F I S C A L I M P A C T R E P O R T

SPONSOR Padilla **ORIGINAL DATE** 2/10/16 **LAST UPDATED** **HM**

SHORT TITLE Add Rett Syndrome to Medicaid **SM** 81

ANALYST Chilton

APPROPRIATION (dollars in thousands)

Appropriation		Recurring or Nonrecurring	Fund Affected
FY16	**FY17**		
	None		

(Parenthesis ( ) Indicate Expenditure Decreases)

SOURCES OF INFORMATION
LFC Files

Responses Received From
Department of Health (DOH)

Responses Not Received From
Developmental Disabilities Planning Council (DDPC)
Human Services Department (HSD)

SUMMARY

Synopsis of Memorial

SM 81, Add Rett Syndrome to Medicaid, asks DOH and HSD to request the addition of patients diagnosed with Rett Syndrome to those eligible for the Developmental Disability Waiver Program (DDWP), due to the severe disabilities almost always seen in patients with this disorder.

FISCAL IMPLICATIONS

Unlikely to be any major fiscal implications, since most patients with Rett Syndrome are already eligible for the DDWP, given that most have severe developmental delay and/or seizure disorders, and many have autistic symptoms.

SIGNIFICANT ISSUES

As noted by DOH, Rett Syndrome is a serious neurodevelopmental disorder almost exclusively affecting females and resulting in degeneration of neurological function, usually beginning between six and eighteen months of age. Application of national incidence figures indicates that about one girl would be born each year in New Mexico would at some time in her life be diagnosed with Rett Syndrome. The disorder causes rapid deterioration in function for several years, then an apparent "plateauing" of function for two to ten years, and then further degeneration. Affected females often live into adulthood, but require on-going care for most activities of daily living.

Individuals with Rett Syndrome are diagnosed on a characteristic pattern of disabilities, now usually confirmed with specific genetic laboratory testing.

TECHNICAL ISSUES

The memorial does not state the criteria for diagnosis, although that diagnosis usually becomes obvious within a short period after onset of symptoms.

OTHER SUBSTANTIVE ISSUES

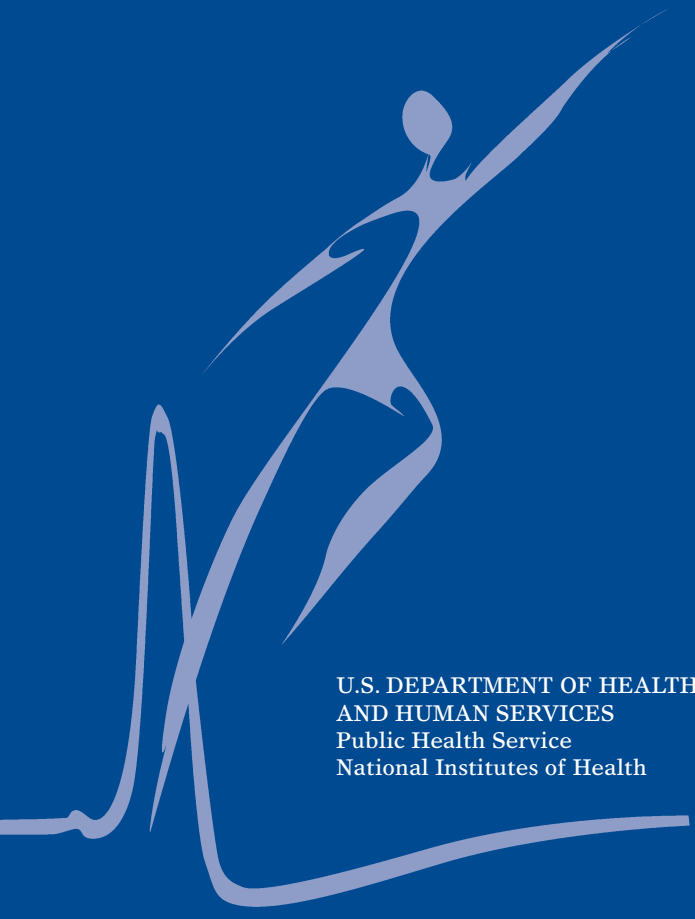
DOH states that "The DDW program is a Medicaid program which is due for renewal on July 1, 2016; however, a request for extension of the current waiver to 2017 is in preparation for submission. The program renewal will include definitions of eligibility for the program and qualifying conditions that would go into effect on the DDW renewal date."

