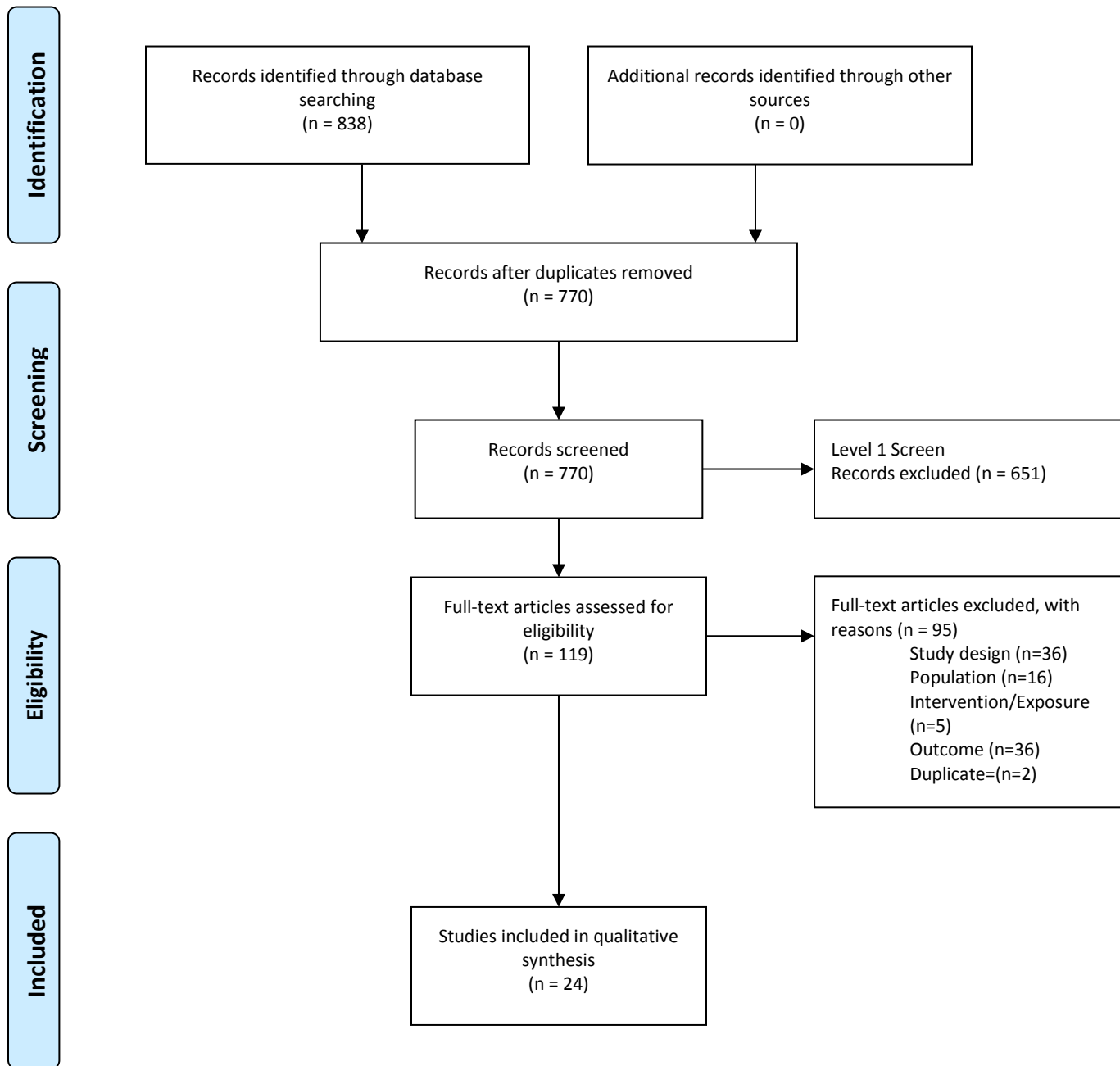


**Table A.1 Search Strategy**

<b>MEDLINE Search Strategy:</b>
((exp Down Syndrome/ or ((down* adj2 syndrome) or (trisomy adj3 "21")).ti,ab,kf.) and (exp Sleep Apnea Syndromes/ or (hypersomnia adj3 periodic respiration).tw,ab,kf. or ((Sleep or obstruct* or nocturnal) adj3 (breath* or airway or ventilat* or apnea* or apnoea* or hypox* or study)).ti,ab,kw. or (hypoventil* or SBD or OSA or CSA or IMV or polysomnograph* or oximetry).ti,ab,kf.) and (english or french).lg.) not (case reports or letter).pt.
<b>Embase Search Strategy:</b>
(Exp Down Syndrome/ or ((down* adj2 syndrome ) or (trisomy adj3 21)).ti,ab,kw.) AND (exp Sleep Disordered Breathing/ or (hypersomnia adj3 periodic respiration).tw,ab,kw. or (hypersomnia adj3 periodic respiration).tw,ab,kw. or ((sleep or obstruct*or nocturnal) adj3 (breath* or airway or ventilat* or apnea* or apnoea* or hypox* or study)).ti,ab,kw. or (hypoventil* or SBD or OSA or CSA or IMV or polysomnograph* or oximetry).ti,ab,kw.) and (english or french).lg. not letter.pt.
<b>CENTRAL Search Strategy:</b>
((down* adj2 syndrome) or (trisomy adj3 "21")).ti,ab,kw. and ((hypersomnia adj3 periodic respiration).tw,ab,kw. or ((sleep or obstruct* or nocturnal) adj3 (breath* or airway or ventilat* or apnea* or apnoea* or hypox* or study)).ti,ab,kw. or (hypoventil* or SBD or OSA or CSA or IMV or polysomnograph* or oximetry).ti,ab,kw.)
<b>CINAHL Search Strategy:</b>
((MH Down Syndrome+ or ((down* N2 syndrome) or (trisomy N2 "21"))) and (MH Sleep Apnea Syndromes+ or (hypersomnia N2 periodic respiration) or ((Sleep or obstruct* or nocturnal) N2 (breath* or airway or ventilat* or apnea* or apnoea* or hypox* or study)) or (hypoventil* or SBD or OSA or CSA or IMV or polysomnograph* or oximetry))

**Figure A.1: PRISMA Flow Diagram**

**Study:** Predictors of sleep-disordered breathing in patients with Down syndrome: A systematic review



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and MetaAnalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097  
For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).

