

Why is my loved one with Down syndrome slowing down, shutting down, or losing skills?

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Adult Down
Syndrome Center
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Please note:

- This presentation is intended for families, caregivers, health care professionals, and service providers of individuals with Down syndrome.
- The information in this presentation is provided for educational purposes only and is not intended to serve as a substitute for a medical, psychiatric, mental health, or behavioral evaluation, diagnosis, or treatment plan by a qualified professional.
- We recommend that you bring specific questions about an individual with Down syndrome to their medical and/or therapy providers.

Objectives

- Describe decline in skills and identify causes of decline in skills, including Down syndrome regression disorder (DSRD) and Alzheimer's disease.
- Identify strategies to assist with diagnosis and treatment of decline in skills.
- Discuss options to access care and resources available to individuals with Down syndrome across the country.

Resource Library

The screenshot shows the top navigation bar with the Advocate Medical Group logo and 'Adult Down Syndrome Center' text. A search bar contains 'I'm looking for...' and a 'MENU' button with a hamburger icon. Below the navigation is the 'Resource Library | All Resources' header. Three featured resource cards are displayed: 'People with Down Syndrome' (with a photo of a young woman), 'Families & Caregivers' (with a photo of a woman and a man), and 'Health Care Professionals' (with a photo of a woman talking to two men). At the bottom, five categories are listed with icons and links: 'Events, Classes & Programs' (with a bell icon and 'See the Schedule' link), 'Video Gallery' (with a play button icon and 'View All' link), 'Related Organizations' (with a sunburst icon and 'See Listing of Links' link), 'Projects' (with a book icon and 'See Our Latest Projects' link), and 'News' (with a document icon and 'View News Articles' link).

Advocate Medical Group
Adult Down Syndrome Center

I'm looking for... MENU

Resource Library | All Resources

People with Down Syndrome

Families & Caregivers

Health Care Professionals

Events, Classes & Programs
[See the Schedule](#)

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<https://adsresources.advocatehealth.com/>

Decline in skills

What is “decline in skills”?

Decreased ability to perform
or use previously mastered
skills or abilities

- Cognition
- Behavior / psychological changes
- Ability to perform activities of daily living
- Motor function
- Speech

Why might a person with DS decline?

- Autism
- Down syndrome regression disorder (DSRD)
- Alzheimer's disease (AD)
- Other

Other causes

Other causes

- Medical conditions
- Adjustment to life events

Medical conditions

- Medication side effects
- Sleep apnea
- Vitamin B12 deficiency
- Endocrine disorders
 - Hypothyroidism or hyperthyroidism
 - Adrenal insufficiency
 - Diabetes mellitus
 - Puberty-related
 - Menopause
- Cervical myelopathy (subluxation, spinal stenosis)
- Seizures
- Chronic pain
 - Dental
 - Sinus
 - Menstrual
 - Gastrointestinal, severe constipation

Medical conditions (cont.)

- Neuropsychiatric disorders
 - Catatonia
 - Mood disorder
 - Obsessive-compulsive disorder
 - Psychotic disorder
 - Complex tic disorder
 - Post-traumatic stress disorder
 - Parkinsonism, dystonia
- Cardiovascular disease
 - Uncorrected congenital heart disease with pulmonary hypertension, congestive heart failure
 - Eisenmenger's syndrome
 - Stroke: thrombotic or hemorrhagic

Medical conditions (cont.)

- Infectious disease
 - Urinary tract infections
 - Pneumonia
 - Sepsis
 - Viral/bacterial meningitis/encephalitis
 - Lyme's disease
- Toxic-metabolic
 - Numerous etiologies
- Visual impairment
 - Glaucoma
 - Retinal detachment
 - Cataracts
 - keratoconus
- Hearing impairment
 - Hypoacusis or hyperacusis
 - Tinnitus
 - Vertigo

Adjustment to life events

- Loss of family, friends, pets
- School graduation
- Work setting changes
- Staff changes
- Physical relocation
- Response to hospitalization or medical condition
- COVID-19 pandemic

Case 1

- 35-year-old man with Down syndrome
 - Noted to be struggling with completing his daily activities at home and at work
 - Weight loss but appetite good
 - Sleeping well
 - “Just don’t feel well”
 - Cause?

