Sleep-Disordered Breathing in Down Syndrome

Chitra Lal, MD, FCCP; David R. White, MD; Jane E. Joseph, PhD; Karen van Bakergem, LMSW; and Angela LaRosa, MD

OSA is associated with significant adverse outcomes with far-reaching health-care implications. OSA is much more common and severe in patients with Down syndrome (DS) than in the general population, yet there is a striking lack of literature in this area. In this review article, we have summarized the current state of knowledge and presented the available data on OSA in DS. The higher prevalence and severity of OSA in patients with DS may be related to unique upper airway anatomic features as well as increased risk for obesity, hypothyroidism, gastroesophageal reflux disease, and generalized hypotonia. Although many of the manifestations of OSA in patients with DS are similar to those seen in the general population, the relative morbidity is significantly higher. For individuals with DS who already face cognitive challenges, the added impact of OSA on cognitive function may hinder their ability to function independently and reach their full potential. Screening and evaluation for OSA should be done in children and adults with DS. Treatment of OSA in DS involves the use of CPAP, upper airway surgery, and dental appliances, along with weight-reduction strategies, nasal steroids, and oral leukotriene modifiers as adjunctive treatments. The treatment plan should be individualized for each patient with DS, taking into account age, comorbid conditions, and barriers to treatment adherence. Future research should aim to better characterize OSA, further evaluate neurocognitive outcomes, and evaluate the efficacy of treatments in patients with DS.

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ABBREVIATIONS: AD = Alzheimer disease; AHI = apnea-hypopnea index; AT = adenotonsillectomy; BPAP = bilevel positive airway pressure; CSA = central sleep apnea; DS = Down syndrome; EF = executive function; PAP = positive airway pressure; PSG = polysomnogram; SDB = sleep-disordered breathing

Sleep-disordered breathing (SDB) refers to a group of disorders characterized by abnormalities of respiration and/or ventilation during sleep. It encompasses central sleep apnea (CSA) syndromes, OSA disorders, sleep-related hypoventilation disorders, and sleep-related hypoxemia disorder. OSA is the commonest of these disorders and has been associated with significant adverse impacts on health, such as stroke, coronary artery disease, hypertension, arrhythmias, and excessive daytime sleepiness resulting in an increased risk of motor vehicle accidents. It is increasingly being recognized that OSA is associated with memory impairment and deterioration in other aspects of cognitive functioning. Down syndrome (DS), defined by an extra copy of chromosome 21, is the commonest genetic disorder, occurring in one out of...
Individuals with DS are at an increased risk of heart defects, gastroesophageal reflux, celiac disease, hypothyroidism, hearing and vision problems, leukemia, and Alzheimer disease (AD), as well as intellectual disability of varying degrees.

The prevalence of OSA in children with DS is 30% to 50% and increases to >90% in adults with DS, as compared with the 2% to 4% prevalence seen in the general population. In addition, OSA is usually more severe in patients with DS, with significant hypoxemia as compared with individuals without DS. Several manifestations of OSA, such as cognitive impairment and cardiovascular disease, are common in individuals with DS, which may obscure the diagnosis of OSA in patients with DS. Thus, clinicians should maintain a high index of suspicion for OSA in patients with DS.

Adults with DS also have a very high risk of developing AD. The added insult of OSA in this highly vulnerable population may exacerbate cognitive difficulties and lead to a greater predisposition to neurodegeneration.

Patients with DS now lead longer and more productive lives. Early recognition and aggressive treatment of OSA in patients with DS can further help to improve quality of life. Despite the significant resources that have been allocated to the study of OSA in the general population, few studies have evaluated the impact of OSA on patients with DS, and available studies are limited by small sample size.

Although not a systematic review, the purpose of this article is to provide a comprehensive review of this topic with a focus on recent developments in the field. Keywords such as “Down syndrome sleep disordered breathing” and “obstructive sleep apnea,” and specific topics such as “cognitive functioning,” “Alzheimer disease,” and “executive functioning,” and databases including PubMed, CINAHL, PsycINFO, and MEDLINE were used in searches, which were limited to English language. In addition to computer searches, the ancestry approach was used. An important goal of this article is to identify published information specific to OSA in individuals with DS; however, given the limited amount of research on OSA in those with DS, evidence regarding OSA in the general population is discussed to make recommendations for further research. Salient studies specifically addressing OSA in patients with DS are listed in Table 1.

