Assessing the health status of patients with late-diagnosed PKU from the retrospective analysis of the full French insurance claims cohort 2006-2018

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Background

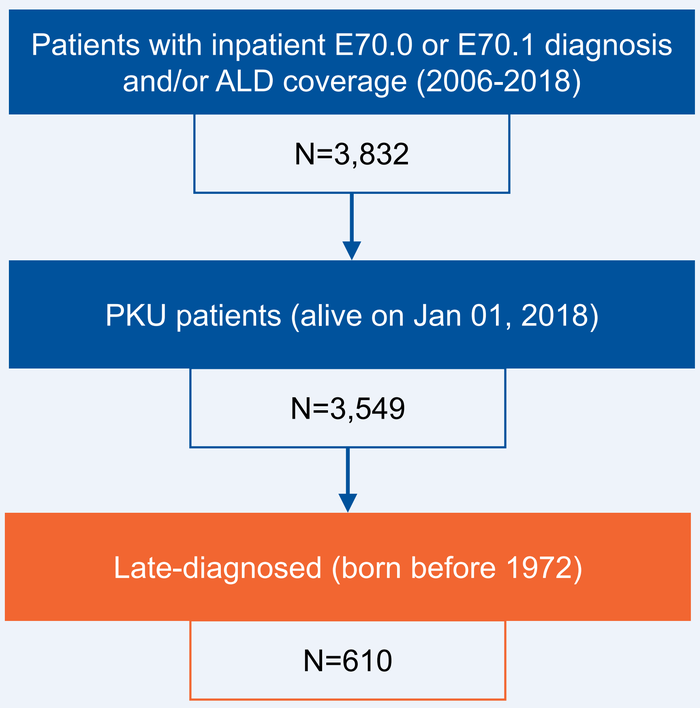
- Phenylketonuria (PKU) is a rare inborn error of metabolism of the essential amino acid phenylalanine
- If left untreated PKU results in global developmental delay or severe irreversible intellectual disability, as well as growth failure, hypopigmentation, motor deficits, ataxia, and seizures
- While the management of PKU in patients born after the implementation of newborn screening is well established, little is known about the long-term burden of illness in adult, late-diagnosed PKU patients born before the nationwide implementation of newborn screening in France before 1972
- **The aim of this study was to evaluate health status and healthcare consumption of patients with late-diagnosed PKU in France**

Methods

- This retrospective observational study used health insurance claims data from the French database SNDS, including data from over 66 million French inhabitants
- PKU patients were identified between 2006-2018 by ICD-10 diagnosis codes E70.0/ E70.1 documented as chronic condition (affection de longue durée – ALD) or in the inpatient setting
- PKU patients born before implementation of the newborn screening in France in 1972 and alive on January 01, 2018, were included and matched to controls without PKU regarding age, gender, and region
- Comorbidities of interest were assessed using the algorithms collected in 2015 by Quantin and the French Sickness Fund[1] for selected diseases
- Medications were assessed using 1-digit Anatomical-Therapeutic-Chemical (ATC) classification codes. Sapropterin was identified via ATC code A16AX07 and dietary amino acid supplements were identified by the PRS_NAT_REF code 3517
- Outcomes were analyzed for the year 2018

Results – Study Population

Figure 1. Flowchart



- Overall, 610 PKU patients were identified and matched to 3,047 controls **(Figure 1)**
- Mean age of the population was 68.5 (±13.5) years (48.9% female) **(Table 1)**
- The mean Charlson Comorbidity Index (CCI) was significantly higher among late-diagnosed PKU patients compared to their controls (1.1 vs 0.5, p<0.01) **(Table 1)**

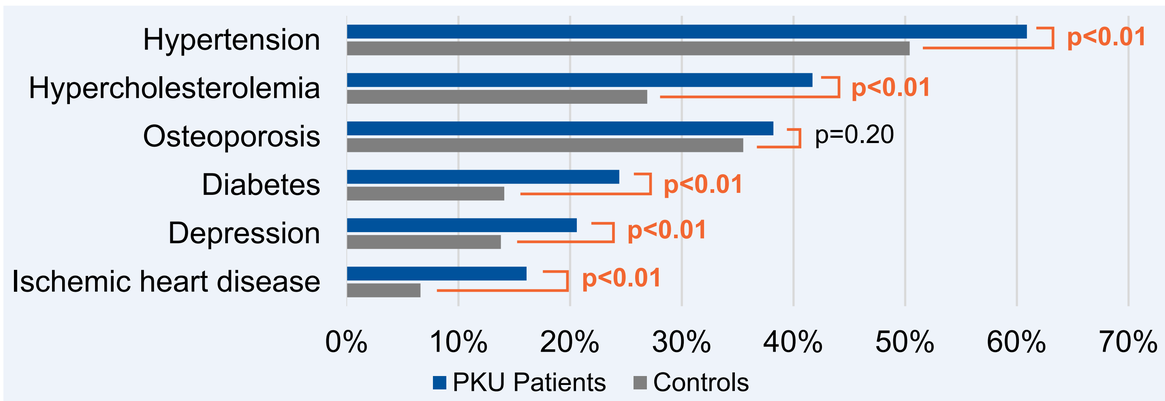
Table 1. Patient Demographics after Matching*

