The UK Myotonic Dystrophy Patient Registry: An Important Tool Linking Patients to National and International Research Projects

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Background

- The UK Myotonic Dystrophy Patient Registry (https://www.dm-registry.org.uk/) is a patient self-enrolling online database, collecting clinical and genetic information about both myotonic dystrophy type 1 (DM1) and myotonic dystrophy type 2 (DM2).
- Established in May 2012.
- Supported by Muscular Dystrophy UK (MDUK) and the Myotonic Dystrophy Support Group (MDSG), assisted by the TREAT-NMD Alliance (www.treat-nmd.org) and coordinated by the John Walton Muscular Dystrophy Research Centre at Newcastle University.
- The registry's primary aim is to facilitate and accelerate clinical research in DM1 and DM2.
- The registry also aims to better characterise and understand DM, and disseminate information relating to upcoming academic and non-clinical studies in DM.

Method

- The registry is used to capture longitudinal, self-reported data through an online portal available to patients and clinicians.
- Patient reported outcomes are entered into a secure portal, combined with clinician verified clinical and genetic details.
- The dataset collected within the registry includes all mandatory and highly encouraged items agreed at the 2009 TREAT-NMD and Marigold Foundation workshop held in Naarden[1].
- This includes **patient reported data items** such as, clinical diagnosis, wheelchair use, myotonia, fatigue/daytime sleepiness, current best motor function, and **doctor reported items** such as heart condition, electrocardiogram, echocardiogram medication, ventilation, age of onset and genetic confirmation.
- The registry can support researchers and industry on various projects by facilitating study/survey recruitment or by providing de-identified patient data

Results

As of April 2021, there were 800 participants enrolled on the UK Myotonic Dystrophy Patient Registry. This includes 409 female and 391 male participants, with an average age of 44.9 years old (range of 0 – 83 years).

*Patients who report a clinical diagnosis as other or unknown may have DM, however the registry requires a discrete choice of DM1 or DM2.

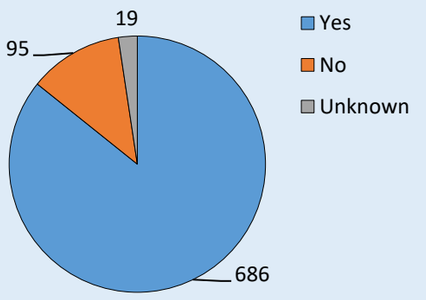

Figure 1. Self-reported positive family history

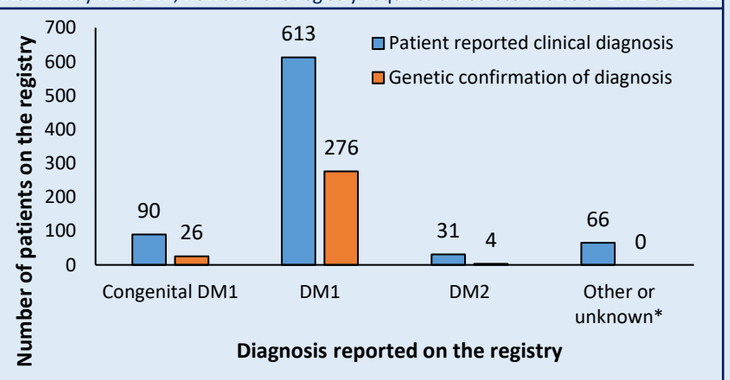

Figure 2. Self-reported clinical diagnosis and doctor reported genetic confirmation of diagnosis

