

# Health Watch Table — Williams Syndrome

Forster-Gibson and Berg 2013

CONSIDERATIONS	RECOMMENDATIONS
<b>1. HEENT (Head, Eyes, Ears, Nose, Throat)</b>	
<p><i>Children:</i> ~60% have chronic otitis media</p> <p>Nearly all have characteristic auditory profile including hyperacusis [84-100%] and paradoxical affinity to music. Early onset phonophobia (fear of noises) also common</p> <p>Noise tolerance improves with age</p> <p>Strabismus and refractive errors such as hyperopia are common</p> <p>Amblyopia and reduced depth perception can cause difficulty in negotiating uneven surfaces and stairs</p> <p>Blocked tear ducts are common</p> <p>Hoarse, deep voice</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Arrange hearing assessment at 6-12 months and annual screen thereafter.</li> <li><input type="checkbox"/> Check for wax accumulation if indicated.</li> <li><input type="checkbox"/> Refer for tympanoplasty, if indicated.</li>   <li><input type="checkbox"/> Encourage caregivers to reduce exposure to loud noises (e.g., electric household appliances and machines, fireworks, thunder) and recommend earplugs in noisy environments.</li> <li><input type="checkbox"/> Use headphones with music in uncomfortable situations, e.g., school-bus ride or watching a noisy event.</li>   <li><input type="checkbox"/> Arrange ophthalmologic exam by 1 year and vision screening annually thereafter.</li> <li><input type="checkbox"/> See also #8, MUSCULOSKELETAL regarding mobility.</li> </ul>
<p><i>Adults:</i> Vulnerable auditory system with risk of hearing loss</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Refer for audiology examination at age 30 and every five years thereafter to assess sensorineural hearing loss.</li> <li><input type="checkbox"/> Check for wax accumulation, if indicated.</li> <li><input type="checkbox"/> Follow general consensus guidelines for DD for vision assessment.</li> </ul>
<b>2. DENTAL</b>	
<p><i>Children:</i> Missing or small teeth, malocclusion and other dental anomalies are common. Visual-motor integration difficulties interfere with dental hygiene</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Arrange early dental evaluation; recommend dental cleaning every four months by adolescence and advise caregiver to provide daily supervision or assistance with brushing and flossing.</li> <li><input type="checkbox"/> Make orthodontic referral by 8 years, as needed.</li> </ul>
<p><i>Adults:</i></p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Refer for dental cleaning every four months and recommend use of sealants.</li> <li><input type="checkbox"/> Supervise brushing and flossing.</li> </ul>
<b>3. CARDIOVASCULAR</b>	
<p><i>Children:</i> Stenosis of medium to large-sized arteries is common; typically supravalvular aortic stenosis (SVAS) in ~45% and/or peripheral pulmonary stenosis (PPS) in ~37%<sup>1</sup></p> <p>Mitral valve prolapse (MVP), usually mild, may be present in ~15%</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Refer for cardiology evaluation in infancy and annually to age 5, then every 3-5 years (or more frequently if clinically warranted).</li> <li><input type="checkbox"/> Close and ongoing monitoring by a cardiologist should be determined by severity of findings.</li> </ul>

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<p>Spontaneous improvement without surgical or catheter-based interventions of mild to moderate lesions may occur in childhood</p> <p>Hypertension (HTN) is common in adolescence but may present earlier</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> 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.</li> <li><input type="checkbox"/> If HTN is present, assess for arterial stenosis, renal disease, and hypercalcemia.</li> </ul>
<p><i>Adults:</i> SVAS is common. Pulmonary artery stenosis may have resolved</p> <p>HTN is common in adults and may be severe</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Arrange cardiac evaluation for mitral valve prolapse, aortic insufficiency, and arterial stenosis.</li> <li><input type="checkbox"/> Measure BP as in children.</li> <li><input type="checkbox"/> If HTN is present, assess for arterial stenosis, renal disease, and hypercalcemia.</li> </ul>
<b>4. RESPIRATORY</b>	
<p><i>Children and Adults:</i> Sleep disorders, such as sleep anxiety, night waking, restless sleep and daytime sleepiness appear to be fairly common and improve with increased age</p> <p>Habitual snoring, obstructive sleep apnea (OSA), have been reported</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Ascertain comprehensive sleep history and refer for sleep study as appropriate.</li> <li><input type="checkbox"/> Consider the possibility that sleep disturbance may have a negative impact on daytime behavior before diagnosis of behaviourally defined disorder is entertained.<sup>2</sup></li> <li><input type="checkbox"/> The use of Melatonin to improve sleep patterns has received anecdotal support.<sup>3</sup></li> </ul>
<b>5. GASTROINTESTINAL</b>	
<p><i>Children:</i> Early failure to thrive, colic, Gastroesophageal Reflux Disease (GERD), vomiting and , hypercalcemia, are common</p> <p>Constipation is variously due to hypercalcemia, to low muscle tone and to low-fibre diet; when chronic, diverticular disease often occurs and occasional bowel perforation has also occurred</p> <p>Sensory issues, notably texture aversion may affect feeding</p> <p>Increased frequency of celiac disease has been reported<sup>4</sup></p> <p>Hernias (inguinal and umbilical) due to connective tissue abnormality, are relatively common and may occur at any age</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Undertake clinical evaluation and history with attention to GERD and feeding difficulties.</li> <li><input type="checkbox"/> Recommend small, frequent, high caloric density meals for infants.</li> <li><input type="checkbox"/> Consider feeding and oral motor therapy for child with significant feeding difficulty.</li> <li><input type="checkbox"/> Measure total serum calcium level every two years.</li> <li><input type="checkbox"/> Ascertain calcium/creatinine ratio in random spot urine annually.</li> <li><input type="checkbox"/> 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 #12 ENDOCRINE).</li> <li><input type="checkbox"/> Advise parent that chronic constipation can lead to diverticular problems.</li> <li><input type="checkbox"/> Consider referral of severe cases to nephrologist (infants may require therapy with pamidronate).</li> <li><input type="checkbox"/> Consider extending period of feeding with pureed food to circumvent sensory aversion to some food textures.</li> <li><input type="checkbox"/> Consultation with a feeding specialist (speech therapist) can help with transition to solid food.</li> <li><input type="checkbox"/> Screen once after 3 years of age or if patient is symptomatic.</li> <li><input type="checkbox"/> Ascertain if present at regular/routine medical visits.</li> </ul>

