



The UK Myotonic Dystrophy Patient Registry: A Key Tool Linking Patients with National and International Research Projects

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Background

- The **UK Myotonic Dystrophy Patient Registry** is a patient self-enrolling online database, collecting clinical and genetic information about myotonic dystrophy type 1 (DM1) and myotonic dystrophy type 2 (DM2).
- Established in May 2012.
- Supported by Muscular Dystrophy UK (MDUK), Cure Myotonic Dystrophy UK Charity (Cure DM) and the Myotonic Dystrophy Support Group (MDSG), affiliated to 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 specialist clinicians.
- Patient reported outcomes are entered into a secure portal, combined with clinician verified clinical and genetic details. Patients are reminded to update their information annually.
- The dataset collected within the registry includes all mandatory and highly encouraged items in the TREAT-NMD Core Dataset for Myotonic Dystrophy.
- 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 June 2022, there are 810 active, UK based participants enrolled on the UK Myotonic Dystrophy Patient Registry. This includes 416 female and 394 male participants, with an average age of 46.4 years old (range of 0 – 84 years). There are currently 55 paediatric patients (under 18) in the registry.

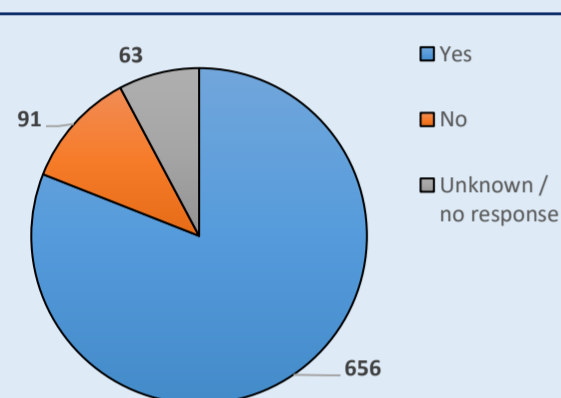


Figure 1. Self-reported positive family history

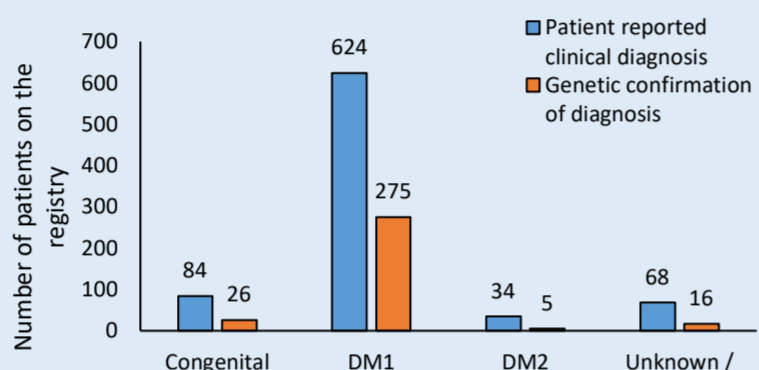


Figure 2. Self-reported clinical diagnosis and doctor reported genetic confirmation of diagnosis