WHAT WILL BE THE CONSEQUENCES OF NOT ENACTING THIS BILL

Children with Rett Syndrome would probably qualify for the DDWP based on symptoms of the disorder, as noted above, but that qualification might be delayed relative to when it might be available based on the inclusion of this category in the DDWP.

LAC/al

Rett Syndrome



U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
Public Health Service
National Institutes of Health

Rett Syndrome

What is Rett syndrome?

Rett syndrome is a neurodevelopmenal disorder that affects girls almost exclusively. It is characterized by normal early growth and development followed by a slowing of development, loss of purposeful use of the hands, distinctive hand movements, slowed brain and head growth, problems with walking, seizures, and intellectual disability.

The disorder was identified by Dr. Andreas Rett, an Austrian physician who first described it in a journal article in 1966. It was not until after a second article about the disorder, published in 1983 by Swedish researcher Dr. Bengt Hagberg, that the disorder was generally recognized.

The course of Rett syndrome, including the age of onset and the severity of symptoms, varies from child to child. Before the symptoms begin, however, the child generally appears to grow and develop normally, although there are often subtle abnormalities even in early infancy, such as loss of muscle tone (hypotonia), difficulty feeding, and jerkiness in limb movements. Then, gradually, mental and physical symptoms appear. As the syndrome progresses, the child loses purposeful use of her hands and the ability to speak. Other early symptoms may include problems crawling or walking

and diminished eye contact. The loss of functional use of the hands is followed by compulsive hand movements such as wringing and washing. The onset of this period of regression is sometimes sudden.

Apraxia—the inability to perform motor functions—is perhaps the most severely disabling feature of Rett syndrome, interfering with every body movement, including eye gaze and speech.

Children with Rett syndrome often exhibit autistic-like behaviors in the early stages. Other symptoms may include walking on the toes, sleep problems, a wide-based gait, teeth grinding and difficulty chewing, slowed growth, seizures, cognitive disabilities, and breathing difficulties while awake such as hyperventilation, apnea (breath holding), and air swallowing.

What are the stages of the disorder?

Scientists generally describe four stages of Rett syndrome. Stage I, called early onset, typically begins between 6 and 18 months of age. This stage is often overlooked because symptoms of the disorder may be somewhat vague, and parents and doctors may not notice the subtle slowing of development at first. The infant may begin to show less eye contact and have reduced interest in toys. There may be delays in gross motor skills such as sitting or crawling. Hand-wringing and decreasing head growth may occur, but not enough to draw attention. This stage usually lasts for a few months but can continue for more than a year.

Stage II, or the rapid destructive stage, usually begins between ages 1 and 4 and may last for

weeks or months. Its onset may be rapid or gradual as the child loses purposeful hand skills and spoken language. Characteristic hand movements such as wringing, washing, clapping, or tapping, as well as repeatedly moving the hands to the mouth often begin during this stage. The child may hold the hands clasped behind the back or held at the sides, with random touching, grasping, and releasing. The movements continue while the child is awake but disappear during sleep. Breathing irregularities such as episodes of apnea and hyperventilation may occur, although breathing usually improves during sleep. Some girls also display autistic-like symptoms such as loss of social interaction and communication. Walking may be unsteady and initiating motor movements can be difficult. Slowed head growth is usually noticed during this stage.

Stage III, or the plateau or pseudo-stationary stage, usually begins between ages 2 and 10 and can last for years. Apraxia, motor problems, and seizures are prominent during this stage. However, there may be improvement in behavior, with less irritability, crying, and autistic-like features. A girl in stage III may show more interest in her surroundings and her alertness, attention span, and communication skills may improve. Many girls remain in this stage for most of their lives.

Stage IV, or the late motor deterioration stage, can last for years or decades. Prominent features include reduced mobility, curvature of the spine (scoliosis) and muscle weakness, rigidity, spasticity, and increased muscle tone with abnormal posturing of an arm, leg, or top

part of the body. Girls who were previously able to walk may stop walking. Cognition, communication, or hand skills generally do not decline in stage IV. Repetitive hand movements may decrease and eye gaze usually improves.

What causes Rett syndrome?

Nearly all cases of Rett syndrome are caused by a mutation in the methyl CpG binding protein 2, or *MECP2* (pronounced meck-pea-two) gene. Scientists identified the gene—which is believed to control the functions of many other genes—in 1999. The *MECP2* gene contains instructions for the synthesis of a protein called methylcytosine binding protein 2 (MeCP2), which is needed for brain development and acts as one of the many biochemical switches that can either increase gene expression or tell other genes when to turn off and stop producing their own unique proteins. Because the *MECP2* gene does not function properly in individuals with Rett syndrome, insufficient amounts or structurally abnormal forms of the protein are produced and can cause other genes to be abnormally expressed.

