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Baseline Polysomnography Prior to Growth Hormone Initiation in Young Infants with Prader-Willi Syndrome: A Multicenter Retrospective Study

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Research Article

Keywords: Prader-Willi syndrome, growth hormone, obstructive sleep apnea, central sleep apnea, polysomnogram, infant

Posted Date: June 21st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-8904627/v1

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Abstract

Purpose: Early growth hormone (GH) initiation is recommended in Prader–Willi syndrome (PWS), yet current guidelines advise baseline polysomnogram (B-PSG) because of concern for worsening obstructive sleep apnea (OSA). Significant OSA has been reported as rare in infants with PWS, and access to polysomnography is limited. We aimed to describe B-PSG findings in infants with PWS, characterize apnea type, and determine how B-PSG results predicted subsequent interventions and post-GH sleep outcomes.

Methods: A multi-institutional retrospective review was conducted of infants with PWS who underwent B-PSG at age≤24 months. B-PSG were classified as OSA, central sleep apnea (CSA), OSA+CSA, or Neither using oAHI≥1.5 and CAI≥5. Post-B-PSG management was categorized as no intervention (NO-INT), Oxygen, Minimal (intranasal steroid), or Invasive (surgery or positive pressure). A subset with GH initiation ≤36 months and follow-up PSG within 12 months comprised the Post-GH-PSG cohort.

Results: Eighty-eight infants had B-PSG: 64.8% had OSA, 3.4% CSA, 19.3% OSA+CSA, and 12.5% Neither. Post-B-PSG, 72.7% had NO-INT, 22.7% Oxygen, 1.1% Minimal and 3.4% Invasive intervention. Compared with NO-INT, the Oxygen group had higher oAHI, %Time<90, and ODI, and lower oxygen saturation. GH did not broadly change sleep-disordered breathing; however, %Time<90 improved in Oxygen group.

Conclusion: In infants with PWS undergoing B-PSG before GH, most did not require intervention; invasive interventions were rare. For clinically stable infants under 6 months, continuous oximetry may be a reasonable alternative to routine B-PSG before GH, whereas PSG should be prioritized in those with respiratory or airway concerns. Further prospective studies are needed to inform future guideline revisions.

BRIEF SUMMARY

Current Knowledge/Study Rationale: Growth hormone (GH) is standard in Prader–Willi syndrome (PWS), yet current guidelines recommend baseline polysomnography (B-PSG) despite uncertainty regarding the prevalence and definition of obstructive sleep apnea (OSA) in infants and variability across studies. Limited access to PSG can delay GH initiation, and prior single-site studies have suggested that central sleep apnea may predominate at this age.

Study Impact: This multi-site analysis demonstrates that although sleep-disordered breathing is common in young infants with PWS, most do not require intervention after B-PSG. When needed, treatment is almost always supplemental oxygen rather than invasive interventions. These findings support a more targeted approach to B-PSG and suggest that continuous nocturnal oximetry may be a reasonable alternative for stable infants with PWS under six months.

INTRODUCTION

Prader-Willi syndrome (PWS) is a multisystem genetic disorder caused by lack of expression of paternally inherited genes on chromosome 15q11-q13, and occurs in 1/10,000-1/30,000 individuals.[1] PWS is characterized by severe hypotonia and failure to thrive during the neonatal period, followed by hyperphagia, behavioral difficulties, and multisystem abnormalities during childhood and into adulthood.[2] Hypothalamic dysfunction is a key characteristic of PWS, resulting in increased risk for multiple endocrine deficiencies, including growth hormone (GH) deficiency.[3] GH deficiency in PWS is associated with short stature with increased weight velocity, decreased lean body mass, decreased strength, and decreased tone.[4] GH therapy additionally improves lean mass and linear growth throughout childhood in PWS.[4-6] Evidence supports that early initiation of growth hormone leads to improved cognition and attainment of motor milestones in those with PWS <2 years old [7,8] Early GH initiation in infants with PWS is therefore widely endorsed.

There are, however, known respiratory risks associated with GH therapy in PWS. A study of 64 cases of death in children with PWS by Tauber et al noted that 44% of those children were on GH. Of those on GH, 75% of deaths occurred within 9 months of starting GH, with respiratory illness noted as the most common cause of death in 61% of all cases.[9]

Sleep apnea is highly prevalent in PWS, and respiratory failure is a leading cause of death in PWS.[10] Both obstructive (OSA) and central sleep apnea (CSA) are described in PWS but the prevalence of each differs among age groups. CSA, characterized by episodic desaturations and usually treated with supplemental oxygen therapy, has been reported more commonly in infants with PWS, with a reported decrease in prevalence to 5% after the age of 2 years.[11,12]

GH therapy has known variable effects on CSA vs OSA. GH treatment has been associated with worsening OSA in PWS,[13] potentially related to accelerated lymphoid tissue growth.[14] In contrast, GH has been associated with improvement in CSA in PWS, likely due to enhanced central respiratory drive.[13,15,16] Given the potential for GH initiation to worsen obstructive sleep-disordered breathing in conjunction of the reports of sudden death within the first year of GH initiation, current consensus recommendations advise obtaining a baseline polysomnogram (B-PSG) prior to GH initiation.[17,18]

To date, there have been a few single-site studies characterizing PSG data in infants under 2 years with PWS that have found a much higher prevalence of CSA compared to OSA.[11,12,19,20] The recommendation to obtain a B-PSG prior to initiation of GH has been questioned given these prior studies noting low rates of OSA in infants with PWS. Secondly, polysomnography is time-intensive, resource-heavy, costly, and difficult to schedule rapidly in many clinical centers, adding feasibility challenges.[21]

As such, the primary objective of this study was to determine whether obtaining a B-PSG prior to GH initiation in infants ≤ 24 months with PWS resulted in clinical treatment or intervention. The secondary objective was to describe post-GH-PSG findings and clinical interventions for this same population.

METHODS

Participants/Procedure

A multi-institutional retrospective chart review was conducted by Cook Children's Medical Center (CCMC) in collaboration with three other sites: Children's Mercy Kansas City (CMKC), Seattle Children's Hospital (SCH), and University of Utah Health (U Health). The study was approved at each participating institution by its respective institutional review board.

Patients were eligible if they 1) had a genetically-confirmed diagnosis of PWS and received care at a study site on or after January 1, 1990; and 2) had a B-PSG performed at ≤ 24 months of age prior to GH initiation, if started. GH initiation was not required for inclusion, as the B-PSG findings were considered clinically informative regardless of GH use. When a patient had more than one PSG at ≤ 24 months and prior to GH initiation, only the initial PSG was included.

For Post-GH-PSG assessment, if a patient was initiated on GH at ≤ 36 months of age, the first PSG occurring within 12 months after GH initiation was included. If a patient received an intervention after GH initiation but prior to the Post-GH-PSG, the B-PSG data were retained; however, the Post-GH-PSG data were excluded because GH effects could not be separated from that of the intervention.

