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Active Presurgical Infant Orthopedics for Unilateral Cleft Lip and Palate: Inter-Center Outcome Comparison of Latham, Modified McNeil, and Nasoalveolar Molding

Michelle Kornbluth, D.M.D., M.Sc., F.R.C.D.(C.)¹, Richard E. Campbell, D.M.D., M.S.², John Daskalogiannakis, D.D.S., M.Sc., F.R.C.D.(C.)³, Elizabeth J. Ross, D.D.S.⁴, Patricia H. Glick, D.M.D.⁵, Kathleen A. Russell, D.D.S., M.Sc.⁶, Jean-Charles Doucet, D.M.D., M.D., M.Sc.⁷, Ronald R. Hathaway, D.D.S., M.S.⁸, Ross E. Long Jr., D.M.D., M.S., Ph.D.⁹, and Thomas J. Sitzman, M.D., M.P.H.¹⁰

¹Clinical Orthodontic Fellow, Department of Dentistry, The Hospital for Sick Children, Toronto, Ontario, Canada

²Assistant Professor and Director of Orthodontics, Division of Pediatric Dentistry, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, United States

³Staff Orthodontist, The Hospital for Sick Children, and Associate Professor, Department of Orthodontics, University of Toronto, Toronto, Ontario, Canada

⁴Instructor, Department of Dentistry, Boston Children's Hospital, Boston, Massachusetts, United States

⁵Co-Director, Barrow Cleft and Craniofacial Center, Phoenix, Arizona, United States

⁶Professor and Head, Division of Orthodontics, Dalhousie University, and Orthodontist, IWK Cleft Palate Team, Halifax, Nova Scotia, Canada

⁷Assistant Professor, Division of Oral and Maxillofacial Science, Dalhousie University, and Oral and Maxillofacial Surgeon, IWK Cleft Palate Team, Halifax, Nova Scotia, Canada

⁸Professor of Surgery and Pediatrics, Division of Craniofacial Plastic and Reconstructive Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, United States

⁹Director, Lancaster Cleft Palate Clinic, Lancaster, Pennsylvania, United States

¹⁰Staff Surgeon, Division of Plastic Surgery, Phoenix Children's Hospital, Phoenix, Arizona, United States

Abstract

Objective—To compare dental arch relationship, craniofacial form, and nasolabial aesthetic outcomes among cleft centers using distinct methods of presurgical infant orthopedics (PSIO).

Design—Retrospective cohort study.

Corresponding Author: Thomas J. Sitzman, M.D., M.P.H., Division of Plastic Surgery, Phoenix Children's Hospital, 1920 East Cambridge Road, Suite 201, Phoenix, AZ 85006, Telephone: 602.933.0500, Fax: 602.933.4320, tsitzman@phoenixchildrens.com.

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Setting—Four cleft centers in North America.

Patients—One hundred ninety-one children with repaired CUCLP.

Main Outcome Measures—Dental arch relationship was assessed using the GOSLON Yardstick. Craniofacial form was assessed by twelve cephalometric measurements. Nasolabial aesthetics were assessed using the Asher-McDade system. Assessments were performed between 6 and 12 years of age.

Results—The Center that used no PSIO achieved the most favorable dental arch relationship and maxillomandibular relationship, with a median GOSLON score of 2.3 ($p<0.01$) and an ANB angle of 5.1 degrees ($p<0.05$). The proportion of children assigned a GOSLON score of 4 or 5, predictive of the need for orthognathic surgery in adolescence, was 16% at the center which used no PSIO and no secondary surgery, compared to 76% at the centers which used the Latham appliance and early secondary lip and nose surgery ($p<0.01$). The center which used no PSIO and no secondary surgery achieved significantly less favorable nasolabial aesthetic outcomes than the centers using Latham appliance or NAM ($p<0.01$).

Conclusions—Effects of active PSIO are multifaceted and intertwined with use of revision surgery. In our study, centers using either the Latham appliance combined with early revision surgery or the NAM appliance without revision surgery achieved better nasolabial aesthetic outcomes but worse maxillary growth, compared to a center using no PSIO and no secondary surgery.

