Pulse Transit Time and Assessment of Childhood Sleep Disordered Breathing

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Objectives: To compare nocturnal polysomnography (PSG) with pulse transit time (PTT) recordings and structured clinical assessments and assess the reliability of these methods as a surrogate for the apnea-hypopnea index (AHI; calculated as the number of apneas/hypopneas per hour of total sleep time) and to test the associations between the clinical assessments and sleep disordered breathing (SDB).

Design: Prospective observational study. The parents of 51 children and adolescents filled out a questionnaire on SDB and the participants underwent examination. Scores from questionnaire and examination items were weighted according to their association with SDB. A total clinical score was assigned combining questionnaire and examination scores.

Setting: Hospital pediatrics department.

Patients: Children and adolescents aged 5 to 17 years undergoing standard PSG with the addition of PTT as part of a clinical investigation for SDB.

Main Outcome Measures: The AHI and associations between the AHI and PTT arousal index (PTT-AI) and questionnaire, examination, and total clinical scores.

Results: We found a significant correlation between the AHI and PTT-AI ($r=0.55$; $P<.001$). The relationship between the AHI and PTT-AI was stronger when the AHI was greater than 3. We also found significant correlations between the PTT-AI and the total clinical score ($r=0.38$; $P=.008$) and the examination score ($r=0.44$; $P=.002$) but not the questionnaire score ($r=0.23$; $P=.12$). There was an association between the AHI and examination score in particular when the AHI was greater than 3.

Conclusions: Pulse transit time shows promise as a screening test for SDB associated with an AHI greater than 3. For less severe SDB, the validity of using the PTT to separate these conditions from primary snoring has not been demonstrated in a clinical setting.

SLEEP DISORDERED BREATHING (SDB) is estimated to affect 10% to 12% of children, of whom 1% to 3% will have obstructive sleep apnea hypopnea syndrome (OSAHS). Sleep disordered breathing encompasses a range of conditions, including primary snoring, upper airway resistance syndrome (UARS), and OSAHS. Diagnosis is important because associated health-related consequences include growth impairment and metabolic derangements (insulin resistance), hypertension, heart and vascular disease, and neuropsychological sequelae (ie, daytime sleepiness, inattention, behavior problems, and impaired cognitive function and school performance), some of which are associated with only a small elevation of the apnea-hypopnea index (AHI).

Clinical examination alone would ideally be sufficient to determine which children have significant SDB. Unfortunately, research to date indicates that the history and examination are unable to reliably identify those most likely to have SDB. Sleep disturbance can be indirectly assessed by overnight measurement of apneas, hypopneas, and reduction in blood oxygen saturation. The gold criterion standard for OSAHS diagnosis is overnight polysomnography (PSG), which is inconvenient, difficult, and expensive to perform. Upper airway resistance syndrome is difficult to diagnose because it is defined by the absence of a significant rise in AHI; esophageal manometry is required to detect the airway obstruction–related changes in intrathoracic pressure that cause arousal without limitation of airflow. Cortical arousal caused by sleep disturbance can be recorded with electroencephalography (EEG). Autonomic or subcortical arousals also occur as a re-
Pulse transit time (PTT) has been used in sleep studies as a marker for autonomic perturbations; a change in PTT from baseline. \(^{12,13}\) Arousal at the termination of an obstructive event causes a transient marked increase in blood pressure, so decreasing PTT. Pulse transit time may be measured noninvasively and can be assessed quickly and objectively. It detects the time taken for a pulse wave generated by ventricular contraction to reach a peripheral detector (usually a finger or toe). Pulse transit time is inversely related to blood pressure; that is, as blood pressure rises (during arousal), PTT decreases. Pulse transit time is influenced by arterial wall stiffness, and this dictates that changes in PTT be measured for individuals in relation to their baseline PTT. For measurement accuracy, PTT is defined as the interval between the R wave of the electrocardiographic waveform to the time of the arrival of the pulse waveform distally (at the finger), was measured as 50% of the height of the maximal point of the waveform (graticule width, 40 milliseconds).

