Craniofacial and upper airway morphology in pediatric sleep-disordered breathing: Systematic review and meta-analysis

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Introduction: Pediatric sleep-disordered breathing is a continuum, with primary snoring at one end, and complete upper airway obstruction, hypoxemia, and obstructive hypoventilation at the other. The latter gives rise to obstructive sleep apnea. An important predisposing factor in the development and progression of pediatric sleep-disordered breathing might be craniofacial disharmony. The purpose of this systematic review and meta-analysis was to elucidate the association between craniofacial disharmony and pediatric sleep-disordered breathing. **Methods:** Citations to potentially relevant published trials were located by searching PubMed, Embase, Scopus, and the Cochrane Central Register of Controlled Trials. The MetaRegister of controlled trials database was also searched to identify potentially relevant unpublished trials. Additionally, handsearching, Google Scholar searches, and contact with experts in the area were undertaken to identify potentially relevant published and unpublished studies. Inclusion criteria were (1) randomized controlled trials, case-control trials, or cohort studies with controls; (2) studies in nonsyndromic children 0 to 18 years of age with a diagnosis of sleep-disordered breathing or obstructive sleep apnea by either a sleep disorders unit, screening questionnaire, or polysomnography; and (3) principal outcome measures of craniofacial or upper airway dimensions or proportions with various modalities of imaging for the craniofacial and neck regions. The quality of the studies selected was evaluated by assessing their methodologies. Treatment effects were combined by meta-analysis with the random-effects method. **Results:** Children with obstructive sleep apnea and primary snoring show increased weighted mean differences in the ANB angle of 1.64° (P <0.0001) and 1.54° (P <0.00001), respectively, compared with the controls. An increased ANB angle was primarily due to a decreased SNB angle in children with primary snoring by 1.4° (P = 0.02). Children with obstructive sleep apnea had a distance from the posterior nasal spine to the nearest adenoid tissue measured along the PNS-basion line reduced by 4.17 mm (weighted mean difference) (P <0.00001) and a distance from the posterior nasal spine to the nearest adenoid tissue measured along the line perpendicular to the sella-basion line reduced by 3.12 mm (weighted mean difference) (P <0.0001) compared with the controls. **Conclusions:** There is statistical support for an association between craniofacial disharmony and pediatric sleep-disordered breathing. However, an increased ANB angle of less than 2° in children with obstructive sleep apnea and primary snoring, compared with the controls, could be regarded as having marginal clinical significance. Therefore, evidence for a direct causal relationship between craniofacial structure and pediatric sleep-disordered breathing is unsupported by this meta-analysis. There is strong support for reduced upper airway width in children with obstructive sleep apnea. Larger well-controlled trials are required to address the relationship of craniofacial and upper airway morphology to pediatric sleep-disordered breathing in all 3 dimensions. (Am J Orthod Dentofacial Orthop 2013;143:20-30)

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The authors report no commercial, proprietary, or financial interest in the products or companies described in this article.
Supported by the Australian Society of Orthodontists Foundation for Research and Education.
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Submitted, April 2012; revised and accepted, August 2012.
0889-5406/$36.00

http://dx.doi.org/10.1016/j.ajodo.2012.08.021

Sleep-disordered breathing is a disorder of breathing during sleep characterized by prolonged increased upper airway resistance, partial upper airway obstruction, or complete obstruction that disrupts pulmonary ventilation, oxygenation, or sleep quality.[1] Pediatric sleep-disordered breathing is a continuum, with primary snoring at 1 end and complete upper airway obstruction, hypoxemia, and obstructive hypoventilation at the other, giving rise to obstructive sleep apnea.[1]

Sleep-disordered breathing is associated with a wide variety of symptoms in children.[2-8] Snoring is the most common nighttime symptom of sleep-disordered breathing in children.[1] Chronic snoring, although common in adults, is considered abnormal in a pediatric population.[7] Other symptoms associated with sleep-disordered breathing can include restless sleep, frequent arousals, snorting, gasping, unusual sleeping positions (eg, sitting), sweating during sleep, and nocturnal enuresis.[2-8] The most prominent daytime symptom of sleep-disordered breathing in adults is excessive daytime sleepiness,[9] which is absent in most children with polysomnography-proven obstructive sleep apnea.[10] Sleep–disordered breathing in children is also associated with behavioral and impaired cognitive or school performance.[6,11,12]

The current view is that adenotonsillar hypertrophy is the major cause of sleep-disordered breathing in otherwise normal healthy children.[13] Adenotonsillar hypertrophy results in upper airway narrowing and, when superimposed with other factors (eg, reduced muscle tone), can lead to a clinically significant dynamic airway obstruction during sleep.[13] Adenotonsillectomy is therefore often the first line of treatment for pediatric sleep-disordered breathing and is deemed curative in approximately 25% to 75% of patients.[14-18] Nasal continuous positive airway pressure is often the next course of treatment, but there is emerging evidence of midface hypoplasia and other craniofacial side effects in children with this approach.[19,20] There is currently no consensus on the best method of managing obstructive sleep apnea in childhood.[21] Kaditis et al[21] proposed a stepwise approach to treatment that starts with weight control and is followed by nasal corticosteroids, adenotonsillectomy surgery, orthodontic devices, continuous positive airway pressure, and, finally, craniofacial surgery or tracheostomy in severe cases.

Craniofacial disharmony can also be an important predisposing factor in the development and progression of pediatric sleep-disordered breathing. Studies in nonsyndromic children have shown a positive association between craniofacial disharmony and pediatric sleep-disordered breathing.[22-25] Other contradictory studies, however, do not report such associations.[26,27] There is no systematic review in the literature of the association between craniofacial and upper airway morphology in pediatric sleep-disordered breathing.

This aim of this study was to conduct a systematic review of the published and unpublished literature. A further aim was that the results of the primary studies would be combined by meta-analysis to statistically elucidate the nature of the association between craniofacial disharmony and pediatric sleep-disordered breathing. This will aid clinicians by increasing the diagnostic sensitivity of sleep-disordered breathing and might provide suggestions for alternative treatments for the children suffering from it.

MATERIAL AND METHODS

Citations to potentially relevant trials published in journals and dissertations were located by searching the appropriate databases (PubMed, Embase, Scopus, and Cochrane Central Register of Controlled Trials). An effort to identify potentially relevant unpublished or ongoing trials was made by searching the MetaRegister of controlled trials database. Additionally, hand-searching, Google Scholar searches, and contact with experts in the area were undertaken to identify potentially relevant published and unpublished studies. The references cited in the reviewed articles were also checked. The search date was December 27, 2011, across all databases, and the search was updated monthly for PubMed and Scopus until April 2012. The Appendix Table shows the search strategy for this systematic review with a list of keywords used.

