We're hungry for a solution to obesity. Imagine that one source could provide breakthrough insight.

Prader-Willi Syndrome is the window of opportunity.
We're hungry for a solution to obesity. Imagine that one source could provide breakthrough insight. Prader-Willi Syndrome is the window of opportunity.

**Fact:** Genomic imprinting — a new area of genetics — is revealing that the mere presence of a gene may not result in a normally functioning gene.

**PWS Breakthrough:** Prader-Willi syndrome was among the first genetic models to reveal the importance of imprinting and has provided other breakthrough insights in the field of genetics.

**Fact:** Neuropeptides — or hormones — help regulate appetite. The hormone, ghrelin, is at its highest levels in the body after periods of fasting.

**PWS Breakthrough:** People with Prader-Willi syndrome have a constantly higher levels of ghrelin than the general population, even just after eating a meal.

**Fact:** Recent research shows that the nerve structures of the brain produce activity in response not only to eating, but also to mere images of food.

**PWS Breakthrough:** For people with Prader-Willi syndrome, the neurobiological activity of the brain in response to eating or viewing pictures of food is very different from — and lasts longer than — that of the general population and the general obese population.

**Fact:** It takes the first two to three years after birth for the microorganisms that balance the energy harvest and fat metabolism from the food we eat to fully populate the gut.

**PWS Breakthrough:** People with Prader-Willi syndrome begin to develop obesity at age two or three — after experiencing decreased fetal activity and “failure to thrive” — prior to their development of a runaway appetite.
A Quick Look at Prader-Willi Syndrome:

- PWS causes in utero damage to the brain and nervous system structures, which control appetite and metabolism. Children with PWS always feel hungry and regularly sneak food.
- In addition to life-threatening obesity, PWS causes low muscle tone, cognitive disabilities, and behavioral challenges.
- Only devoted 24/7 management and supervision keep PWS sufferers from tragic, premature death due to morbid obesity.
- The average life span of a person with PWS is 27 years.
- People with PWS, throughout their lives, need support for their various, PWS-associated social, medical, educational, and vocational problems.
- In recent years, developments of some effective management protocols have made progress in the treatment of PWS, but not progress toward a cure.

Prader-Willi Syndrome is starving for a cure. But it’s too late for... “Penny,” a toddler whose mother found her dead in her crib. An autopsy on the three-year-old revealed that she died from weight-related obstructive sleep apnea and a fatty liver.

Understanding Prader-Willi Syndrome

Prader-Willi syndrome (PWS) is the most commonly known genetic cause of life-threatening obesity. This complex genetic disorder occurs, typically, with a deficiency in a small region of chromosome 15 – a region vital to regulation of appetite and metabolic levels, cognitive function and behavioral patterns.

For the more than 30,000 people in the United States who suffer with PWS, a chronic insatiable feeling of hunger and extraordinarily low metabolism plague their daily lives. These factors lead to excessive eating and life-threatening obesity. Only with constant care and supervision from infancy through adult life can a person with Prader-Willi syndrome avoid a lifetime of chronic health problems, social crises and premature death.

With your help, Prader-Willi Syndrome can open the window to solving obesity.

Give financial support.
Advocate with a strong voice.
Conduct collaborative research.
A Look at Life with Prader-Willi Syndrome

PWS and the Infant: Typically, infants with PWS are born premature. They suffer from low birthweight and quickly experience a “failure-to-thrive.” This inability to suckle properly – breast feed or take food from a bottle – can claim an infant’s life if not responded to rapidly and appropriately by medical personnel. Babies with PWS spend their first few weeks of life in neonatal intensive care units before the hospital discharges them home with complicated care instructions for their parents. Generally, these infants require tube feeding for several weeks or months after birth and their respiratory problems require apnea monitors and oxygen therapy.

PWS and the Child: Because of related developmental delays, toddlers with PWS require constant occupational, physical and speech therapies. At approximately two years old, a child with the syndrome quickly begins to experience weight gain, followed by the development of an insatiable appetite. Children with PWS continue their drive to seek food and eat regardless of the amount consumed. This drive is not satiated with food. Without significant intervention, children with PWS become morbidly obese.

PWS and the Adolescent: Extreme obesity leads to life-threatening health problems and social ridicule for the older child. For parents, helping their child survive becomes a daily vigil of supervising their child with and around food. Parents must lock kitchen cabinets and refrigerators, trash cans cannot house food scraps and mealtimes are a constant struggle – often the catalyst for tantrums. The emotional issues that arise and the temper tantrums that escalate in adolescence increasingly alienate children with PWS from their families and peers. In addition, children with PWS usually have speech problems, communication difficulties and problematic behaviors that increase their frustration and contribute to their social withdrawal. With social rejection – affecting every member of the family – and an increasing financial burden, family units often crumble under the stress of caring for a child with the syndrome.