Keywords

Presurgical infant orthopedics; Cephalometry; Dental arch; Esthetics

INTRODUCTION

Infants born with cleft lip and palate present with significant facial deformities. These deformities involve skeletal and soft-tissue elements of the lips, nose, and facial bones that affect symmetry and esthetics. It is safe to say that there is no consensus on the best approach to treatment of an infant born with a cleft. In fact, there is great variability in protocols of management and surgical interventions among cleft centers (Shaw et al., 2001). Currently, one of the most controversial components of individual protocols is the use of presurgical infant orthopedics.

Any manipulation of the infant's alveolar segments prior to lip and nasal repair is referred to by the umbrella term presurgical infant orthopedics (PSIO). The objectives of PSIO, while neither static nor universally agreed, generally include improving alignment of the child's alveolar segments, facilitating the primary cleft lip and nose repair, and improving the aesthetic outcome of primary repair, ideally without harming facial growth. PSIO can be divided into passive and active devices, although definitions of each type can vary among providers. As applied by the author's in this article, *passive* PSIO utilize an intra-oral appliance (plate) that is fabricated to match the initial alveolar positions without applying active pressure at any point; they achieve reduction of the alveolar cleft width by preventing the tongue from entering the cleft and they prevent collapse of the lateral cleft segment.

Active PSIO use force exerted by the device to actively reposition the alveolar segments to improve alveolar alignment and reduce the width of the cleft before primary surgery. Some types of active PSIO, in particular nasoalveolar molding (NAM), also seek to normalize nasal cartilage shape and elongate the columella. The Dutchcleft randomized controlled trial found that passive appliances do not achieve a sustained improvement in alveolar alignment nor do they improve facial appearance (Prahl et al., 2003, Prahl et al., 2006). Evidence on active PSIO is of much lower quality and much of it is conflicting, yet active orthopedics is used by over 40% of cleft teams in the United States (Sitzman et al., 2008, Uzel and Alparslan, 2011, Sischo et al., 2012).

Multiple types of active PSIO are in use today. The modified McNeil approach consists of an intra-oral acrylic appliance that is progressively reshaped to narrow the cleft width (McNeil, 1950, McNeil, 1956). The Latham approach uses a pin-retained intra-oral appliance with a mechanical screw that is progressively turned to narrow the cleft width (Latham, 1980, Chan et al., 2003). NAM combines the progressively reshaped intra-oral appliance of McNeil with a nasal stent that aims to improve nasal dome projection and position (Grayson et al., 1999, Grayson and Shetye, 2009). All PSIO appliances require at least three months of daily care at home and, in the case of McNeil appliance and NAM, weekly adjustments by an orthodontist or pediatric dentist.

The debate surrounding the benefits of active PSIO has yet to reach a definite conclusion. While the Dutchcleft trial demonstrated that passive approaches provide no sustained benefits, many providers believe that active approaches are substantially different from passive approaches, and thus the trial's findings are not generalizable to current practice. Use of the Latham device has been particularly controversial. Berkowitz et al. (1996) reported that children treated with the Latham and gingiverrhinoosteoplasty (GPP) achieved favorable nasolabial esthetics but substantial midface retrusion, while Chan et al. (2003) reported that midface growth was not affected by use of the Latham appliance. While there is more consistent evidence on the benefits of NAM, evidence is primarily limited to single-center retrospective case series and cohort studies (Barillas et al., 2009, Chang et al., 2010). One prospective non-randomized study found that aesthetic outcomes after cleft lip repair were similar among children who did and did not receive NAM, although children receiving NAM had more severe clefts at the beginning of treatment and thus a greater relative improvement (Broder et al., 2016). In addition to the limited information on the efficacy of each type of active PSIO relative to no orthopedics, there has been no comparison among the different types of active PSIO.

