Royal College of Paediatric and Child Health

Working Party on Sleep Physiology and Respiratory Control Disorders in Childhood.

Standards for Services for Children with Disorders of Sleep Physiology.

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1. Introduction

1.1 Justification and remit.

Despite the relatively high prevalence of sleep problems, awareness is poor amongst paediatricians surveyed in the US. Only 50% of questions relating to sleep disordered breathing were answered correctly and 44% of paediatricians routinely inquired about sleep problems in adolescents [1]. It is unlikely that awareness in UK paediatricians is any different; in a 1998 survey the median total time spent on undergraduate teaching on sleep and sleep disorders in UK medical schools was 5 minutes [2]. A recent survey of paediatricians by the British Paediatric Respiratory Society disclosed a chaotic and unplanned structure of services for sleep disorders in children, often unfunded and frequently perceived as inadequate for local needs [3].

This report presents evidence-based recommendations for the diagnosis and management of disorders of sleep physiology and respiratory control in children, and the organisation of such services nationally in the UK. While it recognises the importance of behavioural sleep disorders, the report does not discuss this area in details. Guidelines already exist for the diagnosis and management of Obstructive Sleep Apnea/Hypopnea Syndrome in adults [4]. Children are sufficiently different to justify a separate approach; they have more varied conditions presenting with sleep disordered breathing, with very different natural histories; they have far more protean and elusive symptoms; and they present different challenges in both diagnosis and treatment.

There are four main presentations which lead to the consideration of an underlying disturbance of sleep physiology or respiratory control. These are:

- symptoms suggesting airway or breathing problems during sleep;
- apparent life threatening events in infancy;
- diurnal symptoms suggesting disturbed sleep, including excessive daytime sleepiness;
- abnormal episodic behaviours during sleep in older children.

In addition, a number of conditions are known to be at high risk of such disorders even without suggestive symptoms.

The organisation of the clinical section of the report will therefore be according to these four presenting patterns of sleep and breathing impairment.

The report aims to aid parents, primary and secondary care physicians and surgeons to recognise the symptoms of sleep disorders, to prioritise referral requests, to identify groups who require screening for abnormalities, and to understand which investigations and treatment modalities are available and appropriate. It also aims to aid clinicians and health service managers involved in providing and commissioning services for affected children in prioritising such commissioning, and in organising pathways of care.

1.2 Overall methodology

For each symptom group a series of questions were asked:

1. What conditions are likely to present in this way?
2. For each conditions, what evidence exists for:
   a. Effective preventive measures in the population or in high risk groups?
   b. How the condition should be identified?
   c. How the condition should be managed
3. Are there any existing standards for any of the above
4. What key clinical information should be used to assess performance.

Literature searches of Medline (1950-2006) and the Cochrane database were performed as stated for each topic. CINAHL was used in some topics, but the additional yield was negligible. Hand searching of existing personal references and of relevant original and review articles was also used. Articles were considered relevant if they provided any evidence bearing on the questions above, relating to children. Statements are evidence-based as far as possible, and have been graded using the SIGN scale [4] for therapy, aetiology, prevention and harm, and the Sackett system [5] for prognosis, diagnosis and economic analysis. Recommendations were derived from discussion among working party members and then refined after further agreement with expert reviewers.

As with the SIGN guidelines, this report is not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor, following discussion of the options with the patient and parents or guardians, in light of the diagnostic and treatment choices available. However, it is suggested that significant departures from the recommendations contained in this report, or any local guideline derived from it should be fully documented in the patient’s notes at the time the relevant decision is taken.

Levels of evidence used, and grades of recommendations are detailed in Appendix 1, and grades of recommendations are summarised below to aid the reader.

The membership of the working party included clinicians from a number of related specialist areas in paediatrics: Respiratory, Neurology, Intensive Care, General and Community. Representatives were invited from the British Sleep Society, and the Association of Respiratory Therapists and Technologists, and from the Muscular Dystrophy Campaign and the Down’s Syndrome Association. A full list of the membership is given in Appendix 3.

In addition to the full report there are summaries of key points for clinicians and a number of lay summaries relating to the different clinical sections.
**GRADES OF RECOMMENDATION**

<p>| | |</p>
<table>
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| A | At least one meta-analysis, systematic review or RCT rated as 1++ and directly applicable to target population; or  
  a body of evidence rated as 1+ consisting mainly of RCTs and directly applicable to target population, and consistent. |
| B | A body of evidence including studies rated as 2++ directly applicable to target population, and consistent; or  
  Extrapolated evidence from studies rated as 1++ or 1+ |
| C | A body of evidence including studies rated as 2+ directly applicable to target population, and consistent; or  
  Extrapolated evidence from studies rated as 2++ |
| D | Evidence level 3 or 4; or  
  Extrapolated evidence from studies rated 2+ |
| E | Extrapolated evidence from studies rated 2+ |

**GOOD PRACTICE POINTS**

√  Recommended best practice based on clinical experience of working party
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADHD</td>
<td>Attention Deficit/Hyperactivity Syndrome</td>
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<tr>
<td>AHI</td>
<td>Apnoea/Hypopnoea Index</td>
</tr>
<tr>
<td>ALTE</td>
<td>Apparent life threatening event</td>
</tr>
<tr>
<td>BIPAP</td>
<td>Bilevel positive airway pressure</td>
</tr>
<tr>
<td>CCHS</td>
<td>Congenital Central Hypoventilation Syndrome</td>
</tr>
<tr>
<td>CPAP</td>
<td>Continuous positive airway pressure</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal Fluid</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiograph</td>
</tr>
<tr>
<td>MSLT</td>
<td>Multiple Sleep Latency Test</td>
</tr>
<tr>
<td>NIV</td>
<td>Non-invasive ventilation</td>
</tr>
<tr>
<td>NREM</td>
<td>Non-Rapid Eye Movement</td>
</tr>
<tr>
<td>OSA</td>
<td>Obstructive Sleep Apnea (includes obstructive hypopnea)</td>
</tr>
<tr>
<td>(P_aCO_2)</td>
<td>Arterial Carbon Dioxide tension</td>
</tr>
<tr>
<td>(PtcCO_2)</td>
<td>Transcutaneous Carbon Dioxide tension</td>
</tr>
<tr>
<td>(P_eCO_2)</td>
<td>End-tidal Carbon Dioxide tension</td>
</tr>
<tr>
<td>PIRCM</td>
<td>Paradoxical Inward RibCage Movement</td>
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<td>PLMD</td>
<td>Periodic Leg Movement Disorder</td>
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<tr>
<td>PRS</td>
<td>Pierre Robin sequence</td>
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<tr>
<td>PSG</td>
<td>Polysomnography</td>
</tr>
<tr>
<td>PTT</td>
<td>Pulse Transit Time</td>
</tr>
<tr>
<td>PWS</td>
<td>Prader Willi Syndrome</td>
</tr>
<tr>
<td>REM</td>
<td>Rapid Eye Movement</td>
</tr>
<tr>
<td>RLS</td>
<td>Restless Legs Syndrome</td>
</tr>
<tr>
<td>SOREM</td>
<td>Sleep onset with REM</td>
</tr>
<tr>
<td>SRBD</td>
<td>Sleep-Related Breathing Disorder</td>
</tr>
<tr>
<td>SpO2</td>
<td>Oxygen saturation measured by pulse oximetry</td>
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<tr>
<td>UARS</td>
<td>Upper airway resistance syndrome</td>
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1.3 **Sleep physiology and developmental changes in childhood**

Any attempt to understand or interpret findings from recordings of breathing during sleep in any child depends on a detailed knowledge of the normal patterns of physiological development during sleep and wakefulness for children of that age.

The newborn infant spends 16-18 hours per day asleep, around 60% of which is in Rapid Eye Movement (REM) Sleep. By the age of 1 year this has fallen to 12-15 hours, with around 30% being REM. From about 3-4 months of age sleep is gradually consolidated into more continuous periods, mostly during the night time hours. The nature of sleep also changes over this age period, with the appearance of differentiation between stages 1-2 and 3-4 non-REM sleep by about 4 months [6]. With increasing age further changes occur, with further shortening and consolidation of the night time sleep period, and reduction of daytime sleep duration such that by the age of 3 years around 45% of children take a regular daily day-time nap, whilst by 5 years of age this has fallen to less than 10%. The distribution of sleep states during day and night time sleep periods also changes with age: at 2 years of age children spend a higher proportion of time in stage 4 non-REM sleep during the day than during the night [7-9]. The function of the different stages of sleep is unclear, but REM sleep (the predominant state during fetal and early post-natal life) may be a basic activation programme for the central nervous system that increases the functional competence of neurons, circuits, and complex patterns before the infant is called upon to use them. The maturation of Quiet Sleep (non-REM sleep) coincides with the formation of thalamocortical and intracortical patterns of innervation and periods of heightened synaptogenesis, and synaptic remodelling. Several studies have shown that information acquired during wakefulness is further processed during both REM and Quiet sleep [7, 8].

During mid to late childhood further changes in the organisation and duration of sleep continue, with a reduction in total sleep time from an average of around 11 hours at 5 years to 8 hours at 16 years [9].

Within sleep the duration of the REM/non-REM cycles also changes, from around 50 minutes in early infancy to 60 minutes at 6 months and to the adult period of 90 minutes during late childhood to early adolescence [10].

During sleep there are marked differences in physiology between different states, and between sleep and waking. During REM sleep, metabolic rate is higher than during non-REM sleep, and in humans (unlike most non-primate mammals) there is active thermoregulatory activity, with a vigorous metabolic response to cold stress [11]. In contrast, during non-REM sleep, the metabolic response to cold stress is less marked, but the ventilatory responses to mild hypoxia or hypercarbia are more marked than in REM sleep. From the age of 3-4 months infants exhibit a fall in body temperature during the early part of the night, followed by a slow rise thereafter; the falls in temperature are oscillatory, being more marked in non-REM sleep [12, 13].
During REM sleep there is inhibition of muscle tone, particularly in postural muscles, with a resulting lack of activity in the intercostals muscles and the abdominal oblique and transversus muscles. In young infants this results in the appearance of intercostals recession during REM sleep as a normal phenomenon, even in the absence of airway obstruction or increased upper airway resistance. Such a pattern is commonly seen in children up to the age of 3 years [14]. At all ages muscle tone in the muscles of the pharynx and upper airway – particularly genioglossus - is reduced or absent in REM sleep, and may result in airway obstruction particularly in the supine position during REM sleep. Infants with relative macroglossia and micrognathia (e.g. Robin anomalad) are at particular risk of such obstruction. Other changes which occur during REM sleep include a reduction and instability of functional residual capacity and increased variability of respiratory rate, heart rate and oxygen saturation [15-17].

1.4 Behavioural sleep problems

The prevalence of behavioural sleep problems, including bedtime resistance and sleep phase disturbances, is high. Moderate or severe sleep problems are reported in 17% of 1 year old children [18], and some form of sleep problem is present in 20% of 5 year olds and 6% of 11 year olds [19]. There is a perceived lack of services for such problems (BPRS survey, 2002). There can be considerable diagnostic difficulty between primary behavioural sleep disorders and those arising from sleep disordered breathing, and it is important that any centre which offers assessment of the latter should have some facilities to deal with behavioural sleep disorders either on site or by onward referral. However, the management of behavioural problems is outside the scope of this report, and will not be considered further here.

1. Any centre which offers assessment of SRBD should establish some resource to deal with behavioural sleep disorders either on site or by onward referral.

1.5 General effects of sleep impairment

A randomised controlled trial showed that higher cognitive function is impaired after experimental sleep restriction in 10-14 year old children in the absence of sleep disordered breathing [20] (level 1). Multiple sleep latency tests (MSLTs) were abnormal after sleep deprivation, with low sleep onset latency (8.5 mins) and increased REM episodes [20].

In a questionnaire survey of sleep habits in US adolescents, associations were found between shorter self-reported total sleep times and poor school performance, negative moods, difficulty controlling emotions and behaviour problems [21]. A survey of 450 students aged 11 – 15 showed associations between daytime sleepiness (measured on a questionnaire scale) and low school achievement, absenteeism, low school enjoyment, low total sleep time and frequent illness [22]. While these associations between impaired daytime functioning and sleep restriction have not been shown to be causal, they are consistent with the experimental findings of sleep deprivation cited above.

Sleep disordered breathing is also associated with daytime dysfunction. In children whose academic performance was poor (lowest 10th centile), 18% were found to have objective evidence of sleep disordered breathing [23]. Furthermore a much higher
incidence of snoring at 2-6 years of age was found in children with poor academic performance at 7-8th grade compared with children with high academic performance raising the concept of long term harm resulting from airway obstruction in earlier childhood [24]. In a community based study of 1144 children, poor academic performance was significantly associated with snoring. There was a dose response relationship between the frequency of snoring and performance [25]. Some aspects of performance were independent of hypoxia, suggesting that poor sleep quality was a more likely mediator, but the depth of the saturation nadir was predictive of poor mathematics performance, with a dose-response effect [26]. Similar data have been obtained from community-based surveys of 835 children [27] and 1014 adolescents [26] showing negative associations between snoring/SRBD on cognition, achievement, attentiveness and grade point averages with an amplified effect in children born prematurely. In two case-control studies children with snoring or minor obstructive sleep apnoea, but insignificant gas exchange abnormalities had worse scores for attention, memory and intelligence than matched controls [28, 29]; these impairments were correlated with measures of sleep disturbance [28]. (Level 2++) A community survey of 4-5 year old children observed poorer parental ratings for attentiveness and behaviour in children with documented sleep disordered breathing [30]. Arousals and sleep fragmentation were predictors of neurocognitive impairment in children with OSA in a case-control study [29]. (Level 2++) Deleterious effects on development of snoring without OSA have also been described in infants [31]. A recent well-conducted systematic review of the literature on behaviour, neurocognition and quality of life in children with SRBD concluded that “there is compelling evidence that sleep-disordered breathing in children is associated with behavioural and neurocognitive problems and leads to reduced quality-of-life. In addition to improvements in sleep, adenotonsillectomy is associated with improvements in behaviour, neurocognition and quality-of-life in these children. However, the lack of uniform criteria for the diagnosis of sleep-disordered breathing in children and variation in methods used to assess the outcome of surgical therapy limit our current knowledge and should be addressed by future research. The high prevalence of sleep-disordered breathing in children should make this research a public health priority.” [32]

**Conclusion**

Inadequate sleep duration or quality leads to impairment in attention, memory, behaviour, and school performance.
2. **Methodology of assessment.**

This section will confine itself to the methodological issues regarding different methods of assessment of sleep and breathing. More detailed discussion of utility of different methods in diagnosing specific conditions will be dealt with under each condition. The purposes of sleep studies for cardiorespiratory disturbances include the assessment of adequacy of ventilation; the identification of different types of respiratory disturbances (e.g. central vs obstructive apnoea); the assessment of cardiac rate and rhythm; and the assessment of the sleep stages in which any disturbances occur. When the degree of sleep disruption is being assessed, or in children with other sleep symptoms it may be necessary to assess sleep architecture, arousals, periodic leg movements and the presence of epileptic activity. In addition, studies of children on non-invasive ventilation will need the facility to measure ventilator pressure waveforms.

*Search strategy:*
*Medline (1966-Dec 2006) search of polysomnography (subheadings: methods / instrumentation / standards), limited to “all child 0-18 years”.*

*Specific searches on individual methodologies*

*Secondary search of references in relevant articles.*

2.1 **Adequacy of Ventilation**

2.1.1 **Arterial Oxygenation**

Measurement of oxygenation is the simplest method of assessing ventilation during sleep. It has the advantage of a robust, non-invasive measurement device but is insensitive to minor degrees of hypoventilation in children with normal lungs. The mainstay of assessment of oxygenation is pulse oximetry, which is well-tolerated, and non-invasive. The sensor is incorporated into a soft cuff that fits around a finger or toe or clips to an ear lobe. Arterial oxygen levels from a pulse oximeter ($S_pO_2$) have been shown to correlate well with measurements of arterial blood gases down to $S_pO_2$ of 70%, provided there is a good arterial pulse wave form at the probe site and the signal is free of movement artefact [33, 34]. There is a significant time delay between changes in ventilation and changes in $S_pO_2$, due partly to the electronic processing of the signal to minimise artefact, and partly to the circulation time from the lungs to the probe site. Oximetry is also affected by movement artefact and by poor tissue perfusion. Visualisation of the pulse waveform improves the differentiation of genuine desaturations from artefact [35].

Widely used criteria of abnormality in nocturnal oximetry recordings are falls of >4% below baseline and desaturations below 90%; abnormal clusters of 4% desaturations have been defined as 5 or more in a 30 minute period [25, 36]. Normative values for baseline $S_pO_2$ levels at night have been published for infants [37-39] and school age children [39, 40]. These studies show that baseline $S_pO_2$ does not increase with age after the first week of life, although desaturations and periodic breathing may be more frequent in early infancy. It should be noted that different oximeters, averaging times and storage algorithms may give different results [41-45], and there are no data confirming the level of abnormality which will predict a clinical benefit from intervention.
In children outside infancy a normal oximetry recording should have:

a) A median $S_pO_2$ level $\geq 95\%$.

b) No more than 4 desaturation of 4% or greater per hour.

c) No abnormal clusters of desaturation.

2. Oximetry recordings should only be performed by clinicians who are skilled in interpretation of the results, and systems should allow graphical inspection of recordings, with adequate facilities for artefact rejection.

Transcutaneous oximetry has been used as an alternative method of assessing oxygenation. However, the inaccuracy of the absolute values, a response time which is even slower than a pulse oximeter, and the need to re-site the heated probe every 3-4 hours makes it much less useful in practice, and it cannot be recommended as a sole indicator of oxygenation in sleep studies.

2.1.2 Measurement of carbon dioxide

The assessment of arterial $CO_2$ tension is an important adjunct to the detection and quantitation of hypoventilation. This can be done indirectly using end-tidal carbon dioxide or transcutaneous $CO_2$ measurements. A non-invasive estimate of alveolar $PCO_2$ levels may be made from the $PCO_2$ value measures at the nose or mouth during the last fifth of expiration. This is termed the end-tidal $PCO_2$ ($P_eCO_2$). This is a reasonable approximation of arterial $PCO_2$ ($P_aCO_2$) in subjects with healthy lungs and unobstructed breathing [46]. Obtaining $P_eCO_2$ measurement is technically difficult, as it requires precise positioning of the probe at the airway opening and maintained vigilance throughout the sleep study to ensure a satisfactory signal. The quality of the signal can be determined from its shape; an end-tidal plateau generally indicates a reliable signal. The signal needs to be interpreted with caution in subjects with lung disease or high respiratory rates, as end-tidal levels will underestimate $P_aCO_2$; in the latter case the error should be evident from the shape of the $PCO_2$ trace. End-tidal $CO_2$ recordings have the advantage that they also provide an indicator of airflow on a breath-by-breath basis.

An alternative non-invasive measure of $PCO_2$ is that of transcutaneous recording ($P_{tc}CO_2$). In this instance, a heated $PCO_2$ electrode is affixed to the skin surface on the chest wall or abdomen. The electrode makes direct recordings of the levels of $CO_2$ diffusing through the skin from the subcutaneous blood vessels. Heating of the site aims to increase local blood flow to make capillary blood gas levels similar to arterial. In adults, the accuracy of $P_{tc}CO_2$ in reflecting $P_aCO_2$ is only moderate, with limits of agreement having a 15 mm Hg (2 kPa) range[47]. Transcutaneous monitoring has been shown to be valuable in infants and young children, but will not give an accurate measure of $paCO_2$ unless calibrated against an arterial blood gas measurement for each individual [48]. Accuracy is decreased by $CO_2$ retention [49]. The limitations of $P_{tc}CO_2$ measurements lie in their inability to detect rapid or transient changes in $PCO_2$; their main strength is in their ability to follow a long term trend. Furthermore, in older children raw $P_{tc}CO_2$ measurements may not reflect true $P_aCO_2$ levels, although the difference tends to remain constant, allowing the monitoring of trends in $PCO_2$ levels.
Because prolonged partial airway obstruction and obstructive hypoventilation forms an important component of obstructive sleep apnoea syndrome in children, PetCO$_2$ and/or PtcCO$_2$ measurements are considered essential for paediatric sleep apnoea syndrome assessments; the use of both modalities in the same subjects increases the number of periods in which CO$_2$ data are available [48, 50].

3. For any investigation of SRBD other than screening studies a measurement of CO$_2$ is essential, and the use of both end-tidal and transcutaneous modalities reduces the number of epochs with unobtainable data and is therefore recommended.

The main disadvantage of P$_{et}$CO$_2$ measurements is the necessity of attaching the probe to the facial region which may be poorly tolerated. It is possible to pick up false obstructive events when the P$_{et}$CO$_2$ signal is lost either because the probe is displaced or the patient adopts mouth breathing. This can be avoided by not relying on P$_{et}$CO$_2$ alone, but to look for corroborative information from other channels (e.g. increased paradoxical movements of rib cage and abdomen, or decreased S$_p$O$_2$ or P$_{tc}$O$_2$).

### 2.2 Evaluation of respiratory disturbance

#### 2.2.1 Respiratory airflow

Several techniques are available – an adult summary statement concluded that there were insufficient data to allow recommendations regarding standardisation of instrumentation [51]).

