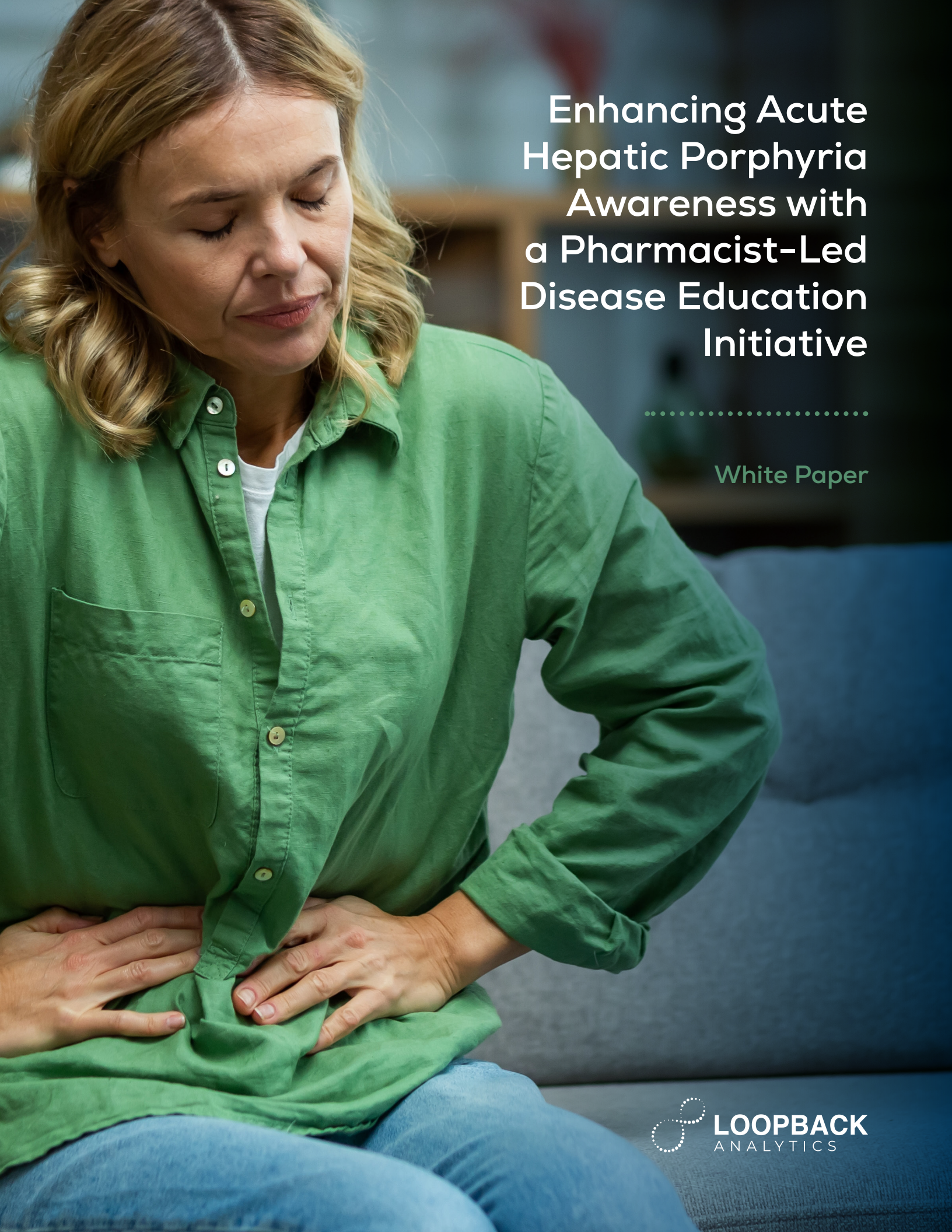


Enhancing Acute Hepatic Porphyria Awareness with a Pharmacist-Led Disease Education Initiative

White Paper

LOOPBACK ANALYTICS

Executive Summary

Acute hepatic porphyria (AHP) is a rare genetic disorder that can cause debilitating health problems for the approximately 10 per 1 million patients impacted with symptomatic AHP in the USA.[1,2] Patients can experience nonspecific symptoms —including severe, diffuse abdominal pain, nausea and vomiting[3,4,5]— resulting in an average diagnostic delay of 15 years from the onset of symptoms.[5]

In partnership with Alnylam, Loopback Analytics implemented a pharmacist-led disease education initiative to enable healthcare providers to better recognize AHP symptoms in order to facilitate timely diagnosis and management. To develop the disease education initiative, Loopback convened an AHP Task Force of health system specialty pharmacy leaders from three academic medical centers. The task force leaders then implemented the disease education initiative across seven health systems, providing targeted education about AHP to 65 healthcare providers practicing in both inpatient and outpatient settings. Recognition of the disorder, appropriate management of AHP and emergency department/hospitalizations were measured at these health systems before and after the educational initiative was provided.