In summary, there is broad utilization of active PSIO in children with cleft lip and palate yet a weak level of evidence to support their efficacy. Furthermore, there are few studies directly comparing clinical outcomes achieved with the different types of appliances. There is thus a pressing need to compare multi-dimensional outcomes across patient cohorts that were treated with each type of appliance therapy. In this study, we compared dental arch relationship, craniofacial form, and nasolabial aesthetic outcomes among centers using four distinct methods of PSIO: Latham, modified McNeil, NAM, and no PSIO. While this inter-center comparison cannot separate the effect of an individual PSIO appliance from the effect of other components of a center's treatment protocol, notably the surgical protocol and the

operator skill, the comparison does contribute to our understanding of whether a specific type of active PSIO enables a center to achieve better treatment outcomes than centers using alternative types of PSIO.

METHODS

Study Design

A multi-institutional retrospective cohort study was performed to compare treatment outcomes at four treatment centers each using a distinct approach to PSIO. Children received all cleft-related treatment at one of four treatment centers, labeled Center 1, 2, 3, and 4. Care at each center was delivered according to pre-specified treatment protocols, adherence to which was confirmed by review of treatment records. Center 4 assembled two cohorts, one cohort from children who received PSIO treatment using a modified McNeil protocol prior to lip repair (Center 4-IO), and a second cohort from children who received nasoalveolar molding prior to lip repair (Center 4-NAM).

Institutional review board approval was obtained at each site prior to the initiation of data collection.

Population

Medical records were reviewed to identify children meeting the following inclusion criteria: Caucasian, complete unilateral cleft lip and palate, receipt of primary cleft lip and palate repair in infancy at the participating center, available dental models, lateral cephalograms, and/or facial photographs obtained between age 6 and 12 years of age at the participating center, and treatment during a calendar period when treatment protocols at the participating center were stable and consistent. Exclusion criteria included the presence of a Simonart's band or a syndromic diagnosis.

Medical records at each center were then reviewed to collect information on subject demographics and treatment history. Information included sex, use of PSIO, surgeon performing the primary lip and palate repairs, occurrence of any secondary lip, nose, or palate surgery, and age at secondary surgery(s).

Collection of Records and Assessment of Outcomes

Clinical records were collected from existing archives at each center. Records included dental models, lateral cephalograms, and facial photographs obtained when children were between 6- and 12-years old. Records were obtained prior to any orthodontic treatment, palatal expansion, incisor alignment, or secondary bone grafting. For each outcome measure evaluated, raters were blinded to treatment center, treatment history, and patient demographic information.

Dental Arch Relationship—Each child's dental models were duplicated in a standard method to prevent identification of the center from appearance of the model. Models from all centers were assembled into a single set and then randomized in order of presentation. Models were rated by six experienced and calibrated raters using the Goslon Yardstick

(Mars et al., 1992). During the ratings, raters had the opportunity to compare each study model with the GOSLON Yardstick – a set of reference models established from the original GOSLON study to indicate discrete examples for each point on the scale. Ratings were performed twice, on separate days, by the same panel of raters. Between the first and second rating session, all models were re-randomized in order of presentation.

Cephalograms—Lateral cephalograms were produced using the cephalometric equipment available at the respective centers, and acquired in either a hardcopy or digital format. Conventional cephalograms were scanned at a resolution of 300 dpi using an Epson Expression 1680 scanner. Digital images were cleared of all center- and subject-identifiers, imported into Dolphin imaging software (version 11.7), and calibrated. Twenty-two landmarks were digitized per radiograph (Figure 1). All radiographs were digitized twice on the same screen by a single investigator with four months between the two digitations. Each tracing was reviewed for accuracy by a professional digitizer with 35 years of experience. A total of seven hard-tissue and five soft-tissue cephalometric measurements were evaluated. Only angular and ratio measurements were undertaken to avoid error from differential magnification of the films.

Facial Photographs—Facial photographs consisting of frontal and cleft-side lateral images were converted to digital format as necessary, cleared of all center- and subject-identifiers, and cropped in trapezoidal format to include only the nasolabial region (Mercado et al., 2011). Photographs from all centers were assembled into a single set and then randomized in order of presentation. Photographs were rated by six experienced and trained raters using the system of Asher-McDade et al (1992), as modified by Mercado et al (2016). Each rater assigned ratings for each component of the scale: nasal frontal form and symmetry, nasal profile, and shape of the vermillion border. During the ratings, raters used the Q-SORT methodology to compare each study photograph with a set of reference photographs previously selected to indicate discrete examples for each point of the scale (Mercado et al., 2016, Stoutland et al., in press). Ratings were performed twice, on separate days, by the same panel of raters. Between the first and second rating session, photographs were re-randomized in order of presentation.

