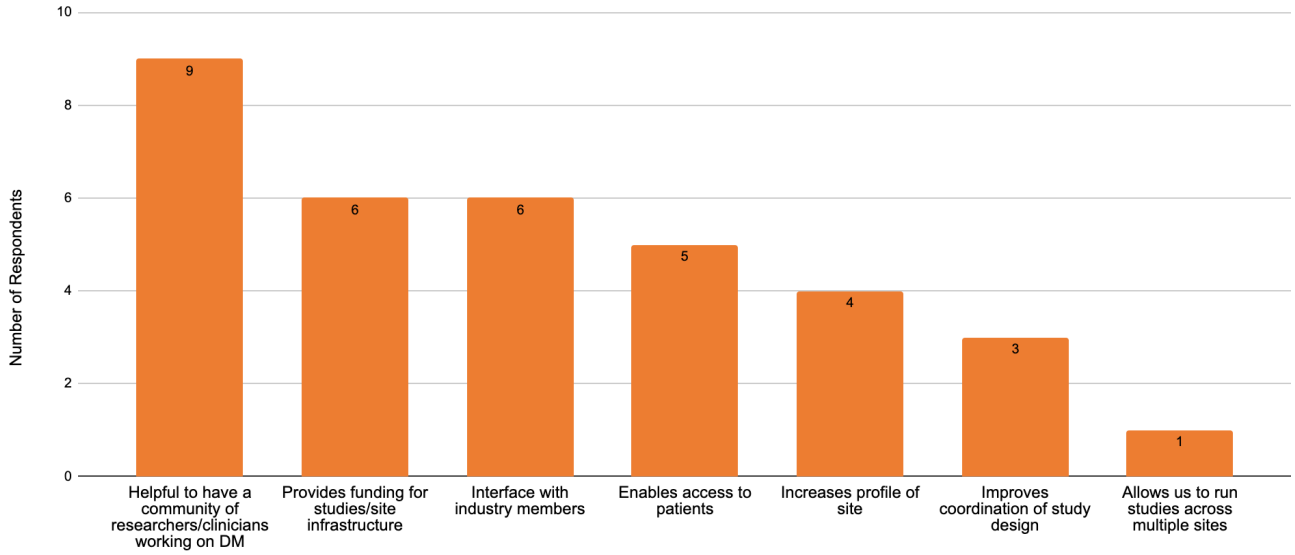
Respondents across both groups had largely positive feedback about the DMCRN, and noted that utilizing a pre-existing research network had great benefits for studies and trials. In particular, respondents praised the DMCRN's patient database, natural history study, and efforts to standardize measurements and staff training. Access to KOLs and researchers' general familiarity with each other and disease expertise were also cited as key advantages of working with the DMCRN. Participants also highlighted the standardized study design and protocol used across DMCRN sites. Several respondents also commended Dr. Nick Johnson's leadership and expertise.

> *"The nice thing about having a network… is the built-in support system and infrastructure, as opposed to going out and randomly picking sites. (Industry)*

The DMCRN has also been an important link to the patient community for many industry partners. Yearly meetings of industry members and principal investigators fosters a sense of community and respect for member sites across the network. Some European respondents also praised the DMCRN's efforts to include European sites.

> *"Formerly, there was always the 'Atlantic Gap,' there were some activities in Europe and a lot in the US, but [these activities were] not bridged. The DMCRN bridges this and regular meetings and exchange helps. (Research)*

Figure 9. Survey - DMCRN Benefits that Support Research (n=9, multiple select[23])



Current Opportunities for the DMCRN

In the interviews, **several researchers and industry partners called for the DMCRN to include more budget and management transparency.** Researchers who expressed these opinions included both DMCRN members and sites outside of the network. One researcher mentioned that they are unable to attend the DMCRN's regularly scheduled meetings, but no minutes are disseminated which makes it difficult to know what goes on at meetings. Likewise, some other members shared similar comments and frustrations that they had put time and resources into the network but had not yet received many results or data.

> *It feels like we're giving a great deal of information in, but not getting any information back. (Research)*

From an industry perspective, it is also important that the DMCRN share this data. One industry partner suggested that the DMCRN push researchers to publish data.

> *The DMCRN has amazing researchers…[but these researchers] are sitting on some amount of data that can be published. We need this data in the public domain to help educate people not in the field about the disease…. If data isn't published, it won't be taken seriously…. [The DMCRN] needs to push academia…to share data and knowledge. (Industry)*

Another respondent mentioned that they felt that the DMCRN did not appropriately involve network members in decision-making.

[23] This question was only asked to survey respondents who indicated that they were part of the DMCRN.

> *[The DMCRN is] a very top-down organization, so a lot of decisions [are] made without input from people in the community…. People involved in the network [have] a sense that you were supposed to do what [the] executive committee [decides] and [the] executive committee [is] very small. It [is] difficult to try to do sub-studies or suggest other ideas. It [feels] like it [is] a pretty closed organization. (Research)*

Two researchers noted that the DMCRN appears to be focusing more on expanding the size of the network, rather than supporting the capacity of existing sites.

> *Their solution is to throw money at new sites that are less experienced rather than supporting the sites that are already up and running. (Research)*

> *The DMCRN has grown so big but hasn't established their mission…. There's a balance between being big and [being] too big. (Research)*

When asked why they would not join the DMCRN, one researcher mentioned a lack of bandwidth to comply with the network's protocols and standards. Another researcher noted that a lack of funding to procure the equipment needed to join the network precluded them from joining.

> *The DMCRN is an excellent network, it's just that it's already big, so I don't see a reason to join… when you do something [with the] DMCRN, you need to follow their protocol – it's almost like doing a clinical trial under pharma. If your plate is already full, you don't have that bandwidth or staff to do this work. (Researcher)*

Some researchers mentioned that they faced challenges trying to reenter the network, even if they had been previously involved at a different research site. Another industry partner discussed that they do not use the DMCRN because their focus is on pediatrics/juvenile DM, and the network is not currently set up to support this type of research.

