Williams Syndrome

Health Watch Table

1. Head, eyes, ears, nose, throat

Considerations	Recommendations
Children: ▸ 60% have chronic otitis media ▸ Nearly all have characteristic auditory profile including hyperacusis [84%-100%] and paradoxic affinity to music. Early onset phonophobia (fear of noises) also common ▸ Noise tolerance improves with age ▸ Strabismus and refractive errors such as hyperopia are common ▸ Amblyopia and reduced depth perception can cause difficulty in negotiating uneven surfaces and stairs ▸ Blocked tear ducts are common ▸ Hoarse, deep voice	▸ Arrange hearing assessment at 6-12 months and annual screen thereafter. ▸ Check for wax accumulation, if indicated. ▸ Refer for tympanoplasty, if indicated. ▸ Encourage family/support persons to reduce exposure to loud noises (e.g., electric household appliances and machines, fireworks, thunder) and recommend earplugs or shooters' ear muffs in noisy environments. ▸ Use headphones with music in uncomfortable situations, e.g., watching a noisy event. ▸ Arrange ophthalmologic exam by 1 year and vision screening annually thereafter. ▸ See also No. 8, Musculoskeletal section, regarding mobility.
Adults: ▸ Vulnerable auditory system with risk of hearing loss	▸ Refer for audiology examination at age 30 and every five years thereafter to assess sensorineural hearing loss. ▸ Check for wax accumulation, if indicated. ▸ Follow general consensus guidelines for IDD for vision assessment.

2. Dental

Considerations	Recommendations
Children: ▸ Missing or small teeth, malocclusion and other dental anomalies are common. Visual-motor integration difficulties interfere with dental hygiene	▸ Arrange early dental evaluation; recommend dental cleaning every four months by adolescence and advise family/support persons to provide daily supervision or assistance with brushing and flossing. ▸ Make orthodontic referral by 8 years, as needed.
Adults: ▸ Visual-motor integration difficulties interfere with dental hygiene may continue to be an issue	▸ Refer for dental cleaning every four months and recommend use of sealants. ▸ Supervise brushing and flossing.

3. Cardiovascular

Considerations	Recommendations
Children: ▸ Stenosis of medium to large-sized arteries is common; typically supravalvular aortic stenosis (SVAS) in ~45% and/or peripheral pulmonary stenosis (PPS) in ~37% ▸ Mitral valve prolapse (MVP), usually mild, may be present in ~15% ▸ Spontaneous improvement without surgical or catheter-based interventions of mild to moderate lesions may occur in childhood ▸ Hypertension (HTN) is common in adolescence but may present earlier	▸ Refer for cardiology evaluation in infancy and annually to age 5, then every 3-5 years (or more frequently if clinically warranted). ▸ Close and ongoing monitoring by a cardiologist should be determined by severity of findings. ▸ Measure BP annually in both arms and legs (to detect stenoses), preferably in a relaxing environment and using manual cuffs, to minimize anxiety-related response. ▸ If HTN is present, assess for arterial stenosis, renal disease, and hypercalcemia.
Adults: ▸ Supravalvular aortic stenosis is common. Pulmonary artery stenosis may have resolved ▸ Hypertension is common in adults and may be severe	▸ Arrange cardiac evaluation for mitral valve prolapse, aortic insufficiency, and arterial stenosis. ▸ Measure BP as in children. ▸ If HTN is present, assess for arterial stenosis, renal disease, and hypercalcemia.

4. Sleep

Considerations	Recommendations
Children and Adults: ▸ Sleep disorders, such as sleep anxiety, night waking, restless sleep and daytime sleepiness appear to be fairly common and improve with increased age ▸ Habitual snoring, obstructive sleep apnea (OSA), have been reported	▸ Conduct comprehensive sleep history and refer for sleep study as appropriate. Consider the possibility that sleep disturbance may have a negative impact on daytime behavior before diagnosis of behaviorally defined disorder is entertained. ▸ The use of melatonin to improve sleep patterns has received anecdotal support.

5. Gastrointestinal

Considerations	Recommendations
Children: ▸ Early failure to thrive, colic, gastroesophageal reflux disease (GERD), vomiting and, hypercalcemia, are common ▸ Constipation is variously due to hypercalcemia, to low muscle tone and to low-fiber diet; when chronic, diverticular disease often occurs and occasional bowel perforation has also occurred ▸ Sensory issues, notably texture aversion may affect feeding ▸ Increased frequency of celiac disease has been reported. ▸ Hernias (inguinal and umbilical) due to connective tissue abnormality, are relatively common and may occur at any age	▸ Perform clinical evaluation and history with attention to GERD and feeding difficulties. ▸ Recommend small, frequent, high-caloric density meals for infants. ▸ Consider feeding and oral motor therapy for child with significant feeding difficulty. ▸ Measure total serum calcium level every two years. ▸ Determine calcium/creatinine ratio in random spot urine annually. ▸ Manage constipation as per general population (e.g., institute regular, routine toilet regimen) and if hypercalcemic, reduce (but do not eliminate) dietary calcium and vitamin D (see No. 12 Endocrine section). ▸ Advise that chronic constipation can lead to diverticular problems.

