Healthcare Resource Utilization Among Fabry Disease Patients in the US: Insights from a Real-world Retrospective Study

Khashayar Azimpour[1], Lucas Olivera[2], Brooklyn Stanley[2], Irene Koulinska[2]
[1]Chiesi Canada Corp Canada, [2]Chiesi USA Inc.

Background

- Fabry disease (FD) is a rare, progressive X-linked lysosomal storage disorder caused by mutations in the galactosidase alpha gene, resulting in a deficiency of the enzyme alpha-galactosidase A.[1,2]

- Current treatments for Fabry disease include enzyme replacement therapy (ERT) with agalsidase-α or agalsidase-β, or chaperone therapy with migalastat to boost enzyme activity. Plant-derived pegylated ERT, like pegunigalsidase-α with longer plasma half-life are also available.

- Other emerging options include substrate reduction therapies (Lucerastat, venglustat), moss α-GAL and gene therapy.[3]

- Despite this advancement, large-scale, real-world studies examining the economic burden and healthcare resource utilization (HCRU) associated with FD in the US remain limited.

Objective

- The objective of this claims-based study was to evaluate the HCRU and costs among patients in the US who were treated for FD versus those who were untreated to better understand the impact of current treatments.

Methods

- Data were obtained from the Komodo Commercial Claims and Encounters (CCAE) database for claims from January 1, 2022, to May 24, 2024.

- The CCAE database includes de-identified healthcare data for more than 300 million commercially insured patients in the US, covering demographics, insurance, diagnoses, procedures, prescriptions, and costs.

- **Inclusion criteria:** Patients with FD were identified using International Classification of Diseases, 10th Revision code E75.21- Fabry (-Anderson) disease. Eligible patients must have had at least two claims with this code, longer than 30 days apart, between January 1, 2022, and December 1, 2023, along with more than six months of continuous enrollment from the index diagnosis date.

- This enrollment requirement was waived for patients with a death event during the study period.

- Patients with missing data on age or sex or those who did not meet inclusion criteria were excluded.

- The number of patients with closed data was 2,029 in 2022 and 1,283 in 2023. Given the larger sample size in 2022 and to avoid potential duplication bias from pooling, we report the 2022 results, which are generally consistent with those from 2023 **(Figure 1).**

- Five distinct treatment groups were defined based on treatment duration and adherence over a two-year period. Categorization was based on treatment status in the target year and the preceding year (lookback year). The lookback year for 2022 was 2021; 2022 served as the lookback year for 2023.

   o Never treated: No treatment recorded at any time

   o Untreated: Less than six months of treatment within the two-year window (<25% treatment)

   o Sparsely treated: 6 to 18 months of treatment total, but <6 months during the target year (25% to 75% of treatment overall with <50% in target year)

   o Newly treated:<6 months of treatment in the lookback year and >6 months in the target year (50% to 75% of treatment overall; >50% in target year)

   o Treated: more than six months of treatment in two years (50% to 100% of treatment overall; >50% in target year)

- The untreated group was selected as a comparator for patients with treatment exposure, as it represents the lowest level of therapy exposure. Using the never-treated group as a comparator may introduce bias due to potential differences in disease severity, age, and comorbidities compared to treated groups.

- The study outcomes included overall visits, inpatient stays, emergency room (ER) visits, physician consultations, procedures, and diagnostic assessments across the treatment groups, as well as the associated costs.