Inclusion criteria were limited to (1) randomized controlled trials, case-control trials or cohort studies; (2) studies of nonsyndromic children 0 to 18 years of age with a diagnosis of sleep-disordered breathing or obstructive sleep apnea by a sleep disorders unit, screening questionnaire, or polysomnography; and (3) principal outcome measures of craniofacial or upper airway dimensions or proportions with various modalities of imaging for the craniofacial and neck regions. The study selection criteria are given in Table I.

The primary author (V.K.) independently reviewed the titles and abstracts of all identified citations. Any studies not fulfilling the inclusion criteria were excluded from further evaluation, and the full articles were retrieved for those meeting the criteria. The primary author and a coauthor (C.N.D.) independently reviewed all full texts.

Data abstraction was performed independently by the same 2 authors using Excel (Microsoft, Redmond,

Table I. Study selection criteria

Criterion	*Definition*
Study characteristics	The studies should be prospective or retrospective in design. Included study designs will be randomized controlled trials, case-control trials, or cohort studies with controls.
Patient characteristics	Nonsyndromic children, 0-18 years of age with a diagnosis of sleep-disordered breathing, primary snoring, or obstructive sleep apnea by a sleep disorders unit, screening questionnaire, or polysomnography. Studies in medically compromised patients and those studying craniofacial syndromes will be excluded.
Study method characteristics	Studies with various modalities of imaging for the craniofacial and neck regions in children will be included.
Outcome characteristics	Trials reporting outcome measures: • Craniofacial dimensions or morphology • Upper airway dimensions or morphology

Wash); this included year of publication, demographic details of the patients, details of the study design, the participants' characteristics, the method of sleep-disordered breathing diagnosis, the measurement tool, a quality assessment, and the statistical details. Any disagreements were resolved by discussion and mutual agreement between the 2 authors. Angular variables were recorded in degrees (± standard deviations), and linear variables were recorded in millimeters (± standard deviations).

Statistical analysis

Revman (version 5.1; Nordic Cochrane Centre, Cochrane Collaboration; 2011) was used for the statistical analysis. The data categories common among the studies were used for the pooled analysis. Because of the expected variability in the trials, a random-effects model was chosen. To identify heterogeneity, the overlap of the 95% confidence intervals for the results of each study was inspected graphically, and the Cochrane test for homogeneity and the I^2 test were calculated to check for heterogeneity and inconsistency, respectively.

Forest plots to calculate the weighted mean differences were generated for the following cephalometric variables (Fig 1) in children with obstructive sleep apnea: (1) SNA angle (angle between sella, nasion, and A-point), (2) SNB angle (angle between sella, nasion, and B-point), (3) ANB angle (difference of SNA and SNB angles), (4)

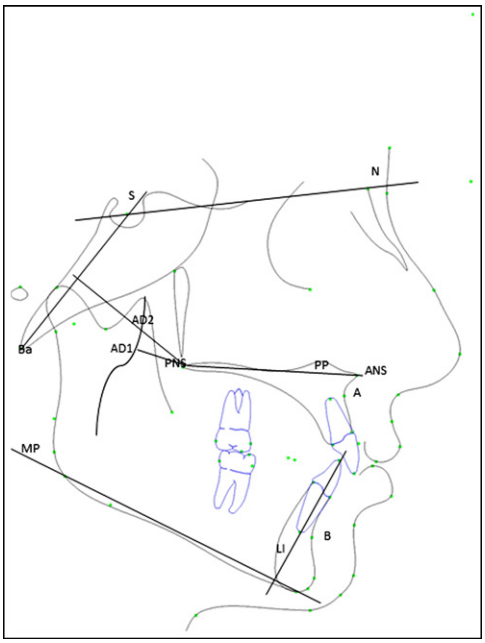

Fig 1. Cephalometric references and landmarks used in the meta-analysis: *S*, Sella; *N*, nasion; *Ba*, basion; *ANS*, anterior nasal spine; *PNS*, posterior nasal spine; *PP*, palatal plane; *A*, A-point; *B*, B-point; *MP*, mandibular plane (gonion-menton); *PNS-AD1*, distance from PNS to the nearest adenoid tissue measured along the line PNS-Ba; *PNS-AD2*, distance from PNS to the nearest adenoid tissue measured along the line perpendicular to S-Ba; *LI*, long axis of the mandibular incisor.

SN-MP angle (angle made by the sella-nasion plane to the mandibular plane), (5) PP-MP angle (angle made by the palatal plane extending from ANS-PNS to the mandibular plane), (6) IMPA (angulation of the mandibular incisor to the mandibular plane), (7) BaSN angle (angle formed between basion, nasion, and sella), (8) PNS-AD1 (distance from the posterior nasal spine to the nearest adenoid tissue measured along the PNS-basion line), and (9) PNS-AD2 (distance from the posterior nasal spine to the nearest adenoid tissue measured along the line perpendicular to the sella-basion line). For children with primary snoring, the analysis was pooled for the SNA, SNB, ANB, and BaSN angles because of the limited data from the primary studies.

The planned subgroup analyses were based on age, sex, body mass index, and apnea-hypopnea index.

The quality of the studies selected was evaluated by assessing their methodologies. The assessment criteria were those from the Centre for Reviews and Disseminations in York, United Kingdom.[28] These are presented in Table II.

