PWS publications April to June 2026

PWS PAPERS OF INTEREST

Listed below along with their abstracts are selected papers on PWS newly appearing in PubMed between 1st January and end of March 2025 in peer reviewed academic journals. All papers are initially listed without their summaries to give a quick overview, then for most of the papers the summaries are included later in the document. They are divided into specific categories: General PWS and families; Genetics and brain imaging; Endocrine including GH; Sensory and physical; Behaviour; Cognition and mental health.

This list has been compiled by Joyce Whittington and by members of the IPWSO Scientific Advisory Committee. If there are papers that you think should have been included, please let Joyce Whittington know (jew1000@cam.ac.uk).

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General PWS and families

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Nueraili Dayimu , Lingli Leng , Gulisitan Kuerbanniyazi , Xiaojing Lin. Loneliness and parental caregiving burden in families of children with Prader-Willi syndrome in China: the moderating effects of family functioning and socioeconomic status. Front Psychol. 2026 May 29:17:1771064. eCollection 2026.

Lauren Schwartz , Abigail TurnWald , Madelyn Roth , Theresa V Strong. Lived Experiences of Teens and Adults in North America Who Grew Up With a Sibling Diagnosed With Prader Willi Syndrome. J Appl Res Intellect Disabil. 2026 May;39(3):e70263.

Joyce Whittington , Anthony J Holland. Review of estimates of birth incidence and population prevalence over time and between countries of the rare neurodevelopmental condition Prader-Willi syndrome. J Med Genet. 2026 Jun 5:jmg-2025-111438. Online ahead of print.

Ayako Konishi , Makiko Tachibana , Yuji Oto , Kenichi Kashimada , Tomohiro Ishii , Yoko Aoki , Koji Muroya , Yutaka Takahashi , Kenji Kurosawa , Tsutomu Ogata , Masanobu Kawai. Health-Related Quality of Life and Its Related Factors in Adolescents and Adults With Prader-Willi Syndrome in Japan. Am J Med Genet A. 2026 May 31. Online ahead of print.

Isidro Miguel Martín Pérez , Sebastián Eustaquio Martín Pérez · Effectiveness and Safety of Hormonal Treatments in Children with Growth Disorders: A Systematic Review of Clinical Evidence. Clin Pract. 2026 May 20;16(5):96.

Jennifer M Miller , Ashley H Shoemaker , Parisa Salehi , Jorge Mejia-Corletto. Diazoxide choline extended-release (DCCR) use in Prader-Willi syndrome: patient selection, dosing, and management. J Endocr Soc. 2026 Apr 30;10(6):bvag099. eCollection 2026 Jun.

Prakriti Pokhrel , Hidhaya S Noorul , Laraib Fatima , Aakash Kumar , Amrah Abdul Samad , Gerardo F Ferrer. Vykat XR (diazoxide choline-extended release): a new FDA-approved treatment for hyperphagia in Prader-Willi syndrome. Ann Med Surg (Lond). 2026 Apr 27;88(5):2728-2730. eCollection 2026 May.

Genetics and brain imaging

Yung-Ling Tseng , Ying-Chung Chen · Incomplete trisomy 15 rescue associated with hypermethylation of the Prader-Willi critical region. Taiwan J Obstet Gynecol. 2026 Jul;65(4):789-793.

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Lorenzo Chiarella , Ramona Cordani , Marco Veneruso , Antonella Barbieri , Flavia Napoli , Mohamad Maghnie , Lino Nobili. Teaching Video NeuroImage: Eating-Related Cataplexy in Prader-Willi Syndrome. Neurology. 2026 Jun 9;106(11):e218016. Epub 2026 May 5.

Erina Nakane , Hiroyuki Ogata , Sohei Saima , Chuichi Kondo , Masaki Seki , Yuji Oto , Hiroshi Ihara. Associations Between Sensory Processing and Irritability in Prader-Willi Syndrome: Beyond Genetic Subtypes and Clinical Backgrounds. Am J Med Genet A. 2026 Apr 29. Online ahead of print.

Cognition and mental health

Lisa Rein , Christine Tørris , Ana Carla Soares Portugal Schippert , Malin Holmström Rising , Astrid Torbjørnsen , Tina Rich Mogensen , Ann Kristin Bjørnnes. What Is Known About Persons with Intellectual Disabilities and Cardiovascular Risk Factors-A Scoping Review. Epidemiologia (Basel). 2026 Apr 25;7(3):59.

Christian Karl Eberlein, Maximilian Jakob , Angelina Jechalke , Gesa Ordon [Psychiatric challenges in Prader-Willi syndrome][Article in German] Nervenarzt. 2026 Apr 23. Online ahead of print.

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Abstracts

General PWS and families

James Luccarelli , Theresa V Strong, Thomas H McCoy Jr. Validation of the Q87.11 ICD Code for Prader-Willi Syndrome. J Intellect Disabil Res. 2026 Jun 24. Online ahead of print.

Abstract Background: Prader-Willi syndrome (PWS) is a rare genetic disorder that is identified by the ICD-10 code Q87.11. Although this code has been used in several large studies, its diagnostic validity has not been evaluated. This study assessed the accuracy of the Q87.11 code for identifying individuals with PWS.

Methods: The electronic health record (EHR) of a large health system was reviewed for patients with the Q87.11 code. Additionally, a 10% random sample of patients with free-text evidence of possible PWS but no code was reviewed. All charts were assessed for PWS using expert review. Diagnostic validity of the Q87.11 code was assessed at both the individual level (i.e., using a single diagnostic code at any point in the EHR to define the patient as having PWS) and encounter level (looking at coding behaviour for individual inpatient or outpatient episodes of care) using sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Results: Of 2 718 218 patients with ≥ 4 recorded encounters, 126 had at least one Q87.11 code; 122 were confirmed to have PWS by chart review. This yielded a PPV of 96.8% (95% CI: 92.0%-99.1%). Full-chart review of patients with text evidence of PWS but no code estimated a code sensitivity of 92.4% (95% CI: 68.9%-100%) and specificity and NPV of 100%. On a per-encounter basis, sensitivity was 79.4% (95% CI: 62.6%-91.1%) for inpatient and 46.0% (95% CI: 44.1%-47.9%) for outpatient visits.

Conclusions: A single use of the Q87.11 diagnostic code produces excellent sensitivity, specificity, PPV and NPV for identifying patients with PWS, although sensitivity is lower for individual outpatient encounters compared with inpatient ones. The overall accuracy of the Q87.11 code supports the validity of using this code in the analysis of administrative claims datasets.

Keywords: Prader-Willi syndrome; coding; cohort studies; detection.
PMID: 42340009 DOI: 10.1111/jir.70140

Nueraili Dayimu , Lingli Leng , Gulisitan Kuerbanniyazi , Xiaojing Lin. Loneliness and parental caregiving burden in families of children with Prader-Willi syndrome in China: the moderating effects of family functioning and socioeconomic status. Front Psychol. 2026 May 29:17:1771064. eCollection 2026.

Abstract Background: Raising a child with Prader-Willi syndrome (PWS) is associated with substantial caregiving challenges for parents. Elevated levels of caregiving burden and loneliness have been documented in this population. However, the relationship between loneliness and caregiving burden, as well as the factors that may shape this association, remains insufficiently understood.

Objectives: This study aimed to examine the association between loneliness and parental caregiving burden, particularly regarding the moderating role of family functioning and family SES.

Methods: A cross-sectional survey was conducted among 1,105 children with PWS and their parent caregivers through *the Prader-Willi Syndrome Care and Support Center* from July to October, 2023. Participants completed a questionnaire assessing sociodemographic factors, self-rated health (EQ-5D-5L), caregiving burden (ZBI-22), loneliness (De Jong Gierveld-11), and family function (Apgar-5). Descriptive statistics and hierarchical multiple linear regression analyses were conducted in R 4.2.2. We employed a nonparametric bootstrapping for sensitivity analysis.

Results: Results indicated: (1) Loneliness was positively associated with caregiving burden. (2) Family SES was negatively associated with caregiving burden. (3) Family functioning negatively moderates the association between loneliness and caregiving burden. (4) Family SES positively moderates the association between loneliness and caregiving burden.

Conclusion: This study identifies that loneliness was positively associated with caregiving burden among parents of children with PWS in China. Family functioning buffers the effect, whereas higher SES may

amplify it. These findings highlight the importance of promoting family cohesion, financial stability, PWS-specific social welfare, and reducing parental loneliness.
Keywords: Prader-Willi syndrome; caregiving burden; family SES; family function; loneliness; primary caregiver; rare disease.
PMID: 42293888 PMCID: PMC13261814 DOI: 10.3389/fpsyg.2026.1771064

Lauren Schwartz , Abigail TurnWald , Madelyn Roth , Theresa V Strong. Lived Experiences of Teens and Adults in North America Who Grew Up With a Sibling Diagnosed With Prader Willi Syndrome. J Appl Res Intellect Disabil. 2026 May;39(3):e70263.
Abstract Background: Prader-Willi syndrome (PWS) is a complex disorder with severe behavioural symptoms that affects the entire family. Relatively little research has focused on the lived experiences of siblings growing up in this unique family environment.
Method: Semi-structured interviews were performed with 25 siblings of individuals with PWS from North America. Participants reflected on their experiences including interpersonal relationships, impacts on well-being, coping, and relationship with food.
Results: Using inductive thematic analysis, we identified several themes: (a) emotion and well-being impacts, (b) impacts on their relationship with food, and (c) relational/social issues. Positive aspects of their family experience and impacts on job path were identified. Key coping resources were highlighted.
Conclusions: This study can inform more family-oriented support efforts in PWS care models to include sibling support. The findings suggest sibling support should focus on addressing difficult emotional experiences, problematic eating behaviours, and seeking connection with other siblings with similar experiences.
Keywords: Prader-Willi syndrome (PWS); eating behaviours; family impact; siblings; support.
PMID: 42286844 DOI: 10.1111/jar.70263

Joyce Whittington , Anthony J Holland. Review of estimates of birth incidence and population prevalence over time and between countries of the rare neurodevelopmental condition Prader-Willi syndrome. J Med Genet. 2026 Jun 5:jmg-2025-111438. Online ahead of print.
Abstract Epidemiological data such as birth incidence or population prevalence for rare conditions is difficult to obtain because of the large sample size required in order to obtain a valid estimate (ie based on a reasonable number of cases) and the difficulty of either identifying all cases or meeting the cost and logistics of screening the whole general population in that large sample. This article illustrates these difficulties in the case of the rare neurodevelopmental condition Prader-Willi syndrome (PWS). Before reviewing attempts that have been made over the years to estimate birth incidence and/or population prevalence in this condition, this review discusses aspects of PWS, clear definitions of the measures themselves and aspects of general populations that are pertinent to estimates of birth incidence and population prevalence. Although most published studies on PWS quote a prevalence (meaning not always clear) estimate, very few quote the original study on which it is based. Our review found very few (12) original studies. These are described in some detail and where relevant methodological details that render the findings suspect are discussed. Finally, we answer the question of the existence of global estimates for birth incidence and population prevalence of PWS, showing that they will vary from one population to another at a given time and from one time period to another for a given population. However, for very similar populations at a given time, the values may lie within a very close range.
Keywords: Demography; Diagnosis; Genetic Diseases, Inborn; Methods
PMID: 42248669 DOI: 10.1136/jmg-2025-111438

