CLINICAL BURDEN OF CLASSICAL HOMOCYSTINURIA IN THE UNITED STATES: A RETROSPECTIVE CLAIMS ANALYSIS

TRAVERE THERAPEUTICS

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RESULTS

Baseline Patient Demographics

- There were 1,875 patients in the HCU cohort (Table 1)
    - Mean age was 53 years and 37.2% of patients were female
    - Most patients (60.5%) were between ages 45 and 64
    - Median follow-up time was 25.1 months
- There were 59,044,824 patients in the non-HCU cohort
    - There was a nearly even gender distribution (52.3% female)
    - The highest proportion of patients were between ages 45 and 64

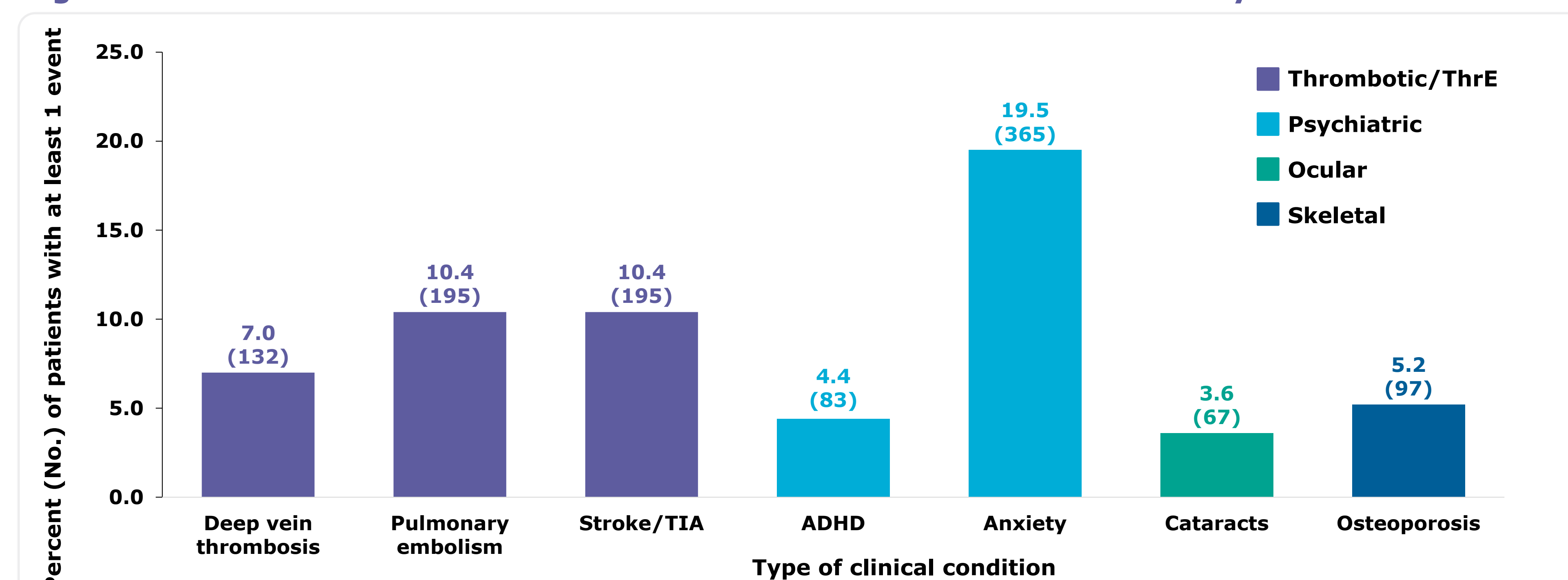### Table 1. Baseline Patient Demographics and Clinical Characteristics

	HCU cohort (n=1,875)
Gender, female, No. (%)	698 (37.2)
Age at index (continuous), y	
Mean (SD)	52.6 (13.4)
Age group at index, y, No. (%)	
<10	6 (0.3)
10–17	17 (0.9)
18–34	167 (8.9)
35–44	281 (15.0)
45–54	458 (24.4)
55–64	677 (36.1)
65–74	207 (11.0)
≥75	61 (3.3)
Unknown or missing	1 (0.1)
Follow-up time, months*	
Median (Q1, Q3)	25.1 (15.5, 40.6)
Charlson comorbidity index, mean (SD)	0.6 (1.1)

Abbreviations: HCU, classical homocystinuria; Q1, 1st quartile; Q3, 3rd quartile; SD, standard deviation; y, years.
*Time based on the end of continuous enrollment during the study.