OSA and DS

Patients with DS are predisposed to upper airway obstruction due to multiple factors (Fig 1). Midface and maxillary hypoplasia have been demonstrated radiologically, resulting in smaller bony dimensions of the airway. Although absolute tongue size is normal, relative macroglossia results because of the smaller bony framework of the small maxilla and mandible. Donnelly et al demonstrated on cine MRI that this relative macroglossia and hypotonia resulted in airway obstruction caused by glossoptosis and hypopharyngeal collapse (also referred to as pharyngomalacia) in nearly two-thirds of children with DS and persistent OSA after adenotonsillectomy (AT). A follow-up study revealed that lingual tonsillar hypertrophy is >10 times more common in children with DS compared with other children with OSA, further contributing to obstruction at the oropharyngeal level. Hypotonia may also cause obstruction at the supraglottic level, with laryngomalacia being demonstrated in nearly 50% of children with DS and upper airway obstructive symptoms. Subglottic and tracheal stenosis are more common in patients with DS than other populations. The association between obesity and OSA in individuals with DS has been demonstrated in several studies.

In a Dutch sample, children with DS were almost twice as likely to be overweight and obese as compared with a control group (25% of boys and 32% of girls with DS were overweight, and 4% of boys and 5% of girls were obese). Women and men with DS were more likely to be overweight, with women more likely to be obese when compared with matched control subjects. It is postulated that fat deposits in the lateral wall of the pharynx reduce the caliber of the upper airway and increase airway collapsibility. Central obesity, defined as increased intraabdominal and subcutaneous fat as measured by waist circumference, has been associated with OSA. Individuals with DS have a higher incidence of central adiposity; however, the actual prevalence relative to the typical population needs further study. In another study, the apnea-hypopnea index (AHI) was found to be highly correlated with the degree of obesity in adults with DS. Obesity is a risk factor for OSA and is more prevalent in patients with DS; thus, it has been suggested that OSA severity in those with DS may be correlated with obesity. Therefore, obesity as a risk factor for OSA should be discussed with all patients with DS.