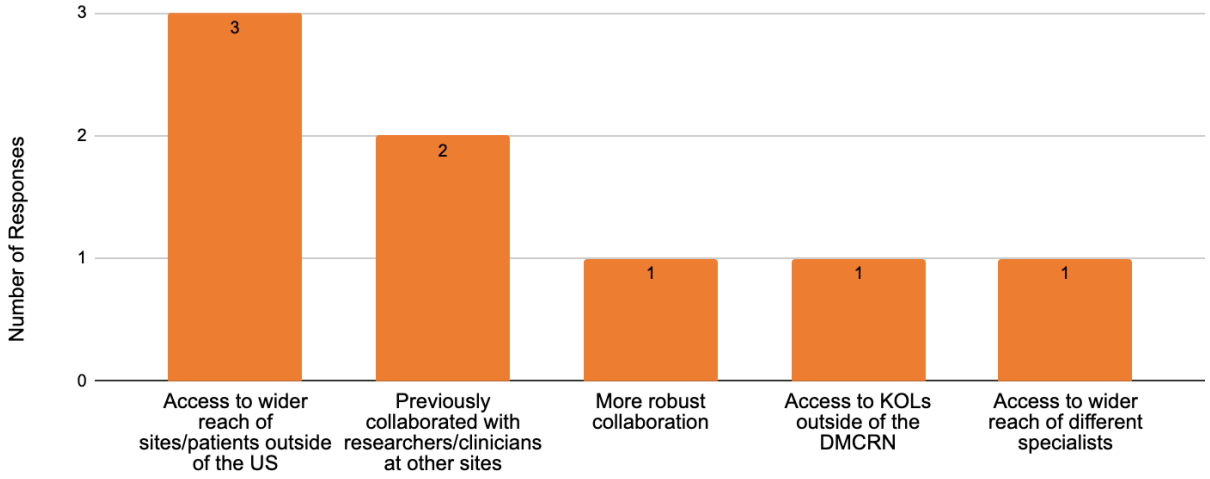
Some European researchers praised the DMCRN's expansion into Europe, while other respondents noted that additional geographic diversity would strengthen the network, indicating a mixed view of the network's current geographic reach. In particular, a few industry partners expressed in interviews that working exclusively with DMCRN sites may limit geographic diversity. Working with sites outside of the DMCRN also provided them with access to a greater diversity of KOLs, as well as access to sites with which they had previously collaborated.

> *Sometimes there are other considerations like geography or the racial and ethnic background of a particular region that make it attractive beyond just what's available to the DMCRN. (Industry)*

When survey respondents were asked why they are not currently a member of DMCRN, the most frequent reasons cited were not being a clinical research site (10), not being invited to join (7), or "other" (12).[24] Of those who selected "other," most were not sure about their membership status or were not eligible because they do not conduct clinical research.

Industry survey respondents who indicated that they use, or will consider using, a trial site or network other than the DMCRN cited reasons such as gaining access to patients outside of the U.S. or previous collaboration or relationships with researchers or clinicians at other sites.

Figure 10. Reasons Industry Survey Respondents Currently Use or Plan to Use Sites Other than the DMCRN (n=6, multiple select)



4.3. Myotonic Dystrophy Foundation: Strengths and Opportunities

4.3.a. MDF Current Strengths

The most common theme across both groups of interview respondents was the key role that MDF plays as a convener and bridge between patients, researchers, industry members, and regulatory bodies. This was coded approximately 50 times across industry and research interviews, including multiple mentions for individual respondents. Both industry and research respondents commended MDF's ability to build bridges between disparate groups and ensure the right voices were included at the right time. Industry partners also noted the

[24] Twenty-nine individuals responded, with two respondents selecting multiple responses. Additional responses were "Lack of bandwidth to follow DMCRN protocol" (1) and "Institution was not interested in joining" (1).

importance of having a neutral convener so companies can learn and work together, as drug development can often be a competitive space.

Many industry partners and researchers spoke highly of MDF's conferences and in-person gatherings, highlighting MDF's ability to act as a convener. Interview respondents stressed the importance of bringing together industry partners, researchers and clinicians, and patients and providing spaces for all of these groups to learn from each other how to best support the patient community. A few researchers also noted the importance of conferences for networking and peer learning from other researchers and clinicians, and in particular the value that this in-person engagement provides to more junior researchers and site coordinators.

> *The educational resources for health providers and patients and the open door for patients to be an equal member at the table for conferences and committees is phenomenal and it's been a great help to us. (Research)*

> *MDF meetings have been really great to see patients, regulators, academic investigators, and everyone sharing knowledge and ongoing collaboration. [MDF is] building that bridge between different groups. (Industry)*

MDF was particularly praised for its advocacy on behalf of the DM community in interviews, and this theme was reflected in survey responses (see Figure 12 below). Interviewees noted the value to both patient and caregiver groups and commended MDF's efforts in these areas. Additionally, industry partners and researchers highlighted MDF's ability to orient newly diagnosed patients and connect them to resources and potential therapies. **Both industry partners and researchers recognized MDF's essential role in advocating on behalf of the patient community at various levels, including with regulators and policymakers.** "Advocacy" was coded nearly 40 times across all interviews, including multiple mentions for individual responses. Relatedly, both groups recognized the importance of MDF's patient and advocacy support groups and acknowledged that this is a core component of MDF's vision.

> *[Having the] nonprofit advocacy voice at the table is so important in highlighting what key issues are. MDF's work with and on behalf of the community is so well received and important. (Industry)*

Industry partners spoke highly of MDF's role in connecting them to patient populations and helping industry prepare for trials. In interviews, nine companies spoke positively about MDF's support role. MDF is particularly useful in helping industry understand patients' realities and needs, as many industry respondents mentioned that they are often disconnected from or unaware of patients' day-to-day challenges. On the flip side, industry partners highlighted the importance of MDF's role in educating patients and ensuring that they are ready–and excited–to participate in trials. For smaller companies, or companies that are new to DM research, this is especially important.

> *Because [our company] is so new, no one in the company has an understanding of DM1. The fact that MDF exists and has been able to connect us with other experts and clinicians has been very valuable to us. MDF is the hub of the wheel in connecting us with key people we need to interact with. (Industry)*

Additionally, some industry partners mentioned that having in-person connections with patients helped them feel greater purpose and stake in their work. Overall, industry partners view MDF as an important and valued partner.

> *I've been to one MDF meeting and it was great not just to meet academic researchers but also to meet patients, which is something I don't have the opportunity to do very often as a researcher. It's very inspiring for researchers and gives us more purpose and momentum. (Industry)*

Similarly, researchers from five different sites also praised MDF for its ability to connect them to patients, noting that incorporating patients' voices has improved research. Partnering with MDF also helps researchers keep patients' voices and needs at the center of their research design and ensure that what they are doing is actually meaningful for patients.

