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

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Background

- The UK FSHD Patient Registry (https://www.fshd-registry.org.uk/) is a patient self-enrolling online database, collecting clinical and genetic information about both FSHD type 1 (FSHD1) and FSHD type 2 (FSHD2).
- Established in May 2013.
- Supported by Muscular Dystrophy UK (MDUK), 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 FSHD.
- The registry also aims to better characterise and understand FSHD, share information on standards of care, and disseminate information relating to upcoming academic and non-clinical studies in FSHD.

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 genetic details.
- The dataset collected within the registry includes all mandatory and highly encouraged items agreed at the 171st ENMC International Workshop[1]. This includes **patient reported data items** such as, clinical diagnosis, wheelchair use, weakness, current best motor function, and **doctor reported items** such as genetic confirmation.
- The registry also captures the **McGill Pain Questionnaire**, an **FSHD Pain Questionnaire**, **the Short Form 36 Health Survey Questionnaire (SF-36)**, the **Individualized Neuromuscular Quality of Life Questionnaire**, and a **Scapular Fixation Questionnaire**.
- 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 May 2021, there were 1,042 participants enrolled on the UK FSHD Patient Registry. This includes 536 male and 506 female participants, both with an average age of 49 years old (overall range of 8 – 86 years).

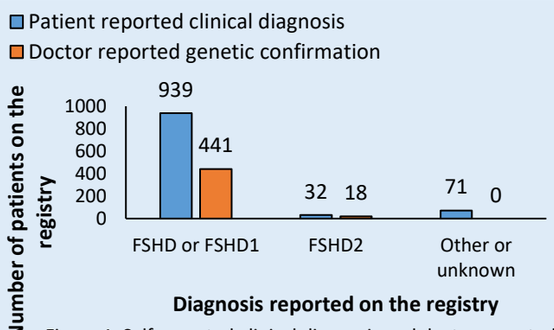

Figure 1. Self-reported clinical diagnosis and doctor reported genetic confirmation of diagnosis

Sixty four percent of patients reported a **positive family history** of FSHD. The most common self-reported **clinical diagnosis** is FSHD/FSHD1 (90%) followed by other/unknown (7%) and FSHD2 (3%). Doctors have provided **genetic confirmation** for 47% of FSHD/FSHD1 patients, and 56% of FSHD2 patients (**Figure 1**).

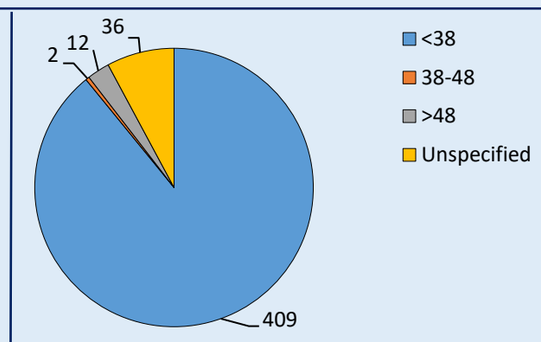

Figure 2. D4Z4 repeat size (kb) as reported by a nominated doctor

The mean (± standard deviation) age of **genetic confirmation** was 38.9 ± 16.3 years. Where doctors on the registry have input genetic data, most patients (89%) on the registry have a **D4Z4 repeat size** less than 38 kilobases (kb), with a small number of doctors (8%) not reporting the D4Z4 repeat size **(Figure 2)**.

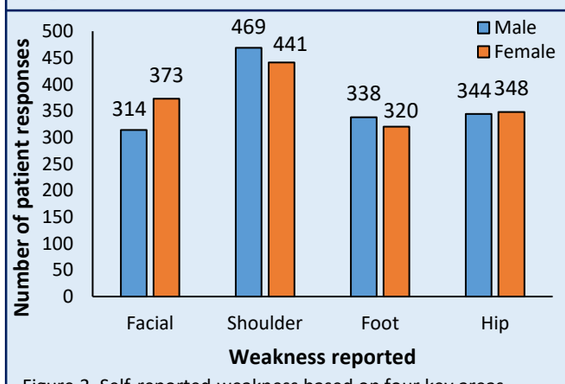

Figure 3. Self-reported weakness based on four key areas

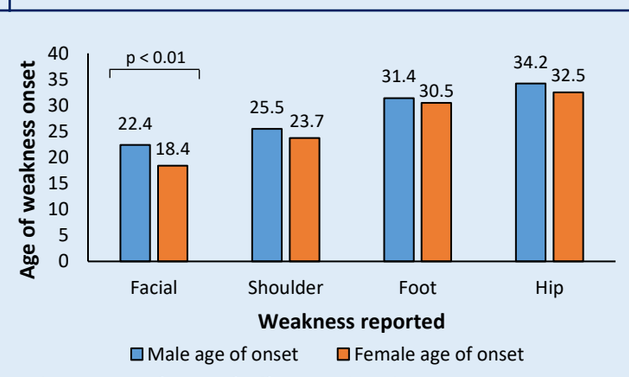

Figure 4. Age of onset of self-reported weakness

The majority of patients reported **weakness** in the shoulder (male – 88%, female – 87%), with considerably more females than males reporting facial weakness too (74% to 59%) (**Figure 3**). A significant difference was observed in the age of onset of facial weakness between males (22.4 ± 17 years) and females (18.4 ± 17.4 years) ($p < 0.01$). There were no significant differences between the age of onset of other areas of weakness, however, the age of onset of hip weakness was the latest, with males reporting 34.2 ± 16.5 years and females reporting 32.5 ± 17.3 years (**Figure 4**).

