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BACKGROUND

- Pyruvate kinase (PK) deficiency is a rare, hereditary, autosomal recessive enzyme disorder characterized by chronic hemolytic anemia¹⁻³
 - PK deficiency is associated with a wide range of symptoms such as fatigue, dyspnea, and jaundice, that negatively impact health-related quality of life (HRQoL)⁴
 - While data are limited, patients with PK deficiency report daily social and physical limitations associated with these symptoms, which negatively impact various aspects of their lives, including the ability to perform at their full potential at work or school^{4,5}
- Further data are needed to understand the impact of PK deficiency on patients' lives, particularly on work and school

OBJECTIVE

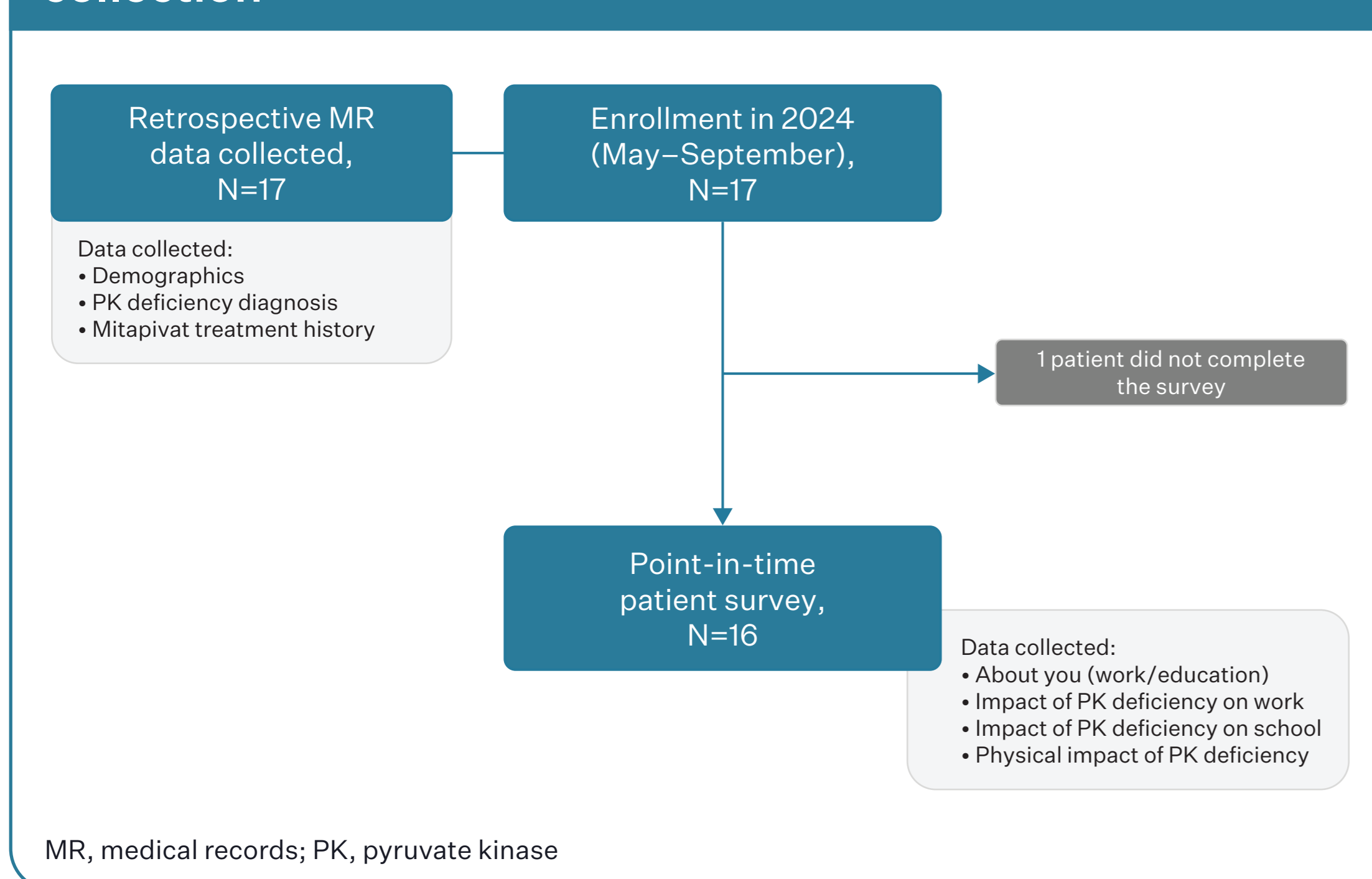
To describe the impact PK deficiency has had on school and work among adults in the US