Statistical Analysis

Intra-rater and inter-rater reliability were evaluated for the GOSLON ratings using weighted kappa statistics. For each model, twelve (six raters, two sessions) individual ratings were made using the five-point scale. For subsequent analysis, each model's score was assigned as the mean from these twelve individual ratings. Among-center comparisons of GOSLON scores were performed using the Kruskal-Wallis test, with Bonferroni adjustment for multiple comparisons. Analyses of the nasolabial ratings were conducted in a manner similar to the GOSLON ratings. Comparisons of predicted need for orthognathic surgery (GOSLON score of 4 or 5) were performed with the Fisher exact test. Intra-rater reliability was evaluated for cephalometric measurements using the intra-class correlation coefficient. Among-center comparisons of cephalometric measurements were performed using analysis of variance (ANOVA), with Tukey adjustment for multiple comparisons. Statistical significance for all analyses was set at $p < 0.05$.

RESULTS

Center-Specific Treatment Protocols

Cleft centers were selected to compare diverse approaches to PSIO. The approaches used at participating centers included: no PSIO (Center 1), Latham appliance (Centers 2 and 3), nasoalveolar molding (Center 4-NAM), and modified McNeil appliance (Center 4-IO). Centers 2 and 3, the two centers using the Latham appliance, routinely performed secondary cleft lip and nasal surgery prior to age seven. All other centers delayed secondary cleft lip and nasal surgery until late adolescence. Details of the treatment protocols for each center are shown in Table 1.

Patient Characteristics

The study cohort included 191 children from four cleft centers in North America. Children were predominantly male ($N = 121$, 63%). All children were born with non-syndromic complete unilateral cleft lip and palate. All children underwent primary cleft lip and palate repair before two years of age. Dental models, cephalograms, and nasolabial photographs were available for 138 (72%), 124 (65%), and 130 (68%) children, respectively. Patient characteristics availability of records, and rates of secondary surgery for each center are shown in Table 2.

Dental Arch Relationship

Dental arch relationship was compared among centers using dental models obtained in mixed dentition and the GOSLON rating system. Intra-rater reliability was excellent for all raters (mean weighted kappa, 0.88; range 0.83–0.93). Inter-rater reliability was also excellent (weighted kappa, 0.87). Distribution of GOSLON scores by center are shown in Figure 2A.

Children treated at Center 1, which used no PSIO, achieved the most favorable dental arch relationship with a median GOSLON score of 2.3 ($p < 0.01$, Kruskal-Wallis). The proportion of children assigned a GOSLON score of 4 or 5, predictive of the need for orthognathic surgery in adolescence, was 76% at Centers 2 and 3 which used the Latham appliance and early secondary lip and nose surgery, 47% at Center 4 which used either NAM or modified McNeil but delayed secondary surgery, and 16% at Center 1 which used no PSIO and delayed secondary surgery ($p < 0.01$, Fisher exact).

Cephalometrics

The intra-class correlation coefficient for hard and soft tissue cephalometric measurements was 0.93 and 0.82, respectively. Results of the cephalometric comparisons are shown in Table 3. Children treated at Center 1, which used no PSIO, achieved a significantly larger mean ANB angle than children treated at Centers 2 and 3, which used the Latham appliance ($p < 0.05$) (see Figure 2B). The mean ANB angle at Center 1 was also larger than the mean angle for children treated with NAM appliance at Center 4 ($p < 0.05$). Similarly, soft tissue A'-N'-B' angle was larger at Center 1 than at all other centers ($p < 0.05$).

Differences in ANB were principally attributable to maxillary projection: Center 1 had the largest SNA angle (79.99°) and Center 2 had the smallest SNA angle (74.81°) ($p<0.05$).