- Demographic information such as gender, age group, geography, and comorbidities was also recorded.
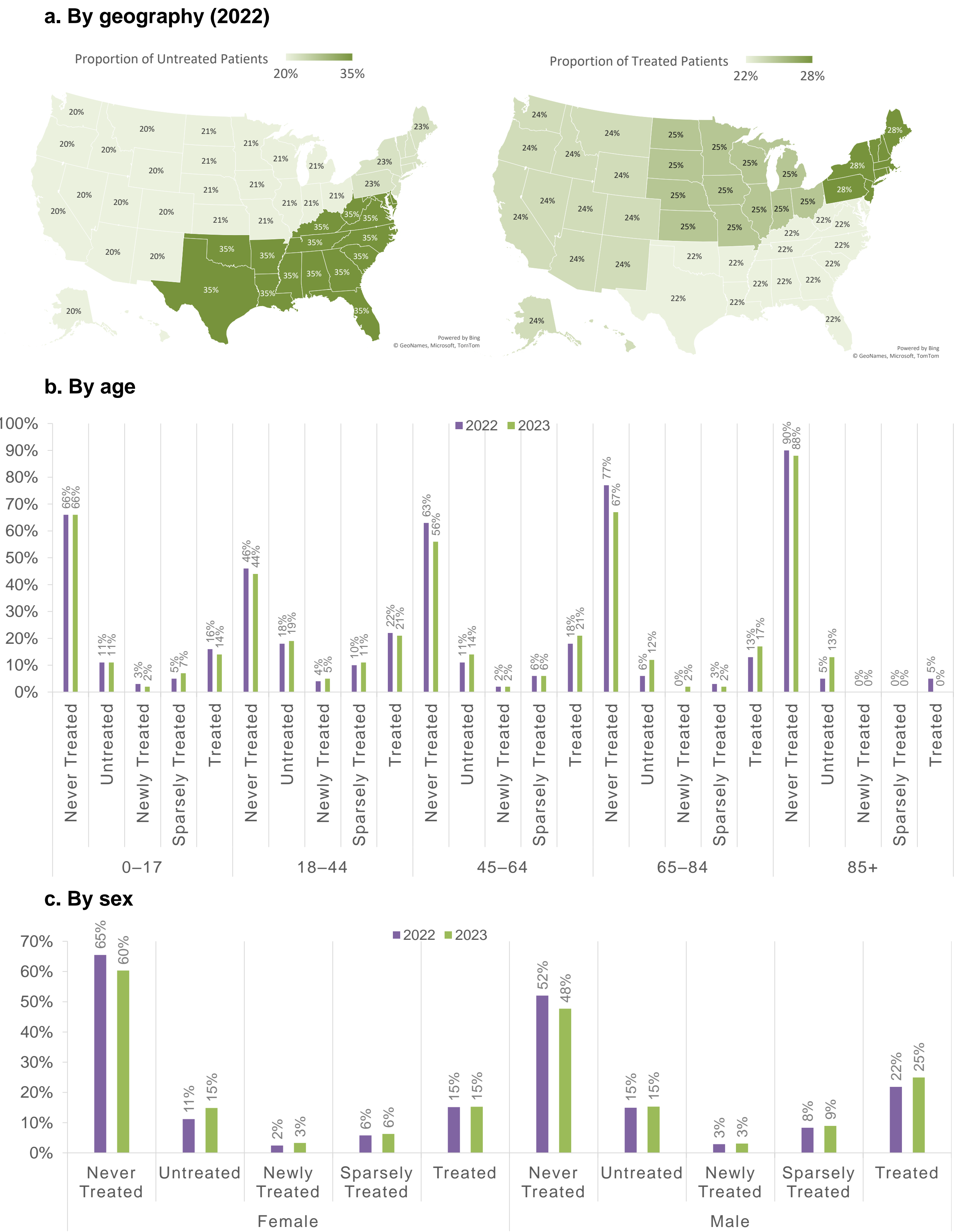
