Recent advances in paediatric sleep disordered breathing

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Shareable abstract (@ERSpublications)
This review of paediatric sleep disordered breathing includes updates on brain and cardiovascular changes, pulse oximetry and home sleep studies for diagnosis, and effectiveness of intracapsular tonsillectomy, weight loss and hypoglossal nerve stimulation. https://bit.ly/3p2SshU

Cite this article as: Garde AJB, Gibson NA, Samuels MP, *et al*. Recent advances in paediatric sleep disordered breathing. *Breathe* 2022; 18: 220151 [DOI: 10.1183/20734735.0151-2022].

Received: 30 May 2022
Accepted: 2 Aug 2022

Abstract

This article reviews the latest evidence pertaining to childhood sleep disordered breathing (SDB), which is associated with negative neurobehavioural, cardiovascular and growth outcomes. Polysomnography is the accepted gold standard for diagnosing SDB but is expensive and limited to specialist centres. Simpler tests such as cardiorespiratory polygraphy and pulse oximetry are probably sufficient for diagnosing obstructive sleep apnoea (OSA) in typically developing children, and new data-processing techniques may improve their accuracy. Adenotonsillectomy is the first-line treatment for OSA, with recent evidence showing that intracapsular tonsillectomy results in lower rates of adverse events than traditional techniques. Anti-inflammatory medication and positive airway pressure respiratory support are not always suitable or successful, although weight loss and hypoglossal nerve stimulation may help in select comorbid conditions.

Educational aims

- To understand the clinical impact of childhood sleep disordered breathing (SDB).
- To understand that, while sleep laboratory polysomnography has been the gold standard for diagnosis of SDB, other diagnostic techniques exist with their own benefits and limitations.
- To recognise that adenotonsillectomy and positive pressure respiratory support are the mainstays of treating childhood SDB, but different approaches may be indicated in certain patient groups.

Introduction

Sleep disordered breathing (SDB) is an umbrella term for disturbed respiratory pattern and function during sleep, including apnoea, hypopnoea and/or hypoventilation. Traditionally, sleep apnoea has been subdivided by cause into obstructive *versus* central sleep apnoea. However, it may be more helpful to think of obstructive *versus* non-obstructive SDB, the latter including patients with central SDB due to reduced respiratory drive and those with more multifactorial non-obstructive SDB. The most common form of paediatric SDB in typically developing children is obstructive sleep apnoea (OSA), characterised by upper airway obstruction resulting in snoring, apnoea and hypopnoea. Children with complex conditions may have more challenging, multifactorial SDB due to factors such as neuromuscular weakness, impaired gas exchange, altered respiratory drive, and craniofacial and skeletal abnormalities. There is often an element of co-existent OSA for these children. Prevalence of SDB in typically developing children is estimated at 3–4% [1]. Prevalence of SDB is much higher in children with pre-disposing conditions such as Down syndrome (DS), where it has been estimated at 75% [2]. The majority of recent publications on paediatric SDB focus on OSA.

SDB is associated with negative health outcomes, including behavioural, cognitive and emotional difficulties and enuresis. In children with complex conditions, it is associated with poor growth and

cardiovascular morbidity [3]. In this article, we review new evidence on clinical effects of SDB, screening and diagnostic tests, developments in treatment approaches, and central SDB and specific conditions needing an adapted approach.

Consequences of sleep disordered breathing

SDB disrupts both sleep quality and cardiorespiratory physiology. It is associated with a range of negative outcomes as mentioned. However, much of the research on the effects of SDB in children has been of low quality and shown inconsistent results. Recent research has focused on quantifying the deleterious effects attributable to SDB, elucidating the causative mechanisms, and determining the modifiability of these effects through treatment.

Neurobehavioural effects and brain imaging

SDB in children is associated with a range of behavioural, cognitive, academic and emotional difficulties [3]. It is unclear whether these effects are purely due to sleep disruption, or whether other elements of SDB, such as intermittent hypoxia, may contribute.

Magnetic resonance imaging (MRI) techniques have identified changes to brain structure and function in children with OSA that may be physical correlates of these difficulties. Lower cortical thickness and lower tissue volume is seen in certain areas of both grey and white matter in children with OSA [4]. Diffusion tensor imaging (DTI) MRI shows lower white matter integrity in children with severe *versus* mild OSA [5]. Functional MRI shows differences in activity in certain brain regions in children with OSA compared to healthy controls [6]. The changes noted on MRI correlate with worse scores on neurocognitive testing, suggesting that OSA might be the underlying cause of these neurobehavioural changes.

It is unclear whether the neurobehavioural effects described in childhood OSA are reversible with treatment. Existing studies into the benefits of treatment have mostly had inadequate control groups. Two recent studies suggest that neurobehavioural effects may be less modifiable than hoped. Waters *et al*. [7] randomised children with mild OSA to early adenotonsillectomy (AT) (within 2 months) or delayed AT (after a cognitive assessment at 12 months). Both groups showed improvements in cognitive scores at 12 months; there was no treatment-attributable improvement in the AT group *versus* the delayed AT group. Similarly, Lushington *et al*. [8] studied children with OSA treated with AT. Despite improvements in sleep, quality of life and polysomnography (PSG) indices at 6 months and 4 years after treatment, there were no significant improvements in behaviour *versus* controls.

Cardiovascular effects

The cardiovascular effects of childhood SDB have been mainly studied in OSA, because in adults, OSA is associated with hypertension, cardiac disease and stroke. In children, severe OSA can contribute to pulmonary hypertension and even the development of cor pulmonale, usually in the context of significant and complex comorbidities such as DS or Prader–Willi syndrome (PWS) [3]. Typically developing children rarely demonstrate clinically significant cardiovascular morbidity. However, there is growing evidence of an association between childhood OSA and adverse subclinical changes to cardiovascular parameters. Treating OSA in childhood could represent an opportunity to modify long-term cardiovascular risk.

Blood pressure

Childhood OSA is associated with adverse changes to blood pressure (BP) profile, and these changes may persist into adulthood. Brooks *et al*. [9] found that children with moderate-severe OSA had higher rates of systolic hypertension than healthy controls. Systolic BP (SBP) and diastolic BP correlate with apnoea–hypopnoea index (AHI) [10]. BP is normally lower during sleep than wake states, known as "night-time dipping". Loss of this normal night-time BP reduction is a precursor to the development of overt hypertension and is a risk factor for adverse cardiovascular outcomes. There is now good evidence of reduced night-time dipping in childhood OSA [9].

A recent 10-year follow-up study showed that childhood OSA has long-term effects on BP parameters that last into adulthood, independent of whether the OSA itself persists. In comparison to healthy controls, those with moderate-severe OSA 10 years earlier (obstructive AHI (OAHI) of $\geqslant 5$ events·h^{-1} on PSG) had higher night-time SBP, reduced nocturnal SBP dipping, higher mean arterial pressure (MAP), and reduced night-time MAP dipping at follow-up (age 16–25 years) [11].

Cardiac effects

The heart may also be affected by childhood OSA, with both ventricular dysfunction and remodelling seen. These changes are typically subclinical but could provide some of the mechanism for cardiovascular morbidity seen in later life. Recent evidence suggests that diastolic dysfunction may normalise after AT, but structural changes persist despite treatment [12]. Further research is required to understand whether diagnosing and treating OSA early in life reduces the risk of permanent cardiac remodelling.

Vascular effects

The effect of OSA on vascular function is another area of current research. While Smith *et al*. [13] found no overt structural or functional changes to the carotid arteries in childhood OSA, there is evidence that endothelial function may be affected. Improvements in endothelial function caused by weight loss were less in obese children with residual OSA than in those without [14].

