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DOI:

[10.1016/j.sleep.2022.10.028](https://doi.org/10.1016/j.sleep.2022.10.028)

*Document Version*

Peer reviewed version

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*Citation for published version (APA):*

Shi, J., Chiang, J., Ambreen, M., Snow, N., Mocanu, C., Mcadam, L., Goldstein, R. S., Rose, L., & Amin, R. (2023). Ambulatory transcutaneous carbon dioxide monitoring for children with neuromuscular disease. *SLEEP MEDICINE*, 101, 221-227. <https://doi.org/10.1016/j.sleep.2022.10.028>

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# **Ambulatory Transcutaneous Carbon Dioxide Monitoring for Children with Neuromuscular Disease**

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**Conflicts of Interest Disclosures:** The authors have no conflicts of interest nor financial relationships relevant to this article to disclose.

**Clinical Trial Registration:** Transcutaneous CO<sub>2</sub> Monitoring at Home for Children with Neuromuscular Disease, <https://clinicaltrials.gov/ct2/show/NCT03478566>, NCT03478566.

**Tables:** 4

**Figures:** 1

**Abstract word count:** 218

**Manuscript word count:** 2520

**Data Sharing Statement:** De-identified participant data and related documents (e.g., study protocol, statistical analysis plan, etc.) will be available for up to 7 years upon request to the author and will be shared by a secure and encrypted method (e.g., VPN).

## **CONTRIBUTOR'S STATEMENT PAGE:**

Dr Shi collected data, carried out the data analysis, drafted the initial manuscript, completed the analysis and interpretation of the data and reviewed and revised the manuscript.

Dr Chiang, Dr McAdam, Dr Goldstein, and Dr Rose all provided substantial contribution to the conception and design of the study as well as the interpretation of the data and critically reviewed and revised the manuscript.

Dr Ambreen, Ms Snow and Ms Mocanu were involved in acquisition of the data and critically reviewed and revised the manuscript.

Dr Amin conceptualized and designed the study, supervised the data analysis and interpretation of the data and critically reviewed and revised all drafts of the manuscript.

All authors drafted/revised the article for intellectual content and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

## **ABSTRACT**

**Objective:** Early screening and diagnosis of nocturnal hypoventilation can slow progression to diurnal hypercapnia and mortality in children with neuromuscular disease (NMD). However, gold standard, laboratory-based polysomnography (PSG) testing is a limited resource. Therefore, we evaluated the diagnostic accuracy of ambulatory transcutaneous carbon dioxide (tcCO<sub>2</sub>) monitoring used in the home compared to PSG in children with NMD.

**Methods:** Prospective, cross-sectional study in children 0-18 years old with a confirmed diagnosis of NMD and a clinically indicated need for PSG. Ambulatory tcCO<sub>2</sub> was assessed by a respiratory therapist in participant's homes. Demographics, and PSG (including tcCO<sub>2</sub>).

**Results:** We enrolled 39 children with NMD; 3 had unusable ambulatory tcCO<sub>2</sub> data because of failure of drift correction on the machine (n=2) or an air bubble (n=1). The remaining 36 patients aged 11 months to 16 years (median (IQR) 12.5 years (6.0-15.8)) had ambulatory tcCO<sub>2</sub> and outpatient level 1 PSG data. Ambulatory tcCO<sub>2</sub> monitoring had a sensitivity of 20.0% (95% confidence interval [CI] 0.5-71.6%) and a specificity of 93.5% (95% CI 78.6-99.2%). Almost all children and/or parents (34/36, 94%) preferred ambulatory monitoring over in-hospital PSG.

**Conclusions:** Ambulatory transcutaneous carbon dioxide monitoring was not sufficiently accurate as a clinical tool for the diagnosis of nocturnal hypoventilation our cohort of children with neuromuscular disease despite being preferred over PSG by both children and parents.

**Keywords:** Pediatrics; diagnostic screening programs; hypoventilation; sleep apnea syndromes; neuromuscular diseases; polysomnography.

**Abbreviations:** sleep-disordered breathing (SDB), neuromuscular disease (NMD), polysomnography (PSG), transcutaneous carbon dioxide (tcCO<sub>2</sub>), end-tidal carbon dioxide (tcCO<sub>2</sub>), partial pressure CO<sub>2</sub> (pCO<sub>2</sub>), non-invasive ventilation (NIV), continuous positive airway pressure (CPAP), forced vital capacity (FVC), body mass index (BMI), respiratory therapist (RT), American Academy of Sleep Medicine (AASM), electroencephalogram (EEG), electro-oculogram (EOG), electromyogram (EMG), oxygen saturation (SaO<sub>2</sub>), capillary blood gas (CBG), Duchenne Muscular Dystrophy (DMD), interquartile range (IQR), receiver operating curve (ROC), area under the curve (AUC), confidence interval (CI), standard error (SE), research ethics board (REB)

**Funding:** This work was funded by Muscular Dystrophy Canada.

**Equipment:** The tcCO<sub>2</sub> monitors were provided for the study in kind by Sentec.

**Role of Funder/Sponsor:** Neither Muscular Dystrophy Canada nor Sentec had any role in the design and conduct of the study.