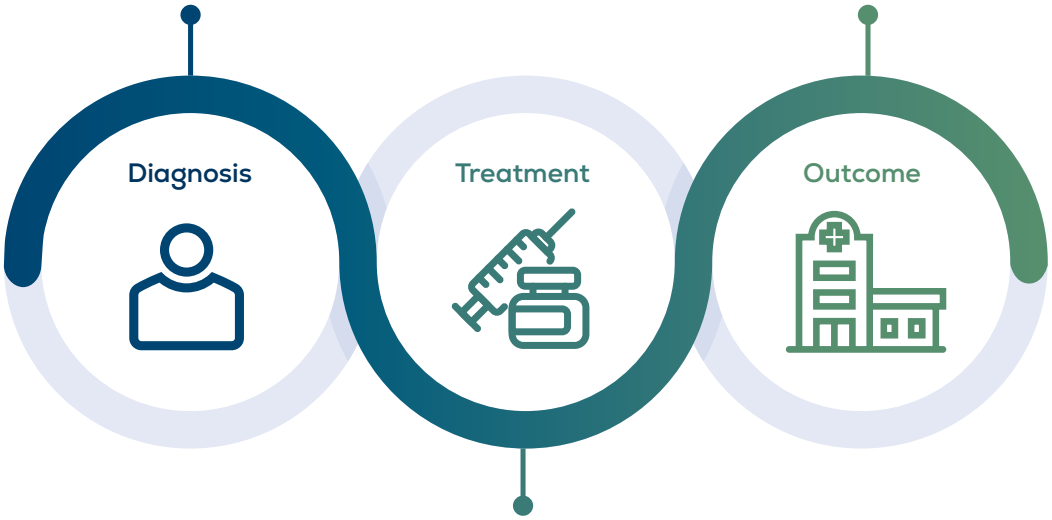
Both task force and non-task force health systems saw increases in AHP diagnoses of ~14% and ~13%, respectively, and improved disease management. Furthermore, there appeared to be a reduction of inpatient visits per eligible patient. The analysis was limited by small patient sample sizes, unequal cohort group sizes and risk profiles, and restricted healthcare utilization data due to the constraints of the available de-identified dataset. Still, these findings highlight the critical importance of healthcare provider education in detection, diagnosis, and effective management of AHP, with the goal of improving patient outcomes and reducing healthcare system burden.

Key Results

Pharmacist-led education initiative with 65 healthcare providers resulted in:

Nearly 14% overall increase in patient identification across health systems participating in the education initiative

~10% reduction in mean inpatient visits per patient for treated AHP patients at health systems participating in the education initiative



38% increase in disease management and treatment options, including usage of FDA-approved AHP therapies

Background

AHP is a family of diseases that occur due to a deficiency in one of the enzymes of heme biosynthesis in the liver.[5] There are four types of AHP, the most common of which is acute intermittent porphyria (AIP). These are distinguished by the location of the enzymatic mutation along the heme biosynthesis pathway. The disease process is similar across types: When the body's heme-producing pathway doesn't work as it should, molecules called porphyrin precursors used to make heme can build up, causing nerve damage and other severe symptoms.

The most common symptom of AHP is severe pain in the abdomen lasting for several days, although pain also can occur in the extremity or back. Women ages 15-45 are the most frequently affected.[6,7] Other symptoms may include, but are not limited to: hypertension, tachycardia, nausea and vomiting, constipation or hyponatremia.

Some patients may develop serious symptoms or attacks. Stress[10], hormonal fluctuations and a fasting or low-calorie diet are among the triggers[8-10] for an attack. When attacks occur, it can be extremely painful and prevent participation in normal daily activities. Beyond acute attack symptoms, more than 50% of patients who experience recurrent attacks report chronic neurologic symptoms, and 35% have received a diagnosis of neuropathy.[11]

Recognizing cases of AHP can be challenging due to the diverse and non-specific clinical presentation.[18] Healthcare providers should consider screening for AHP in women ages 15-50 with unexplained, recurrent severe abdominal pain without a clear etiology.[11] The recommended diagnostic method is biochemical testing with a urine test during an attack to look for elevated levels of porphobilinogen (PBG) as well as measure aminolevulinic acid (ALA) normalized to creatinine. Urine porphyrins alone is nonspecific and should not be used in isolation to diagnose AHP. Once AHP is identified, genetic testing should be performed to confirm the subtype.[4,5,11] However, once AHP diagnosis is confirmed, management should begin immediately, if clinically indicated, without waiting for genetic testing results.[11,12]

Timely diagnosis is critical; if not managed appropriately, patients can experience recurrent attacks, which can be life threatening.[8,15] Patients may also experience long-term complications of AHP, which include liver cancer, chronic kidney disease, neuronal damage and hypertension. Looking at impacts to the health system, patients with AHP reported a mean of 2.8 emergency room (ER) visits and 4.5 overnight hospitalizations lasting an average of 6.6 days for porphyria-related care, according to the EXPLORE study, a prospective, natural history study of 112 patients with AHP from 13 countries. Estimated average annual expenditures based on hospital costs/charge estimates per patient were $398,463 to $655,418.[16]

Ideal management of AHP is multi-fold, depending on individual patient needs. There are two FDA-approved treatments available for this patient population.* In addition there are several other management options available.

