Diagnosis of Nocturnal Hypoventilation in Pediatric Neuromuscular Disorders: A Survey of Clinical Practice in Australia and New Zealand

Adelaide L Withers¹,²,³, Jenny Downs²,³, Andrew C Wilson¹,²,³, Graham Hall²,³

¹Department of Respiratory and Sleep Medicine, Perth Children’s Hospital, Perth,  
²Telethon Kids Institute, Perth,  
³Curtin School of Allied Health, Curtin University Faculty of Health Sciences, Perth, Australia

Objective: Nocturnal hypoventilation is a complication of neuromuscular disorders. There are various recommendations for measuring pCO₂ during polysomnography and numerous national and international definitions of hypoventilation that could contribute to significant variations in clinical practice. We therefore aimed to determine clinical practices implemented by Australasian pediatric sleep physicians.

Methods: Pediatric sleep physicians completed an electronic survey for information regarding pCO₂ measurements and definitions of hypoventilation that are followed for children with neuromuscular disorders.

Results: It was found that transcutaneous measurement of pCO₂ was performed in all centers, with 25% of the centers simultaneously performing capnography. Twelve definitions of hypoventilation were used, including published definitions from the American Academy of Sleep Medicine (AASM) manual and recommendations of the pediatric Australasian Sleep Association/Australasian Sleep Technologists Association. The most commonly used definition of hypoventilation (9/17, 53%) was the 2012 pediatric AASM definition (pCO₂ >50 mmHg for >25% of the total sleep time). There was a discrepancy between centers and individuals within the same center when defining hypoventilation. Answers stating the use of the Australasian definitions (rise in pCO₂ ≥10 mmHg from wake to sleep, average rise in pCO₂ ≥3 mmHg from non rapid eye movement to rapid eye movement sleep) were more frequent when asked specifically via a checkbox (yes/no) compared to free text.

Conclusions: These results confirm the heterogeneity and lack of standardization of clinical practice within Australasia when measuring pCO₂ during polysomnography and defining hypoventilation. The Australasian definitions were not used as frequently as anticipated.

Keywords: Hypoventilation; Neuromuscular disorder; Polysomnography; Pediatric.
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can be measured transcutaneously (ETCO₂) and/or end-tidally (ETCO₂), which is also known as capnography. Both measurement methods are recommended in the American Academy of Sleep Medicine (AASM) manual and by the pediatric Australasian Sleep Association/Australasian Sleep Technologists Association (ASA/ASTA) as appropriate surrogate markers for alveolar pCO₂ during pediatric PSG.⁴⁵

Although hypercapnia while awake is defined as an arterial pCO₂ of >45 mmHg,⁴⁶ there is no clear definition of what constitutes a clinically relevant change in pCO₂ during sleep.⁴ The threshold of hypercapnia associated with morbidity and mortality is unknown, the relationship between hypercapnia and end-organ damage has not been elucidated, and the impact of modulating factors such as peak pCO₂ during hypercapnia, and age of the child is unclear.⁴⁸ Therefore, it is not surprising that the thresholds and values used to define significant hypercapnia and hence hypoventilation during sleep vary worldwide.⁴⁹⁻⁵⁰

Defining hypoventilation is even more challenging in individuals with NMD, as the ‘normal range’ of pCO₂ during sleep has not been defined and hypercapnia is often significant during sleep.⁴¹ Some groups have proposed that individuals to define hypoventilation may be more sensitive to lower thresholds with NMD.⁵²⁻⁵⁳

The most recent 2012 AASM manual defines hypoventilation in adults as an increase in arterial pCO₂ or appropriate surrogate during sleep to >55 mmHg for ≥10 min⁴ and/or a rise in arterial pCO₂ or appropriate surrogate during sleep to ≥10 mmHg compared to awake supine value of >50 mmHg for ≥10 min.⁴ Hypoventilation in children is defined as an increase in arterial pCO₂ or an appropriate surrogate during sleep to >50 mmHg for >25% of the total sleep time (TST).⁴ The AASM manual states that pediatric scoring rules can be used up to the age of 18 years; however, for adolescents aged 13 years and above, adult scoring rules may be used if desired.⁴

