

Target patient population
Individuals with Phelan-McDermid Syndrome

Relevant condition process
Phelan-McDermid Syndrome is a result of haploinsufficiency of the SHANK3 gene, resulting from either 22q13.33 deletions encompassing SHANK3 or pathogenic sequence variants.

Impacts on individuals with PMS that caregivers can report

Sleep impacts
Bedtime resistance | Need help returning to sleep after waking | Need parent in room/bed to fall asleep | Need medication to sleep | Takes very long time to fall back asleep | Tiredness during the day | Wakes very early | Waking up sweating, screaming, and/or inconsolable

Other impacts
Difficulties at school | Difficulty concentrating | Food refusal | Social avoidance

Signs of Phelan-McDermid Syndrome

Autism spectrum disorder
Autism and/or autistic traits | Decreased social functioning and communication | Hyperactivity | Repetitive behavior
Communication disturbance | Deficits in non-verbal communication | Deficits in social-emotional reciprocity | Delayed response to verbal cues | Disruptive/antisocial | Does not seem to listen when spoken to directly or refuses to respond to directions | Echolalia | Flat/inappropriate affect | Inattentiveness | Laughs or appears angry for no apparent reasons | Poor eye contact | Random and inappropriate speech | Resistance to change | Responds to imaginary sounds or sights | Restricted patterns of behavior

Neuropsychiatric signs
Intellectual disability – mild to profound | Aggression | Agitation | Apathy | Appear to be in a stupor | Apraxia | Behavioral abnormalities | Disinhibited behavior | Ignorance of consequences | Impulsivity | Mood cycling

Sensory reactivity
Pica | Mouthing, chewing, or teeth grinding | Reduced response to pain | Self-injury | Self-stimulation | Stereotypic movement | Touch aversion

Developmental delays
Delayed to absent speech | Adaptive behavior | Cognitive behavior | Expressive language | Psycho-motor development

Regression
Developmental regression | Constructive or imaginative play | Expressive language | Fine motor skills | Language | Post psychiatric episodes | Purposeful hand movement | Self-help | Social engagement skills

Gastrointestinal dysfunction
Constipation | Gastroesophageal reflux | Abdominal pain | Choking and gagging | Diarrhea | Fecal incontinence | Vomiting

Sleep disturbance
Sleep disturbance | Difficulty falling asleep | Difficulty staying asleep | Insomnia | Parasomnias | Sleep apnea and sleep disordered breathing

Additional signs
Hypotonia | Seizures | Urinary incontinence | Decreased perspiration | Heat intolerance | Recurrent infections | Restlessness | Tetraparesis | Urinary retention

Other clinical manifestations
Renal anomalies | Anorexia | Attention deficit hyperactivity disorder | Bipolar disorder | Catatonia or catatonic phase | Congenital heart defects | Depressive episodes | Epilepsy | Lymphedema | Manic episodes | Mood swings | Neurologic deterioration | Obsessive-compulsive disorder | Psychiatric disorders | Psychosis | Psychotic symptoms | Schizoaffective disorder | Schizophrenia | Thyroid dysfunction | Unipolar major depressive

Impacts on caregivers

Caregiver responsibilities
Management of constipation | Working with a behavioral therapist | Long length of time to toilet training | Managing pica | Use of probiotics and specialized diets | Worsened behavior of child due to constipation

Social activities
Feeling ostracized from community

Family relationships
Impacts to family functioning | Need or desire for genetic testing

Spouse/partner relationship
Diminished marital satisfaction

Work impacts
Unemployment

Emotional function
Concern about: Ability to identify and treat seizures | EEG and MRI indications and timing | Aggression | Toilet-training | Confusion over EEG results | Parenting stress | Restricted parental freedom and sense of identity
Worry about: Child's safety | Regression | How epilepsy might affect family

Sleep
Awakened by their child during the night | Becoming drowsy while driving | Child awakens earlier than caregiver | Difficulty concentrating at work | Feel tired during the day | Irritability due to tiredness | Lack of sleep | Needing to sleep during the day | Sleep in settings other than their own bed | Too tired to do things

Bold indicates concept was reported with high frequency, in at least four unique peer-reviewed articles. *Italics* indicates domain heading.

- A review of published literature was conducted to identify the *signs* (things another person can observe) and *impacts* (how quality of life is affected) of Phelan-McDermid Syndrome (PMS) experienced by individuals with PMS and their caregivers.
- 15 publications were reviewed, and the information they contained about the signs and impacts of PMS was organized into a conceptual model, which is a way to visualize and understand how a disease or condition like PMS leads to the signs experienced by the individual, which in turn lead to quality-of-life impacts upon the individual and his or her caregiver.
 - The signs and impacts are further organized by grouping them with similar things into groups called *domains* (italicized text in each smaller box in the model).

The most frequently reported signs of PMS are **bolded**:

- 9 articles mentioned “Autism and/or autistic traits” and “Intellectual disability”
- 7 articles mentioned “Constipation,” “Hyperactivity,” “Hypotonia,” “Seizures,” and “Sleep disturbance”
- 5 articles mentioned “Decreased social function and communication,” “Delayed or absent speech,” “Developmental regression,” “Gastrointestinal dysfunction,” “Pica,” “Renal abnormalities,” and “urinary incontinence”

Quality of life impacts on individuals with PMS included sleep disturbances, difficulty concentrating, difficulties at school, social avoidance, and food refusal.

Quality of life impacts on caregivers included emotional impacts (like concern and worry), impacts on family functioning, sleep impacts, and social impacts (like feeling ostracized from broader society).

This conceptual model provides an overview of the many ways that PMS affects those who live with it and the people who care for them. It can be used to expand the knowledge base about PMS and to support pharmaceutical companies that might be interested in developing new treatments. It reflects what can be found in current published literature about PMS. Further research with individuals affected by PMS can help to clarify the things that are the most relevant and important to them.