*For more information, please consult the full Prescribing Information for these products.

Common Symptoms

AHP symptoms are non-specific, making the condition difficult to recognize. Common symptoms include:

Intense abdominal pain

Chest or back pain

Hypertension/ Tachycardia

Nausea and vomiting

Constipation

Hyponatremia

This list does not include all possible AHP symptoms.

> “As integrated members of the care team, specialty pharmacists lead both disease state and medication education. Our pharmacist-led education initiative underscores their impact in raising awareness for rare conditions.”
>
> AHP Task Force Health System Pharmacy Leader

Pharmacist-Led Education Initiative Increases AHP Recognition & Management

To increase awareness around AHP and recognition of a typical patient journey, Loopback and Alnylam partnered to provide education about the disease. Loopback recruited three pharmacists representing seven academic medical centers and their specialty pharmacies to participate in an AHP Task Force. The roles of the pharmacists included a Director of System-wide Specialty Operations, a System Director of Specialty and Home Delivery, and a Specialty Clinical Pharmacist. These pharmacists served as champions for the project. They first developed educational materials about AHP and then delivered that to their colleagues in early 2024. The modes of education delivery included team in-service presentations, sharing education materials via email, and one-on-one education sessions with healthcare providers. A total of 65 physicians, medical residents, and pharmacists (including clinic based, pharmacy based, and residents), from the seven participating academic health systems received the AHP education. These providers worked in internal medicine, emergency medicine, hepatology/gastroenterology, and hematology departments in both the inpatient and outpatient settings.

To assess the impact of this education, Loopback analyzed de-identified patient data from two groups: seven health systems where education was conducted, and 21 additional health systems from various areas of the country that did not receive education. The analysis compared utilization data for AHP patients from 2023 (one year prior to the education period) with those from 2024 (1 year post education period). For the 2023 patient count, individuals were included if they had been diagnosed in 2023 or any year prior. Similarly, the 2024 dataset included patients with an eligible diagnosis from 2024 or any year prior. To be considered eligible, patients needed to have a primary diagnosis of AHP, unspecified porphyria, or other porphyria. Additionally, patients with unspecified porphyria who received an FDA-approved therapy for AHP at any point, or who had a secondary diagnosis of unspecified abdominal pain or other porphyria and received an FDA-approved therapy for AHP use were included in the analysis, as detailed in Table 1.

There are several limitations with this analysis. First, the sample patient populations driving these percent changes are small and may not reflect the true mean observed across larger sample sizes. Additionally, because the sample sizes between the two comparator groups were not matched on size and patient risk factors, there may be other confounding variables driving the observed results in the analysis. Finally, patients may have used hospitals not represented in this dataset, so actual utilization may be higher than what is reported in this analysis.

Table 1. Patient Population Diagnoses (Across 28 Health Systems)

The following table shows the percent change of eligible patients from 2023-2024. Patients were deemed eligible if they had an encounter with a primary diagnosis code as listed below.

Diagnosis Codes	Diagnosis	Percent Change of Patients from 2023 to 2024
E80.29 + R10.9	Other porphyria + unspecified abdominal pain	20.45%
E80.20 + R10.9	Unspecified porphyria + unspecified abdominal pain	14.95%
E80.21	Acute intermittent hepatic porphyria	11.65%
E80.20 + Treatment	Unspecified porphyria + FDA-approved therapy	4.55%
E80.29 + Treatment	Other porphyria + FDA-approved therapy	3.23%

E80.20: unspecified porphyria; E80.21: acute intermittent (hepatic) porphyria; E80.29: other porphyria; R10.9: unspecified abdominal pain

From 2023-2024, the number of new patients across the 28 health systems increased in nearly every subcategory, including a more than 20% increase in the number of patients diagnosed with other porphyria and unspecified abdominal pain, and a nearly 15% increase in the number of patients diagnosed with unspecified porphyria and unspecified abdominal pain.

Table 2. Total Eligible Patients, Segmented by Task Force Participation

The following table shows the total number of eligible patients (met criteria for inclusion based on an encounter with a primary diagnosis code) seen across health systems from 2023–2024 and the respective percent change.

