

Economic Burden of Propionic Acidemia by Age Stratum in the United States

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Background

- Propionic acidemia (PA), a rare inherited metabolic disorder, is associated with significant clinical burden, including episodes of life-threatening acute metabolic decompensation events and other complications^{1,2}
- However, real-world data on the healthcare resource utilization (HRU) and cost for patients with PA is limited

Objective

- To characterize the economic burden of patients with PA in the United States (US) by age stratum

Methods

Study design, data source, and study population

- This retrospective matched cohort study compared patients with PA with matched control subjects without PA using data from the IQVIA PharMetrics® Plus claims database from October 2015 to June 2022
- Eligible patients with PA (International Classification of Diseases, Tenth Edition [ICD-10-CM]: E71.121) and control subjects without PA (absence of ICD-10 diagnosis of PA) had non-missing age
- Patients' follow-up time was stratified into five age strata: 0–2 years, 3–6 years, 7–12 years, 13–17 years, and 18+ years
 - Index date for each age stratum was defined by cohort:
 - For patients with PA, the index date was the first observed PA diagnosis for the first age stratum and first day of continuous health plan enrollment in subsequent age strata
 - For control subjects, the index date was the first medical or pharmacy claim for the first age stratum and first day of continuous enrollment in in subsequent age strata
 - Patients were required to have at least 6 months of continuous eligibility after the index date in each age stratum
 - The observation period was defined as the period between the index date and the earliest date of end of continuous eligibility, end of age stratum, or end of data availability
- Control subjects were exactly matched 1:1 to patients with PA within each age stratum on age at index, index year (± 1 year), month of index date (± 1 month), sex, geographic region, insurance plan type, and partially on follow-up time
 - Control subjects were required to have at least the follow-up time of the matched patients with PA follow-up time rounded down to the nearest 6-month increment; the maximum follow-up requirement for control subjects was 3 years

Statistical analysis

- Patient and clinical characteristics during the 6 months post-index were described and compared between patients with PA and control subjects by age stratum
- Rates of all-cause HRU per patient-year (PPY) were compared during the observation period using generalized estimating equations and reported with rate ratios (RRs) and 95% confidence intervals (CIs)
- Mean and median annualized all-cause costs (inflated to 2022 US dollars) were compared during the observation period using Wilcoxon signed-rank tests and reported with mean cost differences and standard deviation

Table 1. Demographic and clinical characteristics of patients with PA and matched control subjects without PA