Data collected included: birth and neonatal history, PSG reports, anthropometrics, interventions, GH initiation details, and clinical notes from relevant specialists (sleep medicine, pulmonary/sleep medicine, otolaryngology, endocrinology, and genetics). Data were entered into REDCap© at each institution and subsequently transferred to the lead site for analysis.

Data Analysis

Table 1. Abbreviations	
ABBREVIATION	**DEFINITION**
%Time<90	Percent Time Under 90% Oxygen Saturation
BMI	Body Mass Index
B-PSG	Baseline Polysomnogram
BSA	Body Surface Area
CAI	Central Apnea Index
CSA	Central Sleep Apnea
ODI	Desaturation Index
GERD	Gastroesophageal Reflux Disease
GH	Growth Hormone
HI	Hypopnea Index
MinO_2Sat	Minimum Oxygen Saturation
NICU	Neonatal Intensive Care Unit
oAHI	Obstructive Apnea-Hypopnea Index
OAI	Obstructive Apnea Index
OSA	Obstructive Sleep Apnea
Post-GH-PSG	Post-Growth Hormone Polysomnogram
PSG	Polysomnogram
PWS	Prader-Willi Syndrome
Total Sleep Time	Total sleep time on room air

Table 1 displays all abbreviations used in the study and associated definitions.

Table 1 provides a list of all abbreviations and their associated definitions. Descriptive statistics were calculated for demographic characteristics and perinatal history. Obstructive Apnea-Hypopnea Index (oAHI) and Central Apnea Index (CAI) were calculated for each patient. The oAHI was defined as the obstructive apnea index (OAI) plus the hypopnea index (HI), each representing the total number of respective events divided by hours of sleep. CAI was defined as the number of central apnea events divided by hours of sleep. While some studies define OSA as an oAHI ≥ 1, there is much more variability in clinical practice, with clinicians even using oAHI ≥ 2 to define OSA.[22,23] Thus, based on emerging clinical trends along with a previously published study in infants and children with PWS, patients were

categorized as: 1) **OSA**: oAHI ≥ 1.5 and CAI < 5; 2) **CSA**: oAHI < 1.5 and CAI ≥ 5; 3) **OSA+CSA**: oAHI ≥ 1.5 and CAI ≥ 5; and 4) **Neither**: oAHI < 1.5 and CAI < 5.[12,22,24] Severity of OSA was accordingly further stratified as Normal (oAHI < 1.5), Mild (oAHI 1.5 to < 5), Moderate (oAHI 5 to < 10), or Severe (oAHI ≥ 10).[12]

For all remaining analyses, patients were classified based on intervention following B-PSG: 1) **NO-INT** (no intervention); 2) **Oxygen** (oxygen therapy alone); 3) **Minimal** (intranasal steroids only); and 4) **Invasive** (surgery or positive pressure support). Due to sample size limitations, **Minimal** and **Invasive** categories were excluded from statistical analyses.

Any patients who had interventions done after GH intervention but prior to post-GH-PSG had their data included in B-PSG data but had their data removed from the Post-GH-PSG analysis as the effect of the intervention could not be separated from the effect of GH.

Differences in anthropometric measures and PSG indices between groups at B-PSG and Post-GH-PSG were compared using Mann-Whitney U tests. Variables included: age, weight, height, body mass index (BMI), body surface area (BSA), total sleep time, CAI, oAHI, HI, minimum oxygen saturation (MinO2Sat), percent time under 90% oxygen saturation (%Time<90), and oxygen desaturation index (ODI). Differences between groups for the following variables were compared using Mann-Whitney U tests: GH initiation age, daily dose, and percent time on growth hormone from initiation until the time of the Post-GH-PSG. Chi-square tests assessed associations between intervention category (**Oxygen** vs. **NO-INT**) and medical history variables [laryngomalacia, aspiration, seizures, apnea, bradycardia, hypothyroidism, dysphasia, gastroesophageal reflux disease (GERD) or symptom variables (apnea, stridor, snoring)]. Chi-squared tests were also conducted to examine the association between B-PSG intervention group and Post-GH-PSG intervention. Relative risk was calculated for each variable. Within-group changes from B-PSG to Post-GH-PSG were evaluated for the **NO-INT** and **Oxygen** groups to assess for changes following initiation of GH using Wilcox Signed Rank Test. Associations between B-PSG indices (CAI, oAHI, MinO2Sat, %Time<90, ODI, HI) and intervention category were examined using logistic regression.

All analyses were performed using Microsoft Excel 2016 and IBM SPSS Statistics version 25. Portions of this manuscript's language were refined using ChatGPT© (OpenAI) to enhance clarity and grammar. No content was generated or interpreted by AI, and all intellectual contributions and conclusions are solely those of the authors.

RESULTS

Demographics and Perinatal History

A total of 88 patients were included (**Figure 1**). Complete demographic data are provided in **Table 2**. The cohort was 60.2% female and 58.0% white (17.0% black). Paternal deletion subtype was present in 55.7% with maternal uniparental disomy in 28.4%. The median age at PWS diagnosis was 0.7 months (*n* = 86; IQR = 0.6 months). Median gestational age was 38.0 weeks (*n* = 87; IQR = 2.0). Median birth weight was

2.7 kg (*n* = 87; *IQR* = 0.7 kg) and median birth length was 48.3 cm (*n* = 81; IQR = 5.1 cm). Median age at neonatal intensive care unit (NICU) discharge was 0.9 months (*n* = 77; IQR = 0.5 months). NICU feeding status was available for all 88 patients: 44.3% received only nasogastric-tube feeding, 23.9% received only gastrostomy-tube, 15.9% received both assisted feeding tubes, and 15.9% did not require tube-feeding.

At the time of B-PSG, apnea was the most commonly reported clinical condition (*n* = 52, 59.1%), followed by dysphagia (*n* = 46, 52.3%), aspiration (*n* = 27, 30.7%), and hypothyroidism (*n* = 27; 30.7%). Seizures and GERD each occurred in 15.9% (*n* = 14).

Table 2. Demographics (*N* = 88)

	N	**%**
Sex		
Female	53	60.2%
Male	35	39.8%
Race		
White	51	58.0%
Black	15	17.0%
Asian	8	9.1 %
American Indian/ Alaska Native	2	2.3%
Multi-ethnic	1	1.1%
Other	9	10.2%
Unknown	2	2.3%
Ethnicity		
Hispanic / Latino	17	19.3%
Non-Hispanic / Latino	71	80.7%
Genetic Subtype		
Paternal Deletion	49	55.7%
Maternal Uniparental Disomy	25	28.4%
Imprinting Defect	1	1.1%
Unknown	13	14.8%

Table 2 displays demographic data for the cohort.

Baseline Polysomnogram (B-PSG) Results

B-PSG was performed for the cohort (*n* = 88) at a median age of 4.2 months (IQR = 5.9). **Table 3** reports the PSG indices by apnea classification category (**OSA**, **CSA**, **OSA+CSA**, or **Neither**). **OSA** was present in 64.8% (*n* = 57), **CSA** in 3.4% (*n* = 3), **OSA+CSA** in 19.3% (*n* = 17), and **Neither** OSA nor CSA in 12.5% (*n* = 11).

