Economic Burden of Erythropoietic Protoporphyria (EPP) and X-Linked Protoporphyria (XLP): A Large United States (US) Nationwide Claims Analysis

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INTRODUCTION

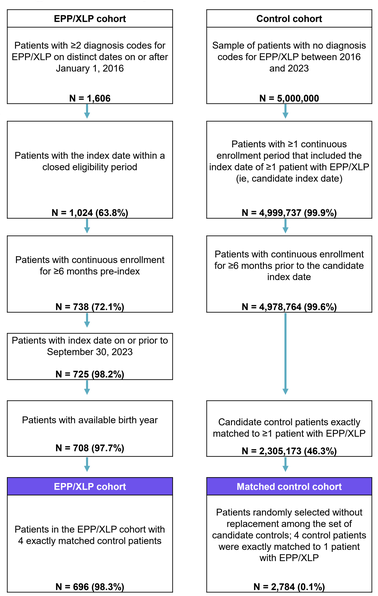
- Erythropoietic protoporphyria (EPP) and X-linked protoporphyria (XLP) are characterized by the accumulation of protoporphyrin IX (PPIX), which leads to severe pain upon exposure to sunlight, with an estimated clinical prevalence of 1:200,000 to 1:57,000 and genetic prevalence of up to 1:17,000[1-6]
- Patients with EPP, inclusive of XLP, often have systemic complications, including mild anemia, iron deficiency, vitamin D deficiency, and osteoporosis[1,7,8]
- Approximately 56% of EPP patients have elevated liver biochemistries and 2.5% develop liver failure that requires liver transplantation[9]
- Given the rarity of the disease, there is a lack of information on the real-world burden of illness among patients with EPP/XLP
- This retrospective real-world study used a large, nationwide claims database to assess healthcare resource utilization (HRU) and costs, as well as to identify predictors of high healthcare costs among patients with EPP/XLP in the US

METHODS

Study Design

- A retrospective, longitudinal cohort study, which included an EPP/XLP cohort and a matched control cohort at a ratio of 1 patient with EPP/XLP to 4 control patients, was conducted
- Patients were identified from the Komodo Research Database between 2016-2023 and matched on index date and key characteristics
- EPP/XLP *index date* was date of first observed EPP/XLP diagnosis (ICD-10-CM: E80.0)
- Patients were required to have 6 months of continuous enrollment pre-index (*baseline*).
- Per-patient-per-year (PPPY) HRU and costs (2023 US dollars) were assessed post-index and compared between cohorts using rate ratios (RRs) estimated from negative binomial regressions for HRU and cost ratios from two-part linear models for costs
- Predictors of high healthcare costs (follow-up costs ≥75th percentile) in the EPP/XLP cohort were identified using linear regression

Figure 1. Sample Selection Flowchart



RESULTS

Table 1. Patient Characteristics

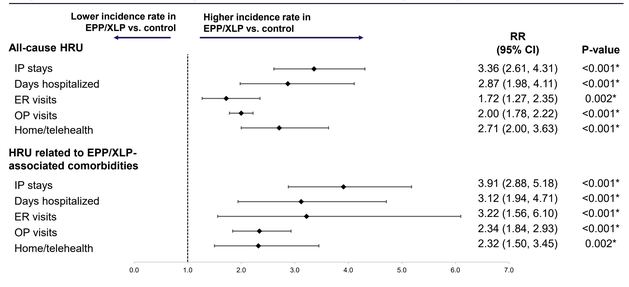
	EPP/XLP cohort (n=696)	Matched control cohort (n=2,784)
Demographic Characteristics		
Age at index (years)[1], mean ± SD [median]	45.4 ± 23.6 [48.8]	45.6 ± 23.9 [48.9]
Female[1], n (%)	383 (55.0)	1,532 (55.0)
White[1], n (%)	383 (55.0)	1,532 (55.0)
South[1], n (%)	227 (32.6)	908 (32.6)
Commercial insurance[1], n (%)	443 (63.6)	1,772 (63.6)
2020-2023 index date, n (%)	351 (50.4)	1,404 (50.4)
Clinical Characteristics		
Modified CCI score[1-2], mean ± SD [median]	0.9 ± 1.7 [0.0]	0.8 ± 1.6 [0.0]
Bone diseases related to vitamin D deficiency[3], n (%)	128 (18.4)	322 (11.6)
Anxiety[3], n (%)	124 (17.8)	277 (9.9)
Depression[3], n (%)	111 (15.9)	239 (8.6)
Liver/biliary conditions[3], n (%)	97 (13.9)	134 (4.8)

[1] Variable used for matching the control patients to the patients with EPP/XLP
[2] Modified CCI score excluded liver disease
[3] Standardized differences >10% in magnitude in EPP/XLP cohort vs matched control cohort
CCI: Charlson Comorbidity Index; SD: standard deviation