	Age strata									
	0–2 years n=32		3–6 years n=32		7–12 years n=36		13–17 years n=24		18+ years n=106	
	With PA	Control	With PA	Control	With PA	Control	With PA	Control	With PA	Control
Demographics on index										
Age, mean \pm SD (years)	0.5 \pm 0.6	0.5 \pm 0.6	4.0 \pm 1.2	4.0 \pm 1.1	8.6 \pm 1.8	8.6 \pm 1.8	14.8 \pm 1.7	14.8 \pm 1.7	40.6 \pm 17.6	40.6 \pm 17.6
Female, n (%)	19 (59.4)	19 (59.4)	15 (46.9)	15 (46.9)	10 (27.8)	10 (27.8)	8 (33.3)	8 (33.3)	55 (51.9)	55 (51.9)
Flu season,* n (%)	19 (59.4)	19 (59.4)	20 (62.5)	20 (62.5)	15 (41.7)	15 (41.7)	12 (50.0)	12 (50.0)	61 (57.5)	63 (59.4)
Insurance type, n (%)										
Commercial/self-insured	29 (90.6)	29 (90.6)	32 (100.0)	32 (100.0)	35 (97.2)	35 (97.2)	24 (100.0)	24 (100.0)	93 (87.7)	93 (87.7)
Medicare	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (10.4)	11 (10.4)
Medicaid	3 (9.4)	3 (9.4)	0 (0.0)	0 (0.0)	1 (2.8)	1 (2.8)	0 (0.0)	0 (0.0)	2 (1.9)	2 (1.9)
Clinical characteristics^b										
PA symptoms, n (%)										
Anorexia/failure to feed	22 (68.8)	11 (34.4)	21 (65.6)	5 (15.6)	12 (33.3)	5 (13.9)	10 (41.7)	1 (4.2)	62 (58.5)	8 (7.5)
Vomiting	19 (59.4)	8 (25.0)	15 (46.9)	4 (12.5)	4 (11.1)	3 (8.3)	9 (37.5)	1 (4.2)	17 (16.0)	0 (0.0)
Metabolic acidosis	11 (34.4)	2 (6.3)	16 (50.0)	0 (0.0)	5 (13.9)	2 (5.6)	2 (8.3)	0 (0.0)	27 (25.5)	4 (3.8)
Seizures	13 (40.6)	0 (0.0)	5 (15.6)	0 (0.0)	2 (5.6)	0 (0.0)	3 (12.5)	0 (0.0)	31 (29.2)	0 (0.0)
Hyperammonemia	5 (15.6)	1 (3.1)	6 (18.8)	1 (3.1)	8 (22.2)	0 (0.0)	3 (12.5)	0 (0.0)	15 (14.2)	4 (3.8)
PA-related comorbidities, n (%)										
Metabolic-related conditions	9 (28.1)	0 (0.0)	4 (12.5)	0 (0.0)	2 (5.6)	0 (0.0)	1 (4.2)	0 (0.0)	2 (1.9)	0 (0.0)
Cytopenias	10 (31.3)	0 (0.0)	14 (43.8)	0 (0.0)	6 (16.7)	0 (0.0)	2 (8.3)	0 (0.0)	6 (5.7)	0 (0.0)
Growth complications	13 (40.6)	0 (0.0)	4 (12.5)	0 (0.0)	1 (2.8)	0 (0.0)	1 (4.2)	0 (0.0)	21 (19.8)	0 (0.0)
Heart conditions	14 (43.8)	3 (9.4)	8 (25.0)	0 (0.0)	8 (22.2)	0 (0.0)	4 (16.7)	0 (0.0)	8 (7.5)	0 (0.0)
Neurologic or CNS/PNS conditions	1 (3.1)	0 (0.0)	1 (3.1)	0 (0.0)	3 (8.3)	0 (0.0)	6 (25.0)	0 (0.0)	12 (11.3)	0 (0.0)
Other comorbidities, n (%)										
Anxiety	11 (34.4)	4 (12.5)	17 (53.1)	3 (9.4)	16 (44.4)	1 (2.8)	8 (33.3)	2 (8.3)	35 (33.0)	7 (6.6)
Type II diabetes	0 (0.0)	0 (0.0)	2 (6.3)	0 (0.0)	2 (5.6)	1 (2.8)	5 (20.8)	0 (0.0)	30 (28.3)	16 (15.1)
Type I diabetes	0 (0.0)	0 (0.0)	1 (3.1)	0 (0.0)	1 (2.8)	0 (0.0)	2 (8.3)	0 (0.0)	38 (35.8)	3 (2.8)
Chronic pulmonary disease	1 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)	5 (13.9)	0 (0.0)	6 (25.0)	0 (0.0)	15 (14.2)	2 (1.9)
Renal disease	2 (6.3)	1 (3.1)	1 (3.1)	2 (6.3)	1 (2.8)	1 (2.8)	3 (12.5)	0 (0.0)	17 (16.0)	6 (5.7)
	1 (3.1)	0 (0.0)	3 (9.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.3)	0 (0.0)	20 (18.9)	0 (0.0)

Highlighted cells indicate statistical difference ($p < 0.05$)

*Flu season was an index date between September and March

^bClinical characteristics were summarized during the 6 months post-index

CNS, central nervous system; PA, propionic acidemia; PNS, peripheral nervous system; SD, standard deviation