Nasolabial Appearance

Nasolabial appearance was evaluated in three domains: nasal frontal form and symmetry, nasal profile, and shape of the vermillion border. Intra-rater reliability was very good to excellent for all raters in all domains (mean weighted kappa, 0.80; range 0.72–0.93). Inter-rater reliability was good, with weighted kappa of 0.64 for nasal frontal form and symmetry, 0.63 for nasal profile, and 0.60 for vermillion border. Ratings for each domain of nasolabial appearance are shown in Figure 3.

Children treated at Center 1, which used no PSIO and performed no secondary lip or nose surgery prior to collection of facial photographs for this study, achieved a significantly less favorable nasolabial appearance in both frontal and profile views than children treated at Center 2, which used the Latham appliance and performed secondary lip and nose surgery for 94% of patients prior to collection of photographs ($p<0.01$). Children treated at Center 1 also achieved a significantly less favorable nasolabial appearance in frontal view than children treated at Center 4 using the NAM appliance ($p<0.01$). Children treated at Center 4 using the NAM appliance achieved the most favorable vermillion border alignment ($p<0.01$ for Center 2 and Center 4-IO, $p<0.05$ for Centers 1 and 3).

DISCUSSION

Cleft lip and palate treatment providers can choose among a broad array of treatment interventions for their patients, including the choice to not offer an intervention. Recognizing that no single intervention occurs in isolation, inter-center outcome comparisons inform treatment providers about interventions used at other cleft centers and the outcomes achieved by centers applying distinct combinations of interventions. Individual providers can use this information to predict the potential benefits and harms of modifying their current treatment protocol to more closely align with another center whose outcomes they know. Outstanding results in cleft care can be achieved by different centers using different protocols, and inter-center outcome comparisons enable providers to determine whether outcomes achieved at another center are so much superior to their own results that they should consider changing their treatment protocol.

The desire to achieve optimal facial aesthetics for children with cleft lip and palate has created strong interest in active PSIO. Active PSIO are currently used by over 40% of cleft teams in the United States, although there is substantial variation in the type of orthopedics used (Sitzman et al., 2008, Sischo et al., 2012). There is a strong interest among cleft providers to understand the merits of each particular type of PSIO, so they can decide which type, if any, to offer their patients. While the present inter-center comparison cannot separate the effect of an individual PSIO method from the effect of other components of a center's treatment protocol, the comparison does evaluate whether the use of a specific type of active PSIO enables a center to achieve overwhelmingly better treatment outcomes than centers using alternative types of PSIO.

In the present study, we compared treatment outcomes among centers using a broad variety of active PSIO and different approaches to timing of revision surgery. We found that Center 2, which used the Latham appliance and performed early revision surgery, achieved the best nasolabial aesthetic outcomes, while the worst aesthetic outcomes were achieved at Center 1, which performed neither PSIO nor early revision surgery. Center 4-NAM, which used nasoalveolar molding but did not perform early revision surgery, achieved aesthetic results between these two extremes: better than Center 1 when evaluated in frontal view, but worse than Center 2 when evaluated in profile. The superior aesthetic outcomes achieved by Centers 2 and 3 with use of the Latham appliance and early revision surgery were offset by substantially worse maxillary growth than the other centers. Using a GOSLON score of 4 or higher as a threshold for orthognathic surgery (Shaw et al., 2005), Centers 2 and 3 would require orthognathic surgery for 75% of children, compared to 16% at Center 1, which did not use PSIO nor early revision surgery. Taken together, our results suggest that: (1) use of Latham appliance with early revision surgery may lead to improved nasal aesthetic outcomes relative to centers offering neither active PSIO nor early revision surgery; (2) use of the NAM appliance without early revision surgery may lead to improved nasal aesthetic outcomes relative to centers offering neither active PSIO nor early revision surgery; and (3) there may be a cost to both Latham and NAM in terms of impeding maxillary growth. Whether the cost of impeding maxillary growth is sufficient to change clinical practice is a provider-specific decision.