5. Gastrointestinal (continued)

Considerations	Recommendations
	▸ Consider extending period of feeding with pureed food to circumvent sensory aversion to some food textures. ▸ Consultation with a feeding specialist (speech therapist) can help with transition to solid food. ▸ Screen once after 3 years of age or if patient is symptomatic. ▸ Check if present at regular/routine medical visits.
Adults: ▸ ~25% have GERD ▸ ~ 50% have constipation ▸ Hypercalcemia may recur periodically and can contribute to constipation and vomiting ▸ Sigmoid diverticulitis occurs with increased frequency and at younger age (<30). Diverticuli of bowel and bladder are also common. Diverticular disease may be associated with chronic abdominal pain. ▸ Celiac disease may be more common, as in children	▸ Follow usual guidelines for GERD and manage constipation as per general population; if hypercalcemic, reduce (but do not eliminate) dietary calcium and vitamin D. ▸ Determine calcium/creatinine ratio in random spot urine annually. ▸ Measure total serum calcium level every two years. ▸ Consider diverticulitis in the differential diagnosis of individuals with recurrent or chronic abdominal pain. ▸ Screen if symptomatic.

6. Genitourinary/Renal

Considerations	Recommendations
Children: ▸ Dysfunctional bladder leading to voiding problems and bladder diverticula, in addition to enuresis, are common. ▸ ~50% have enuresis ▸ ~30% have urinary tract infections ▸ Hypercalcemia is common	▸ Arrange renal and bladder ultrasounds in infancy and every 5 to 10 years or more often, depending on clinical findings. ▸ Refer to urologist regarding management of bladder function and UTIs. ▸ Consider referral of severe cases of hypercalcemia to nephrologist (infants may require therapy with pamidronate)
Adults: ▸ ~30% have recurrent UTIs ▸ The incidence of bladder diverticula increase with age ▸ Hypercalcemia	▸ Arrange renal and bladder ultrasounds every 10 years or sooner, if symptoms warrant. ▸ Perform annual BUN and creatinine testing. ▸ Consider referral of severe cases of hypercalcemia to nephrologist

7. Sexual Function

Considerations	Recommendations
Children: ▸ Adolescent males and females may be fertile ▸ Increased risk of sexual abuse and exploitation given their personality traits (See section No. 11 on Behavioral/Mental Health.)	▸ General consensus guidelines for IDD apply for adolescents. ▸ Genetic counseling referral may be appropriate.
Adults: ▸ Males and females may be fertile	▸ General consensus guidelines for IDD apply. ▸ Genetic counseling referral may be appropriate.

8. Musculoskeletal (MSK)

Considerations	Recommendations
Children: ▸ Hypotonia and lax joints may delay motor milestones and impair gross and fine motor coordination ▸ Hypertonia, hyper-reflexia, and joint contractures may develop over time ▸ Short stature and slow rate of growth. 70% remain below 3rd percentile for mid-parental height ▸ Adolescents may have awkward gait, scoliosis, kyphosis and lordosis	▸ Perform musculoskeletal evaluation with attention to joints and muscle tone. ▸ Arrange physical therapy consultation and appropriate exercise program. ▸ Plot growth on specific growth charts for Williams syndrome.
Adults: ▸ Hypertonia, hyper-reflexia, and joint contractures may develop over time. ▸ Adults may have awkward gait, scoliosis, kyphosis and lordosis	▸ Perform musculoskeletal evaluation with attention to joints and muscle tone. ▸ Arrange physial therapy consult and appropriate exercise program.

9. Neurology

Considerations	Recommendations
Children: ▸ Hypotonia, mild cerebellar and extrapyramidal signs are common.	▸ Refer to neurologist, if indicated. ▸ Consider occupational therapy/physical therapy referral for treatment of delays in activities of daily living and other functional skills. ▸ Consider evaluation for Chiari I malformation if individual complains of headache, dysphagia, dizziness or weakness.
Adults: ▸ There have been some reports of cerebrovascular accidents, possibly due to intracranial stenosis and/or hypertension.	▸ Investigation for and management of symptoms of stroke should follow guidelines for the general population.

10. Dermatology

Considerations	Recommendations
Children and Adults:	▸ Recommend diligent use of sunscreen to reduce vitamin D absorption and hypercalcemia.