PWS and the Adult: Largely due to a lack of appetite control and behavioral problems, adults with Prader-Willi syndrome are unable to live independent lives. Only with constant oversight by one-to-one aides can adults with PWS function in a work setting; therefore, employment opportunities in a competitive general workplace environment remain likely out of reach for most people with Prader-Willi. Marriage and having children usually are not viable life choices for PWS sufferers. The runaway appetite and resulting behavioral and social issues doom an adult with PWS to a lifetime of controlled environments and supervised activities. Many adults with PWS live only an average of 27 years.

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A Quick Look at Prader-Willi Syndrome:

- Obesity and PWS kill and it’s our collective societal problem.
- PWS is an excellent scientific model for the study of obesity.
- If doctors can diagnose PWS at birth, early intervention can save that child from a life of pain and suffering. As many as 20,000 people in the U.S. may be struggling with undiagnosed PWS.
- Historically, treatments with pharmacotherapy or behavior modification techniques have not been effective.
- It’s a sad fact that the average age of death for a person with PWS is 27 years old.
- Caring for a person with PWS can cost families and tax-funded social agencies up to $150,000 per year.

Prader-Willi Syndrome is starving for a cure. But it’s too late for...“Wayne,” a 33-year-old, 390-pound man, who was afraid to be caught sneaking food. In his haste to eat, he swallowed a potato whole. At the hospital, doctors surgically removed the potato and put him on a respirator. Four days later he died.

The Critical Need for Prader-Willi Syndrome Research

Because Prader-Willi syndrome (PWS) is the most commonly known genetic cause of life-threatening obesity, this complex genetic disorder – involving problems with chromosome 15 – needs additional collaborative research, generous funding and societal advocacy to uncover early diagnosis factors and effective treatment options.

Left undiagnosed or poorly managed, a person with PWS lives to eat and doesn’t know when to stop. Compounding that hunger drive, those affected by PWS suffer with extraordinarily slow metabolism and cognitive and behavioral problems, which can mask their understanding of their disorder and their acceptance of their regimented activities, including eating.

With your help, Prader-Willi Syndrome can open the window to solving obesity. Give financial support. Advocate with a strong voice. Conduct collaborative research.
PWS and the Obesity Epidemic: The Centers for Disease Control states that obesity is a problem of epidemic proportions and threatens to overcome tobacco use as the number one public healthcare problem in the United States. Estimates put the cost to the healthcare system in the U.S. at approximately $117 billion per year. Because of the unique genetic and hormonal factors of PWS, advances from PWS research can provide viable treatment options for addressing obesity problems in the population as a whole.

PWS and Studying Extreme Cases: The two hallmark characteristics of Prader-Willi syndrome are extraordinarily low metabolic rates and a chronic, intractable feeling of hunger (hyperphagia). Scientific investigation is most effective when researchers explore extreme conditions in isolated environments. As such, these characteristics, together with the unique genetic profile of PWS and the numerous extreme clinical symptoms – including obsessive-compulsive behavior and dramatic shifts from “failure-to-thrive” in infancy to an unyielding appetite thereafter – make PWS an incomparable scientific model for the study of obesity.

PWS and Early Diagnosis: Only with early diagnosis and treatment – before the onset of weight gain and behavioral problems – can children with PWS, and their families, have any hope of avoiding the major health and lifestyle crises associated with the disorder. Once a person with PWS begins experiencing uncontrolled weight gain, the personal and financial costs of managing the disorder rise dramatically and breaking the momentum of the disorder to recover some semblance of health is difficult. Uncovering the indicators of PWS will improve the lives of those with the syndrome and will help identify the causative factors of other diseases, including obesity.

PWS and Premature Death: PWS is a life-threatening disorder. Without 24/7 supervision, people with PWS will die prematurely from complications of extreme obesity. Based on a review of deaths from 2001 through 2003, conducted by the Prader-Willi Syndrome Association (USA), the average age of death among people with PWS was 27 years old. Advanced treatments stemming from research progress will save and extend the lives not just of PWS sufferers, but also of other people living with obesity.

PWS and Undiagnosed Cases: Though we need further study, existing data estimates that one in 10,000 to 12,000 people are born with Prader-Willi syndrome. Using this incidence rate, there are potentially 25,000 to 30,000 people with Prader-Willi syndrome in the U.S. The Prader-Willi Syndrome Association (USA) has identified only approximately 4,500 cases of PWS. That concludes that there are thousands more people living with PWS – and suffering its consequences – without a proper diagnosis and without proper treatment.

