The Journal of Laryngology & Otology (2017), ***131***, *378–383*.

doi:10.1017/S0022215117000056

REVIEW ARTICLE

Tongue–lip adhesion and tongue repositioning for obstructive sleep apnoea in Pierre Robin sequence: A systematic review and meta-analysis

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Abstract

Objective: To search for studies on tongue–lip adhesion and tongue repositioning used as isolated treatments for obstructive sleep apnoea in children with Pierre Robin sequence.

Methods: A systematic literature search of PubMed/Medline and three additional databases, from inception through to 8 July 2016, was performed by two authors.

Results: Seven studies with 90 patients (59 tongue–lip adhesion and 31 tongue repositioning patients) met the inclusion criteria. Tongue–lip adhesion reduced the mean (± standard deviation) apnoea/hypopnoea index from 30.8 ± 22.3 to 15.4 ± 18.9 events per hour (50 per cent reduction). The apnoea/hypopnoea index mean difference for tongue–lip adhesion was −15.28 events per hour (95 per cent confidence interval = −30.70 to 0.15; $p = 0.05$). Tongue–lip adhesion improved the lowest oxygen saturation from 75.8 ± 6.8 to 84.4 ± 7.3 per cent. Tongue repositioning reduced the apnoea/hypopnoea index from 46.5 to 17.4 events per hour (62.6 per cent reduction). Tongue repositioning improved the mean oxygen saturation from 90.8 ± 1.2 to 95.0 ± 0.5 per cent.

Conclusion: Tongue–lip adhesion and tongue repositioning can improve apnoea/hypopnoea index and oxygenation parameters in children with Pierre Robin sequence and obstructive sleep apnoea.

Key words: Sleep Apnea; Obstructive; Pierre Robin Syndrome; Tongue; Surgical Procedures; Operative

Introduction

Pierre Robin sequence is a disorder characterised by glossoptosis, micrognathia and obstruction in the upper airway, with or without a cleft palate.[1] Even though the tongue of children with Pierre Robin sequence may not be hypertrophic compared to that of children without the disorder, the micrognathia does not allow for the tongue to be in a natural, unobstructing position. In adults with obstructive sleep apnoea (OSA), moving from an upright to a supine position has been shown to decrease the volume of the upper airway by approximately 33 per cent.[2] It follows that in children, the upper airway volume would also decrease significantly when moving from the upright to supine position. Tongue–lip adhesion has been described as an effective surgery for keeping the tongue in an anterior position, so that it does not obstruct the upper airway. Tongue repositioning via subperiosteal release of the floor of mouth has also been performed to move the tongue into a more anterior position.[3]

A systematic review of studies evaluating the effect of tongue–lip adhesion and tongue repositioning on Pierre Robin sequence patients with OSA, with a meta-analysis, would be useful to quantify the overall effects of these treatments. Hence, this review entailed a search of the international literature for studies (e.g. case reports, case series, cohorts, randomised trials) evaluating the effects of tongue–lip adhesion and/or tongue repositioning on Pierre Robin sequence patients with OSA, and the data were used to perform a meta-analysis.

Materials and methods

Information sources

We searched Google Scholar, Web of Science, Cochrane Collaboration databases, and PubMed/Medline. The

Accepted for publication 25 October 2016 First published online 14 February 2017

Preferred Reporting Items for Systematic Reviews and Meta-Analysis ('PRISMA') statement[4] was downloaded and used as a guide for performing this study.

Search

Medical Subject Headings (MeSH) terms, keywords and phrases were tailored to each specific database that was searched. A sample search, which was used in PubMed/Medline, is as follows: 'lingual', 'tongue', 'glossal', 'glossectomy', 'glossopexy', 'tongue-lip adhesion', 'tongue lip adhesion', 'lip/surgery*' (MeSH), 'tissue adhesions' (MeSH) or 'tongue/surgery*' (MeSH), and 'child', 'pediatric', 'paediatric', 'children', 'infant' or 'teenager', and 'Pierre Robin' or 'Pierre-Robin'. Other databases were searched with a similar search strategy, with appropriate modification to meet the requirement for the databases. The database function 'similar articles' (or equivalent) and 'cited by' (or equivalent) were used to search for further articles.

