Healthcare Resource Utilization and Costs Among Patient Segments with Acute Intermittent Porphyria: Analyses from a National Healthcare Database

Stephen Meninger, PharmD, MS, MBA[1], Angelika L. Erwin, MD, PhD[2], Samuel Silver, MD, PhD[3]

[1]Alnylam Pharmaceuticals, Cambridge, MA, USA; [2]Cleveland Clinic, Cleveland, OH, USA; [3]University of Michigan Medical Center, Ann Arbor, MI, USA

Conclusions

- **Patients with acute intermittent porphyria (AIP) exhibited high rates of healthcare resource utilization (HCRU) and high associated costs**
- **Given the substantial burden experienced by patients with AIP—acute attacks, chronic symptoms, and long-term complications—and the resulting burden on the healthcare system overall, the unmet needs of patients with AIP and the burden to the healthcare system are high**
- **Therapeutic strategies that can prevent or reduce AIP attacks, chronic symptoms, and long-term complications are essential in reducing the burden of AIP**

Background

- AHP is a group of rare, chronic, multisystem disorders with acute attacks, progressive elements, and long-term complications requiring proactive management and treatment[1]
- AHP comprises four types of porphyria: acute intermittent porphyria (AIP; the most common), variegate porphyria (VP), hereditary coproporphyria (HCP), and delta-aminolevulinic acid (ALA) dehydratase deficiency porphyria (ALAD)[2]
- The accumulation of ALA and PBG, neurotoxic precursors to porphyrin, is thought to cause injury to the nervous system and organs such as the liver and kidneys[1]
- Patients with AHP can experience potentially life-threatening acute attacks (characterized by symptoms including severe abdominal pain, nausea, vomiting, tachycardia, hypertension, hyponatremia, mental status changes, and muscle weakness) and chronic manifestations including moderate to severe chronic pain, anxiety, depression, and limitations in mobility and activities of daily living—which diminish quality of life[2]
- Patients with AIP are at increased risk for chronic neuropathy, chronic renal disease, and development of liver complications[1]
- Hemin is used to treat acute attacks and has been used prophylactically to treat recurrent attacks[1]
- Givosiran was approved by the US Food and Drug Administration in 2019, after these analyses were performed, and is indicated for the treatment of adults with AHP[3]
- Results from a previous analysis showed that, from 2007 to 2017, patients with AIP being treated with hemin annually spent an average of $188,752 for all-cause HCRU and $113,477 for AIP-related HCRU[4]
- HCRU and cost data for various US patient segments with AIP are limited and warrant further investigation

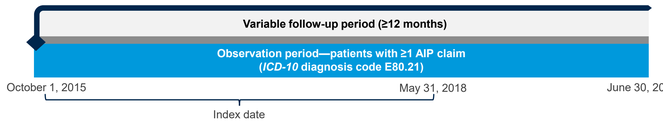
Objective

- To describe the HCRU and costs of AIP among US patient segments differing in AARs, hemin use, chronic symptoms, and long-term complications

Methods

Figure 1. Study Period

- This retrospective, observational study used Merative MarketScan (formerly IBM MarketScan) Commercial and Medicare Supplemental data drawn from the period October 1, 2015 to June 30, 2019 (**Figure 1**)



- Patients with ≥1 nondiagnostic AIP claim from October 1, 2015 to May 31, 2018 and ≥12 months of continuous enrollment with medical and pharmacy benefits after the earliest AIP diagnosis (index date) were included in the analyses
- Clinical characteristics, collected over the variable-length follow-up, included comorbidities, concomitant medications, CCI, and modified CCI, which does not include hepatic or renal conditions
- In segmentation analyses, postindex annualized HCRU and costs were assessed for all patients with AIP and for key segments: AAR/hospitalizations (0, 1, 2, and ≥3 annual attacks, and ≥1 hospitalization), hemin use (any, prophylactic), chronic symptoms (pain, nausea), and long-term complications (hepatic conditions, renal conditions, chronic neuropathy)
- AARs per patient per year were calculated and rounded up to the nearest whole number. Hemin use was determined by medical claims with a Healthcare Common Procedure Coding System code for hemin (J1640). Chronic pain and nausea were identified based on high opioid and antiemetic use, both defined by an MPR that was higher than the third quartile of MPR in the entire sample
- All outcomes were annualized and reported as PPPY
- Patients with AIP and ≥12 months of continuous enrollment with medical and pharmacy benefits before and after the earliest AIP diagnosis (index date) were matched to 10,000 patients without AIP on age, sex, insurance plan type, population density, payer, and length of follow-up, and were included in the multivariable analysis
- Generalized linear models and logistic regression models, adjusted for patient characteristics, were used to assess HCRU and costs of AIP