CONSIDERATIONS	RECOMMENDATIONS
<p><i>Adults:</i> ~25% have GERD ~50% have constipation Hypercalcemia may recur periodically and can contribute to constipation and vomiting</p> <p>Sigmoid diverticulitis occurs with increased frequency and at younger age (&lt;30). Diverticuli of bowel and bladder are also common. Diverticular disease may be associated with chronic abdominal pain<sup>5,6</sup></p> <p>Celiac disease may be more common, as in children</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Follow usual guidelines for GERD and manage constipation as per general population; if hypercalcemic, reduce (but do not eliminate) dietary calcium and vitamin D.</li> <li><input type="checkbox"/> Ascertain calcium/creatinine ratio in random spot urine annually.</li> <li><input type="checkbox"/> Measure total serum calcium level every two years.</li> <li><input type="checkbox"/> Consider referral of severe cases of hypercalcemia to a nephrologist.</li> <li><input type="checkbox"/> Consider diverticulitis in the differential diagnosis of individuals with recurrent or chronic abdominal pain.<sup>7</sup></li> <li><input type="checkbox"/> Screen if symptomatic.</li> </ul>
<b>6. GENITOURINARY</b>	
<p><i>Children:</i> Dysfunctional bladder leading to voiding problems and bladder diverticula, in addition to enuresis, are common<sup>8</sup></p> <p>~50 % have enuresis ~30% have urinary tract infections (UTIs)</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Arrange renal and bladder ultrasounds in infancy and every five to ten years or more often, depending on clinical findings.</li> <li><input type="checkbox"/> Refer to urologist regarding management of bladder function and UTIs.</li> </ul>
<p><i>Adults:</i> ~30% have recurrent UTIs The incidence of bladder diverticula increase with age</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Arrange renal and bladder ultrasounds every 10 years or sooner if symptoms warrant.</li> <li><input type="checkbox"/> Undertake annual BUN and creatinine testing.</li> </ul>
<b>7. SEXUAL FUNCTION</b>	
<p><i>Children:</i> Adolescent males and females may be fertile</p> <p>Increased risk of sexual abuse and exploitation given their personality traits</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> General consensus guidelines for DD apply for adolescents.</li> <li><input type="checkbox"/> Genetic counseling referral may be appropriate.</li> </ul>
<p><i>Adults:</i> Males and females may be fertile</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> General consensus guidelines for DD apply.</li> <li><input type="checkbox"/> Genetic counseling referral may be appropriate.</li> </ul>
<b>8. MUSCULOSKELETAL (MSK)</b>	
<p><i>Children:</i> Hypotonia and lax joints may delay motor milestones and impair gross and fine motor coordination</p> <p>Hypertonia, hyperreflexia, and joint contractures may develop over time</p> <p>Short stature and slow rate of growth. 70% remain below 3<sup>rd</sup></p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Undertake musculoskeletal evaluation with attention to joints and muscle tone.</li> <li><input type="checkbox"/> Arrange physiotherapy consultation and appropriate exercise program.</li> <li><input type="checkbox"/> Plot growth on specific growth charts for Williams Syndrome.<sup>9</sup></li> </ul>