**Quantitative measures.** A pneumotachograph can be attached to nasal prongs, oronasal mask or tracheostomy tube. This gives quantitative assessments of flows, volumes and timings, and may be important in a research setting, or in assessing central hypoventilation. However, from a clinical perspective the technique is little used as it is technically difficult, disruptive to the patient and may be poorly tolerated. Also in infants and children, in particular, the added dead space of the equipment may have an influence on breathing patterns [52, 53].

**Qualitative measures.** Oronasal or nasal thermistors, or nasal CO$_2$ catheters are the most commonly used techniques to detect respiratory airflow. The main disadvantage of these methods is that they require connection to the facial area, which disturbs many children and may be poorly tolerated. In addition the measurements are not quantitative, and thermistors may not reliably detect periods of hypopnoea (partial obstruction with decreased tidal volume) [54]. The sensitivity of thermistors is dependent on make [54]. Pressure transducers attached to nasal cannulae have recently been shown to be useful in identifying airflow interruption, and may be more sensitive to hypopnoea than thermistors, although they are also more prone to displacement, and the best results are gained from a combination of sensors [54-58]

Respiratory inductance plethysmography has been used as an indirect method to quantify airflow (see below).
Sounds recorded by a laryngeal microphone can be used to detect snoring and the presence or absence of airflow in patients with upper airway obstruction [59, 60]. However, the technique is limited as it can only detect complete obstruction (apnoea) and cannot detect partial obstruction (hypopnoea). Sound recordings also give information on the volume and quality of snoring, but snoring history does not quantitate the ventilatory disturbance in children [61]. It is nevertheless useful to have an indication of snoring to correlate temporally with episodes of respiratory disturbance or arousals.

2.2.2 Respiratory Movement / Effort
Oesophageal pressure is the optimal technique for detection of respiratory effort, but is an invasive technique which is not popular among children or parents. When determined efforts were made to pass oesophageal catheters they were only feasible and acceptable in 73% of school age children [62]. In addition, the presence of an oesophageal catheter may cause sleep disruption and result in a sub-optimal study [63]. Non-invasive techniques are usually adequate for clinical purposes, and should assess both thoracic and abdominal effort, to allow detection of thoraco-abdominal asynchrony. A semi-quantitative measure of airflow and tidal volume can be derived from respiratory inductance plethysmography (RIP). This non-invasive technique uses a pair of inductance bands placed around the rib cage and abdominal compartments to detect respiratory excursions allowing volumes and flows to be derived [64]. This method may allow detection of obstructive apnoeas and hypopnoeas as well as central respiratory events. Calibration is necessary to set the gain factors for the thoracic and abdominal components to make the sum equivalent to tidal volume [64-66]. The technique has been demonstrated to work well in detecting obstructive and partially obstructive events in children and adults [67, 68], and for measuring tidal volume in infants [69]. However the calibration is influenced by body position [70] and may be invalid in a subject who sleeps in a number of different positions [71]. RIP alone is not as sensitive as thermistor or capnography in the detection of apnoea in infants [72]. Hypopnoea is best detected by a combination of RIP and nasal pressure transducers [54].

Qualitative measurements of chest and abdominal movements may be made with strain gauge bands placed round the chest and abdominal compartments. These are not calibrated and are therefore not capable of giving measurements of tidal volume or minute ventilation. However they are able to show distinct patterns associated with central apnoea, obstructive apnoea and increased work of breathing. Transthoracic impedance is frequently used to record respiratory efforts in apnoea monitors for hospital or home use. However, this technique is not capable of detecting obstructed breathing [68] and hence is not recommended for sleep laboratory recordings.

2.3 Assessment of cardiac rate and rhythm.
Cardiac rate can be derived from a pulse oximeter. However, it is subject to movement artefact and will not give information on cardiac rhythm. A simple single lead ECG should therefore be used to monitor cardiac rate and rhythm to enable cardiac arrhythmias and changes resulting from respiratory disturbances to be assessed.

4. A single lead ECG is recommended as a minimum for second-line
2.4 **Assessment of sleep state.**

In infants below the age of 6-12 months, sleep staging is generally behavioural, and can be done by visual means, but more accuracy can be achieved using information on muscle tone or movement, stability of R-R interval, respiratory channels and EEG patterns as adjunctive information [73]. No data are available on inter-observer reliability of behavioural sleep staging.

In older children it is important to have a more detailed neurophysiological assessment of sleep stage, in particular to ensure that periods of REM and slow-wave sleep have been recorded. The methodology for this is well described by Rechtschaffen and Kales [74]. The following parameters are required for sleep staging in this age group:

**2.4.1 Electroencephalogram (EEG)**

The International 10-20 system of electrode placement is used to determine surface electrode placement [75]. When EEG is limited to one derivation, the recommended derivation is C4/A1 or C3/A2 [74]. The addition of O1/A2 or O2/A1 is often used to assist in detecting alpha activity associated with the sleep-wake transition [76].

**2.4.2 Electrooculogram (EOG)**

Eye movements are detected by placing surface electrodes near the outer canthus of each eye. The EOG electrodes should be offset from horizontal, one slightly above and one slightly below the horizontal plane to detect both horizontal and vertical eye movements [74, 76].

**2.4.3 Electromyogram (EMG)**

2 surface electrodes are placed either on the mentalis or submentalis to detect muscle activity.

**2.5 Other Measurements**

**2.5.1 Body Position**

Information on body position may be of significance, particularly in patients with upper airway obstruction where the severity of obstruction may be affected by body position. In contrast to adults, children have been found to maintain airway patency better in supine [77]. Abrupt changes in body position may also be useful in identifying arousals and sleep disturbance. Position may be determined from direct observation, video records or from a position sensor attached to the subject. The sensor normally comprises a small capsule attached to the chest wall which electronically senses the patients position (upright, supine, prone, left or right sided). The advantage of the sensor is that it gives a continuous record and shows precisely the time of any positional changes.
2.5.2 Limb movements
Gross body movements and limb movements may be assessed from direct observation, a video record or from recordings of a peripheral EMG recording (see below), or from accelerometer capsules attached to the wrist or ankle (actigraphy). These may be of use in detecting the extent of sleep disturbance, or arousal frequency, and are necessary for assessment of sleep state in infants.
Monitoring the EMG from a leg muscle (conventionally Tibialis anterior) is a useful measure of peripheral skeletal muscle tone and allows assessments of gross body movements and arousals during sleep. Leg EMG can be used to detect PLMS, but actigraphy is not an adequate substitute in children [78].

2.5.3 Oesophageal pH
Gastro-oesophageal reflux may present an important problem in some infants. To assess the extent of the problem and to look for associations between reflux events and changes in cardio-respiratory patterns, it is necessary to have a continuous record of oesophageal pH during the sleep study. Oesophageal pH can be measured with an indwelling pH sensitive catheter passed via the nose and placed in the lower oesophagus [79]. The occurrence of spontaneous reflux episodes should be noted. It should be noted that normative data for reflux indices are based on 20-24 hour recordings, while sleep studies are generally of shorter duration. Disadvantages of simultaneous pH recordings are that the presence of an oesophageal pH probe alters the sleep pattern and respiratory events in infants [63] and in addition, the temporal correlation between reflux events and respiratory events may be poor. The latter point may be improved by the introduction of systems to detect non-acid reflux [80].

2.5.4 Video and sound recording
Good quality video recordings are an important component of a clinical sleep study, and can be made using infra-red or low-light cameras and appropriate microphones. Video and sound recordings can provide useful information on sleep behaviour, snoring, sleep disturbance, breathing patterns. Video can be used to distinguish sleep from wake and can be analysed to detect movement arousals [81]. Snoring can be recorded directly by a microphone in the suprasternal area, or by a bedside microphone.

2.6 Interpretation
An evidence-based manual for scoring sleep in adults and children has been issued recently by the American Academy of Sleep Medicine, and should be referred to for the technical aspects of scoring a polysomnogram [82].

2.6.1 Breathing and heart rate.
Normal values for heart rate [83, 84], respiratory rate [83, 85-88], and oximetry [37, 39, 40] are available for different ages. The movements of rib cage and abdominal compartments are usually in phase. During inspiration, both compartments expand, whilst during expiration they both move inwards. Rib cage contribution, as a percentage of tidal
volume, increases over the first year of life to reach the level seen in adolescents and adults [52].
Paradoxical respiratory movements (Paradoxical Inward Rib Cage Movement, PIRCM) are seen in premature neonates, in term neonates with abnormal respiratory mechanics, and in infants during REM sleep. PIRCM during REM sleep decreases with age, and it is uncommon in non-REM sleep in children over 3 years [89]. PIRCM may be a response to an increased respiratory load [90], or due to diaphragmatic or intercostal muscle impairment. In the absence of other explanations it is suggestive of partial or total upper airway obstruction during sleep.
Parental reports of habitual snoring correlate well with objective recordings [91], but snoring is not a good predictor of OSA [92, 93]. However, temporal associations between snoring and arousals or respiratory events may be helpful in assessing the overnight study.

2.6.2 Respiratory events
Adult criteria for identification of obstructive events should not be used for children, as they may fail to identify clinically significant obstruction.
Obstructive apnoea is the absence of oronasal airflow in the presence of continued respiratory effort. The significance of the apnoea duration depends on the background respiratory frequency, and a duration of 2 respiratory cycle times is a useful measure which corrects for this [94]. However, the majority of children with significant gas exchange abnormalities during sleep do not have repeated complete obstructive events, but show a pattern of obstructive hypoventilation, with cyclical decreases in SaO2, hypercarbia, and paradoxical respiratory efforts [95, 96].
Obstructive hypopnoea is a >50% reduction of airflow in the presence of continued respiratory effort. Paradoxical respiration (thoracic-abdominal asynchrony) and gas exchange abnormalities are often seen as additional features. If evidence of significant hypercarbia is present then it is better described as obstructive hypoventilation.
If hypopnoea or hypoventilation is present with a concomitant decrease in respiratory effort, then it is non-obstructive (for more details of criteria see [94, 97]).
Any respiratory event associated with a significant fall in SaO2 or heart rate should be considered abnormal. Reference values for duration and frequency of respiratory events at different ages are available [86, 97-99].

2.6.3 Sleep staging and arousals
Arousals may be assessed by EEG changes or by other physiological indicators.
Physiological indicators include movement [74, 81] or indices of autonomic arousal such as pulse transit time (PTT) [100] or peripheral arterial tonometry [101]. The different indicators of arousal are correlated with each other, but in children with OSA, 20-25% of either movement or EEG arousals occur without the other being present [102]. In contrast to Mograss [81], who found nearly all obstructive events in 14/15 children with OSA to be terminated by EEG arousals, McNamara [103, 104] found this in only a minority of obstructive events in infants and children. Using detailed respiratory assessment including oesophageal manometry in 34 children, Katz [100] has observed about 50% of obstructive events were associated with an EEG arousal, and that PTT arousal was a more
sensitive and specific indicator of a respiratory obstructive event than EEG arousal. This suggests that PTT may offer a useful surrogate indicator of SRBD, although the clinical importance of different types of arousal on morbidity in children has yet to be established.

Determination of arousals from EEG is not simple. The most robust algorithm for arousal identification is that put forward by the American Sleep Disorders Association [105, 106]. Normative data for EEG arousals [106] and sleep architecture [107-109] in children are available. A simplified modification of infant EEG arousals has been found to give excellent inter-rater agreement after training [110]. Arousals should be categorised as respiratory, technician-induced or spontaneous [81]. Although most modern polysomnography systems offer automated event detection, this remains poorly validated at present, particularly for paediatric use.

<table>
<thead>
<tr>
<th>5. Visual review of the complete recording should be undertaken by a competent observer before a report is issued.</th>
</tr>
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</table>

### 2.7 General Methodology of studies

Three general types of study may be needed:

- **Screening studies** - used to screen for major abnormalities in a high risk population, or as a preliminary assessment of children with obstructive symptoms.
- **Second-line studies** - used to assess children where the diagnosis is in doubt or where treatment decisions cannot be made on the basis of screening studies.
- **Third line studies** - used to assess children where knowledge of sleep neurophysiology and architecture is important to decision-making or diagnosis.

#### 2.7.1 Timing and duration.

While daytime nap studies are more convenient than overnight studies, they have a number of disadvantages: they are behaviourally abnormal in most children over 4 years old, they may not include adequate periods of REM and non-REM sleep, and ignore circadian variability in physiology. In two series comparing nap study with PSG, using chloral hydrate sedation [111, 112], nap studies were found to have a high specificity, but low negative predictive values (17-49%). Severe adverse events have been reported after the use of chloral hydrate in children with OSA [113], and nap studies using sedation cannot be recommended. An alternative method of inducing naps is by sleep deprivation, but this can exaggerate SRBD in infants [114].

| 6. A study of the whole night is the recommended investigation to assess sleep disordered breathing. A minimum of 6 hours sleep is desirable. | ✓ |

#### 2.7.2 Number of studies

A “first night effect” has been described in adults, whereby sleep differs during the first night in a sleep laboratory compared to subsequent nights [115]. Two studies assessing this in children [102, 116] have shown that SRBD parameters are no different between the first and second nights, but differences in sleep architecture were found, more marked in one study [102] than the other (Level 2++).

| 7. A single night study is generally sufficient to assess SRBD. | B |
| 8. Abnormalities in sleep architecture require a second night study for reliable diagnosis. | C |
2.7.3 Measurement conditions and reporting of results

For screening, including variables such as oximetry, capnography, actigraphy and video or audio, unattended home recordings are relatively simple and likely to be more representative of the child’s normal sleep. Home cardiorespiratory studies or PSG has been advocated by some centres [117-119], but others have reported less success [120]. A detailed systematic review of the utility and performance of home and hospital diagnostic studies for sleep apnoea in adults has been conducted [121], but there are few published data for children. Factors which may affect the success and diagnostic accuracy of home monitoring include the specific system used, the specifics of the home environment and the cooperation of the parents; it is also likely to depend on whether the technician or the parent is responsible for sensor placement. It is not therefore possible to make a general recommendation about the usefulness of home studies, although they are clearly more desirable if demonstrated to be of adequate diagnostic accuracy.

Unattended, or partially attended studies in hospital are more common in the U.K. than elsewhere in the world, perhaps due to limited resources. There are no studies documenting the difference in diagnostic accuracy of attended compared with unattended studies in a hospital setting. The presence of video recording is likely to make the interpretation of unattended studies more robust.

It should go without saying that a sleep study can only be performed in a quiet environment, where a child is likely to have reasonably representative sleep. This requires a separate cubicle in a quiet area. Studies cannot be done on an open ward. Because both the equipment, the surroundings, and the interpretation of findings are different in children, and because of the possible need for resuscitation in these patients, it is strongly recommended that all in-patient sleep studies on children are undertaken by staff with adequate training and experience in paediatrics, and in an environment where paediatric resuscitation facilities and skills are readily available. If children are studied in a primarily adult laboratory, it is strongly recommended that a paediatrician with expertise in paediatric sleep medicine oversees the laboratory operations related to children and is involved in the interpretation of results [14].

<p>| | |</p>
<table>
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<tbody>
<tr>
<td><strong>9.</strong> All in-patient sleep studies on children should be undertaken by staff with adequate training and experience in paediatrics and in an environment where paediatric resuscitation facilities and skills are readily available.</td>
<td>✓</td>
</tr>
<tr>
<td><strong>10.</strong> If children are studied in a primarily adult laboratory, a paediatrician with expertise in paediatric sleep medicine should oversee the laboratory operations related to children and be involved in the interpretation of results.</td>
<td>✓</td>
</tr>
<tr>
<td><strong>11.</strong> Sleep studies should only be done in a suitable, quiet environment where normal sleep is possible.</td>
<td>✓</td>
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</table>

Detailed suggestions for parameters which should be reported in a paediatric sleep study have been made by the American Thoracic Society [14].

**Table 2. Recommendations for minimum standards of equipment available.**

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>Ideal</th>
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<tbody>
<tr>
<td>Screening (first line) studies:</td>
<td>Oximetry (adequate storage and replay, with good artefact detection)</td>
<td>CO2 measurement Video and sound Arousal detection</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Second line studies</td>
<td>Above plus: Airflow Effort (thorax and abdomen) ECG Surrogate pCO2 measurement Video and sound Arousal detection</td>
<td>Sleep staging Body position</td>
</tr>
<tr>
<td>Third line studies</td>
<td>Above plus: EEG/EOG/EMG Assessment of PLMS oesophageal pH</td>
<td></td>
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</table>
3. Airway and breathing problems during sleep

3.1 Obstructive sleep apnoea (OSA) and hypoventilation

Search Strategy

Medline 1950-Dec 2006, and Cochrane Database of Systematic Reviews
(Sleep apnoea) or (obstructive sleep apnoea) or (sleep disordered breathing) or (snoring) or (adenotonsillectomy) or (upper airway resistance), limited to “all child 0-18 years” Secondary search of references in relevant articles.

3.1.1 Prevalence of OSA

There is a continuum of upper airway obstruction ranging from snoring to obstructive sleep apnoea/hypopnoea syndrome. Primary snoring is defined as reported snoring without obstructive apnoea, frequent arousals, or gas exchange abnormalities [122]. The prevalence of reported snoring most or every night in 4-5 year old UK children is 12% [123], and remains at a similar level at 7 years, although only half the children snore at both ages [124]. Similar prevalence levels were found in 8-10 year old German children [25, 125]. In a large interview-based survey of adolescents and their parents in the USA, 6% were reported to have habitual snoring [126]. Using a variety of definitions, not all based on formal polysomnography, the prevalence of obstructive sleep apnoea in the general population is between 0.7% and 2.9% [123, 127-129]. The prevalence in morbidly obese children is considerably higher at 13% [130]. It also appears more common in lower socio-economic groups [131].

Diagnosis is often delayed, with up to 31% of patients waiting more than 4 years respectively until treatment was instigated and 40% self referring despite their primary care physician being aware of their symptoms [132].

Although the majority of children with OSA have no underlying condition, there are a number of conditions in which SRBD is common and consequent morbidity more likely (Table 3).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
<th>Prevalence of SRBD</th>
<th>Other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down’s syndrome</td>
<td>1:1,000</td>
<td>70-100%</td>
<td>High risk of pulmonary hypertension, especially if co-incident heart disease.</td>
</tr>
<tr>
<td>Neuromuscular Disease</td>
<td>1:3,000</td>
<td>42%</td>
<td>Difficult to detect clinically. Reduced life expectancy, reversible by treatment.</td>
</tr>
<tr>
<td>Craniofacial abnormalities</td>
<td>1:7,000</td>
<td>Depends on severity; 100% in severe cases</td>
<td></td>
</tr>
<tr>
<td>Achondroplasia</td>
<td>1:25,000</td>
<td>48%</td>
<td></td>
</tr>
<tr>
<td>Mucopolysaccharidoses</td>
<td>1:40,000</td>
<td>&gt;90%</td>
<td>Difficult to detect clinically.</td>
</tr>
</tbody>
</table>
3.1.2 Presenting features of OSA

Night time Features

Symptoms and signs at night which may suggest OSA include snoring, gasps, snorts, witnessed apnoeas, restlessness and laboured breathing. These may be associated with unusual sleep postures such as an extended neck position. Early morning headache and excessive sweating may be features of CO₂ retention. The loudness of snoring does not predict the severity of obstruction. Unusually, carers may witness cyanosis. Enuresis is more common in children with OSA on polysomnography [133].

Daytime Features

The frequent arousal as a consequence of OSA result in fragmentation of sleep especially in REM and this will present with features of sleep deprivation. It is important to emphasise that these can be very non specific and overlap with many feature seen in normal children. Tiredness and irritability on awakening may be reported but excessive daytime tiredness persisting through the day is unusual. Children may have behavioural problems, poor concentration and poor academic performance. Failure to thrive may result from OSA [134, 135] (Level 3). Physical signs suggesting upper airway compromise include nasal obstruction, mouth breathing, adenoidal facies and nasal speech. Examination of the throat may reveal enlarged tonsils, although these are common in normal children. Enlarged tonsils do not predict adenoidal enlargement [136]. While adenoid or tonsillar size has been shown to correlate with OSA in some studies [127, 136-139], others have not found this association [140, 141]. There may be other craniofacial features that may compromise airway calibre such as retrognathia, high arched palate, midface hypoplasia, nasal polyps, deviated nasal septum or choanal stenosis. Harrison’s sulci may result from persistent upper airway obstruction. Marked obesity is associated with OSA in cross-sectional studies [136, 142, 143]; another study found obesity to be equally common in children with snoring and OSA, but more than twice as prevalent than in the general population [144]. In children with predisposing conditions (see Table 3) the presence of SRBD may be clinically impossible to detect and progression insidious; screening may be the only way of detecting SRBD. Similarly in young infants where behavioural sleep and daytime problems are common clinical diagnosis may be difficult and objective evaluation is more often indicated.

3.1.3 Consequences of OSA
Serious morbidity was described in early reports of OSA including failure to thrive, cor pulmonale and mental retardation [96] (Level 3). Failure to thrive in infancy has been confirmed by other reports [135] and was found in 52% of infant under 18 months who had undergone adenotonsillectomy for OSA, 87% of whom had significant increase in weight velocity after surgery [134]. Reversible short stature has also been described [145]. Whilst most children with OSA are not frankly failing to thrive, several further studies of confirmed OSA have shown substantial improvement in weight gain after adenotonsillectomy [146-148] (Level 3).