Ayako Konishi , Makiko Tachibana , Yuji Oto , Kenichi Kashimada , Tomohiro Ishii , Yoko Aoki , Koji Muroya , Yutaka Takahashi , Kenji Kurosawa , Tsutomu Ogata , Masanobu Kawai. Health-Related Quality of Life and Its Related Factors in Adolescents and Adults With Prader-Willi Syndrome in Japan. Am J Med Genet A. 2026 May 31. Online ahead of print.
Abstract Prader-Willi syndrome (PWS) is a rare neurogenetic disorder characterized by endocrine, metabolic, behavioral, and psychiatric features. These manifestations may affect health-related quality of life

(HRQOL). Evidence on HRQOL in adolescents and adults with PWS remains limited. This study evaluated HRQOL and examined sex, age, genetic, and behavioral factors associated with HRQOL in individuals with genetically confirmed PWS aged 16 years and over. A proxy-reported questionnaire survey was conducted through a Japanese national PWS support group, and responses from 119 participants (median age, 25 years) were analyzed. The primary outcome was a EuroQol five-dimension five-level (EQ-5D-5L) index value in the upper tertile of the study distribution (≥ 0.744). The median EQ-5D-5L index value was 0.665 (IQR, 0.549-0.775), and the mean was 0.652 (SD, 0.180). Only 4.3% of participants reported no problems in any dimension. Younger age (16-19 years) (OR, 4.62; 95% CI, 1.42-15.1), the deletion genetic subtype (4.79; 1.15-20.0), and lower problematic food-related behaviors (0.90; 0.83-0.97) were independently associated with an EQ-5D-5L index value in the upper tertile. Support during the transition from late adolescence to early adulthood and attention to problematic food-related behaviors may be important for improving the HRQOL of individuals with PWS.
Keywords: EQ-5D-5L; HQ-CT; HRQOL; Prader–Willi syndrome; adolescent; adult; health-related quality of life.
PMID: 42219582 DOI: 10.1002/ajmg.a.70222

Isidro Miguel Martín Pérez, Sebastián Eustaquio Martín Pérez. Effectiveness and Safety of Hormonal Treatments in Children with Growth Disorders: A Systematic Review of Clinical Evidence. Clin Pract. 2026 May 20;16(5):96.
Abstract Background: Growth disorders, including central precocious puberty and delayed puberty, can significantly affect linear growth, skeletal maturation, metabolic regulation, and psychosocial development during childhood and adolescence. This systematic review synthesizes the current evidence regarding the effectiveness and safety of hormone-based therapies used in children with disorders of pubertal maturation. Methods: A PRISMA-guided systematic search was carried out between January 2016 and March 2026 in different databases, such as MEDLINE (PubMed), EMBASE, CENTRAL, Scopus, Web of Science, CINAHL, LILACS and OpenGrey; the protocol was previously registered in the PROSPERO database (CRD420251068048). Non-randomized, randomized controlled trials and observational research including participants aged 0-18 years receiving hormone therapies were eligible. Risk of bias was assessed using validated, design-specific tools. Results: Twenty studies involving 21,812 participants were included. GnRHa therapy improved final adult height (+3.5 to +4.5 cm) and reduced bone age advancement (-0.6 to -1.3 years) in children with central precocious puberty. rhGH therapy increased growth velocity (+3.0 to +5.0 cm/year) and height SDS (+0.3 to +0.9), particularly in idiopathic short stature and Prader-Willi syndrome. Combined GnRHa plus rhGH therapy showed greater short-term growth benefits than GnRHa alone. Both therapies showed favorable safety profiles, with predominantly mild adverse events and discontinuation rates below 2%. However, the evidence was limited by substantial heterogeneity and moderate-to-serious risk of bias. Conclusions: GnRHa and rhGH therapies are generally effective and safe for improving growth and pubertal outcomes in pediatric endocrine disorders. However, further long-term studies are needed to clarify their metabolic and psychosocial effects in adulthood. Nevertheless, these conclusions should be interpreted with caution due to the study's moderate-to-serious risk of bias and heterogeneity.
Keywords: GnRH; bone age; growth; hormone therapy; pediatric endocrinology; pubertal disorders; sex steroids.
PMID: 42187530 DOI: 10.3390/clinpract16050096

Jennifer M Miller, Ashley H Shoemaker, Parisa Salehi, Jorge Mejia-Corletto. Diazoxide choline extended-release (DCCR) use in Prader-Willi syndrome: patient selection, dosing, and management. J Endocr Soc. 2026 Apr 30;10(6):bvag099. eCollection 2026 Jun.
Abstract Prader-Willi syndrome (PWS) is a rare genetic disorder marked by metabolic, endocrine, and behavioral challenges, with hyperphagia as a central feature contributing to significant health risks. Diazoxide choline extended-release (DCCR; VYKAT™ XR) is a once-daily adenosine triphosphate (ATP)-sensitive potassium channel activator recently approved for the treatment of hyperphagia in individuals with genetically confirmed PWS aged 4 years and older. As this novel therapy enters clinical practice, clinicians require practical guidance on appropriate use. This manuscript provides actionable recommendations for patient selection, baseline assessments, and strategies for optimizing comorbid conditions prior to initiation.

Structured, weight-based dosing and titration protocols are outlined, along with recommendations for monitoring glycemia and edema and managing common adverse events (AEs), including hyperglycemia, peripheral edema, and rash. Special considerations are discussed for patients with diabetes, cardiopulmonary risk factors, and those on concomitant medications with potential drug-drug interactions. The guidance is informed by data from the phase 3 DESTINY-PWS program, long-term extension studies, and real-world clinical experience. Emphasis is placed on early identification and management of AEs and the importance of a multidisciplinary approach to care. These recommendations aim to support clinicians in safely and effectively incorporating DCCR into the management of PWS, improving outcomes for affected individuals. Ongoing research and real-world evidence will continue to refine best practices and address remaining gaps in knowledge.
Keywords: Prader–Willi syndrome; diazoxide choline extended-release; hyperphagia; patient selection.
PMID: 42100354 PMCID: PMC13148164 DOI: 10.1210/jendso/bvag099

Prakriti Pokhrel , Hidhaya S Noorul , Laraib Fatima , Aakash Kumar , Amrah Abdul Samad , Gerardo F Ferrer. Vykat XR (diazoxide choline-extended release): a new FDA-approved treatment for hyperphagia in Prader-Willi syndrome. Ann Med Surg (Lond). 2026 Apr 27;88(5):2728-2730. eCollection 2026 May.
Abstract On March 27, 2025, the U.S. Food and Drug Administration (FDA) approved Vykat XR (diazoxide choline-extended release tablets) for the treatment of hyperphagia in individuals aged 4 years and older with Prader-Willi Syndrome (PWS). This marks the first FDA-approved pharmacologic therapy targeting hyperphagia in this population, addressing a long-standing unmet need and offering new hope for patients, caregivers, and clinicians.
Keywords: Prader-Willi syndrome; Vykat XR; diazoxide choline; hyperphagia.
PMID: 42078615 PMCID: PMC13132293 DOI: 10.1097/MS9.0000000000004938

Genetics and brain imaging

Yung-Ling Tseng , Ying-Chung Chen . Incomplete trisomy 15 rescue associated with hypermethylation of the Prader-Willi critical region. Taiwan J Obstet Gynecol. 2026 Jul;65(4):789-793.
Abstract Objectives: To present a rare prenatal case of incomplete trisomy 15 rescue with hypermethylation in the Prader-Willi critical region and to emphasize the diagnostic challenges associated with discordant results among NIPT, chromosomal microarray, and karyotype, highlighting the critical role of methylation analysis in confirming the diagnosis.
Case report: Our patient of 41-yea-old underwent NIPT showed trisomy 15 but low risk in PWS and Angelman syndrome. Subsequent karyotyping and CGH array provided discordant results possibly due to incomplete trisomy rescue. To clarify the diagnosis, MLPA was performed to confirm the hypermethylation of the Prader-Willi critical region, presenting as atypical PWS.
Conclusion: This case highlights the importance of MLPA test in the diagnosis workflow of atypical PWS caused by incomplete trisomy rescue. Early recognizing of atypical PWS is important due to its variable prognosis reported by current literatures.
Keywords: Atypical Prader–Willi syndrome; Incomplete trisomy 15 rescue; Methylation-specific MLPA; Mosaic trisomy 15; Prenatal diagnosis; Uniparental disomy.
PMID: 42362270 DOI: 10.1016/j.tjog.2025.10.017

Laura Doetsch , Leo Weirauch , Janika Hunger , Tobias Thiemann , Johann Maaß , Constanze Schmidt , Florian Leuschner , Christian P Schaaf , Henning Froehlich. Magel2 deficiency promotes cardiac

remodeling and increases arrhythmogenic susceptibility in a mouse model relevant to Prader-Willi and Schaaf-Yang syndromes. Clin Sci (Lond). 2026 Jun 9:CS20260647. Online ahead of print.
Abstract Prader-Willi syndrome (PWS) and Schaaf-Yang syndrome (SYS) share overlapping phenotypic features, but potential cardiac involvement in both conditions remains poorly understood. Here, we investigated cardiac function in Magel2 knockout (KO) mice, a model relevant to PWS and SYS, to assess the impact of Magel2 deficiency on the heart. Echocardiographic analysis of 20-week-old Magel2-KO mice revealed concentric remodeling of the left ventricle together with reduced left ventricular end-diastolic volume and stroke volume, as well as a modest but significant reduction in ejection fraction. Electrophysiological studies identified sex-dependent alterations, particularly in males, characterized by shortened action potential duration and increased atrial potassium currents. Surface ECG recordings showed no overt arrhythmias and visual inspection confirmed sinus rhythm during the monitoring period; however, the observed cellular alterations indicate increased arrhythmogenic susceptibility. In addition, aged Magel2-KO mice developed adult-onset obesity and exhibited elevated HbA1c levels consistent with impaired glycemic control. Given the minimal expression of Magel2 in cardiac tissue, these findings suggest that systemic and metabolic alterations may contribute to the observed cardiac phenotype. Together, these results demonstrate structural cardiac remodeling and electrophysiological changes consistent with increased arrhythmogenic susceptibility in Magel2-deficient mice, suggesting clinically relevant cardiac involvement in SYS and PWS. Our findings support consideration of structured cardiovascular monitoring to mitigate potential secondary cardiac complications in affected individuals.
Keywords: Concentric cardiac remodeling; Magel2; Prader-Willi syndrome; Schaaf-Yang syndrome.
PMID: 42275194 DOI: 10.1042/CS20260647