Limitations

- The sample size of this study is limited owing to the rare nature of PA, especially within certain age strata. Nevertheless, the current study is the largest and first claims study of PA to our knowledge and within the known literature
- Results may not be generalizable to pediatric patients without commercial insurance (eg, patients covered by Medicaid). Further research in such payer type is needed
- Initial diagnosis of PA may not be recorded in the database

Conclusions

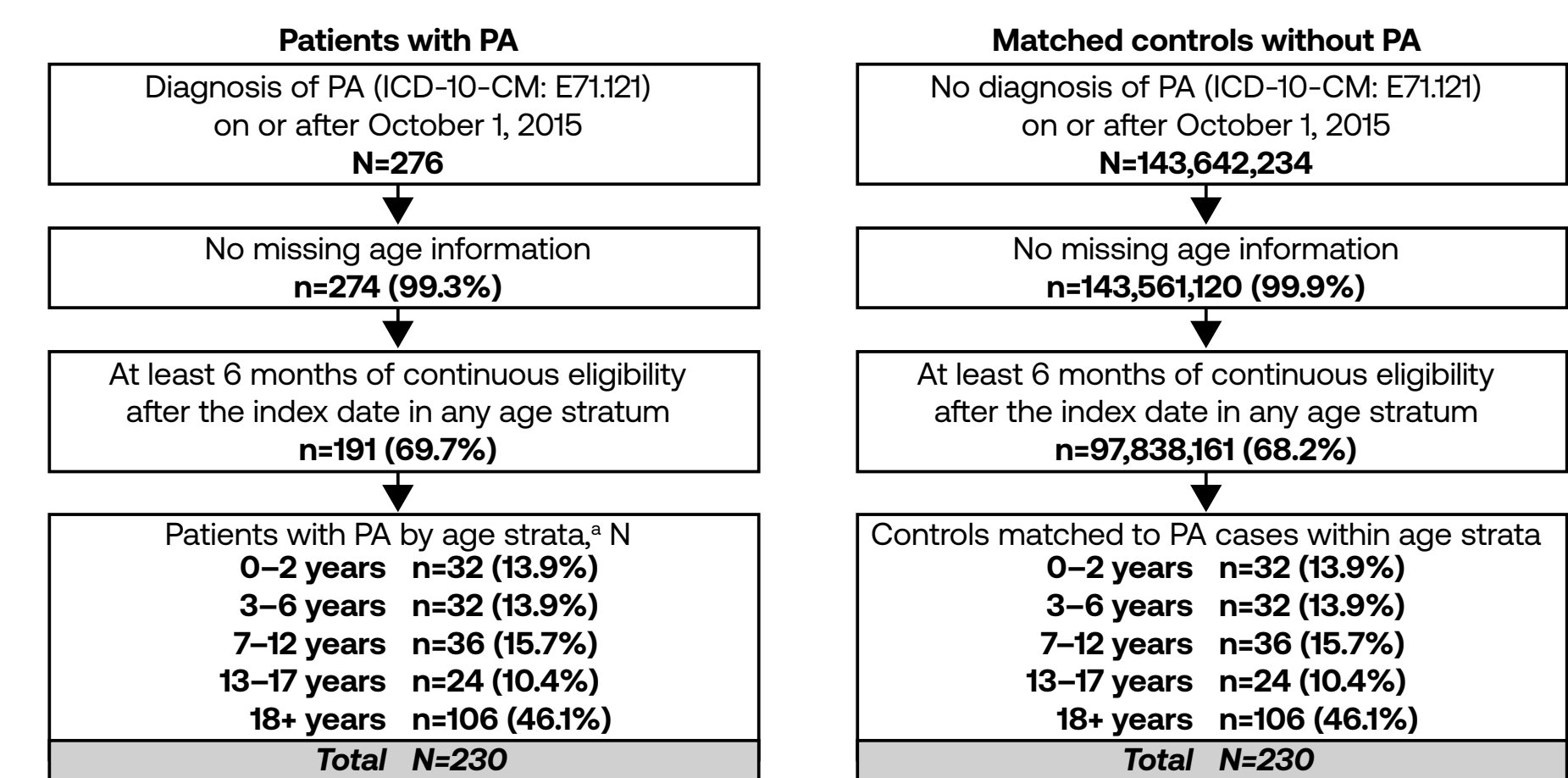
- This is the largest and first claims study of PA to our knowledge and within the known literature, which showed that patients with PA had significant HRU and economic burden compared with matched control subjects without PA across age strata, primarily driven by a higher burden of hospitalization
- Development of efficacious treatments for PA to help reduce the clinical burden, leading to reductions in economic burden