A wide variety of cardiovascular effects have been described ranging from cor pulmonale and pulmonary oedema [149-153] (Level 3), changes in cerebral blood flow (Level 2-) [154], diastolic hypertension [154-156] (Level 2+), and changes in ventricular mass/dimension [157-159] (Level 2+), all reversible after relief of the obstruction. Raised levels of brain natriuretic peptide presumably due to ventricular strain have also been observed [160].

There appear to be substantial effects of OSA on behaviour even in those with very mild airway obstruction [28, 123, 161-163] with improvement with adenotonsillectomy [162, 164-167] (level 2+). In contrast to adults, daytime sleepiness is not a common symptom except in severe cases and those with obesity [168]. The potential effect on neurodevelopment are of particular concern, although the mechanism and causality have not been clearly established (see Section 1.4 for further details.)

There is some evidence for an inflammatory process in OSA. Case-control studies have found raised plasma levels of C-reactive protein [169, 170] and interferon-γ [171], increased sputum neutrophils [172], increased inflammatory mediators in exhaled breath condensate [173] and differences in urinary protein expression [174] in children with OSA. Increased expression of glucocorticoid [175] and leukotriene [176] receptors in adenotonsillar tissue of children with OSA have also been described. However, another study of 141 children with and without OSA found no difference in C-reactive protein levels between groups [177].

Two case-control studies conducted in Israel by the same group have compared health care utilisation in children with OSA prior to diagnosis with matched controls. They found a 226% increase in health care utilisation in the year before diagnosis and a 215% increase from birth to diagnosis [178, 179] (Level 2++).

Conclusions
OSA can cause reversible failure to thrive, and is associated with systemic hypertension, increased left ventricular mass, and changes in cerebral blood flow. Life threatening complications in children include cor pulmonale or pulmonary oedema.
OSA is associated with impaired academic performance in children, even in the absence of nocturnal hypoxia. OSA is also associated with increased health care utilisation.

3.1.4 Identification of OSA
Most children without underlying risk factors will be identified because of concern from a parent or health care professional. There are no data to suggest that screening for asymptomatic children with OSA is worthwhile. While primary snoring may be associated with impaired cognitive and behavioural performance, there are insufficient data to recommend routine intervention in snoring children.

12. At present there is insufficient evidence to recommend intervention in children if primary snoring is the sole symptom.

3.1.5 Assessment of OSA

History and questionnaires. A simple history scoring systems distinguished normal children from a group with severe OSA, but PSG was required for the intermediary group [180]. Another questionnaire was found to have 85% sensitivity and 87% specificity in distinguishing normal children from those with proven SRBD; its usefulness in predicting OSA in children with symptoms is less clear [181]. Clinical history is very sensitive at detecting OSA but not specific enough to differentiate primary snoring from OSA [36, 61, 92, 144, 182-185]. Similarly clinical history can not be relied on to gauge severity of OSA [183, 186, 187]. (Sackett level 2b)

13. Clinical history is a sensitive screen for OSA, but has low specificity and relates poorly to severity.

Most validation studies of different assessment tools have used polysomnography (PSG) as the “gold standard”. However, it is not clear that PSG is necessarily the best predictor of morbidity amenable to intervention. A number of studies have explored alternatives to PSG. Simple saturation monitoring only identified 90 out of 210 children with OSA with 3 children being incorrectly identified as having OSA [36]. (Sackett level 1b). Video with microphone as a sole investigation evaluated by an experienced observer is a sensitive screening tool for home usage [188] but is not specific enough to differentiate primary snoring from OSA (Sackett level 1b). Audiotaping has not shown consistent enough results to be used in clinical practice [92, 93]. Nap studies are insensitive but if positive give a high rate of prediction for OSA [111, 112]. Whilst PSG can accurately diagnose OSA it is not clear which parameters of the PSG are important in determining symptoms or long term sequelae.

Testing with abbreviated PSG using respiratory inductance plethysmography, saturation, ECG and video was compared to full PSG in 21 children over 2 years of age, and detected AHI>3 or 5 with a sensitivity and specificity of 100% although AHI>1 was detected with a sensitivity of 92% and specificity of 100% compared to PSG, [189]. (Sackett level 2b) Care needs to be exercised in interpretation of PSG. Adult criteria can not be used in children [95]. The condition of upper airway resistance syndrome (UARS) has been well described in adults, but there is only one systematic study of this condition in children, using oesophageal pressure measurement. This study suggested that UARS is a relatively common condition in children with suggestive symptoms of SRBD but without clear OSA findings on PSG [190]. Further studies in this area are needed, but the difficulty of routine oesophageal manometry is a limiting factor.
14. Second- or third-line studies are required to gauge correctly the severity of OSA and reliably to discriminate OSA from primary snoring.

15. Second-line studies may be satisfactory in uncomplicated children over the age of 2 years.

16. Saturation monitoring is useful as a screen in otherwise healthy children. If positive it is highly predictive of OSA. A negative result does not exclude OSA.

A flow chart to guide interpretation of overnight oximetry in the context of a child with suspected SRBD is included in Appendix 2.

Adenoid or tonsillar size measured by a variety of techniques has been shown to correlate with a number of aspects of OSA in some studies [127, 136-139] but not in others [140, 141]. No technique has been shown to be sufficiently sensitive or specific enough to reliably discriminate between primary snoring and OSA. Similarly whilst radiographic assessment of the upper airway has identified a number of differences between OSA groups and normal children these are not sensitive or specific enough to make treatment decisions [191-193].

Endoscopic assessment and cine NMR imaging have been described in the diagnosis of OSA but are not practical for routine use [194-196]. Although a recent small study has suggested serum proteomic patterns as a potential diagnostic or screening tool for OSA, this remains speculative at present [197]

17. Adenotonsillar size or other craniofacial abnormalities cannot be relied upon to predict the presence or absence of OSA.

18. Other screening tests are as yet not sensitive or specific enough to make treatment decisions.

19. The symptoms of SRBD may be difficult to identify in children with the underlying conditions listed in Table 3, and screening should be offered in these children, even if apparently asymptomatic.

3.1.6 Management of OSA

No randomised trial of adenotonsillectomy in OSA has been done [198]. Several studies have assessed children before and after surgery and the overwhelming majority of otherwise normal children with uncomplicated OSA, including those under 2 years, [134, 199] will improve both clinically and on PSG following adenotonsillectomy [182] (level 2-) [200, 201] (level 3). Adenotonsillectomy improves OSA even in morbid obesity [202, 203] (level 3), and in patients with cerebral palsy [204] (level 3) Adenotonsillectomy results in improved growth in infants [134, 135] and older children with OSA [147] (Level 2-) [146, 148] (level 3), and improved behaviour and attention even when including children with very mild degrees of upper airway obstruction [164, 166,
One non-randomised case-control study demonstrated an improvement in academic performance following adenotonsillectomy in proven OSA [23] (level 2++); another cohort study failed to show any change in Griffith development score though there were more improvements in day and night behaviour in the adenotonsillectomy group [207] (level 2-). Adenotonsillectomy or tracheostomy improve the majority of cardiovascular complications including cor pulmonale [149-151, 153] (level 3) and changes in ventricular mass/dimension [157-159] (level 2+). Quality of life improves after adenotonsillectomy for OSA [206, 208-211] (level 2+). Three studies have reported an improvement in enuresis after adenotonsillectomy for OSA, at faster than expected rates [212-214] (level 3).

The metabolic consequences of OSA in children are not as clear as in adults, with the majority of effects being due to obesity. One study has found a fall in serum cholesterol after resolution of OSA [215] (level 2-). Adenoidectomy alone is often insufficient [201, 216]. Adenotonsillectomy may work in mild cases [201] but is associated with a higher failure rate [216] (level 3).

The well described craniofacial abnormalities seen in OSA may not be permanent, with one group describing resolution after successful treatment by adenotonsillectomy[217] (level 2+)

---

20. *Children with proven OSA secondary to adenotonsillar hypertrophy C should be referred for adenotonsillectomy.*

Where obesity is a factor in the causation of OSA there may be an urgent necessity to improve the breathing at night. Interventions to treat the obesity should also be considered for longer term management, although there is little evidence to support any specific interventions for childhood obesity [218] (level 1++)

Allergic processes may be involved in adenoidal hypertrophy [219] and OSA [220] and nasal steroids have been shown to reduce apnoea frequency over a 6 week treatment period; they may have a role in the milder patient group [221] (level 1+). Oral steroids appear ineffective [222] (level 3). Benefits have also been described with leukotriene antagonists with or without nasal steroid [176, 223] (level 2+)

---

21. *Nasal steroids and/or leukotriene receptor antagonists may be considered B in mild cases of OSA or where abnormalities persist after adenotonsillectomy.*

---

In a highly selected group of children with malocclusion, oral jaw positioning devices were found to resolve symptoms in about 50% of children [224] (level 1-) and may also be applicable for handicapped children [225] (level 3). They are unlikely to be helpful in children with adenotonsillar hypertrophy or in severe craniofacial problems.

---

22. *Oral jaw positioning devices should be considered for OSA in D malocclusion. Further data and experience are required before this can be recommended for routine practice.*
Craniofacial surgery to advance the mandible or maxilla has been successful in some case series as judged by the avoidance of tracheostomy[226-228] and quality of life was much better when tracheostomy was avoided [229]. (level 3)

23. Mandibular and maxillary advancement surgery may be helpful in the management of OSA in craniofacial syndromes especially in those where tracheostomy is the only alternative.

Uvulopalatopharyngoplasty (UPPP) has only been reported to be successful in case reports specifically identifying abnormal soft palate anatomy or in conjunction with T+A where it is not possible to separate the contribution of each form of surgery [230, 231]. At present it can not be recommended.

24. Uvulopalatopharyngoplasty (UPPP) cannot be recommended in children with OSA.

Supplemental oxygen reduces the severity of desaturation in OSA. There is conflicting results on its effect on apnoea frequency, arousals and sleep quality. In a small number of children it was associated with hypercapnia [232, 233]. (level 2+). It is therefore reasonable to use this as a temporary measure provided hypercapnia is excluded

25. Oxygen may be used as a temporary measure for the management of OSA provided carbon dioxide levels are shown not to rise during treatment.

Nasal continuous positive airway pressure (CPAP) has been shown to be effective in correcting the physiological disturbance in several case series of children with OSA [234-236] (Level 3), including those with neurodisability [236] and infants [237] (Level 2-). Compliance with treatment may prove challenging [238, 239]. CPAP also improves behaviour and alertness and concentration [240] (Level 3). Between 55% and 83% of families tolerate nasal CPAP in the longer term [234, 236, 237]. Bi-level nasal positive airway pressure (BIPAP) has also been used effectively in children with OSA [241]; there are no comparative data of CPAP and BIPAP.

26. CPAP/BIPAP is an effective treatment for the physiological derangement of OSA and should be offered where adenotonsillectomy has failed or is contraindicated if symptoms or physiological disturbance are severe.

Tracheostomy has been used when other medical interventions are ineffective or impossible, and results in complete resolution of symptoms [151, 242]. (Level 3) The mortality from tracheostomy in children under one year of age is around 5% [243].

27. In children with severe OSA where all other options have failed tracheostomy may be required.

28. When a child with abnormal physiology has undergone treatment, a further study to ensure normalisation of the physiology is recommended;
if abnormal gas exchange has been documented, this is mandatory.

**Risk of adenotonsillectomy**

OSA is a risk factor for cardiorespiratory morbidity after adenotonsillectomy [244]. Although selected patients (including those with OSA) can safely be discharged as day cases [245], some risk factors indicate particularly high risk. Post operative complications are higher in children under four years of age [244, 246, 247] and as high as 20% in children under 2 years [199, 248]. They are associated with severity of disease, especially if the saturation nadir is less than 80% or if other medical problems e.g. craniofacial disorders and evidence of right ventricular strain are present [246, 248-250]. (Level 2+). It has been argued that since the severity of disease is difficult to assess on clinical grounds, and the risks of surgery are related to the saturation nadir, all children who have adenotonsillectomy planned for OSA on clinical grounds should have a pre-operative oximetry recording to assess the need for a High Dependency Unit bed [251]. Table 4 lists the factors which should prompt referral to a centre with paediatric intensive care facilities for surgical management.

<table>
<thead>
<tr>
<th>Table 4. Factors predicting need for PICU facilities in children with OSA</th>
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<tbody>
<tr>
<td>Age &lt; 2 years</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
</tr>
<tr>
<td>Severe neurodisability</td>
</tr>
</tbody>
</table>

Children with Down’s syndrome, minor heart defects, or overweight (BMI Standard Deviation Score >2) should be evaluated carefully preoperatively before a decision is made about the optimal setting of surgery.

29. Children with suspected OSA who have associated risk factors listed in Table 4 should only have adenotonsillar surgery in a centre with Paediatric Intensive Care facilities available.

30. Overnight pulse oximetry is a desirable method of assessing the operative risk in children without apparent co-morbidity who are being considered for adenotonsillectomy. If performed, a nadir of <80% or baseline hypoxaemia should prompt referral to a centre with Paediatric Intensive Care facilities available.

The immunological consequences of removing the adenotonsillar lymphoid tissue in early life are uncertain; a conservative attitude towards surgery has been recommended, particularly in younger children [252].
3.2 High Risk Groups

3.2.1 Down’s syndrome.

Search strategy:
Medline 1950-Dec 2006
(Down syndrome/) and (sleep apnoea syndromes/ or sleep/ or sleep disorders/)
(Down syndrome/) and (pulmonary hypertension/)
Secondary search of references in relevant articles.

Prevalence and consequences
Five population studies have attempted to study SRBD in unselected patients with Down’s syndrome; one study did not have evaluable prevalence results[253]. Based on the 197 children reported, SRBD occurs in 58% (95% Confidence Intervals 51-65%) of children with Down’s syndrome [254-257] and between one-third and three-fifths of children with Down’s Syndrome have desaturation below 90% while asleep [254, 257]. Only one study of 17 children failed to find an increase in SRBD in children with Down’s syndrome [256]. Children with Down’s syndrome are at increased risk of pulmonary hypertension, particularly if they have any associated heart abnormality [258, 259] (Level 2++); in one study of 71 patients with Down’s syndrome and upper airway obstruction 34 (48%) had pulmonary hypertension [260] (Level 3). Relief of upper airway obstruction improves pulmonary artery pressure [261, 262] (Level 3). In children with cognitive impairment, adverse effects of SRBD may not be recognised.

Assessment and interventions.
There are no controlled trials of intervention in Down’s syndrome complicated by SRBD. A number of before-and-after studies have shown improvement from intervention varying from adenotonsillectomy to uvulopalatopharyngoplasty, tongue reduction, tongue hyoid advancement, and midfacial or maxillary advancement [225, 260, 263-266] (Level 3). CPAP has generally been found to be effective where tolerated. In a minority of the patients reported in these series, other interventions were ineffective and tracheostomy was performed. An observational study of 19 patients with repeated polysomnography demonstrated significant improvements in both AHI and desaturations after CPAP with or without tonsillectomy, but no improvement in patients who refused therapy or had positional therapy only. Four of the fifteen patients with OSA, and none of the four without, had pulmonary hypertension [257].

Based on the suggestion that untreated obstruction with hypoxaemia carries a risk of pulmonary hypertension, and that upper airway obstruction is generally treatable by some intervention, it is difficult to justify not treating obstruction with hypoxaemia when present. Treatment should be at the lowest level possible: adenotonsillectomy would be a reasonable first option. If there are significant craniofacial or tongue abnormalities then it may be appropriate to correct these. If surgical intervention does not correct the situation adequately, then nasal CPAP should be instituted. Reassessment of benefits of each intervention should be carefully documented with repeated physiological studies. Tracheostomy is a last resort in this situation, and the risks and benefits of treatment versus inaction should be discussed carefully with the parents.

In children with Down’s syndrome who do not respond to adenotonsillectomy and will not tolerate CPAP, oxygen therapy may be helpful in preventing pulmonary hypertension,
but should only be implemented if it can be demonstrated not to increase nocturnal CO$_2$ [232, 233].

Conclusions
Children with Down’s syndrome are at high risk of SRBD and nocturnal hypoxaemia, and the high incidence of congenital heart disease in these children makes the development of pulmonary hypertension a significant risk.
SRBD may be difficult to identify on symptoms in this group.
Adenotonsillectomy may have a lower rate of success, but is still indicated.
Other interventions including CPAP are effective but may be difficult to institute.

| 31. All children with Down’s syndrome should be offered screening for SRBD, using at least oximetry; suggested screening ages are at least once in infancy then annually until age 3-5 years. | ✓ |
| 32. Children with Down’s syndrome with abnormalities on screening for SRBD, or where there is a clinical suspicion of a false negative screening test, should have polysomnography, including oximetry, airflow, effort and CO$_2$ measurement. Video should be included if possible. | ✓ |
| 33. If significant SRBD with hypoxia is present in children with Down’s syndrome, then appropriate treatment should be offered. | ✓ |
| 34. Further research is needed on the benefits and risks of screening for SRBD in Down’s syndrome. | ✓ |

Note. There is no evidence about how long screening should continue in these children. We have arbitrarily taken 3-5 years as including the period of highest risk of OSA. If screening tests are negative up to this age it would seem reasonable not to undertake further tests subsequently unless there are suggestive symptoms.

3.2.2 Neuromuscular disease
Search strategy
Medline 1950-Dec 2006
CINAHL 1982-2006
(muscular diseases/ OR neuromuscular diseases/ or muscular atrophies, spinal/ OR muscular dystrophies/) AND (sleep apnoea syndromes/ OR sleep/ OR sleep disorders/).
(muscular diseases/ OR neuromuscular diseases/ OR muscular atrophies, spinal/ OR muscular dystrophies/) AND (respiration, artificial/ or positive-pressure respiration/).
Search of all OVID EBM databases for neuromuscular AND (sleep or ventilation)
Secondary search of references in relevant articles.

Mechanisms and prevalence.
There are two major patterns of SRBD in neuromuscular disease: obstructive sleep apnoea due to loss of glosopharyngeal muscle tone and hypoventilation due to intercostal and abdominal weakness. If the diaphragm is involved then the hypoventilation is particularly severe during REM sleep[267]. Bulbar palsy and scoliosis both increase the risk of respiratory failure and SRBD.
Respiratory failure at night causes hypoxaemia and alveolar hypoventilation. Children with neuromuscular disease and nocturnal desaturations are more likely to have evidence
of pulmonary hypertension [268]. *(Level 2-)* Evidence from intervention studies (see below) strongly suggests that life expectancy is reduced by SRBD; in one study of Duchenne Muscular Dystrophy the mean survival of five patients with diurnal hypercapnia associated with SRBD was less than 10 months [269].

**Assessment and interventions.**

There are a large number of before-and-after studies of non-invasive ventilation (NIV) in neuromuscular disease, particularly Duchenne Muscular Dystrophy. The results of nocturnal NIV as treatment for nocturnal or diurnal respiratory failure in a total of 246 children and young adults with neuromuscular disease have been reported, with follow-up ranging from 6 to 67 months [269-284]. There is almost universal improvement in oxygenation and ventilation during sleep *(Level 2++)*, and survival appears considerably better than contemporary or historical comparison groups [269, 270] *(Level 2-)*. Only 13 patients (mainly younger children) were reported to have been intolerant of NIV, and in only 2 was it ineffective. A recent historical cohort study has suggested that the chances of surviving to age 25 with Duchenne Muscular Dystrophy are increased from 12% to 53% by non-invasive ventilation [285]. *(Level 2+)*. A meta-analysis of a heterogenous group of patients including those with neuromuscular disease has concluded that NIV improves oxygenation, CO2 levels and survival at one year [286], but few of the subjects in the four included studies were paediatric neuromuscular disease patients.

One randomised study of NIV in Duchenne Muscular Dystrophy has been done, but this intervened early (FVC between 20-50%). Although a minority of patients reported symptoms which might have indicated SRBD, sleep studies were not performed, and patients with daytime hypercarbia were excluded. There was no evidence of benefit, with a possibly increased mortality in the intervention group [287].

**35. Non-invasive ventilation is not indicated routinely in DMD in the absence of SRBD**

Theophylline does not improve SRBD in neuromuscular disease [288].

Oxygen treatment of sleep hypoxaemia in Duchenne Muscular Dystrophy has been shown to improve saturations, but increases the amount of apnoea and hypopnoea during REM sleep. Only short term studies of this intervention have been undertaken [289].

NIV should be part of a package of respiratory care in neuromuscular disease, which is aimed at preventing and effectively treating atelectasis and episodes of lower respiratory infection, optimising nutrition, and effective management of scoliosis. There is no evidence of any intervention delaying the onset of SRBD.

Symptoms of SRBD may be very subtle in neuromuscular disease. In Duchenne Muscular Dystrophy significant SRBD with nocturnal desaturations was present in 9/14 patients without obvious sleep-related symptoms [290]. Even a structured symptom questionnaire has failed to identify patients with advanced neuromuscular disease who have SRBD [291].

A Vital Capacity below 30% predicted has been found to be a predictor of the need for NIV in Duchenne Muscular Dystrophy in one study, with a disability score adding to the predictive model [292]. Another study suggested that the best predictor of death or
institution of NIV in Duchenne Muscular Dystrophy was a Vital Capacity below 1 litre [293]. It is suggested that monitoring for SRBD should be initiated at a slightly higher level of lung function than that known to predict a need for NIV, to ensure that cases are not diagnosed too late.

