Lifetime secondary healthcare resource utilization in phenylketonuria from birth to adulthood in Sweden

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Introduction

- Phenylketonuria (PKU) is a rare genetic disorder caused by deficiency of the phenylalanine hydroxylase enzyme, which results in decreased metabolism and elevated levels of the amino acid phenylalanine in the blood[1]
- In Europe, PKU is typically managed by specialist care and lifelong adherence to medical nutrition therapy. The cornerstone of treatment is lifelong dietary restriction of phenylalanine to prevent severe intellectual disability, epilepsy, and behavioral problems[1–4]
- While the medical aspects of PKU are well understood, less is known about its broader impact, particularly healthcare resource utilization (HRU) and societal costs in Europe
- Sweden's comprehensive national health registers provide an opportunity to investigate lifetime HRU in PKU

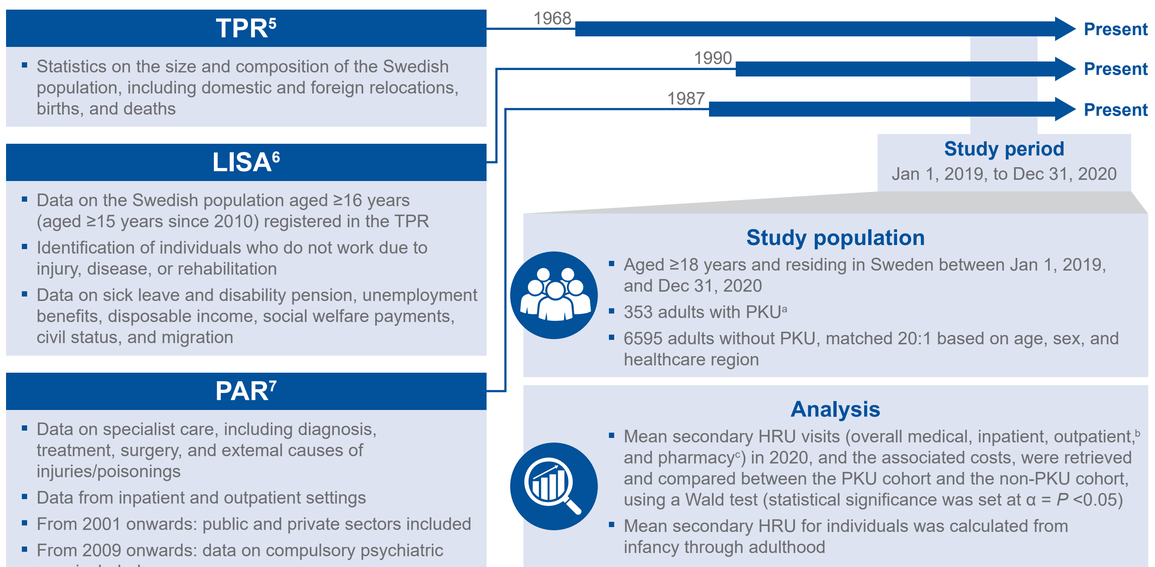
Objective

- To evaluate lifetime secondary HRU from infancy through adulthood in individuals diagnosed with PKU (the PKU cohort) and adults without PKU (the non-PKU cohort) from the general population in Sweden

Methods

- This was a national record-linkage study in Sweden linking population registry data (Total Population Register [TPR] and Longitudinal Integrated Database for Health Insurance and Labour Market Studies [LISA]) and specialist care data (Swedish National Patient Register [PAR]) to compare secondary HRU (and the associated costs) between the PKU cohort and the matched, non-PKU cohort (**Figure 1**)

Figure 1. Study design



[a]Based on at least 1 ICD code for PKU (E70.0 [ICD-10], 270B [ICD-9], or 270.0 [ICD-8]) in PAR between Jan 1, 1965, and Dec 31, 2020.
[b]Outpatient visits only include meetings with, and treatments by, specialized providers. No primary care visits are included.
[c]Pharmacy visits are defined as the number of expedition dates in the Prescribed Drug Registry.
HRU, healthcare resource utilization; ICD, International Classification of Diseases; LISA, Longitudinal Integrated Database for Health Insurance and Labour Market Studies; PAR, Swedish National Patient Register; PKU, phenylketonuria; TPR, Total Population Register.