Table II. Criteria for study appraisal

Strong evidence	*Moderately strong evidence*	*Limited evidence*
• Randomized controlled trials, prospective studies with large study samples • Well-defined and adequate control group • Clearly defined and clinically relevant variables • Low dropout rate • Relevant statistical analysis	• Prospective study, cohort, controlled clinical trial, or well-defined retrospective study with large study group • Clearly defined and clinically relevant variables • Low dropout rate • Relevant statistical analysis	• Cross-sectional study • Clinically inadequate result variables • High dropout rate • No control group • Limited or no statistical analysis • Addressing the issue in question only in part

Adapted from Deeks et al.[28]

RESULTS

No restrictions were placed on year of publication. Restrictions were placed on the participants' ages and the language. In the initial search, we found 875 citations across the 4 databases. Fourteen citations in foreign languages were excluded from this review. The search process is shown in Figure 2. The characteristics of the 9 included trials, including their methodologic quality, are summarized in Table III.[27,29-36] Only 2 trials reported blinding of observers to the diagnosis of children during data collection.[32,33]

Children with obstructive sleep apnea and primary snoring showed increased weighted mean differences in the ANB angle of 1.64° (P <0.0001) and 1.54° (P <0.00001), respectively, in comparison with the controls (Figs 3 and 4). Increased ANB was primarily due to decreased SNB angle in children with primary snoring by a weighted mean difference of 1.4° (P = 0.02) (Fig 5). Children with obstructive sleep apnea had a PNS-AD1 distance reduced by 4.17 mm (weighted mean difference) (P <0.00001) and a PNS-AD2 distance reduced by 3.12 mm (weighted mean difference) (P <0.0001) compared with the controls (Figs 6 and 7).

The weighted mean differences in the SNA, SNB, SN-MP, PP-MP, IMPA, and BaSN for children with obstructive sleep apnea compared with the controls are given in Appendix Figures 1 through 6, respectively. The weighted mean differences in the SNA and BaSN angles for children with primary snoring compared with the controls are shown in Appendix Figures 7 and 8, respectively.

The pooled cephalometric variables in children with obstructive sleep apnea and primary snoring are summarized in Tables IV and V, respectively. There was significant heterogeneity for the variables SN-MP (P = 0.04) and PP-MP (P <0.00001) in children with obstructive sleep apnea. The increased weighted mean difference in the SN-MP angle of 2.74° (P = 0.006) might indicate a trend toward increased lower anterior face height in pediatric obstructive sleep apnea patients. However, this result must be interpreted with caution because of its borderline heterogeneity.

The planned subgroup analyses were not completed because of limited data from the included studies.

DISCUSSION

This meta-analysis supports the argument that children with primary snoring and obstructive sleep apnea show an increased ANB angle on a lateral cephalogram compared with the controls. This increase is due to a decreased SNB angle in children with primary snoring. In addition, children with obstructive sleep apnea have a reduced anteroposterior width of the upper airway at the level of the posterior nasal spine and superiorly at the level of the adenoidal mass.

The mandibular plane angle to the cranial base shows a trend toward hyperdivergence, but with significant heterogeneity across the primary studies. Hence, it was inconclusive from this meta-analysis whether these children have excessive vertical facial patterns.

Most cephalometric measurements have inherent problems with landmark identification, measurement errors, and representation of 3-dimensional anatomic patterns by 2-dimensional analysis. Two included primary studies did not control for the error of the method and reported this to be significant.[29,35]

ANB angle is a measure of the apical base sagittal discrepancy on a lateral cephalogram. ANB angle is affected by the angulations of the maxillary and mandibular incisors, the vertical and horizontal positions of nasion, and the rotation of the jaws during growth.[37,38] Therefore, ANB angle is not a true measure of sagittal jaw discrepancy. This meta-analysis showed a highly significant increase in ANB angle in pediatric sleep-disordered breathing patients compared with the controls; however, the increase of 1.64° might not be clinically significant.

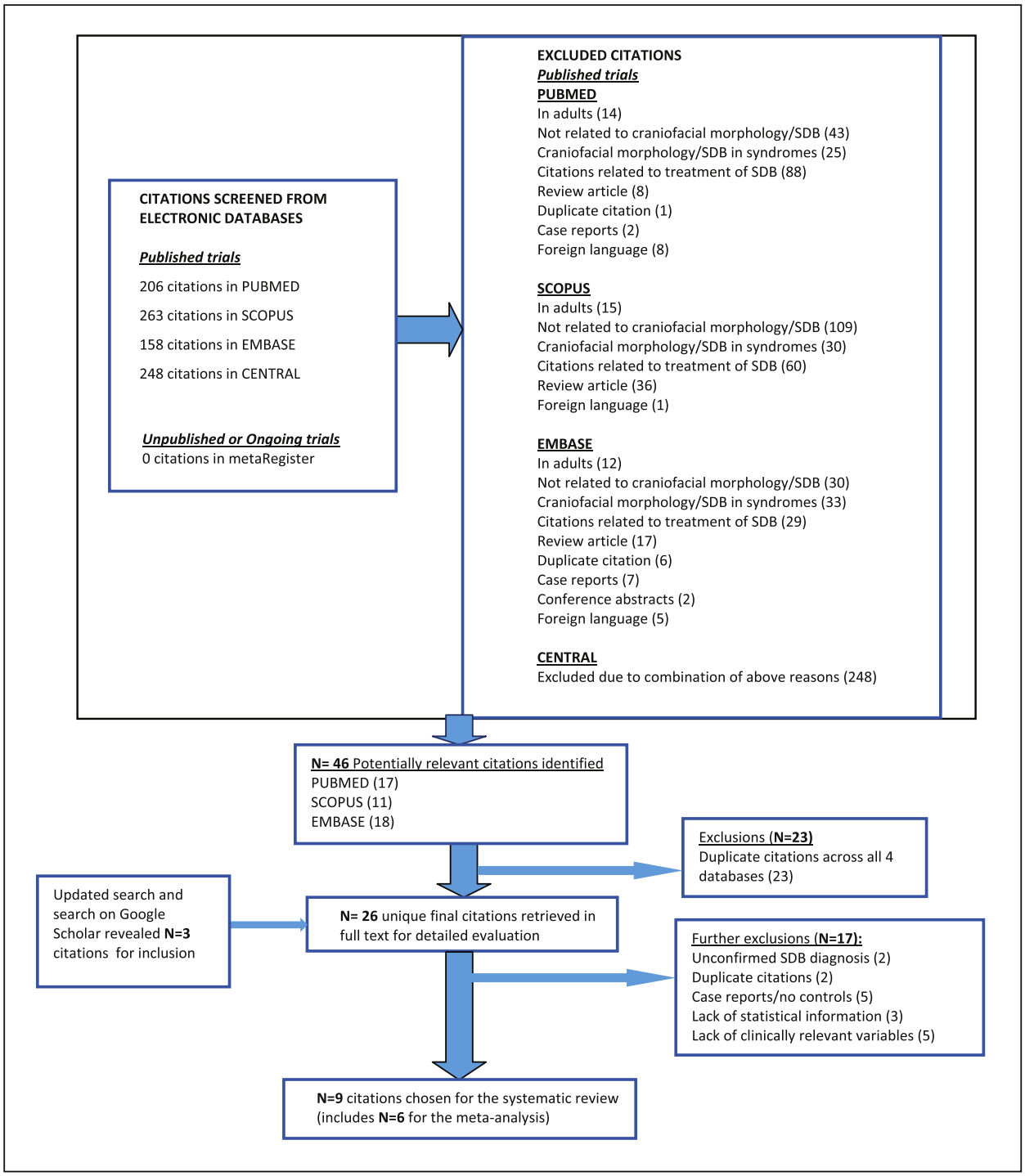

Fig 2. Flow chart of the search process.