PWS and Extraordinary Costs: Largely due to lack of appetite control and behavioral problems, adults with PWS cannot live independent lives. A lifetime of medication and specialized medical and social care – like speech, physical and occupational therapies, special education and 24-hour supervision in structured residential and vocational settings – can average between $100,000 and $150,000 per year, not including the socio-cultural impacts on families, schools and employers. Research into proper diagnosis, better treatment options and healthcare provider education can reduce these costs to the healthcare system.
A Quick Look at Prader-Willi Syndrome:

- People with PWS have specific, unique biological differences – like higher levels of the “hunger” hormone, ghrelin, and altered brain activity in response to food.
- Advances in PWS research could save millions of dollars – money that government programs, insurance companies and private families are paying currently.
- People with PWS suffer from obsessive-compulsive disorder, cognitive disabilities, neurological and behavioral problems, low muscle tone and growth delays.
- Early diagnosis and treatment are critical to managing and mitigating the long-term health effects and financial impact of the disorder.
- Early-onset morbid obesity in PWS causes brain lesions, which affect cognitive function and sentence a child with PWS to significant intellectual challenges.

Prader-Willi Syndrome is starving for a cure. But it’s too late for...“Sam,” who accompanied staff from his group home to a baseball game. During an unsupervised moment, he ate a large quantity of food, bought with stolen money. Later, in pain, he went to the hospital and, within hours, died from complications of a ruptured stomach.

The Unique Research Aspects of Prader-Willi Syndrome

Obesity is the number one public health issue in the United States. As the most commonly known genetic cause of life-threatening obesity, Prader-Willi syndrome (PWS) is a source for providing vital insight into our country’s epidemic of obesity.

Scientific investigation can be most fruitful when researchers explore extreme conditions in an isolated environment. Because of Prader-Willi syndrome’s unique biological profile – involving extreme problems with genetics, hormones, brain and nerve structures, psychological processes and microbial functioning – research on the disorder is the window of opportunity for breakthroughs that are widely applicable to the general population.

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The Unique Research Windows of Prader-Willi Syndrome

**PWS and Genetics:** Scientists first recognized the importance of the phenomenon of genomic imprinting through research on PWS gene abnormalities. Recent study of PWS revealed that the presence of apparently normal chromosome material that is inactive, or “turned off,” might be the cause of the disorder. This has opened the window to a new area of genetic research—genomic imprinting. In addition, research reveals that the gene, *NECDIN*, responsible for controlling the vital process of nerve ending growth and the completion of critical nerve pathways, is absent in people with PWS. Continued research of the genetic component of PWS will yield important answers to the functions of the human genome and will yield revelations that provide key insights into science that will benefit everyone.

**PWS and Hormones:** Studying these unique hormone variances in PWS will provide insight on other metabolic disorders, including obesity. The stomach and intestines produce various hormones, including ghrelin, the so-called “hunger hormone,” which travels in the blood to the brain to control the urge to eat. The levels of these hormones are dramatically different between people with PWS and the general population. In addition, ghrelin levels vary significantly among children, adolescents and adults with PWS.

**PWS and the Hypothalamus:** The hypothalamus of people with PWS is truly unique in its abnormalities. A dramatic difference in people with PWS is the structure and function of the hypothalamic systems that receive and act on the hormone levels. Included among the various problems is an unusual decrease in the “oxytocin neurons.” These nerve endings play a role in satiety and may play a role in AIDS and Parkinson’s disease.

**PWS and Brain Structures:** The study of the formation—or malformation—of nerve endings and the patterns of brain function in people with PWS will have broad implications across the field of neurology. Brain imaging studies, using cutting-edge fMRI technology, show dramatic differences in brain activity before, during and after eating between people with PWS and the general population. In PWS, certain areas of the brain “light up” differently when stimulated by the consumption of food or the sight of food and the activity lasts longer than in control groups. Recently, researchers developed “mouse models” that mimic the genetic patterns unique to PWS. A study, using these models, showed that the action of proteins—the production of which are directed by the abnormal genes in the model—might control nerve growth and maturation.

**PWS and Microorganisms:** The opportunity for scientific discovery abounds with the study of the polarized behaviors in Prader-Willi syndrome and with the further examination of the microbial functions of “energy harvest.” Infants with PWS experience a prolonged period of “failure-to-thrive.” During this time, the newborn usually lacks the ability to cry vigorously or suck adequately. This known symptom of PWS may relate to an interesting and perplexing theory about human development. It is thought that it takes two to three years after birth for the gut to be fully colonized by the microbial community that will aid in digesting food, will extract calories from food and will help regulate how fat is stored in the body. In PWS, after the first few years of failing-to-thrive, children begin having serious issues with obesity, runaway appetite and low metabolism—replacing the “failure-to-thrive” problems with “thriving too well.” Rapidly, this insatiable appetite leads to morbid obesity.
Open the Window

Obesity and PWS kill and it’s our collective societal problem.