The participants were children and adolescents (aged 5-17 years; hereinafter referred to as children) undergoing full nocturnal PSG for investigation of SDB or included as part of a study of sleep qualities among obese children. The Otago Ethics Committee approved the study protocols. Informed written consent was obtained from the participants or from the parents with assent from the child. Inclusion criteria consisted of developmentally healthy children aged 5 to 17 years whose parents reported their child snored frequently and loudly and/or had a body mass index of 30 or more (calculated as weight in kilograms divided by height in meters squared) according to the standards of Cole et al. \(^{19}\) Exclusion criteria consisted of evidence of gross sensory or motor problems, the presence of a parent or guardian who was unable to provide requested information, severe developmental disability, craniofacial abnormalities, neuromuscular disease, or recognized syndromic obesity. Based on these recruitment criteria, participants had a high probability of having SDB. Thus, we used questionnaire and physical examination scores obtained from a system that has high sensitivity (92%) for detecting OSAHS as validated against PSG but low specificity (29.4%), which is useful for contributing to the decision for surgery in a child with a strong clinical history but without recorded PSG. \(^{20}\) All scoring was conducted with raters having no detailed knowledge of the patient’s history while being aware of the research study.

### Questionnaire Score

Parents completed a questionnaire closely based on that devised by Goldstein et al.\(^{20}\) and described in more detail in a subsequent study\(^{21}\) as their score A for assessment of children with obstructive sleep apnea. Questions were tailored to determine the severity of nighttime symptoms (ie, frequency of snoring, gasping, choking noises, restlessness, profuse sweating, awakenings, enuresis, sleeping with the neck fully extended or in the fetal position, and breathing pauses) and daytime symptoms (ie, frequency of daytime sleepiness, morning headaches, irritability, and hyperactive behavior) and general information regarding the child's breathing and airway (frequency of mouth-breathing, chronic rhinorrhea, and number of episodes of tonsillitis per year). The questions all required answers based on a rating scale. One question relating to daytime symptoms included in the assessment by Goldstein et al.\(^{11}\) was graded by detailed discussion with the parent. This question was related to any motor, speech, or cognitive developmental delay. Another question, related to letter grades achieved in the American school system, was not appropriate for the New Zealand system and was thus omitted from the questionnaire. The highest possible score from the questionnaire was 87.

### Physical Examination Score

The physical examination was conducted before the PSG recording. This score was also based on one described by Goldstein et al.\(^{20,21}\) as score B of their assessment\(^{11}\) and included the following objective measures: height, weight, body mass in-
an overnight audiorecording rated for the presence of apnea of adenoidal hypertrophy from a lateral neck radiograph, and of 0). The highest possible physical examination score was 74.

The total clinical score combined the questionnaire score with the physical examination score. Scoring for individual items is provided by Goldstein et al.21 With the slight alteration to the questionnaire (the omission of a school performance measure), the maximum possible overall severity score in this study was 161 (questionnaire total, 87; clinical examination total, 74), whereas that of Goldstein et al21 was 164 (questionnaire total, 90; clinical examination total, 74).

POLYSOMNOGRAPHY

Participants underwent overnight evaluation in a sleep laboratory. The PSG montage involved 2 EEG leads (C4-A1 and C3-A2), 2 electro-oculography leads, submental electromyography, ECG, chest and abdominal wall motion by means of thoracic and abdominal inductance plethysmography (SleepSense; Scientific Laboratory Products), arterial oxygen saturation (Masimo Radical 7 monitor; Masimo Corp), and nasal airflow via nasal prongs (Hudson RCI; Teleflex Medical). A digital recorder (Snorometer; Stowood Scientific Instruments Ltd) incorporated into a clinical diagnostic software system (Visi-3; Stowood Scientific Instruments Ltd) with an external microphone placed 30 cm from the center of the pillow recorded snoring.