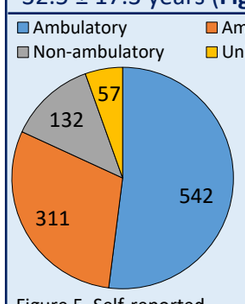

Figure 5. Self-reported current best motor function

Most patients reported their **current best motor function** as either ambulatory (52%) or ambulatory-assisted (30%). A small number of patients reported being non-ambulatory (13%) or did not know (5%) (**Figure 5**).

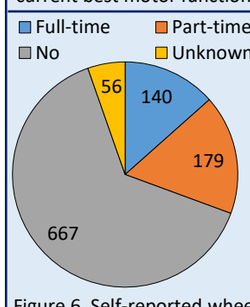

Figure 6. Self-reported wheelchair use

Most patients do not require **wheelchair use**, however 17% report part-time use and 13% report full-time use (**Figure 6**). The average age of wheelchair use was 41.7 ± 17 years.

Non-invasive ventilation was reported by 7% of patients (full time – 9%, part-time - 91%), whilst 1% of patients report using invasive ventilation (full time – 23%, part-time - 73%). The average age of ventilation use was 48.2 ± 14.2 years.

Retinal vascular disease was reported by 2% of patients, with an average age of onset of 37.4 ± 23.8 years.

Hearing loss was reported by 16% of patients with an average age of onset of 40.6 ± 21.6 years.

Scapular fixation surgery was reported by 7% of patients (bilateral – 62%, unilateral – 38%). For those who underwent bilateral surgery, the average age between scapular fixation surgeries was 2.3 years (range of 0-25 years). The average age of either surgery was 27.5 ± 9.5.

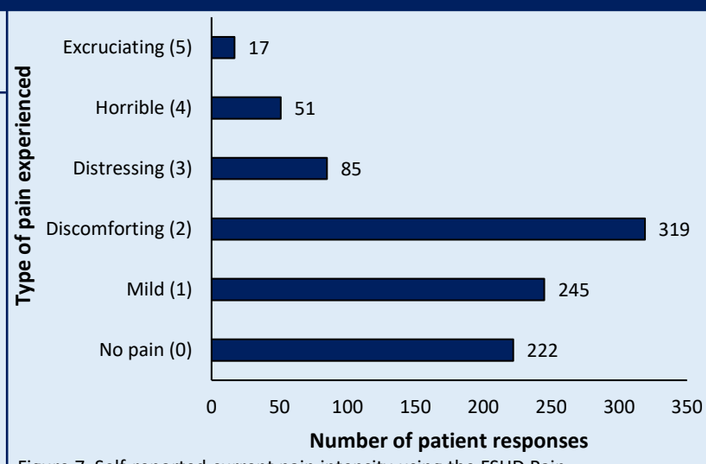

Figure 7. Self-reported current pain intensity using the FSHD Pain Questionnaire captured by the registry

Pain

The FSHD Pain Questionnaire is a universal pain assessment tool developed for the registry which requires further validation.

Thirty four percent of patients who completed this reported their current pain intensity as discomforting, with a further 26% reporting mild pain and 24% reporting no pain. Fewer patients reported their current pain as distressing (9%), horrible (6%) or excruciating (2%) **(Figure 7)**.

Patients who completed the questionnaire reported the least pain in the hands (59%), feet (57%), hips (42%), arms (38%) and legs (34%) in the past 7 days. Pain was reported as discomforting most frequently in the shoulders (29%) and lower back (27%) with similar reporting of mild pain or no pain in these areas too. Distressing pain was most frequently reported in the lower back (12%), shoulders (11%) and legs (11%). The shoulder (9%) and lower back (9%) were the most common locations for pain reported as horrible too **(Figure 8)**.