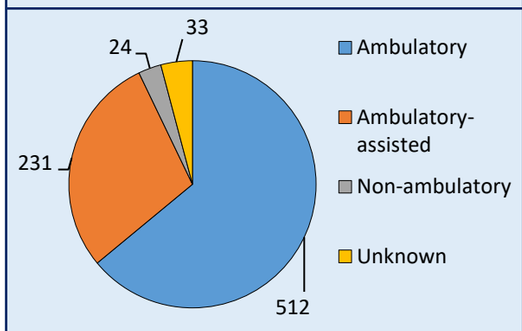

Figure 3. Self-reported current best motor function

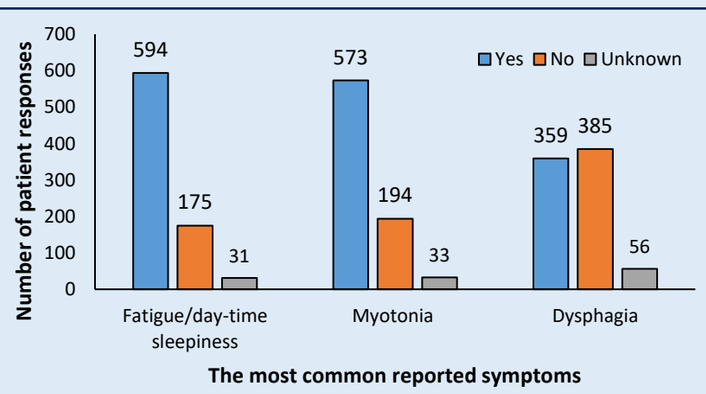

Figure 4. The most common reported symptoms on the registry (fatigue/day-time sleepiness, myotonia and dysphagia.

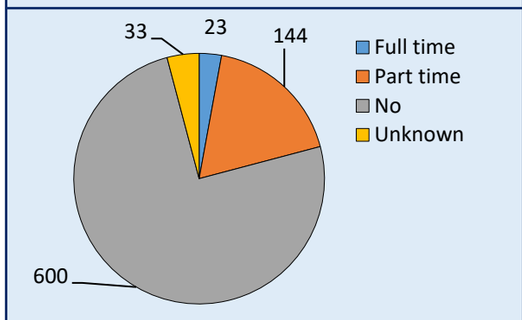

Figure 5. Self-reported wheelchair use

Most patients (86%) on the registry report a **positive family history** of DM (**Figure 1**).

The most common self-reported **clinical diagnosis** is DM1 (76%) followed by congenital DM1 (11%), other/unknown (8%) and DM2 (4%) (**Figure 2**).

Doctors have provided **genetic confirmation** for 45% of DM1 patients, and 29% of congenital DM1 patients (**Figure 2).** The mean (± standard deviation) age of genetic confirmation was 35.1 ± 16.1 years.

Most patients reported their **current best motor function** as either ambulatory (64%) or ambulatory-assisted (29%). A small number of patients reported being non-ambulatory (3%) or did not know (4%) (**Figure 3**).

The most common symptom reported by patients **was fatigue/day-time sleepiness** (74%), followed by **myotonia** (72%) and **dysphagi**a (45%) (**Figure 4**).

Most patients do not require **wheelchair use**, however one fifth report (21%) ether part-time of full-time use. The mean age of wheelchair use was 32 ± 22.9 years, highlighting a large degree of variability (**Figure 5**).

The majority of patients who report their current best motor function as ambulatory, also report myotonia (68%) and fatigue/day-time sleepiness (70%). For patients who report being ambulatory-assisted, most report myotonia (91%) with more than two-thirds reporting severe myotonia (36%). Similarly, 90% of patients report fatigue/day-time sleepiness (90%), with 38% reporting this as severe. Non-ambulatory patients equally reported myotonia and fatigue/day-time sleepiness (58%) (**Figure 6**).

