

AIRWAY MANAGEMENT STRATEGIES IN INFANTS BORN WITH PIERRE ROBIN SEQUENCE (PRS): A SYSTEMATIC REVIEW AND META-ANALYSIS OF EFFECTIVENESS

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ABSTRACT

Background: Pierre Robin sequence (PRS) is characterized by micrognathia, glossoptosis, and upper airway obstruction (UAO). Different management strategies exist, each with its own efficacy and clinical outcomes. **Objective:** To critically evaluate and compare the efficacy of conservative, orthodontic, and surgical airway interventions in neonates and infants with PRS, using polysomnographic (PSG) and clinical outcomes. **Methods:** A systematic review and meta-analysis were conducted per PRISMA guidelines. Databases (PubMed, Embase, Medline, etc.) were searched for studies (2017-2025) reporting pre- and post-intervention PSG data. Seventeen studies (n=1,291 patients) met the inclusion criteria. Risk of bias was assessed using the ROBINS-I tool. A random-effects meta-analysis was performed for Mandibular Distraction Osteogenesis (MDO) outcomes. **Results:** This study analysis reveals a critical finding: while all modalities can be effective, their efficacy is stratified. Conservative management (prone positioning, nasopharyngeal airway) achieved significant improvement, with 84.2% of patients attaining an AHI <5, supporting its role as a first-line strategy. However, MDO demonstrated superior and statistically significant efficacy in resolving severe obstruction, with meta-analysis showing drastic improvements in OAH (MD: -36.29, CI: -43.39 to -29.18, p<0.00001), AHI (p<0.00001), SpO₂ nadir (MD: +12.91%, p<0.00001), and end-tidal CO₂ (p<0.00001). Notably, MDO did not significantly improve weight gain (p=0.24) or sleep efficiency (p=0.51). Tongue-lip adhesion (TLA) was effective (89.5% achieved AHI<5) but was associated with higher recurrence rates than MDO. Orthodontic appliances (SOAP, PEBP) emerged as a highly promising non-surgical intervention, significantly reducing OAH (e.g., from 39.3 to 12.2 events/h, p<0.001) and potentially obviating the need for surgery in selected cases. **Conclusion:** Management of PRS-related UAO requires a severity-based, stepwise algorithm. Conservative and orthodontic interventions are effective first-line options for a majority of patients. For severe, refractory cases, MDO is the most effective surgical intervention for rapidly securing the airway, though its impact on nutritional and sleep quality metrics remains limited.

KEYWORDS: Pierre Robin Sequence; Airway Management; Infants; Airway Obstruction; Respiratory Management; Systematic Review; Meta-Analysis.

INTRODUCTION

Pierre Robin sequence (PRS) is a rare congenital condition defined by the triad of micrognathia, glossoptosis, and upper airway obstruction (UAO) [1]. The estimated incidence ranges between 1:8,500 and 1:14,000 live births [3,4]. Clinical presentation varies from mild feeding and respiratory difficulties to life-threatening airway compromise requiring urgent multidisciplinary intervention [3]. Recurrent obstruction may result in chronic intermittent hypoxemia, malnutrition, pulmonary hypertension, or death, while spontaneous improvement can occur around six months of age due to mandibular growth and neuromuscular maturation [5]. Prognosis differs depending on whether PRS is isolated, syndromic, or associated with additional malformations, while relieving UAO remains the principal therapeutic goal [1].

Management strategies are diverse, yet evidence comparing nonsurgical and surgical approaches is limited. It has been shown that specific patient traits influence clinical decision-making regarding airway interventions [6]. Nonsurgical methods include prone positioning [7], oral appliances with velar extension [8], nasopharyngeal or oropharyngeal tubes, noninvasive ventilation (commonly CPAP), endotracheal intubation, and oxygen supplementation [9]. Positioning alone has been effective in 40–70% of cases [10]. When positioning is insufficient, a nasopharyngeal airway (NPA) may provide temporary relief [11], while CPAP can support infants requiring additional ventilatory assistance [12]. Surgical alternatives comprise tongue–lip adhesion, mandibular distraction osteogenesis, subperiosteal release of the mouth floor, and tracheostomy.

The rationale for this review stems from the scarcity of comparative studies and the absence of standardized criteria to guide therapy selection. Few randomized trials exist, and current practice varies widely, often depending on institutional expertise and clinical judgment [15]. Furthermore, international consensus underscores the need

for a unified protocol for evaluating and treating UAO in PRS [16]. Therefore, this systematic review aims to critically evaluate and compare the efficacy of conservative, orthodontic, and surgical airway interventions in neonates and infants with PRS, using polysomnographic (PSG) and clinical outcomes.

METHODS

Search strategy

PICO Framework:

Population: Neonates and infants diagnosed with Pierre Robin sequence.

Intervention: Nonsurgical airway management strategies (e.g., prone positioning, NPA, CPAP).

Comparison: Surgical interventions (e.g., tongue–lip adhesion, mandibular distraction osteogenesis, tracheostomy).

Outcomes: Short- and long-term measures, including airway patency, feeding ability, growth, respiratory function, complications, and developmental outcomes.

Eligibility Criteria

Eligibility was determined according to the PRISMA-recommended Population, Intervention, Comparison, Outcomes, and Study Design (PICOS) framework (see Appendix). Inclusion criteria were: (1) studies published 2017–2025; (2) neonates (0–28 days) and infants (4 weeks–12 months) with confirmed Pierre Robin Sequence (PRS); (3) reports of pre- and post-intervention data on obstructive airway symptoms or equivalent respiratory outcomes. Exclusion criteria were studies published before 2017, case reports, case series with <10 participants, reviews, studies including children >12 months old, and studies with populations without PRS. Reports without extractable means, standard deviations, or sample sizes for both groups were also excluded.

Information Sources and Search Strategy

PubMed, Google Scholar, ScienceDirect, Medline, Embase, and ClinicalTrials.gov were searched, with additional references from independent journals. Searches followed PICOS-defined terms to ensure relevance.

Selection Process

Two independent reviewers screened peer-reviewed articles, prioritizing high-impact journals to reduce publication bias. References were uploaded into Rayyan.ai for duplicate removal and blinded inclusion/exclusion screening [17]. Disagreements were resolved by a two-member arbitration panel.

Ultimately, 17 studies (n = 1,291) were included. Excluded studies typically had ineligible populations, flawed methodology, inaccurate or incomplete results, or high risk of bias.

Data Extraction

Data from the final 17 studies were charted according to PRISMA guidelines, and a flow diagram was generated (Figure 1) [18]. Only peer-reviewed primary studies were retained. Bias-reduction steps included excluding reviews, mandating disclosure of conflicts of interest, and adhering to the strategies of Chalmers et al. (1990) [19].

