Work complexity in adults with phenylketonuria in Sweden in 2020

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Introduction

- Phenylketonuria (PKU) is an autosomal recessive disorder of phenylalanine (Phe) metabolism that requires lifelong dietary restriction of Phe to prevent severe intellectual disability, epilepsy, and behavioral problems[1,2]
- The socioeconomic impact of PKU – including on educational attainment and the ability to work – is unclear, with prior studies reporting conflicting results[3–5]
- Comprehensive observational data from national health registers in Sweden provide the opportunity to investigate how PKU affects socioeconomic status, including educational attainment, employment, and work complexity
- The impact of PKU on education and employment in Sweden is currently unknown

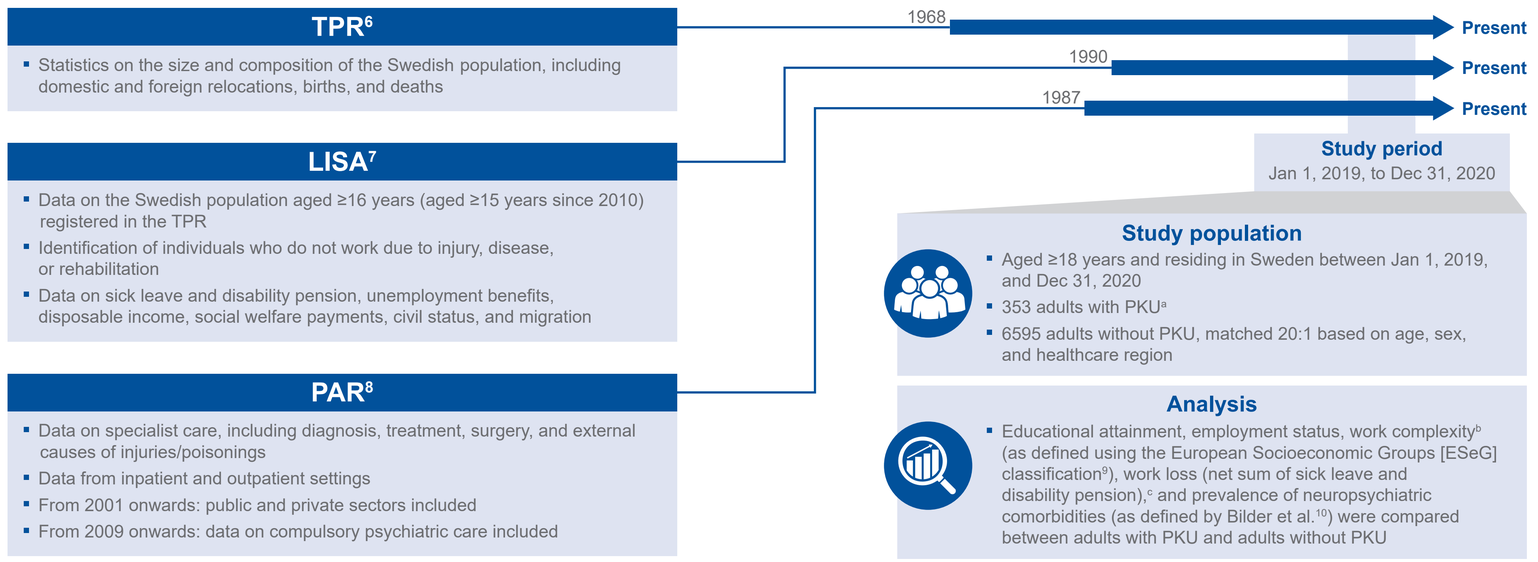
Objective

- To evaluate work complexity in adults 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 educational attainment, employment status, work complexity, work loss, and prevalence of neuropsychiatric comorbidities 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]Higher-complexity jobs: managers, professionals, and technicians and associated professionals. Lower-complexity jobs: clerks and skilled service employees, skilled industrial professionals, and lower-status employees.[9]
[c]The Swedish welfare system provides compensation for sick leave and disability pension (complete or partial). Sick leave is paid by the employer from day 2 to day 14, and episodes of >14 days are recorded by the Swedish Social Insurance Agency, which reimburses the employee for lost income from day 15 onwards. An individual with ≥25% reduced work ability (as evaluated by a physician) expected to last ≥1 year may receive a disability pension. Measure of work loss is the net sum of sick leave and disability pension. A person with 2 days of 50% work loss, for example, is coded as having 1 net day of work loss. Combining sick leave and disability pension gives a unified measure of work loss, comparable over time and insensitive to institutional changes that may move individuals between benefit systems.[11]
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