METHODS

Study design

- This observational, US-based study used data from medical records (MR) and a cross-sectional patient survey among adults (≥18 years) with PK deficiency (**Figure 1**)
- The population was a convenience sample recruited from May to September 2024 via patient outreach channels managed by patient advocacy groups and the Agios patient support program
- Interested individuals were directed to a study website and given the option to enroll
 - Patients were compensated for their participation
 - Patients ever enrolled in a mitapivat clinical trial were excluded

Figure 1. Summary of patient enrollment and data collection



MR, medical records; PK, pyruvate kinase

Data collection, management and analysis

- This study underwent Institutional Review Board (IRB) approval in March 2024
- The PK deficiency cross-sectional survey included questions addressing education and employment status, comorbidities, complications, symptoms and the lifetime impact of the disease on work and school performance
- Questionnaires and MR collection and abstraction were administered via the PicnicHealth research platform
- MR data collection (including retrospective records when available) began upon patient consent and survey data were collected after consent at a time convenient to the patient
- All data were de-identified and managed in compliance with the HIPAA Privacy Rule
- Data were summarized descriptively

RESULTS

- All 17 patients had MR data, and 16 of these patients (94%) completed the survey (**Table 1**)

Table 1. Demographics and study population characteristics

Characteristic	N=17
Sex, n (%)	
Female	12 (71)
Race, n (%)	
White	13 (77)
Black or African American	2 (12)
More than one race	2 (12)
Ethnicity, n (%)	
Hispanic or Latino	1 (6)
Age at enrollment, years	
Median (Q1, Q3)	47.0 (30.0, 59.0)
Min, Max	20.0, 63.0
Age at diagnosis, years	
Median (Q1, Q3)	7.0 (4.0, 20.0)
Min, Max	0.0, 57.0

Max, maximum; Min, minimum; Q, quartile

Education and employment status

- Patient education and employment status are shown in **Table 2** and **Table 3**, respectively

Table 2. Patient education status

Status, n (%)	N=16
Graduate degree or higher	3 (19)
College degree (4 year – Bachelor)	4 (25)
College degree (2 year – Associates)	4 (25)
High school diploma or GED	5 (31)