Jannis Buecking, Baran Enes Güler, Michael Eibl, Azmal Syed Ali, Tobias Walczuch, Tobias Beschauner, Susanne Theiss, Melanie Spanjaard, Katrin Hinderhofer, Freya Herrmann-Sim, Multi-omics profiling reveals MAGEL2-driven defects in human corticogenesis shared across Prader-Willi and Schaaf-Yang syndromes**. [Preprint]** bioRxiv 2026 May 4:2026.05.01.722223.
Abstract The human cortex acquires its advanced cognitive capacity through tightly regulated developmental programs, disruption of which underlies neurodevelopmental disorders such as Schaaf-Yang syndrome (SYS) and Prader-Willi syndrome (PWS). While SYS results from pathogenic variants in the imprinted gene *MAGEL2* , PWS arises from chromosomal deletions, imprinting defects or uniparental disomy encompassing the *MAGEL2* locus. However, the contribution of *MAGEL2* to disease pathogenesis and human corticogenesis is not fully understood. Here, we performed integrated transcriptomic, proteomic, and ubiquitinomic profiling of cortical neurons derived from CRISPR/Cas9-engineered isogenic human pluripotent stem cells (hiPSC) modeling SYS and PWS. Beyond PWS-specific signatures including dysregulated ribosomal processes, we identified *MAGEL2* -dependent defects shared across both disorders. These include reduced progenitor proliferation, accelerated neuronal maturation, impaired migration and adhesion, as well as abnormal synaptic development, collectively linking PWS and SYS at the level of cortical development. Notably, these phenotypes partially overlap with those observed in other neurodevelopmental disorders, suggesting that *MAGEL2* governs core pathways broadly vulnerable in disease. Together, our findings establish *MAGEL2* as a key regulator of human cortical development, provide a unifying mechanistic framework for SYS and PWS, accessible via a web-based platform.
PMID: 42146651 PMCID: PMC13174559 DOI: 10.64898/2026.05.01.722223

Wei Huang , Min Xiao , Xunchang Zou , Tawfiq Mohammed , Zhenyang Feng , Lei Cao. Low dose systemic AAV-exendin-4 gene therapy for Prader-Willi syndrome and dietary obesity. Mol Ther Adv. 2026 Mar 12;34(2):201718. eCollection 2026 Jun 11.
Abstract Prader-Willi syndrome (PWS) patients display developmental delays, endocrine dysfunction, excessive eating, central obesity, and various behavioral abnormalities. Effective and sustained treatments are limited, highlighting the need for new therapeutic strategies. Glucagon-like peptide-1 receptor agonists (GLP-1RA) have revolutionized obesity treatment while their efficacy in PWS population remains inconsistent and data in PWS animal models are lacking. Here, we assessed the efficacy of a newly developed AAV platform to deliver a GLP-1RA exendin-4 via an engineered hybrid capsid Rec2. Intraperitoneal administration of Rec2-exendin-4 at the dose of 2×10^{10} viral genome per mouse normalized

metabolic dysfunction in the *Magel2*-null mouse model of PWS. Systemic Rec2-exendin-4 treatment reversed genotype-driven excessive adiposity, impaired glycemic control, hyperleptinemia, and adipose gene expression signatures. Moreover, intraperitoneal injection of Rec2-exendin-4 (4×10^{10} viral genome/mouse) exerted high levels of efficacy in diet-induced obesity model-decreasing food intake; preventing excessive weight gain and obesity; improving glucose metabolism and insulin sensitivity; and reversing fatty liver. Metabolic improvements were maintained at least 5 months. These data demonstrate the therapeutic potential of a systemic AAV-mediated exendin-4 gene therapy for PWS-related metabolic abnormalities in *Magel2*-null model and dietary obesity.
Keywords: AAV; Magel2; Prader-Willi syndrome; adeno-associated virus; diet-induced obesity; exendin-4; gene therapy; intraperitoneal administration; metabolism; molecular therapy.
PMID: 42137604 PMCID: PMC13148920 DOI: 10.1016/j.omta.2026.201718

Caroline J Vrana-Diaz , Jessica Bohonowych , Jaimie L Richards , Brandon M Wilk , Manavalan Gajapathy , Yael Bar-Peled , Anna C Harris , Jessica J Denton , Donna Brown , Elizabeth A Worthey , Theresa V Strong. Study design with responsible return of results for a fully remote genome sequencing study in individuals with Prader-Willi syndrome. Genet Med Open. 2025 Aug 11:4:103448. eCollection 2026.
Abstract Purpose: Prader-Willi syndrome (PWS) is a complex neurodevelopmental genetic disorder affecting multiple systems. We describe the design and feasibility of a fully remote, patient group-led, genome sequencing (GS) study that will evaluate the impact of genetic variants on the frequency and severity of PWS clinical symptoms, with responsible return of results.
Methods: A total of 50 participants, or their legally authorized representative, provided consent via videoconference discussion and selected which genetic results would be returned. Participants were sent dried blood spot cards for GS and a buccal swab kit for orthogonal pharmacogenomics analysis. A subset of legally authorized representative LARs participated in semistructured interviews about their GS experience.
Results: All 50 participants completed the study and elected to receive their primary findings, and 48 of 49 participants who consented to receive pharmacogenomic information returned the buccal swab kit. Forty-seven participants consented to receive secondary findings per current American College of Medical Genetics guidelines; 2 had actionable results, with online genetic counseling support provided. Three families received medically significant findings related to variants associated with blood clot formation, which is important because individuals with PWS are at an increased risk for thrombotic events. Interview participants expressed a high degree of interest in the findings and emphasized the ease of participating in the study but felt the process was lengthy.
Conclusion: A fully remote GS study is feasible to perform within a rare disease population, and responsibly returning genetic findings that are important to families is achievable.
Keywords: Genome sequencing; Patient advocacy group; Pharmacogenomics; Prader-Willi syndrome; Secondary findings.
PMID: 42111686 PMCID: PMC13156615 DOI: 10.1016/j.gimo.2025.103448

Emilie J Korchak, Gabriella A Soriano, Irina Semenova, Bing Hao, Denis Štepihar, Tara Bayat, Klementina Fon Tacer, Irina Bezsonova. Mechanisms of USP7/MAGEL2 Complex Assembly and Its Mutational Disruption in Neurodevelopmental Diseases. bioRxiv 2026 Apr 28:2026.04.24.720667. **[Preprint].**
Abstract The WASH complex regulates endosomal trafficking and is linked to several neurodevelopmental diseases, including Prader-Willi syndrome, Schaaf-Yang syndrome, and Hao-Fountain syndrome. Its function is tightly controlled by ubiquitination, maintained by the multi-subunit MUST complex containing both a ubiquitin ligase (MAGEL2/TRIM27) and a deubiquitinase (USP7). However, the mechanism underlying the MUST complex assembly remains poorly understood. In this study, we investigate the assembly of USP7 and MAGEL2 components of the MUST complex using NMR spectroscopy, isothermal titration calorimetry, X-ray crystallography, and cellular assays. We show that the USP7/MAGEL2 interaction is bipartite and multivalent. Two distinct domains of USP7, TRAF and UBL1-2, recognize two unstructured but evolutionarily conserved regions of MAGEL2, one of which contains multiple TRAF-binding sites. Furthermore, we determine the high-resolution crystal structure of the

TRAF/MAGEL2 complex and identify Hao-Fountain syndrome-linked mutations in USP7 that disrupt USP7/MAGEL2 complex formation *in vitro* and in cells. These findings provide mechanistic insight into the pathogenic basis of Hao-Fountain syndrome and related Schaaf-Yang and Prader-Willi syndromes.
PMID: 42094436 PMCID: PMC13142314 DOI: 10.64898/2026.04.24.720667

Jie Liu , Zhongxin Huang , Jinhua Cai , Min Zhu , Song Peng , Shuang Ding , Longlun Wang , Wei Tang , Chunlan Sun , Jiaxin Su. Aberrant local and global neural activation patterns in pediatric Prader-Willi syndrome. Front Neurosci. 2026 Apr 15:20:1696114. eCollection 2026.
Abstract Purpose: Although cognitive disorders in children with Prader-Willi syndrome (PWS) are linked to abnormalities in spontaneous neural activation and functional connectivity (FC), the specific neural activation patterns remain uncertain, especially in young children with PWS.
Methods: The current study set out to explore specific local and global neural activation in pediatric PWS using the amplitude of low-frequency fluctuations (ALFF), regional homogeneity (ReHo), and seed-based whole brain FC. Information was gathered from 35 pediatric PWS patients and 33 healthy controls (HC). Both groups' ALFF and ReHo values were computed, and FC were constructed on the basis of altered ALFF and ReHo regions. The relationships between altered ALFF, ReHo, and FC and the Griffiths Developmental Scales (GDS) of the PWS group were analyzed using partial correlation analysis.
Results: Both ALFF and ReHo exhibited decreases in occipital lobe, temporal lobe, and cingulate gyrus, and altered ReHo was present in parietal lobe, frontal lobe, and basal ganglia areas. Moreover, ALFF and ReHo also exhibited increases in occipital and temporal lobes. Decreased FC was detected in the visual network (VN), sensorimotor network (SMN), salience network (SAN), and default mode network (DMN). The SMN-, cingulate-, and occipital lobe-related neural activation patterns were significantly positively correlated with the GDS score.
Conclusion: The PWS group was characterized mainly by decreased neuronal physiological function and the ReHo was similar to ALFF but more extensive. The decreased local and global brain neural activation patterns may serve as early physiological indicators of cognitive abnormalities.
Keywords: Prader–Willi syndrome; functional connectivity; low-frequency fluctuations; magnetic resonance imaging; regional homogeneity
PMID: 42063965 PMCID: PMC13124620 DOI: 10.3389/fnins.2026.1696114

Kunal Bham , Manju Anandakrishnan , Cathy H Wu , Karen E Ross. A network-centric approach reveals novel pathways impacted by Prader-Willi Syndrome. PLoS One. 2026 Apr 28;21(4):e0347773. eCollection 2026.
Abstract Prader-Willi Syndrome (PWS), a rare multi-system disorder characterized by insatiable appetite, growth abnormalities, and cognitive delay, results from genetic defects in a paternally expressed region of chromosome 15, q11.2-q13. This region contains several protein-coding genes and several genes encoding small nucleolar RNA (snoRNAs), including the SNORD116 gene cluster, but their exact role in PWS remains unclear. Since snoRNAs have wide-ranging effects on protein expression and proteins interact in a complex network, the genetic aberrations causing PWS are likely to cause far-reaching indirect effects on protein expression and activity. Here, we mapped PWS gene expression data onto a human protein-protein interaction (PPI) network and used graph learning techniques to 1) identify the most impacted proteins and 2) suggest novel disease mechanisms. We adapted GeneEMBED, a network-based method originally developed to model genetic variants associated with Alzheimer's Disease. Specifically, we integrated PWS or control expression data with the PPI network, calculated node embeddings, and identified proteins with large differences between PWS and control embeddings. These candidate proteins were subjected to functional enrichment analysis to discover altered biological processes in PWS. Candidate proteins were highly enriched for glycosylated proteins. Analysis of candidate glycosylation enzymes suggested abnormalities in mucin-type O-glycosylation, fucosylation, and glycosaminoglycan synthesis. Defects in these glycosylation pathways have been linked to several PWS phenotypes, including obesity, cognitive delay, and production of secondary sex hormones. Homeobox proteins, master regulators of transcription during development, were also overrepresented among the candidate proteins. In particular, we identified homeobox proteins that drive development of GABAergic and dopaminergic neurons. These neuronal pathways regulate appetite and other behaviors that are abnormal in individuals with PWS. Our results were

highly reproducible across PWS model systems. This work offers new avenues for further research in PWS and provides a promising approach that can be applied to other complex diseases.
PMID: 42048351 DOI: 10.1371/journal.pone.0347773

