

Claims-Based Analysis of Homocysteine Testing, Elevated Homocysteine Levels, and Homocystinuria Diagnosis in the U.S.

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Background

- Classical homocystinuria (HCU) is a rare inherited metabolic disorder in which the body is unable to process the amino acid homocysteine (HCY), causing severe developmental and physical disabilities.¹
- HCU is underdiagnosed at birth due to screening that is inadequately sensitive. Newborn screening typically tests for HCU indirectly by measuring the concentration of methionine (a precursor to HCY), rather than HCY itself. As a result, newborn screening often produces false negatives.²
- Recent research has estimated the prevalence of HCU in the U.S. to be 1 in 10,000 people,³ substantially higher than prior estimates of 1 in 100,000-200,000 in the U.S. and 1 in 200,000-335,000 worldwide.⁴⁻⁶ Several studies have estimated the birth prevalence of HCU to be much higher based on genetic modeling.^{7,8}
- Symptoms of HCU can be mistaken for those of other disorders and vary from patient to patient. Adults not diagnosed with HCU during childhood are frequently misdiagnosed or diagnosed later in life due to comorbid conditions and abnormally high blood levels of total homocysteine (tHcy).
- Delayed diagnosis of HCU results in delayed therapy and the earlier development of comorbid conditions.
- Phenylketonuria (PKU), another rare inherited metabolic disorder, is estimated to occur in approximately 1 in 15,000 people in the United States.⁹ Unlike HCU, the newborn screen for PKU is sensitive, and the majority of PKU patients are diagnosed at birth.¹⁰

Objective

- To examine the all-cause healthcare costs and resource utilization between HCU and PKU patients.

Methods

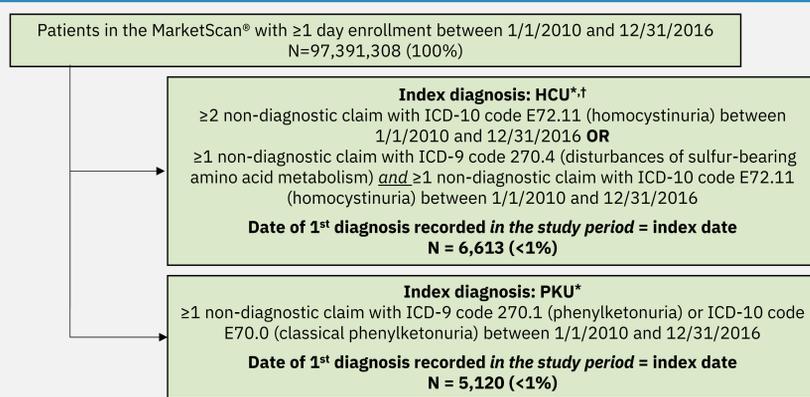
Data Source

- Administrative claims in the IBM® MarketScan® Commercial and Medicare Supplemental Databases from January 1, 2010 through December 31, 2016.

Patient Selection and Study Design

- Figure 1 presents the patient selection criteria.

Figure 1. Patient Selection



*The patient population represents a population with prevalent disease. Patients may have been diagnosed prior to the beginning of the study time period.
†For patients with ICD-9 code 270.4, an accompanying ICD-10 diagnosis code E72.11 was required, as 270.4 is not specific to HCU itself, and patients with this diagnosis may have other sulfur-bearing amino-acid metabolism disorders.
HCU, homocystinuria; PKU, phenylketonuria.

Outcomes and Analysis

- Demographic characteristics (age, sex, region, urban residence, plan type) were captured on the index date.
- All-cause healthcare resource utilization rates (percentage of patients, mean number of visits, mean number of hospital days (inpatient only)) and all-cause costs among HCU and PKU patients were calculated among all patients and compared for the following components of care:
 - Inpatient
 - Outpatient (emergency room [ER], office visits, lab test, other outpatient care)
 - Outpatient pharmacy
- Total all-cause medical costs (inpatient + outpatient) and total all-cause healthcare costs (total medical + outpatient pharmacy) among all patients were also calculated.
- Patient follow-up was variable in length. As such, the number of each claim type (e.g., number of IP admissions) and costs are reported as per patient per month (PPPM).
- Costs were based on paid amounts of adjudicated claims and adjusted for inflation using the Consumer Price Index (CPI) and standardized to 2017 U.S. dollars.
- Costs for services provided under capitated arrangements were estimated using payment proxies that were computed based on paid claims at the procedure level using the MarketScan Commercial and Medicare Supplemental Databases.
- A p-value of 0.05 was considered a priori as the threshold for statistical significance.