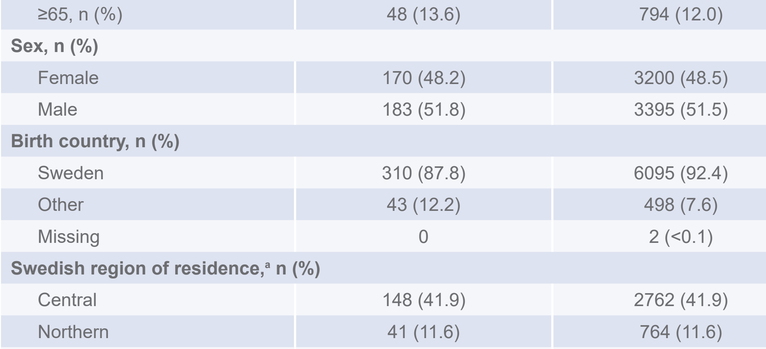
Demographic/ characteristic	PKU cohort (N = 353)	Non-PKU cohort (N = 6595)
Age in 2020, years		
Mean ± SD	43.5 ± 17.6	42.7 ± 17.0
Median (IQR)	40 (28–55)	40 (28–55)
Range, min–max	20–91	20–91
<65, n (%)	305 (86.4)	5801 (88.0)
≥65, n (%)	48 (13.6)	794 (12.0)
Sex, n (%)		
Female	170 (48.2)	3200 (48.5)
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.

Educational attainment

- Individuals in the PKU cohort were less likely than those in the non-PKU cohort to attain post-secondary education, with a difference in proportions of 9.4% (95% confidence interval [CI], 4.7%–14.5%) (**Figure 2**)

Figure 2. Adults attaining each educational level in 2020[a]



[a]Educational attainment was measured based on age in 2020.
[b]"Other" included profession-specific programs and other courses for adults for whom the highest obtained education level was unknown.
CI, confidence interval; PKU, phenylketonuria.

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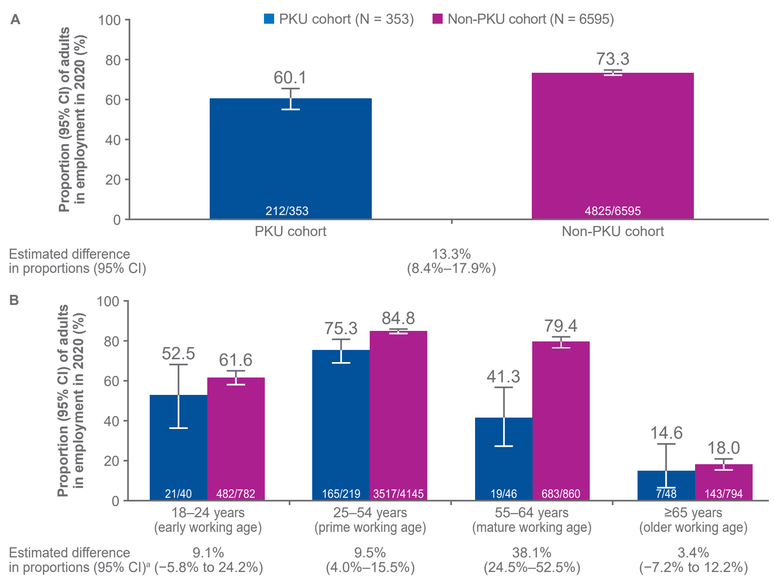
Employment status

- Individuals in the PKU cohort were less likely than individuals in the non-PKU cohort to be employed across all age groups (**Figure 3**)

Figure 3. Adults in employment in 2020: (A) overall and (B) by age[a]