Results

Patient characteristics

- This study included 191 patients with PA and 230 age stratum-matched control subjects without PA (Figure 1)

Figure 1. Sample selection flowchart



*Patients with PA can contribute to multiple age strata. Therefore, the sum of age categories exceeds the total number of patients with PA in the study sample

ICD-10-CM, International Classification of Diseases, Tenth Edition; PA, propionic acidemia

- A total of 91.1% of patients had commercial insurance and 49.7% were female (Table 1)
- Patients with PA were more likely to have symptoms associated with PA, PA-related conditions, and other chronic comorbidities compared with control subjects across age strata in the 6 months after index
 - Across all ages for patients with PA, the most common PA symptoms were anorexia/failure to feed (27.8% overall), vomiting (26.2%), and metabolic acidosis (26.2%)
- Patients with PA had a median (range) of 2.0 (0.5–6.7) years of follow up

Rate of all-cause HRU among patients with PA compared with matched control subjects without PA

- Across all ages, patients with PA had 1.09 inpatient (IP) visits PPY, 24.27 outpatient (OP) visits PPY, and 1.44 emergency department visits PPY (Figure 2)
 - The rate of all-cause HRU was typically higher in younger patients than older patients (Table 2); control subjects had 5.04–9.53 OP visits PPY and <1 IP or emergency department visits PPY across age strata
- Patients with PA had significantly higher all-cause HRU rates compared with control subjects across age strata (RR [95% CI] 0–2 years: IP 10.36 [5.96, 19.85], OP 3.49 [3.20, 3.80]; 3–6 years: IP 78.55 [25.10, 475.12], OP 8.21 [7.34, 9.20]; 18+ years: IP 20.17 [12.23, 36.29], OP 2.62 [2.50, 2.75]; all $p < 0.001$; Table 2)

Healthcare costs among patients with PA and matched control subjects without PA

- Across all age strata, the mean (median) total healthcare costs were \$88,523 (\$16,929) among patients with PA, with medical costs accounting for about 68% of total costs (\$60,385 [\$14,674]; Figure 3)
 - In the overall population with PA, medical costs were driven primarily by hospitalization costs (\$40,621 [\$3254]; 67.3%), followed by outpatient costs (\$10,053 [\$3449]; 16.6%), home health costs (\$6189 [\$85]; 10.2%), and emergency room costs (\$3514 [\$476]; 5.8%)
- The total mean annualized cost difference between patients with PA and control subjects was highest at 0–2 years (\$205,883) and lowest at 7–12 years (\$20,169); adults also showed a significant difference at \$75,095 (all $p < 0.001$; Table 3)