## 1. INTRODUCTION

Early recognition and management of sleep-disordered breathing (SDB), particularly nocturnal hypoventilation, is paramount in reducing mortality in individuals with NMD<sup>1</sup>. The current “gold standard” for diagnosis of nocturnal hypoventilation is a laboratory-based, technician-attended PSG<sup>2</sup>. However, there are currently insufficient resources for the evaluation of sleep-disordered breathing (SDB) in children with neuromuscular diseases (NMD) due to limited and varying resources worldwide<sup>1</sup>. In Canada, it is estimated that 7.5 times more children require polysomnography (PSG) than the current capacity of the healthcare system<sup>3</sup>. The disparity between demand and availability of resources is especially pronounced for children with NMD, as SDB prevalence in this population is estimated to be over 10 times that of the general population, with up to 40% of children with NMD having SDB<sup>4,5</sup>.

SDB is defined as the presence of (1) nocturnal hypoventilation, (2) obstructive sleep apnea and/or (3) central sleep apnea. In children with NMD, nocturnal hypoventilation results from insufficient minute ventilation during sleep secondary to respiratory muscle weakness, scoliosis, or obesity from immobility and/or steroid use<sup>6</sup>. Obstructive sleep apnea can result from increased upper airway collapsibility exacerbated by obesity, retrognathia, or macroglossia<sup>6</sup>. Central sleep apnea occurs when intercostal and diaphragm muscle weakness leads to reduced tidal volumes with associated oxygen desaturations during REM sleep. Central sleep apnea also occurs when overall respiratory instability due to obstructive events or sleep-wake transitions leads to further pauses in respiratory effort<sup>6</sup>. Progressive diurnal respiratory insufficiency is preceded by nocturnal hypoventilation. Timely treatment with non-invasive ventilation (NIV) can reduce hospital admissions and prolong survival<sup>1,7</sup>.

While there is no consensus on screening frequency, British and American Thoracic Societies recommend at least annual PSGs in non-ambulatory children with NMD, and earlier and/or more frequent studies if SDB symptoms are present<sup>8,9</sup>. Objective testing is necessary because children with NMD and nocturnal hypoventilation are often asymptomatic<sup>10</sup>. Furthermore, child and family centered barriers make PSGs more difficult to complete in children with NMD. These barriers include lack of wheelchair accessibility in the PSG labs; need for safe transfer systems, specialized hospital beds, custom commodes, and frequent patient turning; and significant caregiver burden.

Overnight ambulatory transcutaneous carbon dioxide (tcCO<sub>2</sub>) monitoring may be an ideal diagnostic tool because it is noninvasive, comfortable, cost-effective, and portable. To date, only two pediatric studies have evaluated overnight home tcCO<sub>2</sub> monitoring. Felemban and colleagues demonstrated that ambulatory tcCO<sub>2</sub> monitoring was feasible in children with and without NMD who were prescribed NIV<sup>11</sup>. Similarly, Griffon and colleagues showed that ambulatory tcCO<sub>2</sub> monitoring was feasible in children on long term ventilation<sup>12</sup>. However, neither study evaluated diagnostic accuracy. Therefore, our study aimed to evaluate the diagnostic accuracy of ambulatory tcCO<sub>2</sub>, to detect nocturnal hypoventilation in children with NMD compared to the gold standard PSG.

## **2. METHODS**

### **2.1. Study Design and setting**

We conducted a prospective, cross-sectional study between October 1, 2018, and December 31, 2020 at the Hospital for Sick Children in Toronto, Ontario, Canada.



## **2.2. Participants**

Children aged 0 to 18 years old were recruited from the Long-term Ventilation clinic. Inclusion criteria were confirmed NMD diagnosis, clinically indicated PSG as per international societal guidelines<sup>8</sup>, and living within a 100 km radius of the hospital. Clinical indications for PSG include signs and symptoms of SDB (eg. snoring, witnessed apneas) and/or being at risk of developing SDB (eg. loss of ambulation, forced vital capacity <60% predicted)<sup>8</sup>. Although children with different NMD diagnoses have variable clinical trajectories, we chose to be inclusive of all diagnoses as the criteria for hypoventilation is the same from age 0-18 years. Also PSG and tCO<sub>2</sub> monitoring can be done in children of all ages<sup>13</sup>. Exclusion criteria were previously known diagnosis of nocturnal hypoventilation, already commenced on long-term invasive and NIV at home, and physician diagnosis of acute upper respiratory tract infection.