Figure 1: Patient distribution by treatment category
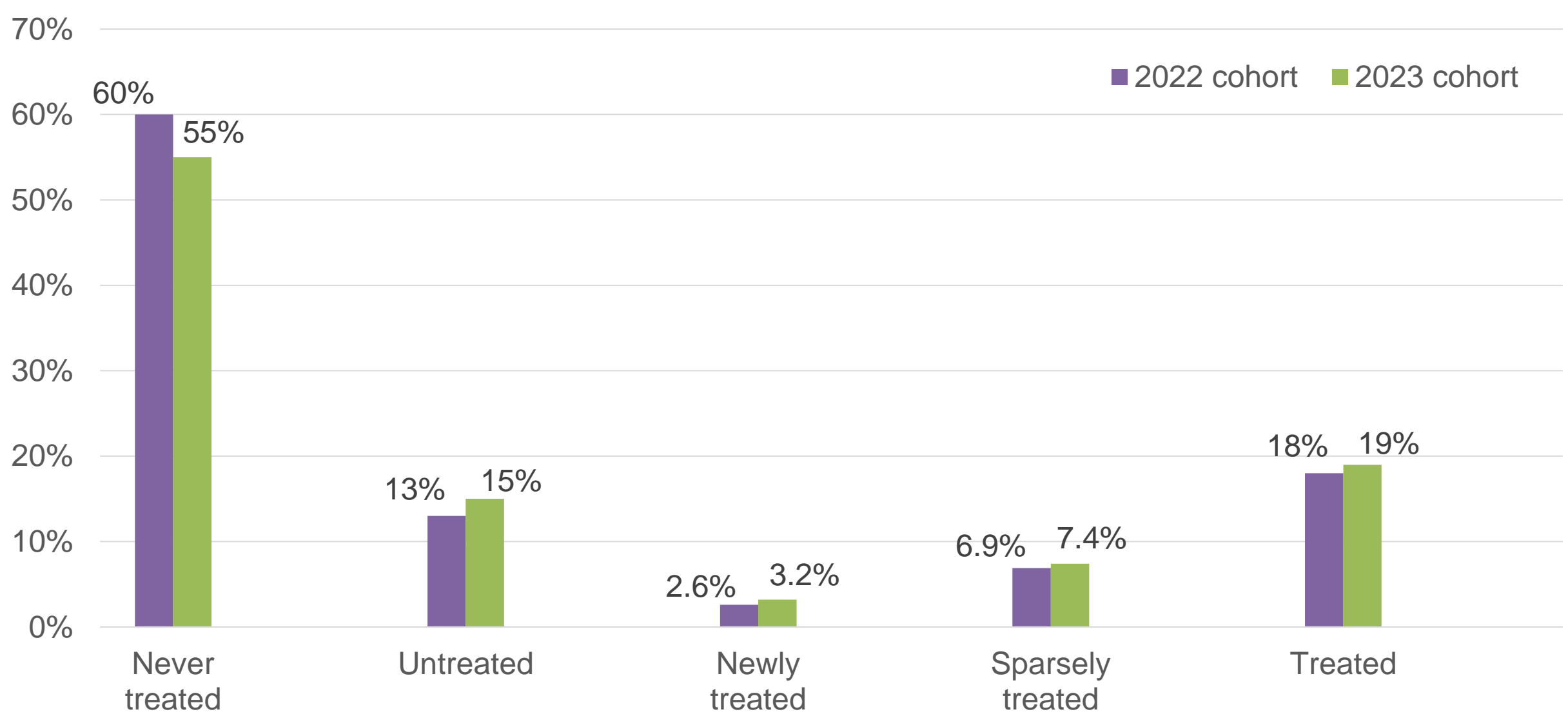
Results