The EEG, electro-oculography, and electromyography signals were relayed through an integrated hardware/software system (PowerLab; AD Instruments Pty Ltd), and the remainder of the signals were relayed through the hardware/software system of the Visi-3 system. The PowerLab and Visi systems were time-synchronized before each recording. Patients were monitored and recorded on videotape using an infrared video camera and were continuously observed by a researcher in a remote laboratory. Sleep recordings were scored in 30-second epochs according to the criteria of Rechtschaffen and Kales23 for total sleep time (TST) (defined as the time from sleep onset to sleep waking minus the time awake), sleep efficiency (calculated as [TST/time in bed] × 100), sleep latency (defined as the time between going to bed and sleep onset), and the arousal index (AI; calculated as the number of arousals per hour).

PULSE TRANSIT TIME

Visi-3 analysis software was used to calculate PTT after the removal of artifacts. Pulse transit time was measured on a beat-to-beat basis using ECG and peripheral pulse oximetry. Pulse transit time was measured from the maximum of the R wave on the ECG trace to the arrival of the pulse waveform taken as 50% of the maximum value of the photoplethysmographic curve (Figure). The inspiratory rise in PTT was measured for each breath and averaged across the night. Pulse transit time arousals were derived from a 4-second moving average of the raw PTT signal to eliminate respiratory variation. A PTT arousal was defined as a decrease in PTT in the averaged signal by at least 15 milliseconds of the baseline lasting at least 5 seconds.24 The PTT-AI was calculated as the number of PTT arousals per hour of TST.

APNEA-HYPOPNEA INDEX

An obstructive apnea was defined as the presence of chest-abdominal wall motion associated with a reduction of airflow by 80% of the baseline rate, lasting for 2 breaths or more, or desynchronization of chest and abdominal movements associated with an arousal for 2 breaths or more.4,5 An obstructive hypopnea was defined as a reduction in airflow associated with a drop in oxygen saturation by pulse oximetry of 4% or more or an arousal35 and was scored when the duration lasted 2 breaths or longer. The AHI was calculated as the number of apneas/hypopneas per hour of TST.

STATISTICAL ANALYSIS

The primary outcome measure was the AHI. We explored associations between the AHI and the PTT-AI, clinical examination score, and clinical examination score without a radiograph. Each association was investigated using Pearson correlation coefficients, in which the AHI was treated as a continuous variable, and using logistic regression, in which the AHI categories were created using cutoff points of 1, 2, 3, and 4. For the latter models, optimal clinical cutoff points in terms of the PTT-AI and clinical examination scores were identified by visually evaluating the sensitivity and specificity graphs. Likelihood ratio tests were used to compare nested models. All analyses were conducted using commercially available statistical software (Stata, version 11.2; StataCorp), with 2-sided P < .05 considered statistically significant in all cases.

Of the 51 participants, 24 were male and 27 were female, with an age range of 5 to 17 years (mean [SD] age, 11.2 [3.5] years) and a mean (SD) body mass index of 26.5 (8.3). Table 1 summarizes the clinical and sleep study results. We found significant correlation between the AHI and PTT-AI when compared as a continuum (r = 0.55; P < .001). There is some debate about the level of AHI considered pathological in children, but there appears to be increasing agreement that an AHI greater than 1 is pathological.7,26 We examined the relationship between the AHI and PTT-AI under different conditions (Table 2). The relationship between the AHI and PTT-AI was stronger when the AHI was greater than 3. We undertook receiver operating characteristic curve analysis, allowing us to visually determine the optimal cutoff points for the PTT-AI and AHI (Table 2). Thus, a PTT-AI greater than 11 will predict an AHI greater than 3 with a sensitivity of 94% and a specificity of 62%. The positive likelihood ratio of 2.45 indicates that a child with SDB is 2.45 times as likely to have a PTT-AI greater than 11.36 compared with a child without SDB (by the criterion of an AHI <3). On the other hand, the negative likelihood ratio of 0.10 demonstrates that a child with SDB is one-tenth as likely to have a PTT-AI less than 11.36 compared with a child without SDB.
There was also significant correlation between the PTT-AI and the total clinical score ($r = 0.38; P = .008$) and the physical examination score alone ($r = 0.44; P = .002$) but not for the questionnaire score alone ($r = 0.23; P = .12$).

