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

Kreher N.[1], Hoffman D.[2], Tuzil J.[3] and Prawitz T.[3]

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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].
- Central obesity is the key feature leading to long-term metabolic complications. Life expectancy in Prader-Willi syndrome ranges between 4 and 7 decades, depending on whether the comorbidities are adequately controlled [1, 5].
- There is no cure to 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].
- Because of the severity of PWS symptoms and implications on patients' health PWS patients accrue considerable costs compared to the general population[6].

OBJECTIVE

Our study aims to provide recent estimates of the relative economic burden of PWS among US pediatric patients (age<18).

Methods

- The all-payer claims dataset (APCD; STATinMED; Dallas, Texas) was used to estimate the costs in patients 0 to 17 years old continuously insured for at least 1 year between 2014 and 2024.
- Patients with 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[7] in sensitivity analysis.
- Economic burden was quantified through ratios of mean costs per person-year[8].

Results

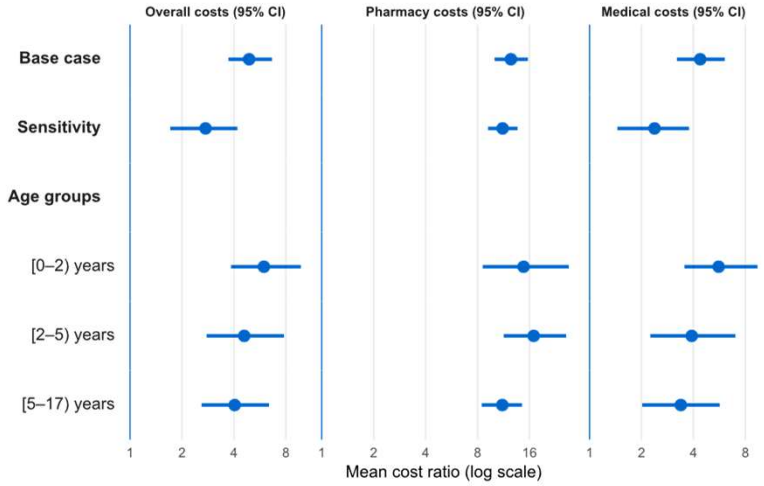
- We identified 2,593 PWS and 16,241 non-PWS patients, respectively.
- The base-case matching provided two balanced cohorts of 2,578 patients in each group. The mean age was 6.2 and 6.5 years, female patients constituted 48% and 47% of the sample and the mean follow-up was 8.2 and 8.4 years, respectively (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%.
- During the follow-up, patients with PWS accrued 4.9 times greater overall costs (p<0.0001), 4.4 times greater medical costs (p<0.0001), and 12.5 times greater pharmacy drug costs (p<0.0001) per year compared to patients without PWS (Figure 1).
  - PWS patients had on average more medical encounters every year- 17.2 vs. 4.4 with an associated rate ratio 3.91 (95%CI 3.88-3.84), driving the over expenditure in medical costs.
  - 77% of pharmacy drug costs were related to growth hormone which was prescribed almost exclusively to PWS patients with an associated odds ratio of 414.1 (95%CI 133.1-1288.7), driving the over expenditure in pharmacy costs.
- Results were consistent in the sensitivity analyses, with significant overspending among patients with PWS, albeit nominal estimates of cost ratios were lower (Figure 1).
- Subgroup analyses revealed the difference in annual costs between patients with PWS and the general population to be higher among patients aged < 2 years at baseline (cost ratio 5.97 (95%CI 3.85-9.77), 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	Mid-west, 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. Mean cost ratios for PWS vs. non-PWS cohorts



Abbreviations: CI = Confidence Interval; PWS = Prader-Willi syndrome.

Limitations

- Our study was conducted on administrative claims data only rand thus only captures billed services of the US insured population. Non-billed services, or services billed on the uninsured could not be considered in our analyses.
- Indirect costs accrued by the patients and their parents / caregivers cannot be quantified. As an example, as children age and become increasingly capable of feeding on their own, the need for a close supervision increases, to ensure that children with PWS do not overfeed, which may translate into productivity loss or reliance on external help. As our analysis does not capture the burden of the disease in terms of productivity costs, non-medical care such as family care, or its global toll on caregivers (e.g., increased stress, isolation), focusing only on the recorded billed medical costs, underestimate the true burden of PWS on the society.
- Few behavioural variables were available for inclusion in the population-adjustment process. For example, due to data missingness no variable reflecting socioeconomic status could be used, hence there is a risk for bias due to unobserved imbalanced confounders.