> *Research is meant to help patients. We need to know what their needs and struggles are so we're doing clinically relevant work.… It's easy for researchers to get so excited about certain things that we forget to check in about whether it's actually meaningful for patients. Having MDF involved will keep things more patient-centric. (Research)*

Finally, respondents across both groups praised MDF's work and CEO, Dr. Tanya Stevenson's leadership, with particular praise for her support of industry partners. Several industry partners mentioned that they had recently been in touch with Dr. Stevenson about ongoing and forthcoming projects, so it is clear that MDF is providing regular support to its partners across the network.

4.3.b. MDF Current Opportunities and Challenges

Survey respondents were asked about the role of advocacy in the success of drug development and clinical trials and study sites, as well as MDF's role in advancing the drug development pipeline. The top answers, shown below,[25] are elaborated in greater detail below based on interview responses. Similar conclusions from interview respondents can be seen in the codebook in Appendix D and are elaborated further in this section.

[25] For the complete list of responses, see Appendix C.

Figure 11. Survey - Role of Advocacy in the Success of Drug Development and/or the Clinical Trial/Study Sites (n=50, multiple select)

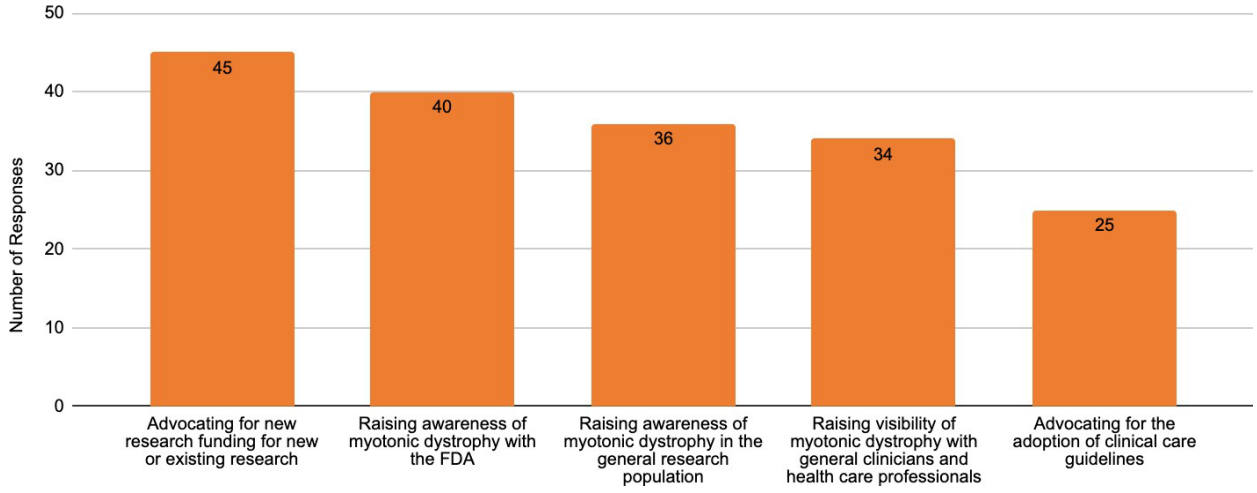
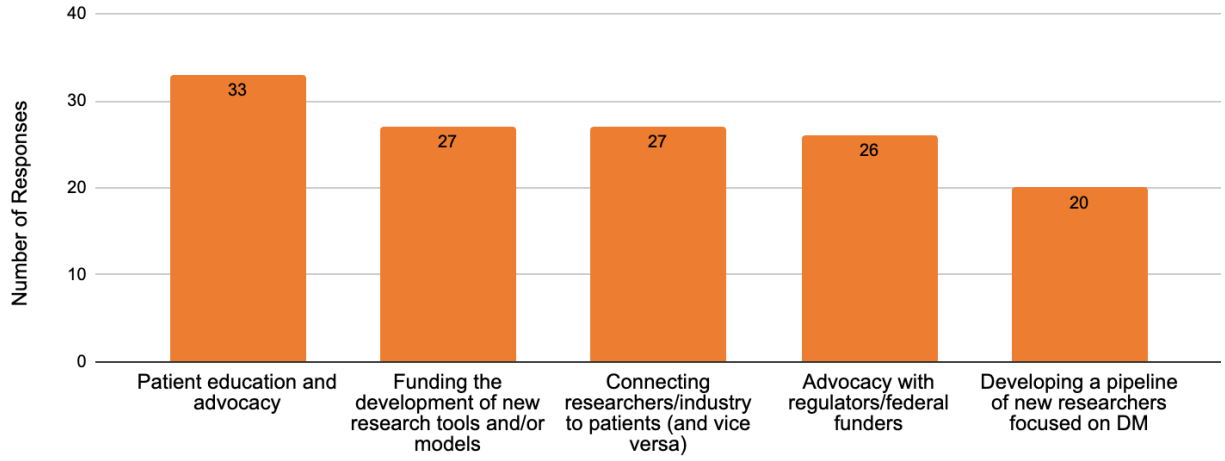


Figure 12. Survey - MDF's Most Valuable Role in Advancing the DM Drug Development Pipeline (n=50, multiple select)



Funding Needs across the DM Ecosystem

Across interviews, funding was a common area for increased support, with approximately 45 coded mentions across industry and research interviews related to areas in which MDF can provide funding support. While many respondents acknowledged that MDF's funding and fundraising capacities are relatively limited given its size, several areas for additional or targeted fund development were mentioned across the interviews. Some respondents suggested that MDF continue to increase their fundraising capacity, perhaps drawing on similar viral fundraising campaigns like the *ALS Ice Bucket Challenge*.

Researchers identified several areas for dedicated funding support. Several researchers expressed frustration with the piecemeal nature of research funding, as the various grant

timelines often leave gaps in the research timeline, inhibiting researchers from running continuous studies. Coding indicated that seven researchers suggested that if MDF were able to provide funding to cover gaps in grant funding for researchers, it would greatly support research continuity. Researchers also identified a need for pilot/startup grant funding. Other suggestions for dedicated research funding areas include DM2 studies, natural history studies, and non-medical research (e.g., physical therapy research).

Approximately ten researchers mentioned in interviews that increased investment for junior researchers would increase the network of DM researchers. Some interview respondents acknowledged that MDF does provide some funding support for junior researchers, but it is unclear how well-known and accessible this funding is among researchers. One European researcher suggested that funding one research fellow per country would also help expand the global scope of researchers. Eventually, this would also help to expand and diversify the number of KOLs, which was identified as an area for network improvement among a number of interviewees. Additionally, a couple respondents mentioned that it would be beneficial to train junior researchers to apply for funding and help to sustain research funding pipelines.

