The High Direct Medical Costs of Prader-Willi Syndrome

Andrew J. Shoffstall, PhD[1], Julia A. Gaebler, PhD[1], Nerissa C. Kreher, MD[2], Timothy Niecko, MS[3], Diah Douglas, MD[1], Theresa V. Strong, PhD[4], Jennifer L. Miller, MD[5], Diane E. Stafford, MD[6], and Merlin G. Butler, MD, PhD[7]

Objective To assess medical resource utilization associated with Prader-Willi syndrome (PWS) in the US, hypothesized to be greater relative to a matched control group without PWS.

Study design We used a retrospective case-matched control design and longitudinal US administrative claims data (MarketScan) during a 5-year enrollment period (2009-2014). Patients with PWS were identified by *Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis code 759.81. Controls were matched on age, sex, and payer type. Outcomes included total, outpatient, inpatient and prescription costs.

Results After matching and application of inclusion/exclusion criteria, we identified 2030 patients with PWS (1161 commercial, 38 Medicare supplemental, and 831 Medicaid). Commercially insured patients with PWS (median age 10 years) had 8.8-times greater total annual direct medical costs than their counterparts without PWS (median age 10 years: median costs $14 907 vs $819; $P < .0001$; mean costs: $28 712 vs $3246). Outpatient care comprised the largest portion of medical resource utilization for enrollees with and without PWS (median $5605 vs $675; $P < .0001$; mean $11 032 vs $1804), followed by mean annual inpatient and medication costs, which were $10 879 vs $1015 ($P < .001$) and $6801 vs $428 ($P < .001$), respectively. Total annual direct medical costs were ~42% greater for Medicaid-insured patients with PWS than their commercially insured counterparts, an increase partly explained by claims for Medicaid Waiver day and residential habilitation.

Conclusion Direct medical resource utilization was considerably greater among patients with PWS than members without the condition. This study provides a first step toward quantifying the financial burden of PWS posed to individuals, families, and society. *(J Pediatr 2016;175:137-43)*.

Prader-Willi syndrome (PWS) is a complex genetic, chronic, life-threatening disorder presenting in childhood with a prevalence at live birth estimated to range from 1 in 10 000 to 1 in 30 000.[1-3] Individuals born with PWS experience a wide variety of medical challenges throughout their lifetime, generating a burden that is likely considerable and spread across medical, nonmedical, productivity, and intangible costs.[3,4]

One of the hallmarks of PWS is hyperphagia, which typically presents as an overriding physiological drive to eat and results in potentially fatal food-seeking behaviors. If unchecked, it may lead to a variety of sequelae and comorbidities.[5]

In addition to hyperphagia, patients with PWS also experience serious physiological and developmental deficiencies.[4,6-9] Infants classically have hypotonia and poor suck, which may warrant the placement of a nasogastric tube along with additional perinatal follow-up care. Severe cases may be cared for in the neonatal intensive care unit for weeks to months.[1] Hypogonadism and growth hormone deficiency may lead to poor skeletal growth, short stature, immature appearance, and osteoporosis. Although recombinant human growth hormone (rhGH) replacement therapy may improve lean body mass and linear growth, it does not have any clinical impact on the hyperphagia in PWS.[10] Other medical issues that frequently arise include dental anomalies, scoliosis, skin picking, strabismus, sleep disturbances and apnea, and psychiatric disturbances.

We sought to understand the impact of PWS on direct medical costs in the US. Using a nationally representative US administrative health care claims database, we estimated the medical resource utilization for individuals in the US with a medical diagnosis of PWS compared with individuals without PWS.

ICD-9-CM	*International Classification of Diseases, Ninth Revision, Clinical Modification*
LOS	Length of stay
PPPY	Per-person per-year
PWS	Prader-Willi syndrome
rhGH	Recombinant human growth hormone

From the [1]Health Advances LLC, Weston, MA; [2]Zafgen, Boston, MA; [3]Niecko Health Economics, LLC, St Pete Beach, FL; [4]Department of Medicine, University of Alabama at Birmingham, Birmingham, AL; [5]Division of Pediatric Endocrinology, University of Florida College of Medicine, Gainesville, FL; [6]Division of Endocrinology, Harvard Medical School, Boston Children's Hospital, Boston, MA; and [7]Division of Research and Genetics, Departments of Psychiatry & Behavioral Sciences and Pediatrics, Kansas University Medical Center, Kansas City, KS

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Methods

We used commercial, Medicare supplemental, and Medicaid data from the MarketScan Research Databases (Truven Health Analytics, Ann Arbor, Michigan) for the years 2009-2014. These data provide a cross-sectional and longitudinal view of health care utilization, expenditures, demographics, and enrollment in the US. Specifically, the databases contain deidentified health insurance enrollment information and fully adjudicated claims data for inpatient and outpatient medical services as well as outpatient medications. The commercial database includes claims from individuals covered by employer-sponsored private health insurance. The Medicare database contains data from retirees with Medicare supplemental insurance paid by employers.

