Healthcare Resource Use and Costs Among Patients With Erythropoietic Protoporphyria and X-Linked Protoporphyria in the United States

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BACKGROUND

- Erythropoietic protoporphyria (EPP) and X-linked protoporphyria (XLP) are rare genetic disorders of the heme biosynthetic pathway that result in severe cutaneous phototoxicity reactions.[1-3] EPP prevalence estimates range from approximately 1:75,000 (The Netherlands) to 1:200,000 (United Kingdom).[4,5] Approximately 90% of protoporphyria cases in the United States (US) are EPP[6]
- Symptoms usually present in early childhood, often during the first few years of life, but there is a long delay to definitive diagnosis,[7] and many patients remain undiagnosed[8]
- Comprehensive studies on the healthcare costs of these disorders in the US are lacking

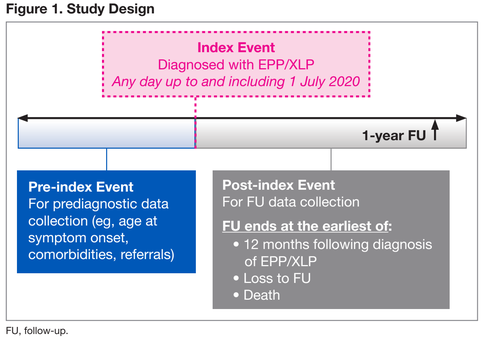
OBJECTIVE

- To document the healthcare resource use and costs among patients with EPP and XLP in routine clinical practice

METHODS

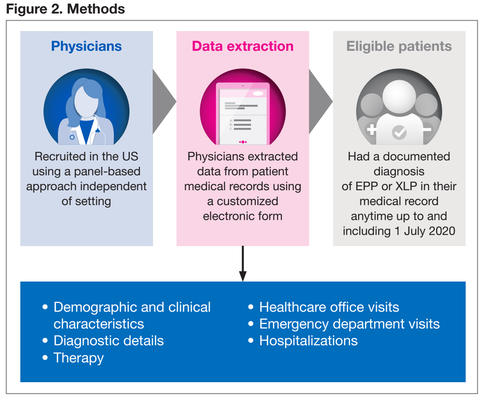
- A retrospective, noninterventional review of de-identified medical records of patients diagnosed with EPP or XLP in the US (Figures 1 and 2)

Figure 1. Study Design



FU, follow-up.

Figure 2. Methods



- Costs were derived from standard cost sources based on 2022 US dollars (Centers for Medicare and Medicaid Services Physician Fee Schedule; Centers for Medicare and Medicaid Services Clinical Laboratory Fee Schedule; IBM Micromedex Red Book; Healthcare Cost and Utilization Project)
- Direct costs were allocated at the patient level (ie, per-patient costs) by multiplying the extracted cost of the relevant procedure/test/visit/therapy by the number of units observed for a patient. Mean per-patient cost was derived
- For the **diagnostic pathway**, costs were based on data that were available in the medical record between the first documented symptom report and diagnosis
  - Prediagnostic costs included tests conducted related to EPP/XLP symptoms and referrals to specialists. Data on the number of prediagnostic tests were not collected. Thus, the analysis assumed only 1 test
- For **postdiagnosis**, costs were based on tests and referrals to specialists within the first year of diagnosis
- **Prescription therapy** included all prescribed therapies from diagnosis to the date of the last available medical record
  - Costs considered the reported dose for the label-recommended frequency
  - If dose information was missing, the mean observed dose was assumed, except for afamelanotide, where the dose was assumed to be 16 mg if dose information was missing, and for hematin, where the dose was assumed to be a 350 mg vial with 7 mg/ml of hematin
  - Prescriptions were assumed to be monthly if prescription frequency information was missing, except for afamelanotide, where the frequency was assumed to be every 2 months, for hematin, where 1 dose was assumed, and for pain relievers, where a 5-day prescription was assumed
  - If prescription duration information was missing, the mean observed duration per prescription was assumed
  - If information on the number of prescriptions was missing, 1 prescription was assumed
- Costs of **hospitalizations** considered the number of hospitalizations and the duration from the first documented symptom report to 1 year postdiagnosis
- Costs of **emergency department** (ED) encounters considered the number of visits reported from the first documented symptom report to 1 year postdiagnosis

RESULTS

- Data were extracted for 386 patients by 136 physicians
- Table 1 presents the derived mean and median per-patient costs
  - Both the diagnostic pathway cost and the postdiagnosis test and referral cost were driven primarily by referrals to specialists
    - Dermatology referrals had the highest costs: mean (standard deviation [SD]) of $109.40 ($137.55) prediagnosis and $81.74 ($110.27) within 12 months postdiagnosis, comprising 33% of both prediagnosis and postdiagnosis specialist referral costs
  - Mean cost for inpatient hospitalizations and ED encounters through 12 months postdiagnosis was $2,731.85, but most patients did not incur this cost, as reflected by a median cost of $0
  - Sixty-eight percent of all patients (n = 263) received a prescription for EPP/XLP; the total mean (SD) per-patient cost of prescription therapy was $27,177.59 ($109,181.97). However, this cost was driven by a small number of patients, as reflected by a median per-patient prescription cost of $192.66
    - Table 2 presents the calculated mean and median per-patient costs of each type of prescription therapy