Table 3. Baseline Anthropometrics and Polysomnogram Data by Apnea Status (*N* = 88)

	OSA (*n* = 57)	**CSA (*n* = 3)**	**OSA+CSA (*n* = 17)**	**Neither (*n* = 11)**
Anthropometrics				
Age (Months)	4.1 (6.9)	5.1 (-)	3.0 (3.2)	8.2 (4.1)
Weight (kg)	4.7 (4.4)	5.7 (-)	4.0 (2.3)	8.0 (2.7)
Height (cm)	57.2 (13.8)	61.0 (-)	54.0 (5.0)	67.8 (12.7)
BMI (kg/m^2)	14.5 (4.6)	14.7 (-)	14.3 (3.4)	15.9 (4.2)
BSA (m^2)	0.29 (0.16)	0.31 (-)	0.25 (0.08)	0.39 (0.09)
PSG Data				
Total Sleep Time	419.5 (136.0)	468.0 (-)	337.0 (263.2)	440.5 (92.0)
oAHI	6.1 (11.4)	0.6 (-)	7.4 (11.2)	0.8 (1.0)
OAI	0.8 (2.5)	0.0 (-)	1.1 (2.8)	0.0 (0.0)
HI	3.7 (6.8)	0.6 (-)	5.8 (4.4)	0.8 (1.0)
CAI	1.4 (2.3)	6.1 (-)	9.0 (7.2)	1.3 (2.3)
MinO_2Sat	80.0 (11.8)	86.0 (-)	78.0 (11.0)	90.0 (8.9)
%Time<90	0.4 (2.3)	0.2 (-)	1.0 (7.2)	0.0 (0.0)
ODI	8.9 (9.9)	7.8 (-)	15.8 (36.0)	4.4 (3.0)

Table 3 displays anthropometrics and PSG data by apnea status. Results are reported as **Median** (IQR). Abbreviations: OSA = patient with Obstructive Sleep Apnea; CSA = patient with Central Sleep Apnea; OSA+CSA = patient with both OSA and CSA; Neither: patient with neither OSA nor CSA; CAI = Central Apnea Index; oAHI = Obstructive Apnea-Hypopnea Index; OAI = Obstructive Apnea Index; HI = Hypopnea Index. The OAI and HI are subcomponents of the oAHI. All units are in events/hour.

Given the high percentage of patients with OSA, severity of OSA was further stratified using oAHI indices as Mild, Moderate, and Severe. Of the 57 patients in the **OSA** only group, the OSA was Mild in 47.4% (*n* =

27), Moderate in 17.5% (*n* = 10), and Severe in 35.1% (*n* = 20). Of the 17 individuals in the **OSA+CSA** group, the OSA was Mild in 23.5% (*n* = 4), Moderate in 47.1% (*n* = 8), and Severe in 29.4% (*n* = 5). When evaluating the individual components of the oAHI for the **OSA** and the **OSA+CSA** groups, the HI component was the predominant contributor compared to the OAI.

Intervention Status after B-PSG

Following B-PSG, 72.7% (*n* = 64) did not receive any intervention (**NO-INT**), and 22.7% (*n* = 20) received oxygen therapy alone (**Oxygen**) (**Figure 1**). Three patients (3.4%) received an invasive intervention (**Invasive**), and one patient (1.1%) received a minimal intervention (**Minimal**). Statistical analyses were completed on **NO-INT** and **Oxygen** groups only: the resulting B-PSG analytic sample was 84 patients. Due to sample size limitations, only descriptive data is included for patients in the **Invasive** and **Minimal** groups.

Comparing Intervention Group B-PSG Results

B-PSG results were compared between the **NO-INT** and **Oxygen** groups (**Table 4**). Compared to **NO-INT,** the **Oxygen** group had significantly higher oAHI (Median: 9.3 vs. 3.8, $p \leq .001$), higher %Time<90 (Median: 1.4 vs. 0.1, $p = .004$), and higher ODI (Median: 12.5 vs 7.0, $p = .003$). The **Oxygen** group also had a significantly lower MinO2Sat (Median: 75.1 vs. 84.0, $p \leq .001$) and lower total sleep time (Median 373.8 vs. 431.0 minutes, $p = .006$) compared to **NO-INT**.

Table 4. Anthropometrics and Baseline Polysomnogram (B-PSG) Data by Intervention Groups					
	Baseline PSG (*N* = 88)		**Mann-Whitney U Test**		
	No-INT (*n* = 64)	**Oxygen** (*n* = 20)	**U**	**Z**	***p***
ANTHROPOMETRICS					
Age (Months)	4.5 (6.9)	2.7 (3.2)	503.0	-1.4	.150
Weight (kg)	5.2 (4.2)	4.2 (2.2)	451.0	-1.9	.057
Height (cm)*	**58.1 (14.0)**	**55.2 (7.9)**	**413.0**	**-2.3**	**.021**
BMI (kg/m^2)	14.7 (4.7)	14.2 (3.5)	526.5	-1.1	.270
BSA (m^2)	0.30 (0.17)	0.25 (0.1)	448.5	-1.9	.053
PSG RESULTS					
Total Sleep Time**	**431.0 (114.6)**	**373.8 (264.1)**	**378.5**	**-2.8**	**.006**
oAHI***	**3.8 (5.9)**	**9.3 (15.0)**	**294.0**	**-3.6**	**≤.001**
OAI*	**0.1 (1.6)**	**1.0 (1.8)**	**410.0**	**-2.5**	**.013**
HI***	**2.6 (4.1)**	**6.7 (14.7)**	**272.0**	**-3.9**	**≤.001**
CAI	1.8 (3.5)	3.2 (5.6)	511.5	-1.4	.177
MinO_2Sat***	**84.0 (10.0)**	**75.1 (13.5)**	**293.5**	**-3.6**	**≤.001**
%Time<90**	**0.1 (0.6)**	**1.4 (4.6)**	**144.5**	**-2.9**	**.004**
ODI**	**7.0 (7.4)**	**12.5 (24.6)**	**208.5**	**-3.0**	**.003**

Table 4 displays the anthropometrics and B-PSG data by intervention group and comparisons using Mann-Whitney U tests. Results are reported as Median (IQR). Abbreviations: oAHI = Obstructive Apnea-Hypopnea Index; CAI = Central Apnea Index; OAI = Obstructive Apnea Index; HI = Hypopnea Index. MinO_2Sat = Minimum Oxygen Saturation; %Time<90 = Percent Time under 90% Oxygen Saturation; ODI = Desaturation Index. The obstructive apnea index and hypopnea index are subcomponents of obstructive-AHI. oAHI, CAI, OAI and HI are in events/hour. Total Sleep Time is in minutes on room air. Significance is marked as follows: * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Clinical Indications of B-PSG Intervention Status

Associations between intervention type (**Oxygen** vs. **NO-INT**) and baseline medical history and sleep-related symptoms during the B-PSG are shown in **Table 5**. Compared with the **NO-INT** group, patients

who required oxygen were more likely to have a history of bradycardia, seizures, aspiration, and apnea, with relative risks ranging from 1.5 to 4.3 (**Table 5**).