For the association with physical examination score, the optimal cutoff at an AHI greater than 3 was a PTT-AI of 11.36. There was an association between AHI and the examination score, particularly when the AHI was greater than 3 with an optimal cutoff score of 18 (Table 3). Thus, the examination score gave a result compatible with SDB as measured by the criterion of an AHI greater than 3 with a sensitivity of 87% and a specificity of 71%. The positive likelihood ratio of 2.95 demonstrates that a child with SDB is 2.95 times as likely to have an examination score (including a radiograph) of 18 or greater compared with a child without SDB (by the criterion of an AHI < 3). On the other hand, the negative likelihood ratio of 0.19 demonstrates that a child with SDB is roughly one-fifth as likely to have an examination score less than 18 compared with a child without SDB.

There was still an association between AHI and the physical examination score when the adenoid radiograph score was excluded from the physical examination score (Table 3). When considered alone, there was no evidence of an association between the AHI category and radiograph score (AHI > 1, $P = .46$; AHI > 2, $P = .96$; AHI > 3, $P = .88$; and AHI > 4, $P = .90$). The addition of PTT-AI to a model already containing the examination score was not consistently statistically significant in predicting an AHI greater than 1 ($P = .47$), greater than 2 ($P = .18$), greater than 3 ($P = .04$), or greater than 4 ($P = .09$). Similar results were found when using examination scores that included radiographs ($P = .46$, $P = .20$, $P = .048$, and $P = .09$, respectively).

### Table 1. Descriptive Results for the Clinical and Sleep Data of the 51 Participants

<table>
<thead>
<tr>
<th>Data</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Questionnaire score a</td>
<td>20.4 (11-27)</td>
</tr>
<tr>
<td>Examination score a</td>
<td>18.6 (12-22)</td>
</tr>
<tr>
<td>Total clinical score a</td>
<td>39 (26-46)</td>
</tr>
<tr>
<td>AHI</td>
<td>3.1 (0.9-3.7)</td>
</tr>
<tr>
<td>PTT-AI</td>
<td>15.6 (8.4-22.7)</td>
</tr>
<tr>
<td>EEG-AI</td>
<td>7.3 (4.3-8.5)</td>
</tr>
<tr>
<td>Sleep latency, min</td>
<td>46.9 (23.9-30.8)</td>
</tr>
<tr>
<td>TST, h</td>
<td>7.4 (7.1-8.0)</td>
</tr>
<tr>
<td>Sleep efficiency, No. (%) b</td>
<td>88.6 (86.7-93.0)</td>
</tr>
<tr>
<td>Snoring, % of TST</td>
<td>18.4 (1.5-21.2)</td>
</tr>
<tr>
<td>Desaturation index, events/h</td>
<td>2.3 (0.15-1.79)</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, apnea-hypopnea index (calculated as the number of apneas/hypopneas per hour of total sleep time [TST]); EEG-AI, electroencephalographic-arousal index (AI) (calculated as the number of arousals per hour of TST); IQR, interquartile range; PTT-AI, pulse transit time–AI.

a Scores were not available for 2 participants.
b Sleep efficiency is calculated as the percentage of time in bed that was total sleep time.

### COMMENT

Distinguishing OSAHS from primary snoring in children is important because of its potential sequelae, to allow parents to be appropriately counseled about treatment choices, and so that health resources may be better allocated. The current New Zealand hospital care model uses prioritization of surgical waiting lists, whereby those more affected by conditions are preferentially offered treatment. Although PSG is considered the criterion standard in the diagnosis of OSAHS, there are problems associated with its use. It requires travel and an overnight stay in a sleep laboratory and is therefore inconvenient for parents and children. In addition, it can lead to underestimation of events due to “first night effects” because children are taken out of their usual environment. Finally, it is expensive and has limited availability in many localities.