Not everyone who has an *MECP2* mutation has Rett syndrome. Scientists have identified mutations in the *CDKL5* and *FOXG1* genes in individuals who have atypical or congenital Rett syndrome, but they are still learning how those mutations work. Scientists believe the remaining cases may be caused by partial gene deletions, mutations in other parts of the gene, or additional genes that have not yet been identified, and they continue to look for other causes.

Is Rett syndrome inherited?

Although Rett syndrome is a genetic disorder, less than 1 percent of recorded cases are inherited or passed from one generation to the next. Most cases are spontaneous, which means the mutation occurs randomly. However, in some families of individuals affected by Rett syndrome, there are other female family members who have a mutation of their *MECP2* gene but do not show clinical symptoms. These females are known as "asymptomatic female carriers."

Who gets Rett syndrome?

Rett syndrome is estimated to affect one in every 10,000 to 15,000 live female births and occurs in all racial and ethnic groups worldwide. Prenatal testing is available for families with an affected daughter who has an identified *MECP2* mutation. Since the disorder occurs spontaneously in most affected individuals, however, the risk of a family having a second child with the disorder is less than 1 percent.

Genetic testing is also available for sisters of girls with Rett syndrome who have an identified *MECP2* mutation to determine if they are asymptomatic carriers of the disorder, which is an extremely rare possibility.

The *MECP2* gene is found on a person's X chromosome, one of the two sex chromosomes. Girls have two X chromosomes, but only one is active in any given cell. This means that in a girl with Rett syndrome only a portion of the cells in the nervous system will use the defective gene. Some of the

child's brain cells use the healthy gene and express normal amounts of the protein.

The severity of Rett syndrome in girls is in part a function of the percentage of their cells that carry a normal copy of the *MECP2* gene. If the active X chromosome that is carrying the defective gene is turned off in a large proportion of cells, the symptoms will be mild, but if a larger percentage of cells have the X chromosome with the normal *MECP2* gene turned off, onset of the disorder may occur earlier and the symptoms may be more severe.

The story is different for boys who have a *MECP2* mutation known to cause Rett syndrome in girls. Because boys have only one X chromosome (and one Y chromosome) they lack a back-up copy that could compensate for the defective one, and they have no protection from the harmful effects of the disorder. Boys with such a defect frequently do not show clinical features of Rett syndrome but experience severe problems when they are first born and die shortly after birth. A very small number of boys may have a different mutation in the *MECP2* gene or a sporadic mutation after conception that can cause some degree of intellectual disability and developmental problems.

How is Rett syndrome diagnosed?

Doctors clinically diagnose Rett syndrome by observing signs and symptoms during the child's early growth and development, and conducting ongoing evaluations of the child's physical and neurological status. Scientists have developed a genetic test to complement the clinical diagnosis, which involves searching

for the *MECP2* mutation on the child's X chromosome.

A pediatric neurologist, clinical geneticist, or developmental pediatrician should be consulted to confirm the clinical diagnosis of Rett syndrome. The physician will use a highly specific set of guidelines that are divided into three types of clinical criteria: *essential*, *supportive*, and *exclusion*. The presence of any of the exclusion criteria negates a diagnosis of classic Rett syndrome.

Examples of *essential* diagnostic criteria or symptoms include having apparently normal development until between the ages of 6 and 18 months and a normal head circumference at birth followed by a slowing of the rate of head growth with age (between 3 months and 4 years). Other essential diagnostic criteria include severely impaired expressive language, repetitive and stereotypic hand movements, and gait abnormalities, including toe-walking or an unsteady, wide-based, stiff-legged walk.

Supportive criteria are not required for a diagnosis of Rett syndrome but may occur in some individuals. In addition, these symptoms—which vary in severity from child to child—may not be observed in very young girls but may develop with age. A child with supportive criteria but none of the essential criteria does not have Rett syndrome. Supportive criteria include breathing difficulties, electroencephalogram (EEG) abnormalities, seizures, muscle rigidity, spasticity and/or joint contractures which worsen with age, scoliosis, teeth-grinding, small hands and feet in relation to height, growth retardation, decreased

body fat and muscle mass (although there may be a tendency toward obesity in some affected adults), abnormal sleep patterns, irritability or agitation, chewing and/or swallowing difficulties, poor circulation of the lower extremities with cold and bluish-red feet and legs, decreased mobility with age, and constipation.