Results

Demographics and characteristics

- Data from 353 adults (aged ≥18 years) with PKU and 6595 adults without PKU, matched 1:20 based on age, sex, and healthcare region, were analyzed (**Table 1**)
  - Median age was 40 years; 51.5% were male
  - Most individuals were born in Sweden; 82% resided in Central or Southern Sweden
  - In PAR, the median follow-up from time of PKU diagnosis to the year 2020 was 25.2 years

Table 1. Demographics and characteristics

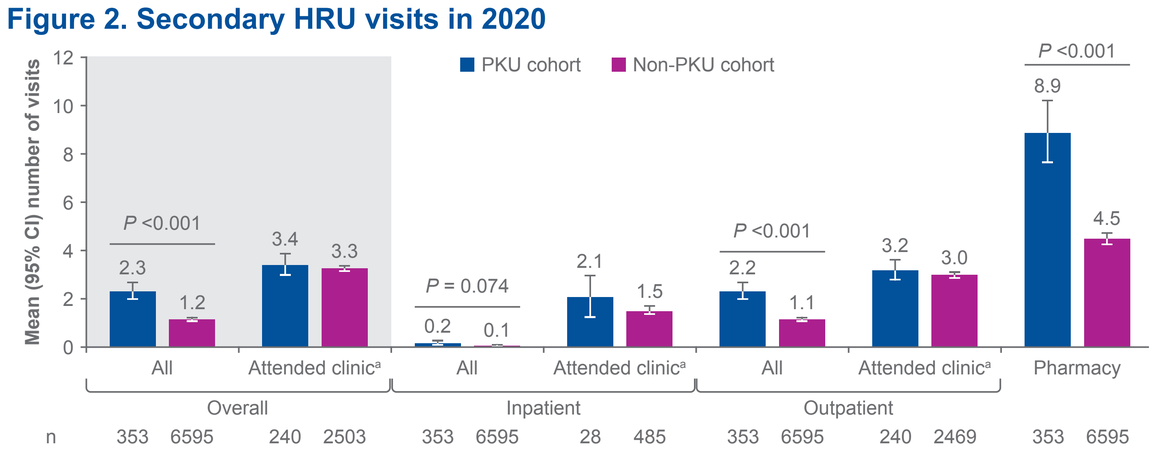
Demographic/characteristic	PKU cohort (N = 353)	Non-PKU cohort (N = 6595)
Age in 2020, years		
Mean ± SD	43.5 ± 17.6	42.7 ± 17.0
Median (IQR)	40 (28–55)	40 (28–55)
Range, min–max	20–91	20–91
<65, n (%)	305 (86.4)	5801 (88.0)
≥65, n (%)	48 (13.6)	794 (12.0)
Sex, n (%)		
Female	170 (48.2)	3200 (48.5)
Male	183 (51.8)	3395 (51.5)
Birth country, n (%)		
Sweden	310 (87.8)	6095 (92.4)
Other	43 (12.2)	498 (7.6)
Missing	0	2 (<0.1)
Swedish region of residence,[a] n (%)		
Central	148 (41.9)	2762 (41.9)
Northern	41 (11.6)	764 (11.6)
Southern	141 (39.9)	2630 (39.9)
Missing	23 (6.5)	439 (6.7)
Follow-up from time of PKU diagnosis to 2020, years		
Mean ± SD	26.5 ± 14.1	N/A
Median (IQR)	25.2 (16.7–38.4)	N/A
Range, min–max	0.1–65.5	N/A

Percentages may not total 100% due to rounding.
[a]Swedish regions of residence represent groups of healthcare regions.
IQR, interquartile range; N/A, not applicable; PKU, phenylketonuria; SD, standard deviation.

Secondary HRU and costs

- Mean secondary HRU in 2020 was higher for the PKU cohort compared with the non-PKU cohort (**Figure 2**)

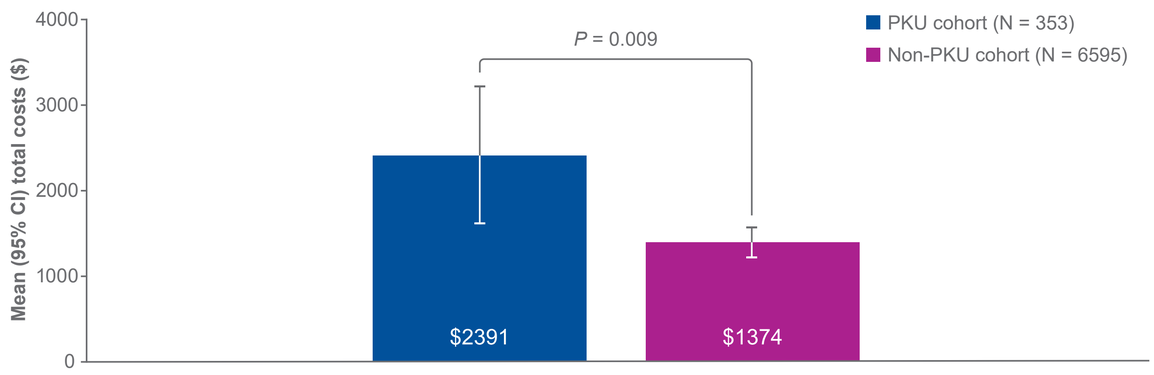
Figure 2. Secondary HRU visits in 2020



*Attended clinic defined as having ≥1 record in the relevant part of PAR (inpatient or outpatient) during 2020.
CI, confidence interval; HRU, healthcare resource utilization; PAR, Swedish National Patient Register; PKU, phenylketonuria.

