Facioscapulohumeral Muscular Dystrophy (FSHD) Age-Related Differences in Symptoms Among Patients Over and Under 40 Years

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Objective

- Describe the age-related management of Facioscapulohumeral Muscular Dystrophy (FSHD) patients compared with matched controls (MCs) in the year following diagnosis for those over and under 40 years of age.

Background

- FSHD is a rare, slowly progressive, genetic skeletal muscle disease caused by aberrant expression of DUX4 transcription factor. Muscle weakness usually presents in the face and upper extremities, eventually extending to the trunk and lower body.[1, 2]
- FSHD is one of the most common forms of muscular dystrophy affecting approximately 16,000-38,000 people in the U.S. by 30 years of age.[1-3]
- Patients experience significant physical limitations, pain, fatigue, and an overall negative impact on wellbeing by the age of 50 years.[4-6]
- Real-world data characterizing the FSHD patient journey and impact of age on the burden of illness are limited.
- Currently there are no approved disease modifying therapies for FSHD, and medical treatment is focused on symptom management.[7]

Design / Methods

- We used PharMetrics deidentified U.S. claims from January 2015 through March 2021 to retrospectively evaluate care for:

1 FSHD patient	RATIO	5 non-FSHD MCs
≥2 FSHD claims ≥30 days apart		No FSHD
First diagnosis date	INDEX DATE	Assigned by matching process

- Cohorts were matched on index month, baseline age, region, gender, plan, and payer types.
- All subjects had one year of data following their index date.
- Costs are the total of member paid plus plan paid. All cost data were adjusted to constant 2020 U.S. dollars.
- Comorbid conditions classified by U.S. Agency for Healthcare Research and Quality (AHRQ) specific categories.
- Services represent the chargeable activities per visit.
- Care days represent unique days where the subjects received medical care or prescriptions.
- Within each age group the FSHD cohorts were compared with the MCs.
- All reported findings are highly significant ($P \leq 0.001$), unless noted.

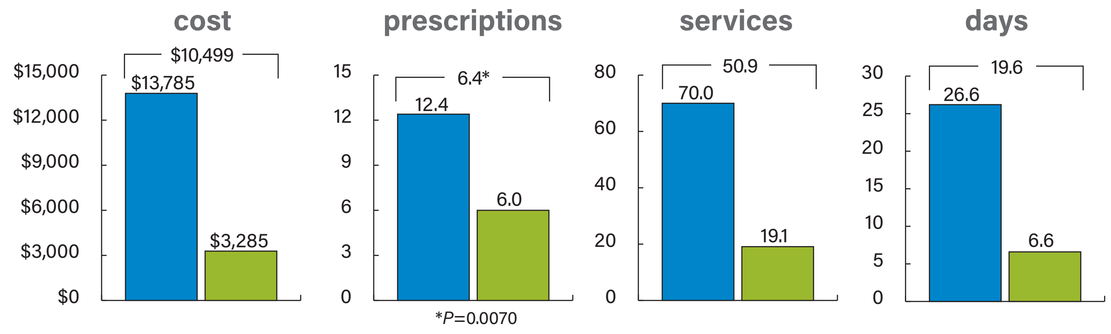
Results

- There were no significant differences between cohorts for age, sex, region of the country, insurance type, or payer type:
  - <40 years, there were 81 FSHD patients (mean 25.7 years, 48.1% female) and 397 MCs (25.8 year, 47.1% female).
  - ≥40 years, there were 199 FSHD patients (56 years, 43.2% female) and 1,003 MCs (56.3 years, 43.8% female).
- Compared with controls in the year following diagnosis, patients with FSHD had higher utilization of healthcare across all locations of care with higher medical costs, more prescriptions, higher use of services, and more days of care in patients under and over 40 years of age.

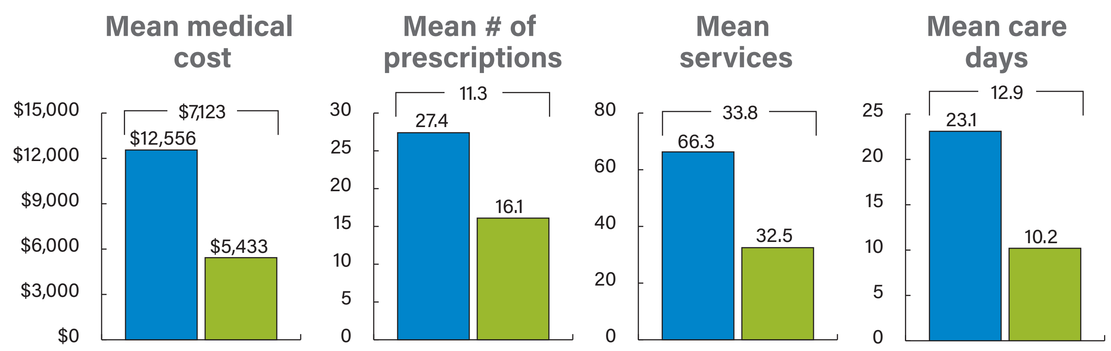
Results (continued)

LEGEND: FSHD patients Non-FSHD MCs

- For those under 40:



- For those 40 and over:



- FSHD patients had a statistically higher prevalence compared to their age group MCs for AHRQ categories in:
  - **Both age groups:** Other nervous system disorders, other connective tissue diseases, other lower respiratory disease, malaise/fatigue, respiratory failure/insufficiency/arrest, administrative/social admission, cardiac dysrhythmias, other acquired deformities, other aftercare, nutritional deficiencies, other ear/sense organ disorders, other GI disorders.
  - **Patients <40 only:** Other non-traumatic joint disorders, paralysis, other hereditary/degenerative nervous system conditions, blindness/vision defects.
  - **Patients ≥40 only:** Systemic lupus erythematosus/connective tissue disorders, immunizations/screening for infectious disease, pleurisy/pneumothorax/pulmonary collapse, other hematologic conditions, acquired foot deformities, multiple sclerosis.

Conclusions

- Patients with FSHD have higher healthcare utilization (medical costs, number of prescriptions, services, and days of care) than MCs in both the under and over 40 cohorts after diagnosis.
- Avidity Biosciences is developing AOC 1020, a first-in-class antibody oligonucleotide conjugate targeting DUX4, the underlying cause of FSHD. Treating the cause of FSHD, should impact the various conditions experienced by patients in both age groups.
  - The U.S. Food and Drug Administration (FDA) has granted orphan drug status and fast track designation to AOC 1020 for the treatment of FSHD.

References

1. Greco A, *et al. Clin Genet.* 2020;97(6):799–814.
2. Statland JM and Tawil R. *Continuum (Minneap Minn).* 2016;22(6):1916–31.
3. Goselink RJM, et al. *Neurology.* 2019;92(4):e378-e85.
4. Hamel J, et al. *Neurology.* 2019;93(12):e1180–e1192.
5. Tawil R and Van Der Maarel SM. *Muscle Nerve.* 2006;34(1):1–15.
6. Statland JM and Tawil R. *Muscle Nerve.* 2014;49:520-527
7. Cohen J, et al. *Trends Mol Med.* 2021;27(2):123-137.

30th Annual FSHD Society International Research Congress • Milan, Italy • June 15 - 16, 2023