Domiciliary oxygen saturation recordings during sleep will detect hypoxaemia at night as well as, or even better than, polysomnography [294] (Sackett level 2b). While they do not identify all patients with SRBD, they probably identify the clinical important problems. In the event of a positive study it is sensible to study the pathophysiology of the sleep hypoxaemia in more detail in order to tailor intervention appropriately and in case of a poor response to initial treatment. However, there is no evidence to support or refute this.

| 36. Overnight oximetry recordings should be carried out on all children with neuromuscular disease if there are symptoms of SRBD, impairment of diaphragmatic function, or a vital capacity below 50% predicted. In conditions such as myopathies, where the risk of early SRBD is particularly high, regular recordings should be carried out even in the absence of any of these indicators. | √ |
| | 37. If feasible, CO₂ recordings should be performed in conjunction with oximetry in children with neuromuscular disease, as they may add useful information. | √ |
| | 38. The optimum frequency of oximetry recordings in high risk children with neuromuscular disease is uncertain. At least annual recordings should be done, with more frequent recordings in higher risk situations. | √ |
| | 39. Limited polysomnography (second-line study) should be performed in neuromuscular patients with abnormal oximetry, but in the presence of severe abnormalities treatment should not be delayed if polysomnography is not readily available. | √ |

There is so much evidence to support the efficacy and tolerability of non-invasive ventilation in neuromuscular disease with nocturnal hypoventilation that it would no longer be ethical to conduct a randomised trial. Positive pressure ventilation is more effective than negative pressure ventilation in these conditions [295]. The use of tracheostomy ventilation when non-invasive ventilation is ineffective is a difficult ethical decision, complicated by varying prognoses in different conditions. Quality of life in tracheostomy ventilated patients with neuromuscular disease is perceived by the patients as satisfactory [296], but it does cause increasing stress for caregivers and patients [297] and requires adequate carer support. It is not a widely available option in the UK.

**Conclusions**

The overall prevalence of SRBD in neuromuscular disease is high, and in progressive conditions it is likely to occur at some stage in most patients. SRBD in neuromuscular disease is associated with increased pulmonary artery pressure. There is good evidence (level 2++) that NIV improves nocturnal and diurnal oxygen saturation and pCO₂ in neuromuscular disease patients who have SRBD, and evidence (level 2+) that NIV
improves survival in these patients, particularly if hypercarbia is present, and that it is generally well tolerated. SRBD and respiratory failure are difficult to detect clinically, and screening in patients at high risk is recommended.

| 40. If SRBD sufficient to cause hypoxaemia at night is demonstrated in an otherwise stable child with neuromuscular disease, then nocturnal NIV should be instituted. | √ |
| 41. If SRBD is associated with nocturnal hypercapnia in a child with neuromuscular disease then nocturnal NIV should be instituted. | C |
| 42. A child with neuromuscular disease on NIV should have repeated studies with oximetry and CO2 recordings to ensure optimal NIV settings. | √ |

3.2.3 Anatomical abnormalities

Search strategy
Medline 1950-Dec 2006
((Obstructive Sleep Apnea) or (Obstructive Sleep Apnea Hypopnea syndrome)) AND ((Mucopolysaccharidosis) or (Pierre Robin syndrome) or (Stickler syndrome) or (Craniofacial syndrome) or (Treacher Collins syndrome) or (Nager syndrome) or (Saethre Chotzen syndrome) or (Achondroplasia))
Secondary search of references in relevant articles.

Background
Airway patency is determined by the fixed size of the bony airway, the varying activity of airway dilator muscles, which can be affected by sleep stage, and by the presence of soft tissues.
It has recently been established by MRI scanning that in otherwise normal children with OSA there is a smaller upper airway, mainly due to adenotonsillar volume [298]. When the bony airway is reduced, a similar degree of adenotonsillar hypertrophy will cause more severe narrowing.

3.2.3.1 Craniofacial syndromes
OSA has been described in virtually all recognised craniofacial syndromes and also in individuals with apparently unique craniofacial anomalies. In a series of children with OSA, those with underlying craniofacial abnormalities had more severe respiratory disturbance indices [191]. Those disorders with poorly formed jaw (Treacher Collins syndrome, PRS) and those with midfacial and palatal involvement (Crouzon, Apert, Saethre-Chotzen, Nager, Pfeiffer and Stickler syndromes) are most likely to have OSA. Isolated craniosynostosis without facial involvement is not associated with OSA [299]. There are also reports of tracheal stenosis secondary to the cartilaginous anomaly often found in craniofacial syndromes [300]. This may complicate the OSA.
Children with craniofacial syndromes are unusual in that they often present with OSA in infancy. However, the airway obstruction may worsen with growth, particularly in midfacial hypoplasia.
Cor pulmonale and sudden death have been described in Pierre Robin sequence (PRS) [301-303].
In the absence of gas exchange abnormalities, intervention should be based on the presence of clinical symptoms suggestive of OSA.

**Treatment**
Older papers only discuss tracheostomy, which was deemed necessary in 19% of 251 subjects in a US study from the early 1990s [304]. Another US study of 109 children with various craniofacial disorders described 60% as requiring airway management interventions with 17% requiring tracheostomy [305]. Recent case series describe successful use of CPAP or BIPAP [306, 307] with improvements in OSA and clinical measures *(level 3)*.

Nasopharyngeal tube placement has been described as successful management for infants with PRS with significant obstruction and hypoxia [308]. A recent series found that nasopharyngeal tube avoided the need for surgery and achieved adequate oxygenation and growth in 22 consecutive patients [309] *(level 3)*.

Major corrective surgery to the midface can improve matters [227]. In children with craniofacial problems, distraction osteotomy of the mandible improved OSA without tracheostomy [310] *(level 3)* and facilitated successful decannulation of tracheostomy especially in PRS [311] *(level 3)*. Denny reported a pilot study of 15 children with PRS (some with associated syndromes) with persisting severe upper airway obstruction despite trials of CPAP, tongue-lip adhesion and nasopharyngeal airway. Distraction osteotomy of the mandible was attempted in 11 children, and all had good outcomes[312]. *(level 3)* Another descriptive case series of mandibular distraction osteotomy in infants with micrognathia and obstructive apnoea refractory to other therapy reported improved airway with avoidance of tracheostomy in 14/17 (82%) [313].

### 43. All children with syndromes involving midfacial hypoplasia or micrognathia should be evaluated for SRBD with a minimum assessment of oximetry, preferably with a measure of CO₂. This should be performed urgently if they have any clinical signs of airway obstruction, and within the first 4 weeks of life in any event. √

### 44. Clinicians should be aware that infants with PRS may have worsening airway obstruction between 4 and 8 weeks and ascertain whether symptoms worsen at this age. If so, repeat assessment should be carried out. √

### 45. Reassessment for SRBD in children with syndromes involving midfacial hypoplasia or micrognathia should occur at 3-6 monthly intervals in the first year of life, and subsequently should be dictated by clinical symptoms and signs. √
46. In infants with PRS or other micrognathia syndromes and with significant airway obstruction or SRBD:
- A nasopharyngeal tube is the first line of treatment.
- If nasopharyngeal intubation is unsuccessful, nasal CPAP or BIPAP should be tried.
- Tracheostomy is necessary if other measures fail.
- Mandibular advancement surgery may have a role in refractory cases, taking into account the degree of expected mandibular growth.
- There is no evidence to support the practice of prone positioning.

47. In children with midfacial hypoplasia and airway obstruction or SRBD:
- A trial of nasal CPAP or BIPAP is indicated.
- If this fails, then surgical options include tracheostomy or surgical reconstruction. If the airway is significantly impaired then tracheostomy remains the immediate treatment of choice.
- The role of craniofacial surgery as an alternative to tracheostomy requires further evaluation.

3.2.3.2 Mucopolysaccharidoses
In a case series of 26 children with various mucopolysaccharidoses, 24 were found to have SRBD, and clinical history was not an adequate detector [314] (Level 3). In order of descending risk the three highest risk syndromes were Hurler’s, Hurler-Scheie and Hunter’s syndrome. OSA in Hurler’s syndrome has been shown to cause cor pulmonale, reversed by nasal CPAP in a case report [315] (Level 3). There are no systematic studies of the effects of identification or intervention for SRBD in this group of patients. In children with cognitive impairment, adverse effects of SRBD may not be recognised. However, the appropriateness of intervention must be considered in the context of the other treatment being offered and the long-term prognosis in each case. The effect of enzyme replacement therapy on SRBD in these conditions has not yet been established.

Conclusions:
Children with mucopolysaccharidoses, particularly Hurler, Hurler-Scheie and Hunter syndromes are at high risk for SRBD.

48. In children with Hurler, Hurler-Scheie and Hunter syndromes:
- a. Screening for SRBD should be offered, after discussion of the possible interventions and benefits.
- b. Adenotonsillectomy should be considered if there is significant SRBD.
- c. In significant SRBD where adenotonsillectomy is unsuccessful or not feasible, nasal CPAP should be considered.

3.2.3.3 Achondroplasia
The predisposing factors for SRBD are a combination of airway obstruction from midfacial hypoplasia and the risk of abnormal respiratory control secondary to brainstem compression. Waters studied 20 children and young adults and found all to have upper airway obstruction with 75% having an apnoea index greater than 5/hr with obstructive, central
and mixed apnoea [316]. In a much larger group of 88 children significant abnormalities on PSG were found in 48% [317].
Pulmonary hypertension and cor pulmonale have been frequent complications in case series selected for SRBD [318, 319]. (Level 3). The overall prevalence of these conditions in achondroplasia is not known.
A good response to adenotonsillectomy has been demonstrated in many, but not all, patients [318, 320]. (Level 3). In patients with cervicomedullary compression and SRBD, decompressive surgery may result in improvement [321]. Nasal CPAP was required in 13/17 children requiring treatment for SRBD, and was found to be effective [320]. (Level 3)
Two children who required tracheostomy for achondroplasia with upper airway obstruction were able to be decannulated after midfacial distraction osteotomy [322]. (Level 3)

Conclusions.
Children with achondroplasia are at high risk of SRBD
Pulmonary hypertension and cor pulmonale are significant risks in SRBD in achondroplasia.
Interventions such as adenotonsillectomy and nasal CPAP are usually, but not always, associated with clinical and polysomnographic improvements.

49. In children with achondroplasia:

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<tbody>
<tr>
<td>a.</td>
<td>Screening for SRBD should be offered to all children with achondroplasia. Ideally this should include oximetry and capnography.</td>
</tr>
<tr>
<td>b.</td>
<td>If initial screening is normal, the optimum frequency of subsequent screening is unclear, but should probably be every 6-12 months in the first 5 years of life.</td>
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<tr>
<td>c.</td>
<td>If significant SRBD is discovered, then adenotonsillectomy should be offered.</td>
</tr>
<tr>
<td>d.</td>
<td>A trial of CPAP should be considered if symptoms or significant gas exchange abnormalities persist after adenotonsillectomy.</td>
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</table>

Note. There is no evidence about how long screening should continue in these children. We have arbitrarily taken 3-5 years as including the period of highest risk of OSA. If screening tests are negative up to this age it would seem reasonable not to undertake further tests subsequently unless there are suggestive symptoms.

3.2.3.4 Prader Willi Syndrome (PWS)

Search strategy:
Medline 1950-Dec 2006
CINAHL 1982-2006
(Prader Willi Syndrome/) AND ((sleep apnea syndromes/) or (sleep apnea, central/) or (sleep/) or (sleep disorders/) or (sleep apnea, obstructive/) or (respiration, artificial/) or (positive-pressure respiration/))
(Prader Willi Syndrome /mortality)
Secondary search of references in relevant articles.
Sleep disturbance and sleep apnoea are included as minor diagnostic criteria of PWS in a consensus document [323]. The prevalence of symptomatic sleep disturbance and apnoeas was 37% in a retrospective chart review of 90 children and adults with PWS [324]. Excessive daytime sleepiness (EDS) is a common feature of PWS, often beginning in early childhood [325]. EDS occurs despite increased quantity of nocturnal sleep in patients with PWS [326]. Disturbed sleep architecture has been reported in PWS with REM sleep occurring earlier in the night than in normal subjects (reduced REM latency). REM sleep onsets (SOREMPs) has been found in 10/23 patients [327, 328] and 8/10 had abnormal sleep latency [328].

**Abnormal ventilatory responses to hypercapnia and hypoxia in PWS**

Hypoxia and hyperoxic ventilatory responses are absent or reduced, and are independent of the degree of obesity [329, 330]. Ventilatory response to CO2 inhalation (chemoreceptor response) is also abnormal in that the PWS patients increase their ventilation at a higher level of arterial CO2 than normal controls [329-331]. Some of this chemoreceptor blunting may be due to obstructive sleep apnoea, since a case report describes an improvement (but not normalisation) in hypercapnic response after tracheostomy and bi-level positive airway pressure during sleep [332]. However abnormal hypercapnic responses have been found even in non-obese subjects [331].

**SRBD in PWS**

Snoring and breathing difficulty during sleep are commonly reported by caregivers [333, 334]. A number of polysomnographic studies have been done in PWS, all confirming the very high prevalence of apnoea and hypoventilation during sleep. Kaplan found only mild obstructive events in 5 patients, although daytime hypoxaemia was common [335]. In contrast, Harris [336] found obstructive SRBD in all 8 patients studied; in 3 patients a improvement in SRBD occurred after weight loss, but daytime somnolence persisted. Hertz demonstrated an association between BMI and SRBD in 43 children and adults with PWS [337]. Richards found abnormal AHI in 12/14 subjects [338]. Manni’s assessment of 14 unselected PWS subjects found only 4 to have abnormal amounts of apnoea/hypopnoea, and these were not severe [328]. A large prospective study of sleep and breathing in 53 pre-pubertal children with PWS found that 49 had an abnormal AHI, but this was mainly due to central apnoea and hypopnoea. Only 8 children in this cohort were obese, and obstructive apnoea was uncommon outside this subgroup[339].

Nocturnal oxygen desaturation, particularly in REM sleep, has been demonstrated in both adults and children with PWS, unrelated to obvious apnoea [335, 340], but positively correlated to obesity [336, 340]. Sleep related hypoventilation and increased central apnoeas in adults and children with PWS have also been described [328, 331, 339].

Thus, some abnormalities of breathing during sleep are common in PWS, being found in 25-100% of patients, but in many cases these are mild. Hypoxaemia is common, and may be multifactorial in origin, due to obesity, OSA and abnormalities of respiratory control.
Conclusions.
SRBD is common in patients with PWS.
Nocturnal hypoxaemia is common in PWS

Consequences of SRBD in PWS.
Some PWS patients have respiratory failure with day and night hypercapnia and hypoxia, and PWS patients die prematurely of cardiorespiratory failure [335]. The annual mortality rate is estimated at 3%, with sudden death being a common cause [341]. (Level 3).

Treatment
Nocturnal non-invasive ventilation has shown to reverse day time ventilatory failure in 4 adults with PWS, with good compliance and continued effects over >4 years [342]. Thus, the respiratory failure is treatable, and identification should prolong life. This evidence is based on a small number of convincing case studies. One case has been described where initiation of CPAP for OSA in a young child improved EDS [343].

Although weight reduction might improve the SRBD, it is not a complete solution to the problem, as abnormalities including hypoxia, central apnoea and hypoventilation are found in non-obese individuals.
There are no good studies evaluating whether clinical symptoms can be used to identify children at risk of respiratory failure. The high prevalence of EDS and obesity in the syndrome suggests that all children should be screened with oximetry on an annual basis. Children with abnormal oximetry should have polysomnography.

50. All children with PWS should be screened with oximetry and capnography on an annual basis. Children with abnormal oximetry should have polysomnography.

Weight reduction leads to improvement both in OSA [336] and nocturnal hypoventilation [344]. (Level 2+) Adenotonsillectomy has been recommended [345], but no data specific to PWS are published. CPAP is effective in controlling OSA, but doesn’t improve non-obstructive REM-related desaturation and is poorly tolerated [346, 347]. Nocturnal non-invasive ventilation has shown to reverse day time ventilatory failure in 4 adults with PWS, with good compliance and continued effects over >4 years [342]. (Level 3)
There is a need for more data on improvements in quality of life as a result of interventions.

Clomipramine has been used in one patient with OSA and daytime somnolence. There was no effect on OSA, but the daytime somnolence improved [348]. (Level 3) Medroxyprogesterone resulted in resolution of nocturnal hypoventilation in a 4 year old obese child with PWS [349]. (Level 3) Growth hormone has been used in PWS to improve growth and reduce obesity. There have been concerns about the possibility of this increasing the risk of sudden death after a case report of worsened sleep apnoea and death after growth hormone treatment [350]. Another child with PWS who died suddenly during growth hormone treatment was
reported to have a normal polysomnogram and no pre-existing obesity [339]. A prospective survey of 338 PWS children who received growth hormone recorded 5 deaths in one year [351]. While there is no evidence of a causal link, these authors recommend that sleep studies should be performed on PWS children prior to starting growth hormone. In the context of these concerns, despite the lack of convincing evidence of risk from growth hormone it would be prudent to assess and optimise breathing during sleep in PWS patients prior to starting growth hormone treatment.

<table>
<thead>
<tr>
<th>51. In PWS with respiratory failure a trial of NIV at night should be initiated</th>
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<tbody>
<tr>
<td>52. In PWS with significant nocturnal hypoxaemia a trial of NIV at night should be initiated</td>
<td>✓</td>
</tr>
<tr>
<td>53. Adequacy of breathing during sleep should be assessed formally in any child with PWS prior to starting growth hormone treatment.</td>
<td>✓</td>
</tr>
</tbody>
</table>
3.3 Congenital Central Hypoventilation Syndrome.

Search strategy
Medline 1950-Jan 2007
(((Congenital central Hypoventilation Syndrome) OR (Ondine's)) AND ((Control AND ventilation) OR (Autonomic nervous system))
Limited to “human”, “all child 0-18”
Additional manual check of review articles

3.3.1 Prevalence.

Congenital central hypoventilation syndrome (CCHS), previously commonly known as “Ondine’s curse” is a rare (between 1 in 50,000 and 1 in 200,000) congenital condition in which there is an abnormality of control of respiration in the absence of any identifiable primary CNS, neuromuscular, lung or cardiac disease. Approximately 800 cases of CCHS have been identified worldwide.

A Strategic Health Authority, with a population of 1–1.5 million, and 10-15,000 births per year will have 3–4 children with CCHS. In the past many children with CCHS may have died in early infancy, but increased awareness of the condition in recent years has led to an increased number of children being diagnosed within a few days of birth [352-355].
Because of the extreme rarity of this condition, virtually all published studies are based upon case reports, case series and expert opinion (i.e. Evidence levels 3 or 4).

Consequences and benefits of identification.

Affected children show hypoventilation during sleep, especially non-REM sleep, but some severely affected patients may also hypoventilate while awake. Untreated children with the more severe forms of CCHS are likely to die within the first few weeks after birth. If not recognised in early infancy, children with the milder forms of CCHS may present with cyanosis, oedema and right heart failure with pulmonary hypertension, as a consequence of recurrent or chronic hypoxemia. Some children may present with apparently life-threatening episodes or apnoeas necessitating resuscitation. Untreated mild to moderate CCHS is compatible with survival for several months, and it is possible for subtle disease to go unnoticed. In the late onset variant that presents around 2–4 years of age there are commonly associated hypothalamic disorders, particularly endocrine dysfunction. There are now several cases reported of presentation of CCHS in adult life, commonly with symptoms dating to early childhood, though in others only being recognised on the diagnosis of CCHS in a child of the affected adult [352-357].

3.3.2 Prevention.
Although the great majority of children with CCHS will be the first affected person in the family, recent studies have identified heterozygous de novo mutations of the PHOX2B gene in more than 90% of children with CCHS [358-360], raising the possibility of prenatal diagnosis. Genetic investigation and counselling should be offered to all newly diagnosed families.

3.3.3 Identification and Diagnosis of CCHS.

Diagnostic criteria.
The clinical and physiological diagnosis of CCHS has been considered to require the following criteria [361, 362] (Level 4):

1. Persistent evidence of hypoventilation during sleep [PaCO$_2$ > 60 mm Hg (8 kPa)]
2. Onset of symptoms usually in the first year after birth
3. Absence of primary pulmonary or neuromuscular disease
4. No evidence of primary heart disease

However, the clinical presentation of CCHS is variable and may reflect the severity of the underlying disorder. Children typically present in the newborn period with duskeness or cyanosis when falling asleep, but no associated increase in respiratory effort. These infants may not awaken during these episodes. Hypoventilation may be present during waking but is generally worse during sleep. Presentation may be with apparent life threatening events (ALTEs), or presentation may be delayed until adult life, as noted above [356].

CCHS is associated with a number of other conditions affecting or derived from the autonomic nervous system. These include neurocristopathies such as Hirschsprung’s disease, abnormalities of a range of autonomic functions (e.g. temperature control, pupil size, heart rate variability), and tumours, including ganglioneuroma, neuroblastoma and ganglioneuroblastoma [353-355, 358-360].

In the evaluation of children with sleep hypoventilation, it is important to exclude primary neuromuscular, cardiac or pulmonary disease or any identifiable brain stem lesions. Other conditions that may cause sleep hypoventilation include congenital myopathy, myasthenia gravis, abnormalities of the airway or intrathoracic anatomy, diaphragm dysfunction, congenital cardiac disease, structural hindbrain or brainstem abnormalities, and metabolic disorders.