Study selection

The inclusion criteria for this article, using the 'PICOS' acronym (participants, interventions, comparisons, outcomes and study designs), were as follows. The participants were children (aged less than 18 years) diagnosed with Pierre Robin sequence and OSA. The interventions were tongue–lip adhesion and/or tongue repositioning. Comparisons of pre- and post-tongue surgery data were made. Quantitative sleep study data were the outcomes assessed (i.e. apnoea/hypopnoea index, apnoea index, respiratory disturbance index, mean oxygen saturation and lowest oxygen saturation). All study types were included in the search: posters, abstracts, case reports, case series, cohorts and randomised trials. The study exclusion criteria were: studies in which other surgical procedures were performed simultaneously, such as mandibular distraction osteogenesis or tracheostomy, and studies in which there were qualitative data without any quantified data.

Methodological quality

The National Institute for Health and Clinical Excellence (NICE) tool for case series was used to individually assess the quality of each study.[5] This comprised eight items scored in terms of 'yes' or 'no' responses.

Hypothesis

The null hypothesis for this systematic review and meta-analysis was that tongue–lip adhesion and tongue repositioning did not change the sleep study variables. To test the null hypothesis, the pre-operative data were compared to post-operative data. Means (± standard deviations) were collected from each study, and were subsequently used to calculate mean differences, standardised mean differences and 95 per cent confidence intervals (CIs). The apnoea/hypopnoea index percentage changes were based on the individual studies and on the overall combined studies.

Statistical calculations

Stata 14.1 statistical software (StataCorp, College Station, Texas, USA) and the Cochrane Collaboration's Review Manager Software (RevMan) version 5.3 were used to evaluate the data.[6] To determine statistical significance, we used $p < 0.05$ as the cut-off. To determine the magnitude of effect for the standardised mean difference, we selected Cohen's guidelines,[7] and reported effects as small (standardised mean difference of 0.2), medium (standardised mean difference of 0.5) or large (standardised mean difference of 0.8). If additional data or outcomes were needed, we emailed or attempted to contact the corresponding authors of the relevant studies using the contact information provided. For studies in which the mean was reported without the standard deviation, and there was no response from the corresponding authors, we calculated and used the weighted average.

Heterogeneity and bias risk

The I^2 statistic was used to evaluate for inconsistency or heterogeneity between studies. The I^2 statistical categories are: low inconsistency = 25 per cent, moderate inconsistency = 50 per cent and high inconsistency = 75 per cent.[8] The Cochran Q statistic was additionally used for determining heterogeneity, and, as recommended in previous studies, statistically significant heterogeneity was defined as a Q statistic p-value of ≤ 0.10.[9]

Data collection

Two authors (EH and MC) systematically searched the literature for relevant articles from 31 January 2016 through to 8 July 2016, and searched from the inception of each database. Initially, the authors reviewed the titles along with the abstracts. Potentially relevant articles were subsequently downloaded in full-text form.

Results

Studies selected

The search identified 244 potentially relevant studies based on the search criteria; 21 of these were potentially relevant after abstract and title review, and were downloaded in their entirety (Figure 1). Seven studies with 90 children met the inclusion criteria. Five studies,[10–14] comprising 59 patients, presented outcomes for tongue–lip adhesion, and 2 studies,[15,16] comprising 31 patients, presented outcomes for tongue repositioning performed via subperiosteal release of the floor of the mouth.

Study characteristics

Table I provides the findings based on the NICE quality assessment tool.