Several characteristics set the MarketScan Databases apart from other similar datasets. The core MarketScan Databases contain more than 180 million patients since 1995 and include private sector health data from approximately 100 payers. Moreover, the MarketScan Medicaid Database contains the pooled health care experience of approximately 6 million Medicaid enrollees from multiple states. Historically, more than 500 million claim records are available in the MarketScan Databases.

This study used a case-matched control design to quantify health care utilization among patients with PWS compared with those without the condition. We used the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code (759.81), which is specific to PWS, to identify the PWS case cohort, and conversely, the absence of the code to define control cohort without PWS. Patients with PWS initially were identified as having at least 1 matching ICD-9-CM code 759.81 within the given study period. Matching controls were matched at a 5:1 ratio to cases with PWS, on the variables of sex, age, and payer type (commercial, Medicare supplemental, and Medicaid). After the initial data extract, we applied additional criteria to increase the robustness of our sample.

To account for extraneous coding errors, we included only cases for which there were at least 2 PWS diagnoses on separate dates. Even though the MarketScan Lab Database includes laboratory test results that could ideally be used to validate diagnosis, these tests are only captured within the patients' enrollment timeframe in our study (maximum 5 years, 2009-2014) and would therefore exclude the patients who became enrolled after their primary diagnosis occurred and would have significantly limited our study population. Finally, we also required patients to be continuously enrolled for at least 12 months within the 5-year study window, which helped to ensure that measured healthcare utilization was not affected by gaps in insurance coverage.

Statistical Analyses

Outpatient service frequency was calculated on the basis of the number of claims reported; outpatient provider visits, as well as emergency department visits, and other billable services were included in this variable. Average component costs associated with inpatient admissions, outpatient services, and prescription medication claims were calculated for individuals with and without PWS. To account for bias in the results caused by differences in lengths of continuous enrollment, utilization statistics were calculated on a per-person per-year (PPPY) basis. Mean and median costs and cost ratios were derived for both patients with PWS and their matched controls. Median costs reflect a typical or standard patient, whereas mean costs may be more relevant for assessments of total costs. Because payers are responsible for paying claims for both typical and outlier cases, we have primarily reported mean costs here.

Statistical tests were performed on costs with the Wilcoxon rank-sum test. Statistics on demographics results in the **Table** were run with χ^2 (categorical variables) and t tests (continuous variables). To study the baseline level of comorbidity in each of the study cohorts, we used a modified Elixhauser methodology to produce a composite comorbidity score from a list of 31 chronic diseases identified by ICD-9-CM codes.[11,12] Statistical analysis was performed with SAS version 9.4 (SAS Institute, Cary, North Carolina).

Results

We identified 2030 individuals with PWS who met the dual PWS diagnosis code and 12-month continuous enrollment inclusion criteria (1161 commercial, 38 Medicare supplemental, and 831 Medicaid). Because of the low number of patients with PWS in the dataset with Medicare supplemental insurance, for these analyses we combined them with the commercial plan patients in the 65+ age cohort. After we matched and applied continuous enrollment criteria, our dataset included 6537 controls without PWS (3945 commercial/Medicare supplement and 2592 Medicaid). Sample demographics are shown after matching and exclusion criteria were applied (**Table**).

Very little variation was observed between the demographic makeup of cohorts with and without PWS, demonstrating effective matching. Of note, 69% of patients with PWS were younger than the age of 18 years (mean: 16 years, commercial/Medicare supplemental; mean: 19 years, Medicaid). Additionally, patients with PWS had longer continuous enrollment duration vs controls without PWS (mean 3.0 vs 2.6 years, commercial/Medicare supplemental; and mean: 4.0 vs 2.6 years, Medicaid). The mean modified Elixhauser composite score was 2.38 for PWS and 0.62 for subjects without PWS with commercial insurance. For the population insured by Medicaid, these scores were 3.92 for subjects with PWS and 1.34 for subjects without PWS.

Prescription medication costs were 15.9 times greater for commercially insured patients with PWS and 7.6 times greater for Medicaid-insured patients with PWS (all-age, ratio of PWS to without PWS). The mean PPPY cost for prescription medications for individuals with PWS varied by