In addition to the essential diagnostic criteria, a number of specific conditions enable physicians to rule out a diagnosis of Rett syndrome. These are referred to as *exclusion* criteria. Children with any one of the following criteria do not have Rett syndrome: enlargement of body organs or other signs of storage disease, vision loss due to retinal disorder or optic atrophy, abnormally small head at birth (microcephaly), an identifiable metabolic disorder or other inherited degenerative disorder, an acquired neurological disorder resulting from severe infection or head trauma, evidence of growth retardation *in utero*, or evidence of brain damage acquired after birth.

Is treatment available?

There is no cure for Rett syndrome. Treatment for the disorder is symptomatic—focusing on the management of symptoms—and supportive, requiring a multidisciplinary approach. Medication may be needed for breathing irregularities and motor difficulties, and anticonvulsant drugs may be used to control seizures. There should be regular monitoring for scoliosis and possible heart abnormalities. Occupational therapy can help children develop skills needed for performing self-directed activities (such as dressing, feeding, and practicing arts and crafts), while

physical therapy and hydrotherapy may prolong mobility. Some children may require special equipment and aids such as braces to arrest scoliosis, splints to modify hand movements, and nutritional programs to help them maintain adequate weight. Special academic, social, vocational, and support services may be required in some cases.

What is the outlook for those with Rett syndrome?

Despite the difficulties with symptoms, most individuals with Rett syndrome continue to live well into middle age and beyond. Because the disorder is rare, very little is known about long-term prognosis and life expectancy. While it is estimated that there are women in their 40s and 50s with the disorder, not enough women have been studied to make reliable estimates about life expectancy beyond age 40.

What research is being done?

Within the Federal government, the National Institute of Neurological Disorders and Stroke (NINDS), the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Institute of Mental Health (NIMH), and the Office of Rare Diseases Research (ORDR) support clinical and basic research on Rett syndrome.

Understanding the cause of this disorder is necessary for developing new therapies to manage specific symptoms, as well as for providing better methods of diagnosis. The

discovery of the main Rett syndrome gene (*MECP2*) in 1999 provides a basis for further genetic studies and enables the use of recently developed animal models such as transgenic mice which are deficient in *MECP2*. These mice have neurologic abnormalities that can be reversed by activating the *MECP2* gene later in life.

One NINDS-supported study looks for mutations in the *MECP2* gene of individuals with Rett syndrome to learn about MeCP2 protein function and dysfunction. Information from this study will increase understanding of the disorder and may lead to new therapies. Other research aims at identifying molecular pathways that are affected by the dysfunction, developing animal models of the disorder, and early-stage therapy development.

Some researchers suggest that the specific type of mutation in the *MECP2* gene affects the severity of symptoms of Rett syndrome. Studies are now underway to understand each mutation that may cause the features of Rett syndrome, and how these mutations might change the features of the syndrome. One NIH-funded study of the natural history of Rett syndrome should also provide new information about these topics.

Scientists know that lack of a properly functioning MeCP2 protein disturbs the function of mature brain cells but they do not know the exact mechanisms by which this happens. Investigators are trying to find other genetic switches that operate in a similar way to the MeCP2 protein. Once they discover how the protein works and locate similar switches,

they may devise therapies that can substitute for the malfunctioning switch. Another outcome might involve manipulating other biochemical pathways to compensate for the malfunctioning *MECP2* gene, thereby preventing progression of the disorder. Gene therapy to achieve regulated expression of a normal *MECP2* gene is also under study in animal models.

Researchers are also trying to find other genes that may be involved in Rett syndrome. Some studies have helped to narrow the search for these genes, but much is still unknown about how these genes may cause or contribute to Rett syndrome.

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
800-352-9424
www.ninds.nih.gov

Information also is available from the following organizations:

International Rett Syndrome Foundation
4600 Devitt Drive
Cincinnati, OH 45246
513-874-5020
800-818-7388
www.rettsyndrome.org

Easter Seals
233 South Wacker Drive
Suite 2400
Chicago, IL 60606
312-726-6200
800-221-6827
www.easterseals.com

RettSearch
716 N. Broadway
Baltimore, MD 21205
443-923-7600
www.rettsearch.org

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31 Center Drive
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www.nichd.nih.gov

National Institute of Mental Health (NIMH)
National Institutes of Health, DHHS
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301-443-4513
866-615-NIMH (6464)
www.nimh.nih.gov

Office of Rare Diseases Research (ORDR)
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