Case 2

- 23-year-old woman with Down syndrome
 - Losing independence in self-care activities
 - Losing writing skills
 - Less conversant
 - More self-talk

Down syndrome regression disorder (DSRD)

DSRD

- First described in 1946 by Rollin – “catatonic psychoses”
- Has been called many names
- Continues to be studied and discussed

DSRD

• Assessment and Diagnosis of Down Syndrome Regression Disorder: International Expert Consensus

- Published in July 2022
- Reached consensus on name, diagnostic work up, and diagnostic criteria

[Link to article](#)



Assessment and Diagnosis of Down Syndrome Regression Disorder: International Expert Consensus

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Objective: To develop standardization for nomenclature, diagnostic work up and diagnostic criteria for cases of neurocognitive regression in Down syndrome.

Background: There are no consensus criteria for the evaluation or diagnosis of neurocognitive regression in persons with Down syndrome. As such, previously published data on this condition is relegated to smaller case series with heterogeneous data sets. Lack of standardized assessment tools has slowed research in this clinical area.

Methods: The authors performed a two-round traditional Delphi method survey of an international group of clinicians with experience in treating Down syndrome to develop a standardized approach to clinical care and research in this area. Thirty-eight

Diagnostic criteria

- Sudden and rapid decline
 - Altered mental status or behavioral dysregulation
 - Cognitive decline
 - Developmental regression with or without new autistic features
 - New focal neurologic deficits on examination and/or seizures
 - Insomnia or circadian rhythm disruption
 - Language deficits
 - Movement disorder (excluding tics)
 - Psychiatric symptoms
- Exclusion of other causes

national down syndrome society
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Regression & Down Syndrome

Down syndrome regression disorder (DSRD), also referred to as regression, is a rare but serious disorder that occurs in some adolescents and young adults with Down syndrome. Regression is used to describe the loss of skills an individual has previously learned. These skills can be daily living, language, movement, or social skills. The loss is often sudden and occurs over a period of weeks to months. Since DSRD may be caused by a variety of factors, the first priority is to determine the most likely cause. Individuals who are younger than 10 years or older than 30 years are very rarely diagnosed with DSRD. If these individuals are experiencing regression-like symptoms, a close look at all other factors must be taken before giving the diagnosis of DSRD. You can download our Down Syndrome Disorder Checklist under the NDSS Resources' tab at the bottom of the page. In 2022, a group of medical experts with experience treating regression in patients with Down syndrome gathered to create the first criteria for diagnosing DSRD. These criteria provide guidance to physicians and families who do not have access to specialists in DSRD. There are eight clusters of symptoms linked to regression, and some are broken down into specific examples. Individuals who are experiencing four or more of the eight symptom clusters are considered "possible" cases of DSRD, meaning further investigation is needed. Individuals who have seven or eight of the eight symptom clusters are considered "probable" cases, meaning they are likely to receive a diagnosis of DSRD if no other cause can be found.

ON THIS PAGE:

- Symptoms
- Treatment
- References

[Download the PDF here](#)

[Regression & Down Syndrome Page](#)

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Down Syndrome Regression Disorder

Down Syndrome Regression Disorder Symptoms Checklist **Date:** _____

Symptoms occurring more frequently within the last three months (check all that apply):

- 1. Behavioral Changes**
Date symptom(s) began: _____
 Eating much more or less than usual
 Confusion or disorientation
 Laughing or crying at inappropriate times
 Frequent changes in mood or rapid fluctuations between happiness, sadness, or anger
- 2. Changes in Thinking and Processing of Information**
Date symptom(s) began: _____
 Decreased visible emotions and empathy
 Lack of motivation or lack of engagement
 Difficulty starting or finishing tasks
 Worsening memory
- 3. Loss of Functional and Social Skills**
Date symptom(s) began: _____
 Loss/worsening of previously learned skills (self-feeding, toileting, dressing, etc.)
 Decreased social interaction with friends, family, classmates, or coworkers
 Decreased eye contact
 Repetitive hand or body movements with no clear purpose
- 4. New seizures or neurological deficits (weakness, slurring of speech, etc.) determined by a physician**
Date symptom(s) began: _____
- 5. Difficulty sleeping or sleeping at irregular times**
Date symptom(s) began: _____
- 6. Language Difficulties**
Date symptom(s) began: _____
 Difficulty producing speech or trouble reading and understanding speech
 No longer using speech or speaking only in a whisper
- 7. Irregular Movements**
Date symptom(s) began: _____
 Lack of movement sometimes with stiff and rigid muscles
 Moving very slowly or using an unusual walk or run gait pattern
- 8. Mental Health Symptoms**
Date symptom(s) began: _____
 New or worsened anxiety
 Delusions (untrue beliefs) or hallucinations (seeing things that are not there)
 Derealization (feeling detached from surroundings) or depersonalization (feeling of observing oneself from outside of the body)
 Obsessive compulsive tendencies like lining up items, only talking about specific topics of interest, and difficulty tolerating changes in routine
 Aggression or agitation toward others

3

[Overview & Symptom Checklist PDF](#)

Catatonia

- Abnormality of movement and behavior
- Can (but may not) be associated with mental illness
- Various presentations
 - Repetitive or purposeless overactivity
 - Resistance to movement

How is DSRD different than other forms of decline in skills?