In 2010, the ASA/ASTA published an addendum to the 2007 AASM manual as it felt that some recommendations were not applicable to the circumstances, population, and equipment available in Australia and New Zealand.²² A further addendum was published specifically for pediatrics in 2011 which recommends using the AASM pediatric definition of hypoventilation; however, an increase in pCO₂ ≥10 mmHg from wake to sleep⁵ and/or an average rise in pCO₂ ≥3 mmHg from non-rapid eye movement (NREM) to REM sleep⁶ were offered as alternative definitions of hypoventilation and REM related hypoventilation, respectively. Other published definitions of hypoventilation are listed in Table 1.

Although an accurate diagnosis of nocturnal hypoventilation in individuals with NMD is imperative to guide treatment decisions, the authors hypothesized that the existence of numerous definitions of hypoventilation and the lack of agreement between sleep physicians are likely to lead to significant variation in methods of measuring pCO₂ during PSG and defining hypoventilation in this vulnerable group. Therefore, this study surveyed pediatric sleep physicians in Australia and New Zealand to assess the usual clinical practice of diagnosing nocturnal hypoventilation in children and adolescents with NMD.

<table>
<thead>
<tr>
<th>Table 1. Proposed definitions of nocturnal hypoventilation</th>
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<tbody>
<tr>
<td><strong>Definition</strong></td>
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<tr>
<td>pCO₂ ≥45 mmHg</td>
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<tr>
<td>Peak pCO₂ &gt;49 mmHg</td>
</tr>
<tr>
<td>Mean pCO₂ &gt;50 mmHg</td>
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<tr>
<td>Peak ETCO₂ &gt;53 mmHg</td>
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<tr>
<td>pCO₂ ≥50 mmHg for at least 5 continuous minutes</td>
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<tr>
<td>pCO₂ ≥55 mmHg for ≥10 minutes</td>
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<tr>
<td>pCO₂ rise of ≥10 mmHg during sleep to &gt;50 mmHg for ≥10 minutes</td>
</tr>
<tr>
<td>pCO₂ rise of ≥10 mmHg from awake to asleep</td>
</tr>
<tr>
<td>Average rise in pCO₂ ≥3 mmHg from NREM to REM sleep</td>
</tr>
<tr>
<td>pCO₂ &gt;50 mmHg for ≥2% TST</td>
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<tr>
<td>pCO₂ &gt;50 mmHg for &gt;5% TST</td>
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<tr>
<td>pCO₂ ≥ 50 mmHg for ≥10% TST</td>
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<tr>
<td>pCO₂ ≥50 mmHg for ≥25% TST</td>
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<tr>
<td>pCO₂ ≥50 mmHg for ≥50% TST</td>
</tr>
<tr>
<td>pCO₂ &gt; 45 mmHg for ≥60% TST</td>
</tr>
</tbody>
</table>

ETCO₂, end tidal CO₂; ASA, Australasian Sleep Association; ASTA, Australasian Sleep Technologists Association; NREM, non rapid eye movement; REM, rapid eye movement; TST, total sleep time.
METHODS

This study was registered on the Child and Adolescent Health Services Governance Evidence Knowledge Outcomes (GEKO) platform, which is a low- and negligible-risk pathway for audits of clinical practice and quality improvement (QA 6245, Accreditation Standard EQuIP 12 Provision of Care). Publication approval was granted via GEKO.

All pediatric sleep physicians in Australia and New Zealand who worked in a hospital setting with access to a sleep laboratory were invited to participate. A fourteen-question electronic survey (SurveyMonkey, www.momentive.ai; Momentive Inc. San Mateo, CA, USA) was emailed via an electronic weblink and a QR code. Responses were anonymous, although potentially identifying information was included to allow grouping of responses by center (such as state of practice and name of the hospital). When the responses were grouped by center, the results were presented ensuring that the individuals could not be identified.