Interestingly, an increased ANB angle was attributed to mandibular retrusion in children with primary snoring but not in children with obstructive sleep apnea, as measured by a reduced SNB angle. Schiffman et al[27] showed no difference in the volume of the mandible in nonsyndromic children with obstructive sleep apnea when compared with the controls. Thus, the position of the mandible in reference to the

cranial base might be at fault rather than mandibular size and shape.

In children diagnosed with obstructive sleep apnea, the upper airway shows narrowing. Upper airway narrowing in children with primary snoring has also been reported in the literature but to a lesser extent in comparison with children with obstructive sleep apnea.[11,32] This is not surprising, since the current view suggests that adenotonsillar hypertrophy causes upper airway narrowing. Adenotonsillar hypertrophy superimposed with other factors—eg, craniofacial anomalies, reduced upper airway muscle tone, and neural reflexes, obesity, or genetics—leads to a clinically significant dynamic airway obstruction during sleep.[1]

A relevant meta-analysis is lacking for comparison. Evidence from case series and some excluded trials suggests that children with mouth breathing, adenotonsillar hypertrophy, or sleep-disordered breathing have increased lower anterior face height, increased mandibular plane angle, retropositioned mandible, narrow maxilla, and smaller airway space.[23,24,29,39,40] This meta-analysis did not show an association between pediatric sleep-disordered breathing and mandibular plane hyperdivergence because of significant heterogeneity across the primary studies.

A narrow maxilla cannot be diagnosed on a lateral cephalogram, since it is a view of the sagittal plane. No pooled variable reported in this meta-analysis indicates the transverse width of the maxilla. Two of the 9 included studies showed statistically significant narrow maxillary intermolar widths, as measured on dental casts in children with sleep-disordered breathed compared with the controls.[29,33] Children with snoring show a similar trend but to a lesser extent.[33] In contrast, Cozza et al[31] showed statistically significant reduced mandibular intermolar width in children with obstructive sleep apnea compared with the controls. The above 3 included studies could not be pooled because of significant heterogeneity in measurement techniques[31,33] and unclear diagnoses of some subjects.[29]

From the literature, it is not possible to determine whether transverse jaw discrepancies are strongly associated with pediatric sleep-disordered breathing. However, there is recent evidence from a randomized clinical trial, with up to a 36-month follow-up, of improvement in apnea-hypopnea index scores with a rapid maxillary expansion device in children with a narrow maxilla and a diagnosis of obstructive sleep apnea.[41,42] This supports the use of the rapid maxillary expansion device in reducing nasal airway resistance[43] and reducing associated symptoms seen in pediatric sleep-disordered breathing, such as nocturnal enuresis, as proposed by Timms.[44,45] Similarly, in a study conducted on a small group of adults and 1 adolescent, Guilleminault and Li[46] showed that surgical maxillomandibular expansion improves sleep-disordered breathing in patients with maxillary and mandibular constriction. In the sagittal dimension, advancement of the mandible in children with obstructive sleep apnea and a diagnosis of mandibular retrognathia by a modified functional appliance shows a significant reduction in apnea-hypopnea index scores from an average of 7.88 to 3.66 and improved sleep quality at the 6-month follow up.[31] This suggests that rapid maxillary expansion and mandibular advancement by a functional appliance might be therapeutic adjuncts or alternatives in managing patients with pediatric sleep-disordered breathing.

Increased lower anterior face height and mandibular plane hyperdivergence is common in adults diagnosed with obstructive sleep apnea.[47] A meta-analysis in adults has shown the strongest correlation between mandibular plane hyperdivergence with the severity of obstructive sleep apnea.[48] However, the correlation is not strong enough to show evidence that craniofacial morphology has a direct causal effect in the development of obstructive sleep apnea in adults.[48] A treatment strategy for severe obstructive sleep apnea in adults is orthognathic surgery. A systematic review and meta-analysis showed pooled surgical success and cure (apnea-hypopnea index score, <5) rates of 86.0% and 43.2%, respectively with maxillomandibular advancement surgery in adults with obstructive sleep apnea.[49] Younger age, lower preoperative weight, apnea-hypopnea index score, and greater maxillary advancement were predictive of increased surgical success.[49] This suggests that craniofacial morphology might have a role in adult obstructive sleep apnea but probably not a major one.

The exhaustive literature search, explicit selection criteria, and validity assessment of the included trials contributed to a thorough and systematic approach in reaching the conclusions. When information was doubtful in a study, the authors were contacted for clarification.

A limitation of this review is the possible language bias, indicated by the exclusion of trials in foreign languages. However, the effect of this exclusion is probably minor as judged from their English abstracts. Having 2 reviewers perform the data abstraction decreased the likelihood of inaccuracy and bias. Additionally, data abstraction was checked several times by the coauthors to prevent errors in data collection. Seven of 9 studies in this meta-analysis were rated as moderately strong for the level of evidence, and 2 studies[35,36] were rated as limited on methodologic validity assessment; this