> *One risk in [DM] is the limited number of KOLs that get used over and over again by everyone. If MDF could help extend this pool to support new academic investigators who could become future KOLs, that would be great. (Industry)*

A few researchers also mentioned that funding to support site coordinators would greatly support site capacity. One researcher also mentioned that a care coordinator could help target traditionally under engaged patients, such as Black and Hispanic patient communities.

Industry partners likewise identified discrete areas for additional funding support. A couple small companies or newer start-ups mentioned that they are currently unable to pursue DM trials due to a lack of funding. Since these companies are eager to work on the disease, providing them with some initial funding or making connections to academic researchers with funding may catalyze trial development.

Additional funding areas identified by researchers and industry partners include travel funding for conferences (particularly for site coordinators), mouse model grants, and funding to support patient travel and logistics.

Research and Trial Development Support

Interview respondents noted some areas where MDF can support the various research and trial barriers mentioned earlier in the report. Coding showed that eight industry partners suggested that MDF continue to support the development of outcome measures and endpoints, as well as trial design more generally. This sentiment was echoed by a few researchers as well.

> *[MDF can help] studies understand design elements that aren't going to work for patients in reality. For example…if [studies] have outcome measures that [patients] are supposed to complete on an iPad, it can be very difficult for them to use a touch screen. If [patients] just used a laptop instead of an iPad, they'd get better data. It's helpful when patient advocacy groups share that kind of information. (Research)*

As mentioned earlier, supporting the development of a biobank is another area for MDF to support.

Regulatory and Policy Advocacy

As noted above, **respondents believe that MDF has done a good job sharing patient voices with regulatory bodies and helping regulators understand patient needs. Maintaining consistent engagement with regulatory bodies and helping regulators to understand patients' needs will help push forward treatments.** In particular, MDF can continue to serve as the patient voice by educating regulators on what specific outcome measures actually mean to patients.

> *MDF has been instrumental in bringing the voice of patients to regulators and making sure they understand the breadth of the disease and how it impacts patients…. It is really important for MDF to engage with regulators and make sure that regulators don't forget about their patients. (Industry)*

> *The best thing MDF could do is speak on behalf and understand what its community's unmet needs are and effectively communicate those unmet needs to the FDA, CDC, Congress, and elsewhere both at the federal and state level. It's really important that MDF does that through patient listening sessions at the FDA and targeted hearings at Congress. (Industry)*

Some industry partners also suggested that MDF continue to work with industry to help define endpoints for regulatory approval.

> *Some therapies aren't getting accepted because they aren't looking at the right endpoints. MDF's role is huge to clear the path to approval and bridge the gap between companies and patients on the ground who suffer from DM1. (Industry)*

Approximately five respondents, including several industry partners and one researcher, noted that MDF could continue to play an important role in policy advocacy. One industry respondent noted that MDF could engage in peer learning from MDA and other patient advocacy groups on how to define policy priorities. Additionally, it was suggested that it would be helpful for MDF to further define its advocacy strategy and communicate this more clearly to their community.

> *It's important that MDF defines its advocacy strategy–which part of the advocacy strategy…are the core part of their mission and which parts are tertiary, and communicates this effectively to their community so members understand what [MDF's] advocacy priorities are. (Industry)*

Patient Education, Engagement, and Recruitment

Patient education was coded 23 times in interviews, including 16 references from industry partners, with an emphasis on supporting patient education around trials. MDF can continue to educate their patient community on what trials are ongoing, what is expected of participation, and what patients can expect to gain from trials. As mentioned earlier, helping to demystify trials and ensure that patients are ready to participate in trials is an area that MDF can continue to support.

> *MDF is doing a good job with this, but lots of patients… are keen on participating in trials but don't understand what involvement entails. Anything MDF can do to explain and educate around clinical trials so the population is really prepared when the trial comes so there's enthusiasm but they're also aware of what they're getting into. (Industry)*

As multiple trials are becoming available, it's particularly important for MDF to support its patient community in accessing and enrolling in these trials and studies.

> *The DM community is going from no treatment or a series of failed treatments to a crowded space with many options. MDF will play a huge role in helping families to ask the right questions of their physician and evaluate options. (Industry)*

In-person community engagement is also an area for continued MDF support. A couple of participants noted the value of family days and other in-person community engagement events, both from an education and a community support perspective, and suggested that MDF support network members in similar events. Respondents spoke highly of MDF's conferences and other opportunities for in-person gatherings, and also recommended that MDF organize more in-person convenings, both for the research network and for community members. In particular, regional convenings would be useful for connecting local network members.

> *[MDF should organize] some smaller regional meetings where sponsors in the community can come together. Last year MDF did their annual conference which was great, but it would be good to do smaller one-day or half-day events in-person. This gives people some facetime, and it could be helpful to have a bit more local presence. (Industry)*

While interview respondents across both groups spoke highly of MDF's patient registry, particularly in the early stages of recruitment, the survey responses were more mixed (Figure 13).[26] Nearly three quarters of respondents did not utilize MDF's research map or patient registry. Of the survey respondents who did not utilize these resources (Figure 14), 37% plan to use the resources in the future, while 39% did not know about the resources and 24% did not find these resources useful, respectively. Of the nine respondents who said the resources were not useful, it is important to note that three respondents expressed that the resources are not useful for studies being conducted outside of the U.S.

Figure 13. Survey - Did You Utilize MDF's Research Map or Patient Registry Data when Engaging in Your Development Work? (n=52)