Research is underfunded. Advocacy is weak. Collaboration is reluctant. We’re all affected. And, we’re all responsible for finding the solution.

You or someone you know is struggling with obesity and the threat of mortality. Society views overweight people as outsiders and, often, they are treated accordingly. The resulting missed work, underperformance at school, social withdrawal and financial difficulties can tear families apart, estrange friends and lead to the depression and anxiety that are such destructive side effects of obesity.

You and everyone you know are paying for the costs of the epidemic of obesity in our country. Caring for people with obesity-related medical problems is taxing our healthcare system and causing individuals and employers to pay increasing medical costs. There is a substantial lack of dedicated funding, research and political advocacy for learning more about obesity, for discovering effective treatment options and, potentially, for finding a cure.

We must come together – and work together – to find a solution, now.

With your help, Prader-Willi Syndrome can open the window to solving obesity.

**Funding** Private donations and government programs have raised limited funding for PWS research. Although government and commercial enterprise funding is substantial in support of finding the solutions for controlling hunger and ending obesity, funding specific to exploring the unique window of research and opportunity that PWS presents is woefully inadequate. Your financial support is vital to finding a cure for PWS and to helping end the epidemic of obesity.

*Give financial support.*

**Collaboration** Studying Prader-Willi syndrome provides a unique case model for many scientific discoveries. PWSA (USA), of course, hopes for a cure to the syndrome to end the suffering of the 30,000 people in the U.S. with the disorder. Presenting the multi-systemic nature of Prader-Willi syndrome as a starting point for understanding other diseases – specifically obesity – will simultaneously facilitate achieving our goals and the goals of the greater healthcare and research communities.

*Conduct collaborative research.*

**Advocacy** Working to develop a voice within influential circles is at the heart of taking the next steps in understanding, treating and potentially curing PWS. Prader-Willi Syndrome Association (USA) seeks to open channels of communication among political figures, publicly and privately funded healthcare institutes, the scientific community and individuals and families dealing with PWS. If you are in a position to elevate PWS awareness and research to a critical priority, we need your help.

*Advocate with a strong, active voice.*

Obesity is everyone’s problem — so is finding the solution.

Prader-Willi Syndrome Association (USA) needs you to help us help others.
Funding: PWSA (USA) is the premier private sponsor of PWS-related research projects and has increased its research funding by almost 1,000% over the past five years.

PWSA (USA) has established a funding goal of Twenty-Five in Five. This aggressive effort will fund medical research involving PWS with $25 million over the next five years. Targeted success will be measured by donations to the PWSA (USA) research fund, by increases in government-funded research and by growth in commercial research programs.

Ambitious goals need assertive patrons: Give financial support.

Advocacy: PWSA (USA) was a key member of the Coalition for Children’s Health and wrote and advocated for the first-ever language adopted by a Senate appropriations committee, which directed the National Institutes of Health (NIH) to study certain aspects of PWS and childhood obesity. As a member of organizations such as FasterCures – The Center for Accelerating Medical Solutions; NIH Rare Diseases Clinical Research Network; Genetic Alliance; and others, PWSA (USA) has been in a leading advocacy position for years.

PWSA (USA) seeks to help people in powerful decision-making positions to understand the unique aspects of the disorder and to recognize the critical need for prioritized PWS research. Creating an extraordinary sense of urgency in PWS research will benefit those who have the puzzling disorder and address the growing epidemic of obesity.

Critical messages need captivating proponents: Advocate with a strong voice.

Collaboration: PWSA (USA) organized and funded the first ever “Roundtable on Obesity in PWS.” The Roundtable – attended by an international group of scientists involved in the study of hyperphagia and obesity – provided a unique platform for exchanging and developing new ideas. For over 25 years, PWSA (USA) has sponsored an annual international symposium for scientists to present and exchange ideas on the syndrome.

PWSA (USA) asserts that any research scientist who studies the key issues of PWS – including appetite control, metabolism, pain, obsessive-compulsive disorder and other difficult behaviors – should always consider PWS as a factor in their research planning. The wealth of knowledge developed by the scientific community and the resources available for research should be shared on a real-time basis to accelerate the progression from scientific idea to practical treatment.

Earnest ideas need eager contributors: Conduct collaborative research.
Obesity and Prader-Will Syndrome kill and it’s our collective societal problem. Help us help others.

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