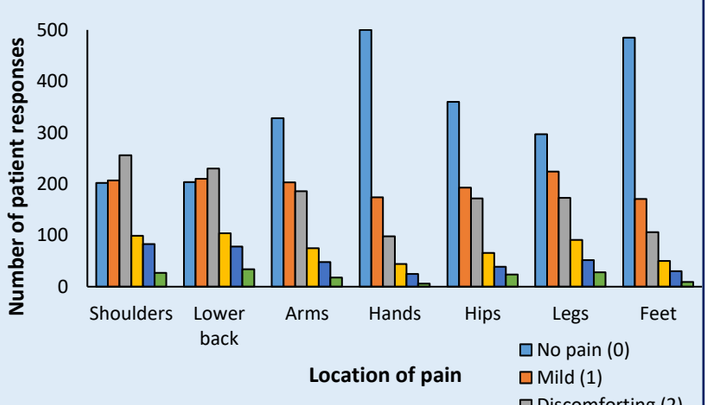

Figure 8. Self-reported level of pain in the past 7 days and its location using FSHD Pain Questionnaire captured by the registry

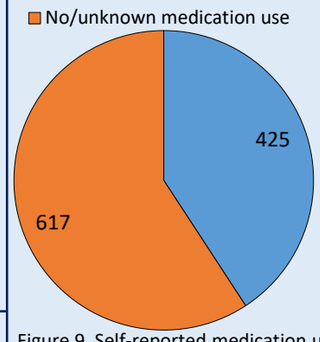

Figure 9. Self-reported medication use for more than one week, to treat pain in the past five years

Medication

Forty one percent of patients reported medication use for longer than one week to treat pain in the past five years (**Figure 9**), and 67% of these are still currently using these medications to treat pain.

The majority of patients use common non-steroidal anti-inflammatory drugs and analgesics to treat their pain. Fewer patients tend to report stronger opioid use such as tramadol (8%) and morphine (3%). Almost 30 different drugs comprise the 18% of patients who reported using **other** less common drugs to treat their pain (**Figure 10**).

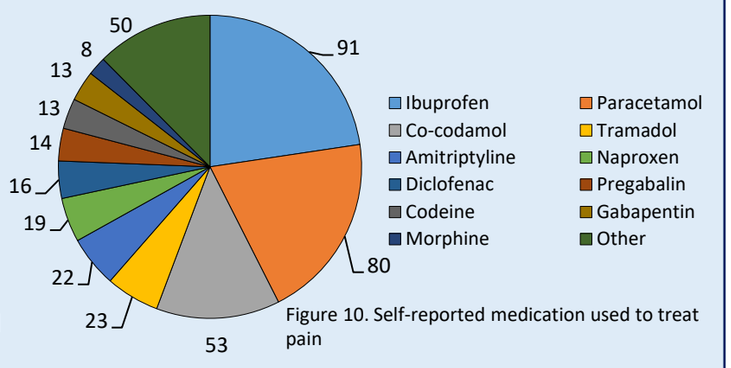

Figure 10. Self-reported medication used to treat pain

Figure 11. Self-reported problems with work or other regular daily activities as a result of current physical health, measured using the SF-36.

Patients most frequently reported their physical health causing them to cut down the amount of time spent on work or other activities, all of the time (28%). Physical health also caused patients to have difficulty with performing work/other activities (25%), limited their work/activities (25%) and accomplishing less than they would like (26%), a little of the time (**Figure 11**).

Figure 12. Self-reported problems with work or other regular daily activities as a result of any emotional problems, measured using the SF-36.

Patients most frequently reported emotional problems (such as anxiety and depression) causing them to cut down the amount of time spent on work or other activities, all of the time (42%). A similar impact was reported on patients accomplishing less than they would like, all of the time (42%) and working or performing other activities less carefully than usual, all of the time (36%) (**Figure 12**).

Registry utilisation in research

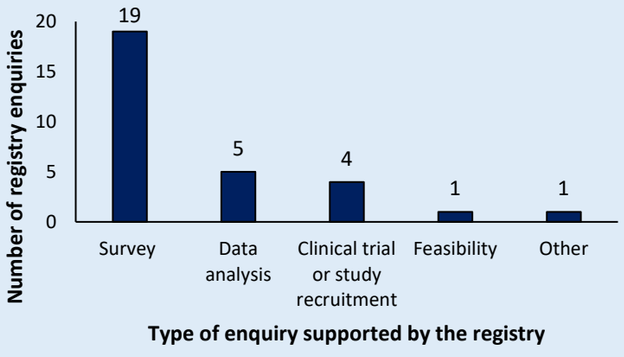

Figure 13. The type and number of registry enquiries supported since 2013

To date the registry has supported **30** enquiries from industry, academics, clinicians and patient organisations. Most registry enquiries have involved online survey distribution (63%) supporting data analysis (17%), or clinical trial and research study recruitment (13%) **(Figure 13).** Since 2020, the registry has supported 13 surveys.

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 10 studies supported by the registry, registry recruitment has ranged from **4%-100%,** with a mean recruitment of **42%.**

The registry has also been involved in **16** 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.

Muscular Dystrophy UK

Acknowledgement to MDUK for their continued support of the registry and to all the patients and clinicians who continue to support the registry.

References

[1] Tawil, R., van der Maarel, S., Padberg, G.W. and van Engelen, B.G. (2010). 171st ENMC international workshop: standards of care and management of facioscapulohumeral muscular dystrophy. Neuromuscular Disorders, 20(7), pp.471-475

Conclusion

The UK FSHD Patient Registry continues to be a versatile, cost-effective research tool that has helped facilitate a range of studies and advance FSHD 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 FSHD community, and plans to further capture the patient voice in the development of new materials.