Also, because obstructive events are frequently not accompanied by EEG evidence of arousal, UARS can go unrecognized unless esophageal manometry is used.27 The latter is uncomfortable and labor intensive. Furthermore, obstructive indices may be lower when an esophageal probe is in place.27 Pulse oximetry has been previously proposed to identify clinically significant SDB, but this does not adequately detect patients with upper airway obstruction not associated with desaturation (or with arousal before a desaturation).28 Pulse transit time may fit the role of a screening test that is simple, inexpensive, well tolerated, and easy to interpret, and it correlates well with the criterion standard test. Pulse transit time has been found to be as accurate as esophageal pressure measurement in adults to separate central and obstructive respiratory events,29,30 and Katz et al31 reported a similar correlation in children. It is less invasive than an esophageal manometry catheter and so should be better tolerated by children and should result in less disturbance of sleep or modification of upper airway dynamics. Children compensate for a relatively narrow airway by increasing upper airway neuromotor tone and central ventilatory drive,13 so the ability of PTT to improve detection of this category of respiratory events increases its appeal in children.

We have shown that the PTT-AI correlates well with PSG-measured AHI, and the receiver operating characteristic curve analyses have shown good screening test performances for a range of diagnostic criteria, with particularly high sensitivity when predicting an AHI greater than 3 and greater than 4 (at 94% and 91%, respectively) while still retaining adequate specificity. Our findings are supported by others; Katz et al31 found PTT arousals to be significantly more likely to be associated with an obstructive event than EEG arousals and the PTT-AI to be significantly higher in children with OSAHS and UARS compared with those with primary snoring. Brietzke et al33 assessed 59 children with simultaneous PTT and PSG recording and found that the PTT-AI strongly correlated with the PSG-measured AHI. The receiver operating characteristic curve analysis suggested 81% sensitivity and 76% specificity for PTT-AI detection of an AHI greater than 1, rising to 97% sensitivity and 91% specificity for an AHI greater than 3.

There remains uncertainty about the relationship between PTT arousals and the respiratory events associated with UARS and mild OSAHS in children. Brietzke...
et al.\(^3\) and we have shown the usefulness of PTT-AI in identifying those with an AHI greater than 3, but our findings show greater variation in the frequency of PT arousal at lower AHI values. Neither study used esophageal monitoring during PSG, and this lack precludes our identifying respiratory event–related arousals. Esophageal monitoring is uncomfortable and not readily acceptable to children and their parents; this makes such monitoring difficult to use as a routine part of PSG. In addition, our patient population was skewed in that most children were at the milder end of the OSAHS spectrum, and to reduce variability there should be a greater spread of participants across the full range of SDB conditions. In elderly patients, the PTT-AI shows a moderate sensitivity for predicting SDB at 70.5% and a specificity of 54.7% for an AHI of 15 or greater.\(^3\) The sensitivity increases to 94.7% for predicating an AHI greater than 3, but our findings in comparison with others suggests that scope remains for further consideration of how the physical examination may be best tailored for predicting SDB in children.

An important finding of our study was that physical examination results were strongly associated with AHI; this finding differed from past studies.\(^5,9,11\) We found that the physical examination score had a greater likelihood of predicting SDB when the AHI was greater than 3. We found that the adenoid radiograph score did not have a significant effect on the predictive ability of the physical examination, meaning that radiography may not be necessary when undertaking clinical assessment of a child suspected of having SDB. Wang et al.\(^8\) reported that loud snoring, witnessed apneas, tonsil size, enuresis, and weight did not have a significant association with the presence of OSAHS as defined by PSG, the predictive value being 30%. Three other studies each failed to show any association between clinical symptoms and severity of OSAHS, with predictive values ranging from 39% to 51%.\(^5,9,11\) Considering our findings in comparison with others suggests that scope remains for further consideration of how the physical examination may be best tailored for predicting SDB in children.

### Table 2. ROC AUC for the AHI vs PTT-AI Using 4 AHI Criteria

<table>
<thead>
<tr>
<th>OSAHS Criterion</th>
<th>AUC (95% CI)</th>
<th>P Value</th>
<th>Optimal Cutoff</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI &gt;1</td>
<td>0.64 (0.47-0.81)</td>
<td>0.16</td>
<td>11.36</td>
<td>66</td>
<td>67</td>
<td>1.97 0.51</td>
</tr>
<tr>
<td>AHI &gt;2</td>
<td>0.74 (0.59-0.88)</td>
<td>0.01</td>
<td>11.36</td>
<td>85</td>
<td>63</td>
<td>2.32 0.24</td>
</tr>
<tr>
<td>AHI &gt;3</td>
<td>0.82 (0.70-0.94)</td>
<td>0.005</td>
<td>12.53</td>
<td>94</td>
<td>62</td>
<td>2.45 0.10</td>
</tr>
<tr>
<td>AHI &gt;4</td>
<td>0.80 (0.66-0.94)</td>
<td>0.005</td>
<td>12.53</td>
<td>91</td>
<td>64</td>
<td>2.53 0.14</td>
</tr>
</tbody>
</table>