GED, general educational development

- 1 patient reported they had never worked because of their PK deficiency

Table 3. Patient employment status

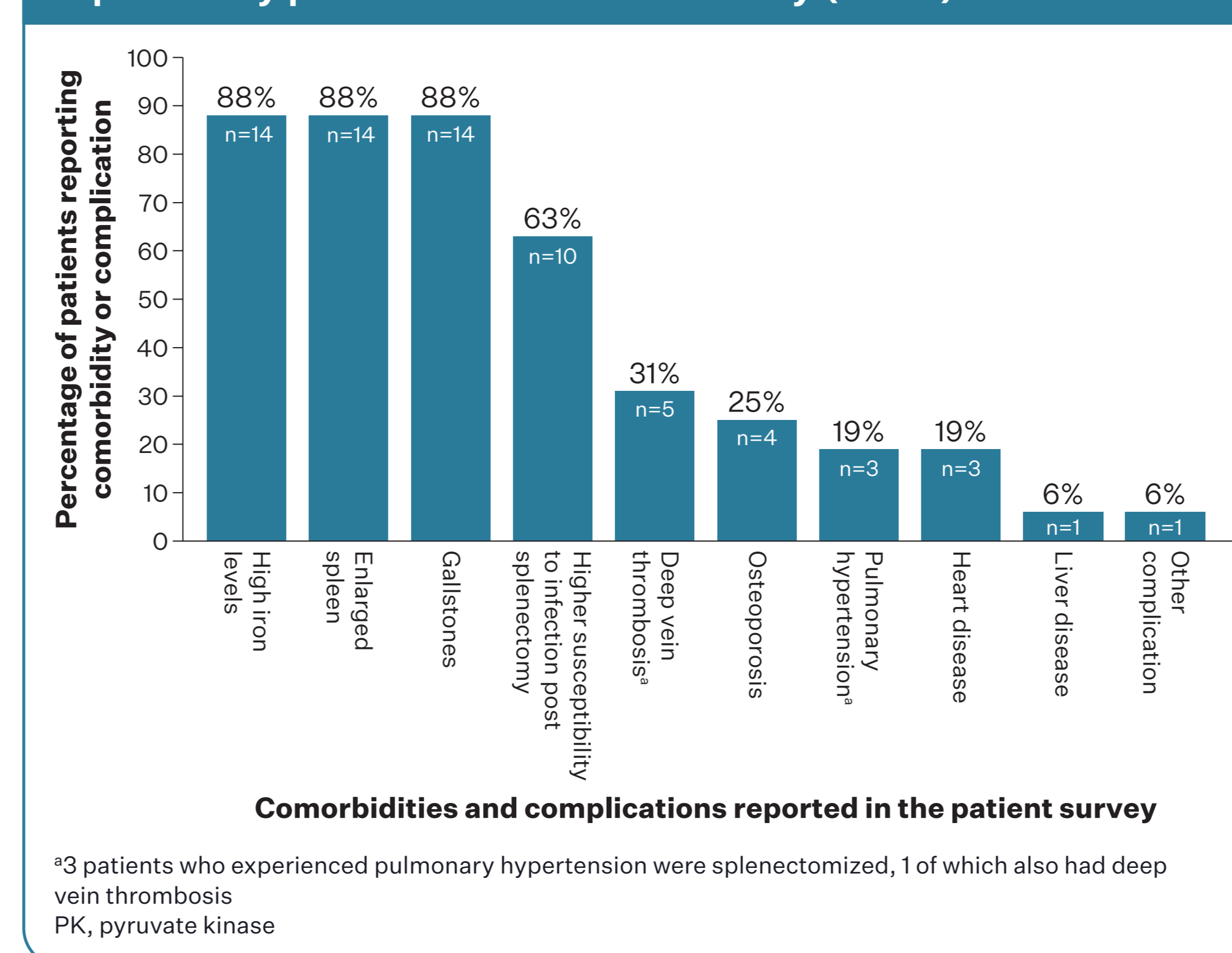
Status, n (%)	N=16
Working full time	5 (31)
Working part time	1 (6)
Retired	2 (13)
Not working, seeking employment	2 (13)
On disability allowance	6 (38)

Patient reported complications and symptoms^a

- All patients who completed the survey reported ever experiencing a comorbidity or complication with their PK deficiency
 - The majority of patients experienced high iron levels, enlarged spleen, and gallstones (88% for each condition, 14/16); deep vein thrombosis (31%, 5/16), and osteoporosis (25%, 4/16) were also reported (**Figure 2**)

^aLifetime history of comorbidities and complications was patient-reported due to incompleteness and limited look-back of the MR data