	PKU Cases	Controls
Gender		
Male	312 (51.1%)	1,557 (51.1%)
Female	298 (48.9%)	1,490 (48.9%)
Age in 2018		
Mean (SD)	68.5 (13.5)	68.5 (13.5)
Median / Min / Max	69.0 / 47.0 / 98.0	69.0 / 47.0 / 98.0
Quartile 25 / Quartile 75	57.0 / 80.0	57.0 / 80.0
Charlson Comorbidity Index		
Mean (SD)	1.1 (1.9)	0.5 (1.1)
Median / Min / Max	0.0 / 0.0 / 14.0	0.0 / 0.0 / 11.0
Quartile 25 / Quartile 75	0.0 / 2.0	0.0 / 0.0

* Based on 610 late-diagnosed PKU patients and 3,047 controls. SD, standard deviation.

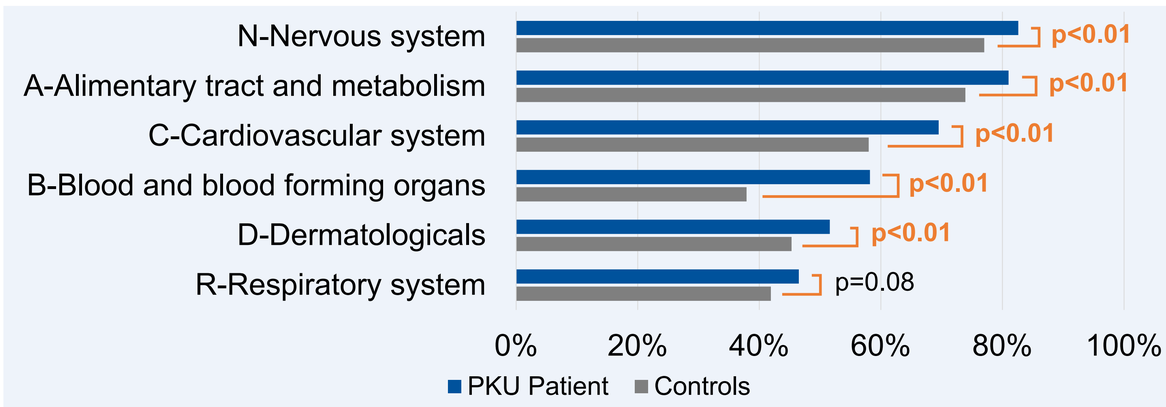
Results – Comorbidities / Medication

Figure 2. Comorbidities of interest in late-diagnosed PKU patients vs. controls*



* Based on 647 late-diagnosed PKU patients and 3,228 controls.

Figure 3. Selected ATC classes in late-diagnosed PKU patients vs. controls*



* Based on 610 late-diagnosed PKU patients and 3,047 controls.

Results – Summary

- Our study indicated higher prevalence of hypertension (60.9% vs 50.4%; p<0.01), hypercholesterolemia (41.7% vs 26.9%; p<0.01), Diabetes (24.4% vs 14.1%; p<0.01), depression (20.6% vs 13.8%; p<0.01), and ischemic heart disease (16.1% vs 6.6%; p<0.01) in PKU patients vs controls **(Figure 2)**
- Consequently, significantly more PKU patients received medication for nervous system (82.6% vs 77.0%; p=0.002) and cardiovascular system (69.5% vs 58.0%; p<0.01) **(Figure 3)**
- Significantly more PKU patients also received medication for blood and blood forming organs (58.2% vs 37.9%; p<0.01), dermatological drugs (51.6% vs 45.3%, p<0.01), and alimentary tract and metabolism drugs (81.0% vs 73.9%; p<0.01) **(Figure 3)**
- Only 0.7% of the PKU patients received sapropterin and 3.4% received dietary amino acids supplements

Discussion

- In this study we analyzed the complete French sickness funds population, leading to the largest PKU population analyzed. However, it is possible that not all late-diagnosed PKU patients were included in this study, as some patients might be treated in nursing homes and hence, are not covered by the sickness funds
- Additionally, the database only contains information concerning care that was reimbursed, and neither self-treatment nor the use of prescribed medications that are not reimbursed can be measured
- Nevertheless, PKU seems to have an overall clinical impact on health status in late-diagnosed PKU patients, with significant higher risk of comorbidities along with increased pharmaceutical prescriptions compared to non-PKU controls
- This study also indicates that few late-diagnosed patients are specifically treated for PKU with sapropterin and dietary amino acids supplements

References

[1] Quantin C and the Caisse nationale d'Assurance maladie des travailleurs salariés. Etude des algorithmes de définition de pathologies dans le système national d'information inter-régimes de l'assurance maladie (SNIIRAM). 2015.

Conflict of Interest

The study, data analysis, writing, editing, and poster production was funded by BioMarin Europe Limited (BioMarin). JBA, FM, and SC received expert honoraria from BioMarin. JT, CJ, and KMS are full-time employees of Xcenda GmbH acting as contractor for BioMarin for the execution of this study. SB is a full-time employee of CEMKA acting as a contractor of Xcenda GmbH for the execution of this study.

Associated Poster

Assessing the health status of ≥16-year-old patients with early-diagnosed PKU from the retrospective analysis of the full French insurance claims cohort 2006-2018.

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