## **2.3. Study Procedures**

We collected the following demographic and clinical characteristics from the medical record: age, sex, height, weight, body mass index (BMI) percentile, primary diagnosis, comorbidities, and spirometry (forced vital capacity (FVC)).

### *Ambulatory Transcutaneous Carbon Dioxide Monitoring*

Ambulatory tCO<sub>2</sub> monitoring was performed in the home using the SenTec Digital Monitor carbon dioxide sensor (Therwil, Switzerland). This fully digital sensor is an electrochemical Severinghaus-type CO<sub>2</sub> tension sensor providing continuous CO<sub>2</sub> recordings. Ambulatory data was collected by a respiratory therapist (RT) who traveled to the participant's home to calibrate

and apply the monitor for one night. Calibration is necessary as all sensor measurements drift over time, so an automated correction factor algorithm is applied after the data collection is complete. Our minimum criterion for acceptable recordings was at least 4 hours of data. For each overnight recording, we documented duration of recording; mean, minimum and maximum  $\text{tcCO}_2$ ; and time and percentage of the night with a  $\text{tcCO}_2 > 50$  mmHg.

### *Polysomnography*

All PSGs were conducted according to the American Academy of Sleep Medicine (AASM) guidelines with a computer based software system (XL-TEK, Oakville, Ontario, Canada)<sup>13</sup>. A standard overnight PSG includes a 6-lead electroencephalogram (EEG) (C3, C4, O1, O2, M1, M2), two bilateral electro-oculogram (EOG) leads, one submental and two tibial electromyograms (EMG). Respiratory measurements include chest wall and abdominal movement using inductance pneumography; airflow using a nasal cannula connected to a nasal pressure transducer (Braebon); oxygen saturation ( $\text{SpO}_2$ ) using a pulse oximeter (Masimo Irvine, CA);  $\text{tcCO}_2$  using a Digital Monitor  $\text{CO}_2$  sensor (SenTec, Therwil, Switzerland); and end-tidal  $\text{CO}_2$  ( $\text{etCO}_2$ ) using a Capnocheck (Smiths Medical, Ashford, Kent, UK). PSG video and audio recordings and body position were obtained as per current clinical standards. PSGs were performed and scored by trained sleep technologists independent of the study team. PSGs were then reported by the principal investigator (RA), who remained blinded to the  $\text{tcCO}_2$  data. We aimed for participants to be booked for a PSG 7-14 days following  $\text{tcCO}_2$  monitoring.

For our primary study objective, nocturnal hypoventilation was defined by a partial pressure  $\text{CO}_2$  ( $\text{pCO}_2$ )  $> 50$  mmHg for  $\geq 25\%$  of the night, as per the pediatric AASM guidelines, which represents the current threshold used for initiation of ventilation. We additionally analyzed

diagnostic accuracy using a more conservative threshold of  $p\text{CO}_2 > 50\text{mmHg}$  for  $\geq 2\%$  of the night, as recommended by the 2018 Duchenne Muscular Dystrophy (DMD) Care Considerations Working Group for initiation of assisted ventilation<sup>14</sup>. This definition may be appropriate for diagnosis of nocturnal hypoventilation in other NMD conditions as well.

### *Patient Experience*

We collected subjective data on participant comfort level during the ambulatory home  $\text{tcCO}_2$  monitoring. Participants (or their parent) were asked to rate their comfort level on a Likert scale with 0 being very uncomfortable and 10 being very comfortable. They were also asked their perception as to the preferred option for diagnostic assessment (i.e., home or in-hospital).

## **2.4. Study Outcomes**

The primary study outcome was accuracy of ambulatory home  $\text{tcCO}_2$  monitoring for diagnosing nocturnal hypoventilation compared to the gold standard  $\text{etCO}_2$  during PSG. A secondary outcome was diagnostic accuracy of ambulatory  $\text{tcCO}_2$  compared to PSG  $\text{tcCO}_2$  monitoring. Additionally, we evaluated the correlations and agreements between ambulatory  $\text{tcCO}_2$  and PSG  $\text{tcCO}_2$  data, comfort level, and diagnostic test preference.

## **2.5. Statistical Analysis**

We performed a sample size calculation based on previous pediatric ambulatory sleep studies without capnography that reported a sensitivity of 75-100% for OSA<sup>15-18</sup>. 37 children achieved 80% power to detect a sensitivity of 90% with an estimated precision of 9%.

We report descriptive statistics (median and interquartile range (IQR) and counts and proportions) to summarize demographic and clinical data. We used Student's t-tests to compare continuous parametric data (total sleep time with  $\text{tcCO}_s > 50$  mmHg), and the Wilcoxon Mann-Whitney U test for nonparametric data (all other data). Distribution normality was determined using the Shapiro-Wilk test and visual inspection methods.