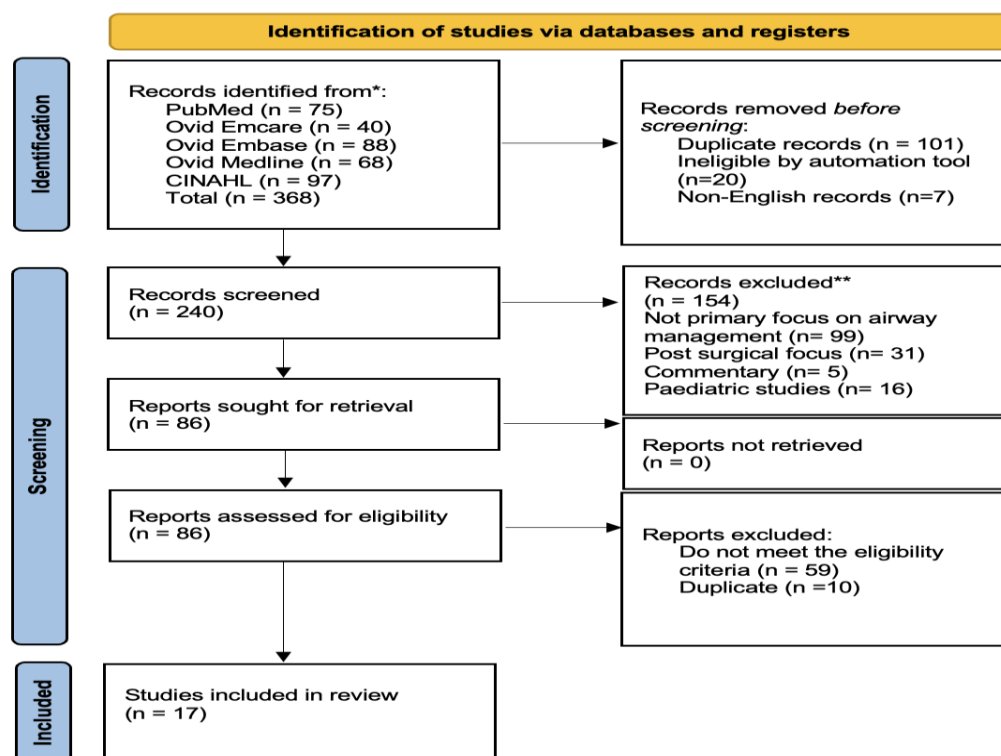


Figure 1: PRISMA guidelines for the included studies (n=17)

Assessment of Research Quality

Risk of bias was assessed using the ROBINS-I tool [20]. Each study was judged against a hypothetical “target trial” across seven bias domains. Ratings were categorized as low, moderate, serious, or critical risk, enabling transparent appraisal of internal validity. Results were summarized in a Figure 2.

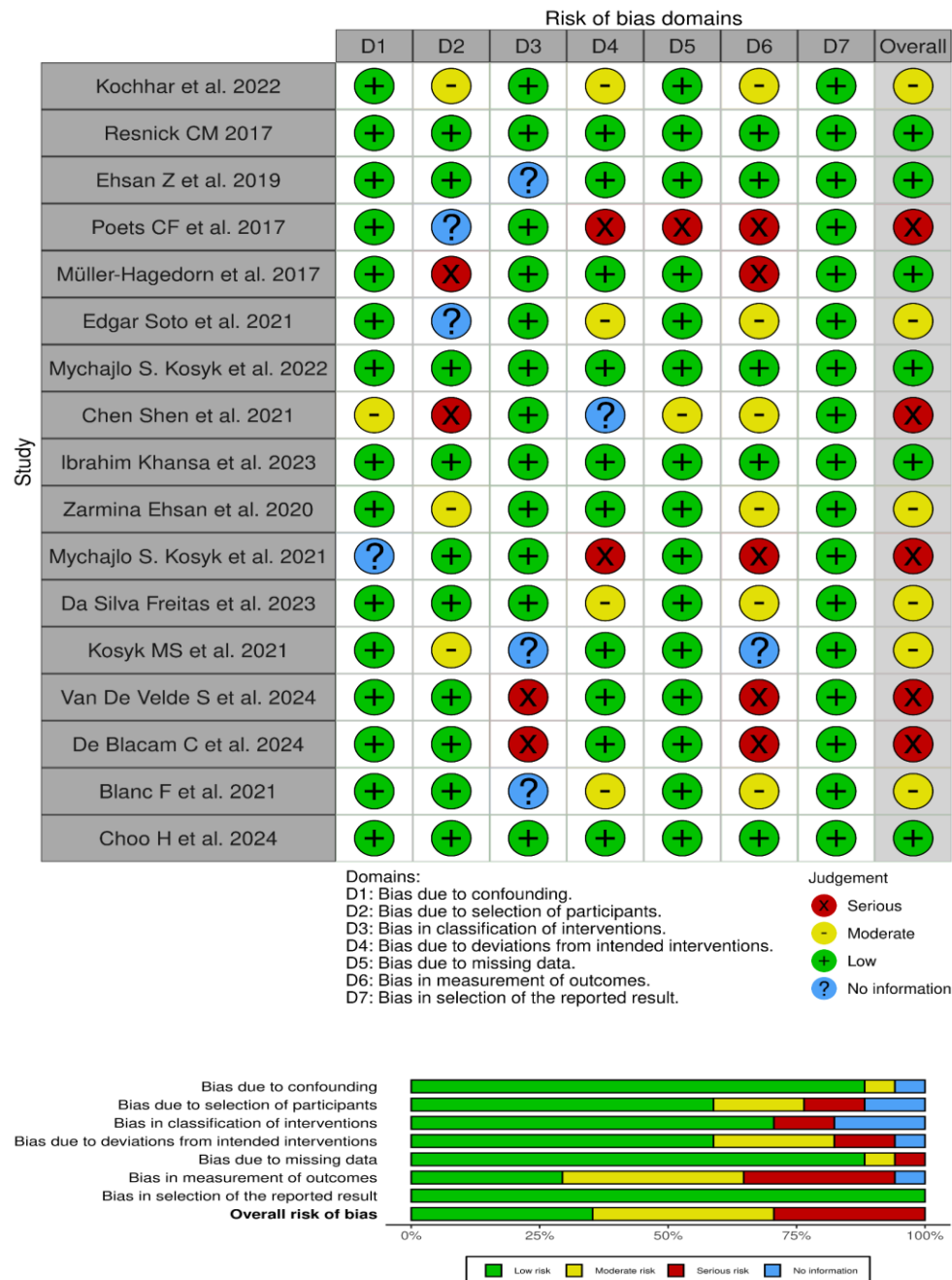


Figure 2: Traffic lights and summary plots for Risk of Bias Assessment (n=17)

Statistical

Of the 17 initially eligible primary studies, eight provided continuous data suitable for pooling. RevMan 5.4.1 was used for meta-analysis [21]. Forest plots were generated, and continuous variables were extracted for effect size computation. For studies reporting medians and interquartile ranges (IQR), means and standard deviations (SD) were estimated using the method of Wan et al. (2014) [22]. Approximations applied were:

$$\text{Mean} \approx (Q1 + \text{Median} + Q3)/3$$

$$\text{SD} \approx (Q3 - Q1)/1.35$$

These conversions standardized heterogeneous data for meta-analysis. Baseline values were pooled across full cohorts, while follow-up outcomes were stratified by syndrome status. Longitudinal comparisons were made by converting group-specific medians and IQRs into means and SDs, then pooling via fixed-effects formulas. One study including a mixed population with only 10% PRS patients was excluded due to lack of stratified data.