Clinical Conditions in Patients With Classical Homocystinuria

- Among patients in the HCU cohort, the most common individual clinical conditions were anxiety (19.5%), pulmonary embolism (10.4%), stroke/TIA (10.4%), deep vein thrombosis (7.0%), osteoporosis (5.2%), attention-deficit/hyperactivity disorder (4.4%), and cataracts (3.6%) (Figure 3)

Figure 3. Most Common Clinical Conditions in Patients With Classical Homocystinuria

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ThrE, thromboembolic; TIA, transient ischemic attack. The denominator for percentages is the total number of patients with each type of category of event (thrombotic/ThrE, ocular, skeletal, etc.).

Clinical Events in Patients With Classical Homocystinuria and Patients in the General Population

- Clinical event rates were generally higher among patients in the HCU cohort
- In the HCU cohort, 83.0% of patients had at least one clinical event and 35.9% had multiple (≥2) clinical events
- The frequency of thrombotic/ThrE events was 21.2% in the HCU cohort and 4.7% in the non-HCU cohort (Figure 2)
- Neurological (3.7%), cognitive impairment (2.1%), psychiatric (23.2%), and skeletal (7.9%) events occurred more frequently in the HCU-cohort (Figure 2)
    - In the non-HCU cohort, neurological, cognitive impairment, psychiatric, and skeletal events occurred at rates of 1.1%, 0.6%, 17.6%, and 6.2%, respectively (Figure 2)

Figure 2. Clinical Events in Patients With Classical Homocystinuria and in the General Population

Abbreviations: HCU, classical homocystinuria; ThrE, thromboembolic.

Other Clinical Events in Patients With Classical Homocystinuria and Patients in the General Population

- Hypertension and hyperlipidemia were the most common of the other conditions assessed in both the HCU cohort and the non-HCU cohort
    - The proportion of patients with hypertension was 53.3% in the HCU cohort and 21.1% in the non-HCU cohort (Table 2)
    - The proportion of patients with hyperlipidemia was 48.7% in the HCU cohort and 13.9% in the non-HCU cohort (Table 2)

Table 2. Other Events in Patients With Classical Homocystinuria and Patients in the General Population

	HCU cohort (n=1,875)	General (non-HCU) cohort (n=59,044,824)
Total patients with other conditions	1,297 (69.2)	15,634,011 (26.5)
Essential (primary) hypertension	1,000 (53.3)	12,436,502 (21.1)
Hyperlipidemia	914 (48.7)	8,213,642 (13.9)
Disorder of pigmentation	16 (0.9)	507,916 (0.9)
Other chronic pancreatitis	4 (0.2)	58,888 (0.1)
Other/primary/secondary spontaneous pneumothorax	0 (0.00)	11,109 (0.0)
Crowding of fully erupted teeth	0 (0.0)	5,840 (0.0)

Abbreviations: HCU, classical homocystinuria. Expressed as No. (%).

CONCLUSIONS

✓ The clinical burden in US patients with HCU identified within the PharMetrics Plus database is substantially higher than in the general non-HCU population

✓ Rates of thrombotic/ThrE conditions, neurological disease, and cognitive impairment occurred at a much higher frequency in patients with HCU

✓ New treatments may help reduce the clinical burden of HCU

ABBREVIATIONS

ADHD, attention-deficit/hyperactivity disorder; HCU, classical homocystinuria; ICD-10, International Classification of Diseases, Tenth Revision; No., number; Q1, 1st quartile; Q3, 3rd quartile; SD, standard deviation; ThrE, thromboembolic; TIA, transient ischemic attack; US, United States; y, years.

