Assessing the Comorbidity Burden of Ehlers-Danlos Syndromes (EDS): An Analysis Using US Real-world Data

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Introduction

- The Ehlers-Danlos syndromes (EDS) are a rare/ultra-rare group of 13 conditions that affect the body's connective tissue and collagen function.[1,2]
- Often misunderstood and misdiagnosed, currently, there are no disease-specific treatments available though patients with EDS experience a high comorbidity burden across multiple organ systems.
- Real-world data quantifying the disease burden among EDS patients compared to the general population are lacking.

Objective

- To characterize the EDS population by comparing the comorbidity burden against a non-EDS control cohort using US real-world data.

Methods

- Data from the Veradigm Network EHR linked to Komodo Health claims were used to identify patients with an EDS diagnosis between 01/01/2010-12/31/2023. Patients were required to have ≥12 months of EHR/claims activity prior to (baseline) and following (follow-up) the index date.
- Patients with EDS were directly matched (1:3) to non-EDS patient by age, sex, index year, and continuous claims enrollment.
- Demographic characteristics were captured at baseline while clinical characteristics were evaluated in both the baseline and follow-up periods.
- To test for differences between the EDS and non-EDS cohorts, t-tests were used for continuous values while chi-square tests for categorical values.

Figure 1: Patient Selection

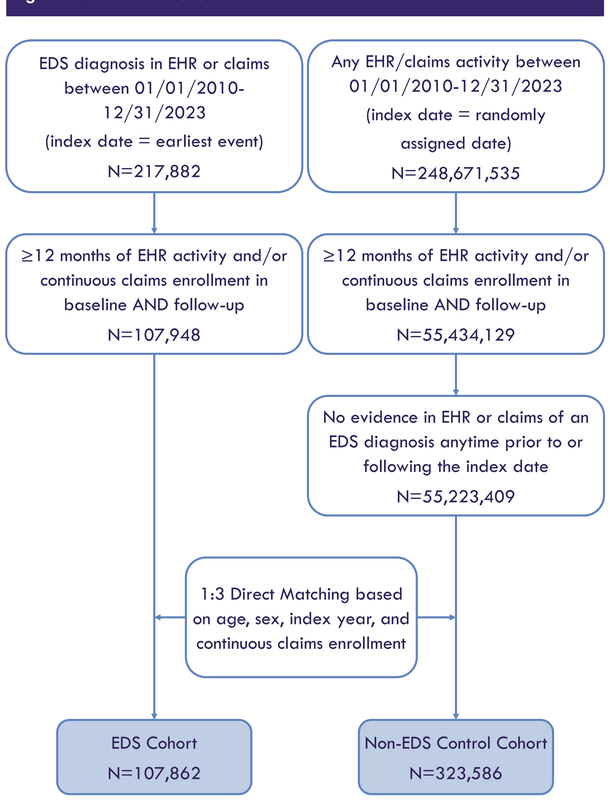


Table 1: Baseline Patient Characteristics

	EDS Cohort	Non-EDS Controls	P[1]
	N=107,862	N=323,586	
Age, Mean (SD)	35.0 (17.3)	35.0 (17.3)	
Sex, Female, N (%)	89,749 (83.2%)	269,247 (83.2%)	
Race, N (%)			**<0.0001**
White	77,780 (72.1%)	177,062 (54.7%)	
Black	2,799 (2.6%)	33,123 (10.2%)	
Asian	2,679 (2.5%)	14,094 (4.4%)	
Other	11,678 (10.8%)	45,699 (14.1%)	
Unknown/Not Reported	12,926 (12.0%)	53,608 (16.6%)	
Ethnicity, N (%)			**<0.0001**
Hispanic	2,617 (2.4%)	17,434 (5.4%)	
Non-Hispanic	75,950 (70.4%)	176,461 (54.5%)	
Unknown/Not Reported	29,295 (27.2%)	129,691 (40.1%)	
Geographic Region, N (%)			**<0.0001**
Northeast	16,746 (15.5%)	53,054 (16.4%)	
Midwest	26,917 (25.0%)	66,279 (20.5%)	
South	37,366 (34.6%)	116,700 (36.1%)	
West	25,307 (23.5%)	78,938 (24.4%)	
Other/Unknown	1,526 (1.4%)	8,615 (2.7%)	
BMI, Mean (SD)	26.7 (7.1)	28.0 (7.0)	**<0.0001**
Physical Characteristics, N (%)			
Chiari Malformation	3,569 (3.3%)	573 (0.2%)	**<0.0001**
Flat Foot/Pes Planus	9,733 (9.0%)	7,876 (2.4%)	**<0.0001**
Abnormal Eyelids	4,832 (4.5%)	5,900 (1.8%)	**<0.0001**
Number of Different Providers Seen PPPY, Mean (SD)	2.4 (4.1)	1.7 (3.0)	**<0.0001**