### Table 3. ROC AUC for the AHI vs Physical Examination Score Using 4 AHI Criteria With and Without the Radiograph Score

<table>
<thead>
<tr>
<th>OSAHS Criterion</th>
<th>AUC (95% CI)</th>
<th>P Value</th>
<th>Optimal Cutoff</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>With Adenoid Radiograph Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI &gt;1</td>
<td>0.70 (0.55-0.85)</td>
<td>0.03</td>
<td>16</td>
<td>68</td>
<td>67</td>
<td>2.03 0.49</td>
</tr>
<tr>
<td>AHI &gt;2</td>
<td>0.72 (0.56-0.88)</td>
<td>0.005</td>
<td>18</td>
<td>74</td>
<td>70</td>
<td>2.46 0.3</td>
</tr>
<tr>
<td>AHI &gt;3</td>
<td>0.84 (0.71-0.97)</td>
<td>0.001</td>
<td>18</td>
<td>87</td>
<td>71</td>
<td>2.95 0.19</td>
</tr>
<tr>
<td>AHI &gt;4</td>
<td>0.78 (0.60-0.95)</td>
<td>0.006</td>
<td>18</td>
<td>90</td>
<td>64</td>
<td>2.51 0.16</td>
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<tr>
<td>Without Adenoid Radiograph Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI &gt;1</td>
<td>0.70 (0.55-0.85)</td>
<td>0.04</td>
<td>16</td>
<td>65</td>
<td>67</td>
<td>1.76 0.62</td>
</tr>
<tr>
<td>AHI &gt;2</td>
<td>0.72 (0.56-0.88)</td>
<td>0.005</td>
<td>16</td>
<td>74</td>
<td>63</td>
<td>2.01 0.42</td>
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<tr>
<td>AHI &gt;3</td>
<td>0.84 (0.71-0.97)</td>
<td>0.001</td>
<td>16</td>
<td>87</td>
<td>65</td>
<td>2.46 0.21</td>
</tr>
<tr>
<td>AHI &gt;4</td>
<td>0.78 (0.60-0.95)</td>
<td>0.005</td>
<td>16</td>
<td>90</td>
<td>59</td>
<td>2.19 0.17</td>
</tr>
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</table>

Abbreviations: AHI, apnea-hypopnea index (calculated as the number of apneas/hypopneas per hour of total sleep time); AUC, area under the curve; OSAHS, obstructive sleep apnea hypopnea syndrome; PTT-AI, pulse transit time–arousal index (calculated as the number of arousals per hour of total sleep time); ROC, receiver operating characteristic.
Pulse transit time seems to fit criteria for a good screening test for SDB associated with an AHI greater than 3; this will allow detection of more severe OSAS. For less severe OSAS and UARS, the reliability of the PTT to separate these conditions from primary snoring has not been demonstrated in a clinical setting. The advantages of PTT include cost, ease of use, and noninvasiveness (particularly important in the pediatric setting). Further research should be aimed at exploring the relationship between SDB and PTT arousals.

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Author Contributions: Drs Bradley, Galland, and Dawes and Prof Taylor had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Galland, Taylor, and Dawes. Acquisition of data: Bakker and Tan. Analysis and interpretation of data: Bradley, Galland, Bakker, Gray, Taylor, and Dawes. Drafting of the manuscript: Bradley, Galland, and Dawes. Critical revision of the manuscript for important intellectual content: Bakker, Tan, Gray, Taylor, and Dawes. Statistical expertise: Gray. Obtained funding: Galland and Tan. Administrative, technical, and material support: Bakker, Tan, and Taylor. Study supervision: Galland and Dawes.

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