Survey questions were worded to ensure that the information collected pertained only to children and adolescents with NMD. The collected data included methods of measuring pCO₂ during PSG for a child or adolescent with NMD and the criteria used to define hypoventilation in children and adolescents with NMD. Definitions of hypoventilation were entered as free text in response to the question, ‘What parameters or rules do you use to decide whether hypoventilation is present or absent?’ After providing free-text definitions of hypoventilation, physicians were asked about the use of pediatric ASA/ASTA definitions via a checkbox (yes/no).

The frequencies, frequency distributions, and calculations were performed using Microsoft Excel (version 2110, Microsoft, Redmond, WA, USA). The free-text responses were coded into published and unpublished definitions of hypoventilation. Unpublished definitions/criteria were further categorized into descriptive pCO₂ trends, pCO₂ criteria with threshold values, and PSG features. Free text comments were grouped into two categories: the potential for pCO₂ measurement to be affected by artifacts and how to best define hypoventilation.

RESULTS

The survey was sent to 58 pediatric sleep physicians, and 17 responses were returned (response rate: 30%). All the physicians who responded worked in dedicated pediatric sleep laboratories in hospital-based settings. Fourteen of the responses came from seven centers in Australia, with three responses from one center in New Zealand. Each of the seven tertiary pediatric centers in Australia had at least one response, with responses per center ranging from to 1–4.

Measurement of pCO₂ was performed using TCO₂ only in six of eight centers (75%), and simultaneously with TCO₂ and ETCO₂ in two of eight (25%) centers. None of the centers used ETCO₂ alone.

Supplementary Material (in the online-only Data Supplement) lists 12 definitions of hypoventilation that were provided. The number of definitions provided by each physician ranged from to 1–5. The coded responses are presented in Table 2. As seen in the Table 2, some definitions included specific thresholds (for example, ‘a rise in pCO₂ of >3 mmHg from NREM to REM’) and others were purely descriptive (‘a rise in pCO₂ during REM’). The most commonly used definition (9/17, 53%) was the 2012 AASM pediatric definition: an increase in arterial pCO₂ or an appropriate surrogate during sleep to >50 mmHg for >25% of the TST.

When specifically asked about the pediatric ASA/ASTA definitions with a check-box (yes/no), 12 (70%) agreed that a rise from awake to asleep pCO₂ of ≥10 mmHg and 10 (59%) claimed that an average rise in pCO₂ ≥ 3 mmHg from NREM to REM indicates hypoventilation. In centers with more than one responding physician, there was occasionally a discrepancy between individuals. For example, in one center, 100% of the responders stated using a rise from awake to asleep pCO₂ of ≥10 mmHg from NREM to REM to define hypoventilation, but only 75% used a rise in pCO₂ of >3 mmHg.

Several physicians commented about the potential for TCO₂ measurement to be affected by artifact and thus be inaccurate, such as the following statements: ‘if you have ETCO₂ tracing, it is useful to recheck whether the rise in TCO₂ was not artefactual’ and ‘our TCO₂ leads tend to over-read, which is why we do not rely on them as a baseline measurement; whereas, a rise in REM is more accurate in our setting.’ Two comments reinforced that the pediatric ASA/ASTA recommendations are not always used in Australasian centers, as follows: ‘we use AASM guidelines solely without the ASA/ASTA recommendations’ and ‘ASA/ASTA recommendations are better characterized as ‘recommended’ rather than ‘recommend’ given the age of that commentary.’ Two physicians commented that they would never use adult rules for pediatric patients, regardless of their age.

DISCUSSION

Although accurate diagnosis of hypoventilation in children with NMD requires consistency when measuring pCO₂ during PSG as well as standardized definitions of hypoventilation, results of this survey confirm the heterogeneity in clinical practice and lack of standardization that exists within Australasia.