Underlying mechanisms for cardiovascular changes

While there is good evidence of cardiovascular changes in childhood OSA, the mechanisms underlying these changes remain unclear. There is some evidence to suggest that OSA is associated with a pro-inflammatory state, with raised cytokines, which may result in these changes [13, 15]. Erythropoietin has been suggested as a potential biomarker candidate for paediatric OSA [16]. In a study of 115 children (mean age 6.8 years), 86 children with OSA had significantly higher serum erythropoietin levels compared to non-OSA children (29 children), their levels correlating with AHI [16]. Another postulated mechanism is elevated sympathetic drive caused by frequent arousals and intermittent hypoxia. The evidence here is both limited and mixed: some studies show higher catecholamine levels in OSA *versus* healthy controls, but others show no effect [9, 17]. This may be due to methods and timing of catecholamine sampling. 24-h urine samples, which have been used in several studies due to their noninvasive nature, reflect sympathetic activity in wakefulness as well as sleep. Variation in sympathetic drive in response to daytime events likely dwarfs that seen during sleep [9]. Further research is needed to clarify the mechanisms of cardiovascular sequelae of childhood OSA.

Modifiability of cardiovascular effects

It is unclear whether adverse cardiovascular changes can be improved by treating OSA. A small study of 12 adolescent subjects with obesity and OSA treated with continuous positive airway pressure (CPAP) for 12 months showed improvements in heart rate and heart rate variability that would be associated with reduction in cardiovascular risk, despite body mass index (BMI) z-score remaining stable [18]. A recent meta-analysis concluded that, overall, clinic and ambulatory BP showed no statistically significant changes after treatment with AT [19]. However, subgroup analysis of patients with pre-existing hypertension showed significant improvements in overall BP parameters. These improvements were more marked at night, with restoration of night-time dipping. This is an area for ongoing research as the current body of literature is limited with very few randomised trials. Most studies also had short follow-up durations, with none longer than 12 months. Longer follow-up might demonstrate more subtle benefits of AT on long-term BP in the non-hypertensive population. Residual OSA after AT is also common (approximately 50% in the studies analysed). Analysis of outcomes for only those whose OSA was successfully treated might demonstrate a stronger beneficial effect.

Diagnosis of sleep disordered breathing

There is a range of investigative techniques available to paediatricians to diagnose SDB [20]. These include validated symptom questionnaires and overnight sleep studies, which range in their complexity. PSG is widely regarded as the gold standard for diagnosing SDB in children. PSG is a multichannel study allowing monitoring of cardiorespiratory status and sleep state. Typical cardiorespiratory channels include ECG, pulse oximetry (peripheral oxygen saturation (S_{pO_2})), end-tidal or transcutaneous carbon dioxide tension (P_{ETCO_2} and P_{tcCO_2}, respectively), airflow, diaphragm electromyography (EMG), and chest and abdominal movements. Sleep stage is monitored using electroencephalography (EEG), electro-oculography, EMG of genioglossus muscle, and leg movements. Concurrent audio and video recordings allow clinical correlation with events. Studies are scored according to American Academy of Sleep Medicine (AASM) scoring criteria for apnoeas and hypopnoeas (table 1).

AHI, the number of events per hour, is used to quantify severity of sleep apnoea. Commonly used classifications of severity in children <16 years of age are OAHI of ⩾1 and <5 events·h^{-1} suggesting mild OSA, ⩾5 and <10 events·h^{-1} moderate, and ⩾10 events·h^{-1} severe. Central AHI (CAHI) of ⩾5 events·h^{-1} is generally taken to be pathological, reflecting central sleep apnoea (CSA) [22]. Nocturnal hypoventilation is present when partial pressure of carbon dioxide (P_{CO_2}) is >50 mmHg (>6.7 kPa) for >25% of the total sleep time [21]. Parameters such as mean and nadir S_{pO_2} can also provide important markers for severity of SDB.

TABLE 1 Summary of American Academy of Sleep Medicine scoring for apnoea and hypopnoea in children aged <16 years [21]

Apnoea	⩾90% reduction in airflow for ⩾2 breaths
Obstructive apnoea	Apnoea plus ongoing respiratory effort
Central apnoea	Apnoea with absent respiratory effort plus ⩾3% S_{pO_2} desaturation or EEG arousal
Hypopnoea	⩾30% reduction in airflow for ⩾2 breaths plus ⩾3% S_{pO_2} desaturation or EEG arousal

S_{pO_2}: peripheral oxygen saturation; EEG: electroencephalography.

PSG is costly and limited to centres where expertise exists in reporting multichannel sleep studies. There has been a longstanding desire to find simpler means of screening for and diagnosing SDB.

When considering the diagnosis of SDB it is vital to consider age- and altitude-dependent reference ranges, as desaturation events are common in healthy, term infants, becoming less frequent and less profound as the child develops (table 2) [23–25]. Normal values at altitude do not match those at sea level due to lower partial pressure of oxygen (P_{O_2}) (table 3) [1, 24]. A review of 16 studies to determine CAHI in normal children at sea level (n=1380) and altitude (n=3575) found the range of median CAHI to be 0.1–0.9 events·h^{-1} at sea level and 0.6–6.9 events·h^{-1} at high altitude [26]. Appropriate altitude reference ranges are therefore crucial to avoid the overdiagnosis of SDB in patients at higher altitude.

Questionnaires

Questionnaires have been the focus of much interest as a potentially low-resource method of screening for SDB. Many have been studied as screening tools for OSA, to select a subpopulation for more detailed diagnostic sleep tests. Recent research has studied whether questionnaires may be specific enough to be used for diagnosis without further testing. Incerti Parenti *et al.* [27] and Patel *et al.* [28] both conducted systematic reviews and meta-analyses of paediatric sleep questionnaires. Of the questionnaires studied, the OSA-18 (18-item OSA questionnaire) had the optimum specificity (73%) but lacked sufficient accuracy to be used as a diagnostic test. Whilst sleep questionnaires have poor diagnostic accuracy, they can add another facet to assessment of the child with SDB. The SRBD-PSQ (sleep-related breathing disorder scale of paediatric sleep questionnaire) has been shown to be predictive of improvements in quality of life,

TABLE 2 Normative oximetry data for healthy children by age

	Evans *et al.* [23]	Evans *et al.* [23]	Vézina *et al.* [24]	Ong *et al.* [25]
Age	1 month	3–4 months	1 year	6 months to 12 years (median 7 years 10 months)
Patients n	45	45	562	66
Average S_{pO_2} %				
Median (10th centile)			97.1 (95.5)	
Mean (95% CI)	97.05 (96.59–97.52)	97.65 (97.19–98.12)		97.57 (97.38–97.76)
S_{pO_2} nadir %				
Median (5th centile)				92.00 (84.35)
Mean (95% CI)	80.4 (78.8–82.0)	84.7 (83.3–86.1)	87.0 (81.0–92.0)	91.09 (90.32–91.86)
ODI3 events·h^{-1}				
Median (90th or 95th centile)			6.7 (90th centile 15.8)	2.58 (95th centile 6.43)
Mean (95% CI)	25.41 (22.00–28.82)	13.92 (11.39–16.47)		2.90 (2.50–3.29)
ODI4 events·h^{-1}				
Median (95th centile)				0.92 (3.00)
Mean (95% CI)	16.16 (13.72–18.59)	8.12 (6.46–9.77)		1.14 (0.93–1.34)
% Time S_{pO_2} <92%				
Median (90th centile)			0.1 (0.6)	0.00 (0.05)
Mean (95% CI)	0.82 (0.60–1.23)	0.25 (0.17–0.44)		0.02 (0.01–0.03)

With increasing age, oxygen saturation nadir rises and desaturation indices fall. S_{pO_2}: peripheral oxygen saturation; ODI3: 3% oxygen desaturation index; ODI4: 4% oxygen desaturation index.

