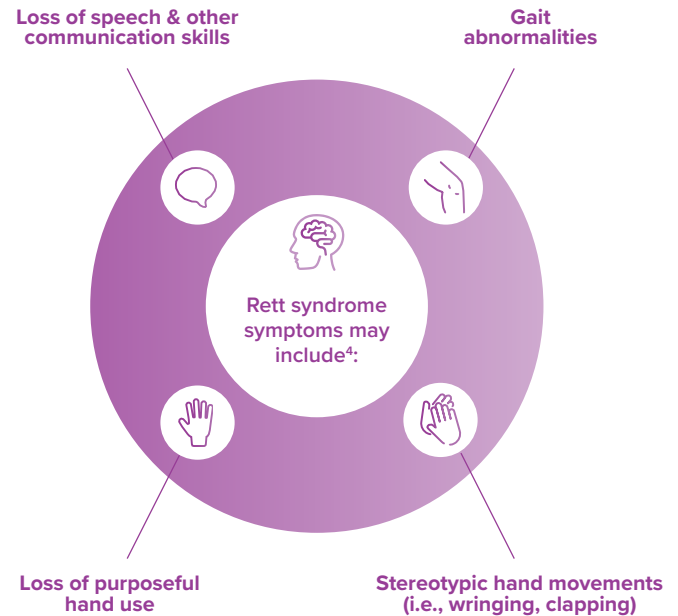


Rett syndrome is a rare, complex, neurodevelopmental disorder that may occur over four stages and affects approximately **6,000 - 9,000 patients in the U.S.**¹⁻³

A child with Rett syndrome exhibits an early period of apparently normal development until six to 18 months, when their developmental progress seems to slow down or stagnate. This is typically followed by a duration of regression when the child loses acquired communication skills and purposeful hand use.³

The child may then experience a plateau period in which they show mild recovery in cognitive interests, but body movements remain severely diminished. As they age, those living with Rett may continue to experience a stage of motor deterioration which can last decades.³



MECP2 Gene Mutation:

Rett syndrome is typically caused by a genetic mutation on the *MECP2* gene.⁵ In preclinical studies, deficiency in *MeCP2* function has been shown to lead to impairment in synaptic communication, and the deficits in synaptic function may be associated with Rett manifestations.⁵⁻⁷

Understanding and Diagnosing Rett Syndrome

According to one study, obtaining a diagnosis of Rett syndrome can be a prolonged journey that varies considerably among cases and can take two to four years between initial presentation of symptoms and diagnosis. The median age of Rett syndrome diagnosis is **approximately three years old.**⁸

Age of diagnosis of Rett syndrome was younger in children with delayed acquisition of pulling to stand, supported walking, independent walking, or finger feeding, but older in children with delayed acquisition of pincer grasp or transfer of objects from hand to hand.⁸

The condition is typically diagnosed by a neurologist, developmental pediatrician or geneticist.⁸

Early symptoms of Rett present similarly to other conditions which may lead to initial diagnoses of **intellectual disabilities, lack of normal physiological development in childhood, failure to thrive, disorders of psychological development, language disorder, degenerative disease of nervous system, Leigh's disease, muscle weakness or specific developmental disorder of motor function.**⁹

Caregiver Impact

Most patients living with Rett syndrome will live into adulthood and require round-the-clock care.^{2,10} The experience of being a caregiver for a child with Rett can be emotionally, physically and financially challenging. Parents and families are often juggling day-to-day life tasks in order to manage the child's condition, while searching for clarity on what the child is experiencing.¹¹



In a study of **caretaker quality of life**, severity of disease was associated with **decreased physical health** scores, and feeding difficulties were associated with **decreased physical and mental health scores**.¹²

Managing Rett Syndrome

Ongoing health concerns for those living with Rett include:²

- **movement disorders**
- **irregular breathing patterns**
- **gastrointestinal issues**
- **epilepsy**
- **scoliosis**

The factors most strongly associated with increased risk of mortality in Rett are **uncontrolled seizures, swallowing difficulties, lack of mobility, pneumonia and compromised lung function due to scoliosis and difficulty swallowing**.¹³

While Rett syndrome causes severe impairment that affects nearly every aspect of a patient's life, there are currently no approved medications that target the disease's root cause. Given the heterogenous nature of Rett syndrome, a multidisciplinary approach is needed to manage the various clinical symptoms.¹⁴ Until recently, there was no available pharmacologic treatment specifically for Rett syndrome.

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