Measurement of ETCO₂ during pediatric PSG is desirable to aid the identification of upper airway obstruction. 4,23 How-
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Table 2. Definitions of hypoventilation used by surveyed paediatric sleep physicians

<table>
<thead>
<tr>
<th>Source</th>
<th>Definition</th>
<th>Number</th>
</tr>
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<tbody>
<tr>
<td>AASM paediatric (2012)</td>
<td>An increase in arterial pCO₂ or appropriate surrogate during sleep to &gt;50 mmHg for &gt;25% TST</td>
<td>9</td>
</tr>
<tr>
<td>ASA/ASTA paediatric (2011)</td>
<td>A rise from awake to asleep pCO₂ of ≥10 mmHg</td>
<td>3</td>
</tr>
<tr>
<td>ASA/ASTA paediatric (2011)</td>
<td>Average rise in pCO₂ ≥3 mmHg from NREM to REM</td>
<td>2</td>
</tr>
<tr>
<td>Descriptive pCO₂ trends</td>
<td>Rise in pCO₂ in REM vs. NREM</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Rise in pCO₂ from wake to sleep</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Other TCO₂ trends (e.g. significant rise in TCO₂, high TCO₂ reading)</td>
<td>5</td>
</tr>
<tr>
<td>pCO₂ criteria with threshold values</td>
<td>A clear rise in pCO₂ ≥5 mmHg from NREM to REM</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Persistent elevation of TCO₂ &gt;50 mmHg in REM</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Persistent elevation of TCO₂ &gt;50 mmHg</td>
<td>2</td>
</tr>
<tr>
<td>PSG features</td>
<td>Sleep breathing</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Hypercapnia and desaturation</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Hypercapnia, desaturation with absence of OSA</td>
<td>2</td>
</tr>
</tbody>
</table>

AASM, American Academy of Sleep Medicine; ASA, Australasian Sleep Association; ASTA, Australasian Sleep Technologists Association; TST, total sleep time; NREM, non rapid eye movement; REM, rapid eye movement; TCO₂, transcutaneous pCO₂; OSA, obstructive sleep apnoea

ever, reliance on ETCO₂ only may be unsuitable in children, as it has been shown to have variable accuracy, particularly in those with NMD, is often poorly tolerated, and artifacts are common due to nasal obstruction. Although TCO₂ is unaffected by nasal obstruction, it cannot measure breath-to-breath changes in pCO₂, has a lag time of approximately two minutes, and artifacts in children are frequent. The potential for TCO₂ values to be affected by artifacts was reinforced by the comments of several physicians in this survey.

Given that both ETCO₂ and TCO₂ have benefits and limitations, simultaneous measurement is desirable to identify artifacts and increase the likelihood that the measured pCO₂ values accurately reflect alveolar pCO₂. In this study, the measurement of ETCO₂ was only reported by 25% of the centers, likely because the equipment and consumables for ETCO₂ measurement are expensive. Perhaps, given the challenges in children and the expense required to measure ETCO₂, this could be reserved for children at a high risk of hypoventilation, such as those with NMD or obesity.

A wide variety of published and unpublished definitions of hypoventilation were used in this study, highlighting the inconsistent application of criteria and the frequent use of parameters or definitions that are not in line with published recommendations. The pediatric AASM definition of hypoventilation was most frequently used, which is unsurprising given that the AASM manual is generally accepted as the definitive reference for PSG scoring. However, despite the AASM manual stating that adult rules can be used for adolescents aged 13 years and above, no physicians reported practicing such, and two specifically commented that they would never use adult rules regardless of the patient’s age. This finding could be explained by the fact that all physicians worked in dedicated pediatric sleep centers; therefore, exposure to adult scoring rules may be limited, and the data required to apply adult definitions (for example, pCO₂ >55 mmHg) may not be easily available to pediatric physicians. However, the most likely explanation is that adult scoring rules have been shown to underestimate the presence of sleep-related pathologies in adolescents, as they are not sufficiently sensitive; hence, pediatric sleep physicians are reluctant to use adult rules.

