Comorbidity Burden of Prader-Willi Syndrome Among Pediatric Patients in the United States

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Introduction

- Prader Willi syndrome (PWS) is a rare, neurobehavioral, genetic disorder affecting 10,000–20,000 people in the United States (US)[1, 2]
- PWS evolves in several phases; in the first year, infants are hypotonic and feed poorly, whilst hyperphagia develops between the age of 4.5 and adulthood[1, 3]
- Hyperphagia in PWS is associated with the lack of a normal satiety response despite adequate energy reserves[1, 3, 4]
- In addition to hyperphagia, PWS patients have reduced energy needs due to decreased basal metabolism[1]
- Central obesity is the key feature leading to long-term metabolic complications. Life expectancy in PWS ranges between 4 and 7 decades, depending on whether the comorbidities are adequately controlled[1, 5]
- There is no cure for PWS; management of its symptoms depends on the patient's age. While specialized feeding techniques and high-calorie supplements are used during the initial phase, restricting food access and intake is critical in the following phases[1, 3]
- Treatment with recombinant human growth hormone can be initiated to improve hypotonia, motor delays, growth, body composition, and adult height[3, 4]
- PWS hyperphagia is currently managed through patient supervision and strict environmental controls. Weight loss medication and bariatric surgery are recommended in the case of advanced obesity[1]
- PWS is associated with a wide range of symptoms, life-threatening health problems, and comorbidities

STUDY OBJECTIVE

In this study we aim to estimate the comorbidity burden that PWS causes on US pediatric patients compared to the general US paediatric population (age <18)

Methods

- The all-payer claims dataset (APCD; STATinMED; Dallas, Texas) was used to estimate the costs in patients 0–17 years old continuously insured for at least 1 year between 2014 and 2024
- Patients with international classification of disease (ICD-10)-CM code Q87.11 on at least two separate occasions were classified as having PWS
- A control group of randomly selected patients was built through 1:1 propensity score-matching on sex, age, race/ethnicity, region, payer type in the base case, and the baseline van Walraven comorbidity score[6] in sensitivity analysis
- Comorbidities were identified through the presence of an ICD-9 or ICD-10 code on at least one medical claim
- Relative comorbidity burden was quantified through risk ratios vs. controls patients among a clinically validated list of comorbidities

Results

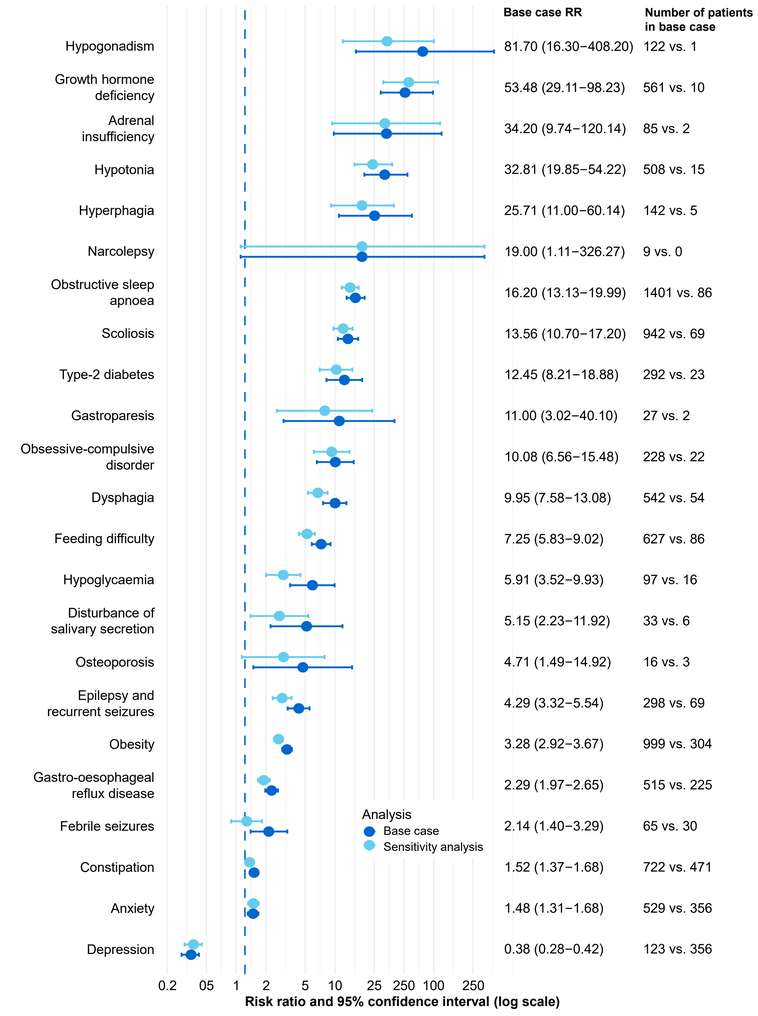
- We identified 2,593 PWS and 16,241 non-PWS patients, respectively. The base-case matching provided two balanced cohorts of 2,578 patients in each group. The mean age was 6.2 and 6.5 years, female patients constituted 48% and 47% of the sample and the mean follow-up was 8.2 and 8.4 years, respectively (**Table 1**)
- In both cohorts, most individuals (52%) were Medicaid-insured, 43% were commercially insured, 1.5% were dual-insured, and 3.4% had other insurance plans
- The baseline comorbidity score was higher among the PWS patients (1.2 vs. 0.4, p<0.001) who were also more likely to be obese 15 % vs. 2.9% (**Table 1)**
- During the follow-up, all pre-specified comorbidities except for depression were more frequent among the PWS patients. The highest was the risk of hypogonadism relative risk (RR)=81.7 (95% CI 16.3, 408.2), growth hormone defficiency RR=53.48 (95% CI 29.11, 98.23), adrenal insufifciency RR=34.20 (95% CI 9.74, 120.14), hypotonia RR=32.81 (95% CI 19.85, 54.22) and hyperphagia RR=17.71 (95% CI 8.89, 35.26) (**Figure 1**)
- Aside from the PWS itself, the 5 most frequent ICD codes recorded during medical appointments were congenital malformation predominantly associated with short stature, immunization, routine health follow-up, obstructive sleep apnea and lack of expected normal physiological development in childhood. These codes are consistent with PWS symptoms (**Figure 2**)
- Comparatively, among patients without PWS, the most frequent ICD codes were routine follow-up, immunization, acute upper respiratory infection, acute pharyngitis, and cough (**Figure 2**). These codes are aligned with expected healthcare resource use from a general paediatric population
- Results were consistent in the sensitivity analyses, with significant risk among patients with PWS, albeit nominal estimates of risk ratios were lower (**Figure 1**)