Higher rates of gastroesophageal reflux disease are seen in patients with DS, which can lead to inflammation and obstruction of the upper airway, thus increasing risk of developing OSA. An increased OSA prevalence of 25% to 35% has been reported in the general population in patients with hypothyroidism. This association
<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Type</th>
<th>N</th>
<th>Population</th>
<th>Outcome/Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcus et al/1991</td>
<td>Prospective</td>
<td>53</td>
<td>Pediatric</td>
<td>Children with DS frequently have OSA, which may contribute to pulmonary HTN.</td>
</tr>
<tr>
<td>Trois et al/2009</td>
<td>Prospective</td>
<td>16</td>
<td>Adult</td>
<td>Abnormal PSG is seen in 94% of subjects with DS.</td>
</tr>
<tr>
<td>Uong et al/2001</td>
<td>Prospective</td>
<td>11</td>
<td>Pediatric</td>
<td>Children with DS without OSA have a reduced UA size caused by soft tissue crowding within a smaller midface.</td>
</tr>
<tr>
<td>Donnelly et al/2004</td>
<td>Prospective</td>
<td>27</td>
<td>Pediatric</td>
<td>Persistent OSA in children with DS after AT is due to macroGLOSSIA, glossophtosis, recurrent enlargement of the adenoid tonsils, and enlarged lingual tonsils.</td>
</tr>
<tr>
<td>Bertrand et al/2003</td>
<td>Retrospective</td>
<td>24</td>
<td>Pediatric</td>
<td>Patients with DS and respiratory symptoms have a high incidence of airway anomalies.</td>
</tr>
<tr>
<td>Jacobs et al/1996</td>
<td>Retrospective</td>
<td>71</td>
<td>Pediatric</td>
<td>Residual symptoms of airway obstruction are common after surgery.</td>
</tr>
<tr>
<td>Dyken et al/2003</td>
<td>Prospective</td>
<td>19</td>
<td>Pediatric</td>
<td>OSA was found in 79% of subjects with DS.</td>
</tr>
<tr>
<td>Shires et al/2010</td>
<td>Retrospective</td>
<td>63</td>
<td>Pediatric</td>
<td>BMI has a statistically significant association with OSA in patients with DS.</td>
</tr>
<tr>
<td>Chen et al/2013</td>
<td>Prospective</td>
<td>29</td>
<td>Pediatric/adult</td>
<td>Individuals with high ratings of sleep disruption showed greater difficulties with EF.</td>
</tr>
<tr>
<td>Breslin et al/2014</td>
<td>Prospective</td>
<td>38</td>
<td>Pediatric</td>
<td>Verbal IQ score was lower in patients with DS and comorbid OSA than in those without OSA, along with poorer performance on cognitive flexibility task.</td>
</tr>
<tr>
<td>Andreou et al/2002</td>
<td>Prospective</td>
<td>12</td>
<td>Adults</td>
<td>Individuals with DS and SDB had very low Mini-Mental and RPM scores.</td>
</tr>
<tr>
<td>Jheeta et al/2013</td>
<td>Retrospective</td>
<td>44</td>
<td>Pediatric</td>
<td>Oximetry has poor sensitivity for OSA in children with DS.</td>
</tr>
<tr>
<td>Ng et al/2006</td>
<td>Prospective</td>
<td>44*</td>
<td>Pediatric</td>
<td>59% of children with DS were found to have OSA. Nearly 40% of children with DS and OSA did not have habitual snoring.</td>
</tr>
<tr>
<td>Shott et al/2006</td>
<td>Prospective</td>
<td>65</td>
<td>Pediatric</td>
<td>57% of the children with DS showed evidence of OSA; 69% of parents reported no sleep problems in their children.</td>
</tr>
<tr>
<td>Austeng et al/2014</td>
<td>Prospective</td>
<td>29</td>
<td>Pediatric</td>
<td>2/3 of 8-y-old children with DS had moderate to severe OSA.</td>
</tr>
<tr>
<td>Shete et al/2010</td>
<td>Retrospective</td>
<td>20b</td>
<td>Pediatric</td>
<td>AT in children with DS improves some parameters of OSA; however, not as markedly as in children without DS.</td>
</tr>
<tr>
<td>Goldstein et al/1998</td>
<td>Retrospective</td>
<td>151c</td>
<td>Pediatric</td>
<td>Postoperative respiratory complications are higher in children with DS undergoing AT.</td>
</tr>
<tr>
<td>de Moura et al/2008</td>
<td>Prospective</td>
<td>24</td>
<td>Pediatric</td>
<td>RME resulted in a reduction in hearing loss, ENT infections, and symptoms of UA obstruction.</td>
</tr>
<tr>
<td>Resta et al/2003</td>
<td>Prospective</td>
<td>6</td>
<td>Adult</td>
<td>Nocturnal respiratory pattern of adults with DS depends on several pathogenetic factors such as age and BMI.</td>
</tr>
</tbody>
</table>

AT = adenotonsillectomy; DS = Down syndrome; EF = executive functioning; ENT = ear, nose, throat; HTN = hypertension; PSG = polysomnogram; RME = rapid maxillary expansion; RPM = Raven Progressive Matrices; SDB = sleep-disordered breathing; UA = upper airway.

a Twenty-two patients with DS, 22 matched control subjects.
b Eleven patients with DS, 9 children without DS.
c Eighty-seven children with DS; 64 matched for age, sex, year of surgery.

may be mediated through narrowing of the pharynx due to soft tissue infiltration by mucopolysaccharides and proteins.\textsuperscript{41} Altered regulatory control of pharyngeal dilator muscles due to neuropathy may also be involved.\textsuperscript{41} Appropriate treatment of hypothyroidism can improve and occasionally cure OSA in studies in the general population.\textsuperscript{39} Thyroid disease occurs more often in patients with DS (4%-18%), with the risk...
increasing with age. Thus, in all patients with DS, thyroid studies are recommended every 6 months until 1 year of age and then annually thereafter. Normal thyroid function or appropriate thyroid management should be verified in individuals with DS presenting with OSA.

Infants with DS have been shown to have a higher prevalence of pulmonary hypertension. Alveolar capillary dysplasia and increased pulmonary vascular resistance have been reported in infants with DS. Pulmonary hypertension and cor pulmonale have also been associated with OSA in patients with DS. It has further been shown that relief of the upper airway obstruction could reverse the pulmonary hypertension in children with DS. Thus, cardiovascular consequences of OSA are likely to be even more dangerous in patients with DS as compared with patients without DS.

Common Symptoms of OSA in Children and Adults With DS

The manifestations and long-term sequelae of OSA in patients with DS are listed in Tables 2 and 3. Although many of the cardinal symptoms of OSA, such as snoring, fatigue, and restless sleep, are common to both children and adults with DS and OSA, children may also present with failure to thrive, hyperactivity, behavioral disruptions, and poor school performance, whereas adults may present with mood dysregulation and depression.