**Table A.2: Summary of study Findings**

Categories of Factors	Factor	Measurement	Findings by study		
			Apnea-Hypopnea Index (AHI)	Obstructive Apnea-Hypopnea Index (oAHI)	Other
Demographics	Age	Mean Age	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (<math>d=-0.74</math>, <math>p=0.09</math>)[1]</li> <li>• No difference between participants with OSA and without (OSA=<math>10.2\pm3.9</math>, non-OSA=<math>10.1\pm3.0</math>)[2]</li> <li>• No difference between participants with OSA and without (OSA= <math>11.5\pm2.16</math>, non-OSA=<math>9.7\pm2.3</math>, <math>p=0.085</math>)[3]</li> <li>• Higher in participants with OSA than those without OSA (OSA=<math>10.2\pm4.2</math>, non-OSA=<math>7.8\pm4.3</math>, (<math>p&lt;0.001</math>) [4]</li> <li>• Lower in participants with OSA than those without OSA (OSA=<math>6.4</math>, non-OSA=<math>9.6</math>, (<math>p&lt;0.001</math>)[5]</li> </ul>		
		Median Age	<ul style="list-style-type: none"> <li>• Higher in participants with OSA than those without OSA when limited to ages 6-12 years (OSA=<math>13.2</math> (10.5-15.7), non-OSA=<math>8.8</math> (8.1-9.7), <math>p=0.018</math>)[6]</li> </ul>	<ul style="list-style-type: none"> <li>• Higher in participants with severe OSA, moderate OSA when compared to participants without OSA (severe OSA=<math>10.3</math>, moderate OSA=<math>7.7</math>, non-OSA=<math>6.3</math>, Kruskal Wallis <math>p&lt;0.001</math>)[7]</li> </ul>	<ul style="list-style-type: none"> <li>• No difference between participants with nocturnal hypoventilation and without (nocturnal hypoventilation=<math>5.9</math> (IQR 2.8,10.55) no nocturnal hypoventilation=<math>4.4</math> (1.8, 7.8), <math>p=0.37</math>)[8]</li> </ul>
		Continuous Age	<ul style="list-style-type: none"> <li>• Age not associated with OSA (<math>p=0.76</math>) [9].</li> <li>• Age negatively associated with AHI (<math>r=-0.195</math>, <math>p&lt;0.00</math>)[5]</li> </ul>	<ul style="list-style-type: none"> <li>• Higher age significantly associated with OSA (OR 1.14 (95% CI 1.03, 1.27), <math>p=0.02</math>)[9]</li> <li>• Age negatively associated with OAHl (<math>r=-0.199</math>, <math>p=0.028</math>)[10]</li> </ul>	
		Dichotomized >4/<4	<ul style="list-style-type: none"> <li>• No difference in presence of SDB (<math>p=0.14</math>)[9]</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in presence SDB (<math>p=0.91</math>)[9]</li> </ul>	
		Age dichotomized < 8 years/ >8 years	<ul style="list-style-type: none"> <li>• Younger age associated with presence of OSA(bivariate analysis OR = 2.9, (95% CI</li> </ul>		

			1.3, 6.4), p<0.05), (logistic regression OR=3.36 (95% CI 1.4, 8.06), p<0.05).[5] <ul style="list-style-type: none"> <li>• Younger age associated with presence of OSA[11]</li> </ul>		
		Dichotomized to <12 and >12 years	<ul style="list-style-type: none"> <li>• No difference in AHI between younger and older children[12][12]</li> </ul>		<ul style="list-style-type: none"> <li>• No difference in central index between younger and older children[12][12]</li> </ul>
		Dichotomized to <2 and ≥2 years		<ul style="list-style-type: none"> <li>• Younger age associated with presence of severe OSA, when compared to moderate, mild and no OSA ((&lt;2 severe OSA=23, moderate OSA=8, mild OSA=12, non-OSA=8), (&lt;2, severe OSA=18, moderate OSA=23, mild OSA=38, non-OSA=22) Chi-square 12.87, p = 0.005)[13]</li> </ul>	
		Stratified into ≤2, 3-10, and >10 years old			<ul style="list-style-type: none"> <li>• Younger age (&lt;2) associated with presence of CSA when compared to older age (&gt;10). No other differences in presence of CSA between groups[14]</li> </ul>
		Stratified into 0-4.9, 5-11.9, 12-18 years old		<ul style="list-style-type: none"> <li>• No difference in median OAHl between children in all age groups [10]</li> <li>• No difference in presence of OSA between younger and older children[10]</li> </ul>	
		Stratified into 3-5 years, 6-10 years, 11-15 years, 16-24 years old	<ul style="list-style-type: none"> <li>• No difference in the percentage of children in different age groups between OSA and non-OSA children (non-OSA 3-5 years=63.2%, 6-10 years=24.6%, 11-15 years=8.8%, 16-24 years=3.5%; OSA 3-5 years=44.4%, 6-10 years=35.6%, 11-15 years=13.3%, 16-24 years=6.7%)[11]</li> </ul>		