Results

- Of the 361 patients with AIP identified (October 1, 2015 to May 31, 2018), 225 had ≥12 months of continuous enrollment after their first AIP claim; only a small proportion of these 225 patients was from each identified segment (**Table 1**)
- For the segmentation analysis, mean age of the patients was 45.6 years; 69.8% of these patients were female
- Of the 225 patients, 87.1% lived in an urban area, and 92.0% were commercially insured; their mean (SD) number of follow-up days was 689 (218)
- For the multivariable analysis, 187 patients with AIP and ≥12 months of continuous enrollment with medical and pharmacy benefits before and after the earliest AIP diagnosis were matched to 10,000 randomly selected patients without AIP. Mean age of the patients with AIP was 46.5 years; 70.6% of these patients were female. Mean age of the patients without AIP was 39.6 years; 53.4% of these patients were female
- The most common concomitant medications were opioids (66.2%), anxiolytics (60.4%), and antiemetics (51.1%)

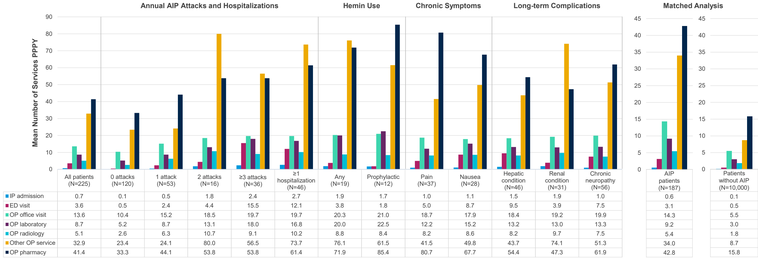
Table 1. Baseline Demographic and Clinical Characteristics of Commercially Insured Patients

Characteristic at Index Date	All Patients (N=225)	Annual AIP Attacks and Hospitalizations					Hemin Use		Chronic Symptoms		Long-term Complications			Matched Analysis	
		0 Attacks (N=120)	1 Attack (N=53)	2 Attacks (N=16)	≥3 Attacks (N=36)	≥1 Hospitalization (N=46)	Any (N=19)	Prophylactic (N=12)	Pain (N=37)	Nausea (N=28)	Hepatic Condition (N=46)	Renal Condition (N=31)	Chronic Neuropathy (N=56)	AIP Patients (N=187)	Patients without AIP (N=10,000)
Age, years, mean (SD)	45.6 (16.4)	46.9 (16.6)	47.6 (16.0)	44.5 (16.5)	39.2 (15.2)	42.4 (17.7)	41.1 (13.9)	43.2 (14.0)	48.4 (12.4)	40.4 (16.3)	44.5 (14.2)	51.8 (14.7)	49.9 (14.8)	46.5 (16.7)	39.6 (21.3)
Female, %	69.8	69.2	69.8	75.0	69.4	69.6	89.5	91.7	78.4	78.6	76.1	83.9	80.4	70.6	53.4
CCI, mean (SD)	1.6 (2.4)	1.1 (1.6)	1.7 (2.4)	3.3 (3.3)	2.5 (3.4)	3.3 (3.6)	2.5 (2.7)	2.4 (1.9)	2.6 (3.1)	1.7 (2.4)	2.8 (3.5)	4.1 (3.9)	2.8 (3.3)	1.7 (2.5)	0.7 (1.5)
Modified CCI,[a] mean (SD)	1.3 (1.9)	1.0 (1.4)	1.5 (2.1)	2.6 (2.6)	1.9 (2.5)	2.6 (2.8)	1.9 (2.0)	1.8 (1.1)	2.0 (2.4)	1.5 (2.1)	2.1 (2.6)	2.6 (3.2)	2.3 (2.5)	1.4 (2.0)	0.6 (1.3)
Concomitant medication, %															
Opioids	66.2	53.3	79.2	81.3	83.3	78.3	84.2	83.3	100.0	82.1	78.3	64.5	82.1	66.8	36.6
Anxiolytics	60.4	47.5	64.2	81.3	88.9	80.4	94.7	100.0	83.8	89.3	76.1	64.5	78.6	62.0	32.2
Antiemetics	51.1	31.7	58.5	93.8	86.1	78.3	89.5	91.7	73.0	100.0	73.9	54.8	69.6	51.3	18.8
MPR, mean (SD)															
Opioids	0.31 (0.39)	0.55 (0.44)	0.69 (0.45)	0.31 (0.40)	0.25 (0.37)	0.41 (0.48)	0.32 (0.37)	0.40 (0.43)	0.93 (0.11)	0.57 (0.43)	0.35 (0.40)	0.47 (0.42)	0.43 (0.39)	0.30 (0.39)	0.07 (0.21)
Antiemetics	0.09 (0.15)	0.09 (0.17)	0.11 (0.21)	0.10 (0.21)	0.06 (0.09)	0.10 (0.12)	0.09 (0.11)	0.08 (0.11)	0.19 (0.24)	0.29 (0.19)	0.08 (0.11)	0.11 (0.18)	0.07 (0.12)	0.10 (0.16)	0.01 (0.05)