- DSRD tends to be more severe and more pervasive.
- The cause can be the same in some instances.

Case 3

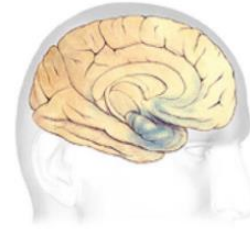
- 22-year-old woman with Down syndrome
 - Over several weeks has a decline in skills:
 - Speech, thought processes
 - Daily tasks
 - Ability to move about the house - “stuck”
 - Sleep changes
 - Mood (depressed)

Alzheimer's disease

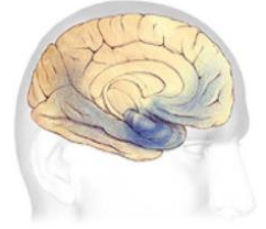
What is Alzheimer's disease (AD)?

- Progressive neurological condition
- Affects the brain
- Is a type of dementia
- Plaques and tangles = the microscopic changes of the brain consistent with AD

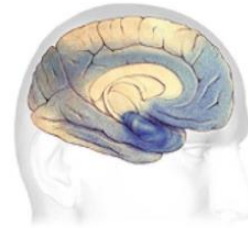
By age 40, nearly all people with Down syndrome have the brain pathology of Alzheimer's disease.



Earliest Alzheimer's



Mild to moderate Alzheimer's



Severe Alzheimer's

Images from [Alzheimer's Association](#)

Mann 1988, Hartley et al. 2014

Why?

- Amyloid precursor protein (APP)
- Chronic inflammation?
- Metabolic abnormalities?

By age 40, nearly all people with Down syndrome have the brain pathology of Alzheimer's disease.

HOWEVER, *symptoms* of Alzheimer's disease are uncommon before age 40.

Prevalence and age of diagnosis

Prevalence of clinical AD

- Estimates vary
- 55% in those ages 50-59
- Greater than 75% in those ages 60 and older

Age of diagnosis

- Mean: about 55 years
- Median: about 54 years

How is AD similar to DSRD?

- Both involve decline in skills
- Both are (probably) neurological conditions that often have psychological symptoms
- Both are challenging for the individual and families
- Both need more research, including ways to support the individual and family

How is AD different than DSRD?

- Alzheimer's disease
 - Age of onset > 40 years old
 - Not reversible
- DSRD
 - Age of onset = teens, early 20s
 - Sometimes reversible
- Not all decline in skills in those age ranges is either AD or DSRD.

Case 4

- 49-year-old man with Down syndrome
 - Seizure (no prior history)
 - Noted over the last few years:
 - Personality changes
 - Less empathetic
 - Less "groove"
 - Memory - not remembering family members' birthdays
 - Siblings report parents have been doing more for him - tasks he could previously do independently

Determining the cause of decline

Determining the cause

- Evaluate for contributing causes
- Ongoing evaluation for additional contributing causes

Diagnostic work up

- History and physical
- Neuroimaging
- Blood work
- Lumbar puncture
- EEG
- Urine studies
- Other

Treatment

Treatment approach

- Treat diagnosable conditions
 - Some specific treatments (e.g., hypothyroidism, catatonia, autoimmune encephalopathy, sleep apnea)
- Treat related signs and symptoms
- Use therapies to help improve function
- Start with “safe” activities

Associated symptoms and/or diagnoses

- Depression
- Anxiety
- Agitation
- Sleep challenges
 - E.g., day/night reversals

Medications

- Natural products
- Prescription medications
 - Review family history
 - Start low, go slow
 - Weaning
 - Genetic testing

*Medication choices are influenced by a patient's particular symptoms and the effects and side effects of the medication.