TABLE 3 Comparison of polysomnography parameters for healthy children tested at low and high altitude

	Vézina *et al.* [24]	Ucros *et al.* [1]
Altitude MASL	645	2560
Patients n	562	32
Age years	1	4–7
Average S_{pO_2} %	97.1 (10th centile 95.5)	93 (5th centile 90.5)
S_{pO_2} nadir %	87.0 (10th centile 81.0)	84 (5th centile 56.6)
ODI3 events·h^{-1}	6.7 (90th centile 15.8)	11.2 (95th centile 15.2)
Obstructive apnoea index events·h^{-1}	0 (90th centile 0.5)	
Obstructive AHI events·h^{-1}		8.8 (95th centile 21.2)
Central apnoea index events·h^{-1}	2.5 (90th centile 7.1)[#]	
Central AHI events·h^{-1}		0.4 (95th centile 2.4)
Hypopnoea index events·h^{-1}	1.2 (90th centile 3.5)	
Total AHI events·h^{-1}	4.2 (90th centile 10.7)	9.2 (95th centile 17.9)

Data are presented as medians with indicated centiles, unless otherwise stated. MASL: metres above sea level; S_{pO_2}: peripheral oxygen saturation; ODI3: 3% oxygen desaturation index; AHI: apnoea–hypopnoea index. [#]: this high central event rate in the lower altitude group is likely to be due to younger age.

sleepiness and behaviour after AT. It therefore complements PSG and clinical examination. It can also provide useful information on the impact of SDB on children's physical and psychological health, which cannot be achieved by PSG [29].

Pulse oximetry

Pulse oximetry is a widely available simple tool and, although limited by its inability to discriminate the cause of desaturations, is frequently used to determine the presence or absence of SDB through quantifying the frequency and severity of desaturation events. The McGill oximetry score (MOS) has previously been validated for diagnosing OSA in typically developing children referred for consideration of ear, nose and throat surgery [30]. However, a recent retrospective study evaluating the diagnostic accuracy of the MOS across the spectrum of pathology characteristically referred to paediatric sleep units demonstrated low specificities and positive predictive values for children with comorbidities. This is presumably due to the increased likelihood of oxygen desaturations in children with pre-existing low baseline oxygen saturations and the increased prevalence of co-existent non-obstructive desaturations in these cohorts of children [31].

Recent research has looked for ways to improve the diagnostic accuracy of pulse oximeters for OSA using other parameters that can be calculated from the pulse oximetry trace. Applying machine learning approaches can detect OSA with increased sensitivity and specificity *versus* standard pulse oximetry. One approach is the development of deep learning algorithms using computational neural networks. These algorithms have been shown to detect OSA more accurately than commonly used parameters such as the 3% oxygen desaturation index (ODI3), particularly for moderate-severe OSA. However, whilst promising, these algorithms still lack sensitivity for diagnosing mild OSA (OAHI <5 events·h^{-1}) [32]. Another method that has been employed to improve OSA detection is use of multi-layer perceptron neural networks of airflow using bispectral analysis in combination with ODI3. When combined, sensitivities and specificities for moderate OSA are 82% and 83%, respectively, significantly improving the sensitivity of oximetry alone [33].

Cardiopulmonary coupling of pulse rate variability and derived respiratory excursions in combination with pulse oximetry data (all using a single sensor) has been evaluated as a diagnostic tool for OSA. This combined analysis was shown to have sensitivities and specificities of 95% and 84%, respectively, for diagnosing OSA in children without comorbidities aged 5–10 years. It had high positive and low negative likelihood ratios, particularly for moderate and severe OSA. The automated calculation of AHI demonstrated excellent agreement with the physiologist-scored PSG studies [34].

It remains questionable as to whether a single night of pulse oximetry monitoring provides adequate data and whether there are certain instances where monitoring over several nights may provide an improved accuracy for diagnosing SDB. Pavone *et al.* [35] have provided evidence that between-night pulse oximetry metric variations are limited in children without comorbidities. However, Galway *et al.* [36] showed that there is likely to be night-to-night variability for children with comorbidities. Further research is required to determine which oxygen saturation indices demonstrate least night-to-night variability and thus might prove most useful diagnostically.

Other methods of improving sensitivity for hypopnoea

Cardiorespiratory polygraphy does not include EEG monitoring, so it is known to underestimate the AHI when compared to PSG, as hypopnoeas that result in arousal without desaturation are not scored. Pulse transit time has been used to accurately detect these events and, when scored in combination with respiratory events, has been shown to more accurately reflect the PSG-determined AHI [37].

However, hypopnoeas can remain underdiagnosed in children, who have a higher arousal threshold than adults. Pulse wave amplitude has been shown to be a sensitive marker of subcortical/autonomic and cortical arousals; it can therefore be used to score hypopnoeas that would otherwise go undetected. When used in a small study by Al-Shawwa *et al.* [38], the mean AHI increased for children originally identified as having mild OSA from 1.4 to 4.8 events·h^{-1}. Since arousals are felt to have an impact on neurocognitive development, identifying subcortical arousals might have an impact on patient management. In this study, the total AHI moved from the mild to the moderate range in five out of 10 children [38].

Methods of assessing airflow

One of the challenges frequently encountered when undertaking PSG and cardiorespiratory polygraphy studies in children is tolerance of the nasal flow sensors [39]. Importantly, these differentiate between central and obstructive events. Recent advances have attempted to detect airflow more readily using other means. Amaddeo *et al.* [40] used a combination of a sensor to detect tracheal sounds (TS) in the suprasternal notch both with and without chest and abdominal wall movement evaluated by inductance plethysmography (TS-RIP and TS, respectively). When compared to the AASM criteria for determining AHI, this sensor provided sensitivities and specificities >90%, suggesting that this might be a simple, effective and well-tolerated tool for diagnosing SDB in children. The study was small, with only 17 children, so further research is warranted in this area.

Home polysomnography

Sleep studies can be performed in either the sleep laboratory or home setting. Increasingly, there is a desire to undertake sleep studies in the home environment, as this is felt to replicate the child's usual sleep patterns more accurately. Recently, an evidence base for home PSG has emerged in children of all ages and a wide range of comorbidities including autistic spectrum disorder, where there are clear advantages to being able to undertake investigations in a familiar environment. Technical acceptability for unmonitored home PSG is reported as 81% but increases to 87% in experienced settings, with failures being related to poor tolerance of nasal flow and the oximetry probe [41, 42]. Home PSG was felt to be acceptable by most patients, with only 8% retrospectively saying that they would have preferred a hospital study.

Emerging diagnostic techniques

There is a flourishing literature in relation to drug-induced sleep endoscopy (DISE) as a tool for evaluating the anatomical site of airway obstruction. A survey by Cousineau *et al.* [43] of practice in Canada identified wide variation, with DISE rarely performed before AT or PSG. It was felt to be helpful in the absence of adenotonsillar hypertrophy or where there was a discrepancy between the clinical findings and severity of sleep apnoea. There is a lack of consensus in the optimal anaesthetic protocols for DISE and the scoring system to define abnormality. A prospective study is needed to assess the potential benefits, in particular its impact on avoiding unnecessary AT.

Other techniques used to diagnose airway obstruction include 3D cone beam computed tomography (CBCT). This is preferred over standard CT due to its low radiation dose. Using CBCT, Hsu *et al.* [44] demonstrated that airway volume and cross-sectional area of the nasopharynx is smaller in children with moderate-severe OSA. This has the potential to be used as a diagnostic tool for OSA but is not ready for clinical practice.

