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Care of Patients with Phenylketonuria (PKU) in Germany – A Claims Data Analysis from 2013 to 2023

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1. BACKGROUND

Phenylketonuria (PKU) is a rare inherited metabolic disorder requiring lifelong management to prevent psychiatric, neurological, physical and maternal complications[1–4]. Since the introduction of newborn screening in Germany in 1969, early treatment has markedly improved outcomes[4–6], but long-term real-world evidence on care and healthcare utilisation remains limited. This study analysed claims data from 2013–2023 to provide insights into epidemiology, comorbidities, treatment patterns, and healthcare resource utilisation, with the aim of identifying gaps in lifelong PKU management.

2. METHODS

Study Design

The present study was designed as a retrospective, non-interventional cohort analysis based on anonymised claims data from the German statutory health insurance (SHI). The data source was the Deutsche Analysedatenbank für Evaluation und Versorgungsforschung (DADB), comprising routinely collected data from 16 SHI funds with approximately 4.4 million insured individuals, corresponding to a representative 5% sample of the SHI population[7].

Study Population

Patients with a confirmed PKU diagnosis (ICD-10-GM: E70.0/E70.1), continuously insured for ≥1 year between 2013 and 2023. Deceased individuals were not excluded.

Analysis Approach

Analyses included descriptive statistics by reporting year and predefined age groups, as well as comparative analyses using a 1:10 matched control cohort (matched by year, age, sex, and follow-up; plus type 1 diabetes for comorbidity analyses). Odds ratios (ORs, 95% CI, p-values) were estimated with conditional logistic regression stratified by year, age, and sex. Results were age- and sex-adjusted, extrapolated to the SHI population, and reported with stratified Wilson intervals. Subgroups with n<10 were not disclosed.

3. Results

Prevalence

Between 2013 and 2023, the annual prevalence of PKU ranged from 0.006% to 0.008% (≈6–8 per 100,000) of insured individuals. The cumulative five-year prevalence (2019–2023) was 0.010% (≈10 per 100,000). Across all study years, females accounted for 51–58% of patients. Prevalence was highest in infants (0–1 years) and children (2–12 years) and declined with increasing age.

Pregnancy

Among 267 women with PKU in the dataset, 34 were identified as pregnant between 2013–2023. Only 46% received dietary therapy during pregnancy. More than 15% of these pregnancies ended in abortion, corresponding to a rate of 187 per 10,000 women, more than triple the national average in Germany (62 per 10,000 in 2024) [8].

Pharmacologic treatment

Less than 15% of patients with PKU received at least one prescription of pharmacological treatment (sapropterin dihydrochloride or pegvaliase) during the study period. The highest treatment rates were observed in young adults (18–24 years), with utilisation declining markedly in older age groups.

3. RESULTS

Comorbidities

Compared to matched controls, patients with PKU showed significantly increased odds for neuropsychiatric conditions, with mental and behavioural disorders. F-diagnoses were analysed as a distinct category due to their clinical relevance. The strongest association was observed for intellectual disability (OR 16.1), with elevated risks for hyperkinetic disorders (OR 2.1), recurrent depressive disorder (OR 1.6), and stress-related/adjustment disorders (OR 1.5), while anxiety, somatoform disorders, and depressive episodes were moderately more frequent (Figure 1).

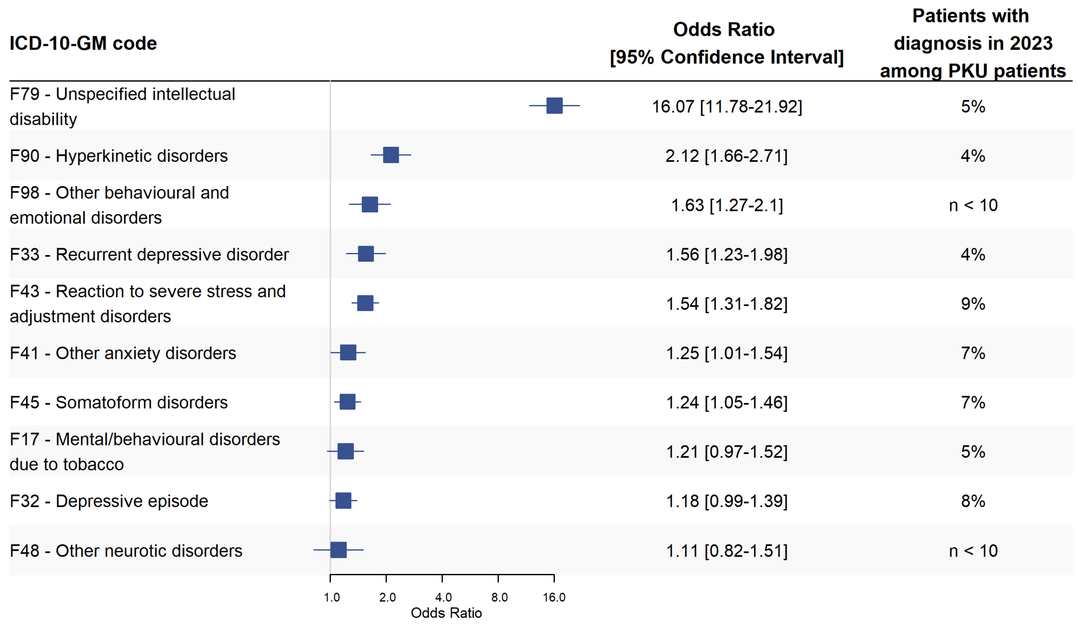

Figure 1. Most frequent F-diagnosis comorbidities based on odds ratios in the PKU population compared to a matched cohort. Odds ratios [±95% confidence interval] from the conditional logistic regression. Percentages are based on SHI extrapolated values.