Fatigue/day-time sleepiness and myotonia

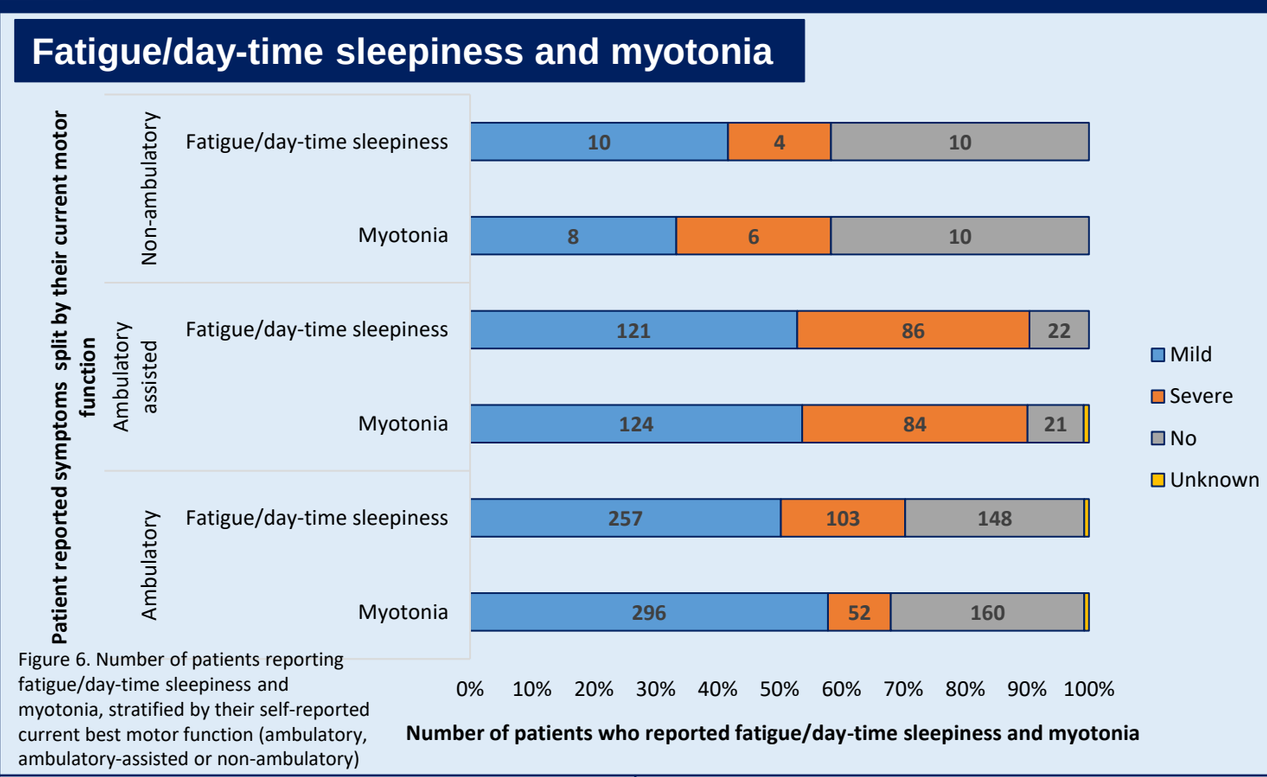

Figure 6. Number of patients reporting fatigue/day-time sleepiness and myotonia, stratified by their self-reported current best motor function (ambulatory, ambulatory-assisted or non-ambulatory)

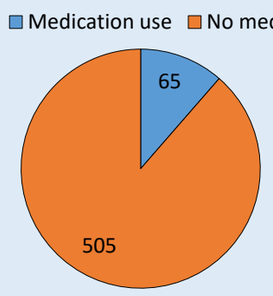

Figure 7. Self-reported medication use for myotonia

Eleven percent of patients report **medication use to treat myotonia** (**Figure 7**)**,** with mexiletine as the most commonly used medication (34%).

Twenty two percent of patients report **medication use for fatigue/day-time sleepiness** (**Figure 8**), with modafinil as the most commonly used medication (87%).

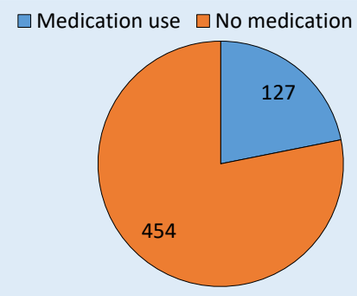

Figure 8. Self-reported medication use for fatigue/day-time sleepiness

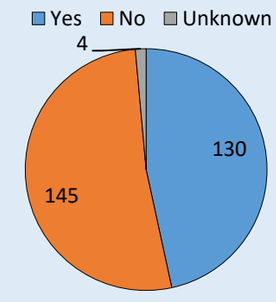

Figure 9. Heart condition as reported by a nominated doctor

Doctors have reported on the **cardiac section** of the registry's doctors form in 35% of patients. Almost half (47%) of these patients have a heart condition (**Figure 9**)**,** with a mean age of onset as 36.3 ± 18.3 years.