	<b>Sex</b>	Dichotomized to male and female	<ul style="list-style-type: none"> <li>• Sex was used as part of a model predicting OSA but was not independently associated with the presence of OSA (OSA % male = 62.2% OSA % female=37.8%, without OSA percent male =57.9%, without OSA percent females=42.1% p=0.69)[11]</li> <li>• No difference in presence of OSA (% male OSA=55, % male non-OSA=54) cut-off of AHI&gt;1 used[4]</li> <li>• No difference in AHI or presence of OSA(mean AHI male=7.7/ OSA=14/14, mean AHI female=12.6 OSA=14/15)[15]</li> <li>• Female sex associated with presence of OSA (% male OSA=20, % male non-OSA=80, Fisher Exact Test p&lt;0.005)[2]</li> <li>• No difference between participants with OSA and without (% male OSA=47, % male non-OSA=16.7, OR=0.22, p=0.13)[1]</li> <li>• Male sex associated with OSA (Bivariate analysis: OR=2.9, (95% CI=1.2, 6.6), P&lt;0.05 Logistic Regression: OR=3.32, CI=1.3, 8.1, p&lt;0.05)[5]</li> <li>• No difference in presence of OSA(% male OSA= 45.8, male non-OSA=50.0, p=1.000)[6]</li> </ul>	<ul style="list-style-type: none"> <li>• Not associated with presence of OSA[10]</li> <li>• Not associated with OAHl[10]</li> <li>• No difference in percentage of males with moderate OSA, mild OSA, and without OSA (% male moderate OSA=46.9 (30/64), % male mild OSA=47.3 (53/11), % male no OSA=50.0 (121/242), Fisher exact test p=0.85)[7]</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in percentage of males with CSA.[14]</li> <li>• When limited to children &gt;2 years, females sex was associated with presence of CSA[14]</li> <li>• When limited to children 3-10 years female sex was associated with presence of CSA (OR=8.93 (95% CI 1.04, 76.7), p=0.46). When adjusted for OSA, BMI and REM % (OR=8.94 (95% CI 1.02, 78.5), p=0.48)[14]</li> <li>• When limited to children &lt;2 years, sex was not associated with the presence of CSA[14]</li> </ul>
	<b>BMI</b>	Mean BMI	<ul style="list-style-type: none"> <li>• No association between mean BMI and presence of OSA (mean BMI OSA=19.48, mean BMI, non-OSA=18.82, p=0.24 d=-0.15)[1]</li> <li>• No difference in between participants with OSA and without (OSA=22.9±9.9, non- OSA=19.5±4.2, p=0.635)[3]</li> </ul>		

		Median BMI			<ul style="list-style-type: none"> <li>No difference in between participants with nocturnal hypoventilation and those without (OSA=16.8 kg/m<sup>2</sup> (IQR 16.25, 21.50) non-OSA=16.5 kg/m<sup>2</sup> (IQR 15, 19.85), p=0.43)[8]</li> </ul>
		Continuous BMI	<ul style="list-style-type: none"> <li>No association between AHI and BMI (R<sup>2</sup>=0.2 p=0.09)[4]</li> <li>Positive association between AHI and BMI (r=0.62 (95% CI 0.23, 0.84), p=0.005)[16]</li> </ul>		
		Dichotomized to healthy weight and overweight (BMI>25)	<ul style="list-style-type: none"> <li>No difference in percentage of overweight participants with OSA and without (% OSA=30, % non-OSA=20)[2]</li> <li>No difference in percentage of overweight participants between OSA and non-OSA children (% overweight OSA=57.9 (11/19), % overweight non-OSA=50.0 (6/12), OR=0.73, p=0.72)[1]</li> </ul>	<ul style="list-style-type: none"> <li>No difference in mean oAHI between overweight and healthy weight children (mean oAHI overweight=20.6± 28 vs mean oAHI normal weight=14.1±24, p=0.170). However, when the study sample was dichotomized into children &lt;12 years, and ≥12 years, overweight children ≥12 years had a higher mean oAHI than non-obese children (p=0.036). There was no difference in mean oAHI between overweight and healthy weight children &lt;12 years, p=0.381)[12]</li> <li>No difference in presence of OSA between overweight and healthy weight children (% OSA overweight=91, % OSA healthy weight=89). When evaluating severe OSA (AHI≥10), there was a difference[12]</li> </ul>	

		Dichotomized to healthy weight and overweight (female BMI >18.69, male BMI > 18.76)	<ul style="list-style-type: none"> <li>• No difference in AHI between healthy weight or overweight children (healthy mean AHI=9.88; overweight mean AHI=11.89)<sup>1</sup>[15]</li> <li>• No difference in presence of OSA (% OSA overweight=88.9% (8/9), % OSA healthy weight= 100.0% (18/18))<sup>1</sup>[15]</li> </ul>		
		Dichotomized to obese, overweight, normal, and underweight	<ul style="list-style-type: none"> <li>• BMI percentile was used in the final predictive model for OSA but there was no difference in the percentage of children in different BMI groups between OSA and non-OSA children(OSA obese=26.7%, overweight=17.8%, normal=51.1%, underweight=4.4%, non-OSA obese=21.1%, overweight=40.4%, normal=35.1%, underweight=3.5%, p=0.089)<sup>2</sup>[11]</li> </ul>		
		BMI greater than 50 <sup>th</sup> percentile	<ul style="list-style-type: none"> <li>• BMI not associated with OSA (BMI&gt;50<sup>th</sup> percentile bivariate analysis OR=0.7 (95% CI=0.3,1.6), p=0.4)<sup>2</sup>[5]</li> </ul>		
		BMI dichotomized to >95 <sup>th</sup> percentile / obese categorized as BMI in >95 <sup>th</sup> percentile	<ul style="list-style-type: none"> <li>• No difference in percentage of obese participants between OSA and non-OSA children(OR=0.40 (95% CI=0.08, 2.05), p=0.27)<sup>3</sup>[9]</li> <li>• Higher risk of OSA in participants with obesity (RR=2.4 95% CI 1.34-4.34, p=0.005)<sup>4</sup>[17]</li> <li>• Higher risk of moderate/severe OSA in participants with obesity when compared to participants with mild/absent OSA(RR= 1.4 (95% CI 1.03,1.82), p= .025)[17]</li> <li>• Mean AHI was higher in children with obesity compared to those without<sup>5</sup> [18]</li> <li>• Obesity associated with presence of OSA<sup>5</sup></li> </ul>	<ul style="list-style-type: none"> <li>• No difference in percentage of obese participants between OSA and non-OSA children (OR=0.71 (95% CI 0.14, 3.63), p= 0.68)<sup>3</sup>[9]</li> </ul>	