	2023	2024	Percent Change
28 Health Systems (HS)	640 patients	723 patients (+83)	12.97%
7 Task Force HS	136 patients	155 patients (+19)	13.97%
21 Non-Task Force HS	504 patients	568 patients (+64)	12.70%

Across the 28 health systems, the total patient count grew from 640 patients in 2023 to 723 in 2024, reflecting an increase of 83 new patients and a 12.97% increase. The health systems that participated in the task force education saw an increase of 19 new patients diagnosed, which equates to a 13.97% percent change, while health systems that did not participate had an increase of 64 new patients, contributing to a 12.7% percent change as seen in Table 2. For context, the incidence of symptomatic acute intermittent prophyria is 0.13 per million per year.[1]

Table 3. Disease Management, Segmented by Task Force Participation

The following table shows the number of eligible patients who received an FDA-approved therapy at task force and non-task force health systems and their total percent change.

	2023	2024	Percent Change
Task Force Health Systems (HS)	16 patients	22 patients	37.50%
Non-Task Force HS	46 patients	42 patients	-8.70%

Tables 4 and 4a. Average Emergency Department (ED) Visits and Inpatient Stays for Patients Receiving Treatment With an FDA-Approved Product

The following tables display the mean number of emergency department (ED) visits and inpatient stays per eligible patient for patients who received treatment with an FDA-approved product in 2023 and 2024.

	2023 AVG ED Visits	2024 AVG ED Visits	Percent Change
28 Health Systems (HS)	1.08 ED visits (n = 51)	1.44 ED visits (n = 54)	33.33%
7 Task Force HS	1.45 ED visits (n = 11)	1.75 ED visits (n = 16)	20.69%
21 Non-Task Force HS	0.98 (n = 40)	1.32 ED visits (n = 38)	35.38%

	2023 AVG Inpatient Stays	2024 AVG Inpatient Stays	Percent Change
28 Health Systems (HS)	0.82 inpatient stays (n = 51)	0.98 inpatient stays (n = 54)	19.51%
7 Task Force HS	1.82 inpatient stays (n = 11)	1.63 inpatient stays (n = 16)	-10.44%
21 Non-Task Force HS	0.55 inpatient stays (n = 40)	0.71 inpatient stays (n = 38)	29.09%

Given the healthcare resource burden associated with AHP, Loopback analyzed data to evaluate healthcare utilization for patients receiving an FDA-approved treatment. Loopback analyzed data across all 28 health systems as well as at the 7 task force and 21 non-task force health systems to understand potential impact of the education initiative. A 33.33% increase in mean emergency room visits per patient and a 19.51% increase in mean inpatient stays per patient were observed across all health systems. A smaller increase in mean emergency room visits per patient was observed for the task force health systems compared to non-task force health systems (20.69% vs. 35.38%). Additionally, a reduction in inpatient stays per patient was observed for task force health systems compared to non-task force health systems (-10.44% vs. 29.09%).

Key Takeaways

The pharmacist-led initiative demonstrates the powerful impact of targeted healthcare professional education in rare genetic disorders like AHP. It also demonstrates the vital role health system pharmacies can play in provider education, and therefore the role they play in the improvement of patient diagnosis and management of rare diseases. The improvements observed across our seven task force health systems show several key takeaways:

Education Drives Awareness

Increased patient diagnoses by nearly 14%

Enhanced understanding of AHP diagnostic criteria and treatment options

Improved Disease Management

Increased utilization of disease management and treatment options for AHP

Potential for more timely, effective patient management

Healthcare System Benefits

Patients at task force health systems receiving appropriate disease management demonstrated a reduction in mean inpatient stays per patient

Future Directions

Our analysis identified several promising avenues for advancing the understanding and management of AHP.

Potential next steps include:

- Conducting a comprehensive analysis of diagnostic timelines to track the journey from symptom onset to treatment
- Expanding our dataset to include historical patient records prior to 2023
- Additional prospective studies to further evaluate the observed reduction in inpatient stays

Another valuable resource would be to bring together experts across health systems to share best practices and challenges related to timely diagnosis and management of AHP. Additionally, creating a clinical dashboard or support tool to help healthcare providers more quickly identify and refer AHP patients to a specialist for further evaluation may be impactful. By continuing to prioritize education and collaborative approaches, we can significantly improve the recognition, diagnosis, and management of AHP, ultimately enhancing patient care.

More information and resources about AHP are available online from the American Porphyria Foundation: **https://porphyriafoundation.org/** and the United Porphyrias Association: **https://www.porphyria.org/.**

Recognition

Thank you also to the Acute Hepatic Porphyria Task Force Committee Members who made this program possible:

- **Rushabh Shah**, PharmD, MBA, AAHIVP, CSP, System Director, Specialty and Home Delivery Pharmacy, UNC Health

- **Melissa Slayton**, PharmD, Specialty Clinical Pharmacist, Regional One Health

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