The results of this study are consistent with reports evaluating individual types of active PSIO, and expand prior findings by providing a direct and multi-dimensional comparison among the different types of active PSIO. Consistent with most prior reports evaluating occlusal relationships and midfacial growth after Latham and GPP (Berkowitz, 1996, Millard et al., 1999, Berkowitz et al., 2004, Matic and Power, 2008), we found this treatment combination was associated with worse dental arch relationship and greater maxillary-mandibular discrepancy compared to the protocol at Center 1 where neither treatment was performed. Interestingly, dental arch relationship and maxillary deficiency were similar between Center 3, which used Latham and GPP, and Center 2, which used Latham but not GPP. While our results on dental arch relationship conflict with the finding by Chan et al (2003) that GOSLON scores were not significantly affected by the use of Latham, we note that sample size in that study was relatively small and that both groups received GPP. In view of the existing literature on Latham and GPP and the results presented here, it seems reasonable to conclude that for centers using Latham, GPP, *and* early revision surgery, discontinuing just one of these interventions may not substantially improve maxillary growth outcomes (Uzel and Alparslan, 2011).

There is a substantial body of cohort studies and case series finding that NAM improves nasolabial appearance. Compared to children not receiving NAM, prospective controlled cohort studies from two centers have shown improvement in height of the nasal dome following NAM (Barillas et al., 2009, Chang et al., 2010). In a recent systematic review, 11 of 12 studies found positive improvements in nasal symmetry by adding NAM to a center's protocol (van der Heijden et al., 2013). In agreement with this pattern, we found that the center using NAM (Center 4-NAM) achieved better appearance of nasal form and symmetry relative to the center performing no PSIO and no lip or nose revision surgery (Center 1).

Further, our finding that nasal frontal form and symmetry were similar between Center 4-NAM and Center 2, which used Latham and early secondary revision surgery, supports the hypothesis made by other investigators that use of NAM may reduce the need for lip and nose revision surgery (Sischo et al., 2012, van der Heijden et al., 2013). Consistent with prior inter-center studies (Peachitlertkajorn et al., 2016), we found that maxillary dental arch relationship and ANB angle appear to be slightly higher (but not significantly different) at the center using NAM relative to the center using no PSIO, although children were not as severely affected as at centers using Latham with early secondary surgery. Overall, these findings add to a body of observational studies that NAM consistently improves nasal appearance across a variety of treatment protocols. Confirmation of these findings in a randomized controlled trial would substantially strengthen the evidence base for NAM, and may lead to broader adoption and universal coverage for this intervention.

Results of this study must be interpreted in the context of the study design. Treatment outcomes were compared across distinct centers whose treatment protocols varied in multiple ways. As such, it is not possible to separate the effects of surgeon skill, surgical technique, sequence of surgical procedures, use of a specific PSIO appliance, and use of secondary surgery. The age of patients examined in this study ranged 6–12 years, and growth-related difference across these ages may confound the results. In addition, information is available only on use of secondary surgery and not the need for secondary surgery. Generalizability of the results may be limited by differing proficiency in active PSIO among orthodontists, or by differing proficiency in cleft lip and palate repair among surgeons. Participating centers were in geographically distinct regions, and there may be bias introduced by ethnic or genetic differences in the patient populations. We attempted to control for this by restricting the sample to Caucasian children with nonsyndromic unilateral complete cleft lip and palate. The results may be confounded by unmeasured differences in cleft severity, including cleft width (Peltomaki et al., 2001, Antonarakis et al., 2015). Assessments were performed at a single time point in mixed dentition: differences in nasolabial aesthetic outcome between centers may have been different at earlier ages and may change by the time children reach adolescence. Finally, aspects of PSIO such as the complexity of care to families, costs to the health care systems, as well as the psychosocial risks and benefits were beyond the scope of this study but are very important aspects of care that need to be considered (Sischo et al., 2015). These are important limitations, and we believe it is essential to be conservative in interpreting results of the present study.