Cognitive Impairment, DS, and OSA: A Triple Threat

Studies have found that decreased slow-wave sleep is seen in children and adolescents with DS who have OSA and that OSA might explain some of the variability associated with verbal IQ, memory, and executive
function (EF) in a DS community cohort.\textsuperscript{18,53,54} Another study found that among children with DS, those with comorbid OSA performed worse on verbal IQ and cognitive flexibility tasks than those without OSA.\textsuperscript{19} EF, which is regulated in the prefrontal cortex, helps to integrate, plan, and organize information to complete a goal-directed task. The prefrontal cortex also regulates working memory, attention, processing speed, arousal, and inhibition. It is hypothesized that the intermittent episodic hypoxemia of OSA and decreased slow-wave sleep can disrupt prefrontal cortical function and thus impact EF. A study of 29 adolescents and young adults with DS found that parents’ rating of OSA and sleep disruption was an independent predictor of executive dysfunction in these subjects.\textsuperscript{18} However, this study was limited by the fact that OSA was not confirmed by polysomnogram (PSG).

Patients with DS are particularly predisposed to developing early-onset AD after the age of 35 years.\textsuperscript{55} The prevalence of AD in DS increases to 75% by the age of 65 years.\textsuperscript{11} Oxidative stress has been implicated in the pathogenesis of premature AD in patients with DS.\textsuperscript{26} Oxidative stress is also a major player in OSA, given the intermittent, episodic hypoxemia and hypoxia-reperfusion injury associated with it.\textsuperscript{29} One could speculate that the added insult of OSA may accelerate the cognitive decline in patients with DS.\textsuperscript{18} This is an area that needs to be explored further in research studies.

Another study found that a higher number of apneas in patients with DS was associated with greater deficiencies in visuoperceptual skills, including orientation, of the right brain hemisphere.\textsuperscript{20} The presence of snoring in children with DS has been associated with a higher prevalence of disruptive school behavior as compared with nonsnoring children with DS.\textsuperscript{50} OSA is a common comorbid condition in adolescents and young adults with DS and depression and may cause further functional decline in patients with DS.\textsuperscript{52} Attention deficit hyperactivity disorder, which is more common in the DS population than in the general population (9% vs 3% to 7%), has been associated with OSA.\textsuperscript{58,59} The presence of OSA in individuals with DS can result in poorer school performance, limited social interactions, and impairment in activities of daily living, thus significantly decreasing quality of life.

### Diagnosis of OSA in DS

Clinical history is helpful in the diagnosis of OSA in patients with DS. However, absence of symptoms does

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### TABLE 2] Common Symptoms and Sequelae of OSA in Adults With DS

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Neurocognitive Manifestations</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease</td>
<td>Excessive daytime sleepiness</td>
<td>Snoring</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>Executive dysfunction</td>
<td>Nocturia</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Impaired attention</td>
<td>Restless sleep</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>Decreased memory</td>
<td>Early morning headache</td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
<td>Mood dysregulation/depressive symptoms</td>
<td>Fatigue</td>
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<td></td>
<td></td>
<td>Gastroesophageal reflux</td>
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<tr>
<td></td>
<td></td>
<td>Polycythemia</td>
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<td></td>
<td></td>
<td>Hypercapnia</td>
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</tbody>
</table>

See Table 1 legend for expansion of abbreviation.

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### TABLE 3] Common Symptoms and Sequelae of OSA in Children with DS

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Neurocognitive Manifestations</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary hypertension</td>
<td>Poor school performance</td>
<td>Failure to thrive</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Inattention</td>
<td>Snoring</td>
</tr>
<tr>
<td></td>
<td>Executive dysfunction</td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td>Decreased memory</td>
<td>Restless sleep</td>
</tr>
<tr>
<td></td>
<td>Behavioral disruptions</td>
<td>Gastroesophageal reflux</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polycythemia</td>
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<tr>
<td></td>
<td></td>
<td>Hypercapnia</td>
</tr>
</tbody>
</table>

See Table 1 legend for expansion of abbreviation.
not obviate the need for a PSG, which is the diagnostic test of choice. Screening oximetry has poor sensitivity for diagnosing OSA in subjects with DS and should not be used as a stand-alone test for diagnosing OSA. Unattended portable monitoring for the diagnosis of OSA has not been evaluated specifically in patients with DS. Thus, we would not recommend using this as a diagnostic modality in patients with DS.

