The Clinical Burden of Friedreich Ataxia: A Retrospective Claims Analysis in the United States

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1. Background

- Friedreich Ataxia (FA or FDRA) is a progressive and systemic neurologic movement disorder, typically characterized by muscle weakness, worsening ataxia and scoliosis, resulting in loss of ambulation (LOA).[1] Speech is affected, and many patients experience loss of vision and hearing
- Cardiomyopathy and diabetes mellitus are also common and serious manifestations of the disease. In Europe, FA prevalence ranges from ~1:20,000 live births in the south-west to 1 in 250,000 in the north and east.[1]
- **This study aimed to characterize and quantify the clinical burden of FA, compared to a non-FA cohort, using a retrospective United States (US) claims analysis.**

2. Methods

Data source: US Merative MarketScan Commercial database (Aug 2010 to Sept 2020)

Inclusion (Figure 1): Children and adults with ≥12 months of follow-up and ≥1 inpatient, or ≥2 outpatient visits separated by ≥30 days, with primary or secondary diagnosis of FA (ICD-9 334.0) prior to Oct 2015 (334.0 was replaced by a non-specific ICD-10 code in September 2015, Figure 2; index was 1st inpatient or 2nd outpatient visit with diagnosis of FA)

Analysis: Demographics and clinical characteristics were summarized descriptively and statistically compared to a 5:1 age-, sex-, and index-year-matched comparison non-FA cohort. Results were stratified by age at index. The presence of loss of ambulation, diabetes, scoliosis, and cardiomyopathy were used as proxies for disease severity.

Figure 1. Cohort selection: inclusion/ exclusion criteria

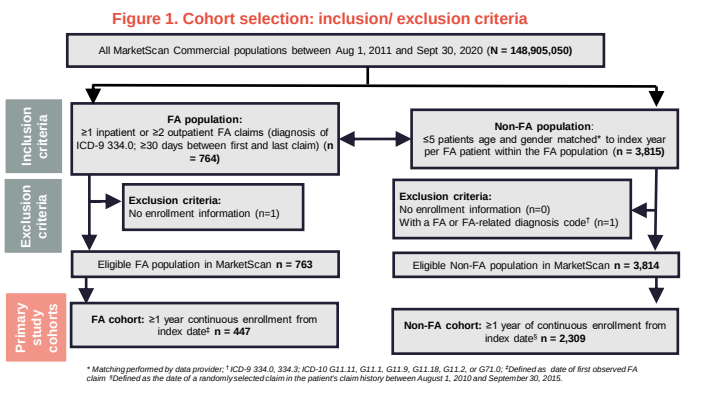
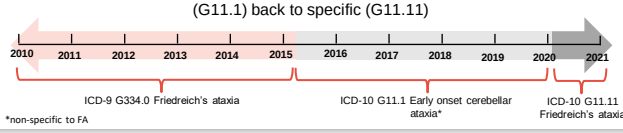


Figure 2. Coding considerations for identifying the study cohort

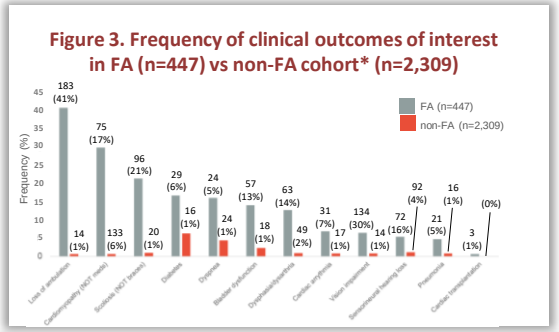
The ICD code has changed over the last 10-years from specific (G334.0) to more general (G11.1) back to specific (G11.11)



3. Results

- 447 patients with FA (mean[SD] age of 34.9[17.5] years at index) and 2,309 non-FA comparison patients (35.8[17.5]) years) met study criteria.
- Over 1-year of follow-up post index date, FA patients had significantly higher comorbidity burden, with a mean(SD) weighted Elixhauser score of 10.4(7.3) compared to 0.3(2.7) among the non-FA patients (p<0.001).
  - 41% of the FA cohort experienced LOA; 30%, cardiomyopathy; 21%, scoliosis; 17% diabetes **(Figure 3)**
- When adjusting for effects of age, sex, index year, and region, the odds of experiencing clinical manifestations were significantly higher among the FA patients (3.8 times higher for diabetes [OR=3.8; 95%CI 2.8-5.3], p<0.001; 113 times [OR=112.6; 95%CI 67-206], p<0.001 for LOA, 75 times higher (95% CI 44 to 139; p<0.001) for cardiomyopathy, 34 times higher (95% CI 21 to 59; p<0.001) for scoliosis).