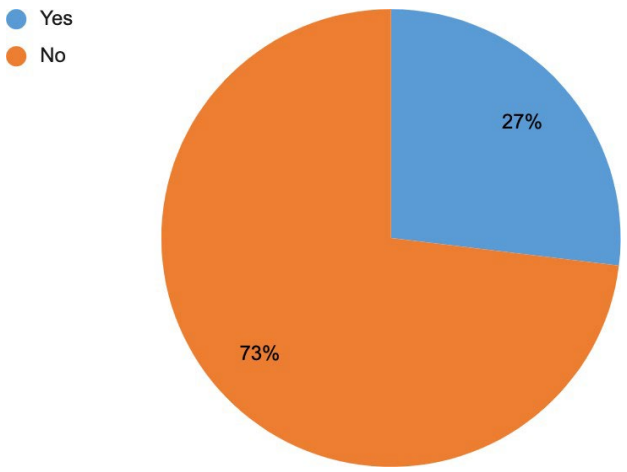
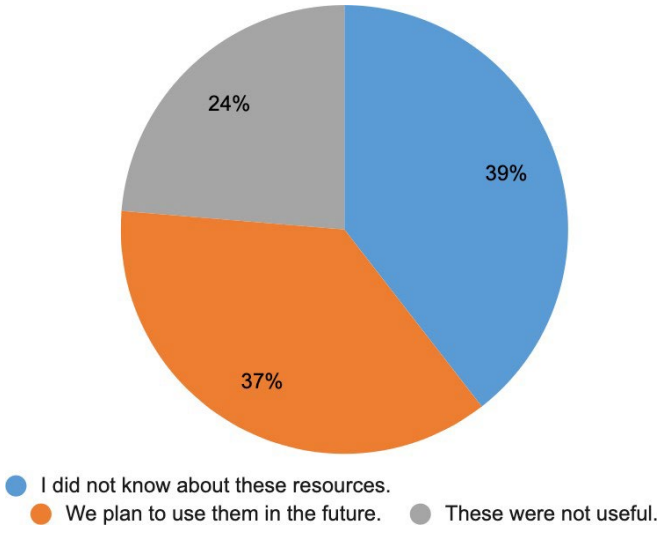


Figure 14. Survey - Reasons for Not Using Resources (n=38)



[26] It is important to note that the survey question did not distinguish between the use of MDF's research map and patient registry; therefore, it is possible that usage for one resource was higher than the other.

Data Sharing and Publication

Another area for continued MDF support is research publication and data sharing. MDF was commended for its research communication, and is viewed as a trusted disseminator of research and other important information. To this end, several participants across both groups encouraged MDF to continue to publish and share research across a range of formats, including white papers, seminars/webinars, and other reports. Across 21 codings for knowledge dissemination and publication, this was flagged 19 times among industry partners, suggesting that additional research publication and data sharing is particularly relevant to industry.

MDF may also work to get researchers to publish more data, which will help in the path to regulatory approval. Some industry partners mentioned the importance of MDF holding researchers accountable to their deliverables and ensuring that researchers share their data in the public domain.

> *MDF needs to be more heavy-handed in what they expect to see as deliverables in the public domain from their research grants. (Industry)*

Industry Support

While comments about MDF's support for industry partners were overwhelmingly positive, some interview participants flagged opportunities for improved communication with industry. One respondent said that it may be useful for MDF to organize industry working groups for a deeper engagement with industry perspectives. Similarly, one researcher suggested that MDF continue to work on bidirectional communication with industry to continue to understand what is working well and what are areas for improvement.

Peer Learning

One recommendation that arose in several interviews was that MDF continue to engage in peer learning from similar organizations working in the neuromuscular disease space, or with other rare disease populations, to learn how to address similar challenges across patient groups. Relatedly, a few respondents also mentioned that it would be helpful to see some type of organizational mapping to illustrate how the various global organizations can work together.

> *MDF can consider how it can learn from others in the neuromuscular disease space who have faced some of these challenges so that it can go quicker and more efficiently for its community…. Collaboration with other nonprofits is definitely a theme that we want to make sure we bring forward. (Industry)*

5. Discussion

Our findings support the following set of opportunities to consider for future investment in the DM research landscape. These opportunities represent the barriers and challenges that are most salient among the sample of interviewees and survey respondents and where MDF may be positioned to contribute both now and in the future. These should not be interpreted as a list of recommendations, but as potential pathways for consideration.

DM Research: Priorities and Barriers

1. **Provide support to directly address top research gaps.**

   There remain gaps in general understanding of the disease across the field, particularly for DM2. Building a more comprehensive understanding of DM alongside drug development is the top priority for research and industry for DM1 and DM2. More specifically, both researchers and industry named identifying appropriate biomarkers for DM1 and DM2 as a priority, and expanding genetic testing and diagnosis as a priority for DM2.

   a. MDF may consider investing in research initiatives that will address foundational gaps in the research and accelerate drug development for DM.
   b. Explore additional strategies to promote genetic testing and improve diagnosis timelines for DM2.

   Follow-up questions for future exploration:

   - *Can general understanding of the disease or identifying appropriate biomarkers be addressed through better knowledge sharing and data publication efforts?*
   - *What are the best ways to catalyze baseline understanding of the disease–launching new research or bolstering research programs already underway?*
   - *How can MDF continue to ensure that DM2 research is prioritized and ensure individuals living with DM2 feel included?*

2. **Fuel the research pipeline by attracting and supporting the next generation of DM researchers and clinicians.**

   MDF's fellowship and grant programs have meaningfully contributed to the development and strength of a collaborative and committed bench of DM researchers. Yet, the future talent pipeline for DM remains a key concern among our sample. MDF may have an ongoing role to play in shaping the future DM workforce.

   a. Continue to provide and potentially expand current research fellowship programs, and explore the potential of initiating a clinical fellowship.[27]
   b. Provide stipends for junior researchers, or those new to the field, to attend the MDF conference.
   c. Provide additional funding for pre- and post-docs focused on DM2.

   Follow-up questions for future exploration:

   - *Is there demand from the field for a clinical fellowship?*
   - *What other rare disease/patient advocacy organizations offer clinical fellowships?*
   - *Can we revisit promotional registration pricing and stipends for the conference to make it more accessible to those more junior in their careers?*

[27] Exploration of launching a DM-focused clinical fellowship is included in MDF's three-year strategic plan (2021 - 2024).

3. **Support early stage research initiatives with pilot grants that will allow researcher teams and institutions to secure larger-scale funding.**

   One opportunity discussed, primarily among researchers, was the challenge of accessing funding for new research initiatives and the toll and resource drain of ongoing funding uncertainty and grant seeking. Given MDF's credibility in the DM landscape, there may be a role to play in helping to seed new research and attract larger institutional funders. Additionally, there may be a role to play in providing funding to cover gaps in larger scale institutional funding to support study or trial continuity.

   a. MDF may consider a pilot funding program, outside of the fellowship program, that will allow researchers to collect initial data sets and position their teams to be more competitive for larger grants from major funding and research institutions.