Analysis

Outcome	Variables
Primary outcomes focused on polysomnography-derived indices of airway obstruction. Five standardized outcomes were:	
Apnea–Hypopnea Index (AHI): number of apneas/hypopneas per sleep hour, an objective marker of obstruction severity.	
SpO ₂ nadir: lowest oxygen saturation during sleep, reflecting hypoxemia burden.	
Sleep efficiency: ratio of total sleep time to time in bed; reductions suggested disrupted sleep from airway obstruction [23].	
ETCO ₂ : elevated end-tidal CO ₂ indicated hypoventilation; reduction after surgery reflect improved ventilation [23].	
Polysomnography composite measures: including apnea indices and oxygen desaturation profiles.	
Secondary outcomes included oxygen desaturation index (ODI), arousal index, sleep architecture, REM/non-REM parameters, hospitalization duration, and intervention-related complications. These were inconsistently reported but summarized descriptively in the appendices.	
Meta-Analysis	

A random-effects model was used because it accounts for variability both within and between studies, acknowledging potential differences in populations, interventions, and methodologies across the included studies. This approach provides more generalized and reliable estimates, especially in the presence of significant heterogeneity, as expected in clinical research. Heterogeneity among studies, representing the variability in effect sizes, was assessed using the I^2 statistic and a chi-squared test for heterogeneity. A P-value of <0.1 was considered statistically significant for heterogeneity, and an I^2 value greater than 50% was interpreted as substantial heterogeneity. This careful approach to data extraction and heterogeneity assessment aimed to ensure robust, reliable results despite potential limitations in the reported data. The left side of the graph represented the [intervention] and the right represented [control] groups. The diamond corresponds to the mean overall effect size of the analysis.

Continuous data were extracted, and coherent outcomes were pooled in a single-arm meta-analysis. The results of the meta-analysis were presented in forest plots, and the potential bias across studies was assessed using funnel plots for all outcome variables.

Bias Assessment

The risk of bias was assessed via the methodology explained earlier. The results of the analysis were determined and presented as a “traffic lights” plot. Further, a summary of the collective risk was calculated and presented as a plot (Figure 2).

RESULTS

Based on the PICOS scheme, 17 studies were included in the final sample. Out of 17, 3 studies reported CM, 6 reported MDO, 2 studies investigated the role of cleft repair, 2 studies collected data on TLA, 3 studies discussed modified palatal plates, 1 study compared all three methods (CM/TLA/MDO), and 1 study further reported the role of surgical osteotomies prior to MDO in pediatric patients under the age of 12 months.

Non-Surgical/ Conservative Management

3 out of 17 studies reported descriptive data on conservative management (CM). Ehsan Z et al. (2019) [26] reported that all the neonates with PRS and OSA, treated conservatively, had an improvement in OAH with advancing age with the median age of OSA resolution at 15 months. Prone positioning and nasopharyngeal tube (NPT) use were considered the modalities for conservative treatment. Another study, Khansa et al. (2023) compared all three modalities, i.e., MDO vs. TLA vs. CM. The PSG outcomes, especially AHI $<5\%$, were achieved by comparable percentages of patients (TLA 89.5%, MDO 96.6%, CM 84.2%). Da Silva Freitas et al. (2023) [35] showed that the mean apnea-hypopnea index was 3.58 (CAI: 1.08; OAI: 2.50), and the minimum oxygen saturation averaged 85%. Da Silva Freitas et al. (2023) followed 56 Pierre Robin Sequence patients under conservative care; in 21 undergoing polysomnography, mean AHI was 0.93 events/hour (CAI 0.3; OAI 0.6), with minimum oxygen saturation averaging 92%, indicating mild residual obstruction. Conservative management showed significant improvement on OAH (events/hr), improving respiratory symptoms in patients. However, long-term outcomes were not reported because the sample size was relatively small and individual patient records were not available 12 months after the postoperative period. All studies investigating the efficacy of CM supported its inclusion in the management algorithm for PRS in all infants and neonates presenting with upper airway obstruction before proceeding to a surgical alternative.

Surgical Management

1. Mandibular Distraction Osteogenesis (MDO)

Seven studies discussed the role of MDO in patients with PRS and all suggested a positive impact in all eligible patients who underwent the surgical procedure. MDO did not only improve obstructive symptoms, but also reduced short-term and long-term complications, such as apneic episodes, cyanosis, and feeding difficulties [34][36]. One of the studies, Edgar Soto et al. (2021) [29], further reported that after MDO, 83% ($n=24/29$) of the

subjects achieved a positive feeding outcome and 86% (n=25/29) achieved a positive airway outcome with no statistical significance between syndromic PRS and isolated PRS ($P = 0.4369$). Nevertheless, no studies reported a significant impact on weight gain in all patients who underwent MDO.

2. Tongue-Lip Adhesion (TLA)/ Palatoplasty

Of 17 studies, only 2 provided both descriptive and quantifiable data on TLA [32] [36]. The combined effect of TLA on all participants showed that all sleep respiratory parameters improved after TLA prior to palatoplasty ($P \leq 0.050$). All PSG parameters remained significantly improved after palatoplasty compared to preoperative values.

3. Modified Palatal Plates

A total of 3 studies investigated the role of palatal plates for patients to attenuate the risks associated with prolonged obstruction, such as early tracheostomy, or long-term NG insertion. Poets CF et al. (2017) [27] included a total of 75 patients, who received individualized hard acrylic palatal plates (PEBP) after polygraphic sleep studies and maxillary casting. The mixed-obstructive apnea index decreased from 15.9 to 0.7 in the 32 infants who underwent a successful 3-month follow-up sleep study. Similarly, the median MOAI decreased from 8.5 (range 0.3–76.0) at admission to 1.1 (0.0–5.2) at discharge ($p < 0.001$), in the study conducted by Müller-Hagedorn et al. (2017) [28]. However, 31 children received only a Tübingen Palatal Plate (TPP), and 5 received additional continuous positive airway pressure (CPAP) or a high-flow nasal cannula. Choo H et al. (2024) employed the nonsurgical methods of treatment using the Stanford Orthodontic Airway Plate (SOAP), which further showed that the mean obstructive apnea-hypopnea index (95% confidence interval) decreased from 39.3 events/h (32.9, 45.7) to 12.2 events/h (6.7, 17.7) ($P < .001$). Interestingly, all patients avoided mandibular distraction osteogenesis or tracheostomy following SOAP. The modified palatal plate treatment demonstrated a potential utility before surgical interventions for neonates with Robin sequence.