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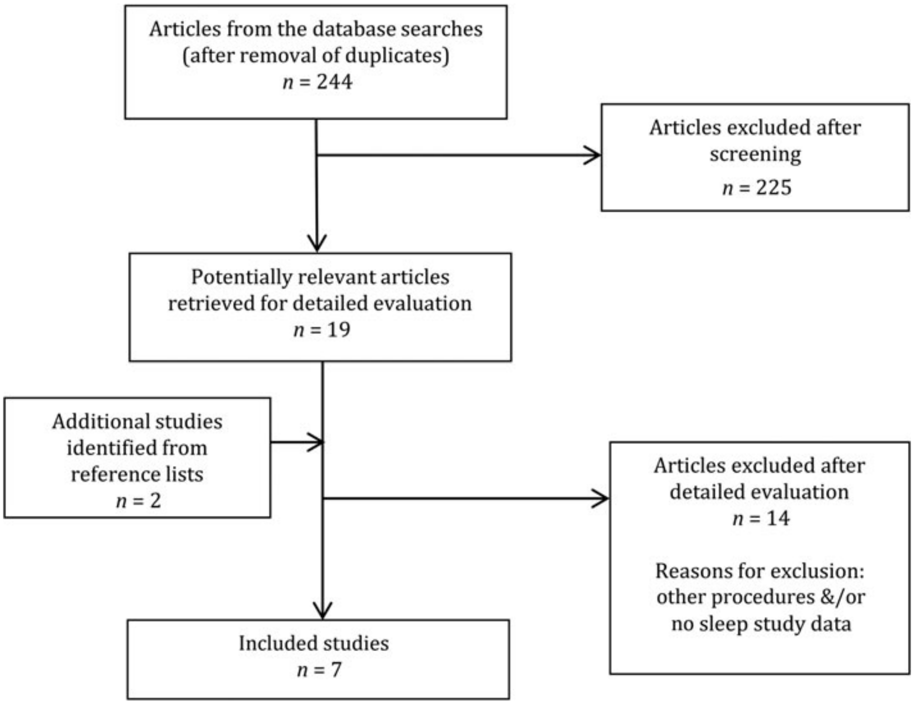

FIG. 1
Study selection flowchart for tongue–lip adhesion and tongue repositioning procedures.

Outcomes

Apnoea/hypopnoea index and tongue–lip adhesion. Five studies presented outcomes for tongue–lip adhesion, with mean apnoea/hypopnoea index improvement from 30.8 ± 22.3 to 15.4 ± 18.9 events per hour in 41 patients (50 per cent reduction) (Table II).[10–14] Random effects modelling in 41 patients demonstrated an apnoea/hypopnoea index mean difference of −15.28 events per hour (95 per cent CI = −30.70 to 0.15; overall effect z = 1.94, $p = 0.05$). The Q statistic was $p = 0.03$ (significant heterogeneity) and $I^2 = 72$ per cent (moderate to high inconsistency). Random effects modelling for apnoea/hypopnoea index standardised mean difference was −1.04 (large magnitude of effect using Cohen's guidelines) (95 per cent CI = −1.51 to −0.58; overall effect z = 4.37, $p < 0.0001$). The Q statistic was $p = 0.63$ (no statistically significant heterogeneity) and $I^2 = 0$ (no inconsistency) (Figure 2).

Apnoea/hypopnoea index and tongue repositioning. Two studies (31 patients) presented outcomes for tongue repositioning via subperiosteal release of the floor of the mouth; the apnoea/hypopnoea index improved

TABLE I
GENERAL CHARACTERISTICS AND NICE QUALITY CRITERIA OF INCLUDED STUDIES

Study	Year	Design	Country	Outcomes analysed	NICE checklist item							
					1	2	3	4	5	6	7	8
Greathouse *et al.*[12]	2016	RMC	USA	AHI	No	No	Yes	Yes	No	No	Yes	Yes
Resnick *et al.*[13]	2016	RCS	USA	AHI, LSAT	No	Yes	Yes	Yes	No	No	Yes	Yes
Flores *et al.*[9]	2014	RMC	USA	AHI, MSAT	No	Yes	Yes	Yes	No	No	Yes	Yes
Caouette-Laberge *et al.*[14]	2012	RCS	Canada	AHI	No	Yes	Yes	No	No	Yes	Yes	Yes
Sedaghat *et al.*[11]	2012	RCS	USA	AHI, LSAT, end-tidal pCO_2, RDI	No	Yes	Yes	Yes	No	No	Yes	Yes
Caouette-Laberge *et al.*[15]	1996	RCS	Canada	MSAT	No	No	Yes	Yes	No	No	Yes	No
Freed *et al.*[10]	1988	RCS	USA	AHI, LSAT	No	Yes	No	No	No	No	Yes	No