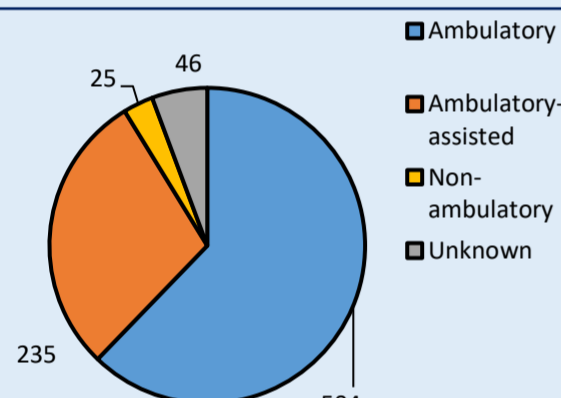


Figure 3. Self-reported current best motor function

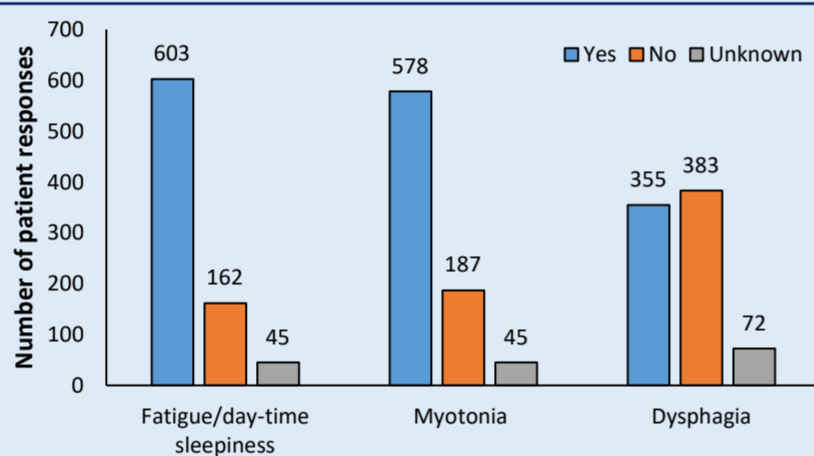


Figure 4. The most common reported symptoms on the registry (fatigue/day-time sleepiness, myotonia and dysphagia).

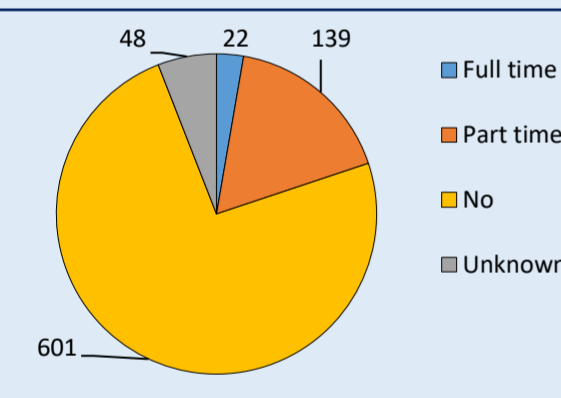


Figure 5. Self-reported wheelchair use

Most patients (81%) on the registry report a **positive family history of DM (Figure 1)**.

The most common self-reported **clinical diagnosis** is DM1 (77%) followed by congenital DM1 (10%), other/unknown (8%) and DM2 (4%) (Figure 2).

Doctors have provided **genetic confirmation** for 44% of DM1 patients, and 30% of congenital DM1 patients (Figure 2).

Most patients reported their **current best motor function** as either ambulatory (62%) or ambulatory-assisted (29%). A small number of patients reported being non-ambulatory (3%), and ambulatory status was unknown for (6%) (Figure 3).

The most common symptom reported by patients was **fatigue/day-time sleepiness** (74%), followed by **myotonia** (71%) and **dysphagia** (44%) (Figure 4).

Most patients do not require **wheelchair use**, however one-fifth (20%) report either part-time or full-time use. The mean age of wheelchair use was 31 ± 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 (69%) and fatigue/day-time sleepiness (73%). For patients who report being ambulatory-assisted, most report myotonia (91%) with 39% describing this as severe. Similarly, 90% of patients report fatigue/day-time sleepiness (89%), with 38% reporting this as severe. Over half of non-ambulatory patients reported myotonia (56%), with fatigue/day-time sleepiness reported more frequently (84%) (Figure 6).

Registry utilisation in research

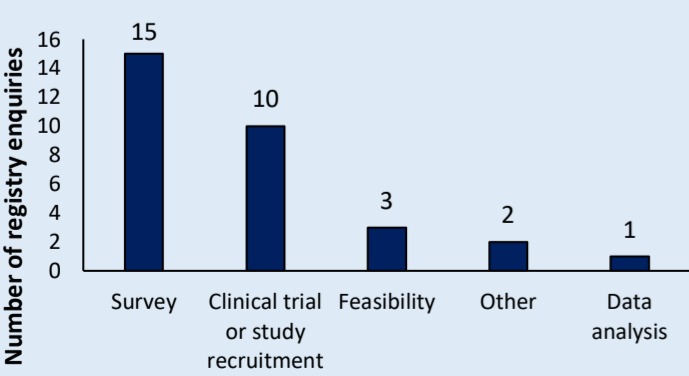


Figure 11. The type and number of registry enquiries supported since 2012

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**.