Given the relevance of upper airway anatomical contributors to obstructive sleep apnea, laryngomalacia was specifically evaluated. Laryngomalacia was present in thirteen patients (14.8%). Among patients with laryngomalacia, 84.6% had dysphagia, 84.6% had a history of apnea, 53.8% had aspiration, and 38.5% had GERD. Laryngomalacia was more frequent among patients in the B-PSG **Oxygen** group, with a 2.74-fold increased relative risk of laryngomalacia compared to **NO-INT** (**Table 4**). Patients in the **Oxygen** group had a 5.76-fold increased relative risk of apnea during the B-PSG compared to **NO-INT (Table 4**).

Table 5. Sleep Symptoms and Medical History by Intervention Type (N = 88)									
	NO-INT (*n* = 64)		**Oxygen** (*n* = 20)		**χ**	**df**	**P**	**Relative risk**	**95% CI**
	n	**%**	***n***	**%**					
Medical History									
Hypothyroidism	20	31.3	6	30.0	0.01	1	.916	0.96	[.45, 2.06]
Adrenal Insufficiency†	1	1.6	1	5.0	0.78	1	.379	N/A	N/A
Laryngomalacia*	**7**	**10.9**	**6**	**30.0**	**4.23**	**1**	**.040**	**2.74**	**[1.04, 7.22]**
Tracheomalacia†	1	1.6	0	0.0	0.32	1	.574	N/A	N/A
Laryngeal Cleft	1	1.6	1	5.0	0.78	1	.379	3.20	[.21, 48.87]
Dysphagia	33	51.6	12	60.0	0.44	1	.509	1.16	[.76, 1.79]
Aspiration*	**16**	**25.0**	**10**	**50.0**	**4.46**	**1**	**.035**	**2.00**	**[1.09, 3.68]**
GERD	11	17.2	2	10.0	0.61	1	.438	0.58	[.14, 2.41]
Seizures*	**7**	**10.9**	**7**	**35.0**	**6.35**	**1**	**.012**	**3.20**	**[1.28, 8.03**
Apnea*	**35**	**54.7**	**16**	**80.0**	**4.09**	**1**	**.043**	**1.46**	**[1.07, 2.00]**
Bradycardia*	**3**	**4.7**	**4**	**20.0**	**4.68**	**1**	**.031**	**5.08**	**[1.03, 25.1]**
Other	4	6.3	3	15.0	1.53	1	.217	2.40	[.59, 9.83]
Sleep Symptoms									
Snoring	6	9.4	4	20.0	1.64	1	.200	2.13	[0.67, 6.81]
Stridor	1	1.6	1	5.0	0.78	1	.379	3.20	[0.21, 48.9
Apnea***	**5**	**7.8**	**9**	**45.0**	**15.17**	**1**	**≤.001**	**5.76**	**[2.18, 15.2]**

Restless Sleep	2	3.1	1	5.0	0.16	1	.693	1.60	[0.15, 16.7]
Gasping/Choking	3	4.7	1	5.0	<0.01	1	.954	1.07	[0.12, 9.69]

Table 5 displays chi-square results examining association between the intervention following the baseline polysomnogram (B-PSG) with medical history and sleep symptoms displayed during the B-PSG. † = Likelihood Ratio. Significance is marked as follows: * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Odds of Receiving Oxygen Intervention by B-PSG Indices

While lower minimum oxygen saturation on B-PSG was independently associated with an increased likelihood of **Oxygen** intervention, no other B-PSG indices were independently associated with **Oxygen** intervention (**Table 6).**

Table 6. Odds of Receiving Oxygen by B-PSG Indices

	b	***SE***	**Wald**	**df**	***p***	**Odds Ratio**	**95% CI**
Total Sleep Time	0.01	0.01	0.85	1	.358	1.01	[0.99, 1.03]
oAHI	1.02	0.77	1.78	1	.182	2.78	[.62, 12.50]
OAI	-2.44	1.43	2.91	1	.088	0.09	[.01, 1.44]
HI	-0.17	0.53	0.11	1	.744	0.84	[.30, 2.37]
CAI	0.25	0.17	2.09	1	.148	1.29	[.92, 1.81]
$MinO_2Sat$*	**-0.29**	**0.12**	**5.64**	**1**	**.018**	**0.75**	**[.59, .95]**
%Time<90	-1.82	1.06	2.93	1	.087	0.16	[.02, 1.30]
ODI	0.01	0.09	0.02	1	.888	1.01	[.86, 1.20]
Constant	14.37	7.96	3.26	1	.071	1737902.91	-

Table 6 displays logistic regression results examining the odds of receiving Oxygen intervention by B-PSG indices. Abbreviations: oAHI = Obstructive Apnea-Hypopnea Index; CAI = Central Apnea Index; $MinO_2Sat$ = Minimum Oxygen Saturation; %Time<90 = Percent Time under 90% Oxygen Saturation; ODI = Desaturation Index. The obstructive apnea index and hypopnea index are subcomponents of obstructive-AHI. oAHI, CAI, obstructive apnea index and hypopnea index are in events/hour. Total Sleep Time is in minutes on room air. Significance is marked as follows: * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Growth Hormone Initiation

Among all 84 patients in the B-PSG analytic sample (**NO-INT** + **Oxygen**), GH was initiated in 83 (98.8%) with median start age of 5.8 months (IQR 2.5 months). When including all 88 patients in the complete

study, 86 started GH, with a median start age of 6.0 months (IQR 7.4 months). By intervention group, GH was started in 95.0% (*n* = 19) of the **Oxygen** group and 100% (*n* = 64) of the **NO-INT** group. In the **Oxygen** group, median age at GH initiation was 4.7 months (IQR = 2.6), and daily dose was 0.20 mg/m^2/day (IQR = 0.39). In the **NO-INT** group, median age at GH initiation was 5.0 months (IQR = 5.7), and daily dose was 0.20 mg/m^2/day (IQR = 0.25). Following GH initiation, 78.9% (*n* = 15) of the **Oxygen** group and 67.2% (*n* = 43) of the **NO-INT** group had a Post-GH-PSG. Between groups, there were no statistically significant differences in age at start, daily dose, duration of time on growth hormone, and percent time on growth hormone by the time of the Post-GH-PSG.