4. Cleft Repair

We found limited evidence in literature concerning cleft repair in patients with RS. The 2 studies that reported cleft repair showed little to no advantage in improving respiratory symptoms [37][40]. However, it is worth noting that individual stratification was not consistently reported across the studies, and PSG outcomes were not followed up in all patients. Assessment of saturation demonstrated higher mean SpO₂ across the group from initial neonatal admission to discharge ($p < 0.002$)

Meta analysis of the interventions

a. Mandibular Distraction Osteogenesis

A total of 5/17 studies discussed the role of MDO in the management algorithm of PRS in infants and neonates. The data collected for the analysis was used from pre-intervention (pre-operative period), specifically at the time of admission. The post-intervention data included the measurement of respiratory outcomes immediately in the post-operative window or within 7 days to <3 months from intervention. The forest plots for the analysis are provided in the figures below (Figure 3 – 7).

01. OAH I - a total of 4 studies reported mean OAH I scores for patients with PRS. As evident from the graph, all 4/4 (100%) studies showed an improvement in obstructive apnea, and significant symptom resolution. The overall effect size for the analysis was estimated to be -36.29 [CI=95% (-43.39, -29.18)]. The $I^2=0\%$ indicates low risk of bias and low heterogeneity in the outcome, with $\text{Chi}^2=2.60$, $\text{df}=3$. Hence, all the evidence suggested that MDO significantly improved the mean OAH I across all populations affected by PRS ($p < 0.00001$). [Figure 3]

We further tested the studies for the individual risk across all domains. The dots represent the estimated heterogeneity. The dots closer to the midline represent a low risk of bias. The funnel plot for this analysis is provided below. [Figure 4]

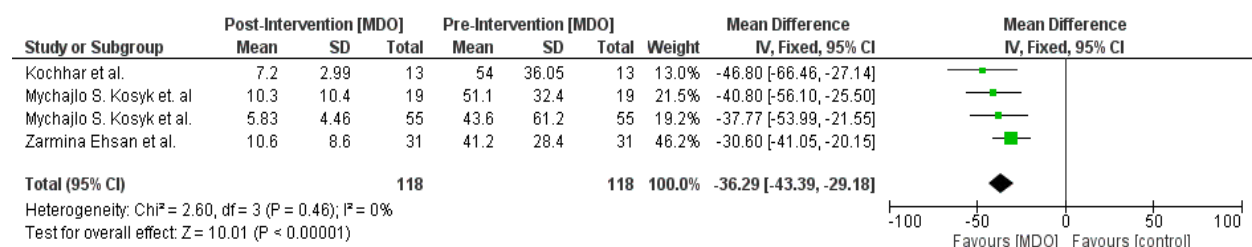


Figure 3: Forest plot for mean OAH I scores before and after MDO in infants and neonates with PRS

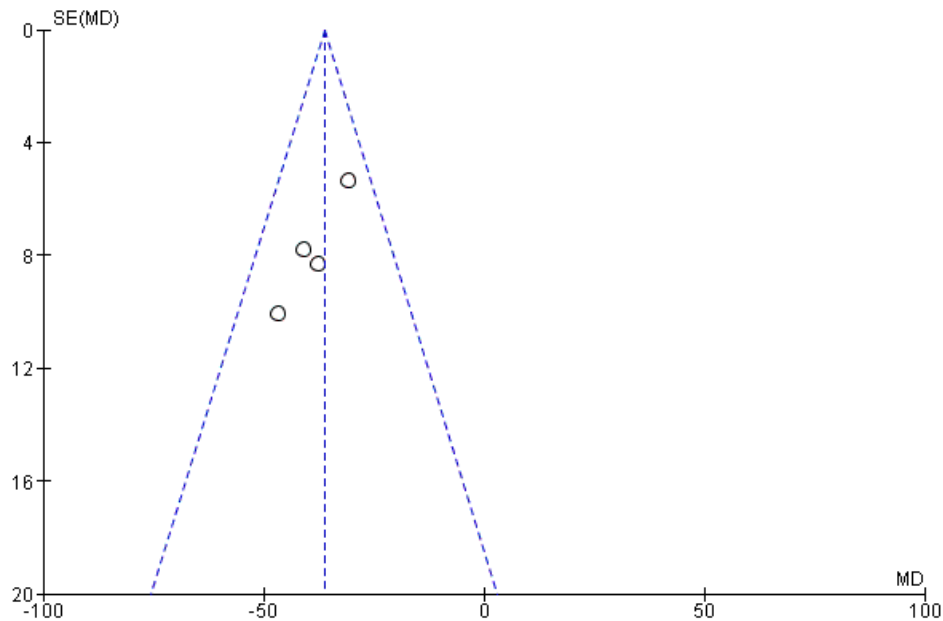


Figure 4: Funnel plot for OAH after MDO

02. AHI - Mean AHI scores were only reported across 2/7 studies investigating surgical management of PRS. Due to a high heterogeneity, the results were inconclusive. However, the overall effect size of the individual studies showed a significant change in AHI in patients postoperatively ($p < 0.00001$). [Figure 5]

The funnel plot for the analysis showed significant heterogeneity in the analysis with a low overall risk of bias in the individual studies. (Supplemental figure)

03. SpO₂ Nadir —patients representing persistently low oxygen saturations during sleep guide the need for surgical intervention such as mandibular distraction osteogenesis to prevent hypoxic complications and ensure adequate gas exchange. A total of 5 studies investigated the change in SpO₂ nadir before and after MDO. All the studies estimated a significant increase in the mean SpO₂ across all the patient population, with an overall effect size of -12.91 [CI=95% $(-15.11, -10.71)$], and comparable heterogeneity. The analysis concluded a positive impact of MDO on SpO₂ nadir ($p < 0.00001$). (Figure 6)

The overall risk and individual risk of bias was calculated to be low with insignificant heterogeneity in the studies. (Supplemental figure)

04. ETCO₂ - Another outcome variable of importance, ETCO₂ is clinically relevant to patients with PRS who have undergone MDO within a 12-month period after birth. A decrease in end-tidal CO₂ capacities advocate an improvement in oxygen retention, and improved oxygen saturations, and consequently improved airway obstruction. The sample sizes across the studies were comparable. The $I^2 = 52\%$ represented an increase in heterogeneity. However, the p-value remained significant ($p < 0.00001$). The analysis concluded that MDO significantly improved the ETCO₂ volumes in infants and neonates, thus relieving airway obstruction. (Figure 7) The funnel plot representing a low overall risk of bias was also created. (See appendix)