Fatigue/day-time sleepiness and myotonia

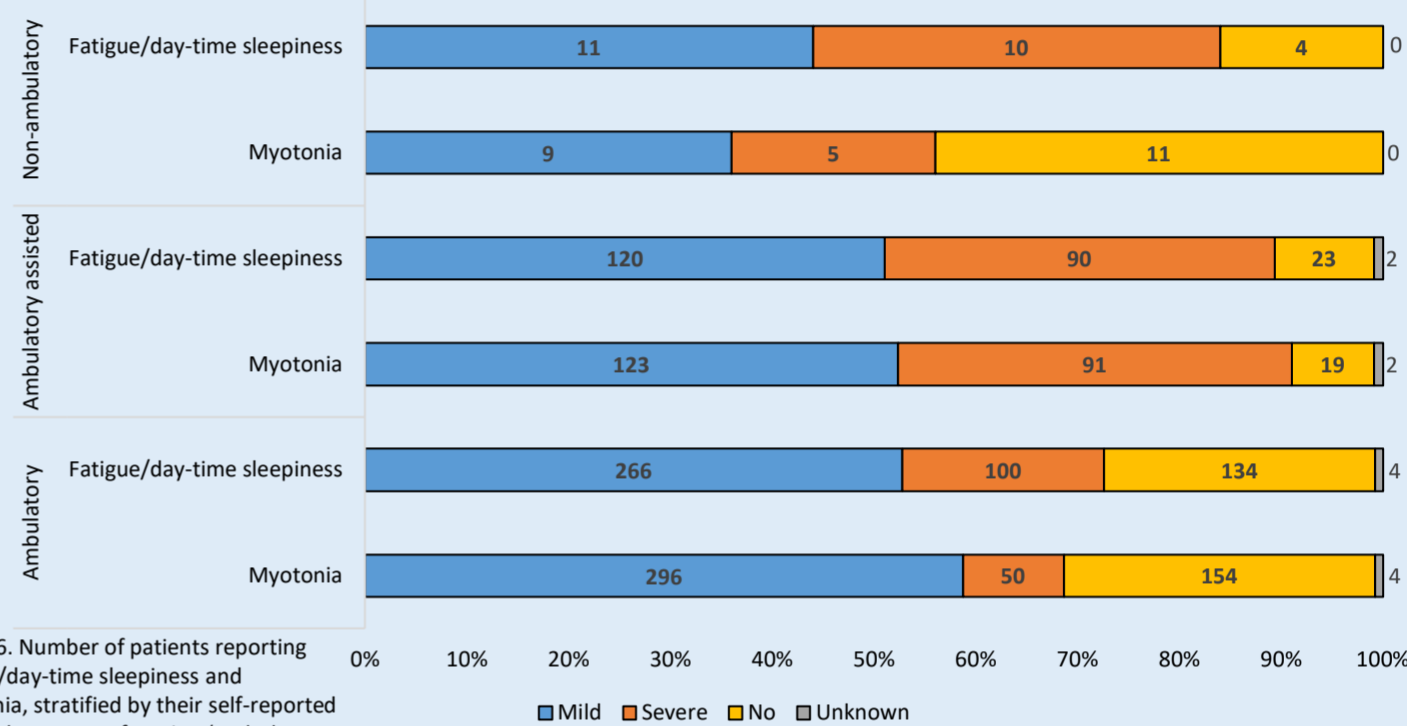


Figure 6. Number of patients reporting fatigue/day-time sleepiness and myotonia, stratified by their self-reported current best motor function (ambulatory, ambulatory-assisted or non-ambulatory)

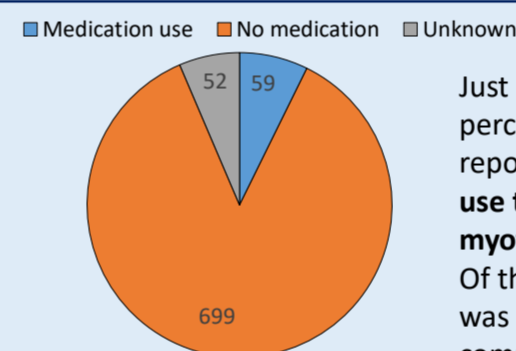


Figure 7. Self-reported medication use for myotonia

Just over seven percent patients report **medication use to treat myotonia (Figure 7)**. Of these, mexiletine was the most commonly used medication (44%).