Post-GH-PSG Results

Comparing Post-GH-PSG Results by Intervention Group

A post-GH PSG was obtained in 60 patients, of whom 58 were in the **NO-INT** and **Oxygen** groups and thus comprised the Post-GH-PSG analytic sample (**Figure 1**). The median age at Post-GH-PSG was 7.0 months (IQR = 3.3) for the **Oxygen** group and 8.5 months (IQR = 6.5) for the **NO-INT** group. The **Oxygen** group had significantly lower MinO_2Sat (Median = 77.0 vs. 81.8, *p* = .047) and lower total sleep time (Median = 328.0 vs 442.0, *p* = .002) compared to the **NO-INT** group (**Table 6**).

Table 7. Post-Growth Hormone Anthropometrics and Polysomnogram Results					
	POST-GH PSG (*N* = 60)		**Mann-Whitney U Test**		
	NO-INT (*n* = 43)	**Oxygen** (*n* = 15)	**U**	**Z**	***p***
ANTHROPOMETRICS					
Age (Months)	8.5 (6.5)	7.0 (3.3)	285.0	-0.67	.505
Weight (kg)	7.1 (3.2)	6.8 (1.9)	305.0	-0.31	.756
Height (cm)	65.4 (12.7)	61.8 (12.4)	235.0	-1.12	.264
BMI (kg/m^2)	16.4 (3.2)	17.2 (3.7)	204.5	-1.69	.090
BSA (m^2)	0.37 (0.1)	0.34 (0.1)	242.5	-0.98	.330
PSG RESULTS					
Total Sleep Time**	**442.0 (106.5)**	**328.0 (259.0)**	**149.0**	**-3.08**	**.002**
oAHI	5.4 (6.7)	4.9 (14.8)	272.5	-0.14	.892
HI	4.6 (5.4)	4.7 (14.6)	276.0	-0.71	.480
OAI	0.4 (1.0)	0.6 (1.5)	226.5	-1.30	.194
CAI	1.6 (3.7)	1.8 (3.8)	267.0	-0.12	.905
MinO_2Sat*	**81.8 (11.0)**	**77.0 (12.0)**	**210.5**	**-1.99**	**.047**
%Time<90	0.2 (1.1)	0.3 (0.8)	105.0	-0.30	.768
ODI	9.1 (11.0)	21.9 (25.6)	157.0	-1.85	.065

Table 7 displays anthropometrics and Post-GH-PSG data by intervention group and comparisons using Mann-Whitney U tests. Results are reported as Median (IQR). Abbreviations: oAHI = Obstructive Apnea-Hypopnea Index; CAI = Central Apnea Index; MinO2Sat = Minimum Oxygen Saturation; %Time<90 = Percent Time under 90% Oxygen Saturation; ODI = Desaturation Index. The obstructive apnea index and hypopnea index are subcomponents of obstructive-AHI. oAHI, CAI, obstructive apnea index and hypopnea index are in events/hour. Total Sleep Time is in minutes on room air. Significance is marked as follows: * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Within-Group Change After GH Initiation

In the **NO-INT** group, there were no statistically significant differences across PSG indices following GH initiation. However, in the **Oxygen** group, %Time<90 decreased significantly following GH initiation (*p* =

.042, Z = -2.035), indicting improvement in oxygenation status following growth hormone initiation, while other PSG indices did not demonstrate significant change (**Table 8**).

Table 8: Within-group Changes from B-PSG to Post-GH-PSG

	B-PSG		**Post-GH-PSG**				
	Median	**IQR**	**Median**	**IQR**	**z-value**	**Sign.**	**Effect size**
NO-INT (n=43)							
Total Sleep Time	426.5	137.5	442.0	106.5	-1.141	0.254	-0.174
oAHI	4.0	5.8	5.4	6.7	-1.024	0.306	-0.156
OAI	0.1	2.0	0.4	1.0	-1.515	0.130	-0.234
HI	2.9	4.7	4.6	5.4	-1.319	0.187	-0.204
CAI	2.7	4.7	1.6	3.7	-1.555	0.120	-0.240
MinO_2Sat	84.0	9.4	81.8	11.0	-0.732	0.464	-0.112
%Time<90	0.2	0.7	0.2	1.1	-0.901	0.368	-0.197
ODI	6.3	5.8	9.1	11.0	-0.547	0.584	-0.094
Oxygen (n = 15)							
Total Sleep Time	349.0	242.5	328.0	259.0	-0.738	0.460	-0.191
oAHI	9.0	14.6	4.9	14.8	-1.258	0.208	-0.349
OAI	1.0	1.9	0.6	1.5	-0.847	0.397	-0.226
HI	6.5	15.5	4.7	14.6	-1.193	0.233	-0.308
CAI	3.4	5.0	1.8	3.8	-1.223	0.221	-0.339
MinO_2Sat	75.0	6.0	77.0	12.0	-0.114	0.910	-0.029
%Time<90*	**1.8**	**6.6**	**0.3**	**0.8**	**-2.035**	**0.042**	**-0.678**
ODI	12.5	25.4	21.9	25.6	-0.524	0.600	-0.145

Table 7 displays within group changes from B-PSG to Post-GH-PSG for NO-INT and Oxygen groups. Results are reported as Median (IQR). Abbreviations: oAHI = Obstructive Apnea-Hypopnea Index; CAI = Central Apnea Index; MinO2Sat = Minimum Oxygen Saturation; %Time<90 = Percent Time under 90% Oxygen Saturation; ODI = Desaturation Index. The obstructive apnea index and hypopnea index are subcomponents of obstructive-AHI. oAHI, CAI, obstructive apnea index and hypopnea index are in events/hour. Total Sleep Time is in minutes on room air. Significance is marked as follows: * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Interventions following Post-GH-PSG

Compared to the **NO-INT** group, patients in the **Oxygen** group had a 2.87-fold increased relative risk of continued oxygen therapy and a lower likelihood of normalization following Post-GH-PSG (**Table 8**). One patient in the **NO-INT** group had adenoidectomy following Post-GH-PSG while two started intranasal steroids, and one discontinued GH.

Table 8. Post-GH-PSG Interventions and Relative Risk by NO-INT and Oxygen Groups.

	NO-INT (*n* = 43)		**Oxygen** (*n* = 15)		**Chi-Square**				
	n	**%**	***n***	**%**	**χ**	**df**	**P**	**Relative risk**	**95% CI**
Normalization*	**31**	**72.1**	**6**	**40.0**	**4.96**	**1**	**.026**	**0.56**	**[0.29, 1.06]**
Oxygen Therapy*	**8**	**18.6**	**8**	**53.3**	**6.7**	**1**	**.010**	**2.87**	**[1.31, 6.28]**
Adenoidectomy†	1	2.3	0	0.0	-	-	.551	-	-
Intranasal Steroids†	2	4.7	0	0.0	-	-	.395	-	-
Discontinued GH†	1	2.3	1	6.7	-	-	.428	-	-

Table 8 shows the results of the Chi-square examining the association between B-PSG intervention groups and the interventions patients received Post-GH-PSG. Due to violating the minimum expected count of 5, † indicates Fisher's exact tests were performed instead. Significant results are bolded. Abbreviations: Post-GH-PSG = post-growth hormone polysomnogram; GH = growth hormone; NO-INT = no intervention received after the baseline-polysomnogram. Significance is marked as follows: * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Descriptive Data of Patients with Invasive Interventions Following B-PSG

Three patients received an **Invasive** intervention following B-PSG. Two of the three patients had moderate OSA based on B-PSG oAHI results and one patient had severe OSA based on B-PSG oAHI results.