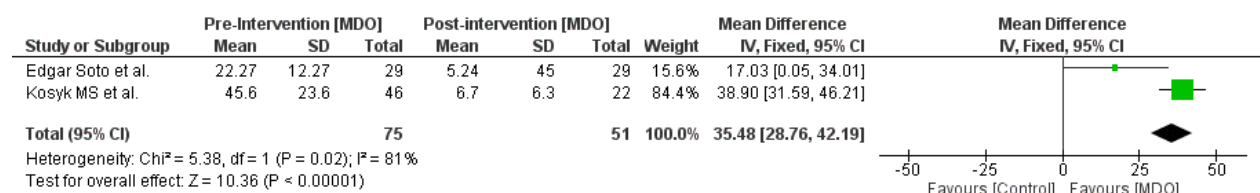


Figure 5: Forest plot for mean AHI scores in patients with PRS after MDO

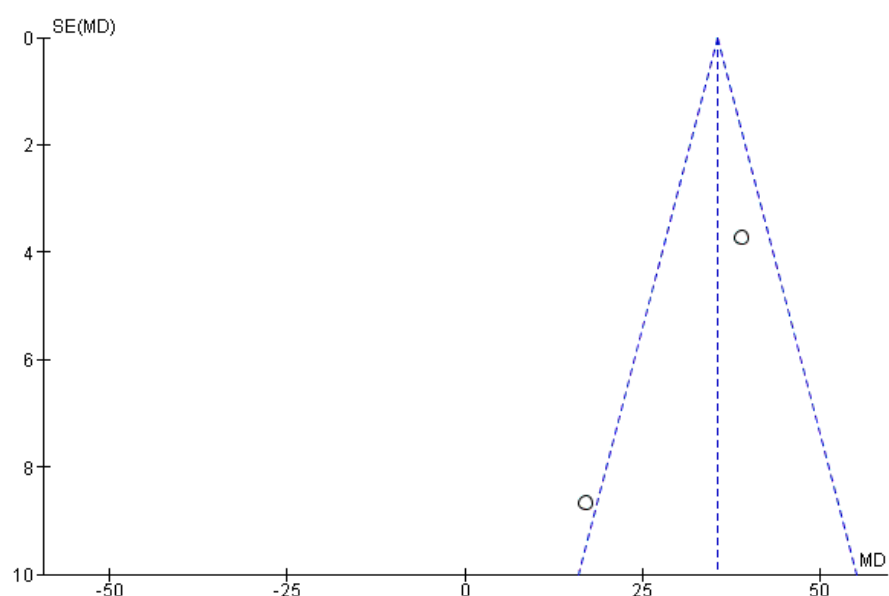


Figure 6: Funnel plot for AHI in patients with PRS

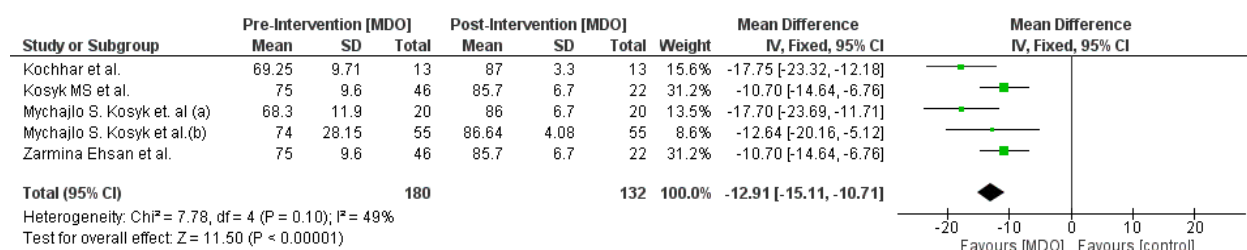


Figure 7: Funnel plot for SpO₂ Nadir scores before and after MDO

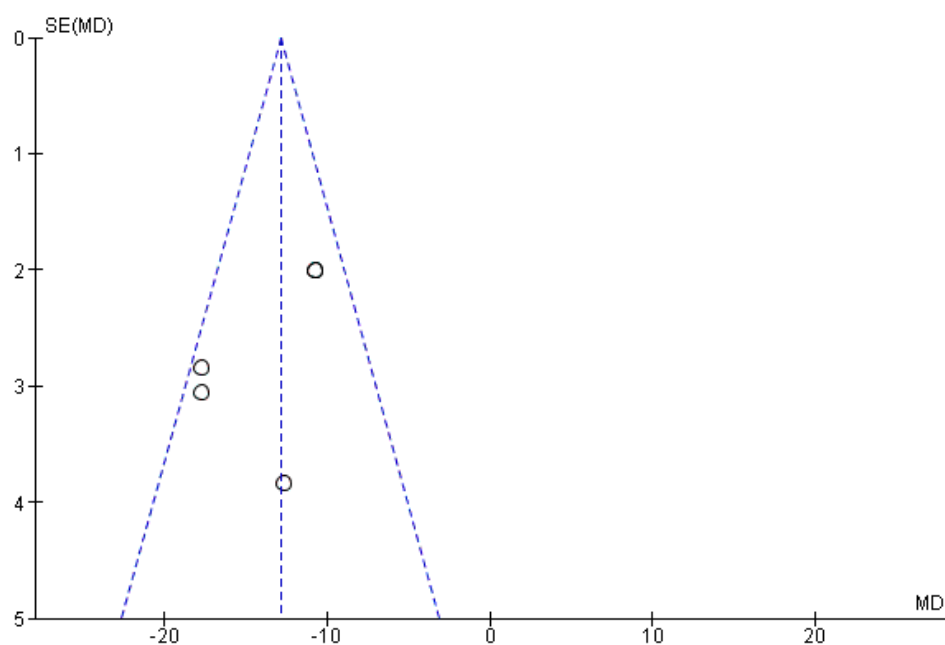


Figure 8: Funnel plot for studies investigating mean SpO₂ Nadir

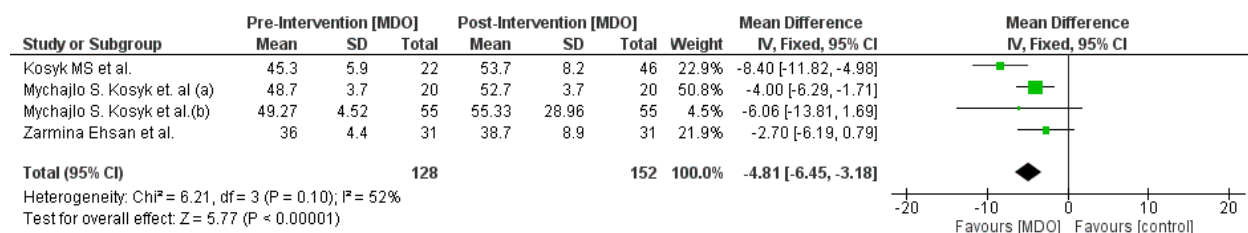


Figure 9: Forest Plot for ETCO₂ volume pre- and post-intervention

05. Sleep Efficiency - only 2 studies reported sleep efficiency out of 17. Consequently, the meta-analysis for this outcome was inconclusive. The p-value was large (p=0.02). Interestingly, Kocher et al. was the only study across the reported evidence that demonstrated a decrease in sleep efficiency after MDO. (Supplemental table)

b. Modified Palatal Plates

Modified palatal plates are often employed when conservative treatment fails to alleviate respiratory symptoms and help in surgical planning by closely monitoring treatment response and avoiding complications during a 3-month follow-up period. Choo H et al. (2024) employed nonsurgical treatment methods using SOAP; the study by Poets et al. investigated the role of a hard acrylic plate (PEBP) [27]; and Muller-Hagedorn studied modified palatal plates and their impact on mandibular anatomy and airway patency [28]. Three outcome variables, i.e., weight gain, desaturation index, and MOAI, were estimated. The studies compared the use of standard palatal and orthodontic plates against conservative management, which included prone positioning and NGT insertion.