Table III. Characteristics of the included studies

Study	*Banabilh et al (2008)*	*Cozza et al (2004)*	*Deng and Gao (2012)*	*Lofstrand-Tidestrom et al (1999)*
Design and participant characteristics				
Design	Prospective case control	Prospective case control	Prospective case control	Prospective cohort
Total number of subjects	60 (30 snorers and 30 controls)	40 (20 OSA and 20 controls)	30 (15 OSA and 15 controls)	21 obstructed subjects and 40 controls for cephalometric examinations; 22 obstructed subjects and 48 controls for study model examinations
Mean age (y) ± SD or range (y); P, participants; C, controls; O, OSA; S, snorer				
P	9.5 ± 2.47	5.91 ± 1.14	9.5 ± 1.0	4.52 ± 0.37
C	10.47 ± 2.28	6.00 ± 0.71	9.6 ± 1.8	4.58 ± 0.25
Sex distribution of subjects				
P	16 M/14 F	10 M/10 F	11 M/4 F	-
C	21 M/9 F	10 M/10 F	11 M/4 F	20 M/20 F
Body mass index distribution of participants (kg/m^2)				
P	21.22 ± 3.12	16.02 ± 3.40	-	-
C	21.42 ± 2.98	20.98 ± 0.48	-	-
Controls matched for age and sex	No	Yes	Yes	Age matched
Methods used				
Method of sleep-disordered breathing diagnosis	Berlin questionnaire for subjects and controls	Overnight polysomnography and Epsworth sleepiness scale in subjects only	Polysomnography for subjects and controls	Polysomnography for subjects; historic controls (cephalometrics); controls from cohort study (study models)
Measurement tool: NHP, natural head position	Cephalogram	Cephalogram and dental models (width between centroids–Moyers method)	Cephalogram in NHP; magnification corrected	Cephalogram in NHP and dental models
Error of the method: NS, not significant	NS	NS	0.5°/0.5 mm	<1.1°/0.6 mm
Study quality appraisal				
Evidence level (L, low; M, moderate)	L	M	M	M
Comments	Diagnosis by parental report; blinding not reported	Apnea, 10 s; OSA, apnea-hypopnea index, >1; blinding not reported	OSA: apnea-hypopnea index, >1; Bonferroni correction for statistics; blinding not reported	Subjects were not subdivided as snorers and OSA; results excluded from meta-analysis

OSA, Obstructive sleep apnea; *Ht*, height; *Wt*, weight.

could have biased the results. No study was assessed as providing strong evidence. Lack of blinding in 7 of the 9 primary studies might have introduced observer bias; hence, the results of this meta-analysis should be interpreted with caution (Table III).

One potential confounding problem in assessing craniofacial morphology is that the lateral cephalogram is taken in an upright position and with the teeth in occlusion while the patient is conscious. Pediatric sleep-disordered breathing is determined under supine conditions, when loss of muscle tone can occur while sleeping. It has been shown that measurements made from awake supine lateral cephalograms show no additional differences between adult obstructive sleep apnea and snoring subjects compared with radiographs taken in the upright position.[50] It is unclear whether the orientation difference has a negligible effect in children with sleep-disordered breathing and

Table III. (*continued*)

Pirila-Parkkinen et al (2009)	*Pirila-Parkkinen et al (2010)*	*Schiffman et al (2004)*	*Zettergren-Wijk et al (2006)*	*Zucconi et al (1999)*
Prospective case control	Prospective case control	Prospective case control	Prospective case control	Prospective case control
123 (41 OSA, 41 snorers, and 41 controls)	140 (70 subjects and 70 controls); subjects, 26 OSA, 27 snorers	48 (24 OSA and 24 controls)	34 (17 OSA and 17 controls)	52 (26 OSA and 26 controls)
(O) 7.2 ± 1.93 (S) 7.2 ± 1.79	(O) 7.7 ± 1.91(S) 7.3 ± 1.61	4.9 ± 1.7	5.6 ± 1.34	4.6 ± 1.5
7.2 ± 1.90	7.3 ± 1.78	4.9 ± 1.8	5.8 ± 1.40	5.1 ± 0.5
(O) 22 M/19 F (S) 22 M/19 F	(O) 14 M/12 F (S) 9 M/18 F	14 M/10 F	10 M/7 F	-
22 M/19 F	34 M/36 F	14 M/10 F	10 M/7 F	-
-	(O) 16.6 ± 3.46 (S) 16.8 ± 2.52	Ht, 109 ± 13 Wt, 19.8 ± 5.7	-	-
-	16.6 ± 2.23	Ht, 108 ± 13 Wt, 20.1 ± 5.5	-	-
Yes	Yes	Yes	Yes	Age-matched
Overnight polysomnography for OSA subjects and snorers only; controls selected by examinations parental reported histories	Overnight polysomnography for subjects only; controls selected by examinations and parental reported histories	Overnight polysomnography in subjects and 12 controls; Brouillette sleep questionnaire for control selection	Overnight polysomnography in subjects; 11 controls had ear-nose-throat examinations; 6 controls from growth study	Validated sleep questionnaire for all subjects and controls; diurnal polysomnography for subjects
Dental models (width between mesiolingual cusps—Moorrees method)	Cephalogram in NHP; magnification, 5%	Magnetic resonance imaging under intravenous sedation	Cephalogram	Cephalogram in NHP; magnification corrected
NS	NS	NS	NS	NS
M	M	M	M	L
Apnea, 10 s; OSA: apnea-hypopnea index, >1; blinding reported	Apnea, 10 s; OSA: apnea-hypopnea index, >1; blinding reported	Apnea, absence of oronasal thermistor signal for 2 respiratory cycles; blinding not reported	OSA: apnea-hypopnea index, >1; Bonferroni correction for statistics; blinding not reported	Apnea, 10 s; OSA: apnea-hypopnea index, >1; blinding not reported

whether the state of consciousness affects the upper airway measurements.

Further standardization of research methods is recommended. The need for standardization includes the establishment and acceptance of valid definitions for normal respiration, sleep-disordered breathing, and overt obstructive sleep apnea. There was considerable variation in the cephalometric measurements used in the included studies, and standardization of appropriate cephalometric measurements is warranted for conclusive evidence. Further studies addressing the 3-dimensional volumetric characteristics of the airway and the positions of the maxilla and the mandible to the cranial base are required to understand not only the sagittal but also the transverse discrepancies in pediatric sleep-disordered breathing.

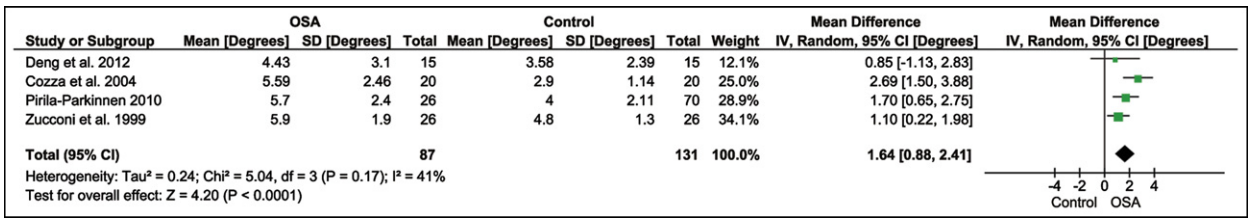

Fig 3. Pooled weighted mean differences in ANB angles between children with obstructive sleep apnea and the controls.

