Real-world healthcare resource utilization in individuals with phenylketonuria: A retrospective observational study in the United States

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Introduction

- Phenylketonuria (PKU) is a rare genetic disorder caused by deficiency of the phenylalanine hydroxylase enzyme, which results in decreased metabolism and elevated levels of the amino acid phenylalanine (Phe) in the blood[1]
- Medical nutrition therapy (MNT) – which includes dietary restriction of Phe, supplemented with specialized medical formula with no/low amounts of Phe – has historically been the cornerstone of treatment of PKU, to prevent severe intellectual disability, epilepsy, and behavioral problems[1–4]
- Although PKU is well understood from a medical perspective, the socioeconomic impact of PKU is unclear[5–7]
- Some studies have suggested a high health economic burden for individuals with PKU, driven particularly by pharmaceutical costs in the US[8–10]
- The impact of PKU on healthcare resource utilization (HRU) in the US needs further research

Objective

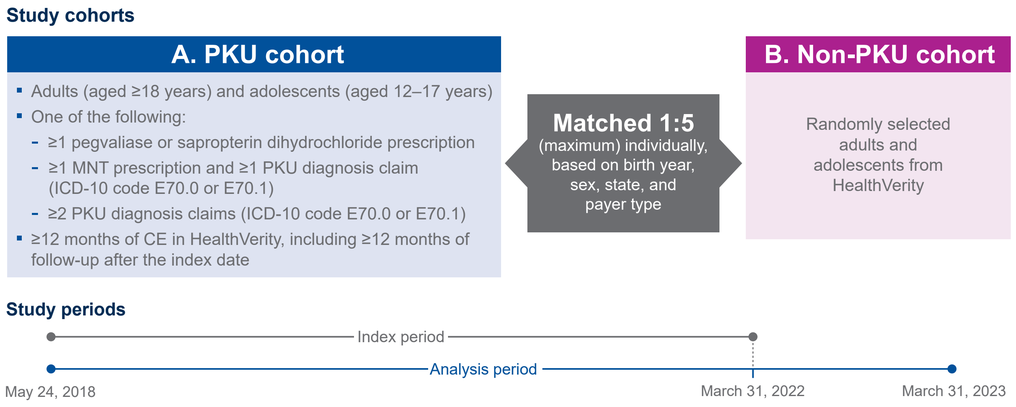
- To assess HRU in adults and adolescents with PKU compared with a matched non-PKU cohort from the general population in the US

Methods

Study design and data source

- This was a retrospective, observational cohort study of adults (aged ≥18 years) and adolescents (aged 12–17 years) with PKU (the PKU cohort) compared with adults and adolescents without PKU (the non-PKU cohort) in the US. The study used de-identified claims data from the HealthVerity database (**Figure 1**)
  - HealthVerity is a de-identified dataset comprising medical and pharmacy claims compiled from >75 data providers covering >330 million individuals in the US[11]
  - Patients with PKU were identified based on International Classification of Diseases (ICD)-10 diagnosis codes or receipt of PKU-related treatment
- This analysis covered a timeframe of May 24, 2018, to March 31, 2023 (analysis period; **Figure 1**)
- The index date served as the starting point for an individual's inclusion in the analysis, and was required to fall between May 24, 2018, and March 31, 2022 (index period; **Figure 1**), to allow a minimum of 12 months of follow-up
- Index date was defined by cohort:
  - (A) PKU cohort: Date of first evidence of PKU diagnosis (for individuals with no record of treatment) or first evidence of treatment with pegvaliase, sapropterin dihydrochloride, or MNT
  - (B) Non-PKU cohort: Date of first evidence of healthcare interaction
- HRU was evaluated after the index date, based on the number of hospitalizations and outpatient visits (by specialty), and the length of inpatient stays

Figure 1. Study design



CE, continuous enrollment; ICD, International Classification of Diseases; MNT, medical nutrition therapy; PKU, phenylketonuria.

Statistical analysis

- Mean differences in annualized HRU between the PKU cohort and the non-PKU cohort were evaluated using Welch's t-test (statistical significance was set at P <0.05)
- Annualized visits represent the number of visits an individual (or group of individuals) would be expected to have in 1 year, based on the observed data, where:
  - Annualized visits = (total number of visits / total first continuous enrollment [CE] duration) × 365.25
  - Total first CE duration is the continuous period within the study timeframe (May 24, 2018, to March 31, 2023) during which an individual remained enrolled in both medical and pharmacy benefits, starting from the first date of CE
- All analyses were conducted separately for adults and adolescents

Results

Demographics and characteristics

- Data from 1721 adults and 405 adolescents with PKU (the PKU cohort) were matched with 6536 adults and 1746 adolescents without PKU (the non-PKU cohort) (**Table 1**)
  - Median age was 35 years among adults and 14–15 years among adolescents; 60.1% of adults and 51.3% of adolescents were female
  - Most individuals were insured under Medicaid or commercial plans