Figure 2. Rate of all-cause HRU among patients with PA by age stratum

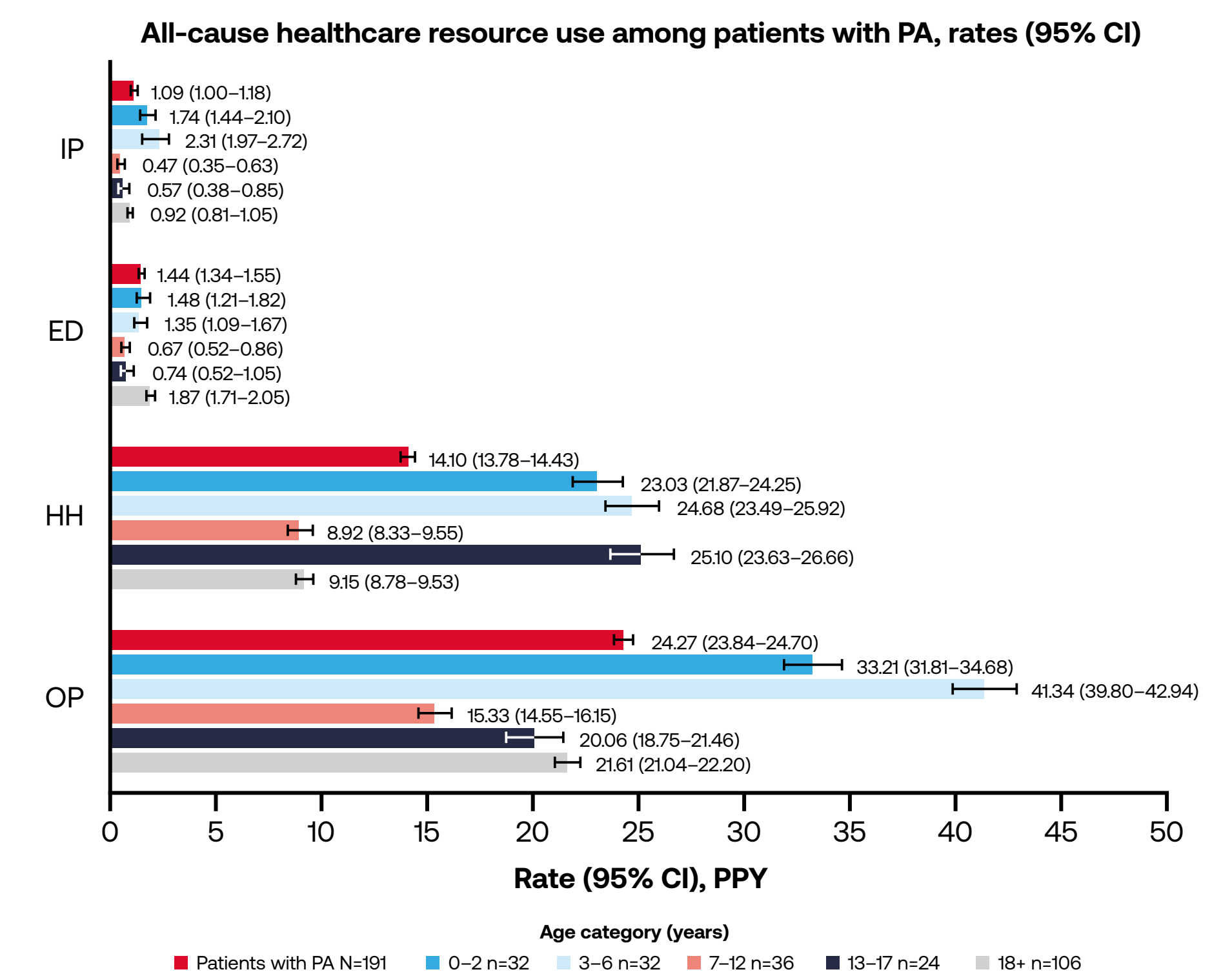


Table 2. Rate ratios of all-cause HRU among patients with PA vs matched control subjects without PA by age stratum

