The UK Myotonic Dystrophy Patient Registry: An Essential Tool in the Facilitation of Translational and Clinical Research

Ben Porter[1], Phillip Cammish[1], Chris Turner[2], Emma Heslop[1], Darren Monckton[3], David-Hilton Jones[4], Margaret Bowler[5], Margaret Phillips[6], Mark Roberts[7], Mark Rogers[8], Michael Rose[9], Richard Orrell[10], Jacqueline Donachie[11], Chiara Marini-Bettolo[1]

1. The John Walton Muscular Dystrophy Research Centre, Institute of Genetic Medicine, Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
2. University College Hospital, National Hospital for Neurology and Neurosurgery, London, UK
3. Institute of Molecular, Cell and Systems Biology, University of Glasgow, Glasgow, Scotland, UK
4. Department of Clinical Neurology, John Radcliffe Hospital, Oxford, UK
5. Myotonic Dystrophy Support Group, Nottingham, UK
6. Department of Rehabilitation Medicine, Derby Teaching Hospitals NHS Foundation Trust, Derby, UK
7. Department of Neurology, Salford Royal NHS Foundation Trust, Salford, UK
8. Institute of Medical Genetics, University Hospital of Wales, Cardiff, UK
9. Department of Neurology, Kings College Hospital NHS Foundation Trust, London, UK
10. Department of Neurology, Royal Free Hospital, London, UK
11. School of the Arts, English and Drama, Loughborough University, Loughborough, UK

Contact: *Ben.porter@newcastle.ac.uk*

Introduction and aims

- The UK Myotonic Dystrophy Patient Registry (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 act as the most comprehensive distributor of information relating to upcoming academic and non-clinical studies in DM.

Patient population overview

- There are 738 patients registered as of August 2019.
- Sex split: 375 (50.8%) females and 363 (49.2%) males.
- Age range of 1 - 85 years (mean age of 44 years).
- On average 9 new registrations per month.
- There are 49.9% of patients who have entered data at ≥2 time points.

Most patients have a clinical diagnosis of DM1 (89.9%), with approximately half of these also having genetic confirmation of their condition (Table 1).

Table 1. Patient clinical diagnosis and genetic confirmation of their condition.

	Clinical diagnosis	Genetic confirmation
DM1	663 (89.9%)	298 (44.9%)
DM2	23 (3.1%)	5 (21.7%)
Unknown or unspecified	52 (7%)	*335

*The total number of patients without genetic confirmation of their condition

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 online portal that are then combined with clinician verified 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, for example, clinical diagnosis, wheelchair use, myotonia, fatigue/daytime sleepiness, and professional report data items such as heart condition, medication, ventilation, age of onset and genetic confirmation.
- The registry actively encourages researchers to enquire (see Figure 1) as the registry is a flexible tool that can facilitate and accelerate research through:
  - Providing non-identifiable aggregate data (for feasibility work).
  - Facilitating study recruitment through identifying eligible patients directly from the registry.
  - Providing services to conduct research (e.g. disseminating, collecting and analysing research questionnaires).

An enquiry is made into the registry

The registry curator provides the enquirer with a form to complete (includes details such as project summary, eligibility criteria, details related to what approvals are in place and the proposed registry use)

10 working days

The enquiry must be submitted to the Registry Steering Committee, comprised of doctors, scientists and patient organisation representatives

10 working days

Data can only be released once approval from two-thirds of the Registry Steering Committee (SC) is obtained

For industry enquiries, Newcastle University Business Development Team will provide the project costing and contracting prior to the release of any data

The registry charges fees on a cost-recovery basis to industry but operates free of charge to academic research

Figure 1. The registry enquiry process for industry and academics to use the UK DM Patient Registry in research.

Patient reported symptoms

- Fatigue/day-time sleepiness is reported in 74.9% of patients (mild - 64.7%, severe - 35.3%).

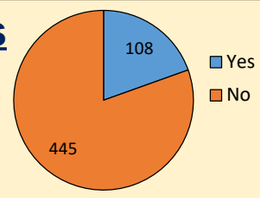

Figure 2. Medication use for fatigue/day-time sleepiness.

- Myotonia is reported in 72.4% of patients (mild - 75.3%, severe - 24.7%).

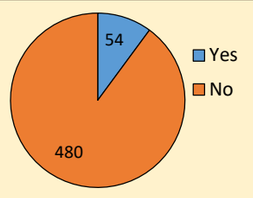

Figure 3. Medication use for myotonia.

Registry use in research

Since 2012, the UK DM Patient Registry has facilitated a number of academic and clinical research enquiries (n = 16) through the use of patient and public involvement, survey distribution, and recruitment to basic scientific studies, observational studies and clinical trials (Figure 4).

Recruitment for "Illuminating Loss", a film study of siblings with DM. Out of 11 participants, **9** were recruited from the registry - artist, Jacqueline Donachie (Loughborough University).

Recruitment for natural history study on the identification of potential biomarkers in DM1, for therapy development. Out of 60 participants, **22** were recruited through the registry – Nottingham University

Recruitment for the international OPTIMISTIC clinical trial where 255 patients were recruited from four European sites. At Newcastle there were 52 participants recruited of which more than **50%** were recruited through the registry.

Recruitment for deep molecular phenotyping of DM1 hiPSC-cardiomyocytes, to facilitate risk stratification and drug evaluation. The registry helped recruit ~**40%** of participants - Nottingham University

Recruitment for PHENO-DM1 where 213 participants were recruited across the London and Newcastle sites, of which ~**40%** were recruited through the registry.

Recruitment for activity monitoring in neuromuscular conditions, where 504 participants expressed interest across all conditions. A total of **21%** came from the registry. Due to study capacity, only **5** patients were included from the registry - PhD study at Kings College London.

Recruitment for DM and autism inheritance film study of parent, with young adults who have DM and comorbid autism spectrum disorder – artist, Jacqueline Donachie (Loughborough University).

2012 2013 2014 2015 2016 2017 2018 2019

Survey distribution capturing tumour history and lifestyle information from **261** participants through the registry – in collaboration with National Institute of Health.

Feasibility enquiry using the registry for AMO Pharma.

Feasibility enquiry to explore pregnancy in DM – Kings College Hospital NHS Foundation Trust.

Recruitment for the phase II clinical trial of tideglusib in DM. The study was set up in Newcastle and 16 participants were recruited, with **~35%** recruited through the registry - AMO Pharma.

Survey distribution to a multi-national cohort about falls and complications. The survey was sent to 510 patients on the registry and **49%** responded.

Feasibility enquiry to explore bradyarrhythmias in childhood-onset DM1 and congenital DM – Newcastle University

Recruitment for the patient preference study, PREFER. There were 67 patients or carers who self-reported interest in this study with **72%** coming from the registry. For the first phase of PREFER, 49 patients took part.

Recruitment for a DM patient/carer advisory group who can provide insight into swallowing disorders to help shape future research. 25 people with DM1 have registered their interest with **84%** coming from the registry - UCL NHS Foundation Trust

Survey distribution to relevant patients or carers about long-term ventilation.

Figure 4. The use of the UK DM Patient Registry in research since it was established in 2012.

Conclusion

The UK DM Patient Registry is an example of a versatile, cost-effective research tool that has helped facilitate a number of studies and advance DM research. Whilst the registry currently has 70 doctors associated with it, a large number of patients remain without genetic confirmation of their condition. This is highlights a potential under reporting especially in DM1 as the true population with genetic confirmation is likely to be even greater. Further work is therefore required to ensure that the registry appropriately captures this information, which in turn will help optimise recruitment to research.

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

[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.