Annualized HRU

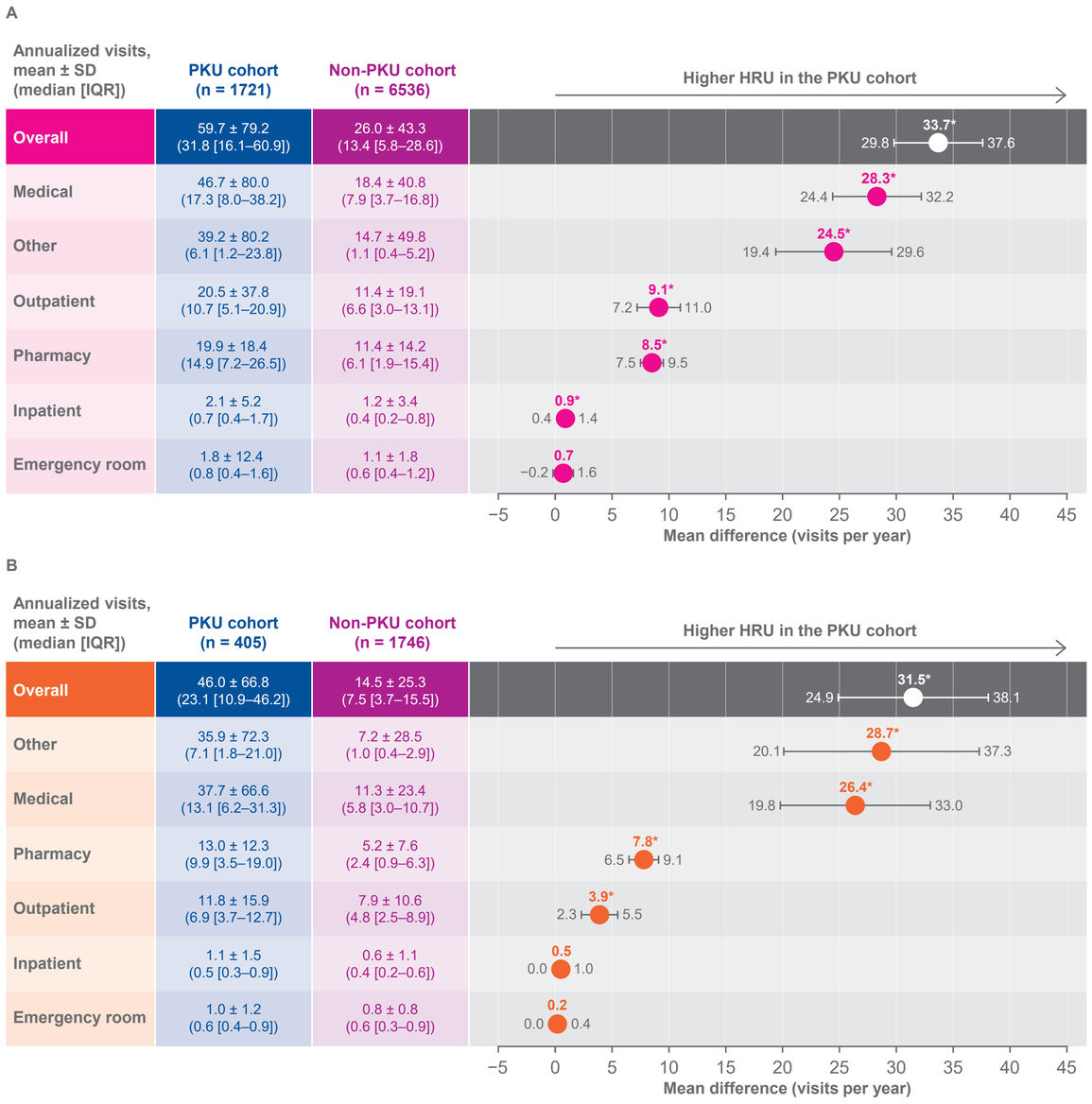
- Overall annualized HRU in adults with PKU was significantly higher than in adults without PKU, including a significantly higher mean number of medical, other, outpatient, pharmacy, and inpatient visits (**Figure 2A**)
  - Length of inpatient stay was significantly longer in the adult PKU cohort (mean ± standard deviation [SD], 50.1 ± 105.5 days; median [interquartile range (IQR)], 3.3 [1.5–26.8] days) than in the adult non-PKU cohort (mean ± SD, 12.3 ± 45.4 days; median [IQR], 1.7 [0.8–4.4] days), with a mean difference of 37.8 days (95% confidence interval [CI], 28.0–47.6)
- Overall annualized HRU in adolescents with PKU was significantly higher than in adolescents without PKU, including a significantly higher mean number of other, medical, pharmacy, and outpatient visits (**Figure 2B**)
  - Length of inpatient stay was numerically longer in the adolescent PKU cohort (mean ± SD, 8.0 ± 15.3 days; median [IQR], 1.9 [1.0–6.5] days) than in the adolescent non-PKU cohort (mean ± SD, 3.1 ± 6.4 days; median [IQR], 1.3 [0.8–2.4] days), with a mean difference of 4.9 days (95% CI, 0.0–9.8)