   Follow-up questions for future exploration:

   - *What type and size of grant funding would meaningfully support pilot research programs?*
   - *What types of researchers and institutions would benefit from this support? How might intervening at this stage affect the field overall, both now and in the future?*
   - *Are other rare disease advocacy organizations and/or funding institutions currently providing this type of support to the field? If so, who?*

DM Research Studies and Trials: Strengths and Opportunities

4. **Make additional investments in DM trial readiness infrastructure to meet future demand for clinical trial sites.**

   Over the past decade, there has been significant growth in the development of active DM programs, studies, and trials. However, the field has indicated that the DMCRN is not fully equipped to meet the near-term demand of the growth trajectory. There is an opportunity to make critical investments to strengthen the capacity DMCRN or other trial sites; specific suggestions from respondents include:

   a. Additional training to bolster capacity of trial site staff (e.g., research coordinators), or funding to hire additional staff.
   b. Enhance site capabilities for more specialized studies and trials through education or procurement of required equipment (e.g., pediatrics, physical therapy), or discuss with DMCRN leadership what it would take to allow existing specialized trial sites to become members of the DMCRN.
   c. Support the reduction in monetary/logistical barriers to trial and study participation for patients and their families (e.g., supplement travel costs, strengthen on-site patient support services and staff). This may be achieved through provision of patient incentives or funding to enhance on-site staffing and resourcing to support patient participation.

   Follow-up questions for future exploration:

   - *What training and support do trial site staff most need?*
   - *How do we help VCU determine what specialized trial sites might be eligible to join the DMCRN? Do they need to develop additional criteria for eligibility?*
   - *If providing patient incentives or support to bolster study or trial participation, how do we determine which to incentivize?*

5. **Continue to invest in patient education efforts.**

Participants overwhelmingly commended MDF on the role it plays in patient education and advocacy. We heard that MDF's ability to bring together stakeholders across the DM ecosystem (patients and their families, physicians, researchers, industry partners) is a tremendous strength and value-add. At the same time, there was a call, particularly related to trial preparation and participation, for more support educating and expectation setting with patients. There may be an opportunity to augment existing patient education programs to better prepare those living with DM and their families to successfully participate in studies and trials.

- Promote the importance of non-treatment focused studies such as the natural history study to strengthen knowledge of the disease and how it affects various body systems across the field.
- Strengthen trial enrollment and increase registry numbers through targeted communications, campaigns, and education.
- General expectation setting for trial and study preparation (e.g., financial implications, timeline, what to expect at appointments, etc.).
- Provide information on, or directly provide, resources to offset personal costs to participate (e.g., travel and lodging costs).

Follow-up questions for future exploration:

- *How do other rare disease organizations prepare their patient populations for study and trial participation? What can we learn from their approaches?*

6. **Promote accountability and data publication and dissemination.**

While it was largely agreed that the DM research landscape is collegial and collaborative, there were also concerns raised, among both research and industry respondents, regarding access to data and knowledge sharing across the ecosystem, both related to general accountability and reducing barriers to knowledge access such as cost.

a. The majority of interviewees noted that access to natural history study data is crucial for advancement of the field at large; two industry members directly named financial barriers to data access as a challenge.
b. Respondents noted that some MDF grantees are not consistently sharing and publishing data, which may require better defining the grant agreement deliverables.
c. Multiple interviewees who are members of the DMCRN noted that the network has an opportunity to strengthen transparency among member sites and improve data sharing.

Follow-up questions for future exploration:

- *What datasets, if any, can be made available at no, or low, cost to the public? Who owns this data? What's keeping the authors from developing and submitting manuscripts?*
- *What are the particular barriers to making widely available data from the natural history study?*
- *Are there particular operational supports that would allow the DMCRN to strengthen member communication and knowledge sharing?*

Other Opportunities to Support the Field

7. **More clearly define MDF's advocacy priorities and strategies.**

   Industry partners and researchers highlighted MDF's crucial role in advocating at the federal level with governing institutions, regulators, and policymakers, but expressed that a more clearly defined agenda and increased transparency around advocacy efforts may help to accelerate progress in specific areas.

   a. Set a clearer agenda for advocacy efforts with regulators and communicate these advocacy priorities more openly to the community.
   b. Continue to share patients' experiences and serve as the patient voice to help develop meaningful outcome measures.
   c. Continue to work with industry members to help define endpoints for regulatory approval.
   d. Better coordinate advocacy efforts with others who share similar interests (e.g., MDA).

   Follow-up questions for future exploration:

   - *Can we make our current advocacy priorities and successes more transparent to the field? How can we best publish/disseminate those priorities?*
   - *Which other rare disease/advocacy organizations have clearly defined advocacy priorities; what are they focused on?*

8. **Define and strengthen MDF's role in the global DM ecosystem to accelerate learning outcomes.**

   MDF is a credible, collaborative, and central player in DM patient advocacy worldwide. While there is agreement that the field is inherently cooperative, international colleagues suggested there remains a divide between North American, European, Latin American, and Asian researchers, both in academic and clinical settings. Additionally, respondents observed that many of MDF's resources and perspectives are U.S.-centric, which causes them to miss out on research advancements happening in other countries. There may be an opportunity for MDF to better define its position internationally and to foster synergies and progress on a more global scale.

   a. In addition to the bi-annual International Myotonic Dystrophy Consortium Meeting (IDMC), arrange less formal, more frequent intercontinental meetings that create conditions for relationship building, brainstorming, and collaboration.
   b. Launch a funding initiative that is exclusively focused on promoting international collaboration.
   c. Support researchers to identify funding opportunities where they would be most competitive.
   d. Continue to engage in peer learning from other rare disease research organizations, both in the U.S. and internationally.
   e. Develop a more global view that encapsulates research and trials happening in other countries and patient communities.

   Follow-up questions for future exploration:

   - *What are the most crucial investments to better promote international collaboration (e.g., translated resources, funding, convenings)?*

Appendices

A. Participating Institutions: Interviews and Focus Groups[28]

AMO Pharma, UK
ARTHEx Biotech, Spain
Avidity Biosciences, US
Biogen, US
Dyne Therapeutics, US
Entrada Therapeutics, US
Expansion Therapeutics, US
GrittGene Therapeutics, US
Harmony Biosciences, US
Houston Methodist, US*
Indiana University School of Medicine, US
Institut de Myologie, France*
Juvena Therapeutics, US
Locana Bio, US
Ludwig Maximilian University of Munich, Germany*
Lupin Neurosciences, Switzerland
N-Lorem Foundation, US
National Health Service (NHS)/University of London, UK*
PepGen, US
Radboud University, Netherlands*
Sanofi, US
Stanford University School of Medicine, US*
Syros Pharmaceuticals, US
University of Auckland, New Zealand*
University of California, Los Angeles, US*
University of Colorado, Denver, US*
University of Florida, Gainesville, US*
University of Iowa, US*
University of Kansas Medical Center, US*
University of Missouri, US
University of Rochester, US*
University of Sherbrooke, Canada*
U of Texas Southwestern, US*
Virginia Commonwealth University, US*
Vertex Pharmaceuticals, US
Wake Forest University, US
Anonymous (3)[29]

[28] Starred sites are members of the DMCRN.
[29] Anonymous participants include two large and one mid-sized pharmaceutical company.