Medications for AD

- Cholinesterase inhibitors
 - donepezil / Aricept
 - rivastigmine / Exelon
 - galantamine / Razadyne
- NMDA receptor antagonist/glutamate regulator
 - memantine / Namenda
- Anti-amyloid therapy
 - aducanumab / Aduhelm
 - lecanemab / Leqembi

Treatments for DSRD

- Medications
- ECT
- Therapy (physical, occupational, art, music, etc.)
- Counseling
- Immunotherapies

Supporting an individual with decline in skills

Diagnosis and treatment

- Be observant
- Share your observations
 - Mood, behavior, function, motor activities, sleep, appetite, any other symptoms you notice
 - What is still “missing” from the person?

Diagnosis and treatment

- Treat condition and function
 - “Safe” activities
 - Re-teach
- Trust yourself!

Non-medicinal strategies

- Sensory strategies
- Create schedules and routines
 - Sleep, healthy eating, physical activity
- Encourage safe social interactions

Caregiver support

- [Regression in Down Syndrome Support Group](#) (Facebook)
- [Down Syndrome and Alzheimer's Disease Support Groups](#) (multiple)

Accessing care

Finding a provider

- Down Syndrome Clinics
 - [NDSC](#)
 - [Global](#)
- Down Syndrome Organizations
 - [NDSC](#)
 - [Global](#)

Finding a provider

- Qualities
 - A belief that all people with Down syndrome deserve the same respect and care provided to any patient
 - A willingness to listen to and learn from individuals with Down syndrome, families, care providers, and other health professionals
 - An understanding that problems that occur are not necessarily “just Down syndrome” (diagnostic overshadowing)

Sharing resources

- [Down Syndrome Medical Interest Group \(DSMIG-USA\)](#)
 - Membership
 - Speaker Series
 - Project ECHO



DSMIG-USA
Down Syndrome Medical Interest Group

FREE RESOURCES

SHARE WITH YOUR HEALTH CARE PROVIDER

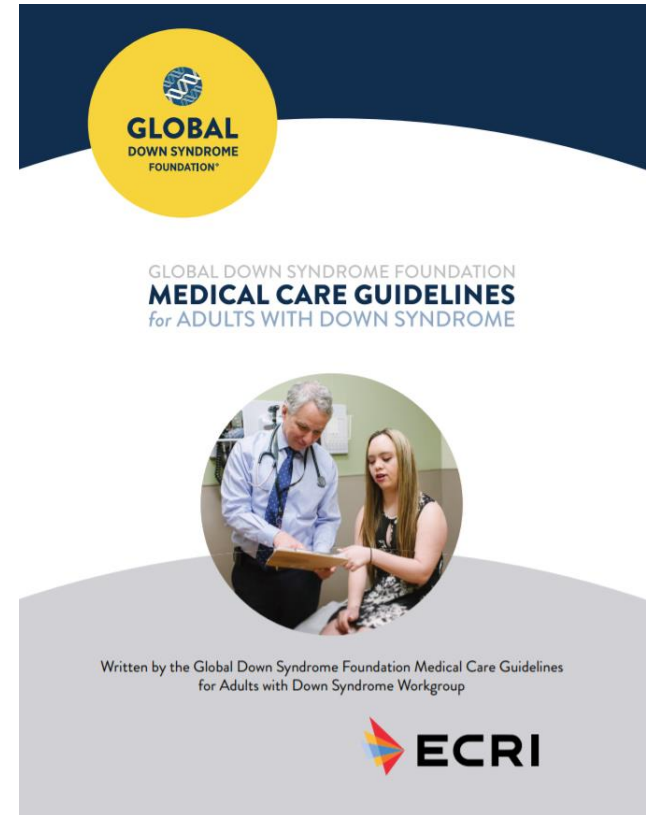
- Down Syndrome Project ECHO is a monthly virtual meeting for health care providers to learn and seek input from expert providers.
- The DSMIG Speaker Series consists of webinars and enduring materials designed to share knowledge and experience related to the care of people with Down syndrome and clinical research related to Down syndrome.
- DSMIG vetted resources including articles and important guidelines related to child and adult health issues, and health utilization by people with Down syndrome.