Table 1. Characteristics of the matched cohorts (base case)

Characteristics at baseline		Non-PWS (N=2,578)	PWS (N=2,578)
Age (years)	Mean (SD)	6.5 (5.7)	6.2 (5.6)
	Median (range)	6 (0–17)	5 (0–17)
	0–2, n (%)	808 (31)	858 (33)
	2–5, n (%)	331 (13)	349 (14)
	5–18, n (%)	1,439 (56)	1,371 (53)
Sex	Female, n (%)	1,215 (47)	1,236 (48)
	Male, n (%)	1,363 (53)	1,342 (52)
Race	Asian, n (%)	3 (0.1)	4 (0.2)
	Black, n (%)	10 (0.4)	13 (0.5)
	White, n (%)	105 (4.1)	104 (4.0)
	Missing, n (%)	2,460 (95.4)	2,457 (95.3)
Region	Midwest, n (%)	575 (22.3)	529 (20.5)
	Northeast, n (%)	420 (16.3)	462 (17.9)
	South, n (%)	949 (36.8)	960 (37.2)
	West, n (%)	634 (24.6)	627 (24.3)
Payer	Commercial, n (%)	1,110 (43.1)	1,125 (43.6)
	Dual, n (%)	40 (1.6)	35 (1.4)
	Medicaid, n (%)	1,335 (51.8)	1,334 (51.7)
	Other, n (%)	93 (3.6)	84 (3.3)
Obesity	n (%)	76 (2.9)	379 (15)
van Walraven score	Mean (SD)	0.4 (2.6)	1.2 (4.1)

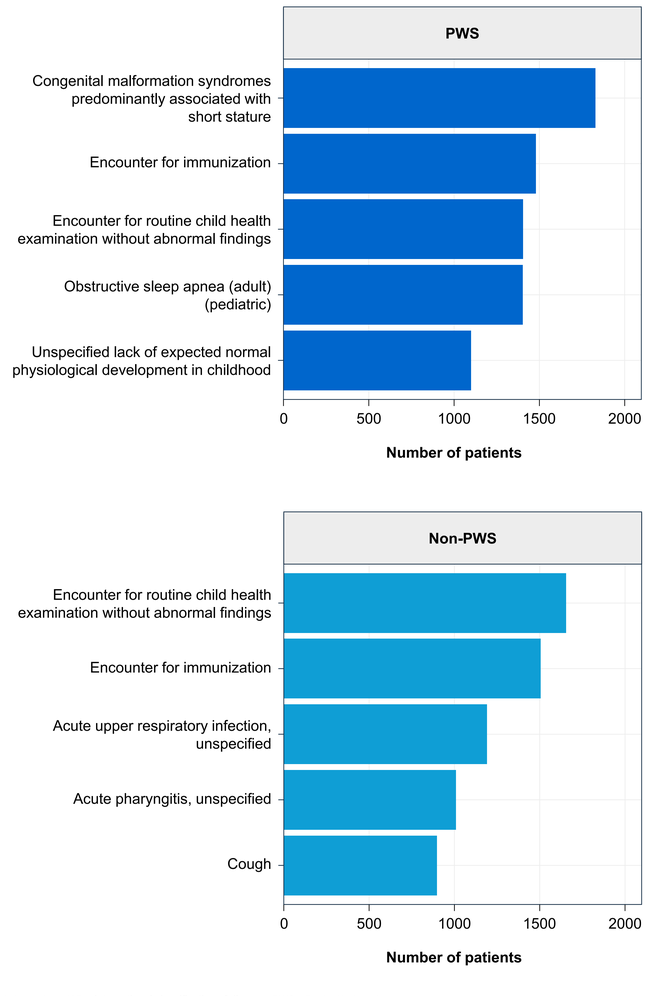
Abbreviations: PWS = Prader-Willi syndrome, SD = standard deviation.

Figure 1. Risk of selected comorbidities for PWS vs. non-PWS patients



Abbreviations: PWS = Prader-Willi syndrome, RR = Risk ratio.

Figure 2. Five most frequent ICD codes recorded during medical encounters



Abbreviations: ICD = international classification of disease, PWS = Prader-Willi syndrome.

CONCLUSION

Our analysis highlights the significant comorbidity burden faced by patients with PWS relative to matched controls and the need for effective interventions to control PWS symptoms

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ACADIA

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