			[18]		
		BMI z-score	<ul style="list-style-type: none"> <li>• Mean BMI z-score not associated with OSA (OSA mean=1.5± 0.8, non-OSA mean=0.9±1.5)[2]</li> <li>• Mean BMI z-scores associated with OSA (p=0.03)<sup>7</sup>[4]</li> <li>• No difference in median BMI z-scores between participants with OSA and without (OSA=0.9 (IQR 0.3, 2.0), median z-score non-OSA= 0.3 (IQR -0.5, 1), p=0.174). When participants with OSA were limited to ages 6-12 years, there was still no association (OSA=0.8 (IQR - 0.05, 1.6), p=0.368)<sup>8</sup>[6]</li> <li>• No association between BMI z-score and AHI (r=0.21, p=0.16)[18]</li> </ul>	<ul style="list-style-type: none"> <li>• BMI z-scores not associated with oAHI<sup>6</sup>[10]</li> <li>• BMI z-score associated with oAHI (Spearman rho = 0.16, p= .035)<sup>4</sup>[17]</li> </ul>	
		Dichotomized to BMI z-score>1.5 and BMI z-score </=1.5	<ul style="list-style-type: none"> <li>• No difference between the percentage of participants with BMI z-score &gt;1.5 between OSA and non-OSA children (% OSA=60, % non-OSA=53)[2]</li> </ul>		
	<b>Weight</b>	Continuous weight (kg)	<ul style="list-style-type: none"> <li>• No difference in weight between participants with and without OSA (OSA=36.9±15.9, non-OSA= 31.4± 11.7)[2]</li> </ul>		
	<b>Height</b>	Mean height (cm)	<ul style="list-style-type: none"> <li>• No difference in mean height between participants with and without OSA (OSA=122.5±15.7, non-OSA=125.7±9.4)[2]</li> </ul>		
		Height greater than 50 <sup>th</sup> percentile	<ul style="list-style-type: none"> <li>• No difference between participants with and without OSA (OR=0.8 (95% CI=0.2, 3.1), p=0.7)[5]</li> </ul>		
	<b>Race and Ethnicity</b>	Dichotomized to white/non-Hispanic and Hispanic and other	<ul style="list-style-type: none"> <li>• No difference in percentage of white/non-Hispanic ethnicity between participants with OSA and without (% OSA=0.474, % non-OSA=0.50), OR=1.11, p=1.00)[1]</li> </ul>		



		Ethnicity dichotomized to not-Hispanic, Hispanic/Latino, or unknown	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OSA= 73.3% non-Hispanic,15.6% Hispanic/Latino,11.1% unknown; non-OSA 70.2% non-Hispanic, 19.3% Hispanic/Latino, 10.5% unknown, <math>p=0.95</math>)[11]</li> </ul>		
		Race dichotomized to White, Black, Asian, other race, multiracial, unknown	<ul style="list-style-type: none"> <li>Race and ethnicity were used in predictive model for OSA but there was no difference in the percentage of children in different racial groups between OSA and non-OSA children (OSA=55.6% White, 6.7% Black, 11.1% Asian, 11.1% other race, 2.2% multiracial,13.3% unknown; non-OSA= 63.2% White, 8.8% Black, 1.8% Asian, 7.0% other race, 7.0% multiracial, 12.3% unknown, <math>p=0.36</math>)[11]</li> </ul>		
<b>Medical and Surgical History</b>	<b>Gastrointestinal comorbidities</b>	Presence of GERD	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OR=0.70 (95% CI 0.28,1.73), <math>p=0.44</math>)[9]</li> <li>No difference in mean AHI between participants with a history of GERD and without (GERD= 9.28, no GERD= 13.56)[4]</li> </ul>	<ul style="list-style-type: none"> <li>Presence of GERD associated with absence of OSA (OR 0.16 (95% CI 0.04, 0.72))[9]</li> </ul>	
		<b>Upper and Lower Respiratory Comorbidities</b>	History of rhinitis/ rhinorrhea/ sinusitis	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OR=2.13 (95% CI 0.90, 5.04, <math>p=0.08</math>)). After multivariate analysis, there was still no difference between participants with OSA and without (OR 2.38 (95% CI 0.80-7.08), <math>p=0.12</math>)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OR 2.22 (95% CI 0.92-5.37), <math>p=0.08</math>). After multivariate analysis, the presence of rhinitis/rhinorrhea/sinusitis was associated with OSA (OR 4.49 (95% CI 1.17-17.19), <math>p=0.029</math>)[9]</li> </ul>
	Asthma/respiration		<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OR 1.65 (95% CI 0.75, 3.61), <math>p=0.21</math>)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OR 1.77 (95% CI 0.77-4.05), <math>p=0.18</math>)[9]</li> </ul>	
	Pulmonary hypertension			<ul style="list-style-type: none"> <li>No association between pulmonary hypertension and SDB[19]</li> </ul>	
	<b>Otolaryn</b>	History of cleft lip/palate		<ul style="list-style-type: none"> <li>No association between cleft lip or palate and SDB [19]</li> </ul>	