National Institute for Health and Clinical Excellence case series checklist items: (1) Case series collected in more than one centre (i.e. multi-centre study)? (2) Is the study hypothesis, aim or objective clearly described? (3) Are the inclusion and exclusion criteria (case definition) clearly reported? (4) Is there a clear definition of the outcomes reported? (5) Were data collected prospectively? (6) Is there an explicit statement that patients were recruited consecutively? (7) Are the main study findings clearly described? (8) Are outcomes stratified (e.g. by abnormal results, disease stage, patient characteristics)? NICE = National Institute for Health and Clinical Excellence; RMC = retrospective matched cohort; AHI = apnoea/hypopnoea index; RCS = retrospective case series; LSAT = lowest oxygen saturation; MSAT = mean oxygen saturation; end-tidal pCO_2 = partial pressure of carbon dioxide at the end of expiration during tidal breathing; RDI = respiratory disturbance index

TABLE II
DEMOGRAPHIC AND SLEEP STUDY DATA PRE- AND POST-TONGUE LIP ADHESION AND TONGUE REPOSITIONING SURGERY*

Study (year) by surgery type	Patients (*n*)	Average age (days)	AHI (events per hour)			LSAT (%)	
			Pre-op	Post-op	% Change	Pre-op	Post-op
Tongue–lip adhesion							
– Greathouse *et al.*[12] (2016)	15	35.5 ± 32.1	38.1 ± 19.2	20.5 ± 25.3	−46.2	–	–
– Resnick *et al.*[13] (2016)	18	28 ± 4.7	15.1 ± 4.3	9.9 ± 4.1	−34.4	73.3 ± 3.4	81.4 ± 3.0
– Flores *et al.*[9] (2014)	15		–	–	–	82 ± 5.1 (52–93)	89.2 ± 6.5 (75–96)
– Sedaghat *et al.*[11] (2012)	8	29 (15–56)	52.6 ± 27.5	18.1 ± 23.9	−65.6	72.9 ± 7.0	82.1 ± 10.7
– Freed *et al.*[10] (1988)	3	–	–	–	–	68 ± 8	85 ± 9.5
– Total	59	–	30.8 ± 22.3	15.4 ± 18.9	−50	75.8 ± 6.8	84.4 ± 7.3
Tongue repositioning							
– Caouette-Laberge *et al.*[14] (2012)	25	–	46.5 (18.2–95.3)	17.4 (4.5–45)	−62.6	–	–
– Caouette-Laberge *et al.*[15] (1996)	6	–	–	–	–	90.8 ± 1.2†	95.0 ± 0.5†

Data represent average values ± standard deviations, with values in parentheses indicating ranges. *In Pierre Robin sequence children with obstructive sleep apnoea. AHI = apnoea/hypopnoea index; LSAT = lowest oxygen saturation; pre-op = pre-operative; post-op = post-operative; – = not reported
†Mean oxygen saturation.

from 46.5 to 17.4 events per hour in 25 patients (62.6 per cent reduction) (Table II).[15,16]

Lowest oxygen saturation and tongue–lip adhesion. Four studies presented outcomes for tongue–lip adhesion, with a mean lowest oxygen saturation improvement from 75.8 ± 6.8 to 84.4 ± 7.3 per cent in 44 patients (an improvement of 8.6 per cent) (Table II).[10–12,14] Random effects modelling in 44 patients demonstrated a lowest oxygen saturation mean difference of 8.13 (95 per cent CI = 6.31 to 9.94; overall effect z = 8.76, $p <$ 0.00001). The Q statistic was $p = 0.62$ (no statistically significant heterogeneity) and $I^2 = 0$ per cent (no inconsistency). Random effects modelling for lowest oxygen saturation standardised mean difference was 1.56 (large magnitude of effect using Cohen's guidelines) (95 per cent CI = 0.79 to 2.32; overall effect z = 4.00, $p < 0.0001$). The Q statistic p-value was 0.11 (no statistically significant heterogeneity) and $I^2 = 51$ per cent (moderate inconsistency) (Figure 3).