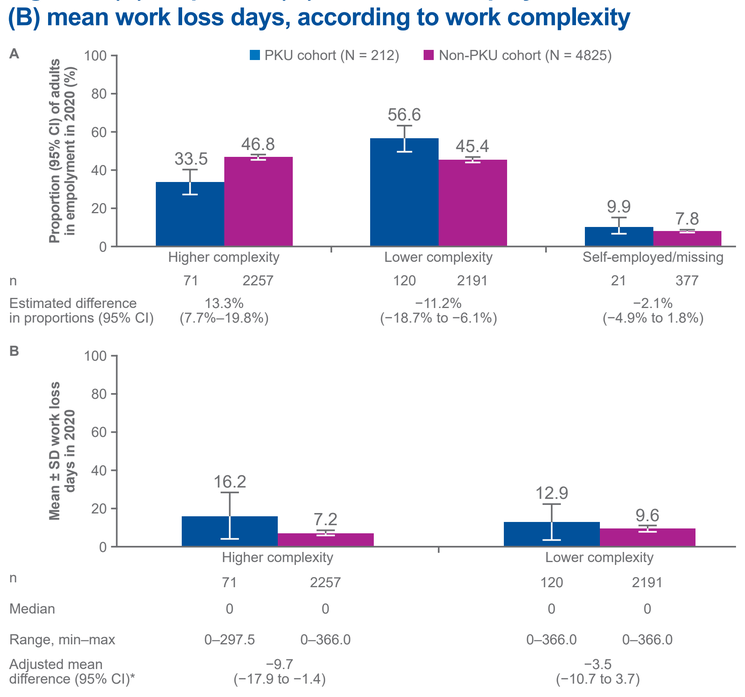


n/N values are shown in each bar.
[a]Missing data are not included.
CI, confidence interval; PKU, phenylketonuria.

Work complexity and work loss days

- Among those employed, a lower proportion of individuals in the PKU cohort held higher-complexity jobs and a higher proportion held lower-complexity jobs, compared with those in the non-PKU cohort (**Figure 4A**)
- Mean work loss days were higher in the PKU cohort compared with the non-PKU cohort. This difference was more pronounced for individuals employed in higher-complexity jobs (**Figure 4B**)

Figure 4. (A) Proportion (%) of adults in employment in 2020 and (B) mean work loss days, according to work complexity

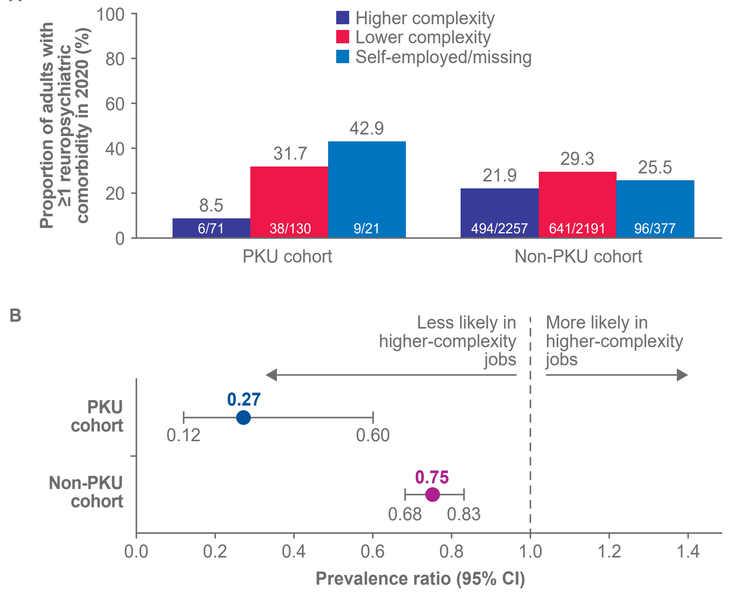


*Mean differences adjusted for matched variables.
CI, confidence interval; PKU, phenylketonuria.

Neuropsychiatric comorbidities

- Adults who had higher-complexity jobs were significantly less likely to have ≥1 neuropsychiatric comorbidity than those with lower-complexity jobs. This difference was more pronounced in the PKU cohort compared with the non-PKU cohort (**Figure 5**)
  - The prevalence of neuropsychiatric comorbidities in individuals with PKU compared with those without PKU in the US was presented at ICIEM 2025[13]

Figure 5. (A) Adults with ≥1 neuropsychiatric comorbidity in 2020, according to work complexity, and (B) prevalence ratio for work complexity (higher vs lower) among individuals with >1 neuropsychiatric comorbidity



n/N values are shown in each bar.
CI, confidence interval; PKU, phenylketonuria.

Conclusion

- Findings show that individuals with PKU are less likely to be employed in higher-complexity jobs, and likely to have more work loss days, compared with individuals without PKU
- Individuals with PKU in higher-complexity jobs have a lower prevalence of neuropsychiatric comorbidities than those in lower-complexity jobs, suggesting a potential association between job complexity and neuropsychiatric burden in this population
  - This association may be driven by the number and/or severity of neuropsychiatric comorbidities among individuals with PKU. Further research to explore this relationship is warranted, given that prior research has suggested a positive correlation between Phe levels and comorbidity severity[12]

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