The UK FSHD Patient Registry: An Important Tool in the Facilitation of Translational and Clinical Research

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Introduction

The UK Facioscapulohumeral Muscular Dystrophy (FSHD) Patient Registry (https://www.fshd-registry.org/uk/) is an online patient driven, clinician verified tool designed to support academic and clinical research. The registry was launched in May 2013 and is funded by Muscular Dystrophy UK (MDUK). It is co-ordinated from the John Walton Muscular Dystrophy Research Centre in Newcastle and developed under the global TREAT-NMD neuromuscular network (http://www.treat-nmd.org). The primary aim of the UK FSHD Patient Registry is to facilitate and accelerate academic and clinical research in FSHD. The registry also aims to act as the most comprehensive distributor of information relating to upcoming studies and development in FSHD standards of care.

Method

The registry is used to capture longitudinal, self-reported data through an online portal available to patients and clinicians. The TREAT-NMD dataset comprises all the items identified at the 171st ENMC (European Neuromuscular Centre) workshop on the care and management of FSHD.[1] This represents a minimal dataset which incorporates potential features that may help define the inclusion and exclusion criteria for clinical trials which are shared by many registries globally (Table 1). The registry also captures the following additional questionnaires:

- McGill Pain Questionnaire
- FSHD Pain Questionnaire – **requires further validation**
- Health and Well-being questionnaire (SF-36)
- Quality of Life questionnaire (INQoL)
- Scapular fixation questionnaire – **requires further validation**

Table 1. Data Items captured by the UK FSHD Patient Registry, which contains all of the mandatory and highly encouraged items outlined in the TREAT-NMD internationally agreed dataset

Mandatory items	Highly encouraged items
Personal data (name, date of birth etc.)	Ventilation
Genetic test results (FSHD1, FSHD2)	Age of onset for selected FSHD symptoms
Clinical data (facial, shoulder, foot and hip girdle weakness)	Retinal vascular disease
Onset of muscle weakness	Hearing loss
Best current motor function	Scapular fixation
Wheelchair use	Pregnancy
	Family history
	Ethnic origin
	Other registry involvement

Results

Between May 2013 and May 2020, 991 patients have registered with the UK FSHD Patient Registry. The clinical diagnosis and genetic confirmation of patients with FSHD can be seen in table 2.

Table 2. The clinical diagnosis of patients registered with the UK FSHD Patient Registry, with their corresponding genetic confirmation of diagnosis (n = 991)

*Clinical diagnosis		**Genetic confirmation of diagnosis	
FSHD or FSHD1	n = 892 (90%)	FSHD1	n = 435 (49%)
FSHD2	n = 32 (3%)	FSHD2	n =18 (56%)

*Self-reported by patient
**Provided by nominated specialist via a genetic/molecular report

To note: 67 patients (7%) selected a clinical diagnosis of "unknown" or did not specify.

4qA D4Z4 repeat array size

- Approximately 96% of patients with genetic confirmation of FSHD1 or FSHD2 have a repeat array size of <38 kb, whilst 3% have 38-48 kb, and 1% have >48 kb.

Treatment sought

- There are currently 861 patients (86%) on the registry who report using medication to treat their condition, with 49% using a named medication. Of those, 29% report using two or more medications to treat their condition.
- Collectively patients reported using 37 different pain medications. Excluding over the counter pain medications; ibuprofen (81%), paracetamol (63%) and co-codamol (44%), the most common pain medications used were tramadol (19%), amitriptyline (18%), naproxen (14%) and diclofenac (11%).
- Over half of all patients on the registry (58%) also report using physiotherapy to help with their condition, with 47% seeking a physiotherapist on two or more occasions.

Patient follow up

- Almost half of all patients (46%) have provided at least one follow up response on the registry.
- In the past year (since May 2019), 61% of patients logged into the registry.

Registry enquiries and impact

The UK FSHD Patient Registry has supported **21** different registry enquiries since its establishment in 2013. Registry enquiries can be categorised into three different types; **research studies** (e.g. clinical trials and natural history studies), **research surveys**, and **research data** enquiries (e.g. for data analysis or feasibility purposes).

Research studies

- A multicentre collaborative study on the clinical features, expression profiling, and quality of life of infantile onset facioscapulohumeral muscular dystrophy *(NCT01437345)*.[2] For the sole UK site in Newcastle, the registry contributed to **42%** of patient recruitment.
- An arm cycling study in FSHD *(NCT04267354).*[3] There were **234** interested registry participants and up to **15** were recruited to reach target recruitment.
- Acceptance and Commitment Therapy for Muscle Disease (ACTMuS) *(NCT02810028).*[4] There were **110** interested registry participants with **23** participants being included. The study team recognised the registry as the most successful recruitment source.
- Activity monitoring in progressive muscle diseases. There were **196** interested registry participants but only **4** were recruited due to limited recruitment capacity.

Research surveys

- Upper limb assessment survey which would inform the arm cycling study.
- Genetic alliance survey to understand how FSHD2 impacts the day to day lives of affected individuals. This was to help the Human Fertilisation and Embryology Authority decide on whether preimplantation genetic diagnosis was suitable in FSHD2.
- English validation of newly developed Dutch Rasch-built patient reported outcome measure. The tool was adapted and circulated to **558** adults on the registry and **287 (52%)** completed the questionnaire.
- Child or young person and caregiver online survey about long-term ventilation. This was sent to a small number of patients on the registry.
- A patient focused survey to assess a proposed clinical study design in patients with FSHD. Compared to sites in the USA, Canada and France, the registry was the best recruitment source, helping recruit **41%** of all patients involved.
- A survey to assess the quality of pain registries.
- MDUK clinical trial capacity questionnaire for FSHD. A survey was circulated to over **30** adult neuromuscular specialists in the UK to understand clinical trial capacity for future studies. The registry was used to identify some of these specialists.
- FSHD Society Voice of the Patient Forum survey. The registry circulated five surveys to over **900** patients in the UK, with **50** completing all surveys within two days.
- Share4Rare neuromuscular pilot and education/employment survey. The registry circulated a new neuromuscular platform and survey to over **900** patients.
- Dysphagia in neuromuscular disorders survey. The registry circulated the survey to over **900** patients to help understand how service delivery may be optimised.

Research data

- Pregnancy for FSHD. Data was analysed from **195** females on the registry.
- Respiratory involvement in ambulant and non-ambulant patients with FSHD.[5] Data was analysed from **100** patients on the registry.
- Semantic data integration study.[6] The registry dataset was extracted to support this study.
- Scapular fixation data. Data was analysed from **50** patients on the registry.
- Phenotypic data for FSHD. [7] Clinical and demographic data from **642** patients on the registry was analysed to better understand the phenotypic aspects of the disease.
- Pain and quality of life data.[8] Data from over **350** patients on the registry was analysed to understand associations between pain and quality of life in FSHD.
- Factors affecting rate of onset of major FSHD symptoms.[9] Data from **730** patients on the registry was analysed, detailing 53 variables including age, sex, symptom onset, D4Z4 length etc.

Conclusion

The UK FSHD Patient Registry is one of the largest FSHD patient registries in the world. The registry aims to help in the planning, development and recruitment to new research and by sharing a common dataset with a growing number of FSHD registries, this should facilitate greater collaborations. Ongoing curation of the registry data will ensure that the quality of patient data is high, optimising data analysis and potential recruitment for academic and clinical studies. The registry is still well placed to inform future clinical research and help develop of standards of care.

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