One patient received Bilevel Positive Airway Pressure (BiPAP) following B-PSG. The patient was born at 36 weeks gestational age and remained in the NICU for 48 days. The neonatal course was notable for respiratory failure requiring positive pressure support, subsequent intubation for respiratory failure, and initiation of sildenafil for pulmonary hypertension. The patient was discharged home on oxygen therapy but restarted on BiPAP shortly before the B-PSG at age 13.2 months due to recurrent respiratory distress. The B-PSG at 13.8 months showed oAHI of 19.4, CAI of 0, $MinO_2Sat$ of 43%, and %Time<90 of 8%. Based on these results, BiPAP was continued. GH was initiated at 17.0 months. A Post-GH-PSG at 24.8 months demonstrated total sleep time of 260 minutes, oAHI of 63.5, CAI of 1.4, $MinO_2Sat$ of 46%,

and %Time<90 of 13.7%. Following GH initiation and the post-GH-PSG, an adenoidectomy was subsequently performed at 25.8 months.

Two patients in the **Invasive** group underwent adenoidectomy following B-PSG. The first was born at 37 weeks gestational age with medical history of hypothyroidism, dysphagia, aspiration, GERD, and apnea. B-PSG at 6.3 months showed oAHI of 14.7, CAI of 0.7, MinO_2Sat of 79%, %Time<90 of 0.4%, and ODI of 15.0. Snoring was present during B-PSG. Adenoidectomy was performed at 8.6 months. GH was not initiated, and a Post-GH-PSG was not performed.

The second patient in the **Invasive** group with adenoidectomy following B-PSG had no additional medical conditions noted and was born at 38 weeks gestational age. Only a nasogastric-tube was placed during the NICU stay. B-PSG at 4.3 months showed oAHI of 7, CAI of 11.8, MinO_2Sat of 81.3%, %Time<90 of 82%, and ODI of 17.6. Adenoidectomy was performed at 10.0 months. Snoring was present during B-PSG. GH was initiated at 10.7 months with a daily dose of 0.28 mg/m^2/day, and a Post-GH-PSG was not completed.

Descriptive Data of Patients with Minimal Interventions Following B-PSG

One patient received a **Minimal** intervention (intranasal steroids) following B-PSG. The patient was born at 38 weeks gestational age and was discharged at 22 days of life. No additional medical conditions were documented. B-PSG at 17.4 months demonstrated total sleep time of 573 minutes, oAHI of 2.0, indicating mild OSA, HI of 0.21, OSA of 0.21, CAI of 0.7, MinO_2Sat of 97%, %Time<90 of 0, and ODI of 0.4. Intranasal steroids were started following the B-PSG. GH was initiated at 19.8 months. Post-GH-PSG at 21.4 months showed total sleep time of 481 minutes, oAHI of 1.7, CAI of 1.10, MinO_2Sat of 86%, and ODI of 1.1. The patient had no sleep symptoms and demonstrated normalization following Post-GH-PSG.

DISCUSSION

To our knowledge, this is the first large, multicenter study of polysomnography data before and after starting growth hormone in infants with PWS and provides multicenter evidence to inform clinical decision-making and surveillance strategies in early infancy for a rare genetic disorder. Following B-PSG, the majority of patients (72.7%) did not receive any intervention, despite 84.1% having some degree of OSA on B-PSG. When an intervention did occur following B-PSG, it was almost always supplemental oxygen (22.7%). Only three patients (3.4%) required an **Invasive** intervention, such as positive pressure support or surgery. Clinical features most associated with the need for oxygen therapy following B-PSG included: bradycardia, seizures, aspiration, apnea, and laryngomalacia. Growth hormone did not broadly alter sleep-disordered breathing indices; however, in those with more severe baseline hypoxemia, GH was associated with a small improvement in oxygenation.

As expected, compared to the **NO-INT** group, infants in the **Oxygen** group demonstrated more pronounced indicators of impaired oxygenation on B-PSG, including higher %Time<90, higher ODI, and

lower $MinO_2Sat$. Although overnight PSG is the current gold standard tool for diagnosing OSA in children, emerging literature suggests that continuous nocturnal pulse oximetry may offer diagnostic value, particularly in resource-limited settings and in centers where access to pediatric polysomnography is limited. A 2016 systematic review of 25 non-PWS pediatric studies with broad ages of infancy through adolescence concluded that at least three desaturation clusters and three events with oxygen saturation <90% on nocturnal oximetry strongly indicated moderate-to-severe OSA.[25] A 2021 systematic review of 20 studies (*n* = 7062 participants; subset of seven studies with *n* = 5098, of broad pediatric ages) evaluating portable oximetry with new mathematical classifiers found pooled sensitivity of 74% (95% CI: 66-80%) and pooled specificity of 90% (95% CI: 85-94%) for detecting AHI ≥ 5 events/hour.[26] Collectively, these findings suggest that continuous pulse oximetry may be a reasonable tool for identifying moderate-to-severe sleep apnea, although additional validation in infants – particularly young infants – is needed.

Although oxygen therapy was the most common intervention in our cohort, it is critical to ensure that early signs predicting future need for an invasive intervention are not missed prior to starting GH. Among infants who required **Invasive** interventions in this study, one required positive pressure support due to significant respiratory compromise beginning at birth, including respiratory failure and persistent respiratory distress requiring positive pressure support before the B-PSG. Thus, clinical signs of respiratory compromise may merit further evaluation with a PSG in infants with PWS.

Respiratory risks in PWS appear to be age-dependent. Caudri et al. completed a large retrospective multicenter Australian study of children with PWS receiving GH over an 18-year period. Their cohort had a median age at GH start of 1.9 years (range 0.1-13.5 years), and 13% subsequently developed moderate-to-severe OSA.[27] Based on these findings, the authors recommended ongoing PSG surveillance before and after GH initiation. In contrast, our cohort had a younger median age at GH start of 6 months, an age when OSA is less prevalent. This difference in age most likely contributes to the difference in our findings. While the Caudri cohort reinforces the importance of post-GH PSG surveillance throughout childhood to detect clinically meaningful worsening of OSA, our study found minimal changes in PSG parameters after GH initiation in infants. These differences underscore the importance of age-specific interpretation of sleep-disordered breathing in infants with PWS.