Assessment

The identification of characteristic abnormalities of the PHOX2B gene – either polyalanine insertions, frameshift or miss-sense mutations [356, 358-360], in more than 90% of children with clinically diagnosed CCHS allows the rapid identification of the diagnosis in the great majority of affected individuals. In the UK, investigation of the
PHOX2B gene is available through the UK clinical genetics testing network. ([http://www.geneticstestingnetwork.org.uk](http://www.geneticstestingnetwork.org.uk)).

Definitive physiological evaluation of CCHS includes a detailed assessment of spontaneous breathing during sleep and wakefulness in a reference sleep physiology laboratory. Good quality polysomnography including an adequate period during both REM and non-REM phases of sleep is essential. The measurements should include at a minimum, tidal volume and flow (pneumotachograph), movement of the chest and abdomen (respiratory inductance plethysmography), pulse oximetry, end-tidal carbon dioxide and ECG, together with EEG and Electro-oculogram (EOG) for sleep state determination. This may be supplemented by invasive blood gas measurements preferably obtained from an indwelling arterial line, to objectively quantify hypoxemia and hypercarbia. Careful observation of tidal volume and respiratory rate of infants during endogenous hypercarbia during sleep and wakefulness may be sufficient to assess central chemoreceptor function. Peripheral chemoreceptor sensitivity to hypoxia may be assessed by measurement of the ventilatory depression caused by hypoxemia from the administration of increased inhaled oxygen concentration. More detailed assessment of chemoreceptor ventilatory responses to hypercarbia may be performed using a rebreathing or steady state challenge with 5% carbon dioxide administered via a head box. Functional MRI imaging has shown abnormalities of CNS responses to both hypoxia and hypercapnia in multiple CNS sites, including the frontal cortex, cerebellar cortex and basal ganglia as well as the midbrain, pons and ventral and dorsal medulla.[361, 363-367].

| 54. Children with suspected CCHS should be referred to a specialist centre with adequate facilities and experience for confirmation of the diagnosis. | ✓ |

### 3.3.4 Management.

Ventilatory support is necessary in almost all children with CCHS. This may be continuous, or during sleep only. In contrast to the generally poor prognosis of untreated infants, more than 60% of patients receiving ventilatory support will survive to later childhood [368]. Most such children with CCHS have an overall high quality of life, though many have persisting hypotonia with varying degree of neurocognitive deficits, and many have multiple autonomic deficits, particularly affecting heart rate variation, blood pressure control, and thermal responses [364-366, 369-374]. Many children with CCHS suffer from seizure disorders and some show evidence of poor growth and delayed puberty. It is difficult to separate the effects of intrinsic CNS abnormalities from the effects of intermittent hypoxemia in determining the neurodevelopmental outcome. Pulmonary hypertension and cor pulmonale occur in some children with CCHS and may be fatal; it is not yet clear whether these can be completely prevented by rigorous ventilatory management, but in order to minimise the risk of cor pulmonale, current
recommendations are to aim to maintain normal levels of both carbon dioxide and oxygen during all periods on ventilatory support [352, 353, 361].

Conventional management of infants with CCHS has been to maintain ventilation via a tracheostomy, but recent reports have shown the feasibility of non-invasive ventilatory support from early infancy for selected infants [352, 353, 375, 376]. With adequate education, support and resources provided to the family and the primary healthcare team almost all children with CCHS can be safely and effectively cared for at home in the longer term [368]. The practicalities of discharging a child on home ventilation in the UK have been dealt with elsewhere [377, 378].

Several ventilatory options are available for these children. With increasing age and as the infant becomes ambulatory, diaphragmatic pacing using phrenic nerve stimulation is an option for children with CCHS who are ventilator dependent for 24 hours a day and who have no evidence of ventilator related lung disease [379-381]. Phrenic nerve electrodes may be bipolar (relatively easier insertion through the neck but somewhat less reliable because of possible displacement) or more recently quadripolar (more difficult transthoracic insertion but more stable position and hence more reliable). The aim is to ensure adequate alveolar ventilation and oxygenation. Because of the more natural breathing pattern, with negative inspiratory intrathoracic pressure, pulmonary ventilation perfusion matching is improved in some patients by the use of phrenic stimulators. Adverse effects of phrenic nerve stimulators include permanent phrenic nerve damage, diaphragmatic fatigue, discomfort associated with surgical implantation, accidental displacements in ambulatory children and the potential need for repeated surgical revisions. The quadripolar electrodes offer greater duration of pacer support, diminished risk of phrenic nerve damage and diaphragmatic fatigue and allow optimisation of the pacing activity during exercise. Despite limitations, parents and children have emphasised the improvements in mobility and quality of life after phrenic nerve stimulator insertion in CCHS [379]. (Level 3). Despite the very high cost of phrenic nerve stimulators and their insertion and maintenance, this option should be explored for all children who require awake as well as asleep ventilatory support. Phrenic nerve stimulators are usually used only during the daytime, with positive pressure ventilation by a ventilator at night, to minimise the risk of phrenic nerve damage from continuous electrical stimulation, though some patients have chosen to use nerve stimulators round the clock for prolonged periods [379].

Children who require ventilatory support only during sleep and who are able to cooperate may be considered for non-invasive facemask ventilation with bi-level positive pressure ventilation. Non-invasive ventilation is generally not recommended for children less than 6-7 years of age, partly because of the likely need for continuous ventilatory support with intercurrent illness, and partly because of the risk of mid-facial growth abnormalities as a consequence of a tightly placed face-mask. Some authors have reported successful use of such techniques in early infancy [354, 355, 376]. If non-invasive ventilation is successfully instituted tracheal decannulation may be performed.
Negative pressure ventilation has been used successfully in one centre in the U.K [375]. However, this is cumbersome and may need significant equipment adjustment over the time. In addition negative pressure ventilation may aggravate any coexisting upper airway obstruction in these children.

Other general supportive measures are also important as many children with CCHS suffer from feeding difficulties and severe gastro-oesophageal reflux necessitating nutritional support, anti-reflux medications and in extreme cases anti-reflux surgery.

Well co-ordinated multidisciplinary care involving members of the primary, secondary and tertiary healthcare teams, and regular review in a paediatric sleep physiology laboratory are central to the successful care of children with CCHS. The monitoring required is well described in the American Thoracic Society guidelines [361].

Unlike other children on home ventilation, children with CCHS do not show ventilatory responses to hypoxemia or hypercarbia, and may hypoventilate more severely when unwell, with increased right to left intrapulmonary shunting. They may show minimal or absent increase in ventilation with exercise, and with infection may develop relative hypothermia rather than fever.

Continuous monitoring of blood oxygen saturation is recommended whenever children with CCHS are on the ventilator, and whenever they are unwell periodic checks of oxygen saturation are also required when awake, as well as assessments of carbon dioxide levels.

Because of their reduced perception of hypoxia and hypercarbia, and the absence of any appreciation of dyspnoea, together with depressed ventilatory responses to exercise, children with CCHS may exert themselves beyond physiological limits, and come to harm. Children with CCHS should be allowed to participate in non contact sports with a moderate level of activity and frequent rest periods. Swimming may be hazardous for these children – the lack of hypoxic response may put them at risk. Underwater swimming is particularly hazardous, but with very careful supervision gentle swimming may be acceptable. Rhythmic activity with the opportunity to develop a learned increase in ventilation may be of value. Dance is particularly helpful in developing appropriate rhythmic increased ventilation with exercise [353, 355, 361, 382].

Children and adolescents with CCHS are at particular risk of severe and potentially fatal hypoventilation on ingestion of alcohol, or use of cannabis. Affected children and their families must be informed and warned of these potential dangers [353, 383].

55. In children with CCHS:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>a.</td>
<td>Ventilatory support is almost always essential for survival. √</td>
</tr>
<tr>
<td>b.</td>
<td>Tracheostomy is indicated for management in the first 6 years of life. √</td>
</tr>
<tr>
<td>c.</td>
<td>Diaphragmatic pacing should be considered in children requiring 24-hour ventilatory support. D</td>
</tr>
<tr>
<td>d.</td>
<td>Care should be supervised by a specialist centre with experience of √</td>
</tr>
<tr>
<td></td>
<td>CCHS management.</td>
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<tr>
<td>---</td>
<td>-------------------------------------------------------------------------------</td>
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<tr>
<td>e.</td>
<td>Oxygen saturation should be monitored continuously during sleep.</td>
</tr>
<tr>
<td>f.</td>
<td>During acute illnesses children with CCHS require checks of oxygen saturation and carbon dioxide levels when awake.</td>
</tr>
<tr>
<td>g.</td>
<td>Carers and children should be advised of the cautions required during exercise, and the specific dangers of alcohol or cannabis use.</td>
</tr>
</tbody>
</table>
4. Unexplained events in infancy- ALTE

Search Strategy:
Medline 1950-Dec2006
For general studies on ALTE:
(ALTE.mp OR life threatening event.mp) limited to (humans and "all infant (birth to 23 months")
For intersection with specific conditions:
(ALTE.mp OR life threatening event.mp OR Critical Illness/ OR Apnea/ OR Sleep Apnea Syndromes/ OR Cyanosis/ OR Monitoring, Physiologic/ OR Airway Obstruction/) limited to (humans and "all infant (birth to 23 months")
intersecting with the specific condition search term

Conditions which present as possible respiratory control disorders in infancy are often described by the term “apparent life threatening events” or ALTEs. A consensus document [384] defines an ALTE as “an episode that is frightening to the observer and that is characterised by some combination of apnoea (central or occasionally obstructive), colour change (usually cyanotic or pallid), marked change in muscle tone, choking or gagging.” The prevalence of ALTE depends on case definition and whether ascertainment is hospital or community based. A prospective community-based study in West Virginia, USA, found a prevalence of 11/1000 live births [385]. In the UK, there are no published data on the prevalence of ALTE, but in Sheffield in 1997 there were 76 ALTEs out of 6,022 births in one year (rate 12.6/1000), and in North Staffordshire, there were 30 ALTEs out of 6,500 live births (rate 4.6/1000) (unpublished data). In the Cheshire area, ALTE was seen in 3.3/1000 infants, after exclusion of preterm infants and infants with congenital anomalies (Mir NA unpublished data).

4.1 Possible conditions presenting as ALTE.

The list of underlying conditions which have been diagnosed after presentation with an ALTE is extensive (Table 5). It is not always clear if the condition was the cause of the ALTE. Congenital heart disease diagnoses include persistent ductus arteriosus and ventricular septal defect which may have been coincidental findings, and prolonged QTc syndrome has not been demonstrated to have a causal relationship in these infants.

4.1.1 Prevalence of ALTE.

The relative prevalence of each condition depends on the method of ascertainment, which varies from consecutive admissions to an A&E department [386, 387] to infants referred for evaluation at a tertiary sleep centre. A systematic review of diagnosed causes of ALTE has described 728 different diagnoses [388] The range of investigations
performed for ALTE is wide: 0-26, mean 15.5 in one study [389], with a low yield contributing to diagnosis (5.9% of 3776 investigations, or 33.5% of positive tests).
Table 5. Causes to which ALTE has been ascribed

Respiratory
- Infection - e.g. respiratory syncytial virus infection, pertussis, pneumonia [387]*
- Upper airway obstruction - e.g. retrognathia, laryngomalacia [387, 390]
- Lower airway obstruction or closure - e.g. tracheo-bronchomalacia [390]
- Intrapulmonary shunting e.g. cyanotic breath holding [391]

Neurological
- Epileptic - seizure induced [387, 390, 392]*
- Intracranial haemorrhage - vitamin K deficiency, child abuse [393, 394]*
- Central hypoventilation - drugs [387, 395], congenital [396]*
- Brain tumour [387]*

Infective
- Septicaemia [392], urinary tract infection [386, 387], gastro-enteritis [386, 387]*
- Meningo-encephalitis [392]*

Autonomic
- Vasovagal [393]
- Gastro-oesophageal reflux [386, 390, 393, 397-399]
- Skin pallor changes

Child Abuse
- Illness fabrication [400]*
- Attempted suffocation [401-408]*
- Poisoning [387]*

Cardiac
- Tachyarrhythmias - Wolfe-Parkinson White and Long-QT syndrome [409, 410]
- Congenital heart disease [392, 393]
- Myocarditis [411]

Inborn areas of metabolism [393, 412]*

Miscellaneous
- Carbon monoxide poisoning*
- Cat smothering
- Abnormal infant holding practices
- Haemorrhagic shock encephalopathy syndrome

Unknown

* Evidence of benefit from identification
Physiological and video monitoring with some form of event capture is particularly helpful in diagnosing some of the rarer causes of recurrent events, including epileptic seizure induced apnoea and imposed suffocation.

Evidence for some rarer causes of ALTE, such as inborn errors of metabolism, is clear-cut. In this report, we focus on the causes which are less clear and may cause confusion, namely:
- gastro-oesophageal reflux
- breath holding
- epilepsy
- child abuse
- upper airway obstruction
- cardiac dysrhythmias

4.1.2 Gastro-oesophageal Reflux and ALTE

Gastro-oesophageal reflux is the most commonly quoted condition associated with ALTE. In two cohorts of ALTE infants referred to sleep units the prevalence of reflux was 62% of 340 infants (diagnosed by barium swallow or milk scan) [390], and 20% of 3799 infants (diagnostic methods not stated) [393]. A systematic search for reflux in 130 infants with ALTE presenting to an emergency room found 26% to have reflux [387]. However, the detection of reflux is highly dependent on the methodology used [414, 415] and studies based on contrast studies or scintigraphy cannot be relied upon [413]. No study has subjected all infants with ALTE to pH monitoring, so the true prevalence of reflux in ALTE is unknown.

Controlled studies suggest that the association between ALTE and GOR is weak. Acid reflux to the proximal oesophagus was not increased in 18 ALTE infants compared to 120 controls [416], or in 50 infants with ALTE compared to another 50 without ALTE [417].

Furthermore, there is poor evidence of temporal association between reflux episodes and pathophysiological events. In 21 infants with ALTE with polygraphically demonstrated apnoeas and episodes of acid reflux, apnoea and reflux were seldom temporally associated; where they were associated, the apnoea generally preceded the reflux episode [399] (Level 3). A study of 26 infants with ALTE found reflux in 19, but no temporal association between reflux and cardiorespiratory events on polygraphic monitoring. In addition, in 3 of 5 infants who underwent fundoplication, the apnoeas persisted [418] (Level 3). Another study of 17 infants with ALTE found 5 who had reflux episodes
associated with apnoea; however in 2 of these infants both the reflux and the apnoea were preceded by a seizure, which was felt to be the primary aetiology [419] Level 3.

Two studies have demonstrated temporal associations. In one study of 15 infants with a history of awake apnoea, 13 had more than one episode of reflux preceding airway obstruction during polygraphic monitoring [420] (Level 2-). In a second study of 16 ALTE infants, reflux was followed by a fall in SpO2 despite normal recordings of breathing movements and ECG [398] (Level 2-).

Recently, a study of intraluminal impedance monitoring for reflux in 22 infants has found that only 22% of reflux demonstrated by this technique would be detected by pH monitoring, and that 30% of apnoeas documented by polygraphy were associated temporally with reflux on impedance monitoring [80, 421] (Level 2-; Level 2-). However, this patient group contained less than 12 patients with ALTE or apnoea on history. Using oesophageal intraluminal impedance rather than oesophageal pH, a study in preterm infants found that while cardiorespiratory events and reflux were common, there was little evidence for a temporal association [421] (Level 2+).

Although gastro-oesophageal reflux features strongly in lists of causes of ALTE, it is debated as to whether all ALTE should have investigation to detect reflux, given the difficulty in knowing whether it is the cause of the disease. Some suggest that only infants with ALTE and a history of vomiting, poor weight gain, feed refusal, etc should be investigated for reflux [422].

There are no randomised controlled trials of the effect of treatment of gastro-oesophageal reflux on ALTE.

**Conclusion:** A causative association between gastro-oesophageal reflux and ALTE has yet to be firmly established.

| 56. Surgical treatment of gastro-oesophageal reflux should not be undertaken in patients presenting with recurrent apnoea or ALTE without evidence of the temporal association of the events with reflux. |

### 4.1.3 Breath holding and ALTE.

Breath-holding attacks are commonly reported by parents [423] and onset may be in infancy [424]. They may present to a health professional as an ALTE. There are no agreed diagnostic criteria for these events. The outcome of breath holding spells is generally thought to be benign [423, 425-428], but some authors have questioned this, reporting deaths occurring as a result of repeated breath holding [391, 429-432].

Iron therapy has been found to reduce breath holding attacks in a randomised controlled trial in 67 children with a high prevalence of iron deficiency and of consanguinity; the response to treatment was greater in those with iron deficiency [433]. (Level 1+)

A randomised controlled trial of the putative nootropic drug, piracetam, showed a reduction in the frequency of breath holding attacks, and a reported 92% of patients with
complete resolution after 2 months treatment, compared to 30% in the placebo group [434]. (Level 1-).

<table>
<thead>
<tr>
<th>57. In the presence of a clear history of breath holding attacks, treatment with iron should be considered, particularly if there is evidence of iron deficiency.</th>
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<tr>
<th>58. Further trials of the safety and efficacy of piracetam in breath holding attacks are needed before this drug can be recommended.</th>
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</table>

### 4.1.4 Epilepsy and ALTE.

Apnoea or ALTE may be a presentation of epilepsy [435-439] (Level 3) and ALTEs presenting to emergency departments, epilepsy has been found in 9-25% of cases [386, 387]. Infants and children may present with no obvious signs apart from episodes of apnoea, cyanosis and change in heart rate. In addition, electroencephalography between seizures is often normal [436-438, 440, 441] (Level 3). Hypoxaemic episodes from non-epileptic ALTEs can also result in secondary and prolonged epileptic seizures [442, 443] (Level 3). Continuous recordings are needed to document an event, and as well as EEG they should include simultaneous measurements of ECG, respiratory effort and airflow, oxygenation and video to determine whether seizure activity precedes or follows the clinical symptoms [400, 436, 444].

<table>
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<tr>
<th>59. In recurrent, unexplained ALTE continuous EEG recording should be undertaken (preferably simultaneously with other physiological monitoring) to attempt to capture an event.</th>
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### 4.1.5 Child Abuse and ALTE

Apnoea, cyanotic episodes and ALTE have been reported as presenting symptoms of child abuse, through mechanisms such as intentional suffocation, intentional head injury and fabricated events [401-407, 445-449]. Child abuse has been found to be a cause of 2.3% of ALTE cases [394]. In a case-control study comparing 33 ALTEs due to child abuse (confirmed by covert video surveillance) with 40 control children who required cardiopulmonary resuscitation for ALTE risk factors for child abuse included petechiae, bleeding from the mouth or nose, and one or more siblings with ALTE or sudden unexplained death [446] (Level 2b). Definitive diagnosis may be achieved by the use of covert video surveillance [407, 418, 446, 450, 451]. Guidelines exist for the use of CVS as part of multi-agency activity following national child protection procedures [452-454]. The surveillance itself is undertaken as a police activity under the Regulation of Investigatory Powers Act 2000 (HMSO).

<table>
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<tr>
<th>60. Child abuse, including fabricated or induced illness by carers, should be considered as a possible cause of ALTE in any of the following</th>
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</table>
circumstances:
- there is a history of severe or repeated attacks with a single witness of the attack onset
- petechiae or bleeding from the mouth or nose
- there is a history of ALTE or sudden death in siblings.

However, none of these features in isolation is diagnostic of child abuse.

61. In cases of ALTE where child abuse is considered a possible cause, referral to a specialist centre may be required for elucidation.

4.1.6 Intrinsic upper airway obstruction and ALTE

A PSG-based study of 29 ALTE and 30 control infants found a significant increase in obstructive apnoeas in the ALTE group [455] (Level 2+). In contrast, a study of 107 term ALTEs using documenting cardiorespiratory monitors and oximetry did not observe a significant difference in apnoeic events in the subsequent 16 weeks compared to 306 healthy term infants [456]. (Level 2+)

A subgroup of patients with ALTEs found to have obstructive sleep apnoea on polysomnography had relatives with a higher risk of SRBD and smaller upper airways than those of ALTE children with normal PSG [457] (Level 3).

Nasal CPAP has been used successfully to treat infants with recurrent ALTE who were found to have upper airway obstruction [237] (Level 3), and has also been shown to normalise autonomic function in these infants [458] (Level 2+). In the absence of randomised controlled trials and the favourable prognosis of most ALTEs, this intervention should be reserved for infants with proven OSA and severe and recurrent symptoms.

62. Polysomnography should be performed in infants with severe and recurrent ALTE.

63. In children with severe and recurrent ALTE due to OSA, a trial of CPAP is indicated.

4.1.7 Cardiac dysrhythmias and ALTE

A case series of 6 patients with cardiac dysrhythmias presenting as ALTE has been reported [409], although in series of patient with ALTE, identified dysrhythmias account for less than 1% of cases [387, 393]. (Level 3). Arrhythmias may also be a presenting feature of metabolic disease [459]. A study of 24 hour ECG recording in 100 infants with ALTE found 62% with one or more dysrhythmias and 30 with a QTc interval above the 97th centile [410]. No control group was studied, the only two patients treated had sinus node dysfunction, and no subsequent adverse events were seen in this cohort.

An electrocardiographic study of 305 infants referred for ALTE did not find dysrhythmia or ECG abnormalities [460].

Conclusion. Cardiac dysrhythmias are a rare cause of ALTE.
While the benefit of routinely measuring the QTc interval in infants with ALTE has not been established, it is a simple investigation and it is reasonable to carry out an ECG in infants presenting with ALTE. Particular attention should be paid to infants with recurrent events, or in those with a family history of sudden death or familial deafness.