Therapeutic options

The main treatment for typically developing children with OSA has been AT with a small proportion progressing to CPAP. Children with more complex comorbidities are more likely to require respiratory support in the form of CPAP or bilevel positive airway pressure (BiPAP), or *via* tracheostomy. Recent publications have advanced our understanding on the specific techniques and outcomes for OSA surgery. Additionally, there is new information on the use of CPAP and its variants, and on alternative methods of treating OSA.

Adenotonsillectomy

AT is the default intervention for those with or without comorbidities who have symptomatic OSA. The procedure is relatively safe but adverse effects include pain, slow return to normal diet, post-operative

infection and bleeding. Young age (<3 years), cardiac comorbidity and pre-existing airway anomaly are associated with a greater risk of peri-operative adverse respiratory events [45]. There is debate about the optimal technique and extent of tissue removal for tonsillectomy and the relative risks of adverse events associated with these.

Traditionally, the whole tonsil and capsule were removed by scalpel: total tonsillectomy (TT). Intracapsular tonsillectomy (ICT) removes most of the tonsillar tissue using a device (*e.g.* microdebrider, radiofrequency ablator) leaving the capsule *in situ*. Recent studies suggest that ICT may have lower rates of adverse effects; this has to be balanced against the risk of tonsillar re-growth requiring revision surgery. This is a rare complication and mainly occurs in very young patients. One study of 1257 patients (median age 4.2 years) who underwent ICT showed quick recovery with no major haemorrhage [46]. Only 2.6% required revision surgery, with risk factors being <2 years old at initial surgery, severe OSA and significant comorbidities. A smaller study of 162 children showed better pain scores in those with ICT *versus* those with TT, with no revision surgery in the ICT group [47]. ICT and TT showed similar behavioural outcome improvement [48]. ICT also appears to be effective in children with comorbidities associated with difficult-to-treat OSA. A study of 320 children with developmental delay due to a range of diagnoses compared ICT and TT. ICT had similar outcomes for symptom resolution but had reduced length of stay, less revision surgery and less need for pain relief [49].

Continuous positive airway pressure

CPAP may be used in those with OSA who are not suitable for AT, or who have persisting obstruction after AT. The two commonly used ways of delivering positive pressure support are CPAP, a single set pressure throughout the respiratory cycle, or BiPAP, a bilevel approach of a background pressure with increases when the device detects or delivers inspiration. Acceptance of this form of therapy can be a significant challenge, with recent evidence confirming that adherence is generally poor. Weiss *et al*. [50] used statistical cluster analysis to examine clinical characteristics and adherence measures for paediatric CPAP patients. Fewer than half of the children were consistently using CPAP for >4 h a night (the level identified in adult literature as bringing tangible gains). Those with high compliance were particularly likely to be those using CPAP after AT, and those with lower BMI, high levels of obstructive events and higher pressures. The least adherent groups tended to be those without developmental delay or with the highest BMI. A large cross-sectional "big data" analysis of those on positive airway pressure (PAP) therapy within a single insurance company in the USA also showed poor compliance. Only 46.3% of 20 533 subjects used PAP for ⩾4 h on 70% of nights in a 30-day period in the first 90 days of treatment [51]. Notably, the use of patient engagement programmes was associated positively with adherence. This may be an important approach to improving compliance. Clinicians should remember that CPAP therapy is clearly not as user friendly as we would like!

Technological advances in PAP therapy

There have been considerable developments in the devices used to deliver PAP over the four decades of this therapy. They all now record data on respiratory indices during use. A recent study sought to examine the accuracy of these data by comparing them to the data obtained during overnight PSG. They found that the device indices tended to underestimate the degree of residual obstruction and therefore could not be relied upon to guide adjustments in treatment [52]. Another facility of modern machines is to deliver a constant tidal or minute volume by adjusting the delivered pressure within set parameters in response to measurements of the patient's breathing. In a study of 19 children with hypoventilation, average volume-assured pressure support (AVAPS) was shown to be superior to conventional BiPAP in control of P_{tcCO_2} parameters [53]. In a study of adolescents, an autotitrating CPAP mode was shown to derive very similar pressures to those recommended following in-laboratory PSG testing [54] (figure 1).

Alternatives to PAP

Owing to the variable acceptance of PAP, there is a desire to find alternatives. Two recent small studies examined the potential for use of high flow nasal cannula (HFNC) therapy in infants and young children with OSA. Kwok *et al*. [55] found it was possible to improve oxygenation and significantly reduce obstruction with HFNC in infants, when using PSG to guide titration. Ignatiuk *et al*. [56] studied 22 young children. They successfully titrated HFNC settings in all subjects, with 19 proceeding to home use. However, of those with 12-month follow-up, nearly half discontinued due to intolerance of the therapy, suggesting that HFNC has similar challenges with adherence.

Medical options, particularly for treatment of mild-moderate OSA, have been suggested as a possible alternative to surgery. A recent Cochrane review found insufficient evidence of benefit from intranasal steroids and mild, short-term improvements to PSG parameters from use of oral montelukast in non-obese

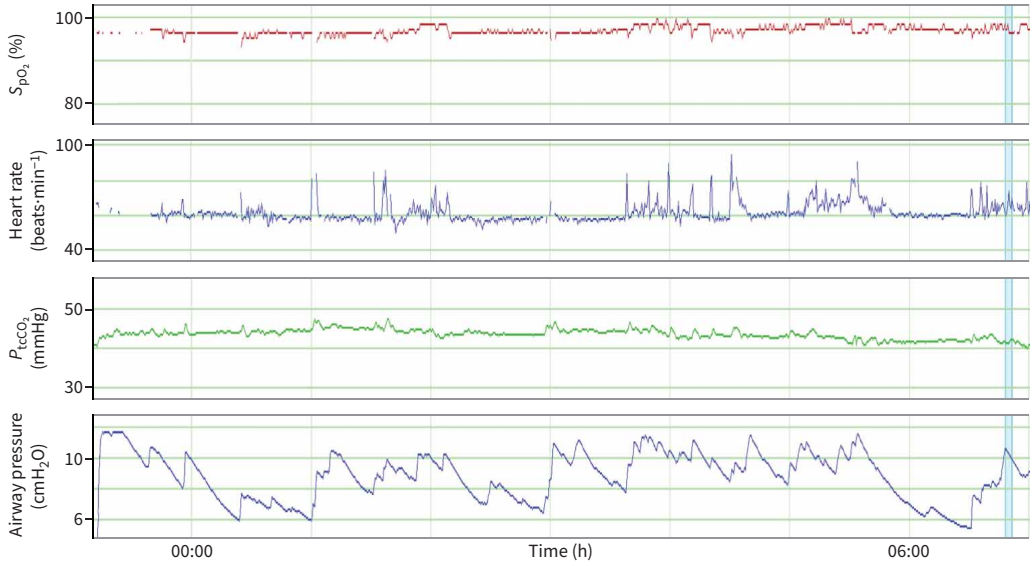

FIGURE 1 Continuous positive airway pressure trace showing frequent pressure changes with autotitration. S_{pO_2}: peripheral oxygen saturation; P_{tcCO_2}: transcutaneous carbon dioxide tension.

typically developing children who had not undergone surgery for OSA [57]. However, there are no long-term data on efficacy, safety or rates of avoidance of surgery, and the authors note the need for more robust research [57].

Myofunctional therapy aims to re-train the muscles of the jaw and tongue to improve tone and positioning and thereby improve maintenance of airway patency, reducing OSA. Many of the studies are small and benefits appear to be limited. A recent meta-analysis of the literature found 10 studies with 241 paediatric patients, mostly with mild OSA. They showed a reduction in AHI from 4.32 to 2.48 events·h^{-1} and an increase in mean S_{pO_2} of just 0.37% [58].