	<b>gologic Comorbidities</b>	Vocal Cord paralysis		<ul style="list-style-type: none"> <li>• No association between vocal cord paralysis and SDB [19]</li> </ul>	
	<b>Congenital Cardiac Abnormalities</b>	Congenital heart disease	<ul style="list-style-type: none"> <li>• No difference in percentage of heart defects between participants with OSA and without (% OSA= 0.58, % non-OSA=0.42, p=0.47, d=0.52)[1]</li> <li>• No difference in percentage of congenital cardiac disease between participants with OSA and without (OR=0.9 (95% CI=0.3, 2.7), p=0.9)[5]</li> </ul>	<ul style="list-style-type: none"> <li>• No association between comorbid congenital heart disease and any diagnosis of sleep-related breathing disorder[19]</li> </ul>	
	<b>Surgical History</b>	Tonsillectomy/adenoidectomy	<ul style="list-style-type: none"> <li>• No difference in percentage with tonsillectomy or adenoidectomy between participants with OSA and without (% OSA=47.4, % non-OSA=66.7, OR=2.22, p=0.46)[1]</li> <li>• No difference in percentage with tonsillectomy or adenoidectomy between participants with OSA and without (% OSA=100.0, % non-OSA=94.7[15]</li> <li>• No difference in history of adenoidectomy between participants with OSA and without (OR=1.8 95% CI=0.7, .6, p=0.2)[5]</li> <li>• No difference in history of tonsillectomy between participants with OSA and without (OR=1.0 95% CI=0.3, 3.2, p=0.8) [5]</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in median oAHI between children with history of upper airway surgery (adenoidectomy, tonsillectomy, adenotonsillectomy) and without when limited to ages 12-18 years[10]</li> <li>• No difference in presence of OSA between children with history of upper airway surgery (adenoidectomy, tonsillectomy, adenotonsillectomy) and without when limited to ages 12-18 years[10]</li> </ul>	
	<b>Developmental history</b>	Gestation at birth		<ul style="list-style-type: none"> <li>• No association between preterm birth and SDB[19]</li> </ul>	
		Failure to thrive	<ul style="list-style-type: none"> <li>• No association with OSA (OR= 0.32 (95% CI=0.04, 2.95), p= 0.29)[9]</li> </ul>	<ul style="list-style-type: none"> <li>• No association with OSA (OR= 0, p= 1.00)[9]</li> </ul>	

	<b>History of Current/ repaired Cardiac Issue</b>	Current Cardiac Issue	• No association with OSA (OR=1.25 (95% CI=0.55, 2.82), p=0.59)[9]	• No association with OSA (OR=1.35 (0.60-3.02), p=0.47)[9]	
		History of repaired cardiac issue	• No association with OSA (OR=1.48 (95%CI 0.70, 3.14), p=0.30)[9]	• No association with OSA (OR=1.35 (95% CI 0.60, 3.02), p=0.47)[9]	
	<b>Psychiatric Comorbidities</b>	Diagnosis of anxiety or ADHD or behavioural issues	• No association with OSA (OR=0.76 (95% CI 0.30, 1.90), p=0.55)[9]	• No association with OSA (OR=1.26 (95% CI 0.48, 3.28), p=0.64)[9]	
	<b>Endocrine Comorbidities</b>	Diabetes/Metabolic Syndrome	• No association with OSA (OR=1.35 (95% CI 0.26, 7.00), p=0.72)[9]	• No association with OSA (OR=2.53 (95% CI 0.49, 12.63), p=0.27)[9]	
		Thyroid disease		• No association between hypothyroidism and SDB[19]	
	<b>Significant comorbidities</b>	Presence of significant comorbidities	• No association between presence of significant comorbidities and OSA[20]		
<b>Musculoskeletal comorbidities</b>	Scoliosis	• No association with OSA (OR=4.19 (95% CI 0.42, 41.49), p=0.19)[9]	• No association with OSA (OR=0.79 (95% CI 0.08, 7.91), p=0.79)[9]		
<b>Physical Examination Findings</b>	<b>Adenotonsillar Size</b>	Continuous tonsil size	• Tonsil size positively associated with AHI ( $r^2=0.75$ , p=0.002)[4]		
		Brodsky Score		• No association with OSA[10]	
		Adenotonsillar Hypertrophy	• No association with OSA (OR=1.16 (95% CI 0.47, 2.86), p=0.74)[9]	• No association with OSA (OR=1.26 (95% CI 0.48-3.28) p=0.64)[9]	
		Adenoid hypertrophy ( $\geq$ grade +3)	• No association with OSA (OR=0.4 (95% CI 0.0, 2.4), p=0.3)[5]		

		Tonsillar hypertrophy ( $\geq$ grade +3)	<ul style="list-style-type: none"> <li>• Tonsillar hypertrophy significantly associated with SDB (OR=4.7 (95% CI=1.4, 15.1), <math>p&lt;0.05</math>)[5]</li> </ul>		
	<b>Dental Examinations</b>	General dental examinations	<ul style="list-style-type: none"> <li>• Dental examinations did not improve the positive or negative predictive value of model to predict OSA. In addition only half of the participants were able to complete these items due to restrictions in age or ability and as such, these variables were excluded from the final model[11]</li> </ul>		
		Malocclusion	<ul style="list-style-type: none"> <li>• No association with SDB (<math>p=0.1</math>)[5]</li> </ul>		
		Mean Gingival Index (GI)	<ul style="list-style-type: none"> <li>• Higher in participants with OSA than those without (OSA= 1.30<math>\pm</math>0.31, non-OSA=0.81<math>\pm</math>0.46, <math>p=0.020</math>)[3]</li> </ul>		
		Mean plaque Index (PI)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=1.34<math>\pm</math>0.34, non-OSA=1.04<math>\pm</math>0.37, <math>p=0.104</math>)[3]</li> </ul>		
		Mean bleeding on probing (BOP) of six sites per tooth	<ul style="list-style-type: none"> <li>• Higher BOP in participants with OSA than those without OSA (OSA=43.62<math>\pm</math>15.81, non-OSA=20.38<math>\pm</math>12.54, <math>p=0.006</math>)[3]</li> </ul>		
		Mean DMFT (decay, missing, filling, tooth) scores	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=6.54<math>\pm</math>3.69, non-OSA=4.71<math>\pm</math>3.90, <math>p=0.425</math>)[3]</li> </ul>		
	<b>Macroglossia</b>	Presence of macroglossia	<ul style="list-style-type: none"> <li>• No association with SDB (OR=0.6 (95% CI=.2, 1.6), <math>p=0.3</math>)[5]</li> </ul>		
<b>Sleep Behaviors</b>	<b>Parental Questionnaires of Sleep Behaviors</b>	SRBD and CSHQ questionnaires	<ul style="list-style-type: none"> <li>• Particular questions from the SRBD and CHSQ questionnaires were among the 15 best discriminated patients with OSA from those without OSA[11]</li> </ul>	<ul style="list-style-type: none"> <li>• No association with OSA[21]</li> </ul>	
		CSHQ daytime sleepiness subscale	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=13.00, non-OSA=14.78, <math>p=0.19</math>, <math>d=0.56</math>)[1]</li> </ul>	<ul style="list-style-type: none"> <li>• No association with OSA[21]</li> </ul>	
		Parental reporting of daytime somnolence	<ul style="list-style-type: none"> <li>• No association with OSA[2]</li> </ul>		

