

Validation of a patient identification algorithm to estimate the prevalence of classical homocystinuria (HCU) in the United States (US)

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Background: Historical US prevalence estimates of HCU range from 1 per 100,000–200,000; a recent study suggests the prevalence is up to 10 times higher. This study aims to estimate the true prevalence of HCU through use of a patient identification algorithm which considers diagnosis codes, total homocysteine (tHcy) values and clinical presentations indicative of HCU.

Methods: This retrospective analysis used IQVIAs PharMetrics® Plus and Ambulatory Electronic Medical Record (AEMR; 2018-2021) databases. A patient identification algorithm was developed with expert clinical input. Strict and broadly defined cohorts were identified based on the presence of ICD codes, tHcy levels, and clinical presentation. The cohorts were used to calculate prevalence estimates, standardized using US Census Bureau data.

Results: Average annual standardized prevalence estimates (2018-2021) were 0.84 (strict cohort) and 3.52 (broad cohort) per 100,000. Overall, 54.1% in the AEMR data during the study period had lab data available; nearly all patients in the strict cohort (99.5%) had tHcy results. Among those with elevated tHcy ($\geq 20 \mu\text{M}$), 80.4% had tHcy $\leq 50 \mu\text{M}$, suggesting their condition may be well managed. In the broad cohort, 81.6% of patients did not have a diagnosis code for HCU; among these patients, 2.4% had tHcy $> 50 \mu\text{M}$ and 34.1% had tHcy between 20 and 50 μM with clinical presentation indicative of HCU. Overall, 57.4% of patients without a diagnosis code for HCU had no tHcy results available but had multiple clinical presentations indicative of HCU.

Discussion/Conclusion: These findings are consistent with a recent analysis using a different database and further confirm that HCU prevalence estimates vary widely based on the approach and cohort definitions. A large proportion of patients with high tHcy levels and clinical presentations indicative of HCU did not have a corresponding diagnosis of HCU, suggesting potential underdiagnosis and/or underreporting.

Characters (with spaces): 1,969/2,000