CONCLUSION

Active PSIO are widely used by cleft teams. In the present comparison, Centers using the Latham appliance combined with early lip and nose revision surgery achieved better nasolabial aesthetic outcomes but worse maxillary growth, compared to a Center using no PSIO and delaying secondary surgery to adolescence. It is not possible in the present study to determine if the use of Latham and/or the use of early secondary revision surgery are responsible for improved appearance and/or inhibited maxillary growth. The Center using NAM also achieved nasolabial aesthetic outcomes superior to the center using no PSIO. Infants treated at the Center using NAM had less severe maxillo-mandibular discrepancy than the Centers using Latham, but their maxilla-mandibular discrepancy was still worse

than the Center using no PSIO. While the nature of our study design prohibits us from establishing causation, our results suggest effects of active PSIO are multifaceted, potentially improving nasolabial aesthetics but also potentially harming facial growth. These results further strength the need for a randomized controlled trial to establish efficacy of active PSIO.

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Hard Tissue Landmarks	
A-point	The deepest point on the anterior contour of the maxillary alveolar process
ANS'	The deepest point on the concavity of the anterior surface of the maxilla in the midline, within 3 mm of the floor of the nose (<i>more reliably and readily located than ANS</i>)
B-point	The deepest point on the anterior contour of the mandibular alveolar process
Ba	Basion: the most anteroinferior point on the margin of the foramen magnum
Gn	Gnathion: the most anteroinferior point on the outline of the chin
Go	Gonion: the most posteroinferior point on the angle of the mandible
Me	Menton: the most inferior point on the outline of the chin
N	Nasion: the most anterior point of the frontonasal suture
Pg	Pogonion: the most anterior point on the outline of the chin
S	Sella: the geometric center of sella turcica
Soft Tissue Landmarks	
A'	Soft tissue subspinal: the point of greatest concavity or convexity in the midline of the upper lip
B'	Soft tissue supramentale: the point of greatest concavity in the midline of the lower lip
CT	Columella tangent: the point of intersection with the nasal outline of a tangent to the columella from Sn
G'	Soft tissue glabella: the most prominent point on the soft tissue drape of the forehead
LS	Labrale superius: the most prominent point on the vermillion border of the upper lip
N'	Soft tissue nasion: the deepest point of the frontonasal curvature
P	Pronasale: the most prominent point on the apex of the nose
Pg'	Soft tissue pogonion: the most anterior point on the soft tissue outline of the chin
Sn	Subnasale: the point where the base of the columella of the nose meets the upper lip

Figure 1. Landmarks for cephalometric analysis
Reference hard- and soft-tissue landmarks are shown on a sample lateral cephalometric tracing, with definitions for each landmark below.

Figure 2. Dental arch relationships among centers

A: Distribution of GOSLON scores by center. B: Mean ANB angles by center with error bars representing 95% confidence intervals.

Figure 3. Nasolabial aesthetic ratings

* $p < 0.01$ denotes level of significance in comparison with the other centers specified.

TABLE 1

Treatment Center Protocols.

Center	1	2	3	4-NAM	4-IO
Characteristic					
Infant Orthopedics	None	Latham *	Latham	NAM	Modified McNeil
Lip Repair	3 mos Tennison	3-4 mos Modified Millard	2 mos Nasolabial adhesion 6 mos Modified Millard	4-5 mos Anatomic Subunit	3 mos Modified Millard
Primary Rhinoplasty	No	Yes	Yes	No	No
Primary Alveolar Repair	No	No	3 mos GPP ^o	No	No
Hard Palate Repair	12 mos Vomer flap	9-12 mos Von Langenbeck + Vomer flap	10 mos Von Langenbeck + Vomer flap	10-14 mos Modified Von Langenbeck/Veau +/- -Vomer flap	12-14 mos Modified Von Langenbeck or Wardill- Kilner +/- Vomer flap
Soft Palate Repair	18 mos Median suture with IVP				
Secondary Bone Grafting	9 yrs	6-10 yrs	9-11 yrs	8-10 yrs	9-12 yrs
Nose/Lip Revisions	14-20 yrs	4-10 yrs	5-11 yrs	14-20 yrs	4-20 yrs
Orthodontists	0	2	1	>4	>4
Surgeons	1	4	2	2	4

* Center 2 used Latham appliance on patients with wide clefts, as determined by the treating surgeon. In this study, 17 of the 36 subjects from Center 2 received the Latham appliance.