We calculated sensitivity, specificity, 95<sup>th</sup> percentile confidence intervals (CI), positive and negative predictive values, and diagnostic accuracy. We generated a receiver operating curve (ROC) using the two definitions of nocturnal hypoventilation as cut-points and calculated the area under the curve (AUC) to determine the discriminative ability of ambulatory  $\text{tcCO}_2$  monitoring as a diagnostic test. We used Cohen's kappa to assess the agreement between ambulatory  $\text{tcCO}_2$  and PSG  $\text{tcCO}_2$  studies and PSG  $\text{etCO}_2$  and PSG  $\text{tcCO}_2$ . We used the Spearman's Rho test due to non-normal distribution of data to determine correlations between mean  $\text{tcCO}_2$  for ambulatory and PSG study parameters. Lastly, we generated Bland-Altman plots to analyse the agreement between tests. Analyses were performed using R Studio (2021.09.1+372).

## **2.6. Ethical Considerations**

This study was approved by the SickKids Research Ethics Board, Toronto, Canada (REB 1000012349242). The study was registered with ClinicalTrials.gov (NCT03478566).

## **3. RESULTS**

### **3.1. Baseline Characteristics**

We enrolled 39 participants. Three had unusable ambulatory tcCO<sub>2</sub> data due to failure of drift correction on the machine (n=2) or an air bubble (n=1). All patients had PSG tcCO<sub>2</sub> data, whereas 3 patients had missing PSG etCO<sub>2</sub> data because of intolerance of application of the nasal sensor. The median (IQR) age of the remaining 36 participants was 12.5 (6.0-15.8) years. Patients lived a median of 41.5 km (IQR 23.3-61.8) away from the hospital and sleep laboratory. Baseline clinical characteristics are described in Table 1.

### **3.2. Comparison of Level 1 Polysomnography vs. Ambulatory tcCO<sub>2</sub> Results**

Table 2 reports level 1 PSG and ambulatory tcCO<sub>2</sub> study results. Median (IQR) time between ambulatory tcCO<sub>2</sub> and PSG was 10.5 days (5.0-20.8 days).

Using AASM criteria, 2 children (5.6%) met criteria for nocturnal hypoventilation using PSG etCO<sub>2</sub>, 5 (13.9%) met criteria using PSG tcCO<sub>2</sub>, and 3 (8.3%) met criteria using ambulatory tcCO<sub>2</sub> measurements<sup>12</sup>. Using DMD specific criteria, 8 children (22.2%) met criteria for nocturnal hypoventilation using PSG etCO<sub>2</sub>, 8 (22.2%) met criteria using PSG tcCO<sub>2</sub>, and 6 (16.7%) met criteria using ambulatory tcCO<sub>2</sub> measurements<sup>13</sup>.

### **3.3. Diagnostic Accuracy of Ambulatory tcCO<sub>2</sub> Monitoring**

Using the diagnostic criteria for nocturnal hypoventilation of CO<sub>2</sub> >50mmHg for ≥ 25% of the night, when comparing to the gold standard PSG we found ambulatory tcCO<sub>2</sub> to have a sensitivity of 0.0% (95% CI 0.0-84.2%) and specificity of 91.2% (95% CI 76.3-98.1%) (Table 3). When comparing ambulatory tcCO<sub>2</sub> to PSG tcCO<sub>2</sub> sensitivity was 20.0% (95% CI 0.5-71.6%) and specificity 93.5% (95% CI 78.6-99.2%) (Table 3).

When using the DMD Working Group criterion for nocturnal hypoventilation of  $\text{CO}_2 > 50\text{mmHg}$  for  $\geq 2\%$  of the night, compared to PSG  $\text{tcCO}_2$ , ambulatory  $\text{tcCO}_2$  sensitivity was 25.0% (95% CI 3.2-65.1%); specificity 85.7% (95% CI 67.3-96.0%) (Table 4). Compared to PSG  $\text{etCO}_2$ , ambulatory  $\text{tcCO}_2$  sensitivity was 25.0% (95% CI 3.2-65.1%); specificity 85.7% (95% CI 67.3-96.0%) (Table 4).

The ROC curve for the two definitions of nocturnal hypoventilation as cut-points is shown in Figure 1. The AUC was 0.595 indicating poor discrimination.

#### **3.4. Agreement Between Level 1 Polysomnography and Ambulatory $\text{tcCO}_2$ Monitoring**

There was no agreement between the ambulatory mean  $\text{tcCO}_2$  measurements and the PSG  $\text{etCO}_2$  measurements, with a kappa coefficient of -0.07 (SE 0.03; 95% CI -0.1 to -0.003). There was only slight agreement between the mean  $\text{tcCO}_2$  measurements from the ambulatory and PSG studies, with a kappa coefficient of 0.2 (SE 0.2; 95% CI -0.5 to 0.5).