		CSHQ sleep-disordered breathing subscale	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OSA=4.40, non-OSA=5.43, p=0.34, d=0.51)[1]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA[21]</li> </ul>	
		Parental reporting of witnessed apneas	<ul style="list-style-type: none"> <li>No association with OSA[2]</li> <li>No association between struggling to breath at night and OSA (OR= 0.79 (95% CI 0.33, 1.90), p=0.59)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA[21]</li> <li>No association between struggling to breath at night with OSA (OR= 1.47 (95% CI 0.56, 3.87), p=0.43)[9]</li> </ul>	
		Parental reporting of gasping	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.05 (95% CI 0.42, 2.62), p=0.93)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA[21]</li> <li>No association with OSA (OR= 1.35 (95% CI 0.49, 3.70), p=0.56)[9]</li> </ul>	
		Parental reporting of struggling to breathe at night	<ul style="list-style-type: none"> <li>No association with OSA (OR= 2.38 (95% CI 0.99, 5.71), p=0.05)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.75 (95% CI 0.67, 4.59), p=0.25)[9]</li> </ul>	
		Parental reporting of mouth breathing during	<ul style="list-style-type: none"> <li>No association with OSA (OR= 0.38 (95% CI 0.12, 1.17), p=0.08)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA (OR= 0.63 (95% CI 0.19, 2.09), p=0.45)[9]</li> </ul>	
		Parental reporting of choking sounds during sleep	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.30 (95% CI 0.52, 3.24), p=0.57)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.35 (95% CI 0.49, 3.70), p=0.56)[9]</li> </ul>	
		Parental reporting of waking up more than twice per night	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.30 (95% CI 0.56, 3.05), p=0.54)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.62 (95% CI 0.62, 4.19), p=0.32)[9]</li> </ul>	
		Parental reporting of restless sleep at night	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.50 (95% CI 0.58, 3.85), p=0.40)[9]</li> </ul>	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.29 (95% CI 0.45, 3.75), p=0.64)[9]</li> </ul>	
		Parental reporting of child's nighttime symptoms	<ul style="list-style-type: none"> <li>No association with OSA (OR= 1.04 (95% CI 0.89, 1.3), p=0.60)[22]</li> <li>No difference between participants with mild OSA, moderate OSA, severe OSA, or without OSA[22]</li> </ul>		
	<b>Snoring</b>	Dichotomized to mild/ moderate/ severe	<ul style="list-style-type: none"> <li>No association with AHI&gt;1 (OSA defined as AHI&gt;1.5) (prob=0.8903)[23]</li> </ul>	<ul style="list-style-type: none"> <li>Snoring was able to predict OSA with a sensitivity of 61.7%, a specificity of 100%, and NPV of 25%.( % snoring with OSA=100, % snoring without</li> </ul>	

				OSA=75)[19]	
		Parental reporting of snoring	<ul style="list-style-type: none"> <li>• No association with OSA[2]</li> <li>• No association with OSA (OR= 1.77 (95% CI 0.57, 5.55), p=0.32)[9]</li> </ul>	<ul style="list-style-type: none"> <li>• No association with OSA[2]</li> <li>• No association with OSA (OR= 0.79 (95% CI 0.24, 2.53), p=0.67)[9]</li> </ul>	
	<b>Sleep Behaviors</b>	Median self-reported hours of sleep scores	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=8.7 (IQR 8, 9.3), non-OSA= 8.3 (IQR 8, 9), p= 0.980). [6]</li> <li>• No difference between participants with OSA and without when participants with OSA limited to ages 6-12 years (OSA 6-12= 9 (8.8-9.5), non-OSA= 8.3 (IQR 8, 9), p= 0.428)[6]</li> </ul>		
		Median self-reported percent sleep efficiency scores	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=100 (IQR 92.3, 100), non-OSA=99.1% (IQR 97.0, 100), p=0.665)[6]</li> <li>• No difference between participants with OSA and without when participants with OSA limited to ages 6-12 years (OSA=100% (93.9-100), non-OSA=99.1% (IQR 97.0, 100), p=0.325)[6]</li> </ul>		
		Median Child Epworth Sleepiness Scale (ESS) scores	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA= 9 (IQR 4.5, 10), non-OSA=10.5 (IQR 6, 13), p=0.374)[6]</li> <li>• No difference between participants with OSA and without when participants with OSA limited to ages 6-12 years (OSA=9 (IQR 5, 10), non-OSA=10.5 (IQR 6, 13), p=0.313)[6]</li> </ul>		
<b>Neuropsychological and Developmental Assessments</b>	<b>Parental Questionnaires of Neuropsychological</b>	Median Parent-rated behaviour: Vineland Adaptive Behavior Scale II (VABS-II) Communication – Receptive scores	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=74.5 (IQR 45, 105), non-OSA=36.5 (IQR 25, 60), p=0.070)[6]</li> <li>• No difference between participants with OSA and without when participants with OSA limited to ages 6-12 years (OSA= 35.5 (IQR 20, 65), non-OSA=36.5 (IQR 25,</li> </ul>		