Patient Baseline Characteristics

- A total of 696 patients with EPP/XLP and 2,784 matched controls were included
- A higher proportion of patients with EPP/XLP had EPP/XLP-associated comorbidities than control patients
- Compared with controls, those with EPP/XLP incurred higher baseline all-cause HRU and costs
  - Inpatient visits (mean PPPY): 0.53 vs 0.17, std diff=29.5%
  - Outpatient visits (mean PPPY): 31.55 vs 16.79, std diff=37.1%
  - Costs (mean PPPY total): $39,440 vs $14,821, std diff=30.3%

Figure 2. HRU During the Follow-up Period (PPPY)

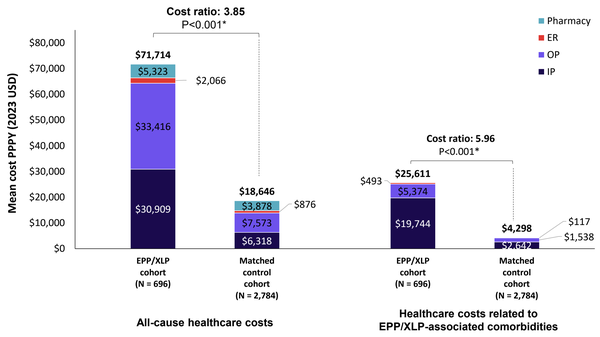


* P < 0.05
CI: confidence interval; ER: emergency room; HRU: health resource utilization; IP: inpatient; OP: outpatient; PPPY: per patient per year; RR: rate ratio

HRU During the Follow-up Period

- During a mean (SD) follow-up period of 30 (23) months, patients with EPP/XLP had consistently higher rates of HRU compared with matched controls
- Among patients with EPP/XLP, IP stays specific to EPP/XLP represented half of all-cause IP stays; OP visits represented more than 10% of all-cause OP visits

Figure 3. Healthcare Costs During the Follow-up Period (PPPY)

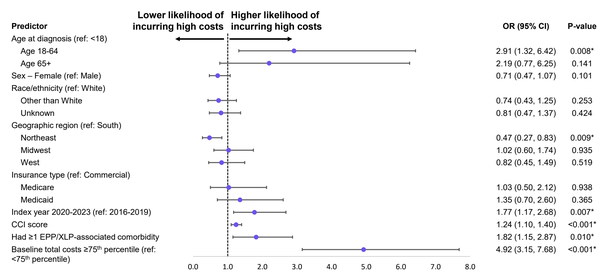


ER: emergency room; IP: inpatient; OP: outpatient; PPPY: per patient per year; USD: US dollar

Healthcare Costs During the Follow-up Period

- During the follow-up period, patients with EPP/XLP incurred higher healthcare costs compared with control patients
- Among patients with EPP/XLP, the total EPP/XLP-specific medical costs PPPY represented approximately one-fourth of total all-cause costs, mainly driven by OP costs

Figure 4. Predictors of High Healthcare Costs During the Follow-up Period



* P < 0.05
CCI: Charlson Comorbidity Index; CI: confidence interval; OR: odds ratio; ref: reference

Predictors of High Healthcare Costs

- Among patients with EPP/XLP, age 18-64 years (vs <18), Northeast region (vs South), an index year in 2020 or later (vs in 2019 or before), CCI score, having ≥1 EPP/XLP-associated comorbidity, and having high healthcare costs during the baseline period (ie, ≥75th percentile) were significant predictors of high healthcare costs during the follow-up period

CONCLUSIONS

- This study demonstrated **significant economic burden** among patients with EPP/XLP, reflected by **>3 times the number of IP stays** and **twice as many OP and ER visits** compared with matched control patients
- Patients with EPP/XLP incur **total healthcare costs that are nearly 4 times higher** than those of matched control patients, mainly driven by higher IP and OP costs
- Age, CCI score, EPP/XLP-associated comorbidities, and high costs in the baseline period significantly predicted high healthcare costs in the follow-up period among patients with EPP/XLP
- These findings emphasize the **significant unmet need** for more effective treatments that could reduce the risk of EPP/XLP-related complications, improve patient outcomes, extend indications to younger patients, and ultimately alleviate the overall burden of disease in this population

References

1. Dickey AK, et al. Annu Rev Med. 2024;75:321-335.
2. Balwani M, et al. Erythropoietic protoporphyria, autosomal recessive. GeneReviews® [Internet]. 2017.
3. Balwani M. Mol Genet Metab. 2019;128(3):298-303.
4. Wang Y, et al. Orphanet J Rare Dis. 2024;19(1):337.
5. Marko PB, et al. Acta Dermatovenerol Alp Pannonica Adriat. 2007;16(3):99-104.
6. Dickey AK, et al. Genet Med. 2021;23(1):140-148.
7. Holme SA, et al. Blood. 2007;110(12):4108-4110.
8. Delaby C, et al. Cell Mol Biol (Noisy-le-grand). 2009;55(1):45-52.
9. Levy C, et al. Hepatol Commun. 2025;9(3):e0657.

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