#### **3.5. Correlation Between Level 1 Polysomnography and Ambulatory $\text{tcCO}_2$ Monitoring**

There was poor correlation between the ambulatory mean  $\text{tcCO}_2$  measurements and the PSG  $\text{etCO}_2$  measurements ( $r = 0.2$ ; 95<sup>th</sup> CI -0.1-0.5;  $p = 0.2$ ). Similarly, mean  $\text{tcCO}_2$  measurements from the ambulatory and PSG studies were also not found to be significantly correlated ( $r = 0.3$ ; 95<sup>th</sup> CI -0.1-0.5;  $p = 0.1$ ). There was also poor correlation between minimum ambulatory  $\text{tcCO}_2$  and PSG  $\text{etCO}_2$  measurements ( $r = 0.2$ ; 95<sup>th</sup> CI -0.2-0.5;  $p = 0.3$ ), maximum ambulatory  $\text{tcCO}_2$  and

PSG etCO<sub>2</sub> measurements (r= 0.2; 95<sup>th</sup> CI -0.2-0.5; p=0.2), time spent >50 mmHg (r= 0.1; 95<sup>th</sup> CI -0.2-0.4; p=0.6), and percentage of time spent >50 mmHg (r= -0.03; 95<sup>th</sup> CI -0.4-0.3; p=0.8).

### **3.6 Bland-Altman Plots Comparing Level 1 Polysomnography and Ambulatory tcCO<sub>2</sub> Monitoring**

Bland-Altman plots were generated to assess the agreement between ambulatory mean tcCO<sub>2</sub> measurements and the PSG etCO<sub>2</sub> measurements (Figure 2) and PSG tcCO<sub>2</sub> measurements (Figure 3). Overall, there was poor agreement between the ambulatory and PSG measurements.

### **3.7. Patient Experience**

The median (IQR) patient comfort level during the ambulatory tcCO<sub>2</sub> study was 8 (8-10). Almost all participants (or parent) (34/36, 94%) preferred ambulatory monitoring over in-hospital PSG. The two patients who preferred PSG monitoring did not leave comment explaining their preference.

## **4. DISCUSSION**

Accurate and early diagnosis and treatment of nocturnal hypoventilation is paramount to slow the development of diurnal hypercapnia, the leading cause of hospitalization and mortality for these children<sup>1</sup>. Our results indicate that current technology for ambulatory tcCO<sub>2</sub> monitoring has limited diagnostic accuracy for nocturnal hypoventilation in a cohort of children with NMD.

To our knowledge, our study is the first to evaluate the diagnostic accuracy of ambulatory tcCO<sub>2</sub> monitoring compared to the gold standard PSG in children with NMD. To date, two studies have

evaluated overnight home tcCO<sub>2</sub> monitoring in children. Felemban et al. compared overnight tcCO<sub>2</sub> and pulse oximetry recordings performed at home and in-hospital in a cohort of 11 children with NMD and 13 children with other disorders treated with long-term NIV<sup>11</sup>. Mean values for at home and in-hospital tcCO<sub>2</sub> measurements were comparable to those in our study<sup>11</sup>. Another study by Griffon et al. analysed tcCO<sub>2</sub> recordings of children treated with or weaned from continuous positive airway pressure (CPAP), NIV or high flow nasal oxygen<sup>12</sup>. Data, however, were not compared to any in-hospital measurements, and neither of these studies evaluated diagnostic accuracy.

End-tidal capnography has also been previously studied in the ambulatory setting with albeit limited success. Fishman and colleagues demonstrated that an ambulatory level III PSG study with etCO<sub>2</sub> similarly had only moderate diagnostic accuracy (sensitivity and specificity to detect SDB was 61.5% and 86.7%, respectively) when compared to a level I PSG. Misinterpretation of falsely high or falsely low measurements can lead to potential mismanagement of these already complex and vulnerable children. As such, our results are congruent with others highlighting the need for increased allocation of healthcare funding for gold standard level I PSG testing to diagnose nocturnal hypoventilation in children with NMD given the existing limitations with ambulatory studies at present<sup>19</sup>.

The same brand of tcCO<sub>2</sub> machines were used for both the PSGs as well as the ambulatory studies. Three participants were excluded due to unusable ambulatory tcCO<sub>2</sub> data. Obtaining accurate tcCO<sub>2</sub> recordings can be technically challenging and labour intensive. The sensor probe is sensitive to temperature, and the heated probe may cause thermal injury (e.g. blisters, burns)<sup>20</sup>.



Falsely elevated  $tcCO_2$  measurements can result from increased capillary blood flow and low temperature, while falsely low  $tcCO_2$  levels can result from a hypo-perfused state, skin edema or sweat, an air bubble in the sensor, or excessive contact gel<sup>20</sup>. Because of these pitfalls, the device requires continuous calibration during PSG. A potential solution would be the performance of the ambulatory test under the supervision of a trained technologist or RT for its duration; however, this would negate some of the cost- and resource-saving goals of ambulatory testing. Therefore, the ambulatory  $tcCO_2$  monitor likely requires further technological advancement resulting in increased ease of use before it can be used in the pediatric ambulatory setting. Overall, in its current state, with limited diagnostic accuracy and feasibility in the home setting, ambulatory  $tcCO_2$  monitoring is unfortunately not yet able to save the long distance that many families need to travel to reach the formal sleep laboratory.