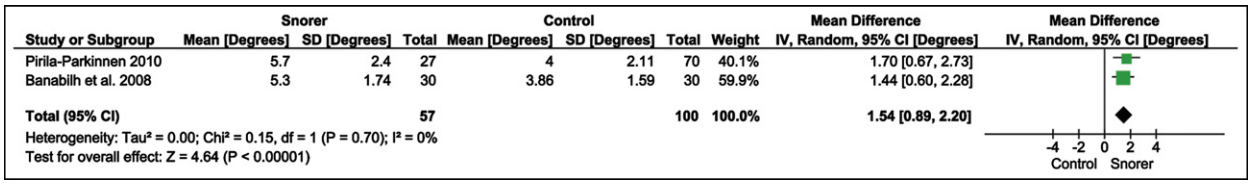

Fig 4. Pooled weighted mean differences in ANB angles between children with primary snoring and the controls.

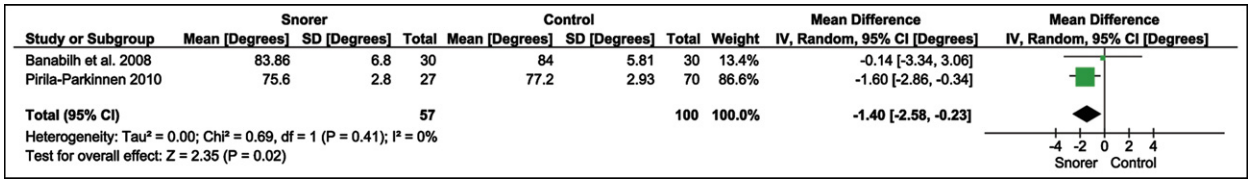

Fig 5. Pooled weighted mean differences SNB angles in children with primary snoring and the controls.

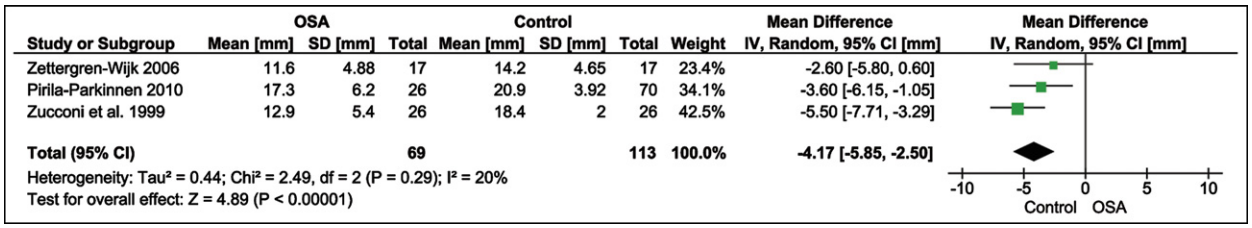

Fig 6. Pooled weighted mean difference in PNS-AD1 between children with obstructive sleep apnea and the controls.

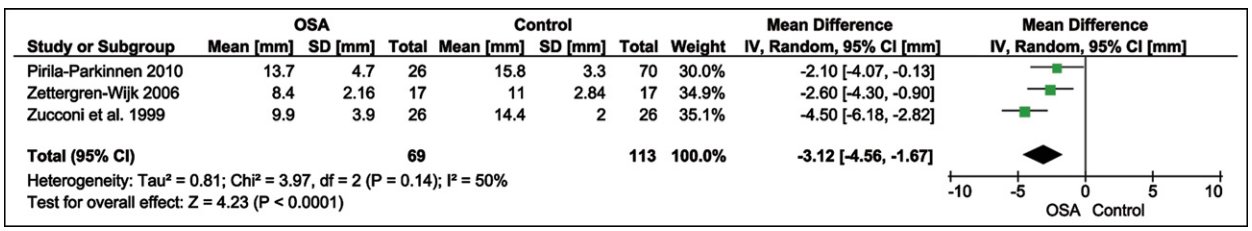

Fig 7. Pooled weighted mean difference in PNS-AD2 between children with obstructive sleep apnea and the controls.

Table IV. Pooled results for cephalometric variables in children with obstructive sleep apnea (OSA) compared with the controls

Cephalometric measurements in children with OSA vs controls	*Weighted mean difference (OSA−control)*	*95% CI*	*Heterogeneity (significance, P <0.05)*	*Statistical significance for overall effect (P)*
SNA (°)	0.61	−0.67 to 1.89	0.16	0.35
SNB (°)	−0.95	−2.09 to 0.20	0.25	0.11
ANB (°)	1.64	0.88 to 2.41	0.17	<0.0001*
SN-MP (°)	2.74	0.80 to 4.68	0.04*	0.006*
PP-MP (°)	6.88	−2.34 to 16.09	<0.00001*	0.14
IMPA (°)	−2.43	−7.26 to 2.41	0.08	0.32
BaSN (°)	3.02	−8.41 to 14.45	0.09	0.60
PNS-AD1 (mm)	−4.17	−5.85 to −2.50	0.29	<0.00001*
PNS-AD2 (mm)	−3.12	−4.56 to −1.67	0.14	<0.0001*

CI, Confidence interval.
*Significant.

Table V. Pooled results for cephalometric variables in children with primary snoring (PS) compared with the controls

Cephalometric measurements in children with snoring vs controls	*Weighted mean difference (PS−control)*	*95% CI*	*Heterogeneity (significant, P = 0.05)*	*Statistical significance for overall effect (P)*
SNA (°)	−1.49	−3.69 to 0.70	0.14	0.18
SNB (°)	−1.40	−2.58 to −0.23	0.41	0.02*
ANB (°)	1.54	0.89 to 2.20	0.70	<0.00001*
BaSN (°)	−1.27	−4.29 to 1.75	0.13	0.41

*Significant.

CONCLUSIONS

There is statistical support for an association between craniofacial disharmony and pediatric sleep-disordered breathing. However, an increased ANB angle of less than 2° in children with obstructive sleep apnea and primary snoring, compared with the controls, could be regarded as having marginal clinical significance. Evidence for a direct causal relationship between craniofacial structure and pediatric sleep-disordered breathing is unsupported by this meta-analysis. There is strong support for reduced upper airway sagittal width in children with obstructive sleep apnea as shown by reduced PNS-AD1 and PNS-AD2 distances. Larger well-controlled trials are required to address the relationship of craniofacial morphology to pediatric sleep-disordered breathing in all 3 dimensions.