**64. An ECG should be recorded, and QTc measured, in all infants presenting with ALTE**

### 4.2 Consequences of ALTE

In three cohort studies of ALTEs presenting to A&E departments [386, 387, 397] there were 2/359 subsequent deaths - a subsequent mortality of 0.6%. A further 3 studies report complete cohorts of infants with ALTE referred to sleep units [390, 392, 393]: 2/1503 (0.13%) infants subsequently died. A systematic review selecting studies with adequate causal investigations found 5 deaths in 643 infants followed for 6-18 months (0.8%) [388]. These deaths occurred in infants with severe gastro-oesophageal reflux (2) and rare congenital metabolic disorders (3). These data suggest that the risk of subsequent death after ALTE is less than 1%. *(Sackett level 1b)*. Despite a number of case reports of individual fatalities after ALTE, these data suggest that the outlook is generally reassuring, although serious underlying conditions must be taken into account. Infants who require repeated vigorous resuscitation appear to be at higher risk of subsequent death [461, 462]. Follow-up into pre-adolescence has found no significant differences in behaviour or IQ between ALTE infants and matched controls [463]. *(Sackett level 2b)*

**Conclusion.** Infants with ALTE where no serious underlying condition is found have a very low risk of subsequent death.

**65. Specialist assessment of ALTE is needed for infants with recurrent
significant events; events where cardiopulmonary resuscitation has
been needed; or those with a family history of unexplained childhood
death.**

### 4.3 Discharge Planning

The plans for follow up of infants and their families need to be individualised and depend on the underlying diagnosis, severity of the event and views of parents, doctors and community staff. Infants with a single mild episode or self-limiting diagnosis do not require follow up.

If an infant who has been admitted to hospital with an ALTE is to be discharged home without a monitor, they should spend some time in hospital without monitors attached. Discharge should be undertaken when the family feel confident and health professionals are happy with the infant's condition.
At the time of hospital discharge, parents require a clear account of what has happened, and the level of medical understanding for the infant's event. Health professionals should be cautious in applying diagnostic labels without good objective evidence, in order to avoid the escalation of treatment for a recurrent condition.

4.4 **Effective interventions.**

The multiplicity of causes means that there are a number of specific interventions which may be effective. In the infant with recurrent ALTEs where no underlying cause has been found there are no studies of effective interventions. Methylxanthine treatment has been used in the presence of an abnormal respiratory pattern and was associated with improvements in pneumogram in an uncontrolled clinical trial [464]; there is no evidence that it affects outcome, and it may worsen gastro-oesophageal reflux and epilepsy.

4.4.1 **Home monitoring**

There has been no randomised controlled trial performed to show that home monitors reduce mortality and they should not be provided on this basis. Practices for offering home monitoring vary widely from those who consider that home monitoring has no role to play to those in whom it is offered to all families.

Cardiorespiratory monitoring is more commonly used in North America and in some other parts of Europe using impedance pneumography and electrocardiography, but this method has not been clinically validated to detect potentially severe apnoeic-hypoxaemic episodes or ALTE [465]. Cardio-respiratory monitors have a high rate of false alarms [466] and may not detect events, deaths having occurred on such monitors [467-469].

In the UK, apnoea monitors that work by detection of body movements are used alone. These have a poor ability to detect hypoxaemic events [470], and deaths have also occurred on these monitors [471]. There is also a theoretical risk of strangulation from such monitors in older infants [472].

An advance in monitor technology in recent years has been the ability to record monitor use and the physiological waveforms prior to an alarm. Such documenting cardiorespiratory monitors have shown bradycardia rather than cessation of breathing movements to precede death/near-death episodes [473]. However, oxygenation was not recorded in these studies; another study recording near death episodes has shown hypoxaemia as the initial changing parameter [400].

Monitoring may increase or lower parental anxiety [474, 475]. Ongoing support is likely to be required for many parents, particularly those who undergo home physiological monitoring.

<table>
<thead>
<tr>
<th>66. There is no evidence to support the routine use of home monitors in ALTE.</th>
<th>✓</th>
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<tbody>
<tr>
<td>67. If a decision is taken to issue a monitor, the parents must understand</td>
<td>✓</td>
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<td><strong>that there is no evidence that it will prevent subsequent death.</strong></td>
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<tr>
<td><strong>68. Cardiopulmonary resuscitation should be taught to any carers who take home an infant with a monitor.</strong></td>
<td>✓</td>
</tr>
</tbody>
</table>
Table 6. Suggested investigations in ALTE.

First line investigations

*If clinically well*

- Full blood count
- Urine culture
- SaO2 measurement/recording
- ECG
- Urine organic acids
- Serum and urine amino acids
- Blood sugar †
- Arterial blood gas †
- Lactate †
- Ammonia †

*If unwell, may also require:*

- Blood culture ± lumbar puncture
- Nasopharyngeal aspirate for viral immunofluorescence and culture
- Pernasal swab for pertussis
- Chest x-ray

Second line investigations (severe/recurrent events)

- Multi-channel physiological recordings / event recording*
- EEG*
- Oesophageal pH monitoring (simultaneous with physiological recording if possible)
- ENT assessment
- Cranial imaging (Ultrasound, CT, MRI)
- Echocardiogram
- Skeletal survey
- Urinary toxicology screen

Third line investigations

- Covert video surveillance (if onset only ever witnessed by one person)

† if close to event/still unwell
* of particular value for documenting pathophysiology during subsequent event

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<table>
<thead>
<tr>
<th>Blood culture</th>
<th>± lumbar puncture</th>
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<tbody>
<tr>
<td>Nasopharyngeal aspirate</td>
<td>for viral immunofluorescence and culture</td>
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<tr>
<td>Pernasal swab</td>
<td>for pertussis</td>
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<tr>
<td>Chest x-ray</td>
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<tr>
<th>Multi-channel physiological recordings / event recording</th>
<th>EEG</th>
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<tr>
<td>Oesophageal pH monitoring</td>
<td>(simultaneous with physiological recording if possible)</td>
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<tr>
<td>ENT assessment</td>
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<tr>
<td>Cranial imaging</td>
<td>(Ultrasound, CT, MRI)</td>
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<td>Echocardiogram</td>
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<tr>
<td>Skeletal survey</td>
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<tr>
<td>Urinary toxicology screen</td>
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<table>
<thead>
<tr>
<th>Covert video surveillance</th>
<th>(if onset only ever witnessed by one person)</th>
</tr>
</thead>
</table>

† if close to event/still unwell
* of particular value for documenting pathophysiology during subsequent event
5. Non Respiratory Causes Of Excessive Daytime Sleepiness In Children

Search strategies: In addition to the searches listed under each section, manual search was also done from textbooks, including the International Classification of sleep disorders. Manual search was also done from index of sleep journals (2002-6), available in personal library, especially Sleep and Journal of Sleep Research

5.1 Narcolepsy

Search strategy:
Medline 1950-Dec 2006
Narcolepsy/

Narcolepsy is a chronic neurological disorder, the core symptoms of which are excessive daytime sleepiness, cataplexy (sudden loss of muscle tone induced by strong emotions), hypnogogic hallucinations (vivid dream like visual images before falling asleep), sleep paralysis (persistence of rapid eye movement sleep atonia on awakening) and night sleep disturbance. It is a life long disorder with striking similarity in symptomatology, age of onset and disease severity across ethnic groups [476].

Narcolepsy with cataplexy is very tightly associated with human leucocyte antigen (HLA) subtype DQB1 0602 with almost all patients with cataplexy positive for this subtype compared to 12 to 38% in general population. However only 40% of patients with narcolepsy without cataplexy are HLA DQB1 0602 positive. Most cases of narcolepsy with cataplexy are associated with loss of hypothalamic neurons containing the neuropeptide hypocretin, identified by measuring CSF hypocretin-1 level [477]. It is hypothesised that destruction of hypocretin neurons occurs by an autoimmune process, though there maybe genetic susceptibility [478].

5.1.1 Prevalence

The prevalence of narcolepsy in a European population survey was 1:2,000 [479], comparable to figures quoted for Americans [480]. In a cohort of 519 narcoleptics in France and French Canada the age of onset was bimodal in distribution. The early-onset group contained 66% of the patients and had a peak age of onset of 14.7 years. Thus onset of symptoms occurs in childhood in at least half of adult narcolepsy sufferers; about 1 in 6,000 fourteen year olds will be affected. (Sackett level 4). Onset before 5 years of age is rare in idiopathic narcolepsy [481].

An underlying causative conditions is present in about 25% of cases of childhood narcolepsy; these conditions include Niemann Pick disease Type C and brain tumours [482, 483]. Children with secondary narcolepsy have an earlier age of onset [482] (Sackett level 4).
5.1.2 Diagnosis

The diagnostic criteria for narcolepsy according to the International Classification of Sleep Disorders are shown in Table 7.

Table 7.

**a. Diagnostic criteria for narcolepsy with cataplexy.**

A. The patient has a complaint of excessive sleepiness occurring daily for at least 3 months.

B. A definite history of cataplexy, defined as sudden and transient episodes of loss of muscle tone triggered by emotions (most reliably laughing or joking) and generally bilateral and transient, is present.

C. The diagnosis of narcolepsy and cataplexy should whenever possible be confirmed by nocturnal polysomnography followed by the MSLT; mean sleep latency on MSLT is less than or equal to 8 minutes and 2 or more SOREM are observed following sufficient nocturnal sleep on preceding night. Alternatively, hypocretin-1 level in the CSF is less than or equal to 110pg/ml or 1/3 of mean normal control values.

D. The hypersomnia is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use or substance use disorder.

**b. Diagnostic criteria for narcolepsy without cataplexy.**

A. The patient has complaint of excessive daytime sleepiness occurring daily for at least 3 months.

B. Typical cataplexy not present though doubtful or atypical cataplexy like episodes (sensation of muscle weakness triggered by emotions such as stress or intense activity/exercise) may be reported.

C. Must be confirmed by nocturnal polysomnography followed by MSLT; same MSLT criteria as in narcolepsy with cataplexy.

D. Hypersomnia not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use or substance use disorder.

**NB.** 10 to 20% of narcolepsy patients without cataplexy, almost all with HLA DQB1 0602, have CSF level of hypocretin less than 110pg/ml (normal value 200-600), often with associate complaints of sleep paralysis and hypnagogic hallucinations present.

MLST- Multiple Sleep Latency Test
SOREM- Sleep Onset with REM
CSF- Cerebrospinal Fluid
The above criteria are valid for the diagnosis of narcolepsy in children with some provisos. Children may deny the occurrence of daytime sleepiness and they may find it difficult to explain the symptoms of hypnagogic hallucinations and sleep paralysis, which are extremely frightening. Sleepy children may present with attention and behaviour problems. Cataplexy, especially partial, may also be difficult to elicit in children [484, 485]. Also, there is a possible link between narcolepsy and weight gain in children, manifested early in the course of the disorder [486], which may cause confusion between obesity-hyperventilation and narcolepsy as possible causes. Because of the difficulty in relying on clinical history in this group, nocturnal polysomnography with subsequent multiple sleep latency test (MLST) is important. As the lower age limit at which one can start applying the MSLT is around 6 years of age [487], for the younger children with narcolepsy diagnosis may have to rely on nocturnal polysomnography features including short sleep onset latency, SOREM and disruption of normal sleep patterns and frequent awakenings [488]. MSLT findings become more abnormal over time, so it may be necessary to repeat the studies in some children before the diagnosis is confirmed [487]. CSF hypocretin measurements may prove to be a useful diagnostic tool in the future [489]. As onset of narcolepsy under the age of 5 is exceptional, it is important to exclude secondary causes, including intracranial pathology, metabolic disorders and chromosome disorders, if symptoms present early.

5.1.3 Consequence Of Not Diagnosing Narcolepsy

Studies have shown that narcolepsy has a profound influence on the quality of life and safety of individuals with this disorder, with negative effect on education, recreation and personality [490, 491]. Children can be misdiagnosed as lazy and may be disciplined in school for falling asleep or poor attention, concentration and memory, or suspected of using illicit drugs [484, 485, 492, 493] (Sackett level 4). This can lead to academic decline and feeling of loss of self worth, with implications for future personal and professional development. The finding that sleep deprivation or restriction affects higher cognitive functions, innovative thinking, flexible decision making [494] and abstract thinking and verbal creativity [20] is of concern for children in whom the diagnosis is delayed. Cataplexy can be misdiagnosed as epilepsy and lead to inappropriate investigations and treatment [484, 493, 495] (Sackett level 4).

69. To confirm a diagnosis of narcolepsy, referral to a centre experienced at PSG and MSLT in children, with clinical experience of narcolepsy is necessary.

5.1.4 Treatment

The management of narcolepsy in children should include medical and non medical management. Supporting the child, parents and school in understanding the disorder and encouraging good sleep hygiene is essential. Breaking the day with short 15 - 20 minute naps can help and it is important that the children do not fight sleep. Special allowances
may need to be made for academic examinations or other competitive performances [496].

Monitoring of school performance and social development is essential and if these are affected, stimulant medication should be considered. Drugs used for excessive daytime sleepiness include the non amphetamine stimulant Modafinil, and amphetamine-based stimulants, including Dexidrene and Methylphenidate. Cataplexy responds to tricyclic antidepressants, with clomipramine most widely used, and also SSRI, including Fluoxetine and Venlaflaxine. There are no RCTs of treatment in children alone. Randomised controlled trials involving children have shown positive effects on sleepiness and cataplexy from modafinil [497] (Level 1-) and selegiline hydrochloride [498]. (Level 1-). Sodium oxybate improves quality of night sleep with increase in slow wave sleep and has shown promising results in alleviating symptoms of cataplexy and excessive daytime sleepiness, in adults with narcolepsy and cataplexy [499-502] (Level 1+). However its safety and efficacy in children and adolescents has not yet been established.

There have been case reports of at least transient improvement in cataplexy in hypocretin deficient children, presenting within a few months of symptom onset, treated with intravenous immunoglobulin [503], but immunosuppression with prednisolone was not found to be successful [504]

Conclusions
A high index of suspicion and a careful history are required to recognise symptoms of narcolepsy in childhood.

70. Management of narcolepsy should only be undertaken under supervision from a clinical service experienced in the condition.

5.2 Idiopathic CNS Hypersomnia

Search strategy
Medline 1950-Dec 2006
(idiopathic AND CNS AND hypersomnia)

Idiopathic CNS hypersomnia is defined as a disorder of presumed central nervous system that is associated with a normal (<10 hours) or prolonged (>10 hours) major sleep episode at night with excessive daytime sleepiness consisting of prolonged (1 - 2 hours) sleep episodes of NREM sleep [481]. There are no prevalence data for this condition, and little information on paediatric presentation, although the commonest age of onset is during adolescence [505] It can be differentiated from narcolepsy by history (no cataplexy episodes or associated features of narcolepsy) and polysomnography which shows normal or >10 hours of night sleep with no SOREM. Mean sleep onset latency is less than 8 minutes (6.2 +/-3) with less than 2 naps with SOREM. It is important to exclude those patients with head trauma who may have transient excessive daytime sleepiness for up to 18 months after the injury.
5.3 **Hypersomnia With Depression**

*Search strategy: Medline 1950-Dec 2006: (Hypersomnia.mp) AND (depression/) AND (children OR adolescents)*

Adolescents with depression may present with excessive daytime sleepiness. A study of 102 patients with major depressive disorder found 17% reported hypersomnia [506]. Yorbik et al. [507] compared the symptoms of major depressive disorder and rates of comorbid psychiatric disorders between depressed children and adolescents. They found that depressed adolescents had significantly more lack of energy/ tiredness and hypersomnia than depressed children. It should also be noted that in a prospective survey of children in a psychiatric clinic who reported daytime sleepiness, 39% were found to have polysomnographic evidence of OSA [508].

5.4 **Chronic Fatigue Syndrome / Myalgic Encephalomyelitis and Excessive Daytime Sleepiness**

*Search strategy: Medline 1950-Dec 2006: (Fatigue syndrome, chronic/) AND (hypersomnia.mp)*

Patients with chronic fatigue syndrome (CFS) or fibromyalgia complain significantly of daytime tiredness and sleepiness [509, 510]. The RCPCH guidelines on CFS [511] emphasise clinical and research evidence of sleep disturbance consisting mainly of phase delay, and sleep interruptions, but non-refreshing sleep, difficulty falling asleep and excessive sleepiness is also reported. Polysonography in a group of teenagers with chronic fatigue syndrome documented more sleep disruption than in matched healthy controls [119]. However, a monozygotic co-twin control study found that though patients with chronic fatigue report increased sleepiness, their MSLT was in the non pathologic range, and not significantly different from their well twin, suggesting they may be mistaking chronic fatigue for sleepiness [512]. In one study of 30 consecutive adult and teenage patients presenting to a referral centre with chronic fatigue syndrome 10 (33%) were diagnosed as having a primary sleep disorder [513].

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**71. Polysomnography may be necessary to rule out a primary sleep disorder in selected cases of suspected CFS where excessive daytime sleepiness is a prominent feature**

5.5 **Insufficient Night Sleep**

Excessive daytime sleepiness may occur in children, especially adolescents because of poor sleep hygiene or other causes of insufficient night sleep. Carskadon et al 1980 showed that adolescents require at least as much sleep as they did as pre-adolescents, in general 8.5 - 9.25 hours each night [514]. In adolescence sleep patterns tend towards later times for both sleeping and waking (phase delay), so that an adolescent, even if maintaining good sleep hygiene, may feel sleepy during the school week, especially with
an early start [515]. Sleep deprivation results in worse cognitive function [20] (Level 1+). These observations emphasise the importance of sleep diaries or actigraphy and trials of extended sleep (up to 9 hours in the case of long sleepers) to exclude sleep deprivation as the cause of excessive daytime sleepiness before undertaking sleep physiology testing.

**Conclusion.** Sleep restriction is common in adolescents and is associated with poor daytime functioning.

| 72. Assessment of sleep habits using diaries or actigraphy is essential in the evaluation of daytime sleepiness. | √ |
| 73. Polysomnography is indicated if a cause is not otherwise apparent. | √ |

### 5.6 Delayed Sleep Phase Syndrome

**Search strategy:** Medline 1950-Dec 2006: delayed sleep phase syndrome

Delayed sleep phase syndrome is a disorder in which the major sleep episode is delayed in relation to the desired clock time, usually more than 2 hours, relative to conventional and socially acceptable times, but once sleep ensues, sleep is reported as normal [481]. Patients present with delayed sleep onset and insomnia or difficulty in waking at the desired time, and excessive daytime sleepiness if forced to maintain socially acceptable morning wake time. When allowed to follow their preferred schedule the patient`s circadian phase of sleep is delayed but stable and attempts to fall asleep earlier are unsuccessful. Although it can occur in younger children, the commonest sufferers are adolescent boys. Almost all patients are "evening" type. Both genetic factors (such as polymorphism in \( hper3 \)) and environmental factors are thought to contribute.[516]

The prevalence of this syndrome is difficult to define as it forms a continuum from normal sleep patterns. A survey of Italian adolescent schoolchildren found a mean daily sleep debt of over 2 hours in the 11% of the population with the most phase delay. This group of adolescents had worse school performance than their peers, with over 40% reporting attention problems at school, and 1 in 5 falling asleep during school [517].

A period of actigraphy may be sufficient to diagnose this sleep - wake cycle disorder. Polysomnography recordings show prolonged, usually greater than 30 minute sleep onset latency, with sleep onset delayed to 1am to 6am and morning wake time from late morning to afternoon. Sleep efficiency tends to be low for age (75% - 85%), most of the inefficiency due to the prolonged sleep latency. Though some patients may show a modest shortening of REM latency, sleep is largely free of arousals once the patient is asleep. [518].

| 74. Delayed sleep phase syndrome is best diagnosed by history and actigraphy. | √ |

The importance of identifying this disorder is that it can be treated. Chronotherapy (steady delay in bed time until the desired time is reached) [519] was successful in an uncontrolled small group of patients (Level 3). Bright light therapy, Vitamin B12 and
melatonin have also been used, separately or in combination. Randomised trials of melatonin in young adults with DSPS have shown short term benefits [520, 521] (Level 1+), but a high rate of relapse in the following year after treatment was stopped [522]. (Level 3). It has also been found to be effective in advancing sleep onset over a 4 week treatment period in pre-pubertal children with sleep-onset delay. Long term benefits were less clear [523] (Level 1+). In a case series of 20 adolescents with DSPS where combinations of the above treatments were tried systematically, 13 (65%) were considered to have been successfully treated [524]. (Level 3). Afternoon melatonin combined with morning bright light with 3 days of gradually advancing, wake up time produced a gradually advancing circadian rhythm, by about an hour a day [525] (Level 3) Melatonin is not currently licensed for these indications in the UK.

| 75. Chronotherapy should be considered in the treatment of delayed sleep phase syndrome. |
| 76. Melatonin may give short term benefits in delayed sleep phase syndrome. |
| 77. The effects of melatonin in delayed sleep phase syndrome are not sustained after cessation of treatment |

### 5.7 Non 24 Hour Sleep Wake Syndrome

The non 24 hour sleep - wake syndrome consists of a chronic steady pattern, comprising 1 - 2 hour daily delays in sleep onset and wake time in an individual living in society [526]. Patients with non 24 hour sleep - wake syndrome exhibit a sleep - wake pattern that is reminiscent of that found in normal individuals living without environmental time cues. In these individuals their sleep phase periodically travels in and out of phase with conventional social hours for sleep. When in phase the patient may have no sleep complaint and daytime alertness is normal. As incremental phase delay in sleep occurs, with difficulty initiating sleep at night, coupled with over sleeping in the daytime hours or inability to remain awake during the daytime. Most of the children and adolescents described in the medical literature have been blind, and some have severe learning difficulties [527, 528]. However Hayakawa et al. [529] studied 57 sighted patients with non 24 hour sleep wake cycle disorder, with onset in teenage years in 63% of the cohort. Psychiatric disorders preceded the onset of the circadian rhythm disorder in 28%, and of the remaining, 34% developed major depression after the onset of the sleep disorder. Diagnosis may be aided by sleep diaries and/or actigraphy. There are anecdotal reports of children with non 24 hour sleep - wake syndrome responding to vitamin B12 [530, 531] (Level 3) and melatonin [532, 533] (Level 3).