- In overall patient population, never treated patients were 60% and 55% in 2022 and 2023 (**Figure 1**). Never treated adult patients accounted for 50% of the total patients in 2022 and 45% in 2023.

- In 2022, among untreated patients in the US, the highest proportion were from the South; among treated patients, the highest proportion were from the Northeast. The same pattern was observed in 2023 (**Figure 2a**). Among never treated patients the highest proportion was observed in the West, in 2022 and in the Midwest in 2023.

- The largest age group across all treatment groups in both years was 45 to 64-year-olds (2022: 38%; 2023: 36%). Older adults (≥65) comprised 14% of the overall patient population annually.

- The percentage of pediatric patients (ages 0 to 17) was consistent across treatment groups, accounting for 14% to 15%.

- A high percentage of older adults remained never treated, (2022: 77% [65 to 84], 90% [≥85]; 2023: 67% and 88%, respectively (**Figure 2b**).

- Although females accounted for most patients across both years (57% vs. 43% for males), they were more likely to be in the never-treated group (63%), whereas the treated groups were predominantly male (52% in 2022 and 55% in 2023) (**Figure 2c**).

Figure 2: Distribution of patient characteristics

a. By geography (2022)

Proportion of Untreated Patients   Proportion of Treated Patients

b. By age

c. By sex

- Across both 2022 and 2023, the most common comorbidities among all patients—regardless of treatment status—included abdominal pain, acid reflux, chronic kidney disease, nausea, renal disease, and chronic pulmonary disease.

- In 2022, the untreated group primarily experienced abdominal pain (59.2%), renal disease (43.5%), and chronic kidney disease (42.7%).

- The treated group in 2022 exhibited a slightly different comorbidity profile, with abdominal pain (55.6%), proteinuria (44.9%), and arrhythmia (42.2%) being the most prevalent conditions.

- Similarly, in 2023, abdominal pain remained the most prominent comorbidity among untreated patients (57%), followed by proteinuria (42.5%) and chronic kidney disease (42.0%).

- For treated patients in 2023, abdominal pain persisted as the most common condition (51.8%), with proteinuria (43.0%) and arrhythmia (43.0%) also being highly prevalent.

- Within the never treated group, abdominal pain (60.1%), acid reflux (44.6%), and chronic pulmonary disease (38.8%) are the most prevalent conditions in 2022. A similar pattern was observed in 2023.

HCRU

- In 2022 and 2023 treated patients were associated with fewer inpatient stays and ER visits compared to untreated patients (neither were statistically significant) (Figure 3).

Figure 3. Overall HCRU (2022)
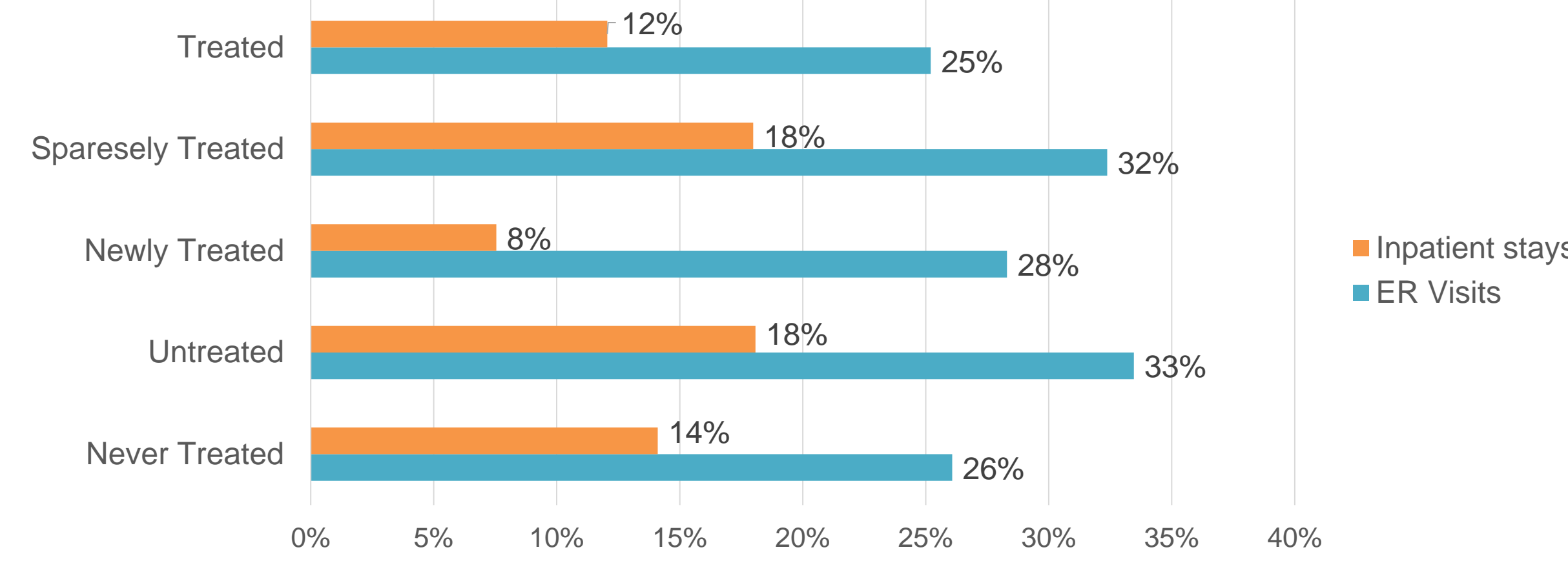
Abbreviation: ER, emergency room

- Across all treatment groups except for the never treated, the highest number of visits were to: 1) General Practitioners, 2) Cardiologists, 3) Nephrologists, and 4) Geneticists (**Table 1**).