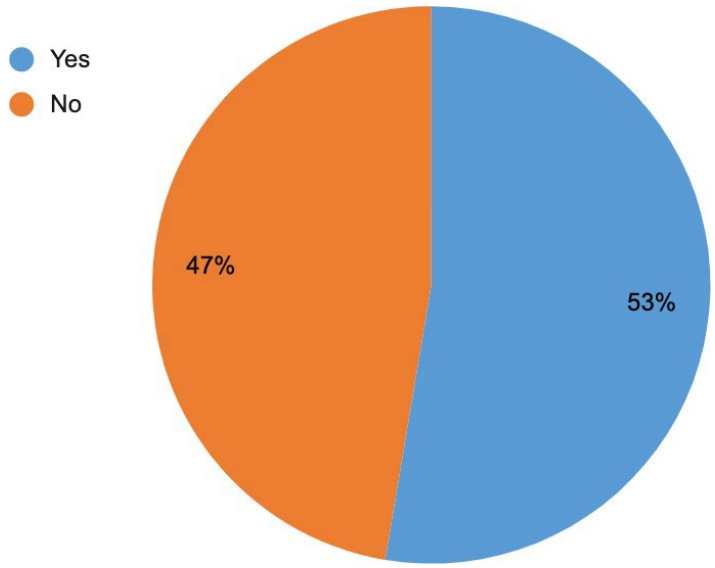
B. Current DMCRN Sites, as of April 2023

Centro Clinico Nemo, Italy[30]
Houston Methodist, US
Institut de Myologie, France
Ludwig Maximilian University of Munich, Germany
Ohio State University Medical Center, US[31]
Radboud University, Netherlands
St. George's University of London, UK[32]
Stanford University School of Medicine
National Health Service (NHS)/University College London, UK
University of Auckland, New Zealand
University of California, Los Angeles, US
University of California, San Diego, US[33]
University of Colorado, Denver, US
University of Florida, US
University of Iowa, US
University of Kansas Medical Center, US
University of Rochester, US
University of Sherbrooke, Canada
University of Texas Southwestern, US
Virginia Commonwealth University, US

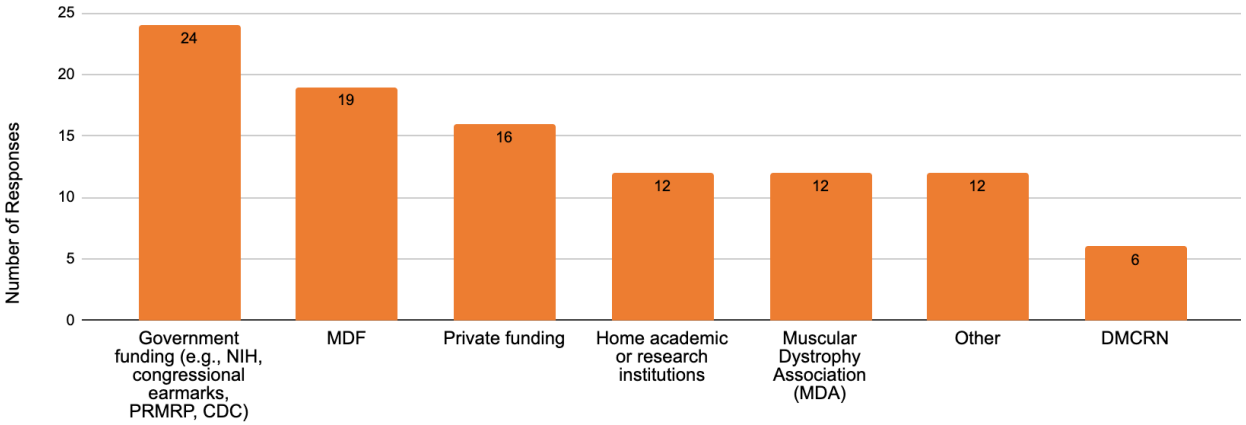
[30] Did not participate in an interview
[31] Did not participate in an interview
[32] Did not participate in an interview but completed survey
[33] Did not participate in an interview

C. Additional Survey Responses

Survey - Have You (or if Applicable, Your Trainees) Been the Recipient of an MDF Research Grant or Fellowship? (n=57)



Survey - Primary Source of DM Funding (n=57, multiple select)



Survey - Barriers and Challenges to DM Research and Treatment Development
(n=50, multiple select)

Barrier or Challenge (select up to 5)	Number	Percentage
Difficulty in drug delivery to muscle	19	12%
Access to tissue samples/ cell lines	18	12%
Lack of funding for study/ trial or other budgetary issues	18	12%
Access to mouse of other animal models	13	9%
Lack of FDA-validated outcome measures/ endpoints	12	8%
Lack of understanding of natural history	12	8%
Site capacity	11	7%
Regulatory challenges	9	6%
Lack of collaboration in the field	7	5%
Difficulty in determining which symptoms/systems to target with treatments	6	4%
Lack of publications on recent longitudinal studies, including RACE, POP, STOPP	6	4%
Identifying and enrolling patients	4	3%
Challenges with caretaker involvement	3	2%
Patients lack understanding of study/ trial	2	1%
Lack of clinical sites near patients	2	1%
Low capacity at DMCRN sites	2	1%
Patient follow through and participation	1	1%
Access to key opinion leaders (KOLs)	0	0%
Other ● NIH in particular NIAMS needs lobbying for DM1 and DM2 if skeletal muscle research in DM is to be funded appropriately ● A sense that this disease has been figured out. Lack of open thought to alternative or additive ideas. This prevails at the PI levels and at funding institutions. Leading to limiting funding access, and limiting thought and voices. ● If researchers have ideal funding and environment, there are several problems that may slow down the progress of therapeutic studies. In my opinion, (1) Link of academic and clinical research, focusing on the therapy as a priority, may be not very efficient. (2) It is always difficult to identify and recruit young researchers (students, postdocs) for academic research. Many labs are understaffed. The research (bench work) should become prestigious for young people. ● Retirement from academia ● Finding effective compounds with low toxicity ● Poorly understood CNS mechanisms ● Geography (Canada) ● Mouse models for DM2	8	5%