^o Center 3 performed GPP when alveolar segments were sufficiently approximated, as determined by the treating surgeon. In this study, 15 of the 19 subjects from Center 3 received GPP.

TABLE 2**Sample Characteristics**

Ages reported as mean and range.

Center	1	2	3	4-NAM	4-IO
Characteristic					
Subjects, total	40	36	19	40	56
Male (%)	24 (60)	25 (69)	14 (74)	26 (65)	32 (57)
Dental Arch Alignment					
Dental models available	38	17	19	28	36
Age at models, y (range)	8.7 (7.0–10.0)	9.1 (7.4–12.5)	9.1 (7.1–11.1)	7.8 (5.8–11.7)	10.3 (6.6–16.3)
Cephalometrics					
Cephalogram available	40	30	18	17	19
Age at cephalogram, y (range)	8.7 (7.0–10.0)	9.1 (5.9–13.4)	9.8 (7.1–11.7)	8.8 (7.5–11.7)	9.5 (7.0–12.0)
Nasolabial Aesthetics					
Photographs available	13	34	19	38	26
Age at photographs, y (range)	8.7 (7.0–10.0)	8.6 (7.3–11.3)	9.1 (7.1–11.1)	7.4 (5.0–11.0)	8.7 (6.0–11.0)
Lip or nose revision prior to photographs (%)	1 (8)	32 (94)	10 (53)	1 (3)	0 (0)

Cephalometric Outcomes

Table 3

Mean values for each measurement are reported, along with standard deviation. Bold numbers are statistically different from one another. SD, standard deviation

Center	1		2		3		4-NAM		4-IO	
Measurement	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Hard Tissue Measurements										
SNA (°)	79.99 * ₂	4.06	74.81 * ₁	4.80	77.51	5.32	77.48	3.80	78.04	4.74
SNB (°)	74.85	3.66	74.63	4.97	76.51	4.83	74.97	4.06	75.36	4.87
ANB (°)	5.13 * ₂	2.68	0.18 * ₁	3.36	0.99 * ₁	3.39	2.50 * ₁	3.69	2.66	3.68
	3 * ₃									
	4-NAM									
Ba-N-A (°)	61.76 * ₂	3.33	56.35 * ₁	4.13	58.84	3.90	60.01 * ₂	2.82	59.74 * ₂	4.31
	4-NAM		4-IO							
A-N-Pg (°)	8.96 * ₂	6.29	-1.67 * ₁	7.97	0.11 * ₁	7.94	3.87	8.73	4.55 * ₂	8.41
	3		4-IO							
SN-MP (SN-GoGn) (°)	34.58	5.01	34.33	5.73	31.86	6.86	35.14	6.08	35.66	4.94
Lower face height ratio (ANS'-Me/N-Me) (%)	58.62	2.13	57.52	2.62	56.74	3.14	57.69	2.64	57.61	2.70
Soft Tissue Measurements										
A'-N'-B' (°)	6.83 * ₂	2.25	3.17 * ₁	3.44	3.47 * ₁	2.38	3.14 * ₁	2.93	2.88 * ₁	2.45
	3									
	4-NAM									
	4-IO									
Nasolabial angle (CT-Sn-LS) (°)	112.72	10.53	115.96 * _{4-IO}	9.55	109.23	12.63	118.27 * _{4-IO}	13.28	105.13 * ₂	10.84
									4-NAM	
Soft tissue convexity (G'-Sn-Pg') (°)	170.14	5.08	172.25	4.21	173.11	4.36	172.76	4.45	173.79	4.21
Nasal projection angle (G'-P-Pg') (°)	31.99	4.90	30.80	6.02	31.07	5.63	29.89	4.79	29.20	6.73

Center	1		2		3		4-NAM		4-IO	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Nasoforn angle (P-N'-Sn) (°)	18.06 ^{*2}	2.14	21.92 ^{*1}	2.99	20.34	2.36	21.09 ^{*1}	3.02	22.07 ^{*1}	4.58

^{*} p<0.05, denotes significant difference in comparison with other centers specified, after adjustment for multiple comparisons using the Tukey method, numerals indicate which centers the value is statistically different from