- The treated group, who had the highest percentage of physician visits, mostly had visits to specialists such as cardiologists, nephrologists, and geneticists, but were less likely to see gastroenterologists, metabolic specialists, and pain specialists (**Table 1**).

- Treated patients also had the highest rates of procedures and diagnostics in the 2022 analysis likely due to routine outpatient-based care

- Electrocardiogram (ECG), echocardiography, and brain imaging (magnetic resonance imaging, computed tomography) were the top 3 procedures among all the groups.

Table 1. 2022 HCRU (physician visits and all-cause procedures and diagnostic assessments)

	Never treated (N=1212)	Untreated (N=260)	Newly treated (N=53)	Sparsely treated (N=139)	Treated (N=365)
Physician visits					
Overall Visits	81.85%	80.77%	88.68%	89.93%	89.04%
Cardiologist	26.65%*	35.77%	28.30%	41.01%	45.48%
Dermatologist	7.92%	8.08%	11.32%	10.07%	11.23%
GP/PCP	68.65%	63.46%	60.38%	68.35%	67.95%
Gastroenterologist	12.13%	8.46%	13.21%	12.95%	9.32%
Geneticist	8.50%*	21.54%	35.85%	25.90%	32.33%
Metabolic specialist	4.79%	3.08%	9.43%	3.60%	4.66%
Nephrologist	9.65%*	30.77%	32.08%	31.65%	34.79%
Neurologist	13.04%	14.23%	18.87%	15.11%	21.10%
Ophthalmologist	15.18%	5.38%	7.55%	9.35%	9.04%
Pain specialist	3.47%	4.23%	1.89%	3.60%	3.84%
All-cause procedures and diagnostic assessments					
Overall Patient per Procedures	43.4%	52.7%	52.8%	59.7%	58.9%
Brain/cerebral imaging (MRI, CT)	12.21%	13.85%	18.87%	14.39%	14.52%
Cardiac biopsy	0.08%	0.77%	0.00%	0.00%	0.55%
Cardiac ECG	30.36%*	40.77%	35.85%	40.29%	43.84%
Cardiac MRI	1.24%	3.46%	11.32%	5.04%	8.77%
Coronary bypass	0.25%	0.00%	0.00%	0.72%	0.00%
Device implant	0.08%	0.77%	0.00%	0.00%	0.82%
Dialysis	1.90%	3.85%	3.77%	2.88%	1.92%
Echocardiography	19.55%	26.15%	28.30%	30.94%	31.23%
Exercise test	3.96%	5.00%	5.66%	5.76%	6.58%
Hearing test	3.30%	3.08%	1.89%	2.88%	2.74%
Holter monitor	2.89%	3.46%	1.89%	2.16%	4.93%
Kidney biopsy	0.25%	1.54%	1.89%	0.00%	0.82%
Renal transplantation	0.08%	1.15%	1.89%	0.72%	0.27%
Renal ultrasound	5.28%	6.54%	0.00%	5.04%	5.21%
Spirometry test	2.97%	6.15%	3.77%	3.60%	4.38%
Stent placement	0.33%	1.15%	0.00%	0.00%	0.00%
Valve replacement	0.08%	0.00%	0.00%	0.72%	0.00%

* rates with significant p-value in comparison with the untreated group;
Greener shades indicate lower rates, while redder shades represent higher rates.

lower rate | higher rate

Note: Some patients included in the 2022 dataset may also be included in the 2023 dataset
Abbreviations: CT, computed tomography, ECG, echocardiogram; GP, general practitioner; MRI, magnetic resonance imaging; PCP, primary care physician

Costs

- In 2022, treated patients incurred lower mean costs for inpatient stays compared to untreated patients

- Treated patients incurred higher mean costs for ER visits compared to untreated patients. However, the cost difference remains modest, suggesting that treatment may not substantially increase short-term acute care expenditures.(**Table 2**)

- For inpatient stays, treated patients had a low mean cost; newly treated patients had a higher mean inpatient cost, suggesting more complex or intensive initial care needs.