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INTRODUCTION

- Classical homocystinuria (HCU) is a rare metabolic disorder characterized by elevated total plasma levels of homocysteine[1,2]
- HCU is a heterogeneous disease affecting the vascular, nervous, ocular, and skeletal systems[2,3]
- This can lead to multiple potential complications including thrombotic/thromboembolic (ThrE) events, developmental delays and intellectual disabilities, ectopia lentis, myopia, and/or skeletal abnormalities[2,3]
- Research on the clinical burden of patients with HCU in the United States (US) compared with the general population is limited
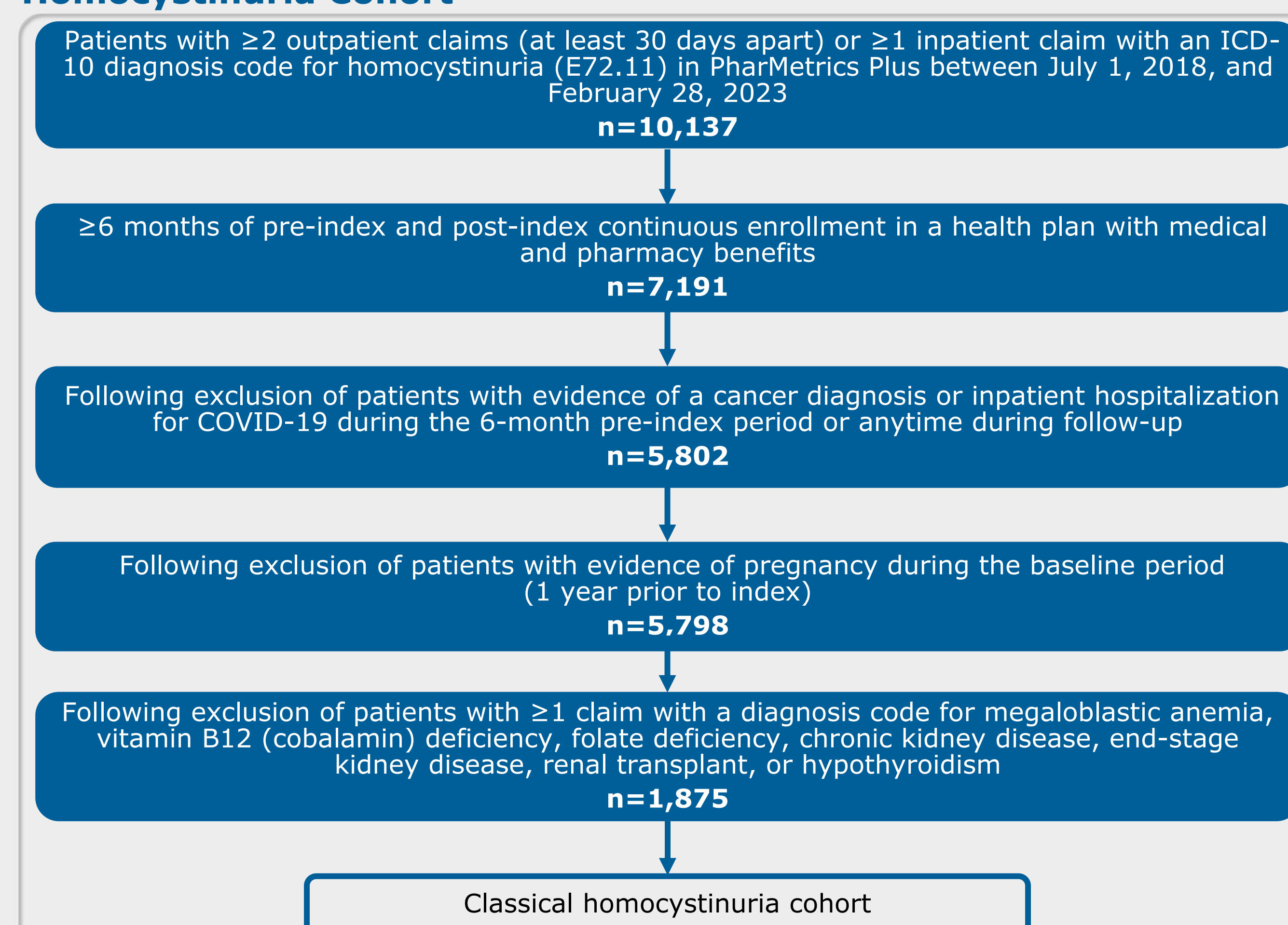
Objective