Aurélien Juven , Catherine Vaurs-Barrière , Franck Court , Bertille Montibus , Philippe Arnaud. Mechanisms Controlling Genomic Imprinting and Their Dysregulation in Human Imprinting Disorders. Ann Endocrinol (Paris). 2026 Apr 15:102552. Online ahead of print.
Abstract Imprinted genes play a pivotal role in regulating growth, development, and behavior through parent-of-origin-specific expression. This allelic specificity is orchestrated by "imprinting control regions" (ICRs), which depend on DNA methylation marks established on only one parental allele. The epigenetic life cycle of imprinting involves dynamic reprogramming: preexisting methylation is erased in primordial germ cells, followed by the establishment of new marks in either the female or male germline. After fertilization, these allele-specific methylation patterns are faithfully maintained throughout somatic development, ensuring proper gene dosage and function. Disruption of this tightly regulated epigenetic cycle, during germline erasure, establishment, or somatic maintenance, can lead to human diseases. Errors in imprinting are linked to at least thirteen congenital imprinting disorders, including Beckwith-Wiedemann syndrome (BWS), Prader-Willi syndrome (PWS), and Silver Russell Syndrome (SRS). Endocrine dysfunctions are central to these conditions, reflecting the critical involvement of imprinted genes in growth regulation and hormonal signalling. In this review, we dissect the molecular mechanisms governing the reset, acquisition, maintenance, and transmission of imprints across development, and examine how perturbations at each stage contribute to the pathogenesis of imprinting disorders.
Keywords: DNA methylation; Epigenetics regulation; Imprinting disorders.
PMID: 41997497 DOI: 10.1016/j.ando.2026.102552

Eman Abuijlan , Shruti Sinha , Sathishkumar Ramaswamy , Ruchi Jain , Ikram Chekroun , Fatma Rabea , Maha El Naofal , Syeda Khadija , Radwa Sharaf , Omer S Alkhnbashi , Fahad Ali , Alawi Alsheikh-Ali , Ahmad Abou Tayoun . Targeted long-read genomic and epigenomic profiling enhances timely comprehensive variant discovery in hypotonia and muscle weakness. BMC Med. 2026 Apr 8. Online ahead of print.
Abstract Background: Identifying the genetic basis of hypotonia and muscle weakness is critical for patient management and family counseling. However, diagnosis is often hindered by diverse genomic alterations, including repeat expansions, structural variants (SVs), and methylation defects. Standard-of-care testing, largely based on short-read sequencing, is limited in its ability to detect this heterogeneous variation landscape, leaving many patients undiagnosed or requiring lengthy sequential testing. Long-read sequencing represents a promising solution. However, its application as a first-tier diagnostic assay for hypotonia remains unexplored.
Methods: We retrospectively analyzed 227 patients with hypotonia to assess diagnostic yield, time-to-diagnosis, and costs associated with standard-of-care testing. A long-read whole-genome sequencing (LR-WGS) workflow with targeted analysis of hypotonia-associated genes was developed to detect and prioritize pathogenic SNVs, SVs, and CNVs, repeat expansions, and methylation changes at key disease loci. The workflow was validated in a reference-positive cohort with known diagnoses (n = 15) and applied to an unsolved cohort (n = 14). Variant interpretation followed ACMG guidelines and was confirmed with orthogonal methods.
Results: Standard-of-care testing achieved a diagnostic yield of 42% with an average time-to-diagnosis of 68.7 days; however, 30% of diagnosed patients experienced significant delays (average 169 days) due to sequential testing. The LR-WGS based approach identified all known pathogenic variants in the positive cohort, including SMN1 deletions, methylation defects at 15q11.2/Prader-Willi locus, FMR1 repeat expansions, and sequence and copy-number variants in > 100 genes underlying myopathies and muscular dystrophies. The targeted long-read pipeline reduced prioritized variant calls by 97.9-99.9% and, in the unsolved cohort, yielded one definitive diagnosis (de novo COL6A3 deletion) and one possible diagnosis (aberrant methylation and copy number at POMK), for an additional 14% yield. Among patients diagnosed after sequential testing (n = 29), LR-WGS is expected to reduce time-to-diagnosis by ~ 85% and decrease cumulative diagnostic delays, with projected healthcare cost savings of $396,000-439,000. Across the entire

227 patient cohort, LR-WGS is anticipated to reduce testing costs by 6.5%, yielding an average savings of $105 per patient.
Conclusions: LR-WGS enables comprehensive discovery of genomic and epigenomic variants in hypotonia and muscle weakness, improving diagnostic yield, shortening diagnostic timelines, and reducing costs compared with current standard-of-care testing.
Keywords: CNVs; DNA methylation profiling; Hypotonia; Muscular weakness; Neuromuscular disorders; STR expansion disorders; SVs; Small SNVs; WG-LRS.
PMID: 41952192 DOI: 10.1186/s12916-026-04850-8

Jennifer Boisgontier , Sarah Charpy , Graziella Pinto , Volodia Dangouloff-Ros , Ludovic Fillon , Ana Saitovitch , Sara Cabet , Khawla Aljabali , Aurélie Fabre , Gwenaëlle Diene , Marion Valette , David Cohen , Monica Zilbovicius , Maïthé Tauber , Nathalie Boddaert. Early neurodevelopmental brain perfusion abnormalities and functional connectivity findings in infants with Prader-Willi syndrome. J Neurodev Disord. 2026 Apr 6. Online ahead of print.
No abstract available
Keywords: Arterial spin labeling; Cerebral blood flow; Functional connectivity; Infancy; Neurodevelopment; Prader-Willi syndrome; Resting-state functional MRI.
PMID: 41937185 DOI: 10.1186/s11689-026-09690-4

Dalibor Pastucha , Darina Aleksijevic , Jiri Hyjanek Ondrej Vesely , Eva Klaskova , Kristyna Kolarikova , Radek Vodicka. Case Report: Schaaf-Yang Syndrome Milder Phenotype Due to Potential Pathogenic Novel Missense Variant as an Unusual Cause of Obesity in a Pediatric Patient. Appl Clin Genet. 2026 Mar 9:19:584482.eCollection 2026.
Abstract According to OMIM and Orphanet databases, Schaaf-Yang syndrome (SYS) (OMIM: 615547, ORPHA: 398069) is a rare genetic disorder that shares certain clinical features with Prader-Willi syndrome (PWS), including hypotonia, developmental delay, and early-onset obesity. However, SYS often exhibits a more complex and variable phenotype. Missense variants in MAGEL2 have been reported only rarely, and their phenotypic spectrum appears milder and more variable than that of truncating mutations. Data on early-onset obesity as a dominant feature in such patients are limited. In this case report, we describe a child with mild phenotype (SYS) carrying the novel missense variant *MAGEL2(NM_019066.5)*:c.1265C>T (p.Pro422Leu) presenting with severe early-onset obesity and a comparatively neurodevelopmental phenotype. We present a case of a boy with neonatal hypotonia, diagnosed with (SYS) at age 9 years, with follow-up to age 11 years. The boy was born at 34+3 weeks of gestation with hypotonia, feeding difficulties, and a persistent ductus arteriosus that required surgical ligation in early infancy. In the following years, he developed severe early-onset obesity, already evident by age 2 despite multidisciplinary care. Genetic testing performed at age 9 years identified a novel missense variant (NM_019066.5)c.1265C>T in the *MAGEL2* gene, which was not inherited from his mother, thereby confirming the diagnosis of (SYS). At the time of the most recent evaluation, at age 11 years, he remained under long-term follow-up. Clinical management over this period included endocrine therapy, cardiac surgery, physical rehabilitation, and dietary interventions, and despite the complexity of his condition, long-term stabilization of his BMI percentile was achieved with consistent non-pharmacological interventions. This case highlights the importance of early multidisciplinary investigation and intervention in SYS, particularly when obesity is the dominant feature. Effective long-term weight stabilization is possible through structured lifestyle management.
Keywords: MAGEL2 mutation; Schaaf-Yang syndrome; developmental delay; hypothyroidism; pediatric obesity; physical activity.
PMID: 41937924 PMCID: PMC13047383 DOI: 10.2147/TACG.S584482

.Thomas W Laver , Preeah Sangha , Lucy Mallin , Michal Cohen , Yağmur Ünsal , Huseyin Demirbilek , Matthew N Wakeling , Jasmin J Bennett , Jayne A L Houghton , Jonna M E Männistö , Emma Dempster , Sarah E Flanagan. Long-read sequencing enables trio-assisted phasing of *de novo* variants in the imprinted gene *MAGEL2*. J Med Genet. 2026 Mar 31:jmg-2025-111282. Online ahead of print

Abstract Schaaf-Yang syndrome and Prader-Willi syndrome are imprinting disorders that result from the disruption of paternally expressed genes within the 15q11-q13 region. Both conditions present with overlapping clinical features including developmental delay, hypotonia and endocrine abnormalities. Schaaf-Yang syndrome specifically results from heterozygous variants in the paternally expressed *MAGEL2* gene. Because these variants are often *de novo*, determining that the variant is on the paternal allele is essential for a definitive diagnosis. Traditional methods, such as methylation-specific PCR, are labour-intensive, while it is challenging to phase variants separated by distances greater than the fragment length (~600 bp) using short-read sequencing. In this study, we used long-read Oxford Nanopore sequencing to perform trio-assisted phasing of a *de novo MAGEL2*, p.(Gln638Ter) variant identified in two unrelated probands referred for congenital hyperinsulinism genetic testing. Long reads spanning both the variant and informative parental heterozygous variants confirmed that the variant was on the paternal allele and was therefore pathogenic and causative of Schaaf-Yang syndrome and associated with hyperinsulinism in both individuals. Our findings demonstrate the clinical utility of long-read sequencing for enabling trio-assisted variant phasing in imprinting disorders, particularly when phenotypes are incomplete or overlapping. Our findings further highlight congenital hyperinsulinism as a rare but important feature associated with Schaaf-Yang syndrome.
Keywords: Genomic Imprinting; Human Genetics; Nanopore Sequencing.
PMID: 41916724 DOI: 10.1136/jmg-2025-111282