The definitions of hypoventilation in this survey included PSG findings that are not part of any currently published definitions, such as the presence of central apnea, hypopnea, sleep-disordered breathing, and oxygen desaturation. Although older definitions of nocturnal hypoventilation often included oxygen desaturation, this was prior to the ability to easily measure pCO₂ continuously during PSG. Currently, hypoventilation is defined as hypercapnia during sleep, rather than oxygen desaturation. Although oxygen desaturation can be associated with hypoventilation, it is important to recognize that oxygen desaturation without hypercapnia is not associated with hypoventilation and is likely secondary to parenchymal lung disease or obstructive sleep apnea. Similarly, the presence of central apnea and/or hypopnea can be associated...
with hypoventilation, but may be physiologic in children due to the instability of the respiratory drive11 and is also seen in NMD, secondary to reduced respiratory drive, diaphragmatic weakness, and cardiomyopathy.1 The presence of central hypoapnea and/or sub-criterion central events without associated hypercapnia is often a precursor to hypoventilation. Therefore, although PSG features, such as central apnea, hypopnea, sleep-disordered breathing, and oxygen desaturation, may be associated with hypoventilation, a diagnosis of hypoventilation requires the demonstration of significant hypercapnia during sleep and should not be based on these PSG findings.

Despite the pediatric ASA/ASTA addendum being developed specifically by Australasian physicians to better reflect their clinical environment, when asked which definitions were used via free text, only 18% used a rise from awake to asleep pCO2 >10 mmHg and 12% claimed the use of an average increase in pCO2 ≥3 mmHg from NREM to REM. There was also a discrepancy between individual physicians working in the same center when using these definitions. This variation in clinical practice and infrequent use of these definitions could be explained by comments that imply that some pediatric sleep physicians felt that the addendum was irrelevant and/or outdated, which justifies a comprehensive review of the definition of hypoventilation.

Of interest, when later asked about the ASA/ASTA definitions via checkbox (yes/no), 70% of physicians agreed that a rise from awake to asleep pCO2 >10 mmHg and 59% that an average increase in pCO2 ≥3 mmHg from NREM to REM indicated hypoventilation. This discrepancy could be explained by the excessive cognitive load associated with remembering multiple definitions of specific values. Further support for the notion of excess cognitive loading is the fact that, when asked to enter definitions via free text, answers including specific thresholds or values were much less frequent than descriptive phrases. As excessive cognitive load on physicians is known to have implications in performance and patient safety,31 this study presents an exciting opportunity to summarize and collate the most clinically useful definitions into a user-friendly reference guideline.

This study has several limitations. The response rate of 30% was low; however, many sleep units operate with a model in which not all physicians who practice sleep medicine are involved in reporting or scoring PSGs for children with NMD. The survey was sent to pediatric sleep physicians working solely in private practices, where exposure to children with NMD is likely to be limited. Therefore, it is likely that many physicians invited to participate in this survey did not respond because the survey was not relevant to their clinical practice.

Although the survey responses included at least one physician from each tertiary pediatric sleep center in Australia and New Zealand, the number of physician responses per center (range 1–4) was not necessarily proportional to the patient load. This reduces the representation of all practices and the likely outcome is an underestimation of heterogeneity.

Data regarding the number of years of experience in reporting and interpreting PSGs were not collected. Although sleep physicians with all levels of experience were invited to participate, a range of experience should have been captured. The use of free text may have underestimated the use of definitions with specific values, because some respondents might have preferentially entered a descriptive response.

In conclusion, this study confirms that despite the accurate diagnosis of nocturnal hypoventilation being of utmost importance in children with NMD to guide clinical decision-making, there is significant variation in normal clinical practice and a lack of standardization when defining hypoventilation in this group. The ability to examine the factors that contribute to this variation, particularly the impact of pediatric sleep physicians’ level of experience, warrants further investigation. The lack of a standardized definition of hypoventilation in children and adolescents with NMD hampers future research collaboration, as well as the comparison and benchmarking of clinical practice between centers. Therefore, a standardized definition of hypoventilation in individuals with NMD that is evidence-based and related to clinical outcomes is urgently required.

Supplementary Materials
The online-only Data Supplement is available with this article at https://doi.org/10.13078/jsm.230005.

Conflicts of Interest
The authors have no potential conflicts of interest to disclose.

ORCID iDs
Adelaide L Withers https://orcid.org/0000-0002-1640-8743
Jenny Downs https://orcid.org/0000-0001-7358-9037
Andrew C Wilson https://orcid.org/0000-0003-0875-2736
Graham Hall https://orcid.org/0000-0002-6217-9494

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