- The objective of this study was to estimate rates of specific clinical events relevant to HCU in a cohort of patients with HCU and in a general (non-HCU) population

METHODS

Study Design and Data Source

- This was a retrospective cohort study using the IQVIA PharMetrics Plus database
- The study period was from January 1, 2018, through February 28, 2023
- Index date was the date of the first claim with an ICD-10 diagnosis code for homocystinuria (E72.11) observed during the study period
- Patients in the HCU cohort were included if they had ≥2 outpatient claims (at least 30 days apart) or ≥1 inpatient claim with an ICD-10 diagnosis code for homocystinuria and at least 6 months of pre- and post-index continuous enrollment (Figure 1)
- Identification of patients with HCU was further refined by excluding those with evidence of secondary causes of elevated homocysteine (eg, megaloblastic anemia, vitamin B12 deficiency, folate deficiency, chronic kidney disease, and end-stage kidney disease) (Figure 1)
- The general (non-HCU) cohort included patients in the IQVIA PharMetrics Plus database with a minimum of 1 month of continuous enrollment and no evidence of HCU during the study period (January 1, 2018-February 28, 2023)
- Major clinical events* were assessed anytime during the study period and included thrombotic/ThrE, neurological disease, psychiatric, ocular, skeletal, and other conditions
- Clinical events were defined as ≥1 claim of event-related inpatient admission, emergency department, or outpatient visit anytime pre- or post-index
- Clinical events were reported descriptively for both cohorts

Figure 1. Inclusion and Exclusion Criteria for the Classical Homocystinuria Cohort

Patients with ≥2 outpatient claims (at least 30 days apart) or ≥1 inpatient claim with an ICD-10 diagnosis code for homocystinuria (E72.11) in PharMetrics Plus between July 1, 2018, and February 28, 2023
n=10,137

↓

≥6 months of pre-index and post-index continuous enrollment in a health plan with medical and pharmacy benefits
n=7,191

↓

Following exclusion of patients with evidence of a cancer diagnosis or inpatient hospitalization for COVID-19 during the 6-month pre-index period or anytime during follow-up
n=5,802

↓

Following exclusion of patients with evidence of pregnancy during the baseline period (1 year prior to index)
n=5,798

↓

Following exclusion of patients with ≥1 claim with a diagnosis code for megaloblastic anemia, vitamin B12 (cobalamin) deficiency, folate deficiency, chronic kidney disease, end-stage kidney disease, renal transplant, or hypothyroidism
n=1,875