Endocrine including GH

Zuzanna Pajak , Natalia Wizner[1], Katarzyna Kania , Zofia Korzonkiewicz , Teresa Wojtowicz , Nikoletta Rauer , Krzysztof Zapart[3], Milosz Janikowski Irisin in Pediatric Obesity: A Narrative Review of Current Evidence. Cureus. 2026 Jun 24;18(6):e111456. eCollection 2026 Jun.
Abstract Obesity in children and adolescents represents an escalating global health challenge associated with chronic low-grade inflammation and dysregulation of myokine and adipokine secretion. Irisin, encoded by the FNDC5 gene, plays a pivotal role in energy homeostasis by promoting the "browning" of white adipose tissue (WAT) and increasing energy expenditure through thermogenesis. The aim of this study was to establish the diagnostic and therapeutic significance of irisin in the context of childhood obesity and to assess its usefulness as a marker for the early detection and monitoring of metabolic disorders. A comprehensive literature search was conducted using the PubMed database. Findings were limited to studies published within the last five years, from April 14, 2021, to April 14, 2026. Only studies in English were included. We used the following keywords and phrases: irisin; FNDC5; obesity; child; children; pediatric; adolescence; adolescent. Twenty studies met the inclusion criteria and were included in this narrative review. Studies confirmed that serum irisin concentration typically correlates positively with BMI and leptin levels, which may be described as a compensatory mechanism for improving insulin sensitivity. In obese adolescent girls with polycystic ovary syndrome (PCOS), irisin levels are lower but increase with a reduction in fat mass. High-intensity interval training (HIIT) stimulates higher irisin release than moderate-intensity training. In rarer conditions, such as Prader-Willi syndrome (PWS), irisin levels are reduced, which is associated with impaired bone metabolism and decreased muscle mass. Irisin can also act as a marker of hepatic steatosis and as a factor supporting executive functions in overweight children. Irisin represents a promising and sensitive biomarker of metabolic status and adipose tissue content in pediatric patients. Its monitoring may allow for a clear assessment of therapeutic effectiveness and dynamic changes in the child's metabolic profile.
Keywords: adolescence; adolescent; child; children; fndc5; irisin; obesity; pediatric.
PMID: 42368235 PMCID: PMC13294640 DOI: 10.7759/cureus.111456

Sydney Englehart , Kathryn S Obrynba, Emily C de Los Reyes. , Jennifer L McKinney . Small-Fiber Neuropathy in an Adolescent With Prader-Willi Syndrome. Pediatr Neurol. 2026 Jun 10:182:1-3. Online ahead of print.
No abstract available
Keywords: Diabetes; Neuropathy; Prader-Willi syndrome; Vitamin B6 toxicity.
PMID: 42348950 DOI: 10.1016/j.pediatrneurol.2026.06.004

Go Yoshimichi . Beyond the GH-IGF-1 Axis: A Network Perspective Integrating Clinical Observations and Mechanistic Insights. Endocr Connect. 2026 Jun 19:EC-26-0317. Online ahead of print.
Abstract Background: Obesity encompasses a heterogeneous group of conditions that include not only simple obesity, but also genetic and endocrine disorders. The growth hormone (GH)-insulin-like growth factor 1(IGF-1) axis plays a central role in body composition, insulin sensitivity, and metabolic regulation. We encountered three patients in whom the clinical courses highlighted distinct interactions between obesity and the GH-IGF-1 axis.
Methods: We reviewed three representative cases. Case 1 involved acromegaly improved by the peroxisome proliferator-activated receptor-α (PPAR-α) agonist pemafibrate. Case 2 involved Prader-Willi syndrome (PWS) with severe obesity treated using dulaglutide. Case 3 involved severe obesity managed with behavioral therapy. Clinical characteristics and therapeutic responses were analyzed.
Results: In Case 1, pemafibrate administration resulted in a marked and sustained reduction in IGF-1 levels despite ongoing lanreotide therapy, suggesting a potential hepatic or pituitary interaction between PPAR-α signaling and GH-IGF-1 regulation. In Case 2, dulaglutide induced weight loss and reduced insulin requirements in a patient with PWS, a condition characterized by high levels of ghrelin. The therapeutic effect may involve modulation of ghrelin, an upstream regulator of GH secretion. In Case 3, behavioral therapy stabilized metabolic deterioration in a patient with a body mass index of 50.7 kg/m2, even though GH and IGF-1 levels remained low after weight reduction, suggesting mechanisms independent of the GH-IGF-1 axis.
Conclusion: These findings support a conceptual shift from a linear GH-IGF-1 axis to an integrated GH-IGF-1 network that connects peripheral signals, hypothalamic regulation, and higher brain functions, offering a novel framework for personalized obesity management.
Keywords: Prader–Willi syndrome; acromegaly; behavioral therapy; growth hormone; heterogeneity; insulin-like growth factor 1; network; obesity.
PMID: 42319153 DOI: 10.1530/EC-26-0317

Yoo-Mi Kim , Young-Jun Rhie , Hyun-Wook Chae , Jaehyun Kim , Young Ah Lee , Hae Sang Lee , Yong Hee Hong , Ja Hye Kim , Moon Bae Ahn , Yejin Jeon , Choong Ho Shin. Accumulated Safety Data of Recombinant Human Growth Hormone Therapy in Korean Children over a 10-Year Period: Interim Results from the LG Growth Study. Endocr Connect. 2026 May 18:EC-26-0073. Online ahead of print.
Abstract Objective: To evaluate the long-term safety outcomes of recombinant human growth hormone (rhGH) administered to Korean pediatric patients with growth disorders, including growth hormone deficiency, Turner syndrome, idiopathic short stature, small for gestational age, chronic kidney disease, and Prader-Willi syndrome, using 10-year interim data from the nationwide LG Growth Study registry in the Republic of Korea.
Design: Prospective, multicenter, observational registry.
Methods: This interim analysis included 5,040 patients from 96 centers, representing 19,878 patient-years of treatment between November 2011 and December 2022. Although the registry spans 10 years, follow-up was limited to periods of active GH treatment and therefore varied across patients. Patients received daily or weekly rhGH. Adverse events (AEs), adverse drug reactions (ADRs), serious AEs (SAEs), and serious ADRs (SADRs) were recorded and compared with international registry data.
Results: Overall, AEs occurred in 34.2% of patients, ADRs in 7.0%, SAEs in 3.2%, and SADRs in 0.3%. The most frequent AE was scoliosis (1.6%), followed by headache (0.8%) and injection site pain (0.5%). Three malignant neoplasms were reported, yielding a standardized incidence ratio of 1.1 (95% confidence interval, 0.21-2.69), comparable to expected national rates. Craniopharyngioma recurrence occurred in 14.3% of affected patients, consistent with international data.

Conclusions: Over 10 years, rhGH therapy in Korean pediatric patients demonstrated a low incidence of ADRs and SADRs, with malignancy and tumor recurrence rates similar to those in global registries. These findings support the long-term safety of rhGH for pediatric growth disorders, with continued surveillance warranted.
Significance: Using 10 years of real-world data from a pediatric registry, conducted in the Republic of Korea, this study provides one of the largest single-nation safety evaluations of rhGH therapy across multiple etiologies of short stature. The low incidence rates of ADRs and SADRs, in alignment with rates reported for other large-scale international registries, provide reassuring evidence of the safety of rhGH for clinicians and caregivers.
Keywords: Growth hormone; Management of endocrine disease; Pediatric endocrinology; Treatment of endocrine disease.
PMID: 42149642 DOI: 10.1530/EC-26-0073

Nikolinka Yordanova , Mila Vasileva , Sonya Galcheva , Violeta Iotova. Metabolic profile in Prader-Willi syndrome patients followed at a single expert center of rare endocrine diseases. BMC Endocr Disord. 2026 May 5. Online ahead of print.
Abstract Introduction: Prader-Willi syndrome (PWS) is a rare imprinting disorder characterized by typical dysmorphic features, lack of satiety, infantile hypotonia, and later morbid obesity with complications, short stature, hypogonadotropic hypogonadism, skeletal and psychiatric problems. From the literature, it is well known that patients with PWS have a more favorable metabolic pattern than healthy controls.
Aim: The aim of the study is to assess the metabolic profile of PWS patients followed at an Expert Center for Rare Endocrine Diseases compared with healthy controls and to look for relations between components of the metabolic syndrome (MetS), adipokines, and the compartments of body composition (BC-lean and fat mass).
Patients and methods: The current study is a cross-sectional evaluation of 25 patients with Prader-Willi syndrome (mean age 11.3 ± 8.2 years), with a total of 183.6 patient-years of regular follow-up (from the first visit to the center to the data collection cutoff date), compared with 24 age-, sex-, and BMI-matched healthy controls (mean age 11.3 ± 3.9 years). Each participant underwent anthropometric measurements, physical examination, biochemical and hormonal blood sampling, and whole-body DXA scan. Statistical analysis (SPSS 15.0 statistical package, Chicago, IL, USA) was performed to assess the relations between the metrics in the PWS group compared with controls.
Results: Patients with PWS showed a better profile of glucose homeostasis with significantly lower serum insulin concentration and calculated HOMA-IR index compared with the controls ($p < 0.05$). Taking into consideration age, sex, and body mass index (BMI) in the PWS group, the analysis showed strong positive correlations between waist circumference (WC) and systolic blood pressure (SBP) ($r = 0.864$, $p < 0.001$), and WC and diastolic blood pressure (DBP) ($r = 0.534$, $p = 0.033$). Partial correlation analysis with respect to age, sex, and pubertal development found significant positive WC correlations with insulin ($r = 0.796$, $p = 0.006$), HOMA-IR ($r = 0.697$, $p = 0.025$), LDL-cholesterol ($r = 0.735$, $p = 0.002$), uric acid ($r = 0.735$, $p = 0.002$), CRP ($r = 0.600$, $p = 0.023$), and leptin ($r = 0.730$, $p = 0.005$). Strong negative correlations existed between WC and SHBG ($r = -0.772$, $p = 0.002$) and HMW adiponectin ($r = -0.998$, $p = 0.044$). Additionally, a negative correlation of HMW adiponectin and SBP was demonstrated. 88% of the patients were treated with recombinant human growth hormone (rhGH). Bone mineral density adjusted for height (BMD/height) was significantly lower in patients with PWS ($p < 0.05$) compared with healthy controls. The analysis did not reveal significant relationships between BC compartments and metabolic and auxological parameters in the PWS group.
Conclusion: Our study confirms that patients with PWS have a favorable metabolic profile compared with healthy controls matched by age, sex, and BMI. Syndromic participants who manifest greater accumulation of abdominal adipose tissue have a higher risk of hemodynamic changes and metabolic disturbances predictive of the development of cardiovascular diseases (CVD) in adulthood. WC could serve as a predictive marker for detecting higher metabolic risk in this syndromic group of patients, and both WC and HMW adiponectin for hypertension. In the future, on this basis, we could possibly implement both of these metrics in clinical practice.
Keywords: Body composition; Cardiovascular risk; Metabolic risk; PWS; Prader-Willi syndrome; Rare disease.