Children with SDB due to craniofacial abnormalities may benefit from corrective surgery. For those with abnormalities affecting the lower face, external mandibular distraction is a technique that has been the focus of recent research. This intervention's effects on PSG were described in 31 neonates with Pierre Robin sequence pre-operatively (mean age 13 days) and post-operatively (mean age 80 days). While there was a significant reduction in obstructive events and improvements in sleep efficiency and oxygenation, 15 of the 31 continued to have severe obstruction with ⩾10 events·h^{-1} [59].

Central sleep apnoea

CSA is generally accepted as a central apnoea index (CAI) of ⩾5 events·h^{-1}. A recent single-centre cohort study of 95 children (aged ⩾1 month, mean±SD age 3.7±4.5 years) with CAI ⩾5 events·h^{-1} at a tertiary sleep clinic found only one case in a child without any comorbidities [60]. In their cohort, CAI ⩾5 events·h^{-1} was associated with Chiari I malformation, complex syndromes including DS, PWS and Beckwith–Wiedemann syndrome, neuromuscular conditions, Pierre Robin sequence, and encephalopathy and epilepsy syndromes. A co-existent significant obstructive element (OAHI ⩾5 events·h^{-1}) was noted in 39% of patients. A variety of treatments were used depending on underlying cause and comorbidities, including supplemental oxygen, ventilatory support, neurosurgery, caffeine and acetazolamide. Groups were too small to evaluate efficacy of individual treatments; however, the vast majority of patients showed improvement in CAI at follow-up, including the 23% managed expectantly. Obstructive parameters did not show a similar improvement.

Congenital central hypoventilation syndrome (CCHS) is a rare condition characterised by alveolar hypoventilation secondary to impaired central respiratory control and associated with other abnormalities of the autonomic nervous system [61]. Patients with CCHS have reduced response to hypoxaemia and hypercapnia, and typically do not experience dyspnoea or increase their respiratory rate to compensate. Therefore, the 2020 guideline from the European CCHS Consortium Project recommends that CCHS patients undergo exercise testing every 1–3 years from the age of 6 years, take frequent breaks during

moderate activity and avoid strenuous activity. However, studies to date of ventilatory changes during exercise in CCHS have been limited.

One recent single-centre study of 15 patients with CCHS showed that patients may develop mild hypoxaemia and hypercapnia during submaximal exercise, despite reporting no symptoms [62]. Subjects (median age 10.5 years, interquartile range 7.9–16.2 years) underwent self-paced 6-min walk testing. Seven patients (47%) desaturated to S_{pO_2} ⩽90%. Three of these patients also developed P_{ETCO_2} of ⩾50 mmHg (6.7 kPa). All patients had normal ventilatory parameters at rest and during sleep with assisted ventilation. It was not possible to predict which individual patients would experience hypoxaemia or hypercapnia based on PHOX2B polyalanine repeat mutation length; however, those with longer repeat lengths were more at risk. Notably, 73% of patients reported participating in mainstream physical education classes at school, and only 27% monitored their S_{pO_2} or P_{ETCO_2} during or after exercise. Exercise testing, particularly submaximal exercise that reflects activities of daily living, may allow more effective personalised exercise plans that account for personal risk.

Specific comorbidities

Down syndrome

It is well recognised that children with DS are particularly prone to multifactorial SDB and are well represented within tertiary sleep services. Waters *et al*. [63] found that PSG scores are generally highest in the first 2 years of life. This may be related to the higher scores we see even in typically developing children at this age. Overall, 78% had moderate to severe OSA at some point, with AT effective in 53% (returning scores to normal–mild). Overall scores tended to lessen over time with successive studies.

As well as there being age-related changes in DS, there may be intrinsic respiratory abnormalities associated with the condition. One study identified that there were lower values of P_{O_2} and higher values of P_{CO_2} in 28 DS children compared to 28 controls matched for age and for AHI scores [64]. They suggested that this was due to poor muscle tone or ventilatory control in DS. Further support for a ventilatory control disorder was found in a study of 14 children with DS and 14 controls where loop gain (a measure of the sensitivity of the negative feedback loop that controls ventilation) was assessed from their PSG. DS children had higher loop gain, indicating an inherent impairment in their ventilatory control, putting them more at risk of SDB [65].

Children with DS are more difficult to treat. A study of 24 DS children with mild OSA (AHI 1–5 events·h^{-1}), followed over 5 years, found that AHI, nadir S_{pO_2} and P_{ETCO_2} did not alter overall, despite medical treatments including intranasal corticosteroids, montelukast or oxygen therapy. They suggested that mild OSA was not responsive to medical treatment and alternative management approaches are needed [66]. In another study of 45 DS children with mild OSA treated over 14 months with intranasal corticosteroids or montelukast, AHI, nadir S_{pO_2} and P_{ETCO_2} did not change, indicating that DS children are less likely to respond. This may be because inflammation within the upper airway is not the sole factor for their SDB [67].

AT remains a mainstay of OSA treatment in DS. However, surgical intervention with AT in DS not only is less effective than in typically developing children, but also has a higher rate of complications, with medical intervention for complications in one study being needed in 78 out of 251 DS children (32%) [68]. This was more likely in those with severe OSA, previous intensive care unit admission, aerodigestive problems and in those with ASA score >2 (American Society of Anethesiologists Physical Status Classification System).

CPAP also appears to be less effective in DS than typically developing children. While MacDonagh *et al*. [69] found that CPAP was better adhered to by 44 DS children than 62 controls (79% *versus* 72%), individuals with DS continued to have higher AHI scores. This study found higher mask leak in the DS cohort and felt attention to mask leak may be an important factor in treatment efficacy.

Considering that in DS children, inhaled corticosteroids, montelukast and CPAP are not that effective, there has been active consideration of other therapies for significant residual OSA in DS after AT [70]. Alternative surgical techniques have included tongue-base reduction, lingual tonsillectomy, revision adenoidectomy, epiglottopexy, supraglottoplasty, inferior turbinate reduction, uvulopalatopharyngoplasty, midline posterior glossectomy and genioglossus advancement. While there was insufficient evidence for any of these therapies, weight management was considered important, and hypoglossal nerve stimulation showed some promise as a safe and effective therapy for OSA in 20 non-obese DS children with severe OSA and failed CPAP after AT. Hypoglossal nerve stimulation resulted in a median 85% reduction in

AHI [71]. Assessment of neurocognitive scores and behaviour before and 6.5 months after surgery in nine DS individuals (mean age 15 years) showed clinically significant improvements in all [72].

Prader–Willi syndrome

Individuals with PWS are known to have a high rate of SDB and this can be aggravated by initiation of growth hormone therapy. One study of 112 PWS children assessed before and after starting growth hormone therapy at a median age of 1.9 years (range 0.1–13.5 years) found that 13% developed worsening OSA needing medical intervention after initiation [73]. Thus, these children need assessment after starting growth hormone, although a recent longitudinal study of 62 PWS children found that starting growth hormone early (<12 months of age) did not result in more OSA. In this study, severity of OSA lessened in both younger and older children with time, perhaps reflecting another age-related effect on OSA scores [74].

PWS children may be helped by AT, with a meta-analysis of seven studies finding a mean post-operative improvement in AHI of 7.7 events·h^{-1} [75]. It is important to recognise that the most common complication of AT (in 14%) was velopharyngeal insufficiency [75].