Survey - Top Research Priorities for DM1 (n=53, multiple select)

Top research priorities for DM 1 (select up to 5)	Percentage	Number
Identifying appropriate biomarkers	11%	26
More research on central nervous system	10%	22
Drug development	9%	21
General understanding of disease	8%	19
Developing clinical endpoints	8%	19
Helping patients manage symptoms	7%	15
Building out multidisciplinary research teams	6%	13
Lack of research and data/publications on DM1 localization and impact in the brain, endpoints and outcome measures for CNS targeting therapies, etc.	6%	13
Expanding genetic testing and diagnosis	5%	12
Clinical trial readiness	4%	10
More research on gastrointestinal symptoms	4%	9
Developing natural history	3%	8
Expanding patient registries	3%	7
More research on how targeting one body system affects other symptoms	3%	7
Access to natural history data	3%	6
More research on cardiovascular system	3%	6
Other	2%	4
Improving DMCRN oversight, administration, and management	2%	4
Patient education	1%	3
Publishing and disseminating more research	1%	3
Developing research infrastructure	1%	2
N/A (haven’t worked on DM1)	0%	1
Number and capacity of experienced clinical trial sites	0%	0

Survey - Top Research Priorities for DM2 (n=35, multiple select)

Top research priorities for DM2 (select up to 5)	Percentage	Number
General understanding of disease	14%	23
Drug development	11%	18
Expanding genetic testing and diagnosis	11%	17
N/A (haven't worked on DM2)	9%	14
Identifying appropriate biomarkers	8%	13
Developing natural history	7%	11
Developing clinical endpoints	6%	10
Clinical trial readiness	5%	8
More research on central nervous system	4%	7
Expanding research network	4%	7
Expanding patient registries	4%	6
Helping patients manage symptoms	3%	5
Access to natural history data	2%	3
More research on cardiovascular system	2%	3
Developing research infrastructure	2%	3
Developing unique studies/data sets	2%	3
More research on how targeting one body system affects other symptoms	1%	2
Building out multidisciplinary research teams (e.g., physical therapists, nutritionists, endocrinologists)	1%	2
Publishing and disseminating more research	1%	2
Other	1%	1
Number and capacity of experienced clinical trial sites	1%	1
Improving DMCRN oversight, administration, and management	1%	1
Patient education	0%	0
More research on gastrointestinal symptoms	0%	0
Lack of research and data/publications on DM2 localization and impact in the brain, endpoints and outcome measures for CNS targeting therapies, etc.	0%	0

Survey - Role of Advocacy in the Success of Drug Development and/or the Clinical Trial/Study Sites (n=50, multiple select)

Role of Advocacy (select all that apply)	Percentage	Number
Advocating for new research funding for new or existing research	21%	45
Raising awareness of myotonic dystrophy with the FDA	19%	40
Raising awareness of myotonic dystrophy in the general research population	17%	36
Raising visibility of myotonic dystrophy with general clinicians and health care professionals	16%	34
Advocating for the adoption of clinical care guidelines	12%	25
Advocating for legislation	9%	20
Advocating for report language for the NIH	5%	10
Other	0%	1

Survey - MDF's Most Valuable Roles in Advancing the DM Drug Development Pipeline, (n=50, multiple select)

Barrier or Challenge (select up to 5)	Percentage	Number
Patient education and advocacy	15%	33
Advocacy with regulators/federal funders	12%	26
Connecting researchers/industry to patients (and vice versa)	13%	27
Maintaining an updated patient registry	5%	10
Funding the development of new research tools and/or models	13%	27
Developing a pipeline of new researchers focused on DM (e.g. engaging early career researchers through fellowships and other opportunities)	9%	20
Developing grants for specific research projects	6%	13
Promoting translational research/sharing research	6%	13
Building community for people living with myotonic dystrophy and their caregivers	9%	19
Other	0%	1
Supporting caregivers	2%	5
Developing more website resources (e.g. guidelines and best practices for clinicians)	2%	4
Ensuring support and transparent management for the DMCRN	4%	8
Outreach, capacity building, and assistance in bringing more centers into DM research and care	5%	10

D. Qualitative Analysis Code Book

Codes (most salient codes are in bold)	Number of Mentions
1 Intro	
1.1 DM program/trial	57
1.2 Personal intro	50
2 Trials	
2.1 Therapies/treatment	**17**
2.2 Gene therapy	5
2.3 Congenital/Children	12
2.4 Areas for improvement	11
2.5 Biobank/human samples	8
2.6 Biomarkers	**21**
2.7 CNS	10
2.8 Drug delivery	9
2.9 Endpoints	**17**
2.10 Enrollment/recruitment	**51**
2.10.1 Patient education	**15**
2.10.2 Logistical challenges/demands	**29**
2.10.3 Caregivers	16
2.10.4 Patient apathy/cognitive challenges	12
2.10.5 Inclusion/exclusion criteria	8
2.11 Genetic testing/diagnosis	8
2.12 Models	9
2.13 Money/funding	**31**
2.14 Natural history	**32**
2.15.1 END-DM1	7
2.16 Outcome measures	**15**
2.17 Research sites	**36**
2.18 Regulatory path	10
4 DMCRN	**41**
4.1 DMCRN Negative	**28**
4.2 DMCRN Positive	**36**

Codes (most salient codes are in bold)	Number of Mentions
5 DM Priorities	
5.1 DM2	**23**
5.2 DM1	**23**
6 MDF support	
6.1 Advocacy	**38**
6.1.1 Patient education	**23**
6.2 Caregiver support	1
6.3 Convener	**49**
6.4 Funding	**46**
6.5 Knowledge dissemination/publication	**21**
6.6 MDF & Industry	**31**
6.7 MDF & regulators	**25**
6.8 MDF & researchers	**23**
6.9 MDF admin/organization	9
6.10 MDF areas for improvement/support	**70**
6.11 MDF challenges	4
6.12 Patient registry	14
6.13 Policy work/advising	8
6.14 Recruitment support	13
6.15 Research tools	8
6.16 Support groups/community	9
7 International inclusion	**32**
8 General DM info	
8.1 COVID	10
8.2 Genetic nature/family impact	9
8.3 Patient care	1
8.4 Research publication/data sharing	2
8.5 General DM challenges	2
8.6 Collaboration	6
8.7 Variability/multisystemic	**30**
8.8 Diversity (Race/ethnicity/gender)	**7**