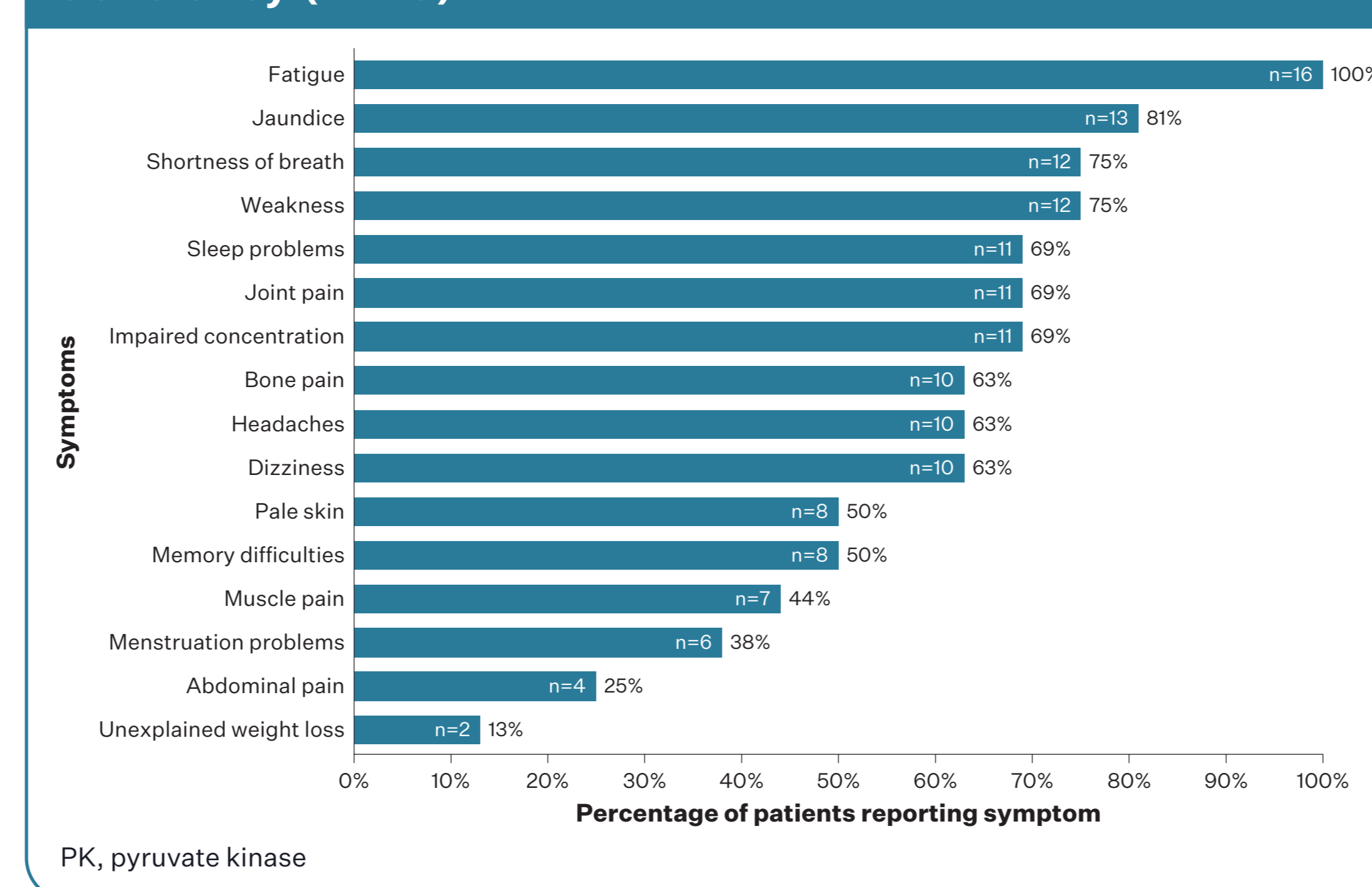
Figure 2. Lifetime history of comorbidities and complications reported by patients with PK deficiency (N=16)



^b3 patients who experienced pulmonary hypertension were splenectomized, 1 of which also had deep vein thrombosis PK, pyruvate kinase

- All patients reported lifetime history of physical symptoms of PK deficiency
 - Fatigue (100%, 16/16), jaundice (81%, 13/16), weakness (75%, 12/16), shortness of breath (75%, 12/16), brain fog/impaired concentration, joint pain, and sleep problems (69% each, 11/16) were among the most common (**Figure 3**)

Figure 3. Lifetime history of symptoms related to PK deficiency (N=16)