There were a few notable limitations to our study. First, our study was likely underpowered as only five study participants had a PSG diagnosis of nocturnal hypoventilation. The presence of hypoventilation was not an inclusion criterion as we took a pragmatic approach to studying a cohort of children referred to our sleep laboratory for evaluation of SDB. Therefore, there is a need for future studies to investigate the utility of ambulatory  $tcCO_2$  monitoring in a pediatric and adult cohort with a higher prevalence of nocturnal hypoventilation. Second, for our evaluation of diagnostic accuracy, we compared ambulatory  $tcCO_2$  to  $etCO_2$  recordings during PSG rather than arterial blood gas (ABG) for two reasons. Firstly, this was done for ease of collection for the child. Second, technically comparing one continuous  $CO_2$  data recording to another continuous recording was chosen rather than to an ABG, a single time point measurement, given the known variability of  $CO_2$  levels overnight with progression through

sleep stages. Third, ambulatory tcCO<sub>2</sub> used total recording time instead of total sleep time which may have inflated the denominator for calculating the percentage of time spent with tcCO<sub>2</sub> >50 mmHg. This inability to accurately capture TST is a well-described limitation of home sleep apnea tests. Potential proposed solutions include adding additional leads (ECG, respiratory effort monitoring) to quantify sleep using autonomic physiology, or recording subjective TST, though this is also commonly inaccurate<sup>21</sup>. As there are currently no well-established methods of accurately determining TST from home sleep testing, the underestimation of TST remains a risk as it can lead to the under detection of sleep-disordered breathing and hypoventilation, which in turn can affect therapeutic decision making and patient care.

## **5. CONCLUSION**

Although ambulatory tcCO<sub>2</sub> monitoring appears to be well tolerated and preferred by patients and families, it is not yet a practical clinical tool for the diagnosis of nocturnal hypoventilation in children with NMD due to its low diagnostic accuracy and technical challenges in the home setting. Future directions for this work include an evaluation of diagnostic accuracy of ambulatory tcCO<sub>2</sub> compared to PSG in a cohort of children and/or adults with established hypoventilation.

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**Table 1: Baseline Characteristics of the Study Cohort**

<b>Characteristic (N=36)</b>	
<b>Age (years)</b>	12.5 (6.0-15.8)
<b>Female sex</b>	11 (31)
<b>Body mass index (kg/m<sup>2</sup>)</b>	19.2 (15.0-23.1)
<b>Distance from hospital (km)</b>	41.5 (23.3-61.8)
<b>Forced vital capacity (% predicted)</b>	69.0 (55.0-77.0)
<b>Diagnosis</b>	
<b>Duchenne muscular dystrophy</b>	13 (36.1)
<b>Congenital myopathy</b>	6 (16.7)
<b>Congenital muscular dystrophy</b>	5 (13.9)
<b>Spinal muscular atrophy type I</b>	2 (5.6)
<b>Spinal muscular atrophy type II</b>	1 (2.8)
<b>Spinal muscular atrophy type III</b>	2 (5.6)
<b>Juvenile amyotrophic lateral sclerosis</b>	2 (5.6)
<b>Neuromuscular disease NYD</b>	2 (5.6)
<b>Myasthenia gravis</b>	1 (2.8)
<b>Ataxia-telangiectasia</b>	1 (2.8)
<b>Becker muscular dystrophy</b>	1 (2.8)

Data are either presented as median (interquartile range [IQR]) or number (percentage). Forced vital capacity (FVC) was able to be completed in 26 patients. IQR = interquartile range. NYD = not yet determined.