11. Behavioral/Mental Health

Considerations	Recommendations
Children: ▸ Full-scale IQ can be misleading with most in mild to moderate range of impairment ▸ Typical cognitive profile includes: strengths in verbal short-term memory and language; unusual degree of interest and enjoyment of music; weakness in fine motor skills (e.g., buttoning, handwriting, drawing) contrast with strength in visual recognition (e.g., reading achievement)	▸ Arrange developmental and neuropsychological evaluations to assist in developing early intervention and special education programs, and vocational training programs. ▸ Make psychiatric referral, if appropriate. ▸ Consider occupational therapy, physical therapy and speech language therapy, as well as behavioral and pharmacological therapy for anxiety and other disorders.

11. Behavioral/Mental health (continued)

Considerations	Recommendations
▸ Common behavioral concerns include overfriendliness, excessive empathy, attention deficit, anxiety, and specific phobias	
Adults: ▸ May have increasing anxiety and social withdrawal	▸ Follow general consensus guidelines for IDD, keeping specific behavioral concerns in mind.

12. Endocrine

Considerations	Recommendations
Children: ▸ Hypercalcemia occurs in ~15% ▸ Central precocious puberty also occurs with greater frequency compared to the general population ▸ Subclinical hypothyroidism is particularly frequent	▸ Measure calcium/creatinine ratio in random spot urine annually. ▸ Measure total serum calcium level every two years. ▸ Do not prescribe multivitamins containing vitamin D. ▸ May require consultation with pediatric endocrinologist. ▸ Evaluate thyroid function annually.
Adults: ▸ Hypercalcemia may recur periodically ▸ Some individuals with WS may have an increased risk of osteopenia/osteoporosis at an earlier age. ▸ Diabetes mellitus is relatively common. ▸ Subclinical hypothyroidism is particularly frequent	▸ Measure calcium/creatinine ratio in random spot urine annually. ▸ Measure total serum calcium level every two years. ▸ If hypercalciuria found, repeat investigations and, if it persists, refer for renal ultrasound for nephrocalcinosis. ▸ Do not prescribe multivitamins containing vitamin D. ▸ Management can be difficult, given the tendency to hypercalcemia. While bisphosphonates have been used, there is concern about giving vitamin D and calcium supplements and if this approach is taken, close monitoring for hypercalcemia is important. ▸ Offer anticipatory guidance at earlier age to minimize risk of diabetes. ▸ Perform oral glucose tolerance test (OGTT) at age 30 and every 5 years thereafter. ▸ Repeat thyroid function tests annually.

13. Other

Considerations	Recommendations
Children and Adults:	▸ Arrange genetic assessment to review any genotype-phenotype correlations, as differing deletion sizes correlate with different degrees of IDD and cardiovascular problems. ▸ Small but increased risk of adverse outcomes with anesthesia reported. Anesthesia consult, including clearance from cardiologist and laboratory tests (e.g., Ca, BUN, T4, TSH), should be undertaken prior to procedures requiring anesthesia.

Health Care Guidelines

Published Williams Syndrome health care guidelines reviewed and compared:

- Committee on Genetics. American Academy of Pediatrics: Health care supervision for children with Williams syndrome. Pediatrics. 2001 May;107(5):1192-204. pediatrics.aappublications.org/content/107/5/1192.full. Accessed June 2025.
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- Pober BR. Medical progress: Williams-Beuren syndrome. N Engl J Med. 2010 Jan 21;362(3):239-52.
- Pober BR, Morris CA. Diagnosis and management of medical problems in adults with Williams-Beuren syndrome. Am J Med Genet C Semin Med Genet. 2007 Aug 15;145C(3):280-90.
- The Williams syndrome Guideline Development Group. Management of Williams syndrome: a clinical guideline. UK: Williams Syndrome Foundation; Dyscerne; 2012. https://williams-syndrome.org.uk/wp-content/uploads/2018/07/williams_syndrome_guidelines_pdf.pdf Accessed June 2025.
- Waxler JL, Levine K, Pober BR. Williams syndrome: a multidisciplinary approach to care. Pediatr Ann. 2009 Aug;38(8):456-63.
- Wilson G, Cooley WC. Williams syndrome. In: Preventive health care for children with genetic conditions: providing a primary care medical home. 2nd ed. Cambridge, UK ; New York: Cambridge University Press; 2006. p. 238-41.

Resources

Williams Syndrome websites that may be useful for families and support persons:

- The Williams Syndrome Association (WSA) (USA) www.williams-syndrome.org. Accessed June 2025.
- Williams Syndrome Foundation (UK) – Clinical guidelines https://williams-syndrome.org.uk/wp-content/uploads/2018/07/williams_syndrome_guidelines_pdf.pdf. Accessed June 2025.

Developed by Forster-Gibson C, Berg J, & Developmental Disabilities Primary Care Initiative Co-editors.

Expert Clinician Reviewers

Thanks to the following clinicians for their review and helpful suggestions.

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This tool was reviewed and adapted for U.S. use by physicians on the Toolkit's Advisory Committee.

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