Table 1. Demographics and characteristics

	Adults		Adolescents	
Demographic/ characteristic	**PKU cohort (n = 1721)**	**Non-PKU cohort (n = 6536)**	**PKU cohort (n = 405)**	**Non-PKU cohort (n = 1746)**
Age, years				
Mean ± SD	40.4 ± 18.0	40.0 ± 16.8	14.3 ± 1.7	14.5 ± 1.8
Median (IQR)	(35 [26.0–54.0])	(35 [26.0–53.0])	(14 [13.0–16.0])	(15 [13.0–16.0])
Range, min–max	18–94	18–91	12–17	12–17
Sex				
Male	692 ± 40.2	2599 ± 39.8	208 ± 51.4	839 ± 48.1
Female	1029 ± 59.8	3937 ± 60.2	197 ± 48.6	907 ± 51.9
Geographic region				
South	547 ± 31.8	2084 ± 31.9	130 ± 32.1	601 ± 34.4
Midwest	390 ± 22.7	1368 ± 20.9	100 ± 24.7	427 ± 24.5
Northeast	407 ± 23.6	1595 ± 24.4	80 ± 19.8	349 ± 20.0
West	375 ± 21.8	1482 ± 22.7	94 ± 23.2	367 ± 21.0
Unknown	2 ± 0.1	7 ± 0.1	1 ± 0.2	2 ± 0.1
Payer type				
Medicaid	664 ± 38.6	2602 ± 39.8	229 ± 56.5	962 ± 55.1
Commercial	720 ± 41.8	3219 ± 49.3	152 ± 37.5	784 ± 44.9
Medicare Advantage	167 ± 9.7	715 ± 10.9	0	0
Dual	159 ± 9.2	0	19 ± 4.7	0
Unknown	11 ± 0.6	0	5 ± 1.2	0

Data are n (%) unless otherwise specified.
Percentages may not total 100% due to rounding.
IQR, interquartile range; PKU, phenylketonuria; SD, standard deviation.

Figure 2. Mean difference in annualized HRU between (A) adults with and adults without PKU and (B) adolescents with and without PKU



*P <0.05. Error bars are 95% CIs.
Annualized visits calculated among individuals with records of each respective visit type. Overall visits: Includes medical and pharmacy visits. Other visits: Visit type could not be determined due to missing type of bill/place of service codes. Medical visits: Includes all visits except pharmacy visits.
CI, confidence interval; HRU, healthcare resource utilization; IQR, interquartile range; PKU, phenylketonuria; SD, standard deviation.

Conclusion

- Total HRU among both adults and adolescents with PKU was higher compared with those without PKU, highlighting the significant economic burden of PKU on the healthcare system in the US

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References

1. van Spronsen FJ, et al. *Nat Rev Dis Primers.* 2021;7:36; **2.** van Wegberg AMJ, et al. *Mol Genet Metab.* 2025;145:109125; **3.** Ashe K, et al. *Front Psychiatry.* 2019;10:561; **4.** MacDonald A, et al. *Orphanet J Rare Dis.* 2020;15:171; **5.** Pessoa ALS, et al. *Orphanet J Rare Dis.* 2022;17:302; **6.** Bosch AM, et al. *J Inherit Metab Dis.* 2007;30:29–34; **7.** Simon E, et al. *Health Qual Life Outcomes.* 2008;6:25; **8.** Trefz F, et al. *Mol Genet Metab Rep.* 2021;27:100764; **9.** Darbà J. *J Med Econ.* 2019;22:1025–29; **10.** Rose AM, et al. *Mol Genet Metab Rep.* 2019;21:100523; **11.** HealthVerity. HealthVerity Marketplace. Accessed September 24, 2025. https://healthverity.com/marketplace/

Acknowledgments

Medical writing and formatting support was provided by Samantha Booth, PhD, at Aspire Scientific Ltd (Manchester, UK), funded by BioMarin Pharmaceutical Inc. (Novato, CA, USA), under the direction of the authors.

Disclosures

Karly S Louie and **Paul Okhuoya** are employees of, and hold stock or stock options in, BioMarin (UK) Ltd. **Sindhu Shivaramu** and **Komal Wadhwa** are employees of Definitive Healthcare, which provided analytical services to the sponsor. **Erin Muller** is an employee of BridgeBio. **Kristin Lindstrom** and **Erin Muller** are/were employees of, and hold stock or stock options in, BioMarin Pharmaceutical Inc.

Presented at the ISPOR EU 2025 Meeting: November 9–12, 2025, Glasgow, Scotland, UK