Table 2. Mean costs for inpatient, and ER visits (2022)

	Mean Costs				
	Never treated	Untreated	Newly treated	Sparsely treated	Treated
Inpatient stays	$22,646	$20,938	$30,101	$19,600	$17,375
ER visits	$513	$459	$355	$422	$484

Abbreviation: ER, emergency room

- Physician office costs were highest per patient for treated individuals at $1,383, second were untreated patients, with mean of $979 (P-value = 0.007).

- Treated patients had a mean cost for overall procedures at $714 compared to the untreated group. In contrast, untreated patients incurred the highest mean of $1,623, indicating a patient group with high individual spending (P-value=0.001).

> **Treated patients had a lower mean cost for overall procedures compared to untreated patients**

- These patterns suggest that while treated patients incur significant individual costs, their overall HCRU reflects more consistent and preventative care compared with other groups due to more routine outpatient-based care and efficient care pathways that reduce reliance on high-cost acute services.

- The treated group also had the highest rate of procedures and diagnostic assessments, which shows that patients receiving therapy are closely monitored, imply a higher HCRU.

- Costs associated with HCRU show that while treatment may not reduce ER and inpatient costs, it likely shifts expenses toward outpatient management and long-term monitoring.

Limitations

- Claims data are primarily collected for billing, therefore, patients in this study may have been misclassified due to miscoding or misdiagnosis. Treatment and mortality data may be incomplete, and relevant clinical history prior to 2017 or between diagnosis and index date may be missing.

- The number of closed cases in 2023 was lower than in 2022, which may limit the robustness of year-over-year comparisons

- Inpatient costs vary widely across US health systems and type of hospitalizations which may not represent actual HCRU expenditures.

- Cost output was based on Medicare FFS pricing or imputed all-payer allowed amounts from a Komodo Health algorithm, reflecting allowed costs and not true costs.

- The lack of matching between treated and untreated groups may introduce bias, and findings may not be generalizable to uninsured or underrepresented populations.

- The data were not matched for comorbidities, therefore, high variant comorbidities could interfere with the results.

Conclusions

- Patients with FD who receive consistent treatment tend to have lower rates of inpatient stays and ER visits compared with untreated or newly treated patients. This indicates that treatment adherence can help reduce acute health emergencies and hospitalizations, promoting better disease management.

- The untreated group generally reflects patients with poorly controlled disease who may have had interruption in therapy. Higher ER and inpatient visits among this group may indicate that delayed initiation or inconsistent adherence to treatment could lead to poorer clinical outcomes and higher reliance on emergency services.

- Fewer visits to pain specialists by the treated group may suggest effective symptom management through treatment, while the presence of specialist visits indicates appropriate ongoing monitoring.

- In terms of costs, treated group had higher costs compared to untreated likely due to outpatient management and long-term monitoring

- Higher rates of specialist visits among the treated groups indicates more comprehensive disease monitoring and multidisciplinary care.

- The findings of this study highlight the value of early and sustained therapy in reducing acute HCRU and related costs.

References: 1. NORD. "Fabry Disease." https://rarediseases.org/rare-diseases/fabry-disease/; 2. Beck et al. Eur J Clin Invest. 2004;34(12):838-44; 3. Umer M, Kalra DK. Treatment of Fabry Disease: Established and Emerging Therapies. Pharmaceuticals (Basel). 2023 Feb 20;16(2):320. doi: 10.3390/ph16020320. PMID: 37259462; PMCID: PMC9967779. 4. US Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761161s000lbl.pdf