We thank Michael Draper, librarian at the University of Adelaide, for assistance with the comprehensive literature search.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ajodo.2012.08.021.

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APPENDIX

Table. Literature searches and keywords

Databases	*Keywords*
Databases of published studies PubMed Searched via The University of Adelaide customised version (December 27, 2011). Updated monthly until April 2012	(cephalometry[mh] OR cephalometr*[tw] OR cephalogram*[tw] OR lateral neck radiograph*[tw] OR MRI[tw] OR Tomography, X-Ray[mh] OR x-ray tomography[tw] OR computed tomography[tw] OR Cone-Beam CT [tw] OR Volumetric CT[tw] OR Spiral Cone Beam[tw] OR Spiral Volume [tw]) AND (child[mh] OR child*[tw] OR juvenile*[tw] OR infant*[tw] OR preschool*[tw] OR Adolescen*[tw] OR teen*[tw] OR pubert*[tw] OR youth*[tw] OR paediatric[tw] OR pediatric[tw] OR neonat*[tw] OR newborn*[tw]) AND (sleep apnea, obstructive[mh] OR obstructive sleep apnea*[tw] OR obstructive sleep apnoea*[tw] OR disordered sleep breathing[tw] OR sleep disordered breathing[tw] OR sleep breathing disorder*[tw]) AND ((structural[tw] OR airway [tw] OR craniofacial [tw] OR dentoskeletal[tw]) AND (trait*[tw] OR dimension*[tw] OR morpholog*[tw] OR feature*[tw] OR character*[tw] OR structur*[tw] OR shape*[tw]) OR (facial bones[mh] OR pharyn*[tw] OR skull [mh:noexp] OR maxillofacial[tw] OR cranial suture*[tw] OR jaw*[tw] OR mandib*[tw] OR maxilla*[tw] OR dental arch*[tw] OR palat*[tw] OR Nasopharyn*[tw]))
EMBASE Searched via the University of Adelaide (December 27, 2011)	(cephalomet*:de,ti,ab OR 'computer assisted tomography'/exp OR cephalogram*:ti,ab OR 'lateral neck radiography':ti,ab OR 'lateral neck radiograph':ti,ab OR 'MRI':ti,ab OR 'x-ray tomography':ti,ab OR 'computed tomography':ti,ab OR 'Cone-Beam CT':ti,ab OR 'Volumetric CT':ti,ab OR 'Spiral Cone Beam':ti,ab OR 'Spiral Volume':ti,ab) AND (child/exp OR child*:ti,ab OR infant:de,ab,ti OR preschool*:ab,ti OR juvenile*:ab,ti OR adolescent/exp OR adolescen*:ti,ab OR teen*:ti,ab OR youth*:ti,ab OR paediatric:ti,ab OR pediatric:ti,ab OR newborn:ti,ab OR neonat*:ti,ab) AND ("sleep apnea syndrome":de OR "obstructive sleep apnea":ab,ti OR "obstructive sleep apnoea":ab,ti OR 'obstructive sleep apnoeas':ab,ti OR 'obstructive sleep apneas':ti,ab OR "disordered sleep breathing":ab,ti OR "sleep disordered breathing":ab,ti OR "sleep breathing disorder":ab,ti OR "sleep breathing disordered":ab,ti) AND ((structural:ti,ab OR airway:ti,ab OR craniofacial:ti,ab OR dentoskeletal:ti,ab) AND (trait*:ti,ab OR dimension*:ti,ab OR morpholog*:ti,ab OR feature*:ti,ab OR character*:ti,ab OR structur*:ti,ab OR shape*:ti,ab) OR (pharyn*:de,ab,ti OR 'facial bone':de,ab,ti OR 'facial bones':ab,ti OR palat*:ab,ti))
SCOPUS Searched via the University of Adelaide (December 27, 2011) and updated monthly until April 2012	(child* OR infant* OR preschool* OR juvenile*) AND ("sleep apnea" OR "sleep apnoea" OR "disordered sleep breathing" OR "sleep disordered breathing" OR "sleep breathing disorder" OR "sleep breathing disordered") AND (mouth OR teeth OR pharyngeal OR pharynx OR 'structural abnormality' OR 'airway abnormality' OR 'airway morphology' OR 'craniofacial malformation' OR 'craniofacial abnormality' OR 'craniofacial anomaly' OR 'craniofacial deformity' OR 'craniofacial structure' OR 'craniofacial structural' OR 'craniofacial morphology' OR 'facial bone' OR 'mouth malformation' OR tongue* OR palate OR 'maxillofacial development' OR (airway* AND (shape* OR structur*)))
Cochrane Central Register of Controlled Trials (CENTRAL) (1991-December 2011)	((sleep disordered breathing OR obstructive sleep apnoea) AND children AND craniofacial morphology)
Databases of research registers Meta-Register of Controlled Trials Searched via www.controlled-trials.com (December 2011 and April 2012)	(sleep disordered breathing in children and craniofacial morphology)

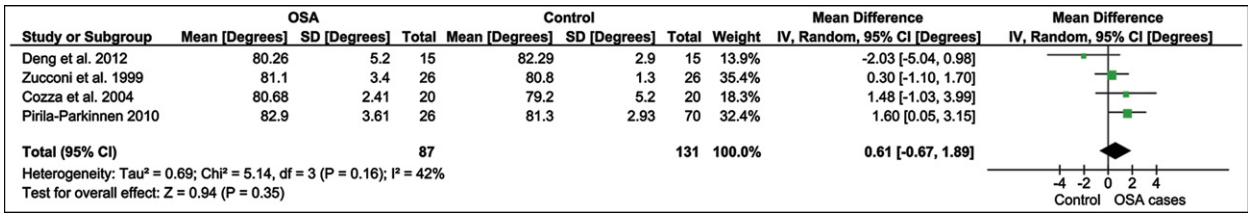

Fig 1. Pooled weighted mean differences in SNA angles between children with obstructive sleep apnea and the controls.