The reported data was approximated because no two studies reported follow-up data within the same period. For example, Poets et al. reported outcome data at discharge, and Choo et al. reported data at discharge as well as at 3-month follow-up. The change in MOAI and ODI scores was statistically significant with all 3 interventions (p<0.0001). (Figure 8)

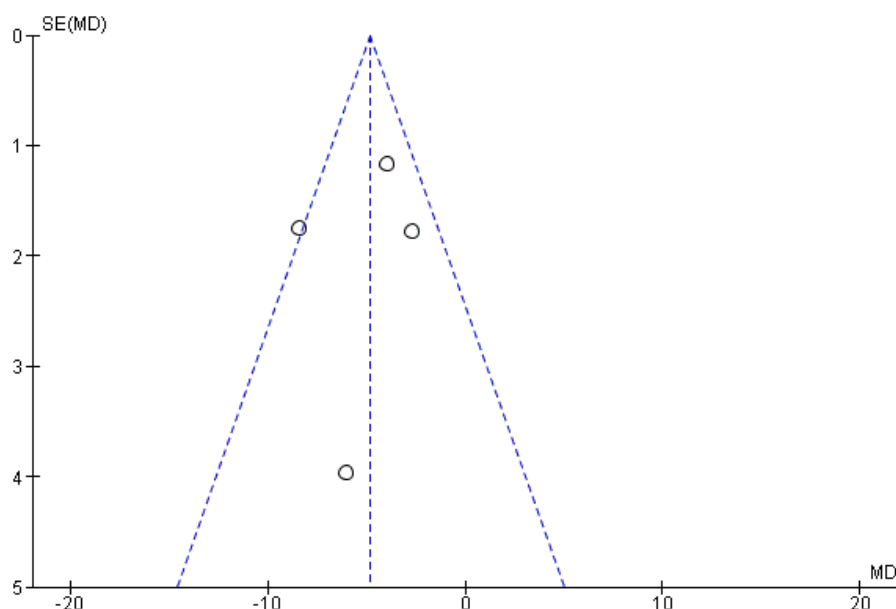


Figure 10: Funnel plot for bias across the studies investigating ETCO₂

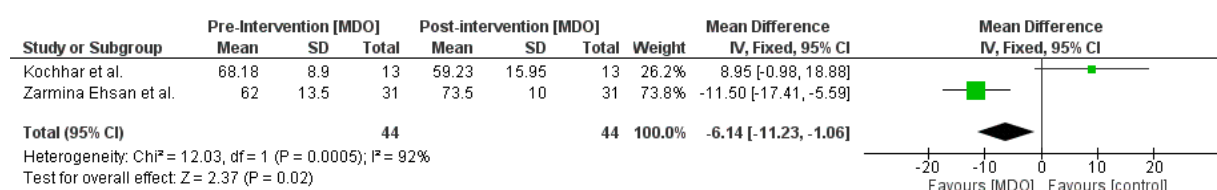
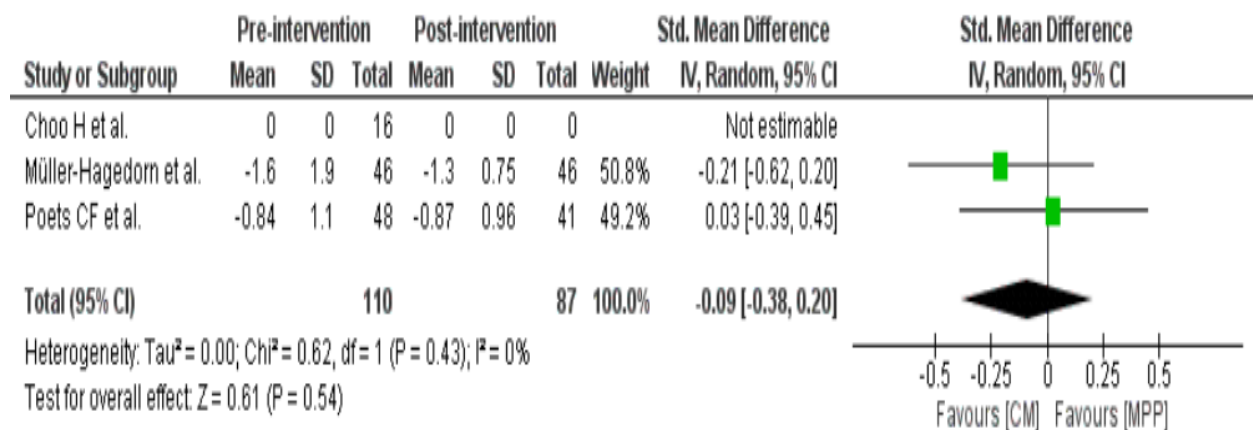
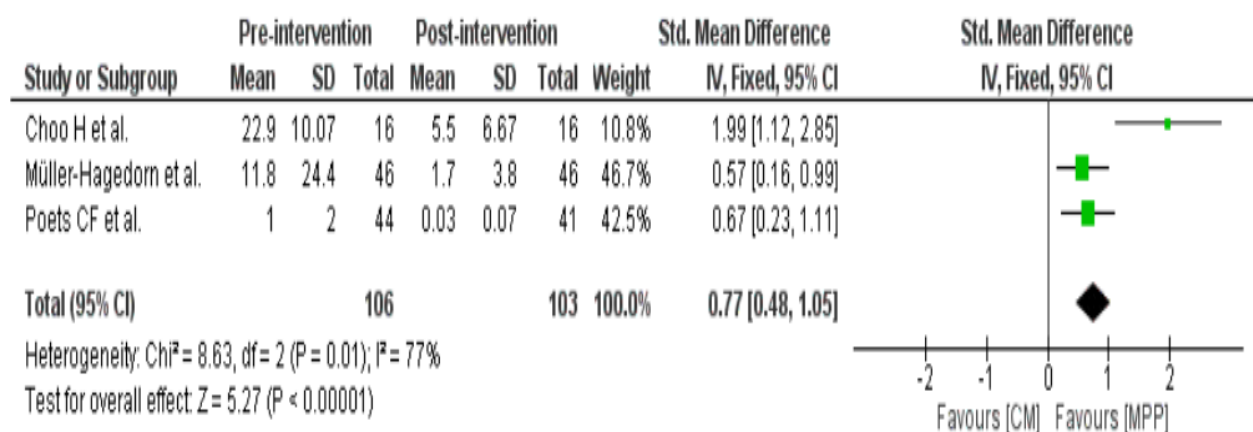