Mean oxygen saturation and tongue repositioning. Caouette-Laberge *et al*. reported that mean oxygen saturation improved from 90.8 ± 1.2 to 95.0 ± 0.5 per cent in six children (Table II).[16]

Discussion

There are three main findings from this systematic review with meta-analysis. First, tongue–lip adhesion improved the apnoea/hypopnoea index by approximately 50 per cent, from 30.8 ± 22.3 to 15.4 ± 18.9 events per hour. The small mandible of children with Pierre Robin sequence predisposes them to obstruction at the level of the base of the tongue. Tongue–lip adhesion and anterior displacement of the tongue allows for an improved retrolingual airway, resulting in a significant improvement in the apnoea/hypopnoea index. Given that the traditional alternatives are tracheostomy, which would bypass the upper airway, or mandibular distraction, which would allow for a skeletal improvement in the mandible, the overall decision will involve a long discussion with the patient and their family. Pierre Robin sequence children who have undergone tongue repositioning surgery and a sleep study are fewer in number, indicating that tongue repositioning is not performed as often.

Second, oxygen saturation improves with both tongue–lip adhesion and tongue repositioning procedures. The lowest oxygen saturation in children who underwent tongue–lip adhesion improved by 8.6 per cent. For tongue repositioning, mean oxygen saturation improved from 90.8 to 95.0 per cent (improvement of 4.2 per cent). It is assumed that anterior displacement of the tongue during sleep leads to an improvement in airflow, with fewer obstructions. Additionally, when there are obstructions, the airway is less likely to be obstructed for as long a duration, which improves the overall mean saturation and the overall lowest oxygen saturation. In order to fully determine the

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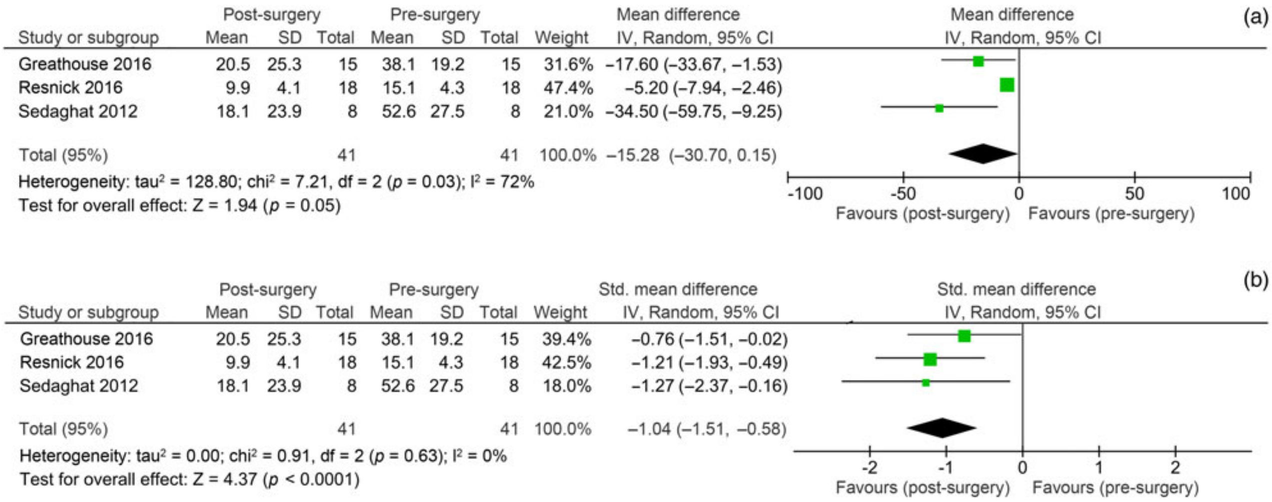