**Table 2: Level I Polysomnography and Ambulatory Transcutaneous Carbon Dioxide Monitoring Results**

Characteristic	Level I PSG	Ambulatory tcCO <sub>2</sub> Monitor	P-value
<b>Recording time (minutes)</b>	454.3 (430.6-502.1)	580.5 (528.5-644.8)	<0.0001
<b>Total sleep time (minutes)</b>	387.0 (399.5-414.0)	N/A	
<b>Transcutaneous CO<sub>2</sub> (mmHg)</b>			
<b>Minimum</b>	36.5 (32.0-41.0)	36.1 (32.8-38.4)	0.6
<b>Maximum</b>	47.5 (43.0-51.8)	45.7 (43.9-49.5)	0.6
<b>Mean</b>	43.5 (39.3-47.0)	42.5 (40.0-45.3)	0.6
<b>Time &gt;50 mmHg (minutes)</b>	35.6 (85.9)	29.6 (92.3)	0.6
<b>%Time &gt;50 mmHg</b>	9.2 (22.6)	5.9 (19.0)	0.7
<b>End-tidal CO<sub>2</sub> (mmHg)</b>			
<b>Minimum</b>	28.0 (25.5-32.0)	N/A	<0.001*
<b>Maximum</b>	51.0 (46.0-54.0)	N/A	0.2*
<b>Mean</b>	43.0 (40.3-44.5)	N/A	0.7*
<b>Time &gt;50 mmHg (minutes)</b>	17.5 (50.2)	N/A	0.9*
<b>%Time &gt;50 mmHg</b>	4.4 (12.5)	N/A	0.7*
<b>OAHl (events/h)</b>	1.4 (0.3-5.4)	N/A	
<b>CAHI (events/h)</b>	0.9 (0.3-1.7)	N/A	
<b>Hypoventilation – AASM<sup>+</sup></b>			
<b>Using tcCO<sub>2</sub></b>	5 (13.9%)	3 (8.3)	
<b>Using etCO<sub>2</sub></b>	2 (5.6%)	N/A	
<b>Hypoventilation – DMD<sup>++</sup></b>			
<b>Using tcCO<sub>2</sub></b>	8 (22.2%)	6 (16.7)	
<b>Using etCO<sub>2</sub></b>	8 (22.2%)	N/A	

Data are either presented as median (interquartile range [IQR]), mean (standard deviation [SD]), or number (percentage).

OAHl = obstructive apnea-hypopnea index. CAHI = central apnea-hypopnea index. CO<sub>2</sub> = carbon dioxide. tcCO<sub>2</sub> = transcutaneous CO<sub>2</sub>. DMD = Duchenne Muscular Dystrophy

\*p-value comparing end-tidal CO<sub>2</sub> from PSG to tcCO<sub>2</sub> from ambulatory study.

<sup>+</sup>Nocturnal hypoventilation as defined by a CO<sub>2</sub> recording >50mmHg for ≥ 25% of the night.

<sup>++</sup>Nocturnal hypoventilation as defined by a CO<sub>2</sub> recording >50mmHg for ≥ 2% of the night, using 2018 Duchenne Muscular Dystrophy (DMD) Care Considerations Working Group<sup>13</sup>.

**Table 3: Sensitivity and Specificity of Ambulatory tcCO<sub>2</sub> Monitoring compared to Polysomnography etCO<sub>2</sub> and tcCO<sub>2</sub> Measurements using AASM Criteria**

	<b>Comparison to PSG etCO<sub>2</sub> (95<sup>th</sup> CI)</b>	<b>Comparison to PSG tcCO<sub>2</sub> (95<sup>th</sup> CI)</b>
<b>Sensitivity</b>	0.0% (0.0-84.2%)	20.0% (0.5-71.6%)
<b>Specificity</b>	91.2% (76.3-98.1%)	93.6% (78.6-99.2%)
<b>Positive Predictive Value</b>	0	33.3% (5.2-82.0%)
<b>Negative Predictive Value</b>	93.9 % (93.3-94.5%)	87.9% (82.3-91.9%)
<b>Accuracy</b>	86.1 (70.5-95.3)	83.3 (67.2-93.6)

tcCO<sub>2</sub> = transcutaneous carbon dioxide; etcCO<sub>2</sub> = end-tidal carbon dioxide; CI = confidence interval.

American Academy of Sleep Medicine criteria: Nocturnal hypoventilation as defined by a CO<sub>2</sub> recording >50mmHg for ≥ 25% of the night<sup>12</sup>.

**Table 4: Sensitivity and Specificity of Ambulatory tcCO<sub>2</sub> Monitoring compared to Polysomnography etCO<sub>2</sub> and tcCO<sub>2</sub> Measurements using DMD Specific Criteria**