Figure 11: Forest plot for Sleep Efficiency

Weight Gain



ODI - Desaturation Index



MOAI - Mixed Obstructive Apnea Index

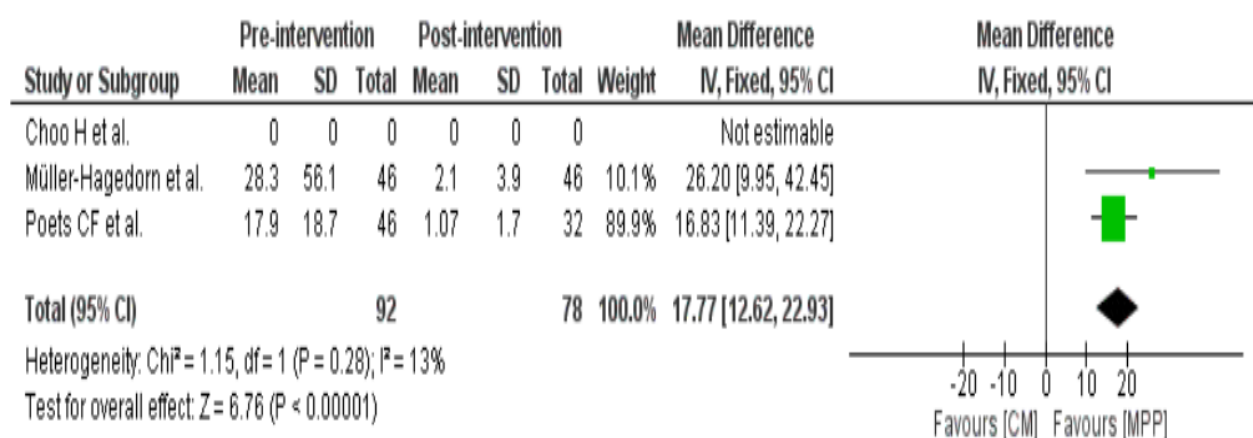


Figure 11: Forest plots for comparison Modified Palatal and Orthodontic Plates

Table 1: Study characteristics (n=17)

<i>Author ID</i>	<i>Location</i>	<i>Study design</i>	<i>Mean age</i>	<i>Sample Size</i>	<i>Population</i>	<i>Intervention</i>	<i>Population characteristics</i>	<i>Key findings</i>	<i>Conclusion</i>
<i>Kochhar et al. (2022)</i>	New York	Retrospective	1.47 (1.09) mo	13	Infants ≤1 yr with severe UAO	MDO	Severe OSA: OAH1 ≥10/h, O2 nadir <90%	Median OAH1 ↓ from 33 to 2.35/h; O2 nadir ↑ from 73% to 90%	PSG guides MDO extent for obstruction relief
<i>Resnick (2017)</i>	USA	Retrospective	86 d	17	Neonates with PRS refractory to non-invasive care	MDO (VSP osteotomies)	Linear, inverted-L, multiangular designs	80% complete OSA remission, minimal residual OSA	MDO with VSP effective for neonatal airway
<i>Ehsan et al. (2019)</i>	Ohio	Retrospective cohort	0.9 ±0.7 mo	21	PRS neonates with PSG + follow-up ≥12 mo	Conservative	No prior surgery	OAH1 improved with age; OSA resolved median 15 mo	Conservative therapy may allow spontaneous resolution; long-term growth effects unclear
<i>Poets et al. (2017)</i>	Germany	Retrospective cohort	5.0 (5.4) wk	75	Infants <1 yr with RS	PEBP	Individualized plates with endoscopic adjustment	Apnea score ↓ 15.9→0.7; desaturation index normalized	PEBP effective for OSA relief and weight gain
<i>Müller-Hagedorn et al. (2017)</i>	Germany	Retrospective cohort	<3 mo	46	Infants with syndromic RS	Modified palatal plates + MOT	56/68 completed treatment	MOAI ↓ 8.5→1.1; 5 required CPAP	Modified plates safe, effective for airway obstruction
<i>Soto et al. (2021)</i>	Alabama	Retrospective cohort	78 d (2–712)	29	iPRS and sPRS neonates	MDO	Bilateral, for decannulation/avoiding trach	83% feeding, 86% airway success; no sPRS vs iPRS difference	MDO effective; sPRS carries higher morbidity
<i>Kosyk et al. (2022)</i>	Philadelphia	Prospective cohort	37 (23–105) d	20	RS with severe OSA	DISE + MDO	Pre/post MDO laryngoscopy	OAH1, O2 nadir, airway width improved significantly	DISE + MDO improves obstruction, oxygenation, intubation
<i>Shen et al. (2021)</i>	New York	Retrospective	63.8 d	12	Neonates with severe PRS	MDO	5-yr review	AHI ↓ 34.8→7.3 (p=0.0024); no tracheostomy needed	MDO safe and prevents trach in high-risk infants
<i>Khansa et al. (2023)</i>	Ohio	Retrospective cohort	29/21/27 d	67	Neonates with ≥1 yr FU, baseline + FU PSG	TLA / MDO / CM	19 TLA, 29 MDO, 19 CM	FU AHI comparable (MDO 1.3, TLA 4.2, CM 4.5); weight stable	All 3 modalities effective; each has role in RS care
<i>Ehsan et al. (2020)</i>	Kansas City	Retrospective cohort	13 (5–34) d	31	Neonates with severe OSA	MDO	Pre/post PSG	OAH1 ↓ 38.3→9.4	PSG before/after MDO recommended for objective tracking

<i>Kosyk et al. (2022)</i>	Philade lphia	Retrospectiv e cohort	37 (17– 81) d	129	RS with TBAO	MDO ± CPAP	FU PSG	OAHl ↓ in both groups; CPAP duration ~1 yr	CPAP effective adjunct, esp. in syndromic RS post-MDO
<i>Da Silva Freitas et al. (2023)</i>	Brazil	Retrospectiv e descriptive	1.5 ±2.09 mo	21	PRS neonates	Conservative (prone, NPT)	42 d avg NPT, some gastrostomy	AHI 3.58; O2 nadir 85%; palatoplasty at 20.7 mo	Conservative therapy reduces OSA; good outcomes in PRS
<i>Kosyk et al. (2021)</i>	Philade lphia	Retrospectiv e	1.4 (1.6) mo	80	PRS with cleft palate repair	MDO vs TLA	Groups matched except more syndromic in MDO	Both improved PSG parameters pre/post palatoplasty	Both safe/effective prior to palatoplasty
<i>Van De Velde et al. (2024)</i>	Netherl ands	Retrospectiv e	57.3 (12.0) d	53	iRS (n=35) + syndromic (n=18)	Cleft repair	Compared to iCP infants	Higher PRD in RS vs iCP (OR=4.16)	RS infants at higher PRD risk
<i>Blanc et al. (2021)</i>	France	Retrospectiv e	7.2 ±3.4 mo	150	PRS children	Conservative (groups by severity)	Group 1: none; 2: prone; 3: NT/surgery	Oral feeding delayed (1 vs 11 vs 39 d, p<.0001); 53% NG tube; 8% gastrostomy	Conservative management feasible, but feeding support common
<i>Choo et al. (2024)</i>	Califor nia	Retrospectiv e	1.1 (0.3– 5.1) mo	16	Neonates with RS + cleft	SOAP	PSG	OAHl ↓ 39.3→12.2; O2 nadir ↑ 79.9%→88.2 % (p<.001)	SOAP improves PSG indices; potential pre- surgical option
<i>De Blacam et al. (2024)</i>	Ireland	Case series	3–6 mo	69	RS infants with cleft palate				