FIG. 2

Pre- and post-tongue–lip adhesion outcomes in terms of: apnoea/hypopnoea index mean difference (a) and standardised mean difference (b). SD = standard deviation; IV = interval variable; CI = confidence interval; Std. = standardised

effect of tongue–lip adhesion and tongue repositioning procedures on oxygen saturation, we recommend that authors report the following four variables: mean oxygen saturation, lowest oxygen saturation, oxygen desaturation index and the percentage of sleep time spent under 90 per cent oxygen saturation.

Third, additional research is recommended. Tongue–lip adhesion seems to be more easily performed than tongue repositioning via subperiosteal release of the floor of the mouth. This might explain why there are more publications on tongue–lip adhesion. Although tongue repositioning in children with Pierre Robin sequence has demonstrated a large improvement in the apnoea/hypopnoea index (62.6 per cent reduction), the procedure is not as commonly performed. It is possible that tongue repositioning could serve as an alternative to tongue–lip adhesion in children with Pierre Robin sequence; however, thus far, only Caouette-Laberge and colleagues have reported outcomes for apnoea/hypopnoea index and oxygen saturation. It is unclear whether other surgical procedures, such as base of tongue reduction, would also benefit Pierre Robin sequence patients. Given that not all institutions have surgeons who are comfortable performing mandibular distraction, there may be circumstances where surgeons may consider other tongue surgical procedures or even tracheostomy given the nuances of individual patient circumstances.

Limitations

It is possible that, despite our best efforts, we could have missed a relevant study in the literature.

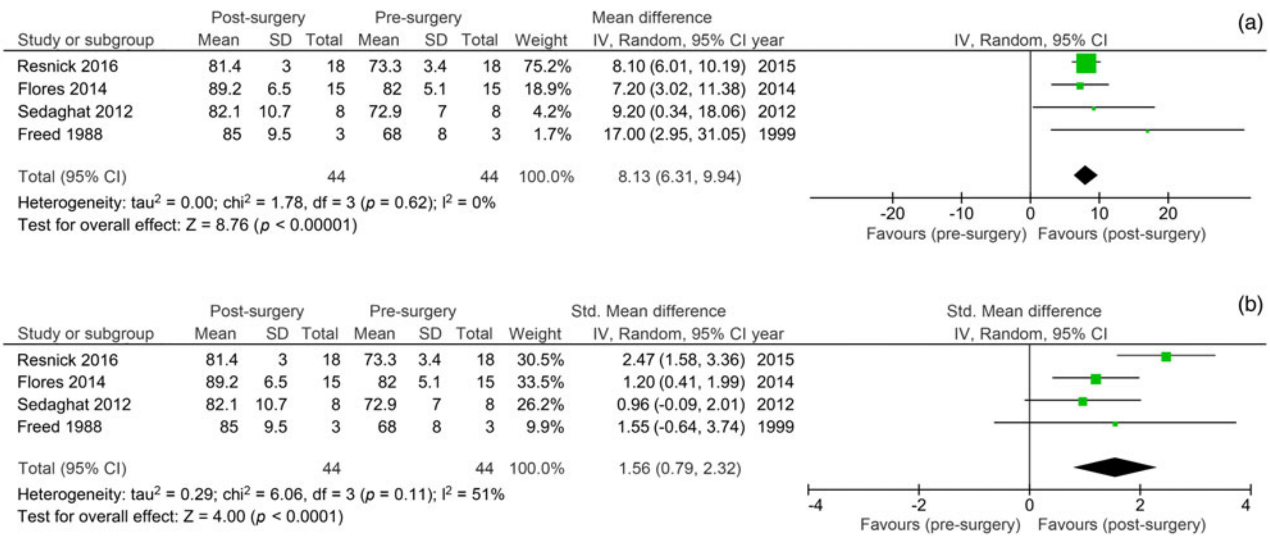

FIG. 3

Pre- and post-tongue–lip adhesion outcomes in terms of: lowest oxygen saturation mean difference (a) and standardised mean difference (b). SD = standard deviation; IV = interval variable; CI = confidence interval; Std. = standardised