Significant neuropsychiatric burden in PKU

Nutritional Therapy

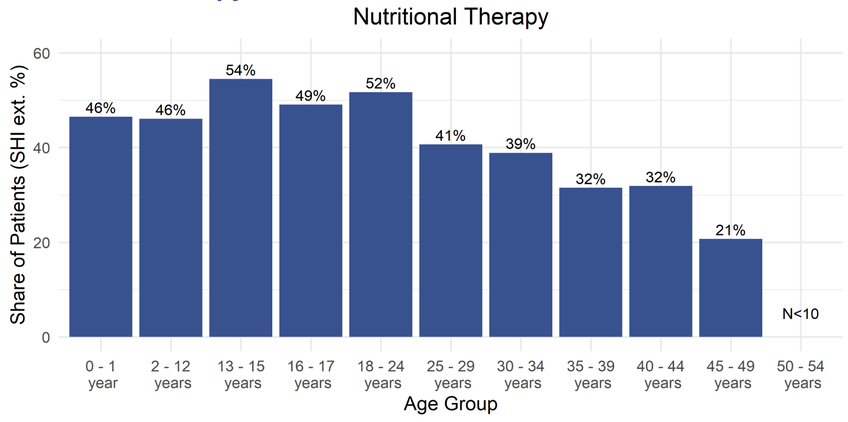

Figure 2. Age-stratified documentation of nutritional therapy among PKU patients across all years (2013-2023) (SHI extrapolated %). The proportion of patients with documented prescriptions for nutritional therapy (ATC code V06 or relevant EBM codes) across age groups is shown.

The proportion of PKU patients with documented prescriptions for nutritional therapy increased from 31% (2013) to 43% (2023). Prescription rates were higher in minors (<18 years: 48%) than in adults (≥18 years: 23%), peaking in early adolescents (13–15 years: 55%) and young adults (18–24 years: 52%), and subsequently declining with age to 21% in patients aged 45–49 years (Figure 2). Of note, only very few patients >49 years obtained nutrition therapy (50-54 years), and no patients >54 years, i.e. before introduction of the newborn screening in Germany.

Rehabilitation

Table 1. Presents the most common diagnoses associated with rehabilitation cases, based on three-character ICD-10 codes recorded in the same case ID as the rehabilitation measure. For each age group, the 10 most frequent diagnoses are shown; ties are included where case numbers are equal.

Age Group	Diagnosis	Description	Share (SHI ext. %)
Minor	F80	Specific developmental disorders of speech and language	
	F83	Mixed specific developmental disorders	
	E10	Type 1 diabetes mellitus	
	F82	Specific developmental disorder of motor function	
	F84	Pervasive developmental disorders	
	F89	Unspecified developmental disorder	
	G81	Hemiparesis and hemiplegia	
	H52	Disorders of accommodation and refraction	
	I61	Intracerebral haemorrhage	
	J45	Bronchial asthma	
Adult	H91	Other hearing loss	
	Q21	Congenital malformations of cardiac septa	
	I10	Essential (primary) hypertension	
	M16	Coxarthrosis [arthrosis of the hip joint]	
	M54	Back pain	
	F32	Depressive episode	
	M17	Gonarthrosis [arthrosis of the knee joint]	
	I25	Chronic ischaemic heart disease	
	M51	Other intervertebral disc disorders	
	I63	Cerebral infarction	
	F43	Reactions to severe stress and adjustment disorders	

PKU patients had a higher utilisation of rehabilitation services compared with matched controls, with the largest difference observed in minors aged 2–12 years (5.6% vs. 0.3%). Elevated rates were also seen in adolescents (13–15 years: 0.7% vs. 0.2%; 16–17 years: 1.2% vs. 0.0%) and in adults aged 25–54 years (2.3% vs. 1.0%). In minors, rehabilitation was primarily related to neurodevelopmental disorders and other development disorders. In adults musculoskeletal, cardiovascular, and mental health conditions were most frequent (Table 1).

4. Conclusion

This real-world study shows current prevalence of PKU in Germany and highlights persistent gaps in lifelong care. Key findings include difficulties in pregnancy management, low utilisation of pharmacologic treatments, insufficient nutritional support in adulthood, a significant burden of psychiatric comorbidities, and high use of rehabilitation services in childhood. These results underscore the need for integrated, guideline-concordant care structures that ensure continuity through vulnerable transitions and provide sustained, age-appropriate management across the lifespan. Rare diseases like PKU require long-term attention, investment and coordinated strategies beyond childhood.

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