Beckwith–Wiedemann syndrome

A small study of tongue reduction surgery for macroglossia in 36 patients with Beckwith–Wiedemann syndrome (age 7 days to 51.3 months) evaluated the effect on OSA in a subset of 12 patients with both pre- and post-operative PSG. Post-operative PSG showed a significant reduction in AHI *versus* pre-operative PSG, from 30.9±21.8 to 10.0±18.3 events·h^{-1} (p=0.019). However, it should be noted that residual AHI remained high, and patients would be likely to require further OSA treatment [76].

Sickle cell disease

OSA is an important complication in sickle cell disease and has been found to be associated with neurological complications (OR 1.50, 95% CI 1.02–2.21) and acute chest syndrome (OR 1.34, 95% CI 1.08–1.67) in a review of 203 705 hospital discharges. Treatment with noninvasive ventilation may influence the risk of these complications [77].

Obesity

It is known that obesity has respiratory consequences for children: it reduces lung volumes and residual volume, contributing to a higher prevalence of SDB [78]. One study of 1017 children (mean age 13.1 years) found 12.8% of obese children had OSA, compared to 5.8% of non-obese children [79]. Katz *et al*. [80] studied 71 children aged 8–17 years with obesity (BMI >95th centile) and found higher neck circumferences associated with OSA severity. Neck circumference to body height ratios predicted worse OSA, warranting earlier PSG. While treating obesity may be thought difficult, a study randomising 44 obese children aged 7–18 years to either high intensity interval training (HIIT) and resistance training three times per week for 8 weeks, or usual care, found that AHI fell significantly more in the HIIT group at 16 weeks [81]. The absolute differences were small (*e.g.* AHI decreased in the HIIT group from 1.3 to 0.6 events·h^{-1}), but it showed that exercise may help sleep measures. S_{pO_2} measurements did not change over time in either group [81]. Encouragingly, a review of 10 studies of multidisciplinary interventions for weight loss found that 90% showed a reduction in AHI, with normalisation in 46–80%. AHI fell by 0.51 events·h^{-1} (range 0.08–0.94 events·h^{-1}) and ODI fell by 0.28 events·h^{-1} (range 0.05–0.50 events·h^{-1}). Small steps for a large problem [82].

Conclusion

Recent evidence reflects a growing appreciation of the complexity of paediatric SDB. There are many promising techniques with an emerging evidence base, which may allow more tailored management of complex patients. It is our hope that the next few years will lead to an increased understanding of the right diagnostic techniques and treatment approaches for the right patient. This would move us closer than ever to the goal of providing personalised care [83].

Key points

- Childhood SDB can have a long-term impact on cardiovascular health, brain structure and function.
- Pulse oximetry, especially in combination with new data-processing techniques, may be adequate to confirm OSA, with low night-to-night variability in typically developing children.
- Intracapsular tonsillectomy has similar efficacy to total tonsillectomy, but has a lower adverse event rate.
- Adherence limits use of positive airway pressure in OSA persistent after adenotonsillectomy, but weight loss and hypoglossal nerve stimulation may benefit patients with specific comorbidities.

Self-evaluation questions

1. How would you expect respiratory indices to change at altitude?
   a) Lower rate of obstructive respiratory events, higher rate of central respiratory events, lower mean S_{pO_2}, lower saturations nadir
   b) Higher rate of obstructive respiratory events, lower rate of central respiratory events, lower mean S_{pO_2}, lower saturations nadir
   c) Higher rate of obstructive respiratory events, higher rate of central respiratory events, lower mean S_{pO_2}, lower saturations nadir
   d) Higher rate of obstructive respiratory events, higher rate of central respiratory events, lower mean S_{pO_2}, higher saturations nadir
2. Which of these features of BP are associated with childhood OSA?
   a) Increased incidence of systemic hypertension
   b) Increased night-time dipping of BP
   c) BP changes that fully resolve with OSA treatment
   d) Increased systolic BP and decreased diastolic BP
3. Which paediatric sleep questionnaire is sufficiently sensitive and specific that it can be used as a stand-alone diagnostic test for OSA?
   a) OSA-18
   b) SRBD-PSQ
   c) Paediatric OSA screening tool
   d) None of the above
4. Which feature is associated with poor compliance with PAP therapy?
   a) Developmental delay
   b) Higher BMI
   c) Higher PAP pressure
   d) Residual OSA after AT
5. In DS, which treatment has evidence of benefit in intractable OSA?
   a) Lingual tonsillectomy
   b) Tongue-base reduction
   c) Hypoglossal nerve stimulation
   d) Epiglottopexy

Conflict of interest: A.J.B. Garde has nothing to disclose. N.A. Gibson has nothing to disclose. M.P. Samuels has nothing to disclose. H.J. Evans has nothing to disclose.

References

1 Ucros S, Granados C, Hill C, *et al.* Normal values for respiratory sleep polygraphy in children aged 4 to 9 years at 2,560 m above sea level. *J Sleep Res* 2021; 30: e13341.
2 Hill CM, Evans HJ, Elphick H, *et al.* Prevalence and predictors of obstructive sleep apnoea in young children with Down syndrome. *Sleep Med* 2016; 27–28: 99–106.
3 Kaditis AG, Alonso Alvarez ML, Boudewyns A, *et al.* Obstructive sleep disordered breathing in 2- to 18-year-old children: diagnosis and management. *Eur Respir J* 2016; 47: 69–94.
4 Musso MF, Lindsey HM, Wilde EA, *et al.* Volumetric brain magnetic resonance imaging analysis in children with obstructive sleep apnea. *Int J Pediatr Otorhinolaryngol* 2020; 138: 110369.
5 Mei L, Li X, Zhou G, *et al.* Effects of obstructive sleep apnoea severity on neurocognitive and brain white matter alterations in children according to sex: a tract-based spatial statistics study. *Sleep Med* 2021; 82: 134–143.
6 Ji T, Li X, Chen J, *et al.* Brain function in children with obstructive sleep apnea: a resting-state fMRI study. *Sleep* 2021; 44: zsab047.
7 Waters KA, Chawla J, Harris MA, *et al.* Cognition after early tonsillectomy for mild OSA. *Pediatrics* 2020; 145: e20191450.
8 Lushington K, Kennedy D, Martin J, *et al.* Quality-of-life but not behavior improves 48-months post-adenotonsillectomy in children with SDB. *Sleep Med* 2021; 81: 418–429.
9 Brooks DM, Kelly A, Sorkin JD, *et al.* The relationship between sleep-disordered breathing, blood pressure, and urinary cortisol and catecholamines in children. *J Clin Sleep Med* 2020; 16: 907–916.
10 Kang KT, Chiu SN, Weng WC, *et al.* 24-hour ambulatory blood pressure variability in children with obstructive sleep apnea. *Laryngoscope* 2021; 131: 2126–2132.
11 Chan KCC, Au CT, Hui LL, *et al.* Childhood OSA is an independent determinant of blood pressure in adulthood: longitudinal follow-up study. *Thorax* 2020; 75: 422–431.