Figure 3. Frequency of clinical outcomes of interest in FA (n=447) vs non-FA cohort* (n=2,309)



- When stratified by age at index (**Figure 4**):
  - LOA, cardiomyopathy, scoliosis were the most frequently observed clinical manifestations over the follow-up period
  - Scoliosis was highest among those aged 7-14 and decreased with age
  - Cardiac transplantation, pneumonia, vision impairment were generally rare
  - Patients with FA consistently had significantly higher observed frequencies of these outcomes compared to the age-, sex- matched non-FA cohort (p<0.001)
- Among those with more disease indicators, the median age at index was younger, while those with fewer disease indicators had an older median age at index
- Of note, 2.4% of FA patients had an ICD code for attempted suicide compared to 0.2% among the non-FA cohort (p<0.0001)

Figure 4. Clinical outcomes of interest, by age at index among patients with FA

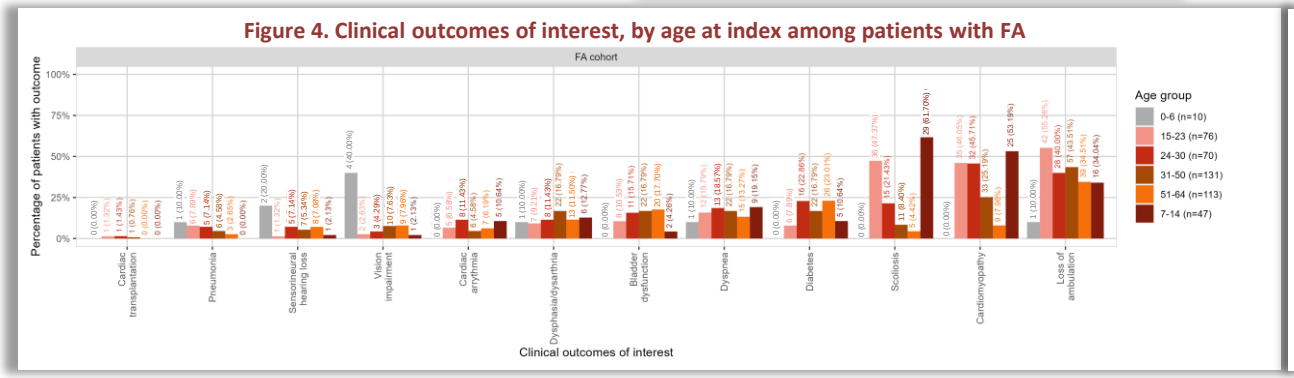
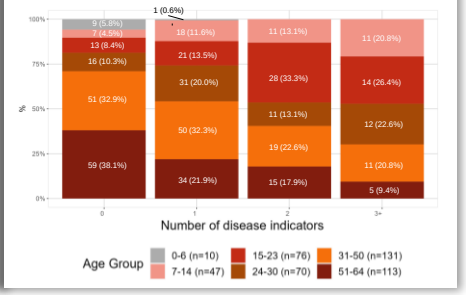


Figure 5. Number of disease severity indicators within the first year, by age at index



5. DISCUSSION

- This study found that:
  - FA patients had significantly higher comorbidity burden compared with the non-FA cohort. (p<0.001).
  - The adjusted odds of experiencing clinical manifestations were significantly higher across all 4 disease indicators (diabetes, LOA, cardiomyopathy, scoliosis) among the FA patients (p<0.001)
- Patients with FA in comparison to age- and sex- matched individuals without -FA experience significant clinical manifestations (both primary and secondary complications due to FA), in particular loss of ambulation, cardiomyopathy, and scoliosis (p-value <0.001).

6. CONCLUSIONS

This study provides real-world estimates of this disease burden, for commercially insured patients with FA in the US, underlying the unmet medical need in this population.

7. LIMITATIONS

- This study using a large, real-world, U.S. dataset allowed identification of a substantial number of FA patients for robust analyses.
- Some limitations of this study included:
  - Given that the data source consists of patients on commercial insurance, patients with FA with later-onset disease (and who are able to maintain employment into adulthood) are potentially over-represented in the cohort.
- Due to the small sample sizes in those aged 0 to 6, outcomes may not be representative of the overall FA population of that age
- Due to the limited amount of follow-up available, it is not possible to ascertain the onset of clinical outcomes.
- Due to the lack of a specific ICD-10 code for FA between September 2015 and September 2020, the results from this study are limited to a cohort of patients identified in or before 2015 and generalizability to cohorts diagnosed since then is uncertain.

Disclosures
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References
1. Cook A & Giunti. British medical bulletin. 2017:1-12