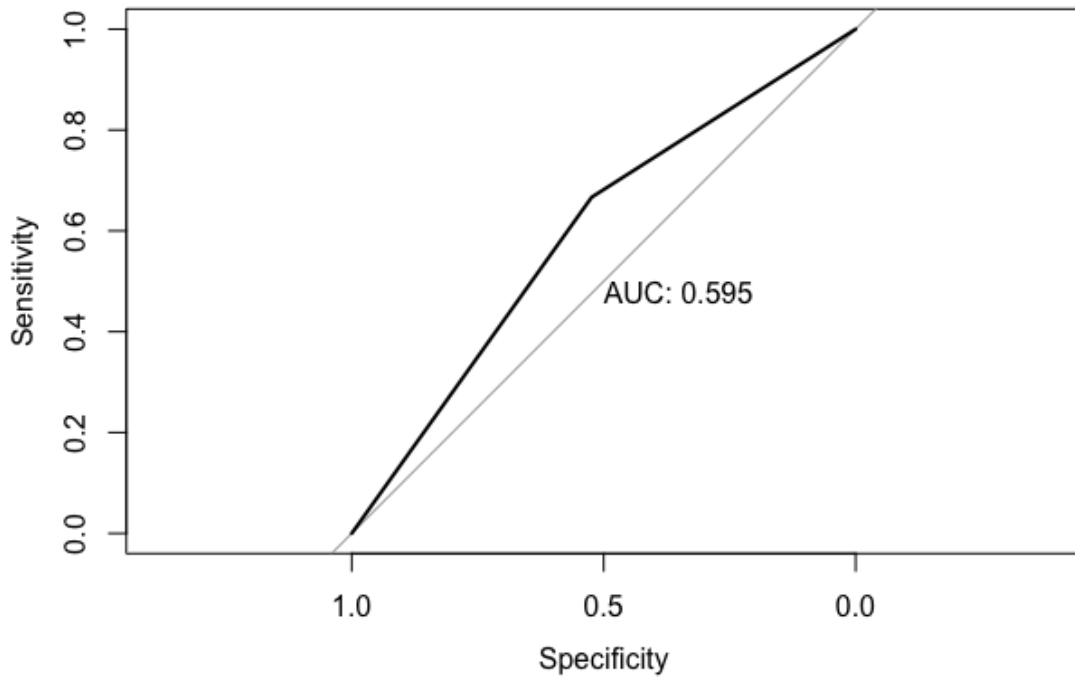
	<b>Comparison to PSG etCO<sub>2</sub> (95<sup>th</sup> CI)</b>	<b>Comparison to PSG tcCO<sub>2</sub> (95<sup>th</sup> CI)</b>
<b>Sensitivity</b>	25.0% (3.2-65.1%)	25.0% (3.2-65.1%)
<b>Specificity</b>	85.7% (67.3-96.0%)	85.7% (67.3-96.0%)
<b>Positive Predictive Value</b>	33.3% (10.0-69.2%)	33.3% (10.0-69.2%)
<b>Negative Predictive Value</b>	80.0% (72.3-86.0%)	80.0% (72.3-86.0%)
<b>Accuracy</b>	72.2 (54.8-85.8)	72.2 (54.8-85.8)

tcCO<sub>2</sub> = transcutaneous carbon dioxide; etcCO<sub>2</sub> = end-tidal carbon dioxide; CI = confidence interval.

Duchenne Muscular Dystrophy specific criteria: Nocturnal hypoventilation as defined by a CO<sub>2</sub> recording >50mmHg for ≥ 2% of the night<sup>13</sup>.

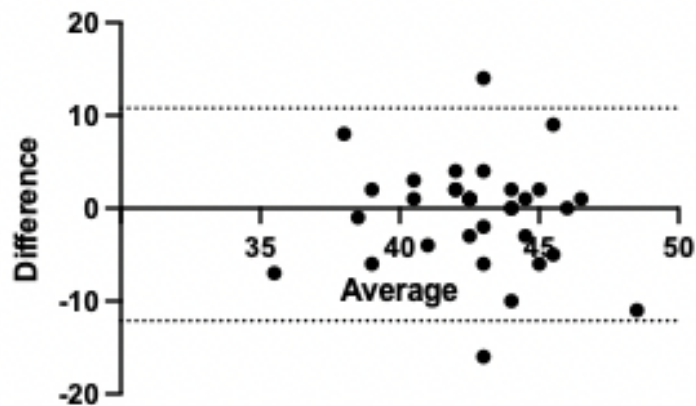


**Figure 1: Receiver Operating Characteristic Curve for Ambulatory tcCO<sub>2</sub> Monitoring**



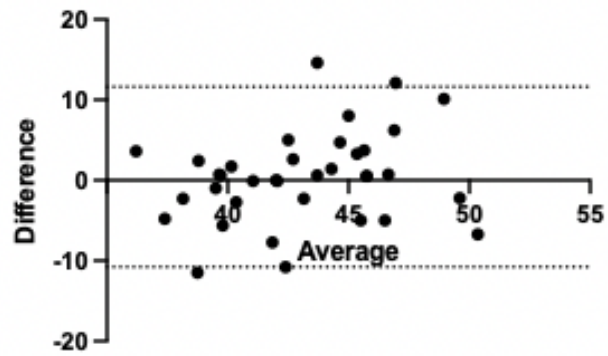
tcCO<sub>2</sub> = transcutaneous carbon dioxide; AUC= area under the curve.

**Figure 2: Bland-Altman Plot comparing Ambulatory tcCO<sub>2</sub> Monitoring against Polysomnography etCO<sub>2</sub>**



*Bias 0.4 mmHg, SD 5.7 mmHg*  
*Dotted line = bias, dashed lines = 95% limits of agreement*

**Figure 3: Bland-Altman Plot comparing Ambulatory tcCO<sub>2</sub> Monitoring against Polysomnography tcCO<sub>2</sub>**



*Bias -0.7 mmHg, SD 5.8 mmHg  
Dotted line = bias, dashed lines = 95% limits of agreement*