	Rate ratio (95% CI): PA vs control				
	0–2 years n=32 pairs	3–6 years n=32 pairs	7–12 years n=36 pairs	13–17 years n=24 pairs	18+ years n=106 pairs
Hospitalization	10.36 (5.96–19.85)	78.55 (25.10–475.12)	51.65 (11.28–915.66)	–	20.17 (12.23–36.29)
Outpatient visits	3.49 (3.20–3.80)	8.21 (7.34–9.20)	1.89 (1.74–2.06)	3.23 (2.83–3.70)	2.62 (2.50–2.75)
Home health visits	117.72 (72.49–209.41)	69.81 (47.81–107.45)	89.76 (52.17–173.43)	71.21 (45.08–121.79)	33.51 (27.14–41.98)
Skilled nursing facility visits	–	–	–	–	37.49 (8.05–667.77)
Emergency room visits	2.79 (1.93–4.11)	3.99 (2.57–6.46)	2.40 (1.57–3.74)	2.23 (1.23–4.25)	4.46 (3.68–5.44)
Prescription fills	6.28 (5.44–7.30)	8.75 (7.15–10.85)	8.75 (5.35–6.98)	8.82 (7.40–10.60)	3.81 (3.63–3.99)

All rate ratios are statistically significant at $p < 0.05$

CI, confidence interval; ED, emergency department; HH, home health; HRU, healthcare resource utilization; IP, inpatient; OP, outpatient; PA, propionic acidemia; PPY, per patient-year; RR, rate ratio

Figure 3. Annualized all-cause healthcare costs among patients with PA vs matched control subjects without PA by age stratum