12 Domany KA, Huang G, Hossain MM, *et al.* Effect of adenotonsillectomy on cardiac function in children age 5–13 years with obstructive sleep apnea. *Am J Cardiol* 2021; 141: 120–126.
13 Smith DF, Schuler CL, Hossain MM, *et al.* Early atherosclerotic inflammatory pathways in children with obstructive sleep apnea. *J Pediatr* 2021; 239: 168–174.
14 Jacobs S, Mylemans E, Ysebaert M, *et al.* The impact of obstructive sleep apnea on endothelial function during weight loss in an obese pediatric population. *Sleep Med* 2021; 86: 48–55.
15 Danisi JM, Fernandez-Mendoza J, Vgontzas AN, *et al.* Association of visceral adiposity and systemic inflammation with sleep disordered breathing in normal weight, never obese adolescents. *Sleep Med* 2020; 69: 103–108.
16 Kalogritsas ND, Lachanas VA, Liakos P, *et al.* Erythropoietin levels in children with obstructive sleep apnea. *Int J Pediatr Otorhinolaryngol* 2021; 151: 110932.
17 Sica E, de Bernardi F, Nosetti L, *et al.* Catecholamines and children obstructive sleep apnea: a systematic review. *Sleep Med* 2021; 87: 227–232.
18 Kirk VG, Edgell H, Joshi H, *et al.* Cardiovascular changes in children with obstructive sleep apnea and obesity after treatment with noninvasive ventilation. *J Clin Sleep Med* 2020; 16: 2063–2071.
19 Kang KT, Chiu SN, Lee CH, *et al.* Effect of adenotonsillectomy on blood pressure in children with obstructive sleep apnea: a meta-analysis. *Sleep Med* 2021; 84: 334–342.
20 British Thoracic Society (BTS). Guideline for diagnosing and monitoring paediatric sleep disordered breathing. On behalf of the BTS paediatric sleep disorders guideline development group. Draft for public consultation. February 2022. https://www.brit-thoracic.org.uk/media/455743/bts-guideline-for-paediatric-sleep-disorders-consultation-feb-2022.pdf
21 Berry RB, Abreu AR, Bibbs ML, *et al.* The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 2.6. Darien, American Academy of Sleep Medicine, 2020. https://aasm.org/clinical-resources/scoring-manual/
22 McLaren AT, Bin-Hasan S, Narang I. Diagnosis, management and pathophysiology of central sleep apnea in children. *Paediatr Respir Rev* 2019; 30: 49–57.
23 Evans HJ, Karunatilleke AS, Grantham-Hill S, *et al.* A cohort study reporting normal oximetry values in healthy infants under 4 months of age using Masimo technology. *Arch Dis Child* 2018; 103: 868–872.
24 Vézina K, Mariasine J, Young R, *et al.* Cardiorespiratory monitoring data during sleep in healthy Canadian infants. *Ann Am Thorac Soc* 2020; 17: 1238–1246.
25 Ong JWY, Williams D, Gavlak JC, *et al.* Observational study to define reference ranges for the 3% oxygen desaturation index during sleep in healthy children under 12 years using oximetry motion-resistant technology. *Arch Dis Child* 2021; 106: 583–586.
26 Restrepo-Gualteros SM, Villamil-Osorio M, Rodriguez-Martinez CE. Prediction of normal values for central apnea-hypopnea index at different ages and altitudes above sea level in healthy children. *Sleep Med* 2021; 78: 182–188.
27 Incerti Parenti S, Fiordelli A, Bartolucci ML, *et al.* Diagnostic accuracy of screening questionnaires for obstructive sleep apnea in children: a systematic review and meta-analysis. *Sleep Med Rev* 2021; 57: 101464.
28 Patel AP, Meghji S, Phillips JS. Accuracy of clinical scoring tools for the diagnosis of pediatric obstructive sleep apnea. *Laryngoscope* 2020; 130: 1034–1043.
29 Rosen CL, Wang R, Taylor HG, *et al.* Utility of symptoms to predict treatment outcomes in obstructive sleep apnea syndrome. *Pediatrics* 2015; 135: e662–e671.
30 Nixon GM, Kermack AS, Davis GM, *et al.* Planning adenotonsillectomy in children with obstructive sleep apnea: the role of overnight oximetry. *Pediatrics* 2004; 113: e19–e25.
31 Trucco F, Rosenthal M, Bush A, *et al.* The McGill score as a screening test for obstructive sleep disordered breathing in children with co-morbidities. *Sleep Med* 2020; 68: 173–176.
32 Vaquerizo-Villar F, Alvarez D, Kheirandish-Gozal L, *et al.* A convolutional neural network architecture to enhance oximetry ability to diagnose pediatric obstructive sleep apnea. *IEEE J Biomed Health Inform* 2021; 25: 2906–2916.
33 Barroso-García V, Gutiérrez-Tobal GC, Kheirandish-Gozal L, *et al.* Bispectral analysis of overnight airflow to improve the pediatric sleep apnea diagnosis. *Comput Biol Med* 2021; 129: 104167.
34 Hilmisson H, Berman S, Magnusdottir S. Sleep apnea diagnosis in children using software-generated apnea-hypopnea index (AHI) derived from data recorded with a single photoplethysmogram sensor (PPG): results from the Childhood Adenotonsillectomy Study (CHAT) based on cardiopulmonary coupling analysis. *Sleep Breath* 2020; 24: 1739–1749.
35 Pavone M, Cutrera R, Verrillo E, *et al.* Night-to-night consistency of at-home nocturnal pulse oximetry testing for obstructive sleep apnea in children. *Pediatr Pulmonol* 2013; 48: 754–760.
36 Galway NC, Maxwell B, Shields M, *et al.* Use of oximetry to screen for paediatric obstructive sleep apnoea: is one night enough and is 6 hours too much? *Arch Dis Child* 2021; 106: 58–61.