[a]Does not include hepatic or renal conditions, as these could be long-term complications of AIP.

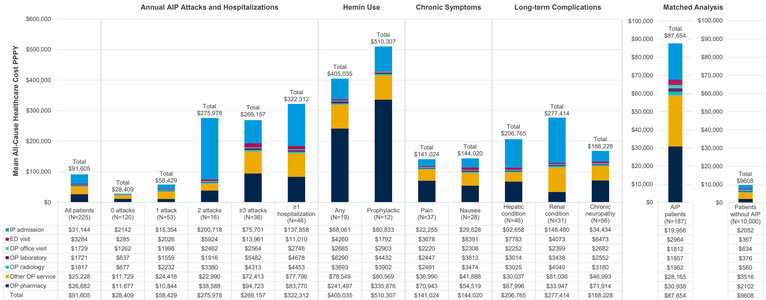
- **Figure 2** shows that patients with increasing annual AIP attacks experienced greater HCRU; those with 1, 2, and >3 AIP attacks had 0.5, 1.8, and 2.4 inpatient admissions and 2.4, 4.4, and 15.5 ED visits, respectively
- Among patients with a selected comorbidity, inpatient admissions were highest in those with a renal condition (1.9) and those with a hepatic condition (1.5)
- Patients with chronic pain and prophylactic hemin use had the highest outpatient pharmacy utilization (80.7 and 85.4, respectively)
- In the matched analysis, the mean total cost was $87,654 and $9608 for patients with AIP and matched patients without AIP, respectively
- In the multivariable adjusted analysis of the matched AIP and non-AIP populations, the mean total costs were $74,686 and $10,152, respectively, per patient
- Mean annualized total costs ranged from $141,024 to $510,307 among segments with high HCRU (**Figure 3**)
- Across all patient segments, hemin users incurred the highest mean total costs ($405,035 for any use, $510,307 for prophylactic use)
- Patients experiencing ≥1 hospitalization/year incurred a mean cost of $322,312
- For patients experiencing 2 and ≥3 annual attacks, healthcare costs were $275,978 and $269,157, respectively
- For patients with hepatic conditions, renal conditions, or chronic neuropathy, the mean annual costs were $206,765, $277,414, and $168,228, respectively
- Mean healthcare costs for patients experiencing chronic pain and nausea were $141,024 and $144,020, respectively