One study found that 97% of children with DS who snored had OSA. This study included 33 children with a mean age of 4.9 years, and none had previously undergone AT. On the other hand, not all children with DS who have OSA are habitual snorers. Given the unique medical and developmental needs of children with DS, specific health supervision guidelines for this patient population have been published. These recommend that at least once during the first 6 months of life, providers should discuss OSA symptoms with parents, including heavy breathing, snoring, uncommon sleep positions, frequent nighttime awakenings, daytime sleepiness, apneic pauses, and behavior problems. If any of these symptoms are endorsed, referral to a physician with expertise in pediatric sleep disorders is recommended. This history should be reviewed at every well-child visit. Parental reports of OSA symptoms and results of PSG do not always correlate; hence, it is recommended that all children with DS should have a sleep study by 4 years of age regardless of symptoms. It is our practice at the Medical University of South Carolina’s Down Syndrome Center to repeat a PSG at 8 years of age in children with DS given the high risk, lack of symptom correlation, and potential long-term sequelae of untreated OSA; however, published guidelines for OSA screening in older children are not available. A recently published article looking specifically at OSA in 8-year-old children with DS found a significantly higher prevalence of moderate to severe OSA when compared with the general population. Additional PSG testing is recommended outside of this age range if symptoms of OSA are present.

*Treatment of OSA in DS

**Nonsurgical Treatments:** Habitual snoring has been shown to be associated with smoking, environmental pollution, atopy, and viral infections. Thus, simple measures like avoidance of noxious fumes and treatment of nasal allergies with antihistamines and intranasal steroids such as budesonide can decrease the severity of snoring. Oral leukotriene modifiers such as montelukast can improve milder forms of SDB. In a case series, oral care and treatment of xerostomia in three children with OSA and DS caused resolution of the snoring and apneas. The exact mechanism of the association between xerostomia and OSA is unknown.

Weight loss by exercise and dietary programs may help decrease OSA severity in individuals with DS. In patients with DS and OSA, thyroid function should be checked and hypothyroidism should be treated.

Positive airway pressure (PAP) remains the cornerstone of treatment of OSA in adults, and this is also true for adults with DS. PAP can be applied as CPAP or bilevel PAP (BPAP). Patients with DS represent a unique and challenging group, however, as far as PAP compliance is concerned. At least one study has shown that of the nine adults with DS who were prescribed CPAP, five had excellent compliance. Improvements in daytime functioning and excessive daytime sleepiness were seen in CPAP-compliant patients in this study. Cognitive behavioral therapy may be used to improve PAP compliance in patients with DS, although large studies in this regard are lacking. Other measures that can be taken to improve PAP adherence include more “hands-on” education for patients and caregivers, and clinic and telephone follow-up.

Dental appliances are useful in treating mild to moderate OSA in the general population. However, they have not been studied specifically in patients with DS. Dental appliances can be tongue-retaining devices, which retain the tongue in a forward position using a suction cup or mandibular advancing devices. Although tongue-retaining devices may be somewhat difficult for patients with DS to tolerate, mandibular advancing devices may be a viable treatment option for mild to moderate OSA in patients with DS.

The efficacy of dental appliances for treatment of OSA is considerably less than that of CPAP, with only a 50% to 60% reduction in the respiratory disturbance index, but patient compliance is better than with CPAP. Given the upper airway obstruction at multiple levels in patients with DS, it is possible that dental appliances maybe less efficacious in these patients than in the general population. Dental appliances should be custom made for each individual patient and may not be appropriate in young children with immature dentition or ongoing facial growth.