	<b>Testing</b>		60), p=0.958][6] <ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Median Parent-rated behaviour: Vineland Adaptive Behavior Scale II (VABS-II) Communication – Expressive scores	<ul style="list-style-type: none"> <li>• Higher in participants with OSA than those without OSA (OSA=86 (IQR 66.5, 115.5), non-OSA= 50 (IQR 47, 81), p=0.055)[6]</li> <li>• No difference between participants with OSA and without when participants with OSA limited to ages 6-12 years (OSA= 66.5 (IQR 42, 78), non-OSA= 50 (IQR 47, 81), p=0.635)[6]</li> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Scales of Independent Behaviour-Revised standard score	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=51.56±17.36, non-OSA=60.25±29.16, t (Mann-Whitney U)=1.03, effect size (d)=0.36, p=0.31)[1]</li> </ul>		
		Conners ADHD Index	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=6.76±5.75, non-OSA=7.67±5.57, t (Mann-Whitney U)=0.42, effect Size (d)=0.16, p=0.68)[1]</li> <li>• No difference between participants with OSA and without[2]</li> </ul>		
	<b>Cognitive Function</b>	Development Quotient	<ul style="list-style-type: none"> <li>• Development Quotient negatively associated with AHI (rho=-0.62, p &lt;0.0001)[24]</li> <li>• Severe Global developmental delay (calculated as development quotient/Intelligence quotient) positively associated with AHI (mild global development delay (50-69) mean AHI= 4.3 (95% CI 1.8, 6.9); moderate global development delay (35-49) mean AHI= 8.67 (95% CI 6.6, 10.7); severe global development delay (20-34) mean AHI= 14.8 (95% CI 8.5, 21.1)[24]</li> </ul>		

		Verbal IQ scores - Kaufman Brief Intelligence Test, Second Edition	<ul style="list-style-type: none"> <li>• Lower in participants with OSA than those without (OSA=45.11±8.83, non-OSA=54.42±11.54, d=0.91, p=0.006),[1]</li> </ul>		
		Non-Verbal IQ - Kaufman Brief Intelligence Test, Second Edition	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=48.53±9.92, non-OSA=52.67±13.55, d=0.35, p=0.46)[1]</li> </ul>		
		Full-scale Intelligence Quotient (FSIQ) - Kaufman Brief Intelligence Test, Second Edition	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=43.84±6.18, non-OSA=48.92±10.65, d=0.58, p=0.21)[1]</li> </ul>		
		Median Full Scale Intelligence Quotient (FSIQ) - Wechsler Intelligence Scale for children	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA= 43.5 (IQR 41, 49.5), non-OSA= 45.5 (IQR 44, 54), p=0.296)[6]</li> <li>• No difference between participants with OSA and without when participants with OSA limited to ages 6-12 years (OSA=44.5 (IQR 43, 48), non-OSA= 45.5 (IQR 44, 54), p= 0.635)[6]</li> </ul>		
		Stanford-Binet Intelligence Scale 4th edition: Vocabulary, Comprehension, Pattern Analysis, Quantitative, Bead Memory and Memory for Sentences	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Wechsler Preschool and Primary Scale of Intelligence - Vocabulary (WPPSI-R)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (OSA=99 (IQR 68.5, 137), non-OSA= 70.5 (IQR 56, 82), p=0.082)[6]</li> <li>• No difference between participants with</li> </ul>		



			<p>OSA and without when participants with OSA limited to ages 6-12 years (OSA=63 (IQR 55, 83), non-OSA= 70.5 (IQR 56, 82), <math>p=0.635</math>)[6]</p> <ul style="list-style-type: none"> <li>• WPPSI-R was associated with OSA, when adjusted for age and FSIQ (coefficient -9.773 (95 % CI -19.478, -0.069), <math>p=0.049</math>)[6]</li> </ul>		
		Woodcock–Johnson Tests of Achievement Revised: Letter–Word Identification, Applied Problems and Dictation (Reading, spelling and arithmetic skills)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Median Developmental NEuroPSYchological Assessment (NEPSY) Visuomotor Precision scores	<ul style="list-style-type: none"> <li>• Higher in participants with OSA than those without (OSA=86.5 (IQR 64, 127), non-OSA=51 (IQR 42, 61), <math>p=0.008</math>)[6]</li> <li>• No difference between participants with OSA and without when participants with OSA limited to ages 6-12 years (OSA=59.5 (IQR 49, 81), non-OSA=51 (IQR 42, 61), <math>p=0.313</math>)[6]</li> <li>• WPPSI-R was associated with OSA, when adjusted for age and FSIQ (coefficient 6.515 (95% CI -5.520, 18.550), <math>p=0.261</math>)[6]</li> </ul>		
		Purdue Pegboard Test (Fine motor skills) scores	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Beery Development Test of Visual–motor Integration (visual-motor skills)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		

		scores			
		CANTAB Paired-Associates Learning Task mean errors to success	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OSA=8.18±4.04, non-OSA=6.05±3.89, t (Mann-Whitney U)=133.00, effect size (d)=-0.54, p=0.13)[1]</li> </ul>		
		CANTAB Intra-Extra dimensional Set Shift stages completed	<ul style="list-style-type: none"> <li>Higher number of CANTAB Intra-Extra Set Shift changes completed in participants with OSA than those without OSA (OSA=5.32±3.59, non-OSA=8.09±0.83, t (Mann-Whitney U)= 55.50, effect size (d)=1.06, p=0.03)[1]</li> </ul>		
		CANTAB Simple Reaction Time task median correct latency	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OSA=706.58±280.64, non-OSA=745.05±203.26, t (Mann-Whitney U)=85.00, effect Size (d)=0.19, p=0.42)[1]</li> </ul>		
		Experimenter Rating of Attention	<ul style="list-style-type: none"> <li>No difference between participants with OSA and without (OSA=3.93±0.71, non-OSA=4.22±0.55, t (Mann-Whitney U)=1.11, effect Size (d)=0.46, p=0.28)[1]</li> </ul>		
		Total Child Behavior Checklist Scores	<ul style="list-style-type: none"> <li>Child Behaviour Checklist scores positively associated with AHI in participants ages 3-5 years (rho=0.77, p &lt; 0.0001)[24]</li> <li>Child Behaviour Checklist scores positively associated with AHI in participants ages 6-12 years (rho=0.83, p =0.0001)[24]</li> </ul>		
		Child Behavior Checklist externalizing behaviour scores	<ul style="list-style-type: none"> <li>Child Behaviour Checklist subscores positively associated with AHI in participants ages 3-5 years (rho=0.68, p = 0.0001)[24]</li> <li>Child Behaviour Checklist subscores positively associated with AHI in participants ages 6-12 years (rho=0.52, p</li> </ul>		