Figure 2. Mean Number of Services PPPY



	All patients (N=225)	0 attacks (N=120)	1 attack (N=53)	2 attacks (N=16)	≥3 attacks (N=36)	≥1 hospitalization (N=46)	Any (N=19)	Prophylactic (N=12)	Pain (N=37)	Nausea (N=28)	Hepatic condition (N=46)	Renal condition (N=31)	Chronic neuropathy (N=56)	AIP patients (N=187)	Patients without AIP (N=10,000)
IP admission	0.7	0.1	0.5	1.8	2.4	2.7	1.9	1.7	1.0	1.1	1.5	1.9	1.0	0.6	0.1
ED visit	3.6	0.5	2.4	4.4	15.5	12.1	3.8	1.8	5.0	8.7	9.5	3.9	7.5	3.1	0.5
OP office visit	13.6	10.4	15.2	18.5	19.7	19.7	20.3	21.0	18.7	17.9	18.4	19.2	19.9	14.3	5.5
OP laboratory	8.7	5.2	8.7	13.1	18.0	16.8	20.0	22.5	12.2	15.2	13.2	13.0	13.3	9.2	3.0
OP radiology	5.1	2.6	6.3	10.7	9.1	10.2	8.8	8.4	8.2	8.6	8.2	9.7	7.5	5.4	1.8
Other OP service	32.9	23.4	24.1	80.0	56.5	73.7	76.1	61.5	41.5	49.8	43.7	74.1	51.3	34.0	8.7
OP pharmacy	41.4	33.3	44.1	53.8	53.8	61.4	71.9	85.4	80.7	67.7	54.4	47.3	61.9	42.8	15.8

Figure 3. Mean All-Cause Healthcare Costs PPPY Among Commercially Insured Patients



	All patients (N=225)	0 attacks (N=120)	1 attack (N=53)	2 attacks (N=16)	≥3 attacks (N=36)	≥1 hospitalization (N=46)	Any (N=19)	Prophylactic (N=12)	Pain (N=37)	Nausea (N=28)	Hepatic condition (N=46)	Renal condition (N=31)	Chronic neuropathy (N=56)	AIP patients (N=187)	Patients without AIP (N=10,000)
IP admission	$31,144	$2142	$15,354	$200,718	$75,701	$137,858	$68,061	$80,833	$22,255	$29,628	$92,658	$148,490	$34,434	$19,956	$2052
ED visit	$3294	$285	$2026	$5924	$13,961	$11,010	$4260	$1792	$3678	$8391	$7783	$4073	$6473	$2964	$367
OP office visit	$1729	$1262	$1998	$2462	$2564	$2746	$2685	$2903	$2220	$2308	$2252	$2399	$2692	$1812	$634
OP laboratory	$1721	$637	$1559	$1916	$5482	$4678	$6290	$4432	$2447	$3813	$3014	$3438	$2552	$1857	$376
OP radiology	$1817	$677	$2232	$3380	$4313	$4453	$3693	$3902	$2491	$3474	$3025	$4040	$3180	$1962	$560
Other OP service	$25,228	$11,729	$24,416	$22,990	$72,413	$77,796	$78,549	$80,569	$36,990	$41,888	$30,037	$81,036	$46,993	$28,165	$3516
OP pharmacy	$26,682	$11,677	$10,844	$38,588	$94,723	$83,770	$241,497	$335,876	$70,943	$54,519	$67,996	$33,947	$71,914	$30,938	$2102
Total	$91,605	$28,409	$58,429	$275,978	$269,157	$322,312	$405,035	$510,307	$141,024	$144,020	$206,765	$277,414	$168,228	$87,654	$9608

Limitations

- The study population was limited to patients with commercial health insurance coverage or private Medicare Supplemental coverage; observed results may not be generalizable to patients with AIP without health insurance coverage, Medicare Advantage, or standard Medicare without commercial supplementation
- Given the overlap of symptoms between AIP and other diseases, potential coding errors, and lack of clinical information in administrative claims, the study had the potential to misclassify patients with AIP
- For patients who die, and those on long-term disability because of serious health conditions, follow-up may be shorter than the 12-month minimum used in the study. Therefore, patients who use healthcare resources the most may not have been captured in the segmentation and multivariable analyses

Abbreviations: AAR, annualized attack rate; AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; ALA, delta-aminolevulinic acid; ALAD, delta-aminolevulinic acid dehydratase deficiency porphyria; CCI, Charlson Comorbidity Index; ED, emergency department; HCP, hereditary coproporphyria; HCRU, healthcare resource utilization; *ICD-10, International Classification of Diseases, 10th Revision;* IP, inpatient; MPR, medication possession ratio; OP, outpatient; PBG, porphobilinogen; PPPY, per patient per year; VP, variegate porphyria.

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