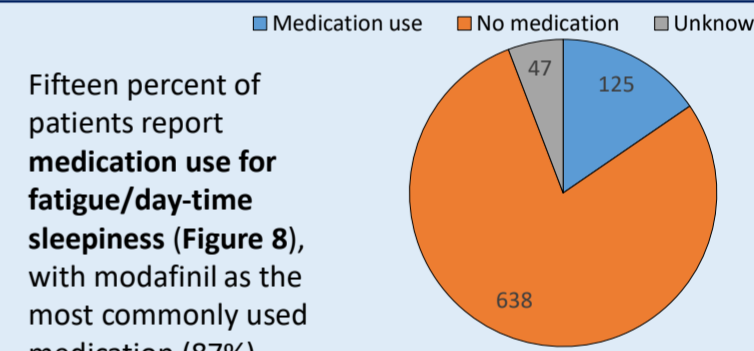


Figure 8. Self-reported medication use for fatigue/day-time sleepiness

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

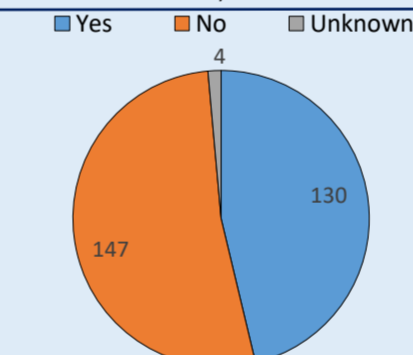


Figure 9. Heart condition as reported by a nominated doctor

Doctors have provided data on the **cardiac section** of the registry's doctors form in **35% of patients**. Almost half (46%) of these patients have a heart condition (Figure 9).

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

- Conduction block in 42% of cases
- Arrhythmia or conduction block in 34% of cases
- Arrhythmia in 16% of cases
- Other in 5% of cases

Medication use for a heart condition was reported in 28% of cases.

An **electrocardiogram** was reported for 171 active patients (21%) on the registry. The mean PR interval was 187.5 ± 38.2 milliseconds (ms), and the mean QRS duration was 106.8 ± 31.6 ms.

An echocardiogram was reported for 76 active patients (9%) and the mean **left ventricular ejection fraction (LVEF)** was 62.3 ± 10.5%. The below LVEF ranges were recorded in 52 patients:

- Hyperdynamic (LVEF >70%) in 6 cases (12%)
- Normal (LVEF 50%-70%) in 42 cases (81%)
- Mild dysfunction (LVEF 40%-49%) in 3 cases (6%)
- Moderate dysfunction (LVEF 30%-39%) in 1 case (2%)

The results of **pulmonary function testing** were reported in 23% of patients, with forced vital capacity (FVC) recorded as (Figure 10):

- Normal in 51% of cases
- Moderate in 13% of cases
- Moderately severe in 13% of cases
- Severe in 14% of cases
- Unknown in 10% of cases

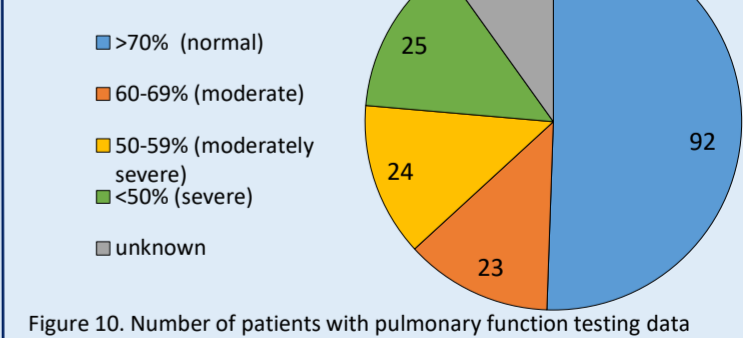
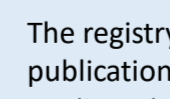


Figure 10. Number of patients with pulmonary function testing data



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 of our valued funders MDUK, MDSG and CureDM, and to all the patients and clinicians who continue to support the UK DM Patient Registry.