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However, we searched for several months in an independent fashion. Additionally, we limited our investigation to publications with sleep study data in order to quantify the improvement in sleep apnoea outcomes, specifically apnoea/hypopnoea index and oxygen saturation.

Conclusions and relevance

The international literature demonstrates that tongue–lip adhesion and tongue repositioning can improve apnoea/hypopnoea index and oxygenation parameters when used as isolated treatments for OSA in children with Pierre Robin sequence.

References

1 Reddy VS. Evaluation of upper airway obstruction in infants with Pierre Robin sequence and the role of polysomnography–review of current evidence. *Paediatr Respir Rev* 2016;**17**:80–7
2 Camacho M, Capasso R, Schendel S. Airway changes in obstructive sleep apnoea patients associated with a supine versus an upright position examined using cone beam computed tomography. *J Laryngol Otol* 2014;**128**:824–30
3 Siddique S, Haupert M, Rozelle A. Subperiosteal release of the floor of the mouth musculature in two cases of Pierre Robin sequence. *Ear Nose Throat J* 2000;**79**:816–19
4 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;**6**:e1000097
5 National Institute for Health and Clinical Excellence. *Methods for Development of NICE Public Health Guidance*. London: National Institute for Health and Clinical Excellence, 2009
6 Review Manager (RevMan) [computer program], version 5.3. Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration, 2014
7 Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd edn. Hillsdale, NJ: Erlbaum, 1988
8 Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557–60
9 Lau J, Ioannidis JP, Schmid CH. Quantitative synthesis in systematic reviews. *Ann Intern Med* 1997;**127**:820–6
10 Flores RL, Tholpady SS, Sati S, Fairbanks G, Socas J, Choi M *et al*. The surgical correction of Pierre Robin sequence: mandibular distraction osteogenesis versus tongue-lip adhesion. *Plast Reconstr Surg* 2014;**133**:1433–9
11 Freed G, Pearlman MA, Brown AS, Barot LR. Polysomnographic indications for surgical intervention in Pierre Robin sequence: acute airway management and follow-up studies after repair and take-down of tongue-lip adhesion. *Cleft Palate J* 1988;**25**:151–5
12 Sedaghat AR, Anderson IC, McGinley BM, Rossberg MI, Redett RJ, Ishman SL. Characterization of obstructive sleep apnea before and after tongue-lip adhesion in children with micrognathia. *Cleft Palate Craniofac J* 2012;**49**:21–6
13 Greathouse ST, Costa M, Ferrera A, Tahiri Y, Tholpady SS, Havlik RJ *et al*. The surgical treatment of Robin sequence. *Ann Plast Surg* 2016;**77**:413–19
14 Resnick CM, Dentino K, Katz E, Mulliken JB, Padwa BL. Effectiveness of tongue-lip adhesion for obstructive sleep apnea in infants with Robin sequence measured by polysomnography. *Cleft Palate Craniofac J* 2016;**53**:584–8
15 Caouette-Laberge L, Borsuk DE, Bortoluzzi PA. Subperiosteal release of the floor of the mouth to correct airway obstruction in Pierre Robin sequence: review of 31 cases. *Cleft Palate Craniofac J* 2012;**49**:14–20
16 Caouette-Laberge L, Plamondon C, Larocque Y. Subperiosteal release of the floor of the mouth in Pierre Robin sequence: experience with 12 cases. *Cleft Palate Craniofac J* 1996;**33**:468–72

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Dr M Camacho takes responsibility for the integrity of the content of the paper
Competing interests: None declared