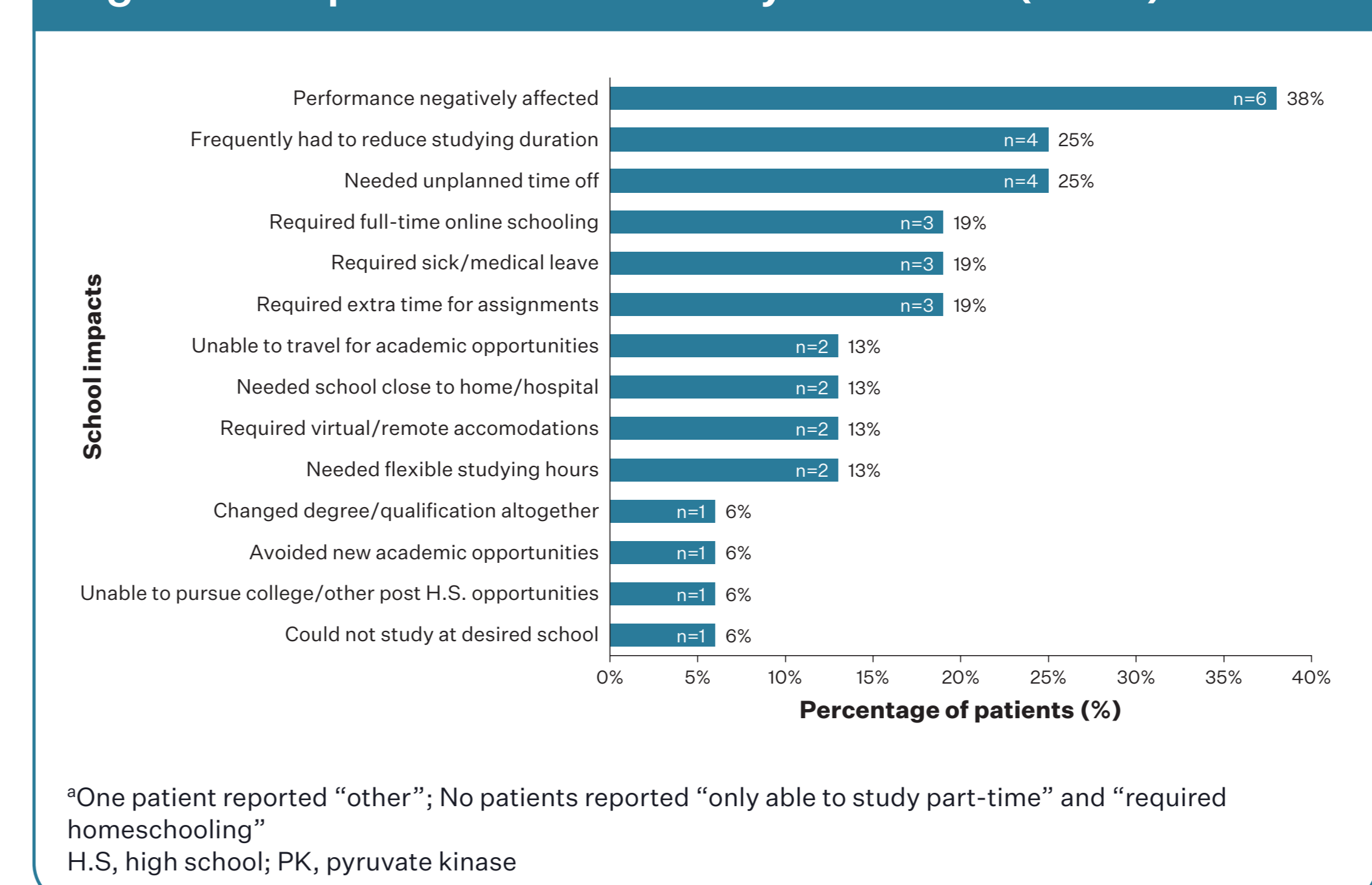


PK, pyruvate kinase

Impacts of PK deficiency on school

- When patients were asked to reflect on their experiences at school, 10 (63%) of the 16 patients reported that schooling had ever been affected by PK deficiency, including reduced performance (38%, 6/16), unplanned time off from school (25%, 4/16), and reduced time studying (25%, 4/16) (**Figure 4**)
- Among the 10 patients who reported a negative impact on school, PK deficiency symptoms included fatigue (70%, 7/10), brain fog/impaired concentration (70%, 7/10), memory difficulties (50%, 5/10), and appearance causing unwanted attention (40%, 4/10)