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Minshun Zhu , Qiang Sun , Jian Zhang , Kuo Cai , Zhipeng Guo , Qing Wu , Yueling Wang , Jiaping Chen. Endocrine-informed monitoring of scoliosis in Prader-Willi syndrome: integrating neuroendocrine pathophysiology, growth hormone therapy, and pubertal transition. Front Endocrinol (Lausanne). 2026 Apr 13:17:1803919. eCollection 2026.

Abstract Prader-Willi syndrome (PWS) is a neuroendocrine disorder characterized by hypothalamic dysfunction, congenital hypotonia, abnormal growth trajectories, and impaired pubertal development, all of which contribute to a markedly increased risk of scoliosis, with a cumulative prevalence reaching up to 70-80% by skeletal maturity, significantly exceeding that of idiopathic scoliosis. Unlike idiopathic scoliosis, spinal deformity in PWS follows a distinct bimodal pattern, with critical vulnerability during infancy and a second acceleration during pubertal transition. Growth hormone (GH) therapy, a cornerstone of PWS management, substantially improves linear growth, body composition, and muscle strength, yet its relationship with scoliosis onset and progression remains a clinical challenge due to the potential for accelerated growth during critical developmental windows, which may unmask or exacerbate underlying spinal instability. Current scoliosis surveillance strategies in PWS are largely extrapolated from idiopathic scoliosis and fail to account for the unique neuroendocrine and biomechanical context of this syndrome. In particular, endocrine modifiers such as GH treatment status, growth velocity, hypogonadism, pubertal stage, body composition, and genotype-specific phenotypes are rarely integrated into structured monitoring protocols. In this narrative review, we synthesize epidemiological, mechanistic, and clinical evidence to elucidate the neuroendocrine and biomechanical pathways underlying scoliosis development in PWS, including the roles of hypotonia-related instability, altered vertebral growth modulation, and delayed epiphyseal maturation. We critically examine the dualistic effects of GH therapy, the impact of pubertal maturation, and genotype-phenotype associations as key determinants of scoliosis risk and progression. Building on this evidence, we propose an endocrine-informed, risk-stratified scoliosis monitoring framework that integrates growth dynamics, hormonal status, body composition, and spinal parameters to guide surveillance intensity, imaging strategies, and multidisciplinary referral. By shifting the focus from isolated curve detection to longitudinal, endocrine-guided surveillance, this review provides a clinically actionable model to optimize early identification and management of scoliosis in children and adolescents with PWS. This framework aims to support coordinated endocrine-orthopedic care and inform future prospective studies designed to refine outcome measures and ultimately improve long-term musculoskeletal and quality-of-life outcomes in this vulnerable population.

Keywords: Prader-Willi syndrome; endocrine monitoring; growth hormone therapy; puberty; risk stratification; scoliosis

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Graziano Grugni , Adele Rocchetti , Carm Bucolo , Raffaele Buganza , Giorgia Buoncuore , Annamaria Colao , Domenico Corica , Antonino Crinò , Francesca Dassie , Luisa de Sanctis , Maurizio Delvecchio , Francesca Di Candia , Maria Felicia Faienza , Danilo Fintini , Donatella Greco , Laura Guazzarotti , Valentina Lo Preiato , Pietro Maffei , Michela Mariani , Enza Mozzillo , Uberto Pagotto , Roberta Pajno , Giuseppa Patti , Irene Rutigliano , Marco Salvatore , Alessandro Sartorio , Emanuela Scarano [23], Sofia Siena , Gianluca Tamaro , Gianluca Tornese , Rossella Vitale , Malgorzata Wasniewska , Giuseppe Zampino , Paola Torreri , Mohamad Maghnie. Correction: Understanding the burden of endocrine and metabolic disorders in Prader-Willi syndrome: data from the Italian registry. J Endocrinol Invest. 2026 Apr 28. Online ahead of print.

No abstract available

PMID: 42048045 DOI: 10.1007/s40618-026-02875-7

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Italian registry. .J Endocrinol Invest. 2026 Feb 12. doi: 10.1007/s40618-026-02832-4. Online ahead of print.PMID: 41678013

Anthony M Saad , Haider Zaki , Adarsh Menon , Mark Hausdorff , Brian Manzi · Growth Hormone-Induced Stridor in a Patient With Prader-Willi Syndrome. Clin Case Rep. 2026 Mar 12;14(3):e72265.eCollection 2026 Mar.

Abstract While growth hormone therapy has been associated with the potential risk of upper airway obstruction and hypertrophy, it may also cause glottic or subglottic edema and stridor, even in patients without adenotonsillar tissue. Clinicians should consider medication-induced airway changes in Prader-Willi Syndrome patients with complex airway histories to optimize management.

Keywords: Prader–Willi syndrome (PWS); complex airway anatomy; glottic edema; growth hormone therapy; laryngomalacia; pediatric airway; stridor; subglottic stenosis
PMID: 42016677 PMCID: PMC13093715 DOI: 10.1002/ccr3.72265.

Yukiko Hashimoto , Kazutaka Nanba , Yosuke Konishi , Takashi Matsukura , Naoko Yano , Takeshi Yoshida. Two siblings with Schaaf-Yang syndrome treated with growth hormone. Clin Pediatr Endocrinol. 2026 Apr;35(2):186-191. Epub 2026 Feb 5.

Abstract Schaaf-Yang syndrome (SYS) is a rare neurodevelopmental disorder with overlapping features with Prader-Willi syndrome (PWS). We report two Japanese siblings with SYS harboring a rare *MAGEL2* variant (NM_019066.5:c.1621C>T, p.(Q541*)). Both patients had GH deficiency and received GH therapy. The older sibling presented with neonatal hypotonia, joint contractures, and severe autism, while the younger sibling showed milder features but developed obesity and behavioral problems. GH therapy led to only modest improvement in their growth. The limited effect may have been related to the late initiation of treatment, marked non-adherence to therapy, and GH doses. This report highlights the phenotypic variability of SYS and demonstrates difficulties and potential issues of GH treatment as well as clinical response to GH treatment in this rare disorder.

Keywords: GH deficiency; MAGEL2; Schaaf-Yang syndrome; hypothalamic dysfunction; neurodevelopmental disorders
PMID: 41923794 PMCID: PMC13038379 DOI: 10.1297/cpe.2025-0105

Sensory and physical

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Yasuhide Nagoshi. Vortioxetine-Lurasidone Augmentation for Compulsive Scratching Behavior in Prader-Willi Syndrome. Neuropsychopharmacol Rep. 2026 Jun;46(2):e70145:

Abstract Background: Prader-Willi syndrome (PWS) is a rare genetic disorder frequently associated with repetitive and self-injurious behaviors such as skin picking. Effective pharmacological treatments for compulsive scratching behavior in PWS remain limited.

Case presentation: We report the case of a 19-year-old woman with PWS presenting with severe, persistent scratching behavior resulting in repeated excoriations. Escitalopram produced partial improvement but was discontinued because of sedation. Treatment was switched to vortioxetine, which reduced the frequency of scratching but did not achieve remission. Subsequent augmentation with lurasidone resulted in marked improvement, with episodes decreasing from daily occurrences to once every 1-3 months and lasting only a few minutes. The patient remained stable for 2 years without recurrence of severe symptoms.

Conclusion: This case suggests that vortioxetine and lurasidone may represent a potential pharmacological option for severe scratching behavior in PWS. Further studies are needed to clarify the therapeutic role of this combination approach.

Keywords: Prader–Willi syndrome; lurasidone; obsessive-compulsive–related symptoms; skin picking; vortioxetine.
PMID: 42309520 PMCID: PMC13275168 DOI: 10.1002/npr2.70145

Haley Fishman , Emma Wen , Colin Massicotte , Indra Narang , Jackie Chiang , Sundeep Bola , Munazzah Ambreen , Allison Zweerink , Reshma Amin. A comparison of therapeutic oxygen versus medical air for the treatment of central sleep apnea in infants with Prader-Willi syndrome; A proof-of-concept randomized crossover trial. Sleep Med. 2026 Jun 9:146:109079. Online ahead of print.

Abstract Background: Central sleep apnea (CSA) is common in infants with Prader-Willi syndrome (PWS). Although supplemental oxygen is frequently used to manage CSA, its mechanism of action remains unclear; comparison with medical air may help determine whether therapeutic benefit is mediated by inspired oxygen or by flow-related effects on respiratory control.
Study design and methods: In this randomized crossover trial, growth hormone-naïve infants <2 years with genetically confirmed PWS and CSA (CAHI >5 events/hr) underwent an overnight polysomnogram receiving medical air and supplemental oxygen in randomized order. Treatments were blinded to scoring sleep technologists and interpreting physicians. The primary outcome was the difference in CAHI between supplemental oxygen and medical air. Secondary outcomes included sleep architecture, obstructive apnea-hypopnea index (OAHI), and gas exchange.
Results: Of 20 infants screened, 10 were randomized; 4 (40%) were male, with a median age of 6.0 months (IQR 4.2-13.2 months). Baseline median CAHI was 9.0 events/hr (IQR 6.3-10.3). Supplemental oxygen reduced CAHI compared with medical air (adjusted difference -7.7 events/hr, 95% CI -15.2 to -0.1; $p = 0.048$; adjusted means 1.8 vs 9.4 events/hr). Compared with medial air, supplemental oxygen increased oxygen saturation nadir (+8.2%, $p < 0.001$), and mean oxygen saturation (+2.1%, $p = 0.009$), and reduced the oxygen desaturation index (-12.3 events/hr, $p = 0.046$). Mean transcutaneous CO_2 was modestly lower with oxygen (-2.2 mmHg, $p = 0.024$), with no clinically meaningful hypercapnia. Sleep architecture and obstructive indices were unchanged.
Interpretation: In comparison to medical air, the administration of supplemental oxygen reduces CSA and improves oxygenation in infants with PWS without adverse effects on CO_2 or sleep architecture, supporting its use as first-line therapy in this population.
Keywords: Central sleep apnea; Control of breathing; Infants; Prader Willi syndrome; Rrandomized clinical trial; Sleep disordered breathing.
PMID: 42287973 DOI: 10.1016/j.sleep.2026.109079

Luo-Hua Yu , Hsin-Chi Wu , I-Shiang Tzeng , Yan-Ting Luo , Li-Ping Tsai , Valeria Chiu. Diagnostic Utility of Muscle Ultrasound for Sarcopenia in Prader-Willi Syndrome: A Cross-Sectional Study. J Cachexia Sarcopenia Muscle. 2026 Jun;17(3):e70326.