Respiratory risks in PWS additionally vary by apnea subtype. Cohen et al. evaluated 44 patients with PWS, including 23 under 2 years of age, using the same oAHI and CAI cutoffs as our study and reported that CSA is more common in infants under age 2 years, whereas OSA typically emerged after age 2 years.[12] In their cohort, CSA was present in 26% of infants, OSA in 35% (mostly mild), and combined OSA+CSA in 17%. Other single-site PWS infant studies also reported higher rates of CSA relative to OSA in this age group.[11,19,20] In contrast, we found that 64.8% had OSA, of whom 47.4% had mild OSA, 17.5% had moderate OSA, and 35.1% had severe OSA. Combined OSA+CSA was found in 19.3% of our cohort, of whom 23.5% had mild OSA, 47.1% moderate OSA, and 29.4% severe OSA.

The markedly higher rate of infant OSA in our cohort compared with prior PWS infant studies is notable. One key difference is age at initial PSG. Infants in the Cohen cohort had a median PSG age of 1.0 year, whereas our cohort underwent B-PSG at a much younger median B-PSG age of 0.35 years.[12] Similarly, the median age of infants in the three other PWS infant PSG studies exceeded 0.5 years.[11,19,20] The younger age of our cohort may be one key explanation for this difference as sleep-disordered breathing patterns may differ between infants with PWS under 6 months of age and those older than 6 months of age, like the variability seen in typically developing infants.[28] Notably, previously published infant PWS sleep studies do not report the specific hypopnea component of the oAHI. In contrast, examination of the separate oAHI components in our cohort demonstrated that hypopneas predominated in both the OSA and OSA+CSA groups, which may influence clinical management decisions, as hypopneas are often treated with supplemental oxygen. Because hypopneas contributed disproportionately to the oAHI in our cohort, differences in how hypopneas are captured and reported may partially account for the higher observed prevalence of OSA compared with prior infant PWS studies. Further studies are needed to better characterize how individual oAHI components vary across infancy in PWS.

As hypopneas are often managed with oxygen, this finding may explain why a substantial proportion of infants with OSA in our cohort received oxygen therapy. Intermittent desaturations often associated with hypopneas can be detected on pulse oximetry, supporting the potential utility of continuous oximetry as an initiation tool for evaluating sleep-disordered breathing in very young infants with PWS. Importantly, there are limitations to continuous oximetry, as it cannot distinguish whether the desaturations originate from obstructive apneas or hypopneas, central apneas, or hypoventilation and may additionally miss mild forms of OSA. Combined oximetry-capnography may be one method to detect both desaturations along with hypoventilation.[29]

Physiologic differences in lymphatic and airway development may contribute to PSG differences between infants under and over 6 months of age. Measurable adenoidal tissue can be present as early as age 3 months but typically enlarges throughout early childhood, with peak size between ages of four and eight years.[30] Two patients in our study underwent adenoidectomy following B-PSG and prior to GH initiation, with the earliest at 8.6 months. Adenoidectomy prior to 6 months is rare, consistent with our findings. Tonsillar tissue is generally absent early in life but becomes more immunologically active and demonstrates growth between ages three and ten years.[31] These developmental patterns suggest a potential window – before 3-6 months of age – during which GH initiation may pose minimal risk for adenoidal hypertrophy-related worsening of OSA. These findings may help guide clinicians in determining when polysomnography is most clinically informative during early infancy.

Anatomic causes of OSA unrelated to adenotonsillar hypertrophy should also be considered, particularly laryngomalacia and laryngeal clefts.[32,33] Laryngomalacia typically presents with stridor, choking, feeding difficulties, aspiration, cyanosis, or apnea.[33] Laryngeal clefts may present with chronic cough, feeding difficulties, aspiration, recurrent pneumonia, stridor, or cyanosis.[34] A retrospective non-PWS study of 130 pediatric patients found a significant association between neurodevelopmental disorders and

synchronous airway lesions such as laryngomalacia or laryngeal clefts.[35] Although airway evaluations in infants with PWS are limited, hypotonia combined with high rates of dysphagia and aspiration increases the likelihood of co-existing laryngomalacia or laryngeal clefts.[36-38] Importantly, aspiration in PWS is reported to be almost exclusively silent, heightening the risk of missed airway pathology.[36,38]

There are no published studies systematically evaluating the impact of GH therapy in young infants with PWS and concomitant upper airway anomaly. Although adenoidal hypertrophy is uncommon in early infancy, it remains theoretically possible that GH-associated changes in upper airway tone or lymphoid tissue growth later in infancy could exacerbate airway obstruction in the presence of a concurrent structural lesion such as laryngomalacia or a laryngeal cleft. Therefore, if stridor, recurrent pneumonia, feeding-related symptoms, or persistent aspiration are present, otolaryngology consultation for upper airway evaluation should be strongly considered. Polysomnography has been shown to be a valuable diagnostic tool in infants with these upper airway anomalies.[33,39]

Even in the absence of respiratory or anatomic concerns, PSG plays a critical role in infants with PWS around 6 months of age, when adenoidal tissue growth may begin – particularly if the infant has already been receiving GH for several months. For infants younger than 6 months with baseline respiratory concerns or features suggesting upper airway abnormalities, PSG should be strongly considered. In this study, among very young infants with PWS under 6 months of age without concerning baseline respiratory findings or suspected airway anomalies, when intervention was recommended following B-PSG, it was almost always oxygen – whether the infant had OSA, CSA, or OSA+CSA.

This study is limited by its retrospective design. Transcutaneous carbon dioxide measurements were unavailable for most PSGs and could not be included. As minimum oxygen saturation pulse oximetry measurement was not standardized between patients and site, confounding influences (e.g., movement and placement of pulse oximeter) may have inflated low recordings. Additionally, variation in PSG availability and clinical practice patterns across centers may reflect real-world care environments. Future studies of PSG findings in infants with and without PWS under 6 months of age, as well as studies incorporating continuous oximetry with longitudinal GH outcomes and further details on post-GH interventions, are needed to validate and expand upon these findings.

CONCLUSIONS

In our multi-center study of young infants with PWS who underwent B-PSG under age 2 years and prior to GH initiation, 73% required no intervention, 23% required oxygen alone, and only 3% had an invasive intervention. For infants who required oxygen after B-PSG, this intervention was indicated by minimum oxygen saturations, a measure that could be ascertained with a more accessible tool such as continuous nocturnal oximetry. Earlier evaluations and treatment are critical for timely GH initiation. Among the three infants requiring an invasive intervention, the youngest age at adenoidectomy was after age 8 months, and the single infant requiring positive airway pressure was already receiving support before the B-PSG. Thus, in infants under 6 months of age without concerning respiratory or anatomical findings,

routine B-PSG may not be strictly necessary prior to GH initiation, and continuous oximetry may serve as a reasonable alternative screening modality. Further validation of these results should support reconsideration of current guidelines for GH initiation in young infants with PWS.

DECLARATIONS

Ethics Approval and Consent to Participate

This study was performed in accordance with the ethical principles as laid out in the 1975 Declaration of Helsinki. This study was approved by Institutional Review Board at Cook Children's (#2023-088), Children's Mercy Kansas City (STUDY00001860), Seattle Children's Hospital (PIROSTUDY15958), and University of Utah Health (IRB_00176038). As decided by the ethics committees, informed consent was waived for this study.