↓

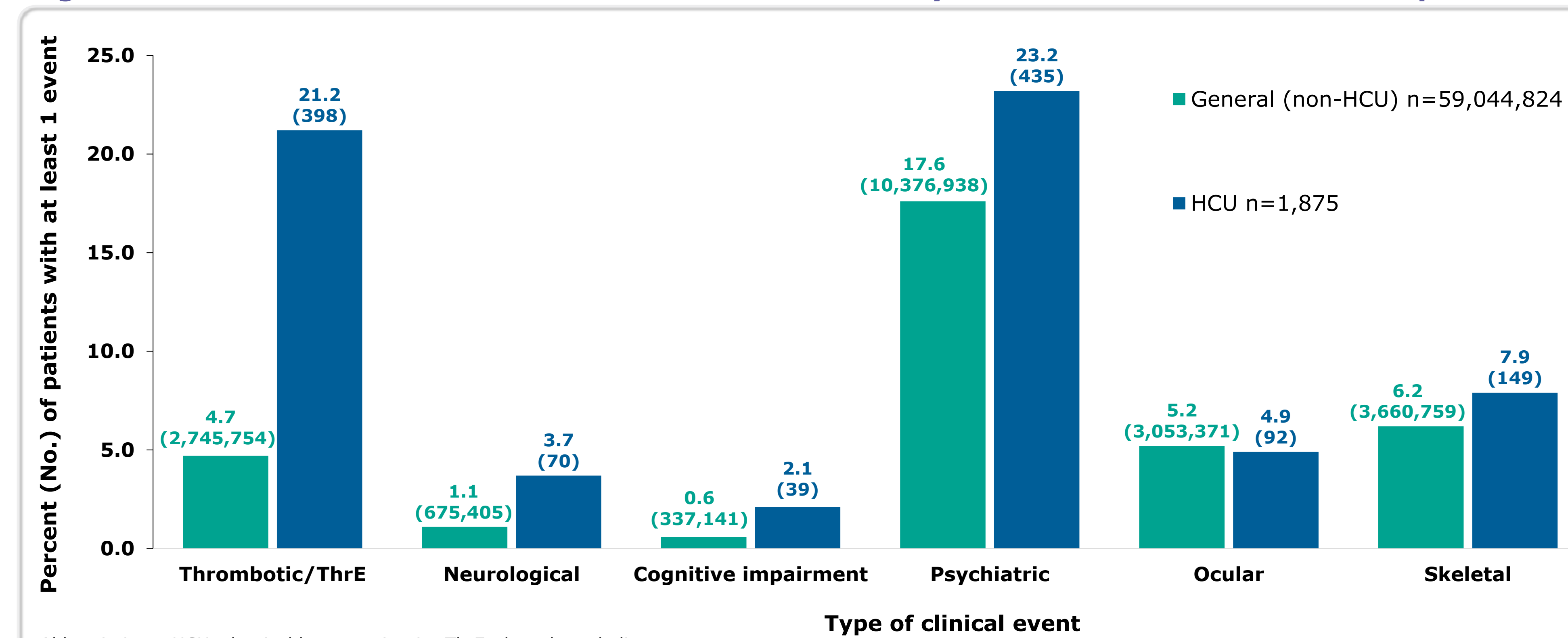Classical homocystinuria cohort

Abbreviations: ICD-10, International Classification of Diseases, Tenth Revision.

*Major clinical conditions included thrombotic/thromboembolic conditions (deep vein thrombosis, pulmonary embolism, renal vein/portal vein/sinus/cerebral venous/arterial thrombosis, myocardial infarction, stroke, transient ischemic attack), neurological disease (white matter disease, epilepsy, aphasia, hemiplegia/hemiparesis, extrapyramidal and movement disorder), cognitive impairment (mild cognitive impairment, intellectual disability, developmental delay), psychiatric conditions (depression, anxiety, attention-deficit/hyperactivity disorder, obsessive compulsive disorder, psychosis, anxiety), ocular conditions (retinal detachment, lens dislocation, myopia, glaucoma, cataracts, strabismus, iridodonesis), and skeletal conditions (osteoporosis, scoliosis, pectus excavatum, pectus carinatum, pes cavus, genu valgum, marfanoid habitus, fractures, kyphosis, skeletal fragility, bone mass deficiency). All remaining conditions (hyperlipidemia, hypopigmentation, hypertension, spontaneous pneumothorax, chronic pancreatitis, dental crowding) were grouped under other.

DISCUSSION

- Overall, these results demonstrate that the clinical burden of patients with HCU is substantially higher than in the general (non-HCU) population
- This was most notable in rates of thrombotic/ThrE events, neurological disease, and cognitive impairment
    - These events occurred at rates nearly 5 times (thrombotic/ThrE) and 3 times (neurological and cognitive impairment) higher in the HCU population
- Similarly, rates of hyperlipidemia and hypertension were also notably higher in the HCU population
- Anxiety, pulmonary embolism, and stroke/TIA were the most common clinical conditions in patients in the HCU cohort

Limitations

- This study was limited to data in the IQVIA PharMetrics Plus database and data may not be representative of the entire US population
    - Data on race is not included and patients 65 years and older are underrepresented in the database
- Claims data are not collected solely for research purposes; missing and incorrect data in detection of HCU-related terms in a patient record could introduce bias
- The ICD code used in the patient identification algorithm may have over-captured HCU patients as it is not specific to HCU
- Data on newborn screening in US-based databases is limited, resulting in potential underestimation of clinical events. In addition, the study may not be capturing patients' initial diagnoses, limiting the amount of follow-up used to assess rates of events