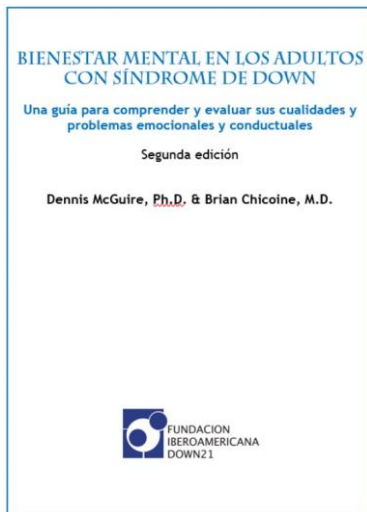
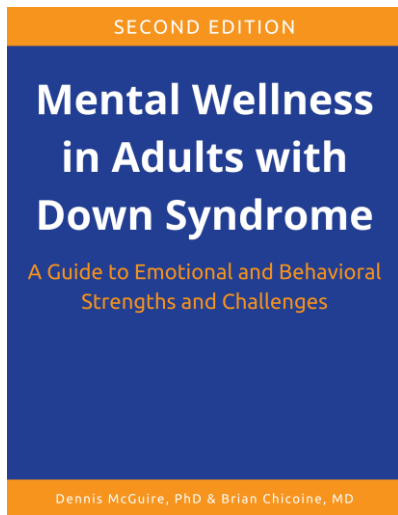
find out more at:
DSMIG-USA.ORG

Resources

- [GLOBAL Medical Care Guidelines for Adults with Down Syndrome](#)



Mental Wellness book



**Available as a free
PDF in English
and Spanish**

<https://adsresources.advocatehealth.com/mental-wellness-in-adults-with-down-syndrome-2nd-edition/>

Resources from our library

- [Alzheimer's disease & dementia](#)
- [Decline in skills/regression](#)
- [Grief and loss](#)
- [Mental health](#)

Takeaways

- There are many possible causes of decline in skills.
- A thorough history and physical exam are important when evaluating for decline in skills.
- Some causes of decline in skills are treatable.
- After the underlying cause is treated, there is usually a need to help the person “get going again” (re-establish healthy routines).
- Even if there is not a cure for the underlying cause, there are many ways to help optimize quality of life.

Resource Library:

adsresources.advocatehealth.com



Facebook:

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Email Newsletter:

eepurl.com/c7uV1v



References

- Akahoshi, K., Matsuda, H., Funahashi, M., Hanaoka, T., Suzuki, Y. (2012). Acute neuropsychiatric disorders in adolescents and young adults with Down syndrome: Japanese case reports. *Neuropsychiatric Disease and Treatment*, **8**, 339-345. doi: [10.2147/NDT.S32767](https://doi.org/10.2147/NDT.S32767)
- Ballard, C., Mobley, W., Hardy, J., Williams, G., & Corbett, A. (2016). Dementia in Down's syndrome. *The Lancet Neurology*, **15**(6), 622–636. doi: [10.1016/S1474-4422\(16\)00063-6](https://doi.org/10.1016/S1474-4422(16)00063-6)
- Castillo, H., Patterson, B., Hickey, F., Kinsman, A., Howard, J.M., Mitchell, T., Molloy, C.A. (2008). Difference in age at regression in children with autism with and without Down syndrome. *Journal of Developmental and Behavioral Pediatrics*, **29**(2), 89-93. doi: [10.1097/DBP.0b013e318165c78d](https://doi.org/10.1097/DBP.0b013e318165c78d)
- Chicoine, B & Capone, G. (2019) "Regression in adolescents and adults with Down syndrome" in Prasher, V & Janicki, M (eds), Physical Health of Adults with Intellectual and Developmental Disabilities. (pp 121-140). Switzerland: Springer Nature. doi: [10.1007/978-3-319-90083-4_7](https://doi.org/10.1007/978-3-319-90083-4_7)
- Coppus, A., Evenhuis, H., Verberne, G.J., et al. (2006). Dementia and mortality in persons with Down's syndrome. *Journal of Intellectual Disability Research*, **50** (Pt 10), 768-777. doi: [10.1111/j.1365-2788.2006.00842.x](https://doi.org/10.1111/j.1365-2788.2006.00842.x)
- Devenny, D.A., Matthews, A. (2011) "Regression: Atypical loss of attained functioning in children and adolescents with Down syndrome" in R.M. Hodapp (ed), International Review of Research in Developmental Disabilities, vol. 41 (pp 233-264). Oxford, UK: Academic Press. doi: [10.1016/B978-0-12-386495-6.00007-2](https://doi.org/10.1016/B978-0-12-386495-6.00007-2)