[1]P-values were not computed for matching variables (patient age and gender). PPPY, per patient per year; SD, standard deviation.

Table 2: Estimated Prevalence of EDS in the US, by Sex

	All EDS Patients	
	Proportion	Prevalence
Total Population	0.04%	1 in 2,337
Male	0.02%	1 in 5,818
Female	0.07%	1 in 1,473

Results

- At baseline, mean (SD) age for patients was 35 (17.3) years and majority were female (83.2%), White (EDS: 72.1% vs non-EDS: 54.7%, $p<0.0001$), and resided in the South geographic region (EDS: 34.6% vs non-EDS: 36.1%, $p<0.0001$) **(Table 1)**.
- Patients with EDS had an increased significant proportion of Chiari malformation (3.3% vs non-EDS: 0.2%), flat foot/pes planus (9.0% vs non-EDS: 2.4%), and abnormal eyelids (4.5% vs non-EDS: 1.8%), compared to non-EDS patients (all $p<0.0001$).

Figure 2: Proportion of Comorbidities by EDS Diagnosis, Baseline Period, all $p<0.0001$

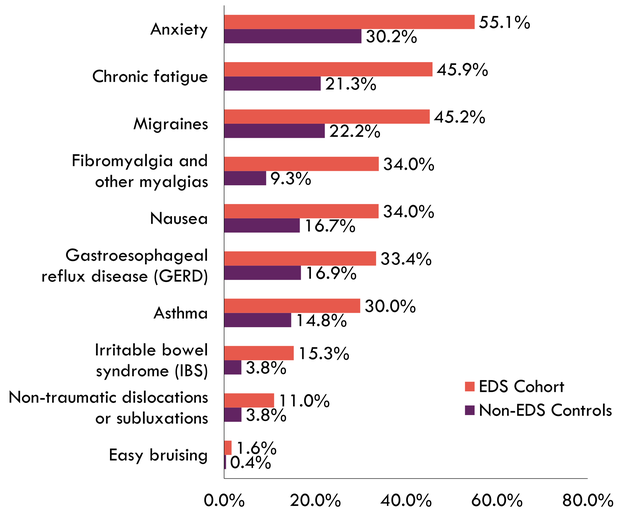


Figure 3: Proportion of Comorbidities by EDS Diagnosis, Follow-up Period, all $p<0.0001$