**Surgical Treatments:** The first-line surgical treatment of OSA in children is AT. In children with DS, AT is effective in reducing obstructive AHI but usually does not normalize it. Sleep-related hypoxia and hypercapnia resolve even less frequently. In fact, no postoperative change in arterial oxygen saturation...
nadir was noted by Shete et al\textsuperscript{25} in 11 children with DS who underwent AT. Goldstein et al\textsuperscript{26} noted a respiratory complication rate five times higher than control subjects in children with DS undergoing AT, along with a prolonged recovery of adequate oral intake. Mortality after AT is reported at between one in 10,000 and one in 30,000 in the general population, with most episodes related to respiratory events.\textsuperscript{71} Mortality figures specific to patients with DS undergoing tonsillectomy have not been reported. DS as a separate risk factor is difficult to separate from other risk factors, such as obesity and severe sleep apnea, which have been shown to increase posttonsillectomy complication rates. In any case, a thorough airway evaluation and a sleep study should be performed before AT in patients with DS.\textsuperscript{72} Since comorbidities, craniofacial abnormalities, and moderate to severe OSA are all considered indications for postoperative hospital observation in children undergoing AT, children with DS should be observed in the hospital (intensive care unit if obesity and/or severe OSA are present) after AT in contrast to their peers who are generally managed as outpatients.\textsuperscript{73} Because of the high rate of persistent OSA in children with DS, a postoperative sleep study is indicated 2 to 3 months after AT.

Children who have persistent OSA after AT should undergo additional airway evaluation, since airway abnormalities in this population are complex and may include multiple levels of obstruction. Surgical management is typically driven by outcomes from studies such as sleep endoscopy and cine MRI, both of which may be used to evaluate the entire airway during a state of induced sleep, to identify sites of dynamic airway collapse.

Lateral pharyngoplasty (tonsillar pillar plication) has been shown to be no better than AT alone.\textsuperscript{70} Uvulopalatopharyngoplasty was shown to reduce AHI from 27 to 9 in five children with DS, but it is not clear whether any patients had resolution of OSA.\textsuperscript{74} Combined genioglossus advancement and radiofrequency ablation of the tongue base was demonstrated to reduce AHI below 5 in 12 of 19 patients, with concomitant improvement of hypoxia and hypercapnia.\textsuperscript{75} Lingual tonsillar hypertrophy is more common in children with DS who have persistent OSA after AT than control subjects with the same history, but to date there is no study comparing preoperative sleep studies to postoperative results after lingual tonsillectomy.\textsuperscript{30,76}

In patients with nasal obstruction, inferior turbinate reduction and revision adenoidectomy may be

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Figure 2 – Treatments for sleep-disordered breathing in children and adults with Down syndrome.

* These approaches may not be appropriate in young children with immature dentition or ongoing facial growth.
+ When tonsillar hypertrophy is present
indicated. In adults and older children, septoplasty may be indicated as well. Maxillary (palatal) expansion may be indicated, especially in patients with severe maxillary hypoplasia. Supraglottoplasty, a procedure whereby redundant collapsing tissue is removed endoscopically from the supraglottis, may be indicated to address severe laryngomalacia. Subglottic and tracheal stenosis may be amenable to reconstructive procedures. Mandibular distraction osteogenesis is a procedure used to lengthen the mandible, which may be useful in patients with micrognathia. The resultant forward movement of the tongue base widens the oropharyngeal airway. There is, however, no substantial literature examining the outcomes of these procedures specifically in patients with DS and OSA. In instances of persistent severe OSA not amenable to other treatment, tracheostomy may be necessary. A treatment algorithm for children and adults with DS is outlined in Figure 2.

CSA in DS
Congenital central hypoventilation syndrome, characterized by the presence of PHOX2B gene, has been associated with DS and Hirschsprung disease. This rare disorder mandates lifelong mechanical ventilation, as patients do not breathe during sleep, despite progressive hypoxia and hypercapnia. Less catastrophic CSA can also be seen in patients with DS. CSA has been reported to constitute 10.8% (in patients with no upper airway abnormalities) to 89.4% of all respiratory events during sleep in patients with DS. CSA is treated with PAP, such as CPAP, BPAP BPAP with a backup rate (BPAP ST mode), and adaptive servventilation. As patients with DS age, the preponderance of respiratory events may become obstructive in nature because of increasing narrowing of the upper airway.

Conclusions
The literature to date suggests that OSA prevalence and long-term sequelae are greater in those with DS than in the general population; however, further research is needed to better define specific risk factors, outcomes, and evidence-based treatment approaches for this potentially modifiable condition.

The full impact of OSA on cognitive functioning in patients with DS needs to be further explored via standardized measures of cognition. Improved identification and treatment of OSA in patients with DS may have long-term effects that could decrease the risk of developing AD. Given the unique pathophysiology seen in those with DS, large studies evaluating the efficacy of current treatment modalities for OSA and new treatment modalities should be undertaken. Prompt diagnosis and treatment of OSA may help to improve the overall quality of life and longevity in patients with DS.

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