Results

Patient Selection and Patient Characteristics

- A total of 6,613 HCU patients and 5,120 PKU patients met the selection criteria outlined above (Figure 1).
- The mean length of follow-up was 12.7 (standard deviation 12.4) months for HCU patients, and 26.4 (standard deviation 22.1) months for PKU patients.
- The average age of HCU patients (55.5 years) over the study time period was 38 years older than that for PKU patients (17.5 years; Table 1).
- Both cohorts were just less than half male, mostly resided in urban areas, and were primarily covered by EPO/PPO plans (Table 1).

Table 1. Patient Demographic Characteristics on Index Date, HCU vs. PKU

	HCU N=6,613	PKU N=5,120
Average age, years, mean (SD)	55.5 (14.8)	17.5 (21.0)*
Male, %	49.2%	47.0%*
Region, %		
Northeast	12.4%	17.7%
North Central	23.8%	19.8%
South	43.5%	34.2%
West	20.0%	27.1%
Missing	0.3%	1.2%
Residence in an urban area, %	90.4%	85.1%*
Plan type, %		
Comprehensive	12.9%	2.7%
HMO	6.5%	10.9%
EPO/PPO	56.1%	64.0%
POS/POS with capitation	7.4%	6.5%
Other	14.8%	9.9%
Unknown	2.2%	6.0%

*p<0.05, HCU vs. PKU. EPO, exclusive provider organization; HMO, health maintenance organization; HCU, homocystinuria; PKU, phenylketonuria; POS, point of service; PPO, preferred provider organization; SD, standard deviation.

Results

All-Cause Healthcare Resource Utilization, HCU vs. PKU

- Compared with PKU patients, HCU patients had significantly more all-cause:
 - Inpatient admissions (0.04 ± 0.49 vs. 0.01 ± 0.08 PPPM, p=0.001).
 - ER visits (0.05 ± 0.29 vs. 0.04 ± 0.27 PPPM, p=0.049).
 - Lab tests (2.4 ± 5.5 vs. 1.2 ± 3.6 PPPM, p<0.001).
 - Outpatient prescriptions (2.5 ± 3.1 vs. 1.0 ± 2.4 PPPM, p<0.001).