CONSIDERATIONS	RECOMMENDATIONS
<p>percentile for mid-parental height</p> <p>Adolescents may have awkward gait, scoliosis, kyphosis and lordosis</p>	
<p><i>Adults:</i> Hypertonia, hyper-reflexia, and joint contractures may develop over time. Adults may have awkward gait, scoliosis, kyphosis and lordosis</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Undertake musculoskeletal evaluation with attention to joints and muscle tone.</li> <li><input type="checkbox"/> Arrange physiotherapy consult and appropriate exercise program.</li> </ul>
<b>9. NEUROLOGICAL</b>	
<p><i>Children:</i> Hypotonia, mild cerebellar and extrapyramidal signs are common<sup>10</sup></p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Refer to neurologist, if indicated.</li> <li><input type="checkbox"/> Consider Occupational Therapy (OT) referral for sensory integration.</li> <li><input type="checkbox"/> Consider evaluation for Chiari I malformation if individual complains of headache, dysphagia, dizziness or weakness.</li> </ul>
<p><i>Adults:</i> There have been some reports of cerebrovascular accidents, possibly due to intracranial stenosis and/or hypertension<sup>11</sup></p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Investigation for and management of symptoms of stroke should follow guidelines for the general population.</li> </ul>
<b>10. DERMATOLOGICAL</b>	
<p><i>Children and Adults:</i></p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Recommend diligent use of sunscreen to reduce vitamin D absorption and hypercalcemia.</li> </ul>
<b>11. BEHAVIOURAL/MENTAL HEALTH</b>	
<p><i>Children:</i> Full-scale IQ can be misleading with most in mild to moderate range of impairment</p> <p>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)</p> <p>Common behavioural concerns include overfriendliness, excessive empathy, attention deficit, anxiety, and specific phobias</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Arrange developmental and neuropsychological evaluations to assist in developing early intervention and special education programs, and vocational training programs.</li> <li><input type="checkbox"/> Make psychiatric referral, if appropriate.</li> <li><input type="checkbox"/> Consider occupational therapy (including sensory integration), physiotherapy and speech language therapy, as well as behavioural and pharmacological therapy for anxiety and other disorders.</li> </ul>
<p><i>Adults:</i> May have increasing anxiety and social withdrawal</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Follow general consensus guidelines for DD, keeping specific behavioural concerns in mind.</li> </ul>
<b>12. ENDOCRINE</b>	
<p><i>Children:</i></p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Measure calcium/creatinine ratio in random spot urine annually.</li> </ul>

CONSIDERATIONS	RECOMMENDATIONS
<p>Hypercalcemia occurs in ~15%</p> <p>Central precocious puberty also occurs with greater frequency compared to the general population</p> <p>Subclinical hypothyroidism is particularly frequent</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Measure total serum calcium level every two years.</li> <li><input type="checkbox"/> Do not prescribe multivitamins containing vitamin D.</li> <li><input type="checkbox"/> May require consultation with pediatric endocrinologist<sup>12</sup>.</li> <li><input type="checkbox"/> Evaluate thyroid function annually.<sup>13-15</sup></li> </ul>
<p><i>Adults:</i> Hypercalcemia may recur periodically</p> <p>Some individuals with WS may have an increased risk of osteopenia/osteoporosis at an earlier age<sup>16</sup></p> <p>Diabetes mellitus is relatively common<sup>17</sup></p> <p>Subclinical hypothyroidism is particularly frequent</p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Measure calcium/creatinine ratio in random spot urine annually.</li> <li><input type="checkbox"/> Measure total serum calcium level every two years.</li> <li><input type="checkbox"/> If hypercalciuria found, repeat investigations and, if it persists, refer for renal ultrasound for nephrocalcinosis.</li> <li><input type="checkbox"/> Do not prescribe multivitamins containing vitamin D.</li> <li><input type="checkbox"/> 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.<sup>18</sup></li> <li><input type="checkbox"/> Offer anticipatory guidance at earlier age to minimize risk of diabetes.</li> <li><input type="checkbox"/> Undertake oral glucose tolerance test (OGTT) at age 30 and every five years thereafter.</li> <li><input type="checkbox"/> Repeat thyroid function tests annually.<sup>13-15</sup></li> </ul>
<b>13. OTHER</b>	
<p><i>Children and Adults:</i></p>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Arrange genetic assessment to review any genotype-phenotype correlations, as differing deletion sizes correlate with different degrees of DD and cardiovascular problems.</li> <li><input type="checkbox"/> 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.</li> </ul>

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#### **PUBLISHED HEALTH CARE GUIDELINES REVIEWED AND COMPARED**

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## RESOURCES

### **Williams Syndrome websites that may be useful for families and caregivers:**

Canadian Association for Williams Syndrome [www.caws-can.org](http://www.caws-can.org)

The Williams Syndrome Association (WSA) (USA) [www.williams-syndrome.org](http://www.williams-syndrome.org)

Williams Syndrome Foundation (UK) – Clinical guidelines

<http://wsf.bigorangesoftware.co.uk/vebo/index.php?idPage=102>

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### **Expert Clinician Reviewers**

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

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