### 5.8 Episodic Hypersomnia / Kleine Levin Syndrome

Search strategy: Medline 1950-Dec 2006: Kleine Levin syndrome/

Recurrent hypersomnia or Kleine Levin syndrome is a disorder characterised by recurrent episodes of hypersomnia that typically occur weeks or months apart. The episodes of
hypersomnia can be associated with binge eating, with or without transient behaviour changes, which include irritability, aggression, impulsive behaviours, restlessness or sexual hyperactivity. A monosymptomatic form of the disorder with hypersomnia only can occur without binge eating or hypersexuality. Typically the episodes last several days to several weeks and appear on average twice a year but can occur as many as 12 times a year, with patients sleeping as long as 18-20 hours of the day during somnolent episodes, waking only to eat and void [526].

Onset is usually adolescence, but can occur in younger children [534]. Although the original reports were confined to males, it is also seen in females [535]. Long term follow up studies of patients with Kleine Levin syndrome have not been performed, but anecdotal evidence suggests that the disorder may remit spontaneously over several years, but can persist into young adult life. There is no randomised controlled study of treatment response. Case reports of lithium treatment suggest a response [534, 536], and a systematic review of 186 cases in the literature suggested that lithium was effective in preventing relapses (41% vs 19% in untreated cases) and that sleepiness responded to stimulants in 40% of 75 treated cases. Carbamazepine and other antiepileptics appeared ineffective. [537]. (Level 3)

5.9 Restless Leg Syndrome / Periodic Leg Movement Disorder

Search strategy:
Restless leg syndrome limited to “All child (age 0-18 years)”

Restless leg syndrome (RLS) is a disorder characterised by disagreeable leg sensation that usually occurs prior to sleep onset and causes an almost irresistible urge to move the legs. The complaint is often associated with periodic limb movement disorder (PLMD), characterised by periodic episodes of repetitive and highly stereotype limb movements that occur during sleep. These are more frequent in the first part of night occurring in NREM sleep. Monitoring of EMG from the anterior tibialis muscle show repetitive contractions, each lasting 0.5 to 5 seconds (mean duration 0.5 - 2.5 seconds), with inter movements interval, typically 20 - 40 seconds. The PLM index is the number of movements per hour of total sleep time and is determined by polysomnography of the major sleep episode. An index of 5 or more is regarded as abnormal [526, 538]. Both RLS and PLMD were considered disorders of middle age, but in the last decade there has been an increased recognition of RLS in children including in some who present to orthopaedic services with "growing pains"[539, 540]. A familial pattern is seen in 50% of patients with primary RLS, with autosomal dominant inheritance and anticipatory onset in some. Secondary RLS can occur in several other medical disorders. Complaints associated with the disorder include sleep onset insomnia, disturbed night sleep, and daytime tiredness / sleepiness [481].

5.9.1 Prevalence and consequences.

In a study of adults with RLS symptoms, over 1/3 reported onset of symptoms before the age of 10 [541]. In a questionnaire survey of 62% of a target population of 1400 US children, restless legs were reported in 17%, and growing pains particularly in bed in 8%
Kotagal and Silber identified RLS in 5.9% of 538 children below the age of 18 attending their sleep disorder centre. 72% had family history of RLS, especially in the mothers, with sleep onset or sleep maintenance complaint the most common presenting symptom [543]. The prevalence of objectively documented PLMD in a general childhood population has not been estimated, but abnormal indices of periodic leg movements have been found in 8.4% of children referred to sleep services [544]. Associations have been demonstrated between PLMD and daytime tiredness or inattention [539, 542] (Level 3), and in such patients daytime tiredness has improved on dopaminergic treatment [539]. (Level 3)

Associations have been found between PLMD and Attention Deficit/Hyperactivity Disorder (ADHD). In a population of children referred to a sleep centre, 129 were found to have PLMD (>5 PLM/hour), and 117 had ADHD, although no control data were obtained. In only 3/16 children with moderate or severe PLMD (>25 PLM/hour) had the PLMs been recognised before the sleep evaluation [539] (Level 3). A systematic review of the literature from 1970-1998 found that the only objective difference between ADHD and control children was in movements during sleep [545] (Level 1). More recently, a case-control study of sleep-clinic and community-based patients with ADHD found that whereas the sleep-clinic patients had abnormal levels of PLMs, community-based patients were no different to controls [546]. (Level 2++) In contrast, a case-control study of 34 children with ADHD recruited from neurology or psychiatry clinics found 5 with PLMD, compared to 0/32 matched controls [547] (Level 2++). The use of stimulants for ADHD does not affect movements during sleep [545] (Level 1+).

The Stanford group found PLM in 23% of pre pubertal children attending a sleep disorder centre, studied prospectively. Of the 58 children with PLM, sleep related breathing disorder was found in 29 children, and other medical and sleep syndromes in the remaining, with only 2 children having isolated PLM. 11 children in the total group had ADHD, with PLM in 7, though 2 also had sleep related breathing disorder. In 2 children PLM were associated with RLS (Level 3). The authors acknowledge that PLM can be associated with a number of conditions but recommend a search for PLM in children with complaints of chronic fatigue, sleepiness and difficulty in initiating or maintaining sleep [548]. Though there was increase in reports of leg pains and leg pains worsening at night in the PLM group, the authors were reluctant to emphasise the significance of this symptom, because of the associated comorbidity and the difficulty in describing symptoms by some of the very young children. Five of the 6 children treated with pramipexole had improvement in clinical complaint and included reduction in hyperactivity in a child with ADHD. Adults with RLS had more ADHD symptoms compared to age adjusted insomnia patients or controls [549]. Reviewing the literature on RLS and ADHD, Cortese et al concluded that the evidence from clinical studies, though limited, demonstrates an association between RLS and ADHD or ADHD symptoms. [550]

| 78. A history of restless legs or growing pains should be sought in children with daytime symptoms suggestive of a sleep disturbance, including attention problems. |
|---------------------------------------------------------------|---|
| 79. The current evidence is not yet adequate to warrant screening for PLMD in children with ADHD. | --- |
5.9.2 Diagnosis

The criteria for diagnosing RLS in children under age 12 include report of an urge to move the legs caused by unpleasant and uncomfortable sensation (described in the child’s own words that is consistent with discomfort), the unpleasant sensation being worse during periods of rest or inactivity mainly in the evening or night, and partially or totally relieved by movements. If the child appears to have the symptoms but is unable to describe in their own words consistent with discomfort, the diagnosis can be considered if 2 of the following 3 features are present: a sleep disturbance for age, a biological parent or sibling with definite RLS, and a PLM index of 5 or more on polysomnography [481].

5.9.2 Treatment

In most children, specific pharmacological therapy will be unnecessary unless the disorder is causing significant functional disturbance, such as insomnia or excessive daytime sleepiness. Case reports in children have reported reduced symptoms and improved daytime alertness from levodopa or pergolide [539, 551] (Level 3). Clonazepam has been found to be beneficial in adults [552], and in 4/5 children with restless legs syndrome associated with William’s syndrome [553] (Level 3). Gabapentin has also been found to be effective in adults in a randomised controlled crossover trial [554], and in children in a case report [555]. Since there are links between PMD and iron deficiency in adults, Simakajornboon [556] looked at the iron status in consecutive children with PLMD and found that 28/39 (72%) children) had ferritin level <50 micrograms per litre and 76% of these children had reduced frequency of PLMs after iron therapy (Level 3). Kotagal and Silber also found low serum ferritin level in 20/24 (72%) children with RLS [543].

| 80. Iron deficiency should be sought and treated in children diagnosed with RLS. | C |
| 81. If PLMD/RLS is associated with significant functional disturbance, then treatment with levodopa, dopamine agonists, gabapentin or clonazepam should be considered. | D |
6 Episodic behaviours in sleep after infancy

Parasomnias are undesirable physical phenomena that occur predominantly during sleep. The International Classification Of Sleep Disorders [481] sub-divide parasomnias into disorders of arousal from NREM sleep, parasomnias usually associated with REM sleep and other parasomnias which include sleep related groaning or eating, enuresis etc.. The new classification separately categorises the sleep related movement disorders such as rhythmic movements in sleep e.g. head banging, and also bruxism and periodic leg movements in sleep, and nocturnal leg cramps. The classic disorders of arousal from NREM sleep are sleep walking, sleep terrors and confusional arousals. Disorders associated with REM sleep are sleep paralysis, hypnogogic and hypnopompic hallucinations, nightmares and REM behaviour disorder

6.1 NREM Arousal Disorders

Sleep terror, sleep walking and confusional arousals are clustered together because episodes share many features in common, including automated behaviour, relative non reactivity to external stimuli, difficulty in being aroused, fragmentary or absent dream recall, mental confusion and disorientation when awakened and retrograde amnesia for the episode the next morning. Sleep terrors first appear after 18 months of age, sleep walking occurs in slightly older children of pre-school and school age years and confusional arousals can occur at any age [557]).

Arousal disorders occur 1 - 3 hours after sleep onset at a time of transition from NREM Stage 4 (deep sleep) to REM sleep. Approximately 3% of children have night terrors, which occur predominantly in pre-pubertal children, but can occur at any age [526]. In a Swedish survey of children aged 6-16 the annual prevalence of sleepwalking varied from 6-17%, with 40% of children sleepwalking at some point [558]; even persistent sleepwalking was not associated with significant psychopathology. In contrast, adolescents with sleep terrors and/or sleep walking had more psychiatric diagnoses and problems than matched controls [559] (Level 2++). As arousal disorders are difficult to predict because they occur sporadically, monitoring in a sleep laboratory is usually not helpful, though if persistent and frequent, sleep studies may be indicated to exclude a primary sleep disorder such as RLS or sleep related breathing disorder [560] which may be lowering the arousal threshold in a child predisposed to NREM arousal parasomnia. A home video recording of the episodes can often provide diagnostic information. Occasionally epileptic seizures may be misdiagnosed as parasomnias [561, 562] and further studies, including video telemetry may be indicated especially if the episodes are frequent and occurring throughout the night [561-563]. (Level 3).
Most often reassurance and explanation as well as common sense safety precautions to limit injury is sufficient, with advice on sleep hygiene but psychotherapeutic support maybe needed. The anticipatory waking technique described by Lask [564] can be valuable in some children in whom the timing of the night behaviour is consistent.

6.2 Sleep–related Movement Disorders

Sleep-related movement disorders include periodic leg movements in sleep (see above), nocturnal leg cramps, bruxism and rhythmic movement disorders (head banging and body rocking). The rhythmic movement disorders are most likely to come to the paediatrician’s attention. These behaviours are common in infants and less so in older children. When intense rocking or head banging persists in the older child, parents may seek help as the noise disturbs the family, there is concern about injury and in the older child, may lead to social restrictions with the child reluctant to have sleep-overs. Emotional factors may be relevant in some children, with lack of environmental stimulation proposed as factors. Self-stimulation and auto-erotic behaviour may be observed, particularly in children with learning difficulties. The activity may also be a way of getting attention or a form of passive aggressive behaviour [526]. Guidance and support to make sure that the child is safe from injury is usually sufficient. Etzioni et al [565] reported a positive response to a programme of sleep restriction combined with a short course of hypnotic.

6.3 REM Parasomnias

The most common REM parasomnia is nightmares, which are frightening arousals from REM sleep, associated with dream reports that are anxiety laden. Stress of various kinds may be triggers and also medication, including beta blockers and withdrawal of drugs that suppress REM sleep. Nightmares usually start between the age of 3 - 6 and affect 10 - 50% of children in that age group severe enough to disturb their parents. Nightmares occur later in the night and are well remembered in the morning in contrast to night terrors, which occur in the first 3 hours of sleep and there is no memory [557].

REM sleep behaviour disorder [566] is characterised by intermittent return of muscle tone during REM sleep, resulting in restored motor function and the appearance of elaborate behaviours in apparent association with dream mentation. Punching, kicking, leaping and running from the bed usually correlate with reported dream imagery [557]. REM behaviour disorder is rare in childhood and in the few reported cases, a neurological lesion has been identified or the condition occurred in association with other sleep disorders, such as narcolepsy. However, in 33 cases of a parasomnia overlap disorder involving sleep walking, sleep terrors and REM sleep behaviour disorder, 22 were idiopathic. In this group the age of onset of the parasomnia was in childhood (mean age 8.8 years. Suggestive features on polysomnography included REM onset of behaviour disturbance with little autonomic activation during episodes occurring from REM sleep. Ninety percent of the patients treated responded to clonazepam and/or carbamazepine [567] (Level 3)
82. Most episodic events occurring during sleep are benign and do not warrant investigation.

83. Episodes which are frequent, or occur throughout the night, require more evaluation, including EEG and video monitoring to exclude epilepsy.

84. Persistent troublesome events during sleep may require full polysomnography, including video and EEG, to exclude treatable factors.

7. Current provision of services

A preliminary survey was conducted by the working party in 2002, with a questionnaire sent to all consultant paediatricians in the UK, asking them about sleep services in their area, and where they would send five exemplar cases (OSA, neuromuscular patient with suspected nocturnal hypoventilation, possible narcolepsy, ALTE, unusual night awakening.) The median number of different referral targets listed by doctors from a single Strategic Health Authority ranged from 2 to 3. Contradictory referral patterns were identified. In more than one area a tertiary recipient of referrals for a case would themselves refer the case elsewhere. In one area the neurology services said that they referred to the respiratory paediatricians and vice versa. Respondents were invited to add free text comments, and 88 (34%) did so. The commonest comment (86%) was that there was a large unmet need for sleep services in the area. The points which emerged from this survey were:

- Poor awareness of local facilities, particularly if a full service is not available.
- Inconsistent referral patterns, with adjacent hospitals often referring to widely different centres.
- A widely perceived need for better provision and organisation of services.

Further to the 2002 survey, a more detailed and directed survey of paediatric PSG facilities was conducted by Dr Cathy Hill in 2005 (unpublished data). This identified 21 possible paediatric sleep centres from 3 sources: the British Sleep Society UK Provider Directory, information from commercial companies providing sleep systems and data from the original 2001 survey. A survey questionnaire was sent to all possible centres, of whom 18 (86%) responded, one of whom was not a provider of PSG services. 12 centres were offering full PSG, 2 were in transition to such a service and 5 were offering extended cardiorespiratory monitoring only. Some centres offered mainly electrophysiological investigation and some mainly cardiorespiratory investigation.

The number of PSG studies performed by each centre per year varied from 20 to over 500 (reported by a single centre). Studies were done in a variety of settings with only 6 centres having a specialised paediatric sleep laboratory in which to conduct studies. Two centres conducted home PSGs, two had mixed adult/paediatric laboratories, and one used
HDU. Two centres could only perform studies in an open paediatric ward. A total of 10 specialised paediatric sleep laboratory beds were identified nationally. Eleven centres have the ability for electrophysiological sleep staging of studies, 5 can do full EEG recording with sleep studies, and 7 can record leg EMG. Ten centres reported that their studies were fully attended overnight, with others relying on intermittent nurse surveillance. 8/17 centres employ a total of 22 sleep technologists or physiologists, but the other 9 centres are without any specialised staff for the PSG. Paediatricians in 5 centres were reported to be competent to set up, score, and report a PSG. Concern was expressed by many respondents about quality control, since there was no identified mechanism for external review of studies in any centre, and most are working in isolation.

The problems identified in the current provision of service are:
- Very variable quality and quantity of services in different geographical areas.
- Lack of awareness of tertiary facilities available within secondary care centres.
- Diagnostic sleep facilities generally poorly staffed, often with unqualified personnel, and in inappropriate clinical areas.
- Few arrangements in place for quality control of studies.

A list of the UK NHS centres currently believed to have the ability to provide full polysomnography with neurophysiological sleep staging (“third line” studies) is provided in Appendix 4. It should be noted that this is derived from self-reported information and no objective data are available on accuracy on on quality of service provided. It is not possible to make an accurate list of centres which can provide adequate tertiary-level studies (i.e. cardiorespiratory assessments and ventilation titrations), and there is a clear need for some form of quality control in centres providing second- and third-line studies (i.e. tertiary and quaternary centres).

8. Organisation of Services

In the light of the information in section 7 there appears to be a clear perception that current services are not meeting the diagnostic and treatment needs of children. The literature includes descriptions of clinical investigation pathways [568] but no comparative data of varying service models. What does exist is from North America, where health service organisation is not comparable to the UK. There is one UK review [16], which describes a recommended set of practices based on literature evidence.

Previous discussion in this report makes it clear that children with unrecognised sleep physiology disorders make heavy use of medical services [178], under-perform academically [22-26] and behaviourally [28-30] and derive measurable benefit from diagnosis and treatment [165]. The consequences of failing to address the current erratic and patchy paediatric sleep services in the UK can be deduced from much of the preceding report. These include:
• Continuing behavioural and cognitive problems (section 1.5)
• Continuing difficulties is assessing OSA (section 3.1.5)
• Failure to recognise severe OSA with increased peri-operative risk of ENT surgery (section 3.1.6)
• Continued inequality of services for children and adolescents with muscle disease (section 3.2.2)
• Continued inequality in services for infants/children with craniofacial problems, storage disorders, skeletal abnormalities and PWS (section 3.2.3)
• Potential difficulties in accessing investigation in cases of ALTE (section 4)
• Inadequate access to detailed studies to diagnose narcolepsy (section 5.1) and to differentiate other excessive daytime sleepiness (section 5.2 to 5.9)

Any recommendation of service has currently to be based on expert opinion of the shape of service that will minimise the chances of morbidity that could be addressed by efficient readily available diagnostic and treatment services. Ideally respiratory and neurology expertise will be available within the service. In addition paediatric sleep investigation services need to work closely with colleagues in ENT and airway surgery.

8.1 Training and education.

Effective provision of services in the field of sleep related physiological disorders in childhood will require the implementation of education and training for all clinical staff dealing with children at the primary, secondary or tertiary level, in order to identify those children for whom referral to secondary or tertiary services will be appropriate.

Detailed description of appropriate training and educational approaches is beyond the scope of this report, but as noted previously, a basic knowledge of sleep physiology and its development in childhood should be incorporated into undergraduate and postgraduate training prospectuses for a wide range of health care professionals. Appropriate multi-professional postgraduate training packages will also need to be developed at different levels for those taking part in the assessment and treatment of these conditions. These packages need to be specific for children.

8.2 Available facilities and expertise.

In order to meet the suggested standards for investigation, diagnosis and treatment of children with sleep related physiological disturbances set out in Sections 1-6 of this report, relevant expertise and facilities will need to be provided at primary, secondary, tertiary and quaternary levels of care. An outline of the minimum recommended levels of expertise, staffing and facilities based upon these standards is set out below. These estimates include only those staff directly employed in the provision of the services, and must be fully supported by appropriate levels of administrative and secretarial staff, plus appropriate technical support for care and maintenance of the complex equipment required.
8.2.1 Primary Care.

Information on relevant symptomatology and possible consequences of disorders of childhood sleep physiology should be incorporated into training for health visitors, school nurses and those involved in developmental screening in childhood. The development and incorporation of appropriate questionnaires on sleep into routine developmental screening and more widespread recognition of the potential contribution of sleep disorders to poor school performance and behavioural problems are likely to increase the appropriate and early recognition and referral of affected children.

8.2.2 Secondary Care.

The high prevalence of many disorders of sleep physiology in childhood (e.g. OSA, ALTE) means that most children with suggestive symptoms will most appropriately be seen, investigated and treated by the local paediatric secondary care service. This will require, in addition to the appropriate level of training for consultant paediatricians, the availability of the necessary equipment (with robust artefact detection or signal extraction facilities) to carry out overnight recordings of pulse oximetry on children at home. Because of the limitations of non-observed home oximetry recordings (see Section 3.1.5), some secondary care services will also benefit from the availability of facilities to make more detailed recordings – e.g. expired carbon dioxide and/or overnight infrared or low-light video recordings. In a secondary care Paediatric service serving a population of 50-60,000 children, with 3,000 births per year, a single recording oximetry system is likely to be sufficient for this purpose. Some provision for this service must be made in job plans for medical and support staff, though the time commitment is likely to be small (approximately one PA of consultant time per month). It is essential that the clinicians involved in this service work in liaison with the tertiary centre to ensure a smooth patient journey.

8.2.3 Tertiary Care.

Tertiary level investigational and treatment services for children with disorders of sleep physiology should be available in all tertiary care centres serving 2, 3 or more Strategic Health Authorities.