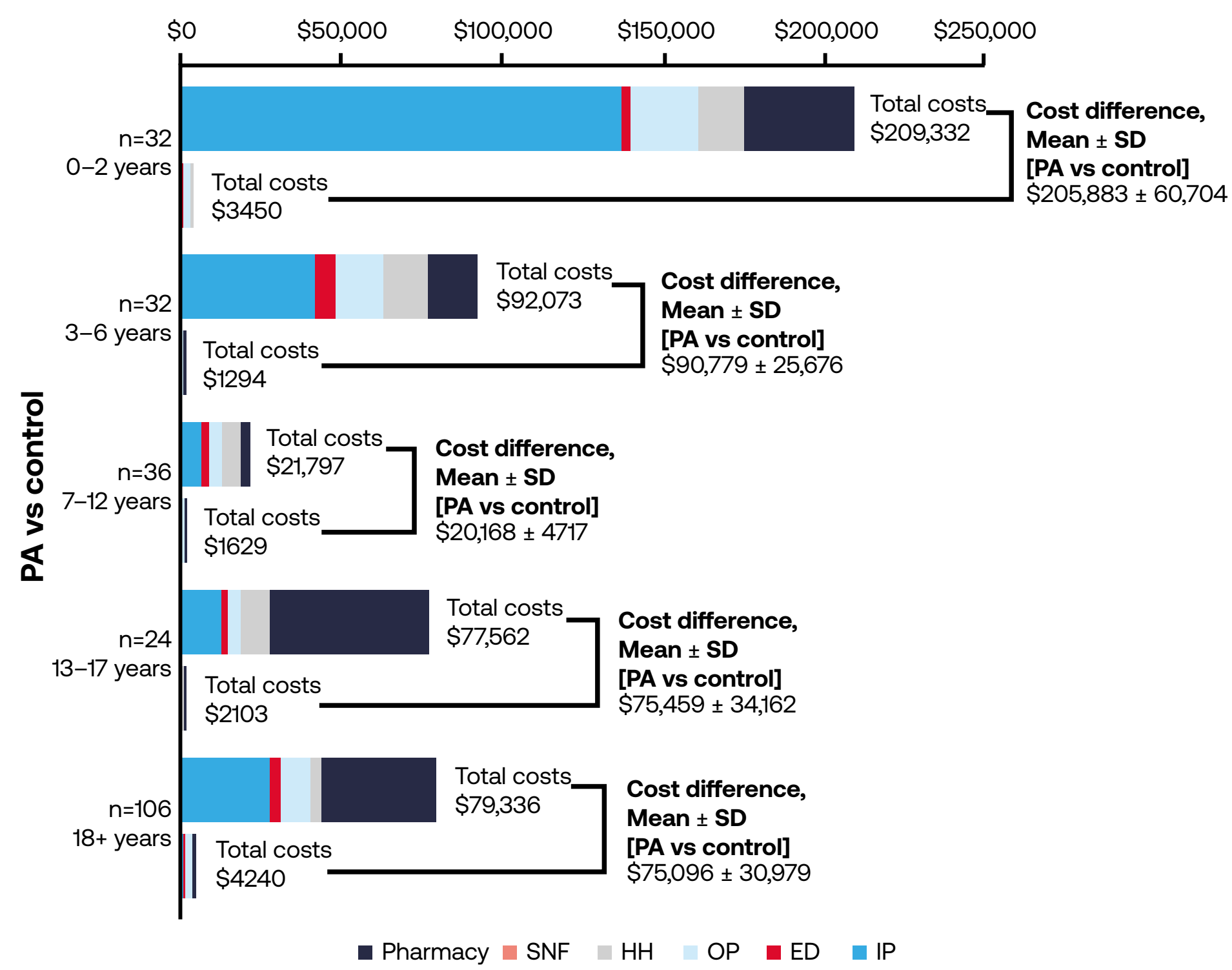


Table 3. Cost differences of annualized all-cause healthcare costs among patients with PA vs matched control subjects without PA by age stratum

	Cost difference, mean \pm SD: PA vs control				
	0–2 years n=32 pairs	3–6 years n=32 pairs	7–12 years n=36 pairs	13–17 years n=24 pairs	18+ years n=106 pairs
Total medical and pharmacy costs	\$205,883 \pm 60,704	\$90,779 \pm 25,676	\$20,168 \pm 4,717	\$75,459 \pm 34,162	\$75,096 \pm 30,979
Total medical costs	\$171,377 \pm 49,986	\$75,661 \pm 22,541	\$17,314 \pm 4,434	\$26,695 \pm 8,280	\$39,750 \pm 8,197
Hospitalization costs	\$137,046 \pm 43,495	\$41,674 \pm 15,425	\$6,966 \pm 3,564	\$12,972 \pm 6,082	\$26,861 \pm 6,603
Outpatient visit costs	\$18,435 \pm 6,155	\$14,347 \pm 4,134	\$3,929 \pm 856	\$3,883 \pm 855	\$7,075 \pm 2,268
Home health visit costs	\$13,903 \pm 4,389	\$13,708 \pm 8,184	\$5,585 \pm 1,866	\$7,910 \pm 2,961	\$2,727 \pm 587
Skilled nursing facility costs	\$0 \pm 0	\$21 \pm 21	\$0 \pm 0	\$0 \pm 0	\$7 \pm 7
Emergency room costs	\$1,994 \pm 559	\$5,911 \pm 4,186	\$835 \pm 369	\$1,930 \pm 772	\$3,079 \pm 902
Total pharmacy costs	\$34,506 \pm 19,863	\$15,118 \pm 13,955	\$2,855 \pm 1,191	\$48,764 \pm 31,077	\$35,346 \pm 29,760

All cost differences are statistically significant at $p < 0.05$, except for skilled nursing facility costs

ED, emergency department; HH, home health; IP, inpatient; OP, outpatient; PA, propionic acidemia; SD, standard deviation; SNF, skilled nursing facility

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Acknowledgments

Editorial, layout, and formatting assistance was provided by Sarah Millard, of Caudex, a division of IPG Health Medical Communications, and was funded Moderna, Inc. This study was funded by Moderna, Inc.

Disclosures

GB and VS are employees of and stockholders in Moderna, Inc. FM, MC, EC, AZ, JLL, and LZ are employees of Analysis Group, Inc, which receives research funding from Moderna, Inc.