Table 2. Post-Index† All-Cause Healthcare Utilization, HCU vs. PKU

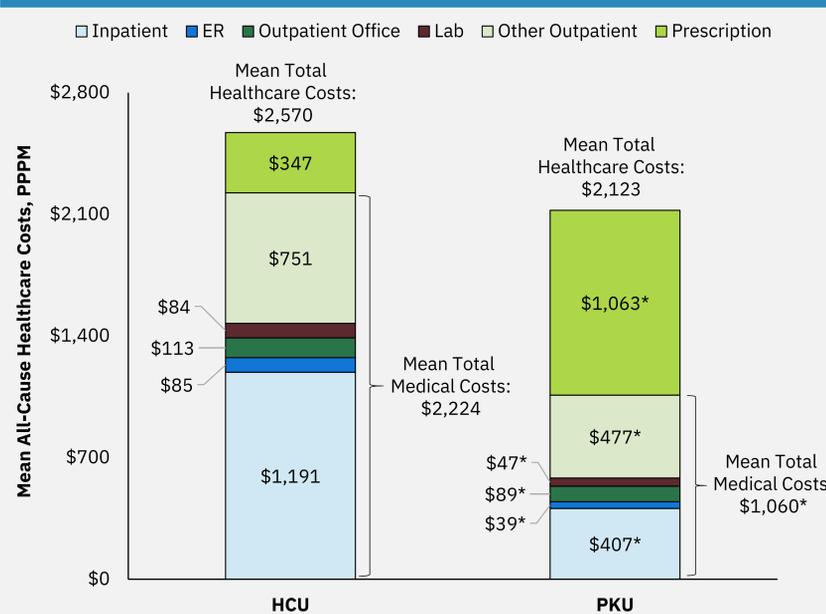
	HCU N=6,613	PKU N=5,120
Inpatient (IP) admissions		
Patients with ≥1 IP admission, %	13.5%	12.3%
Number of IP admissions PPPM, mean (SD)	0.04 (0.49)	0.01 (0.08)*
Total days of hospitalization PPPM, mean (SD)	0.17 (1.70)	0.08 (0.68)*
Emergency room (ER) visits		
Patients with ≥1 ER visit, %	20.4%	30.8%*
Number of ER visits PPPM, mean (SD)	0.05 (0.29)	0.04 (0.27)*
Outpatient (OP) office visits		
Patients with ≥1 OP office visit, %	96.1%	95.0%*
Number of OP office visits PPPM, mean (SD)	0.97 (1.23)	0.65 (1.56)*
Lab tests		
Patients with ≥1 OP lab test, %	80.6%	87.3%*
Number of OP lab tests PPPM, mean (SD)	2.4 (5.5)	1.2 (3.6)*
Other OP visits		
Patients with ≥1 other OP visit, %	91.7%	95.1%*
Number of other OP visits PPPM, mean (SD)	1.5 (2.3)	1.0 (4.8)*
OP prescriptions		
Patients with ≥1 OP prescription, %	89.1%	81.0%*
Number of OP prescriptions PPPM, mean (SD)	2.5 (3.1)	1.0 (2.4)*

†Post-index period is variable length, from the index date through the end of patient's MarketScan enrollment, or 12/31/2016 (whichever is earlier); *p<0.05, HCU vs. PKU.
ER, emergency room; HCU: homocystinuria; PKU, phenylketonuria; PPPM, per patient per month; OP, outpatient; SD, standard deviation.

All-Cause Healthcare Costs, HCU vs. PKU

- Compared with PKU patients, HCU patients had:
 - Nearly three time higher all-cause inpatient admission costs (\$1,191 ± \$26,270 vs. \$407 ± \$4,564 PPPM, p=0.035).
 - Twice as high all-cause ER costs (\$85 ± \$514 vs. \$39 ± \$178 PPPM, p<0.001).
 - 80% higher all-cause lab costs (\$84 ± \$333 vs. \$47 ± \$176 PPPM, p<0.001).
 - Double the total all-cause medical costs (\$2,224 ± \$26,689 vs. \$1,060 ± \$6,777 PPPM, p=0.002).

Figure 2. Post-Index† All-Cause Healthcare Costs, HCU vs. PKU



†Post-index period is variable length, from the index date through the end of patient's MarketScan enrollment, or 12/31/2016 (whichever is earlier); *p<0.05, HCU vs. PKU.
ER, emergency room; HCU, homocystinuria; PKU, phenylketonuria, PPPM, per patient per month.

Conclusion

- HCU patients had higher rates of all-cause healthcare utilization in nearly all components of care captured compared to their PKU counterparts.
- Additionally, HCU patients incurred higher monthly all-cause medical costs. compared to PKU patients, with more than half of the medical costs for HCU patients attributable to IP admissions.
- Better physician understanding and awareness of the diagnosis and management of HCU and improved screening, diagnosis, and treatment are necessary to reduce the medical care resource utilization and costs associated with HCU.

Limitations

- This study was limited to only those individuals with commercial health coverage or private Medicare supplemental coverage. Results of this analysis may not be generalizable to individuals with other insurance or without health insurance coverage.
- The data in this study was limited to data found in administrative claims, which is subject to data coding limitations and data entry error. There is also potential for misclassification of diagnoses or other study outcomes, based on the limitations of claims data.
- The analysis was conducted during the study time period between January 1, 2006 and March 31, 2016. Any temporal differences that may exist were not captured in this study.

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