			= 0.0078)[24]		
		Child Behavior Checklist internalizing behaviour scores	<ul style="list-style-type: none"> <li>• Child Behaviour Checklist subscores positively associated with AHI in participants ages 3-5 years (<math>\rho=0.42</math>, <math>p = 0.0253</math>)[24]</li> </ul>		
		Child Behavior Checklist (ratings of behaviour)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Child Behaviour Teacher Report Form (ratings of behaviour)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Child Behavior Checklist (ratings of attention)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> <li>• Child Behaviour Checklist subscores positively associated with AHI in participants ages 3-5 years (<math>\rho=0.69</math>, <math>p = 0.0001</math>)[24]</li> <li>• Child Behaviour Checklist subscores positively associated with AHI in participants ages 6-12 years (<math>\rho=0.53</math>, <math>p= 0.0061</math>)[24]</li> </ul>		
		Child Behaviour Teacher Report Form (ratings of attention)	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without[2]</li> </ul>		
		Conner's Hyperactivity Index Parent and Teacher Version	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without (Parent and Teacher version) [2]</li> </ul>		
<b>Miscellaneous</b>	<b>Family Income/ Educatio</b>	Family income <40,000	<ul style="list-style-type: none"> <li>• No difference in percentage with family income &lt;40,000 between OSA and non-OSA children (% OSA=26.3, % non-OSA=16.7, OR=0.56, <math>p=0.68</math>)[1]</li> </ul>		

	<b>n Level</b>	Education level of primary caregiver	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without ( OSA=15.8±1.76, non-OSA=15.00±2.86, d=-0.08, p=0.89)[1]</li> </ul>		
	<b>Urine Metabolic Markers</b>	Urinary biomarkers	<ul style="list-style-type: none"> <li>• Presence of the following four urinary makers associated with OSA: nighttime norepinephrine (p=0.037), AM/PM norepinephrine (p=0.004), AM/PM dopamine (p=0.043), AM/PM taurine (p=0.011) [18]</li> <li>• Presence of the following four urinary makers associated with AHI &gt;5: (ROC AUC) nighttime taurine (0.76) and morning taurine (0.94)[18]</li> <li>• No association between presence of the following urinary markers and OSA: Night Epinephrine per Crtn (p=0.680), Night Norepinephrine per Crtn (p=0.037), Night Dopamine per Crtn (p=0.142), Night DOPAC per Crtn (p=0.094), Night Serotonin per Crtn (p=0.695), Night 5-HIAA per Crtn (p=0.472), Night Glycine per Crtn (p=0.108), Night Taurine per Crtn (p=0.601), Night GABA per Crtn (p=0.142), Night Glutamate per Crtn (p=0.152), Night PEA per Crtn (p=0.876), Night Histamine per Crtn (p=0.297), Morning Epinephrine per Crtn (p=0.230), Morning Norepinephrine per Crtn (p=0.285), Morning Dopamine per Crtn (p=0.898), Morning DOPAC per Crtn (p=0.898), Morning Serotonin per Crtn (p=0.566), Morning 5-HIAA per Crtn (p=0.117), Morning Glycine per Crtn (p=0.980), Morning Taurine per Crtn (p=0.178), Morning GABA per Crtn (p=0.717), Morning, Glutamate per Crtn (p=0.899), Morning PEA per Crtn (p=0.608), Morning Histamine per Crtn (p=0.679), AM/PM Epinephrine per Crtn</li> </ul>		

			<p>(p=0.863), AM/PM Norepinephrine per Crtn (p=0.004), AM/PM Dopamine per Crtn (p=0.043), AM/PM DOPAC per Crtn (p=0.143), AM/PM Serotonin per Crtn (p=0.494), AM/PM 5-HIAA per Crtn (p=0.909), AM/PM Glycine per Crtn (p=0.141), AM/PM Taurine per Crtn (p=0.011), AM/PM GABA per Crtn (p=0.318), AM/PM Glutamate per Crtn (p=0.091), AM/PM PEA per Crtn (p=0.260), AM/PM Histamine per Crtn (p=0.120) [18]</p> <ul style="list-style-type: none"> <li>• Variables from urine metabolic markers did not improve the positive or negative predictive value of model to predict OSA. In addition only half of the participants were able to complete these items due to restrictions in age or ability and as such, these variables were excluded from the final model[11]</li> </ul>		
	<b>Anthropometric Measurements</b>	Lateral cephalograms	<ul style="list-style-type: none"> <li>• Variables from the lateral cephalograms did not improve the positive or negative predictive value of model to predict OSA. In addition only half of the participants were able to complete these items due to restrictions in age or ability and as such, these variables were excluded from the final model[11]</li> </ul>		
		3D photographs	<ul style="list-style-type: none"> <li>• Variables from 3D photographs did not improve the positive or negative predictive value of model to predict OSA. In addition only half of the participants were able to complete these items due to restrictions in age or ability and as such, these variables were excluded from the final model[11]</li> </ul>		
		3D anthropometric measurements	<ul style="list-style-type: none"> <li>• No difference between participants with OSA and without OSA[25]</li> </ul>		

<sup>1</sup> International child-specific centiles

<sup>2</sup> Percentiles not reported

<sup>3</sup> DS-specific centiles

<sup>4</sup> CDC SAS height and weight z-scores

<sup>5</sup> CDC 2000 growth curves

<sup>6</sup> Flemish growth curves for boys and girls

<sup>7</sup> CDC age and gender adjusted BMI z-scores

<sup>8</sup> Age and gender-specific z-scores

Of note: where ages are specified, this indicates subgroup analysis of a select age group of the study population

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