Figure 4. Impact of PK deficiency on school (N=16)^a

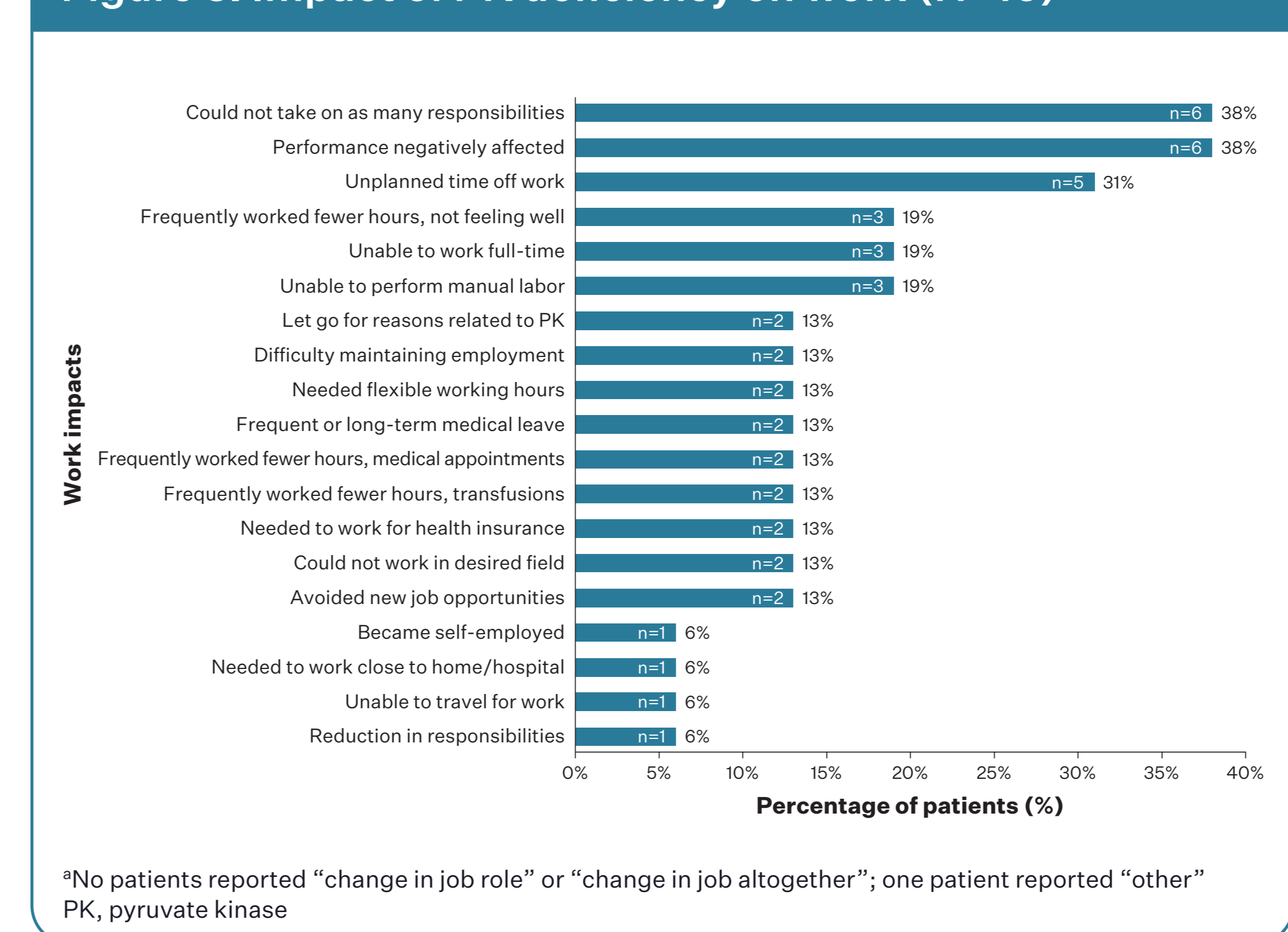


^aOne patient reported "other"; No patients reported "only able to study part-time" and "required homeschooling" H.S, high school; PK, pyruvate kinase

Impacts of PK deficiency on work

- Of the 16 patients who completed the survey, 11 (69%) patients reported ≥1 areas of employment or career path ever being affected by PK deficiency, including reduced performance (38%, 6/16), taking on fewer responsibilities than desired (38%, 6/16), and unplanned time off (31%, 5/16) (**Figure 5**)

Figure 5. Impact of PK deficiency on work (N=16)^a



^aNo patients reported "change in job role" or "change in job altogether"; one patient reported "other" PK, pyruvate kinase

- Among the six patients who reported reduced performance at work, PK deficiency symptoms that negatively impacted performance included fatigue (100%, 6/6), brain fog/impaired concentration (83%, 5/6), memory difficulties (33%, 2/6), and appearance causing unwanted attention (33%, 2/6)
- Among the 16 patients, 56% (9/16) ever applied for disability status. Out of the nine patients who ever applied for disability status, 67% (6/9) were granted disability status

STUDY LIMITATIONS

- This study has limited generalizability due to the small sample size and geographical recruitment limited to US only
- Recruitment efforts were based on convenience sampling and results may not be generalizable to the entire PK deficiency population
 - Selection bias may have also contributed to lack of generalizability as recruitment efforts for this study included the Agios patient support program and patient advocacy outreach
- Patients self-reported their medical history data, the accuracy of which has not been confirmed via medical records
- Furthermore, as patients were adults at the time of the survey, their reporting of lifetime impacts of PK deficiency, particularly on their schooling, may be subject to recall bias

CONCLUSIONS

- In this real-world observational study, most patients reported that PK deficiency negatively impacted various aspects of both work and schooling
- Fatigue and brain fog/impaired concentration were symptoms that markedly contributed to negative impacts of PK deficiency on work or schooling
- These results build on prior findings that revealed the impact of PK deficiency symptoms on various aspects of daily life⁵

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