The **heart conditions** reported by doctors were:

- Conduction block in 44% of cases
- Arrhythmia **or** conduction block in 33% of cases
- Arrhythmia in 15% of cases
- Other in 8% of cases

Medication use for a heart condition was reported in 22% of cases.

An **electrocardiogram** was reported for 243 patients (30%) on the registry. The mean PR interval was 187.3 ± 38.2 milliseconds (ms), and the mean QRS duration was 107 ± 31.6 ms.

An echocardiogram was provided for 129 patients (16%) and the mean **left ventricular ejection fraction** (LVEF) was 61.3 ± 10.5%. The below LVEF ranges were recorded in 100 patients:

- Hyperdynamic (LVEF >70%) in 10 cases (10%)
- Normal (LVEF 50%-70%) in 84 cases (84%)
- Mild dysfunction (LVEF 40%-49%) in 4 cases (4%)
- Moderate dysfunction (LVEF 30%-39%) in 2 cases (2%)

The results of **pulmonary function testing** were reported in 22% of patients, with forced vital capacity (FVC) recorded as **(Figure 10):**

- Normal in 53% of cases
- Moderate in 13% of cases
- Moderately severe in 13% of cases
- Severe in 20% of cases

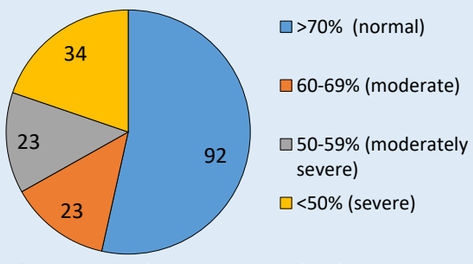

Figure 10. Number of patients with pulmonary function testing as reported by a nominated doctor

Registry utilisation in research

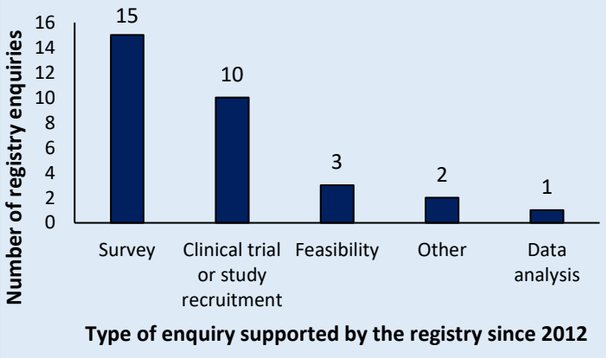

Figure 11. The type and number of registry enquiries supported since 2012

To date the registry has supported **31** enquiries from industry, academics, clinicians and patient organisations. Most registry enquiries have involved online survey distribution (48%) or supporting clinical trial and research study recruitment (32%). Since 2020, the registry has supported 11 surveys, and 1 confidential industry enquiry.

For transparency and to highlight the versatility of the registry, enquiries that the registry has supported are now documented on the registry website.

From the available data of 17 studies supported by the registry, recruitment has ranged from **17%-84%,** with a mean recruitment of **55%** when supporting clinical trials and research studies.

The registry has also been involved in **28** publications most of which include studies where the registry has supported recruitment

These are also now documented on the registry website and are routinely updated.

Conclusion

The UK DM Patient Registry continues to be a versatile, cost-effective research tool that has helped facilitate a range of studies and advance DM research around the world. Additional work continues to be done to improve engagement with more doctors in the UK and the reporting of genetic information on the registry. There are also future data linkage plans between the registry and the Newcastle Research Biobank for Rare and Neuromuscular Diseases. As well as supporting research projects, the registry continues to develop new and engaging communication materials for the UK DM community, and plans to further capture the patient voice in the development of new materials.

Acknowledgement to MDUK and MDSG for their continued support of the UK DM Patient Registry.

References

[1] Thompson R, Schoser B, Monckton DG, Blonsky K, Lochmüller H. Patient registries and trial readiness in myotonic dystrophy–TREAT-NMD/marigold international workshop report. Neuromuscular Disorders. 2009 Dec 1;19(12):860-6.