37 Cheung TW, Lam DS, Chan PC, *et al.* Comparing respiratory polygraphy with pulse transit time analysis versus overnight polysomnography in the diagnosis of obstructive sleep apnoea in children. *Sleep Med* 2021; 81: 457–462.
38 Al-Shawwa B, Cruz J, Ehsan Z, *et al.* The challenges in scoring hypopneas in children: is pulse wave amplitude drop the answer? *Sleep Med* 2021; 81: 336–340.
39 Trang H, Leske V, Gaultier C. Use of nasal cannula for detecting sleep apneas and hypopneas in infants and children. *Am J Respir Crit Care Med* 2002; 166: 464–468.
40 Amaddeo A, Sabil A, Arroyo JO, *et al.* Tracheal sounds for the scoring of sleep respiratory events in children. *J Clin Sleep Med* 2020; 16: 361–369.
41 Ioan I, Weick D, Schweitzer C, *et al.* Feasibility of parent-attended ambulatory polysomnography in children with suspected obstructive sleep apnea. *J Clin Sleep Med* 2020; 16: 1013–1019.
42 Russo K, Greenhill J, Burgess S. Home (level 2) polysomnography is feasible in children with suspected sleep disorders. *Sleep Med* 2021; 88: 157–161.
43 Cousineau J, Prévost AS, Battista MC, *et al.* Management of obstructive sleep apnea in children: a Canada-wide survey. *J Otolaryngol Head Neck Surg* 2021; 50: 53.
44 Hsu WC, Kang KT, Yao CCJ, *et al.* Evaluation of upper airway in children with obstructive sleep apnea using cone-beam computed tomography. *Laryngoscope* 2021; 131: 680–685.
45 Katz SL, Monsour A, Barrowman N, *et al.* Predictors of postoperative respiratory complications in children undergoing adenotonsillectomy. *J Clin Sleep Med* 2020; 16: 41–48.
46 Amin N, Bhargava E, Prentice JG, *et al.* Coblation intracapsular tonsillectomy in children: a prospective study of 1257 consecutive cases with long-term follow-up. *Clin Otolaryngol* 2021; 46: 1184–1192.
47 Wang J, Dang PH, Chang HH, *et al.* Subtotal intracapsular tonsillectomy may be the first choice for tonsillectomy in children. *J Int Med Res* 2021; 49: 3000605211011930.
48 Sjölander I, Borgström A, Larsson JO, *et al.* Randomised trial showed no difference in behavioural symptoms between surgical methods treating paediatric obstructive sleep apnoea. *Acta Paediatr* 2020; 109: 2099–2104.
49 Mukerji SS, Rath S, Zhang WQ, *et al.* Extracapsular versus intracapsular tonsillectomy: outcomes in children with a focus on developmental delay. *Int J Pediatr Otorhinolaryngol* 2022; 152: 110978.
50 Weiss MR, Allen ML, Landeo-Gutierrez JS, *et al.* Defining the patterns of PAP adherence in pediatric obstructive sleep apnea: a clustering analysis using real-world data. *J Clin Sleep Med* 2021; 17: 1005–1013.
51 Bhattacharjee R, Benjafield AV, Armitstead J, *et al.* Adherence in children using positive airway pressure therapy: a big-data analysis. *Lancet Digit Health* 2020; 2: e94–e101.
52 Mihai R, Ellis K, Davey MJ, *et al.* Interpreting CPAP device respiratory indices in children. *J Clin Sleep Med* 2020; 16: 1655–1661.
53 Saddi V, Thambipillay G, Pithers S, *et al.* Average volume-assured pressure support vs conventional bilevel pressure support in pediatric nocturnal hypoventilation: a case series. *J Clin Sleep Med* 2021; 17: 925–930.
54 Khaytin I, Tapia IE, Xanthopoulos MS, *et al.* Auto-titrating CPAP for the treatment of obstructive sleep apnea in children. *J Clin Sleep Med* 2020; 16: 871–878.
55 Kwok KL, Lau MY, Leung SY, *et al.* Use of heated humidified high flow nasal cannula for obstructive sleep apnea in infants. *Sleep Med* 2020; 74: 332–337.
56 Ignatiuk D, Schaer B, McGinley B. High flow nasal cannula treatment for obstructive sleep apnea in infants and young children. *Pediatr Pulmonol* 2020; 55: 2791–2798.
57 Kuhle S, Hoffmann DU, Mitra S, *et al.* Anti-inflammatory medications for obstructive sleep apnoea in children. *Cochrane Database Syst Rev* 2020; 1: CD007074.
58 Bandyopadhyay A, Kaneshiro K, Camacho M. Effect of myofunctional therapy on children with obstructive sleep apnea: a meta-analysis. *Sleep Med* 2020; 75: 210–217.
59 Ehsan Z, Weaver KN, Pan BS, *et al.* Sleep outcomes in neonates with Pierre Robin sequence undergoing external mandibular distraction: a longitudinal analysis. *Plast Reconstr Surg* 2020; 146: 1103–1115.
60 Ghirardo S, Amaddeo A, Griffon L, *et al.* Central apnea and periodic breathing in children with underlying conditions. *J Sleep Res* 2021; 30: e13388.
61 Trang H, Samuels M, Ceccherini I, *et al.* Guidelines for diagnosis and management of congenital central hypoventilation syndrome. *Orphanet J Rare Dis* 2020; 15: 252.
62 Ghosh RN, Guglani L, Westbrook AL, *et al.* Impaired ventilation during 6-min walk test in congenital central hypoventilation syndrome. *Pediatr Pulmonol* 2022; 57: 1660–1667.
63 Waters KA, Castro C, Chawla J. The spectrum of obstructive sleep apnea in infants and children with Down Syndrome. *Int J Pediatr Otorhinolaryngol* 2020; 129: 109763.
64 Richard N, Beydon N, Berdah L, *et al.* Nocturnal hypoventilation in Down syndrome children with or without sleep apnea. *Pediatr Pulmonol* 2020; 55: 1246–1253.
65 Siriwardhana LS, Nixon GM, Davey MJ, *et al.* Children with Down syndrome and sleep disordered breathing display impairments in ventilatory control. *Sleep Med* 2021; 77: 161–169.
66 Howard JJM, Sarber KM, Yu W, *et al.* Outcomes in children with Down syndrome and mild obstructive sleep apnea treated non-surgically. *Laryngoscope* 2020; 130: 1828–1835.

67 Yu W, Sarber KM, Howard JJM, *et al.* Children with Down syndrome and mild OSA: treatment with medication versus observation. *J Clin Sleep Med* 2020; 16: 899–906.
68 Cottrell J, Zahr SK, Propst EJ, *et al.* Morbidity and mortality from adenotonsillectomy in children with trisomy 21. *Int J Pediatr Otorhinolaryngol* 2020; 138: 110377.
69 MacDonagh L, Farrell L, O'Reilly R, *et al.* Efficacy and adherence of noninvasive ventilation treatment in children with Down syndrome. *Pediatr Pulmonol* 2021; 56: 1704–1715.
70 Ravutha Gounden M, Chawla JK. Management of residual OSA post adenotonsillectomy in children with Down syndrome: a systematic review. *Int J Pediatr Otorhinolaryngol* 2022; 152: 110966.
71 Caloway CL, Diercks GR, Keamy D, *et al.* Update on hypoglossal nerve stimulation in children with Down syndrome and obstructive sleep apnea. *Laryngoscope* 2020; 130: E263–E267.
72 Grieco JA, Hartnick CJ, Skotko BG, *et al.* Preliminary neurocognitive results post hypoglossal nerve stimulation in patients with Down syndrome. *Laryngoscope* 2021; 131: 2830–2833.
73 Caudri D, Nixon GM, Nielsen A, *et al.* Sleep-disordered breathing in Australian children with Prader–Willi syndrome following initiation of growth hormone therapy. *J Paediatr Child Health* 2022; 58: 248–255.
74 Zimmermann M, Laemmer C, Woelfle J, *et al.* Sleep-disordered breathing in children with Prader–Willi syndrome in relation to growth hormone therapy onset. *Horm Res Paediatr* 2020; 93: 85–93.
75 Clements AC, Dai X, Walsh JM, *et al.* Outcomes of adenotonsillectomy for obstructive sleep apnea in Prader–Willi syndrome: systematic review and meta-analysis. *Laryngoscope* 2021; 131: 898–906.
76 Cohen JL, Cielo CM, Kupa J, *et al.* The utility of early tongue reduction surgery for macroglossia in Beckwith–Wiedemann syndrome. *Plast Reconstr Surg* 2020; 145: 803e–813e.
77 Tsou PY, Cielo CM, Xanthopoulos MS, *et al.* The burden of obstructive sleep apnea in pediatric sickle cell disease: a Kids' inpatient database study. *Sleep* 2021; 44: zsaa157.
78 Hochart A, Nève V, Drumez E, *et al.* Dramatic impact of morbid obesity on child lung development. *Arch Pediatr* 2021; 28: 186–190.
79 Fraire JA, Deltetto NM, Catalani F, *et al.* Prevalence of sleep-disordered breathing among adolescents and its association with the presence of obesity and hypertension. *Arch Argent Pediatr* 2021; 119: 245–250.
80 Katz SL, Blinder H, Naik T, *et al.* Does neck circumference predict obstructive sleep apnea in children with obesity? *Sleep Med* 2021; 78: 88–93.
81 Longlalerng K, Sonsuwan N, Uthaikhup S, *et al.* High-intensity interval training combined with resistance training improved apnea-hypopnea index but did not modify oxygen desaturation index and oxygen saturation nadir in obese children with obstructive sleep apnea. *Sleep Breath* 2020; 24: 571–580.
82 Roche J, Isacco L, Masurier J, *et al.* Are obstructive sleep apnea and sleep improved in response to multidisciplinary weight loss interventions in youth with obesity? A systematic review and meta-analysis. *Int J Obes* 2020; 44: 753–770.
83 Siriwardhana LS, Nixon GM, Horne RSC, *et al.* Journey towards a personalised medicine approach for OSA: can a similar approach to adult OSA be applied to paediatric OSA? *Paediatr Respir Rev* 2020; 36: 128–135.

Suggested answers

1. c.
2. a.
3. d.
4. b.
5. c.