- Mean total secondary HRU costs were 1.7-fold higher in the PKU cohort compared with the non-PKU cohort (**Figure 3**)

Figure 3. Secondary HRU costs in 2020

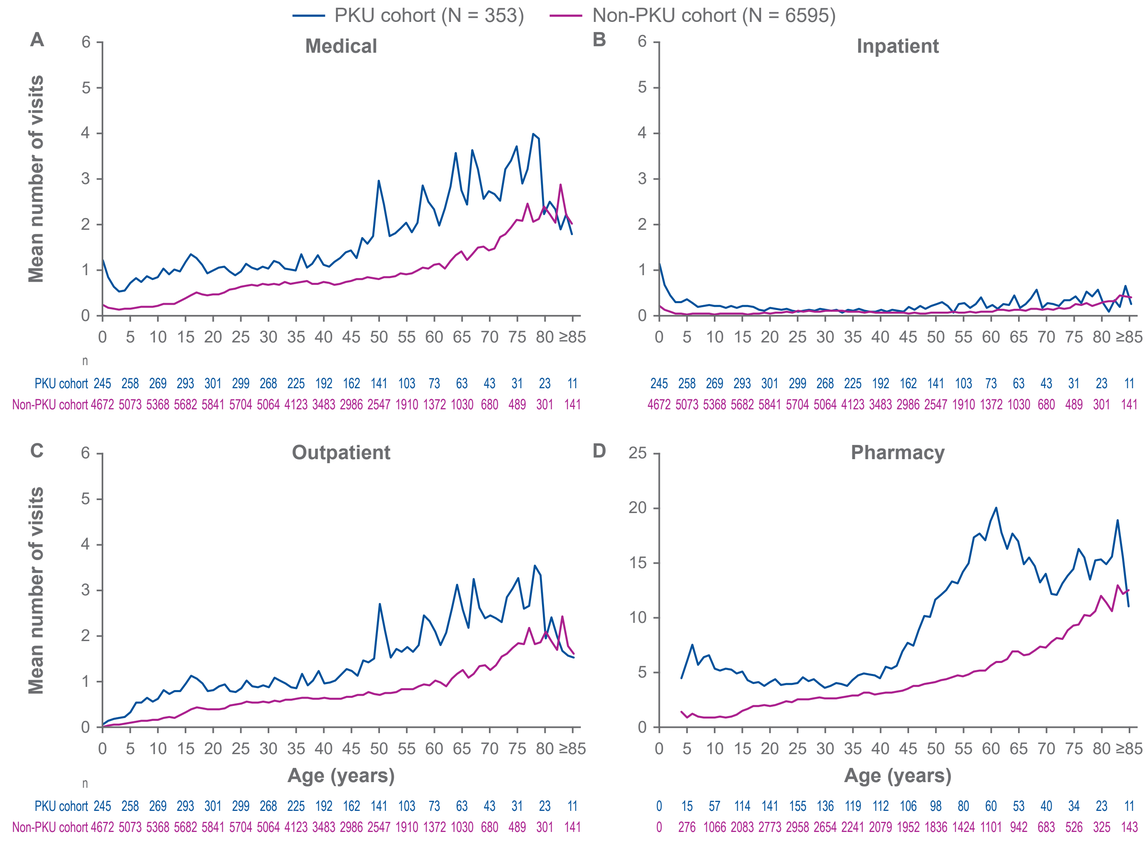


CI, confidence interval; HRU, healthcare resource utilization; PKU, phenylketonuria.

Lifetime HRU

- Across the lifespan, the PKU cohort had higher mean secondary HRU compared with the non-PKU cohort until approximately 80 years of age, except for inpatient visits (**Figure 4**)
- For both groups, secondary HRU was lowest during infancy and increased with age (**Figure 4**)

Figure 4. Mean number of (A) medical, (B) inpatient, (C) outpatient, and (D) pharmacy visits, by age



PKU, phenylketonuria.

Conclusion

- Findings highlight a lifelong personal burden for individuals with PKU compared with the general population, alongside an economic burden on the healthcare system, as shown by significantly higher secondary HRU and associated costs in individuals with PKU compared with those without PKU

References

1. van Spronsen FJ, et al. *Nat Rev Dis Primers*. 2021;7:36; **2.** van Wegberg AMJ, et al. *Mol Genet Metab*. 2025;145:109125; **3.** BMJ Best Practice. Phenylalanine. Accessed September 18, 2025. https://bestpractice.bmj.com/topics/en-gb/867; **4.** Robertson L, et al. *Nutrients*. 2022;14:576; **5.** Ludvigsson JF, et al. *Eur J Epidemiol*. 2016;31:125–36; **6.** Ludvigsson JF, et al. *Eur J Epidemiol*. 2019;34:423–37; **7.** Lund University Population Research Platform. The Swedish National Patient Register. Accessed September 17, 2025. https://www.lupop.lu.se/lupop-researchers/population-data/swedish-registers/swedish-national-patient-register

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