Consent to Participate

Each participating institution received a waiver of consent for the study, and all authors provided written agreement for its publication in *Orphanet Journal of Rare Diseases*.

Availability of Data and Material

Cook Children's implements a direct-to-requester data sharing approach to maximize data utility while protecting participant privacy. Key data products, including de-identified datasets, analysis scripts, and detailed protocols, will be made available to qualified researchers upon reasonable request and execution of a data sharing agreement.

Competing Interests

SMR has been a consultant and/or investigator for Soleno, OT4B, Aardvark, and Acadia Pharmaceuticals. EP and KH have been investigators for Acadia and Saniona Pharmaceuticals and the Foundation for Prader-Willi Research. PS has been a consultant, speaker and investigator for Soleno Therapeutics, PS has been an investigator for Acadia and Lilly. For industry-sponsored clinical trials, funding was provided to the investigators' institutions. Investigators may have received salary or effort-based support through their institutions. All organizations above had no role in the design and conduct of the study. For the remaining authors none were declared.

Funding

This work was supported by a grant from the Foundation for Prader-Willi Research.

Author's Contributions

Sani M Roy: conceptualization, funding acquisition, methodology, supervision, writing – original draft, writing – review and editing, and project administration; **Andrea Fagerman:** data curation, formal

analysis, visualization, writing – original draft, writing – review and editing; **Deborah Rafferty:** formal analysis, visualization, writing – original draft, writing – review and editing; **Emily Paprocki:** writing – review and editing; **David Ingram:** writing – review and editing; **Kelsey Halpin:** writing – review and editing; **Parisa Salehi:** writing – review and editing; **Maida Chen:** writing – review and editing: **Annabelle Wilcox:** writing – review and editing; **David Viskochil:** writing – review and editing; **Keisha Shaheed:** conceptualization, writing – review and editing.

Acknowledgements

The authors acknowledge the Foundation for Prader-Willi Research (FPWR) PWS Clinical Investigator Collaborative for grant-funded support of this work and support of the CCMC Endowed Chair program for SMR; Dr. Jessica Duis and Amy Trejo for input on study design; Svetlana Camacho (CCMC) for assistance in data extraction; and the following individuals for data collection/regulatory support: Amy Trejo (CCMC), Aliza Elrod (CMKC), Jade Turner (SCH), Carrie Bailey (UH), and Avery Giblin (UH). Additionally, the authors acknowledge the CCMC Schwarz Health Sciences Library for literature review; and their patients and patients' families.

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Figures

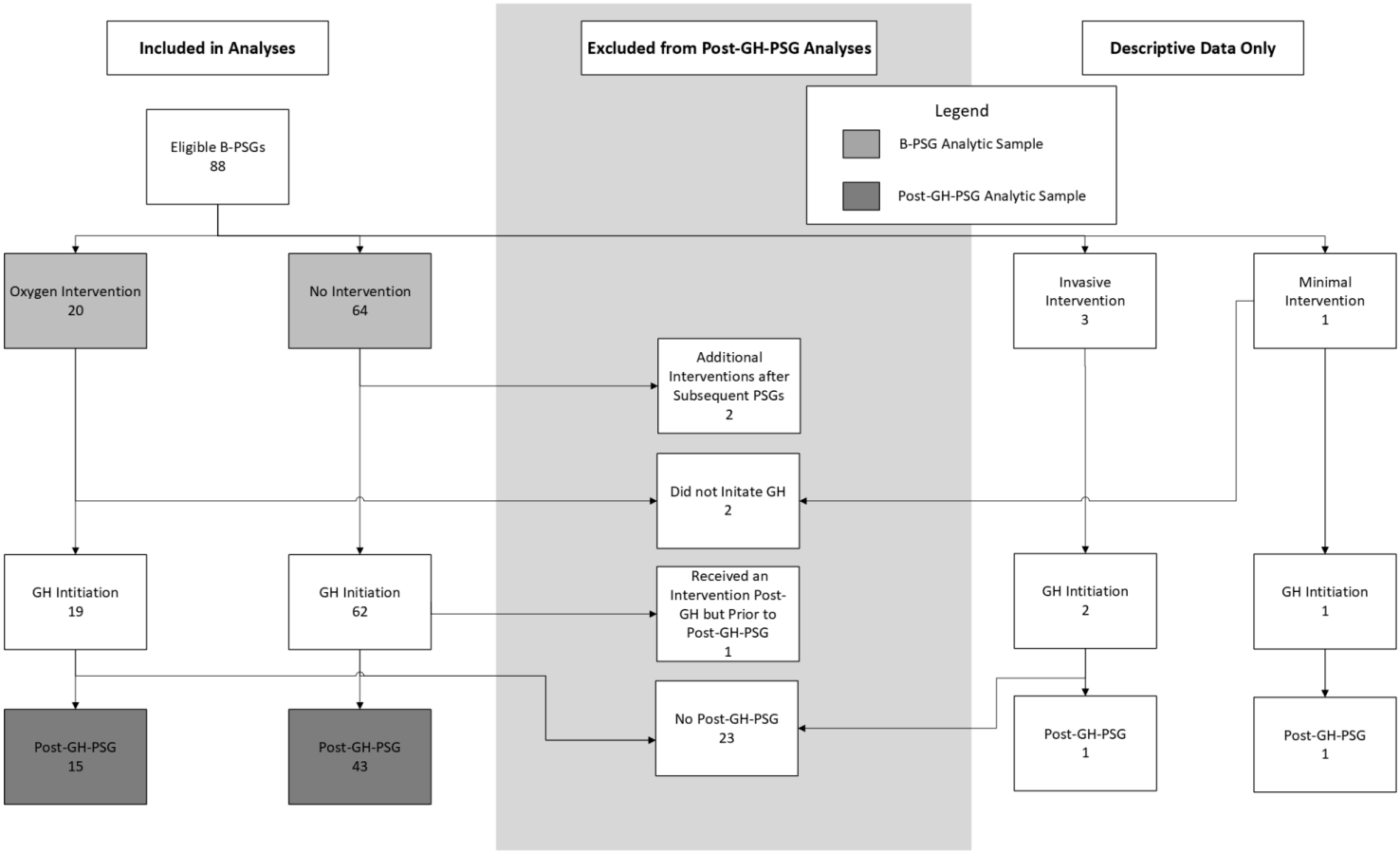


Figure 1

Flowchart of Study Cohort

Figure 1 shows the flowchart of the study cohort. Patients in the shaded gray area were excluded from statistical analyses due to confounding factors or not meeting Post-GH-PSG inclusion criteria. Although Minimal and Invasive Intervention groups were excluded from statistical analysis due to sample size limitations, their descriptive data is still included. Abbreviations: PSG = polysomnogram; CSA = central sleep apnea; OSA = obstructive sleep apnea; B-PSG = baseline polysomnogram; GH = growth hormone; Post-GH-PSG = post-growth hormone polysomnogram.