Table 1. Condition-Related Unadjusted Overall Total Per-Patient Costs

Cost type	N (%) of patients using the resource	Calculated per-patient cost	
		Mean (SD)	Median (Q1, Q3)
Total diagnostic pathway	377 (98%)	$601.54 ($518.50)	$511.86 ($288.96, $770.37)
Specialist referrals	279 (72%)	$330.64 ($432.35)	$237.24 ($0.00, $355.86)
Diagnostic tests	372 (96%)	$270.90 ($199.33)	$314.24 ($60.08, $376.23)
Postdiagnosis tests and referrals	343 (89%)	$397.68 ($432.02)	$283.69 ($98.87, $558.52)
Specialist referrals	244 (63%)	$244.21 ($320.57)	$118.62 ($0.00, $355.86)
Diagnostic tests	325 (84%)	$153.47 ($270.81)	$91.36 ($29.60, $196.10)
Hospitalizations and ED encounters	141 (37%)	$2,731.85 ($7,270.04)	$0.00 ($0.00, $953.72)
Prescription therapies and procedures	263 (68%)	$27,177.59 ($109,181.97)	$192.66 ($0.00, $6,050.54)

Table 2. Unadjusted Per-Patient Costs of Prescription Therapies and Procedures

Prescription therapy/procedure	N (%) of patients receiving a prescription	Calculated per-patient cost	
		Mean (SD)	Median (Q1, Q3)
Afamelanotide	68 (18%)	$25,400.51 ($108,806.29)	$0.00 ($0.00, $0.00)
Hematin	26 (7%)	$1,061.15 ($7,418.88)	$0.00 ($0.00, $0.00)
Cholestyramine	50 (13%)	$121.66 ($807.41)	$0.00 ($0.00, $0.00)
Ursodeoxycholic acid	43 (11%)	$126.41 ($730.83)	$0.00 ($0.00, $0.00)
Antidepressant	54 (14%)	$103.66 ($692.71)	$0.00 ($0.00, $0.00)
Activated charcoal	7 (2%)	$74.11 ($1,115.28)	$0.00 ($0.00, $0.00)
Liver transplant	5 (1.3%)	$71.71 ($626.82)	$0.00 ($0.00, $0.00)
NSAID	49 (13%)	$83.96 ($488.98)	$0.00 ($0.00, $0.00)
Anti-anxiolytic	39 (10%)	$67.17 ($349.44)	$0.00 ($0.00, $0.00)
Plasmapheresis	16 (4.1%)	$24.62 ($118.52)	$0.00 ($0.00, $0.00)
Oral beta-carotene	106 (27%)	$16.68 ($71.04)	$0.00 ($0.00, $3.03)
Iron	38 (10%)	$11.76 ($59.64)	$0.00 ($0.00, $0.00)
Cysteine	22 (6%)	$6.18 ($50.50)	$0.00 ($0.00, $0.00)
Vitamin E	25 (6%)	$2.49 ($16.91)	$0.00 ($0.00, $0.00)
Zinc	20 (5%)	$2.32 ($16.55)	$0.00 ($0.00, $0.00)
Vitamin D	65 (17%)	$1.70 ($12.91)	$0.00 ($0.00, $0.00)
Opioid pain reliever	21 (5%)	$1.27 ($8.55)	$0.00 ($0.00, $0.00)
Vitamin C	26 (7%)	$0.24 ($1.89)	$0.00 ($0.00, $0.00)

NSAID, nonsteroidal anti-inflammatory drug.

DISCUSSION

- Based on real-world data from the US, average costs from symptom onset to diagnosis of EPP or XLP were approximately $600 per patient. Once diagnosed, average costs of referrals and tests in the first year were approximately $400 across all patients
  - However, resource use was based on data available in the medical record to which the physician had access and may not reflect the patient's full usage
  - Moreover, costs were derived for Medicare payments under the Physician Fee Schedule and do not reflect commercial insurance costs or out-of-pocket costs to the patient
- Inpatient hospitalizations and ED encounters specifically related to EPP or XLP are uncommon. However, when they occur, these encounters are costly, resulting in a mean of approximately $2,700 across all patients
  - This may be an underestimate because data were available only from the medical record to which the abstracting physician had access. If a patient visited a hospital or ED outside the physician's network, this visit would not be recorded
  - These costs were derived from the Healthcare Cost and Utilization Project, which encompasses all payer information
- Two-thirds of the sample received a prescription or procedure for EPP or XLP symptoms, with oral beta-carotene (27%) and afamelanotide (18%) being the most common. Total average costs of prescriptions and procedures were over $27,000 across all patients
  - Costs were derived based on the average wholesale price paid by providers. This is not necessarily a reflection of the actual price paid to wholesalers and does not reflect insurance costs or out-of-pocket costs to the patient

CONCLUSION

- EPP and XLP are associated with significant healthcare costs and require multiple specialist referrals and testing

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DISCLOSURES

KH and AH are employees of RTI Health Solutions, which received funding to conduct this study. MC is an employee of Mitsubishi Tanabe Pharma America, Inc.

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