Facilities should include the full range of “second line” investigations (see section 2.7.3), together with appropriate staff and resources to conduct such investigations in hospital – on paediatric wards or preferably also in specialised sleep laboratories – and in the community – particularly for children receiving continuing treatments such as invasive or non-invasive ventilatory support.

The workload for such a tertiary care facility, serving a population of 3-4 million people will be such that dedicated consultant and support staff time will need to be identified and funded. From the workload of such centres currently undertaking this level of service provision this is likely to be in the range of 5 – 8 consultant PA’s per week, plus 2 – 3
WTE nurse specialists (or technical staff) for a centre that does not also provide quaternary level services (see below).

8.2.4 Quaternary Care.

Some (but not all) tertiary level services will also need to provide more complex investigational facilities and expertise (e.g. quantitative recordings of minute ventilation, combined neurophysiological and respiratory recordings), for children with complex neurological disorders affecting sleep physiology, and those with disorders of respiratory control (e.g. CCHS).

The staffing requirements for such quaternary services will be determined by the precise services and investigations provided, the complexity of the case-mix and the configuration of the sleep laboratory. For a centre providing detailed investigational and treatment facilities for children with complex neurological and respiratory control disorders from a population of 5-6 million people, the additional staffing required (based upon the current workload in Bristol at present) is approximately 1 WTE physiologist, plus 3 PA’s per week of consultant time, in addition to that specified for tertiary centres. Thus a centre providing full polysomnography will require at least 1 WTE consultant, 2 nurses/technicians or equivalent, and 1 WTE physiologist as a minimum. The overall numbers will also depend on whether the centre is conducting attended studies, and the configuration of beds in the laboratory. Two nurses or technicians can set up a maximum of three studies in a laboratory per night, and a 2-3 bedded laboratory will allow a more cost-efficient service than a single bedded unit, particularly if studies are attended. These numbers would allow for attended studies on 2-3 patients for 3 nights of the week. Larger throughput would require a proportionate increase in staffing. Smaller laboratories would have a lower capacity with little reduction in staffing. Multiple Sleep Latency testing involves another full day of physiologist time, and a centre undertaking significant number of these tests would need extra staff for this purpose.

9. Quality control and Audit of services

9.1 Local implementation

These UK recommendations will present a challenge to those running existing services as well as to areas of the country where these clinical issues have not yet been as well addressed. The exact configuration of service will vary due to geographic issues and established referral routes. However, clinicians and managers have a responsibility to implement the recommendations to enhance the provision of NHS care for this group of children. A system of managed clinical networks is recommended forging relationships between the tertiary and quaternary centres in a region and those offering secondary care level services.
9.2 Quality Control

There are at present no systems for quality control of diagnostic or therapeutic services in this field. Sleep laboratories are often limited to a single expert who is able to score and assess polysomnographic studies. This poses a considerable clinical governance risk and there is an urgent need to institute more robust systems. In the first instance it is recommended that any centre offering diagnostic sleep facilities should take part in an external quality control system. This should consist of an annual visit from clinicians and physiologists from another centre, who will review the equipment and algorithms used and the outcome and throughput data for the centre, comparing with the recommendations in this report. The visiting team will independently score five randomly selected studies (this may be done in advance of the visit) and compare results with the original scoring. A standardised report proforma will be used for each visit, with recommendations for development. It is hoped that a network of tertiary/quaternary centres will be developed, and where major discrepancies are demonstrated between two centres these can be resolved by others in the network.

9.3 Resource implications

Our surveys have demonstrated that current provision across the UK falls well short of the standards described in this document. There is likely to be significant need for further professional time (consultant, nurse and physiologist/technician) and a more modest need for new equipment, in particular, the provision of modern recording oximeters with high quality artefact rejection. There needs to be clear designation of the Quaternary centres, which will require proper investigation facilities as described in section 8.3.4.

9.4 Key points for Audit

- Availability of good quality pulse oximetry at secondary care level.
- Prompt referral to ENT services or tertiary care for those with positive or unclear diagnosis.
- Proportion of positive diagnoses from those tested.
- Local rate of adenotonsillectomy for OSAHS.
- Follow up assessment of children with abnormal physiology after intervention.
- Proportion of children deemed to need further treatment.
- Proportion of those deemed to need CPAP who are established on therapy for greater than 4 hours per night.
- Annual review of all those on non-invasive or invasive ventilatory support.
- Peer review of clinical service, outcomes, polysomnography raw data and reporting.

10. Declaration of Interests

No funding was received by the working party from any commercial bodies.
Appendix 1. Levels of evidence:

a) SIGN gradings for therapy/prevention/aetiology/harm

LEVELS OF EVIDENCE

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of RCTs, or RCTs with very low risk of bias</td>
</tr>
<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews or RCTs with low risk of bias</td>
</tr>
<tr>
<td>1-</td>
<td>Meta-analyses, systematic reviews or RCTs with high risk of bias</td>
</tr>
<tr>
<td>2++</td>
<td>High quality systematic reviews of case control or cohort studies. Well conducted case control or cohort studies with a very low risk of confounding or bias and a high probability of causal relationship</td>
</tr>
<tr>
<td>2+</td>
<td>Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability of causal relationship</td>
</tr>
<tr>
<td>2</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that relationship is not causal.</td>
</tr>
<tr>
<td>3</td>
<td>Non-analytical studies- e.g. case reports, case series</td>
</tr>
<tr>
<td>4</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>
## GRADES OF RECOMMENDATION

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review or RCT rated as 1++ and directly applicable to target population; or a body of evidence rated as 1+ consisting mainly of RCTs and directly applicable to target population, and consistent.</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++ directly applicable to target population, and consistent; or Extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+ directly applicable to target population, and consistent; or Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated 2+</td>
</tr>
</tbody>
</table>

### GOOD PRACTICE POINTS

- Recommended best practice based on clinical experience of working party
b) Sackett gradings for Prognosis, diagnosis and economic analysis
Levels of evidence and grades of recommendations

<table>
<thead>
<tr>
<th>Grade of recommendation</th>
<th>Level of evidence</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1a</td>
<td>SR (with homogeneityd) of inception cohort studies; or a CPG® validated on a test set</td>
</tr>
<tr>
<td></td>
<td>1b</td>
<td>Individual inception cohort study with ≥ 80% follow-up</td>
</tr>
<tr>
<td></td>
<td>1c</td>
<td>All-or-none case series</td>
</tr>
<tr>
<td>B</td>
<td>2a</td>
<td>SR (with homogeneityd) of either retrospective cohort studies or untreated control groups in RCTs</td>
</tr>
<tr>
<td></td>
<td>2b</td>
<td>Retrospective cohort study or follow-up of untreated control patients, in an RCT; or CPG not validated in a test set</td>
</tr>
<tr>
<td></td>
<td>2c</td>
<td>“Outcomes” research</td>
</tr>
<tr>
<td></td>
<td>3a</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3b</td>
<td>Independent blind comparison of an appropriate spectrum, but the reference standard was not applied to all study patients</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>Case series (and poor quality prognostic cohort studies)</td>
</tr>
<tr>
<td>D</td>
<td>5</td>
<td>Expert opinion without explicit critical appraisal or based on physiology, bench research or “first principles”</td>
</tr>
</tbody>
</table>

Diagnosis

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>SR (with homogeneityd) of level 1 diagnostic studies; or a CPG validated on a test set</td>
</tr>
<tr>
<td>1b</td>
<td>Independent blind comparison of an appropriate spectrum of consecutive patients, all of whom have undergone both the diagnostic test and the reference standard</td>
</tr>
<tr>
<td>1c</td>
<td>Absolute SpPins and SnNouts</td>
</tr>
<tr>
<td>2a</td>
<td>SR (with homogeneityd) of level ≥ 2 diagnostic studies</td>
</tr>
<tr>
<td>2b</td>
<td>Independent blind comparison but either in non-consecutive patients or confined to a narrow spectrum of study individuals (or both), all of whom have undergone both the diagnostic test and the reference standard; or a diagnostic CPG not validated in a test set</td>
</tr>
<tr>
<td>2c</td>
<td>Analysis without accurate cost measurement, but including a sensitivity analysis incorporating clinically sensible variations in important variables</td>
</tr>
<tr>
<td>3a</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td></td>
</tr>
</tbody>
</table>

Economic analysis

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>SR (with homogeneityd) of level 1 economic studies</td>
</tr>
<tr>
<td>1b</td>
<td>Analysis comparing all (critically validated) alternative outcomes against appropriate cost measurement, and including a sensitivity analysis incorporating clinically sensible variations in important variables</td>
</tr>
<tr>
<td>1c</td>
<td>Clearly as good or better, but cheaper. Clearly as bad or worse but more expensive. Clearly better or worse at the same cost</td>
</tr>
<tr>
<td>2a</td>
<td>SR (with homogeneityd) of level ≥ 2 economic studies</td>
</tr>
<tr>
<td>2b</td>
<td>Analysis comparing a limited number of alternative outcomes against appropriate cost measurement, and including a sensitivity analysis incorporating clinically sensible variations in important variables</td>
</tr>
<tr>
<td>3a</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td></td>
</tr>
</tbody>
</table>

C

<table>
<thead>
<tr>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference standard was not applied independently or not applied blindly</td>
</tr>
</tbody>
</table>

D

<table>
<thead>
<tr>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert opinion without explicit critical appraisal or based on physiology, bench research or “first principles”</td>
</tr>
</tbody>
</table>

Analysis with no sensitivity analysis

<table>
<thead>
<tr>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert opinion without explicit critical appraisal or based on economic theory</td>
</tr>
</tbody>
</table>
Notes

These levels were generated in a series of iterations among members of the NHS R&D Centre for Evidence-Based Medicine (Chris Ball, Dave Sackett, Bob Phillips, Brian Haynes, and Sharon Straus).

Recommendations based on this approach apply to “average” patients and may need to be modified in light of an individual patient’s unique biology (risk, responsiveness, etc.) and preferences about the care he or she receives.

Users can add a minus sign (−) to denote the level that fails to provide a conclusive answer because of: either a single result with a wide confidence interval (such that, for example, an ARR in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm); or an SR with troublesome (and statistically significant) heterogeneity. Such evidence is inconclusive, and therefore can only generate grade D recommendations.

By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a “−” at the end of their designated level.

See note “c” for advice on how to understand, rate and use trials or other studies with wide confidence intervals.

Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.

Met when there are no reports of anyone with this condition ever avoiding (all) or suffering from (none) a particular outcome (such as death).

An “absolute SpPin” is a diagnostic finding whose specificity is so high that a positive result rules in the diagnosis. An “absolute SnNout” is a diagnostic finding whose sensitivity is so high that a negative result rules out the diagnosis.

Good, better, bad, and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.

By poor-quality cohort study, we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded) objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study, we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same blinded, objective way in both cases and controls and/or failed to identify or appropriately control known confounders.

By poor-quality prognostic cohort study, we mean one in which sampling was biased in favor of patients who already had the target outcome, or the measurement of outcomes was accomplished in < 80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.

(based on Table 7.2 in “Sackett DL, Straus S, Richardson S, Rosenberg W, Haynes RB. Evidence Based Medicine, How to Practice and Teach EBM (2nd Edition), London, Churchill Livingstone 2000”)
Appendix 2. Flow Chart for interpretation of overnight pulse oximetry in a child suspected of sleep-disordered breathing.

Baseline $\geq 95\%$?

- Yes
  - Consider
    - Lung disease
    - Obstructive hypventilation
    - Cyanotic heart disease
    - Extra-cardiac right to left shunting
    - (Abnormal haemoglobin)

- No
  - Abnormal desaturations?
    - No
      - Excludes significant nocturnal hypoxaemia.
      - Does not exclude obstructive sleep apnoea.
      - Refer for further investigation if symptoms cause continued diagnostic concern.
    - Yes
      - Consider
        - Obstructive sleep apnoea
        - Other causes of sleep apnoea / hypoventilation
        - Movement artefact

- Abnormal desaturations?
  - Yes
    - Saturation nadir <80%?
      - Yes
        - Increased anaesthetic risk.
        - Needs further evaluation.
        - Surgery should only be undertaken in a hospital with Paediatric Intensive Care facilities.
      - No
        - May be suitable for adenotonsillectomy in secondary care setting, depending on other risk factors.
  - No
    - Excludes significant nocturnal hypoxaemia.
    - Does not exclude obstructive sleep apnoea.
    - Refer for further investigation if symptoms cause continued diagnostic concern.
**Appendix 3. Members of Working Party**

<table>
<thead>
<tr>
<th>Name</th>
<th>Professional role and site</th>
<th>Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Robert Primhak</td>
<td>Consultant Paediatrician, Sheffield</td>
<td>Paediatric Respiratory Medicine/Sleep</td>
</tr>
<tr>
<td>(Chair)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ms Rachel Davies</td>
<td>Sheffield</td>
<td>Down’s Syndrome Association</td>
</tr>
<tr>
<td>Dr Michelle Eagle</td>
<td>Physiotherapist, Newcastle</td>
<td>Muscular Dystrophy Campaign</td>
</tr>
<tr>
<td>Prof Peter Fleming</td>
<td>Professor of Paediatrics, Bristol</td>
<td>Sleep/Paediatric Intensive Care</td>
</tr>
<tr>
<td>Dr Neil Gibson</td>
<td>Consultant Paediatrician, Glasgow</td>
<td>Paediatric Respiratory Medicine /Sleep</td>
</tr>
<tr>
<td>Dr Imelda Hughes</td>
<td>Consultant Paediatric Neurologist, Manchester</td>
<td>Neurology</td>
</tr>
<tr>
<td>Prof Paul Johnson</td>
<td>Professor of Physiology, Oxford</td>
<td>Physiology</td>
</tr>
<tr>
<td>Dr Ruth Kingshott</td>
<td>Sleep Physiologist, Sheffield</td>
<td>Sleep Physiologist</td>
</tr>
<tr>
<td>Dr Rod Lane</td>
<td>Clinical Scientist, Great Ormond Street Hospital, London</td>
<td>Sleep Physiologist</td>
</tr>
<tr>
<td>Dr Simon Lenton</td>
<td>Consultant Paediatrician, Bath</td>
<td>Community Paediatrics</td>
</tr>
<tr>
<td>Dr Christopher O’Brien</td>
<td>Consultant Paediatrician, Newcastle upon Tyne</td>
<td>Paediatric Respiratory Medicine /Sleep</td>
</tr>
<tr>
<td>Dr Martin Samuels</td>
<td>Consultant Paediatrician, Stoke</td>
<td>Sleep/Paediatric Intensive Care</td>
</tr>
<tr>
<td>Dr John Shneerson</td>
<td>Consultant Physician, Cambridge</td>
<td>British Sleep Society</td>
</tr>
<tr>
<td>Dr Zenobia Zaiwalla</td>
<td>Consultant Paediatric Neurophysiologist, Oxford</td>
<td>Neurophysiology</td>
</tr>
</tbody>
</table>
Paediatric Sleep Disorders Service Review

Institution:

Type of Laboratory: Adult + Paed / Paed only

Director of sleep service:

Other clinicians involved (career grades):

<table>
<thead>
<tr>
<th>Physiologists and technicians:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
</tr>
<tr>
<td>Training and experience</td>
</tr>
</tbody>
</table>

Key clinical interfaces:

Respiratory:

Neurophysiology:

Neuromuscular:

ENT:

Adult Transition service:

Other:
Date of visit:

Details of workload in previous 12 months:

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic oximetry:</td>
<td></td>
</tr>
<tr>
<td>Oxicapnography:</td>
<td></td>
</tr>
<tr>
<td>Cardiorespiratory PSG:</td>
<td></td>
</tr>
<tr>
<td>Full PSG:</td>
<td></td>
</tr>
<tr>
<td>MSLT</td>
<td></td>
</tr>
</tbody>
</table>

What percentage of studies are attended overnight:

Sleep Laboratory:

How many PSG studies can be done at once?

Facilities

N of fully equipped rooms set aside solely for sleep laboratory use:

N of rooms used for purposes including sleep laboratory work:

N of studies done using mobile equipment in ward side room: (per annum):

N of studies done using mobile equipment in open ward: (per annum):

Sleep Laboratory office: Yes / No
What systems are available for PSG:

Channels available

<table>
<thead>
<tr>
<th>Channel</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
</tr>
<tr>
<td>SaO2</td>
</tr>
<tr>
<td>ETCO2</td>
</tr>
<tr>
<td>tcpCO2</td>
</tr>
<tr>
<td>tcpO2</td>
</tr>
<tr>
<td>Thermistor airflow</td>
</tr>
<tr>
<td>Nasal Cannula Pressure</td>
</tr>
<tr>
<td>Pulse transit time</td>
</tr>
<tr>
<td>Body position</td>
</tr>
<tr>
<td>Actimeter (N)</td>
</tr>
<tr>
<td>Effort strain bands (N)</td>
</tr>
<tr>
<td>Respiratory Impedance Plethysmography</td>
</tr>
<tr>
<td>Pneumotachography flow</td>
</tr>
<tr>
<td>BIPAP pressure</td>
</tr>
<tr>
<td>Oesophageal pH</td>
</tr>
<tr>
<td>EEG (N of leads)</td>
</tr>
<tr>
<td>EOG</td>
</tr>
<tr>
<td>Submental EMG</td>
</tr>
<tr>
<td>Leg EMG</td>
</tr>
<tr>
<td>Video</td>
</tr>
<tr>
<td>Microphone</td>
</tr>
<tr>
<td>Real time sound</td>
</tr>
<tr>
<td>Other:</td>
</tr>
</tbody>
</table>

Other facilities:

<table>
<thead>
<tr>
<th>Facility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actigraphy (N)</td>
</tr>
<tr>
<td>Recording oximetry (systems):</td>
</tr>
<tr>
<td>Recording capnography (systems):</td>
</tr>
</tbody>
</table>
Outcome data:

Diagnostic Oximetry:
Median waiting time for initial study:
Visual inspection and interpretative reporting: Yes / No
Median time to issue report:
Follow up studies for abnormal results after surgery: %
Oxicapnography:
Median waiting time for initial study:
Visual inspection and interpretative reporting: Yes / No
Manual sleep staging: Yes / No
Median time to issue report:
Polysomnography:
Median waiting time for initial study:
Manual reporting and interpretation of results:
Median time to issue report:
Quality Control:

**Oximetry interpretation** (comment on studies evaluated, agreement and areas of disagreement):

**Polysomnography interpretation** (comment on studies evaluated, agreement and areas of disagreement):
Opportunities for continuing professional development (include ongoing training taken up in last 3 years):

*Medical Staff:*

*Paramedical staff:*

Appendix 5. Current centres believed to be offering third line studies* in the UK†

<table>
<thead>
<tr>
<th>Centre</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birmingham Children’s Hospital</td>
<td>Dr Satish Rao</td>
</tr>
<tr>
<td>Bristol Children’s Hospital</td>
<td>Prof Peter Fleming</td>
</tr>
<tr>
<td>East Surrey Hospital</td>
<td>Dr Ivor Lewis</td>
</tr>
<tr>
<td>Evelina Children’s Hospital, London</td>
<td>Dr Paul Gringras</td>
</tr>
<tr>
<td>Great Ormond Street Hospital, London</td>
<td>Dr Rod Lane</td>
</tr>
<tr>
<td>Leicester Royal Infirmary</td>
<td>Dr David Luytf</td>
</tr>
<tr>
<td>Oxford Children’s Hospital, John Radcliffe Hospital, Oxford</td>
<td>Dr Anne Thomson/Dr Zenobia Zaiwalla</td>
</tr>
<tr>
<td>Royal Cornwall Hospital, Truro</td>
<td>Dr Anne Prendiville</td>
</tr>
<tr>
<td>Royal Hospital for Sick Children, Edinburgh</td>
<td>Dr Steve Cunningham</td>
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<tr>
<td>Royal Hospital for Sick Children, Glasgow</td>
<td>Dr Neil Gibson</td>
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<tr>
<td>Royal Victoria Infirmary, Newcastle</td>
<td>Dr Chris O’Brien</td>
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<tr>
<td>Sheffield Children’s Hospital</td>
<td>Dr Heather Elphick</td>
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<tr>
<td>Southampton University Hospitals</td>
<td>Dr Catherine Hill</td>
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<tr>
<td>St Mary’s Hospital, London</td>
<td>James di Pasquale</td>
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<tr>
<td>University Hospital of North Staffordshire, Stoke on Trent</td>
<td>Dr Martin Samuels</td>
</tr>
<tr>
<td>University Hospital of Wales, Cardiff</td>
<td>Dr Hazel Evans</td>
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* These centres have the facility to perform full polysomnography with neurophysiological monitoring and sleep staging.
† Information based on self-reporting. No objective information is yet available about level or quality of service at any centre. This list may not be exhaustive.
11. References


Brouillette RT, Jacob SV, Waters KA, Morielli A, Mograss M, Ducharme FM. Cardiorespiratory sleep studies for children can often be performed in the home. Sleep. 1996;19:S278-80.


Johnson EO, Roth T. An epidemiologic study of sleep-disordered breathing symptoms among adolescents. Sleep. 2006;29:1135-42.


Ruboyianes JM, Cruz RM. Pediatric adenotonsillectomy for obstructive sleep apnea. Ear Nose Throat J. 1997;75:430-3.


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Puntis JW, Booth IW. ALTE and gastro-oesophageal reflux.[comment]. Arch Dis Child. 2005;90:653; author reply


Gau SF, Soong WT. The transition of sleep-wake patterns in early adolescence.[see comment]. Sleep. 2003;26:449-54.