Abstract Background: Prader-Willi syndrome (PWS) is characterized by sarcopenic obesity; however, validated screening tools for muscle mass in clinical settings are lacking. This study aimed to evaluate the diagnostic utility of muscle ultrasound (US) for detecting low muscle mass in individuals with PWS.
Methods: This observational, cross-sectional study recruited 48 individuals with genetically confirmed PWS (International Classification of Diseases, 10th Revision Code Q87.1) from a specialized clinic (October 2022-June 2024). Appendicular skeletal muscle index (ASMI) via dual-energy x-ray absorptiometry (DXA) served as the primary outcome. Sarcopenia was defined based on Asian Working Group for Sarcopenia (AWGS) 2019 criteria. US predictors included muscle thickness (MT) of the rectus femoris (RF), vastus lateralis and gastrocnemius medialis (GM); pennation angle; and RF cross-sectional area (CSA). Analysis included Spearman's correlation (ρ), multivariable linear regression (B) and receiver operating characteristic (ROC) curves.
Results: The cohort (n = 48; 47.9% women; median age 19.5 years, interquartile range [IQR] 12.3-26.8) had a 100% prevalence of obesity (median BMI 27.1 kg/m^2, IQR 22.2-31.4). All participants (100%) had a history of growth hormone treatment; 62.5% exhibited the deletion subtype. Low muscle mass was observed in 60.4% (n = 29), confirmed sarcopenia in 52.1% (n = 25) and severe sarcopenia (including low physical performance) in 20.8% (n = 10) participants. GM MT showed the strongest correlation with ASMI ($\rho = 0.689$, $p < 0.001$, 95% confidence interval [CI] 0.50-0.81), followed by RF CSA ($\rho = 0.587$, $p < 0.001$).

Multivariable regression identified GM MT as a significant independent predictor of ASMI (B = 0.957, p = 0.011) after adjusting for BMI (B = 0.128, p < 0.001), age (B = 0.020, p = 0.044) and sex (B = -0.376, p = 0.029; R^2 = 0.67). ROC analysis for detecting low muscle mass yielded an area under the curve for GM MT of 0.759 (95% CI 0.616-0.901, p = 0.003), with an optimal cut-off of 1.69 cm (sensitivity 86.2%, specificity 63.2%).
Conclusions: Sarcopenia affects 52.1% of patients with PWS, with 20.8% meeting criteria for severe sarcopenia. Ultrasound of the gastrocnemius medialis is a valid, radiation-free predictor of skeletal muscle mass and serves as a practical diagnostic tool for sarcopenic obesity in PWS.
Keywords: Prader–Willi syndrome; body composition; sarcopenia; ultrasonography.
PMID: 42259520 PMCID: PMC13246224 DOI: 10.1002/jcsm.70326

Alessia Aureli , Francesco Carlomagno , Antonino Crinò , Sarah Bocchini , Sonia Battaglia , Daniela Camanni , Emanuela Ceriati , Michela Mariani , Stefano Delli Noci , Melania Manco , Francesco De Peppo , Andrea M Isidori , Stefano Cianfarani , Danilo Fintini. Sleeve Gastrectomy in Paediatric and Transition Age Patients with Prader-Willi Syndrome: A 5-Year Longitudinal Study. J Clin Endocrinol Metab. 2026 May 25:dgag210. Online ahead of print.
Abstract Objective: To evaluate the long-term effectiveness of laparoscopic sleeve gastrectomy (LSG) in paediatric and transition-age patients with Prader-Willi syndrome (PWS).
Design: Single-centre, longitudinal, retrospective cohort study.
Methods: We reviewed EHRs of 110 patients with PWS and 268 subjects undergoing LSG. We included 16 patients with PWS and severe obesity (PWS-LSG) and 32 matched non-syndromic patients with obesity (OB-LSG), both undergoing LSG, and 16 patients with PWS receiving lifestyle intervention only (PWS-LS). The primary endpoint was ΔBMI-SDS% at 5 years.
Results: In PWS-LSG, BMI-SDS decreased from 5.18 to an early nadir at 1-2 years (median ΔBMI-SDS% ~-26%), then partially rebounded to 4.75 at 5 years, with ΔBMI-SDS% -16.9% (p= 0.012). Conventional metrics confirmed this attenuated response, with %BMI change -2.8% and absolute ΔBMI-SDS -1.10 at 5 years. In OB-LSG, BMI-SDS declined from 4.95 to 2.24, with larger and more sustained improvement (ΔBMI-SDS% -57.4%; p<0.001 within-group; p=0.002 vs PWS-LSG), corresponding to a %BMI change -40.1% and absolute ΔBMI-SDS -2.81 at 5 years. In PWS-LS, BMI-SDS increased from 2.25 to 3.19 (ΔBMI-SDS% +36.4%, p=0.003). The mean number of obesity-related comorbidities decreased in PWS-LSG (2.69±1.66 to 1.94±1.18; p=0.041) and in OB-LSG (1.25±0.88 to 0.56±0.76; p<0.001), but increased in PWS-LS (1.56±0.96 to 2.44±1.32; p=0.004).
Conclusion: In PWS, LSG produces clinically relevant early weight loss with partial maintenance at 5 years, but markedly attenuated long-term benefit compared with non-syndromic peers. Nevertheless, when interpreted against the progressive worsening of obesity and cardiometabolic comorbidities observed with lifestyle intervention alone, LSG appears to modify disease trajectory in PWS.
Keywords: Prader-Willi syndrome; metabolic disorders; obesity; obstructive sleep apnoea; sleeve gastrectomy.
PMID: 42178926 DOI: 10.1210/clinem/dgag210

Trees Kempen , Mieke Boon , Anneleen Dereymaeker , Anne Rochtus , Renee Proost , Katrien Lemmens , Katrien Jansen. Polysomnographic findings and brain maturation in infants with Prader-Willi syndrome: a retrospective observational study. Sleep Breath. 2026 May 19;30(3):164.
Abstract Purpose: Prader-Willi syndrome (PWS) is a rare genetic disorder characterized by hypothalamic dysfunction and brainstem immaturity, contributing to central sleep apnea (CSA), hypoventilation and hypersomnolence. Obstructive sleep apnea (OSA) is more common in older children with PWS due to adenotonsillar hypertrophy and obesity. Data on polysomnographic findings in infants remain scarce. This study aimed to assess sleep-disordered breathing and its possible association with brain maturation, based on electroencephalography (EEG) findings, in infants (< 12 months) with PWS.
Methods: We conducted a retrospective analysis of polysomnography (PSG) and EEG data, from seven growth hormone-naive infants with PWS. Statistical comparisons were made between neonatal and older infants, and between those with age-appropriate versus dysmature EEGs.

Results: One infant died suddenly and unexpectedly before PSG could be completed. The median central apnea index was 1.42/h; none of the infants met criteria for CSA. OSA was present in 66.6% of PSGs, with a median obstructive apnea-hypopnea index of 3.94/h. All infants had low arousal indices. Delayed brain maturation was observed in three infants on EEG, with no correlation found between EEG maturity and apnea indices.
Conclusion: OSA also presents in infants with PWS and is mainly caused by hypotonia and a narrow oropharynx. No correlation was found between EEG-based brain immaturity and central apnea severity. Given the respiratory vulnerability of these infants, a baseline PSG is strongly recommended. Larger studies are needed to confirm these findings and to clarify their clinical implications, including the potential role of EEG in early risk stratification.
Keywords: Brain maturation; Infants; Obstructive sleep apnea; Prader-Willi syndrome; Sleep-disordered breathing.
PMID: 42154139 DOI: 10.1007/s11325-026-03709-9

Álvaro Hidalgo-Robles , Daniele Soares-Marangoni , Olena Chorna , Pragashnie Govender , Roslyn Livingstone , Ginny Paleg , Riclef Schomerus , Javier Merino-Andrés , Andrea Guzzetta. Beyond "low tone". What do the General Movements Assessment and Motor Optimality Score tell us about infants with developmental central hypotonia? A scoping review. Early Hum Dev. 2026 May 14:221:106583. Online ahead of print.
Abstract Developmental central hypotonia is a broad clinical term describing low muscle tone secondary to non-degenerative brain impairment. Because there is no widely implemented, standardized way to quantify hypotonia in young children, and low tone is still judged largely through subjective clinical examination, early motor phenotyping remains challenging. We conducted a scoping review to map how Prechtl's General Movements Assessment (GMA) and the Motor Optimality Score-Revised (MOS-R) have been used in infants with developmental central hypotonia aged <5 months corrected age. PubMed, Scopus, ProQuest, Web of Science and the Cochrane Library were searched from inception to November 2025. Included studies assessed preterm or term infants with developmental central hypotonia using GMA and/or MOS-R. Fourteen studies met inclusion criteria, covering 12 diagnoses and etiologies (including Cornelia de Lange syndrome, hypotonic cerebral palsy, Cri du chat syndrome, Down syndrome, Prader-Willi syndrome, Smith-Magenis syndrome, and West syndrome). Across conditions, spontaneous motor behavior showed a consistent pattern: reduced variability and complexity, a below-age-expected repertoire, and atypical posture, with predominantly slow or monotonous movement character. Atypical fidgety patterns were frequent, although fidgety movements could still be present in infants diagnosed with Down syndrome or Prader-Willi syndrome. Evidence was limited and heterogeneous, with most studies small and descriptive. GMA and MOS-R are feasible, reliable tools to assess early motor phenotypes in developmental central hypotonia and may strengthen detection and surveillance pathways. Prospective longitudinal studies should standardize MOS-R subdomain reporting and evaluate clinical utility by examining associations with later functional and hypotonia trajectories, and responsiveness to early intervention.
Keywords: Down syndrome; General movement assessment; Hypotonia; Low tone; Motor Optimality Score; Motor repertoire
PMID: 42143978 DOI: 10.1016/j.earlhumdev.2026.106583

Aysha M Alsindi , Rehab G Amer , Lara M Boustros , Minoosh M Nasef. Prader-Willi Syndrome Presenting With Early Infantile Hypotonia: A Case Report. Cureus. 2026 Mar 17;18(3):e105369.. eCollection 2026 Mar.
Abstract Prader-Willi syndrome (PWS) is a genetic disorder resulting from the loss of paternally expressed genes on chromosome 15q11.2-15q13.3. It is characterized by distinct clinical features and multisystem involvement, including endocrine, neurodevelopmental, and metabolic abnormalities. Early diagnosis can be challenging because clinical manifestations in infancy are often subtle; therefore, molecular testing is essential for confirmation. This report describes a one-year-old child newly diagnosed with PWS, aiming to highlight the clinical presentation and correlate the findings with current genetic and phenotypic evidence.