- Ghaziuddin, N., Nassiri, A., Miles, J.H. (2015). Catatonia in Down syndrome: A treatable cause of regression. *Neuropsychiatric Disease and Treatment*, **11**, 941-949. doi: [10.2147/NDT.S77307](https://doi.org/10.2147/NDT.S77307)
- Hithersay, R., Startin, C. M., Hamburg, S., Mok, K. Y., Hardy, J., Fisher, E., Tybulewicz, V., Nizetic, D., & Strydom, A. (2019). Association of dementia with mortality among adults with Down syndrome older than 35 years. *JAMA Neurology*, **76**(2), 152–160. doi: [10.1001/jamaneurol.2018.3616](https://doi.org/10.1001/jamaneurol.2018.3616)
- Jacobs, J., Schwartz, A., McDougale, C.J., Skotko, B.G. (2016). Rapid clinical deterioration in an individual with Down syndrome. *American Journal of Medical Genetics: Part A*, **170**(7), 1899-902. doi: [10.1002/ajmg.a.37674](https://doi.org/10.1002/ajmg.a.37674)
- Lott, I. T., & Head, E. (2019). Dementia in Down syndrome: Unique insights for Alzheimer disease research. *Nature Reviews Neurology*, **15**(3), 135–147. doi: [10.1038/s41582-018-0132-6](https://doi.org/10.1038/s41582-018-0132-6)
- Mann, D. M., & Esiri, M. M. (1989). The pattern of acquisition of plaques and tangles in the brains of patients under 50 years of age with Down's syndrome. *Journal of the Neurological Sciences*, **89**(2-3), 169–179. doi: [10.1016/0022-510x\(89\)90019-1](https://doi.org/10.1016/0022-510x(89)90019-1)
- McCarron, M., McCallion, P., Reilly, E., & Mulryan, N. (2014). A prospective 14-year longitudinal follow-up of dementia in persons with Down syndrome. *Journal of Intellectual Disability Research*, **58**(1), 61–70. doi: [10.1111/jir.12074](https://doi.org/10.1111/jir.12074)

- Miles, J. (2017, July). *Catatonia as a cause of regression in Down syndrome*. Presentation at the annual symposium of the Down Syndrome Medical Interest Group-USA, Sacramento, CA.
- Mircher, C., Cieuta-Walti, C., Marey, I., Rebillat, A.S., Cretu, L, Milenko, E., Conte, M., Sturtz, F., Rethore, M.O., Ravel, A. (2017). Acute regression in young people with Down syndrome. *Brain Sciences*, **7**(6), E57. doi: [10.3390/brainsci7060057](https://doi.org/10.3390/brainsci7060057)
- Prasher, V. (2002). Disintegrative syndrome in young adults [Letter to the editor]. *Irish Journal of Psychological Medicine*, **19**(3), 101. doi: [10.1017/S0790966700007205](https://doi.org/10.1017/S0790966700007205)
- Rollin, H. (1946). Personality in mongolism with special reference to the incidence of catatonic psychosis. *American Journal of Mental Deficiency*, **51**(2), 219-37.
- Rosso M, Fremion E, Santoro SL, et al. Down syndrome disintegrative disorder: A clinical regression syndrome of increasing importance. *Pediatrics*. 2020;145(6):e20192939. doi:[10.1542/peds.2019-2939](https://doi.org/10.1542/peds.2019-2939)
- Santoro, S.L, Cannon, S., Capone, G., et al. Unexplained regression in Down syndrome: 35 cases from an international Down syndrome database. *Genet Med* 22, 767-776. doi: [10.1038/s41436-019-0706-8](https://doi.org/10.1038/s41436-019-0706-8)
- Stein, D.S., Munir, K.M., Karweck, A.J., Davidson, E.J., Stein, M.T. (2013). Developmental regression, depression, and psychosocial stress in an adolescent with Down syndrome. *Journal of Developmental and Behavioral Pediatrics*, **34**(3), 216-218. doi: [10.1097/DBP.0b013e31828b2b42](https://doi.org/10.1097/DBP.0b013e31828b2b42)

- Wiseman, F. K., Al-Janabi, T., Hardy, J., Karmiloff-Smith, A., Nizetic, D., Tybulewicz, V. L., Fisher, E. M., & Strydom, A. (2015). A genetic cause of Alzheimer disease: mechanistic insights from Down syndrome. *Nature reviews. Neuroscience*, *16*(9), 564–574. doi: [10.1038/nrn3983](https://doi.org/10.1038/nrn3983)
- Worley, G., Crissman, B.G., Cadogan, E., Milleson, C., Adkins, D.W., Kishnani, P.S. (2015). Down syndrome disintegrative disorder: New-onset autistic regression, dementia, and insomnia in older children and adolescents with Down syndrome. *Journal of Child Neurology*, *30*(9), 1147-1152. doi: [10.1177/0883073814554654](https://doi.org/10.1177/0883073814554654)