CONCLUSIONS:

- **Our analysis echoes previously published analyses highlights the significant costs incurred by PWS patients relative to matched controls**
- **Over expenditures mostly results from more frequent medical encounters and growth hormone prescriptions.**
- **There is an unmet need for safe and effective interventions to control PWS symptoms in paediatric patients and to prevent the use of costly healthcare resources.**

References

1. Fermin Gutierrez MA, Daley SF, Mendez MD. Prader-Willi Syndrome. StatPearls. Treasure Island (FL); 2024.
2. Bohonowych J, Miller J, McCandless SE, Strong TV. The Global Prader-Willi Syndrome Registry: Development, Launch, and Early Demographics. Genes (Basel). Sep 14 2019;10(9).
3. Goldstone AP, Holland AJ, Hauffa BP, Hokken-Koelega AC, Tauber M, speakers contributors at the Second Expert Meeting of the Comprehensive Care of Patients with PWS. Recommendations for the diagnosis and management of Prader-Willi syndrome. J Clin Endocrinol Metab. Nov 2008;93(11):4183-4197.
4. Deal CL, Tony M, Hoybye C, et al. GrowthHormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi syndrome. J Clin Endocrinol Metab. Jun 2013;98(6):E1072-1087.
5. Alves C, Franco RR. Prader-Willi syndrome: endocrine manifestations and management. Arch Endocrinol Metab. May-Jun 2020;64(3):223-234.
6. Sholtsall AJ, Gaebler JA, Kreher NC, et al. The High Direct Medical Costs of Prader-Willi Syndrome. J Pediatr. Aug 2016;175:137-143.
7. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care. Jun 2009;47(6):626-633.
8. Zhou XH, Melfi CA, Hui SL. Methods for comparison of cost data. Ann Intern Med. Oct 15 1997;127(8 Pt 2):752-756.

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Online supplementary material: PWS patient selection

Total records extracted from the database

104,483 patients
11,148,916 encounters

Patients with any PWS diagnosis recorded during any encounter

4,487 patients
708,204 encounters

- No PWS diagnosis misspelled
- All PWS diagnoses corresponding to the ICD version

Patients excluded with reasons

- 4 patients with only single ICD-9 code 75981

Patients with two ICD-10 PWS diagnoses recorded during two encounters

4,483 patients
707,601 encounters

Patients or records excluded with reasons

- 19,670 encounters after the 31st of January 2024
- 1 patient with encounters after the 31st of January 2024 only*

Patients with two ICD-10 PWS diagnoses recorded during two encounters, encounters during the study period 2014-2023

4,482 patients
687,931 encounters

Patients or records excluded with reasons

- 39 encounters recorded outside the coverage period (tolerance +/- 30 days)†
- 65 patients with less than 365.25 days of continuous insurance coverage
- 16 patients with negative age

Patients with two ICD-10 PWS diagnoses recorded during two encounters, with encounters during the study period, with at least 365.25 days of continuous insurance coverage

4,401 patients
681,952 encounters
37,208 patient-years

Patients or records excluded with reasons

- 1,754 adult patients
- 54 patients with Medicare plan

Non-adult patients with two ICD-10 PWS diagnoses recorded during two encounters, with encounters during the study period, with at least 365.25 days of continuous insurance coverage

2,593 patients
420,992 encounters
20,943 patient-years

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Online upplementary material: Non-PWS patient selection

Total records extracted from the database

104,483 patients
11,148,916 encounters

Patients with no PWS diagnosis recorded during any encounter

99,996 patients
10,440,712 encounters

Patients excluded with reasons

- 3 patients with encounters after the 31st of January 2024 only

Patients with no PWS diagnosis recorded during any encounter, encounters during the study period 2014-2023

99,993 patients
10,268,840 encounters

Patients excluded with reasons

- 1176 encounters recorded outside the coverage period (tolerance +/- 30 days)†
- 1 patient with records only outside the coverage
- 214 patients with less than 365.25 days of continuous insurance coverage
- 7 patients with negative age

Patients with no PWS diagnosis recorded during any encounter, encounters during the study period 2014-2023, with at least 365.25 days of continuous insurance coverage

99,771 patients
10,258,414 encounters
822,662 patient-years

Patients or records excluded with reasons

- 83,292 adult patients
- 238 patients with Medicare plan

Non-adult patients with no PWS diagnosis recorded during any encounter, encounters during the study period 2014-2023, with at least 365.25 days of continuous insurance coverage

16,241 patients
707,041 encounters
135,667 patient-years

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