Keywords: endocrine dysfunction; genetic mutation; hypotonia; prader-willi syndrome; sleep disorders.
PMID: 42005177 PMCID: PMC13085484 DOI: 10.7759/cureus.105369

Graziano Grugni , Alessandro Sartorio , Antonino Crinò , Danilo Fintini . The pharmacological management of obesity in Prader-Willi syndrome: what does the future hold? Expert Opin Pharmacother. 2026 Apr 7:1-4. Online ahead of print.
No abstract available
Keywords: Carbetocin; GLP-1 receptor agonists; Prader-Willi syndrome; diazoxide; hyperphagia; obesity; oxytocin.
PMID: 41925226 DOI: 10.1080/14656566.2026.2655969

Surya Kant Tiwari , Poonam Joshi , Nihar Ranjan Mishra , Rimjhim Sonowal , Niladri Sekhar Bhunia. Severe respiratory complications in late-diagnosed Prader-Willi syndrome: a case report. J Med Case Rep. 2026 Mar 31. Online ahead of print.
Abstract Background: Prader-Willi syndrome is a rare neuroendocrine genetic disorder that causes hypothalamic dysfunction, hyperphagia, and morbid obesity. Early diagnosis is critical to prevent life-threatening complications. This case report details the fatal outcome of a patient with late-diagnosed Prader-Willi syndrome, highlighting the consequences of diagnostic delay and management challenges in a low-resource setting.
Case presentation: A 17-year-old Asian male individual with a known diagnosis of Prader-Willi syndrome (confirmed by multiplex ligation-dependent probe amplification at age 15 years) presented to the emergency department with acute respiratory distress, generalized edema, and decreased urinary output. His medical history was significant for premature birth, hyperphagia from early childhood, morbid obesity (body mass index 40.63 kg/m^2), type 2 diabetes mellitus, hypertension, and social withdrawal. Despite a prior admission 3 months earlier, where he was stabilized with noninvasive ventilation, metformin, glucagon-like peptide-1 agonists, enalapril, and dietary planning, he was lost to follow-up. On readmission, he was in severe respiratory failure (SpO_2 46% on room air) with acidosis. Physical examination revealed tachycardia, tachypnea, cyanosis, bilateral pitting pedal edema, and crepitations on lung auscultation. Investigations confirmed severe pneumonia, metabolic acidosis, and poorly controlled diabetes. Despite aggressive interventions, including mechanical ventilation and intravenous antibiotics, the patient suffered a fatal cardiorespiratory arrest.
Conclusion: This case underscores that late diagnosis of Prader-Willi syndrome can lead to irreversible, fatal complications. A multidisciplinary management plan is insufficient without addressing profound socioeconomic and educational barriers that hinder its execution. The delay in diagnosis prevented life-changing interventions such as growth hormone therapy. This report emphasizes the need for early diagnosis and holistic, family centered care adapted to the patient's socioeconomic reality to prevent such adverse outcomes.
Keywords: Case report; Late diagnosis; Morbid obesity; Obstructive sleep apnea; Prader–Willi syndrome; Respiratory insufficiency.
PMID: 41918032 DOI: 10.1186/s13256-026-05922-2

Behaviour

Xin-Yu Xu , Dong-Lei Lu , Ya-Nan Zhao , Min Sha , Zhan-Peng Feng , Si-Jie Tan , Mei Wang. Impact of Physical Activity Intervention on Physical Health in Children With Prader-Willi Syndrome:A Systematic Review. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2026 Apr;48(2):315-327.

Abstract Objective To systematically evaluate the effects of acute and long-term exercise interventions on the physical health of children with Prader-Willi syndrome (PWS). Methods A systematic review was conducted following the preferred reporting items for systematic reviews and meta-analyses of non-randomized studies of interventions guidelines.Relevant studies from 1987 to 2023 were retrieved from PubMed,Web of Science,and EBSCO databases.Eligible studies were primarily non-randomized controlled trials focusing on acute or long-term exercise interventions in the children with PWS.Outcome measures included cardiorespiratory function,muscle strength,body composition,metabolism,and inflammation. Results A total of 19 studies were included.Studies of acute exercise showed that the children with PWS had lower cardiorespiratory function and muscle strength than normal or obese children,but similar metabolic responses.Long-term exercise interventions resulted in significant body mass index reduction,increased muscle mass,improved cardiorespiratory function,and regulation of inflammation markers such as interleukin-8.In addition,exercise improved the quality of life in the children with PWS. Conclusions Exercise interventions positively impact the health of children with PWS by reducing the body mass index,increasing the muscle strength,improving the cardiorespiratory function,and regulating inflammation.Exercise intervention combined with hormone therapy and nutritional intervention can serve as an effective rehabilitation regimen for the health management of children with PWS.Future research should explore optimal exercise prescriptions and long-term effects and mechanisms.
Keywords: Prader-Willi syndrome; exercise; physical health.
PMID: 42136341 DOI: 10.3881/j.issn.1000-503X.16606

Lorenzo Chiarella , Ramona Cordani , Marco Veneruso , Antonella Barbieri , Flavia Napoli , Mohamad Maghnie , Lino Nobili. Teaching Video NeuroImage: Eating-Related Cataplexy in Prader-Willi Syndrome. Neurology. 2026 Jun 9;106(11):e218016. Epub 2026 May 5.
No abstract available
PMID: 42085621 DOI: 10.1212/WNL.0000000000218016

Erina Nakane , Hiroyuki Ogata , Sohei Saima , Chuichi Kondo , Masaki Seki , Yuji Oto , Hiroshi Ihara. Associations Between Sensory Processing and Irritability in Prader-Willi Syndrome: Beyond Genetic Subtypes and Clinical Backgrounds. Am J Med Genet A. 2026 Apr 29. Online ahead of print.
Abstract Irritability is a core challenge in Prader-Willi syndrome (PWS). This study investigated the independent contribution of sensory processing to irritability while controlling for clinical and genetic backgrounds in a cohort of 101 individuals with PWS (77 deletion, 24 maternal uniparental disomy [mUPD]). Caregivers completed the Japanese version of the Short Sensory Profile (SSP-J) and the irritability subscale of the Aberrant Behavior Checklist (ABC-J). Hierarchical multiple regression analysis was performed. In Step 1, age, sex, genetic subtype, and psychotropic medication use explained 22.3% of irritability variance ($R^2 = 0.223$, $p < 0.001$). Adding sensory variables in Step 2 explained an additional 38.2% ($\Delta R^2 = 0.382$, $p < 0.001$), totaling 60.6% ($R^2 = 0.606$). Auditory filtering ($\beta = 0.262$), under-responsiveness/seeking sensation ($\beta = 0.201$), and visual/auditory sensitivity ($\beta = 0.194$) were significant independent predictors ($p < 0.05$). Notably, the effect of the mUPD subtype became non-significant after accounting for sensory variables. Sensory processing is a robust predictor of irritability, independent of genetic subtype and medication. Evaluating sensory profiles is essential for environmental adaptations and behavioral interventions in PWS.
Keywords: Prader–Willi syndrome; genetic subtype; hierarchical regression; irritability; sensory processing.
PMID: 42052935 DOI: 10.1002/ajmg.a.70184

Cognition and mental health

Lisa Rein , Christine Tørris , Ana Carla Soares Portugal Schippert , Malin Holmström Rising , Astrid Torbjørnsen , Tina Rich Mogensen , Ann Kristin Bjørnnes. What Is Known About Persons with Intellectual Disabilities and Cardiovascular Risk Factors-A Scoping Review. Epidemiologia (Basel). 2026 Apr 25;7(3):59.

Abstract Background/objectives: Adults with intellectual disability are known to experience complex health needs, including an elevated presence of chronic conditions. Cardiovascular risk factors are a concern, yet the evidence base is fragmented, and the scope and focus of current research are not well understood. Methods: We conducted a scoping review to map the existing evidence on cardiovascular risk factors among adults with intellectual disability. The review included studies reporting on risk factor prevalence as well as participant characteristics (ethnicity, living arrangements, age, sex, and type of disability). Cardiovascular-related outcomes were extracted to clarify the health disparities documented in this population.
Results: Searches of seven databases for studies published from 2013 onward yielded 15,598records, of which 85 met the inclusion criteria. Evidence was dominated by cross-sectional studies, with a few randomized controlled trials. Hypertension, Type 2 diabetes and obesity were commonly reported. Patterns appeared to reflect lifestyle, medication effects, genetic syndromes-particularly Down syndrome and Prader-Willi syndrome-and the severity of the disability. A notable share of the studies originated from the United Kingdom and the United States. Findings reveal a complex cardiovascular risk profile, emphasizing the need for tailored prevention and management.
Conclusions: Adults with intellectual disability face a substantial burden of cardiovascular risk factors. Evidence on effective interventions remains limited, highlighting a need for targeted, evidence-informed approaches to improve cardiovascular health and long-term outcomes.
Keywords: MetS; Prader–Willi syndrome; cardiovascular risk factors; downs syndrome; intellectual disability; metabolic syndrome; obesity; overweight; scoping review; waist.
PMID: 42201203 PMCID: PMC13214662 DOI: 10.3390/epidemiologia7030059

Christian Karl Eberlein, Maximilian Jakob , Angelina Jechalke , Gesa Ordon [Psychiatric challenges in Prader-Willi syndrome][Article in German] Nervenarzt. 2026 Apr 23. Online ahead of print.

Abstract Background: Prader-Willi syndrome (PWS) is highly associated with psychiatric comorbidity. Objectives: This article investigates the prevalence of mental disorders in PWS, explores their association with neurobiological foundations, and outlines the resulting clinical recommendations.
Methods: An evaluation of the scientific literature in the context of clinical experience from the special outpatient clinic for mental health in rare syndromic disorders at Hannover Medical School.
Results: Psychiatric manifestations are present in 44-89% of PWS patients, with disruptive behavior, skin picking, psychosis, compulsive symptoms, and affective disorders being the most common. PWS psychosis differs from schizophrenic psychosis and can be difficult to treat in some cases. Treatment approaches exist for disruptive behavior, affective symptoms, and compulsive symptoms.
Conclusions: Knowledge of the neurobiological basis of PWS is necessary for the adequate treatment of psychiatric disorders. In addition to pharmacological therapies, behavioral interventions and environmental control should also be included.
Keywords: Antipsychotic agents; Compulsive behavior; Psychotic disorders; Selective serotonin reuptake inhibitors; Skin picking.
PMID: 42024161 DOI: 10.1007/s00115-026-01971-6

Klaus Sarimski. [Neurocognitive profile and vulnerability for mental health problems in selected genetic syndromes with disorders of intellectual development][Article in German]. Nervenarzt. 2026 Apr 14. Online ahead of print.

Abstract The analysis of individual cognitive profiles and the assessment of executive function components contributes to a better understanding of the problems that children, adolescents, and adults with intellectual disabilities experience in coping with social demands. Characteristic profiles and abnormalities in executive functions in Down syndrome, fragile X syndrome, and Prader-Willi syndrome are described. These examples illustrate associations with psychological problems-so-called behavioral phenotypes-in children, adolescents, and adults with these genetic syndromes.
Keywords: Cognition; Down syndrome; Executive function; Fragile X syndrome; Prader-Willi syndrome
PMID: 41979662 DOI: 10.1007/s00115-026-01962-7