DISCUSSION

Our review of the 17 studies demonstrates that both non-surgical and surgical interventions effectively relieve upper airway obstruction (UAO) in infants with Pierre Robin sequence (PRS). Conservative measures, particularly prone positioning and nasopharyngeal airway (NPA), were associated with marked reductions in obstructive apnea–hypopnea indices (OAH). Surgical strategies, especially mandibular distraction osteogenesis (MDO), produced the most significant improvements in polysomnographic (PSG) parameters. Across modalities, a high proportion of infants achieved residual apnea–hypopnea index (AHI) <5: TLA 89.5%, MDO 96.6%, conservative therapy 84.2%. These findings confirm earlier reports that most PRS infants can avoid invasive surgery. For example, a five-year retrospective review showed that 96% of infants managed with prone positioning and NPA required no surgery [41], and Haas et al. reported that nearly two-thirds of infants were successfully treated without operative intervention [42].

The pooled analysis reinforces the effectiveness of conservative strategies as initial treatments. Positioning and NPA often stabilize infants until spontaneous mandibular growth occurs, aligning with international recommendations for stepwise care. However, when surgical intervention is necessary, MDO consistently outperforms other techniques. MDO produced highly significant improvements in OAH, AHI, oxygen saturation nadir, and end-tidal CO₂. Zhang et al. (2021) reviewed 693 PRS patients and found that 95% of those managed with MDO avoided tracheostomy compared with 89% with tongue–lip adhesion (TLA) [43]. Feeding outcomes also favored MDO, with 87% achieving full oral feeding versus 70% for TLA. Khansa et al. similarly demonstrated a postoperative mean AHI of 1.5 following MDO, superior to TLA or conservative approaches [44]. Our analysis confirms MDO’s strong efficacy, though we observed no significant gains in weight or sleep efficiency, consistent with Runyan et al., who found no long-term nutritional or speech differences between surgical and non-surgical groups. Importantly, both Runyan and our synthesis showed that tracheostomy is associated with poorer outcomes and should be reserved for complex cases due to higher morbidity.

TLA retains value for infants with mild-to-moderate obstruction. Camacho et al. reported that TLA halved mean AHI (30.8 to 15.4 events/hour) and improved oxygen nadir (75.8% to 84.4%). In our review, 89.5% of TLA-treated infants achieved AHI <5, but residual or recurrent obstruction was more common after TLA than MDO (22–45% vs. 4–6%) [43]. These data indicate that while TLA can be effective, MDO provides more durable relief. Emerging non-invasive devices broaden treatment options. Dental-orthodontic appliances such as the Stanford Orthodontic Airway Plate (SOAP) and the European Pre-Epiglottic Baton Plate (PEBP) demonstrated promising outcomes. Choo et al. reported that SOAP reduced the mean obstructive AHI from 39.3 to 12.2 events/h, the obstructive apnea index from 14.1 to 1.0, and improved the oxygen nadir from 79.9% to 88.2% [44]. None of the infants subsequently required MDO or tracheostomy. Poets et al. found an 85% median reduction in mixed–obstructive apnea index after PEBP insertion [27]. Our pooled analysis confirmed statistically significant improvements ($p < 0.001$) with both devices, supporting their use as first-line or adjunct therapies. Properly designed palatal plates may achieve outcomes comparable to surgery and remain underutilized.

The strengths of this meta-analysis include its comprehensive search across multiple databases, use of PRISMA methodology, and reliance on objective PSG outcomes. Inclusion of both surgical and non-surgical modalities allowed comparison across the full spectrum of interventions. Our findings are consistent with Runyan et al. (2018) [45] and Pendem et al. (2024) [46], further validating the pooled results.

Future research should aim for standardized outcome definitions (e.g., uniform AHI thresholds) and longer-term follow-up. Prospective multicenter cohorts or ethically designed randomized trials are needed to clarify patient selection for different therapies. Further investigation into predictors of severity, refinement of orthodontic devices, and integration of PSG metrics into treatment algorithms are priorities. Cost-effectiveness analyses would also inform guideline development. As emphasized by Poets et al. [27], international collaboration is essential to accumulate robust data on this rare condition. Our meta-analysis demonstrates that conservative measures successfully stabilize most infants with PRS, but MDO provides the most reliable long-term airway correction when surgery is required. TLA and palatal appliances also have defined roles, though tracheostomy should be limited to refractory cases. These findings highlight the importance of individualized, multidisciplinary management and provide a foundation for evidence-based clinical guidelines in PRS airway care.

Limitations

This meta-analysis has several limitations. Significant heterogeneity was present across studies in diagnostic criteria, outcome measures, and intervention protocols, limiting comparability. Most studies were retrospective case series or cohorts, restricting causal inference due to selection and reporting bias. Polysomnographic outcomes, including AHI and SpO₂ nadir, were inconsistently reported, hindering uniform effect size analysis. Sample sizes were generally small, with most studies conducted in single centers, reducing external validity. Furthermore, long-term outcomes such as speech, neurocognition, and quality of life were rarely assessed, preventing evaluation of durability.

CONCLUSION

This meta-analysis shows that a stepwise, individualized approach to airway management in PRS is effective and evidence based. Routine screening for associated abnormalities in neonates is recommended. Early recognition and management of respiratory and feeding difficulties are essential, given their frequency and potential severity, particularly in syndromic cases. Conservative strategies—such as prone positioning, nasopharyngeal airways, and palatal plates (PEBP, SOAP)—achieve significant improvements in polysomnographic outcomes and reduce the

need for invasive interventions in most patients. Treatment decisions should be based on obstruction severity, feeding status, syndromic involvement, and institutional expertise. Multidisciplinary input remains critical for optimal outcomes. Future prospective studies and international registries will be vital in refining treatment algorithms, identifying ideal candidates for each modality, and optimizing long-term outcomes for infants with PRS.

Declarations of interest

Ethical approval

Not available

Acknowledgment

Not available

Data availability

Competing Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper."

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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