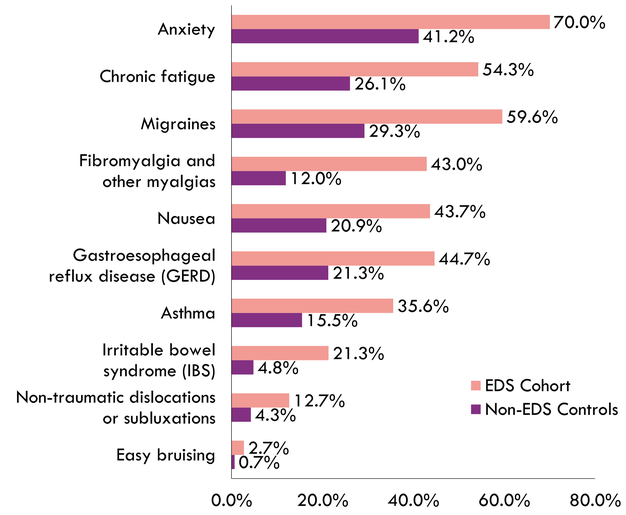
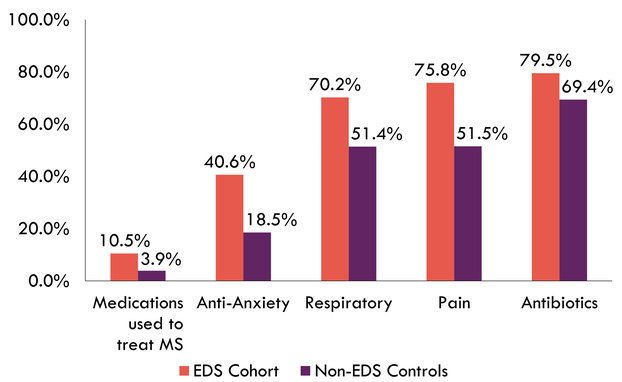
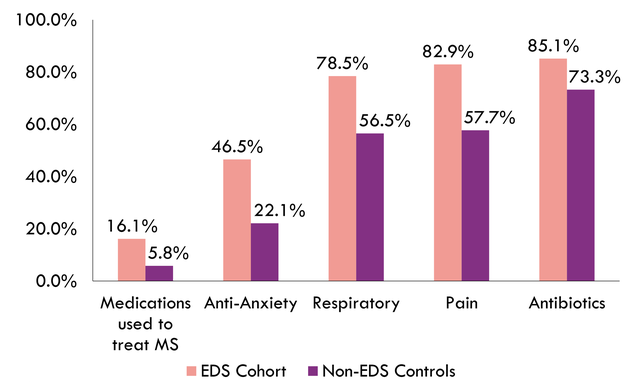


Figure 4: Prevalence of Selected Top Medication Use by EDS Diagnosis, Baseline Period, all $p<0.0001$



MS, multiple sclerosis.

Figure 5: Prevalence of Selected Top Medication Use by EDS Diagnosis, Follow-up Period, all $p<0.0001$



MS, multiple sclerosis.

Results (cont'd)

- During the baseline period, the mean (SD) number of different individual providers seen per patient per year was 1.4x significantly higher for patients with EDS (2.4 [4.1]) as compared to those in the non-EDS control cohort (1.7 (3.0), $p<0.0001$).
- Prevalence estimates of EDS were 0.07% for females and 0.02% for males, representing an overall prevalence of 0.04% in the study database **(Table 2)**.
- Compared to the non-EDS cohort, EDS patients had significantly higher proportions of all measured comorbidities during the baseline and follow-up periods with anxiety, chronic fatigue, and migraines most commonly seen in both cohorts (all $p<0.0001$) **(Figures 2 and 3)**.
- Similarly, EDS patients had significantly higher baseline medication use across antibiotics, pain, respiratory, anti-anxiety, and medications used to treat multiple sclerosis **(Figure 4)**; this was also seen through follow-up (all $p<0.0001$) **(Figure 5)**.

Conclusions

- Our study highlights the increased comorbidity burden among patients with EDS compared to non-EDS controls.
- Moreover, our study demonstrates the increased challenge in the journey to an EDS diagnosis as shown by the number of different providers seen per patient per year.
- With no disease-specific treatment options, this puts into perspective the continued need for personalized management of patient conditions and symptoms.

References

1. Malfait F, et al. *Am J Med Genet C Semin Med Genet*. 2017; 175(1):8-26.
2. The Ehlers-Danlos Society. What is EDS? https://www.ehlers-danlos.com/what-is-eds/
3. Demmler JC, et al. *BMJ Open*. 2019; 9(11):e031365.

Disclosures

C Basch is a student at Wesleyan University. M Allen is an employee at Damon Runyon Cancer Research Foundation. J Cheng, N Coenen, M Ajose, and J Manjelievskaia are employees of Veradigm which funded and provided the data used in the execution of this study.