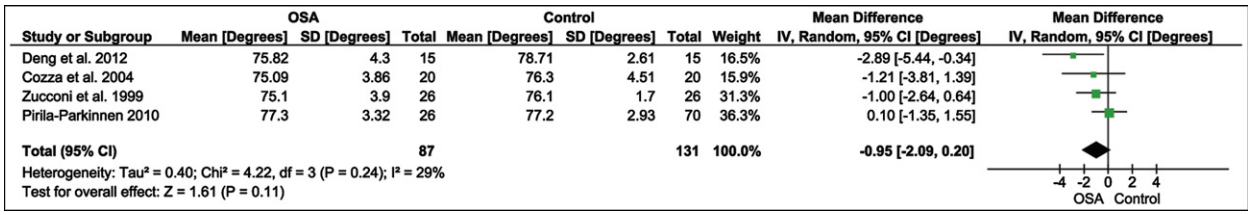

Fig 2. Pooled weighted mean differencse in SNB angles in children with obstructive sleep apnea and the controls.

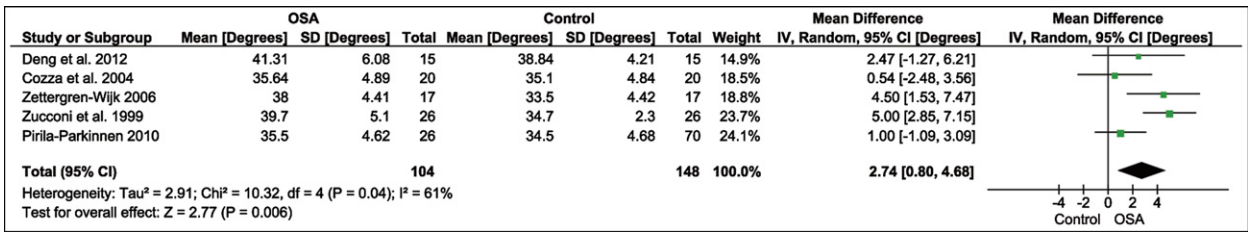

Fig 3. Pooled weighted mean differences in SN-MP angles in children with obstructive sleep apnea and the controls.

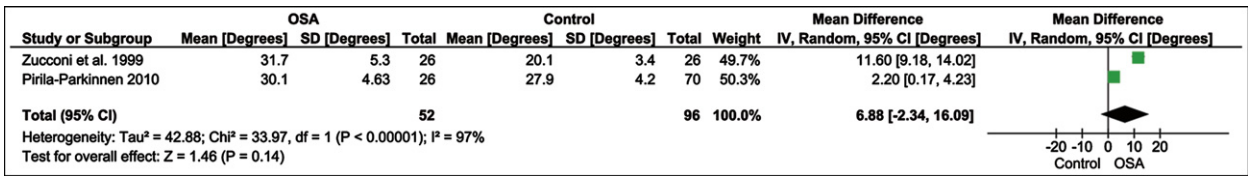

Fig 4. Pooled weighted mean differences in PP-MP angles in children with obstructive sleep apnea and the controls.

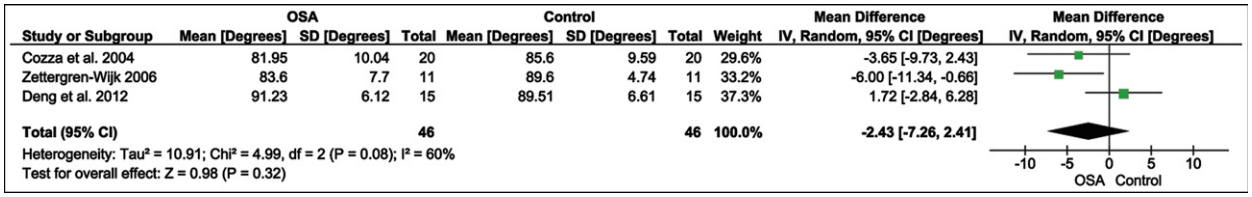

Fig 5. Pooled weighted mean differences in mandibular incisor to MP angles in children with obstructive sleep apnea and the controls.

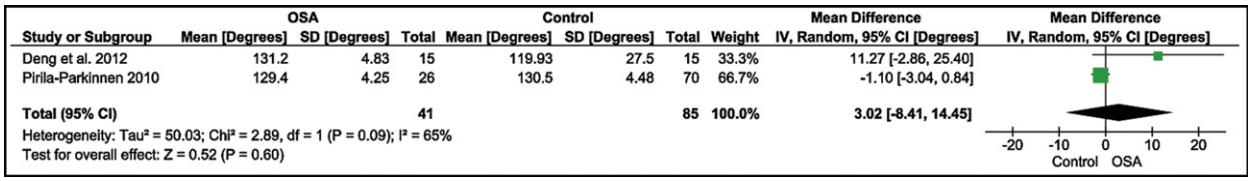

Fig 6. Pooled weighted mean differences in BaSN angles in children with obstructive sleep apnea and the controls.

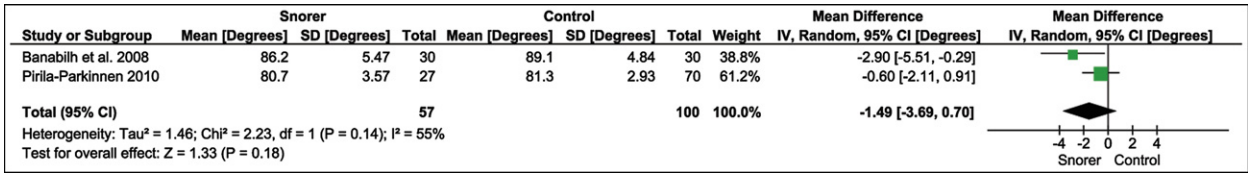

Fig 7. Pooled weighted mean differences in SNA angles in children with primary snoring and the controls.

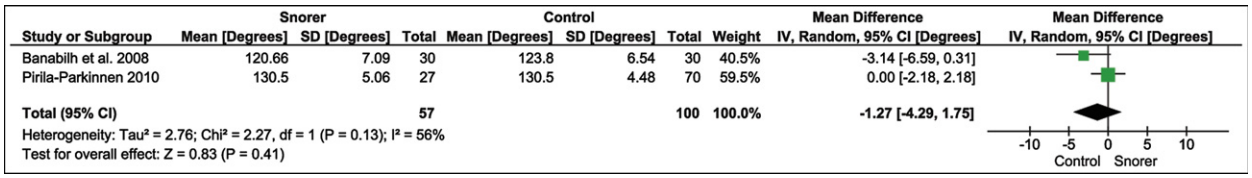

Fig 8. Pooled weighted mean differences in BaSN angles in children with primary snoring and the controls.