Abstract

Pre-surgical infant orthopedics (PSIO) in treatment of cleft lip with or without cleft palate (CL/P) refers to treatment provided within weeks of birth, up to lip closure surgery at 3-6 months of age. Current research supports limited benefits of PSIO including improved nasal symmetry and decreased need for revision surgeries. PSIO requires frequent appointments, as well as daily maintenance of treatment appliances by primary caregivers. It has been suggested that the limited benefits provided by this treatment may not justify the increased burden; however, proponents suggest that objective measures of burden are not appropriate as PSIO may relieve caregiver anxiety and provide a sense of empowerment. At present, studies investigating the psychological effects of PSIO on caregivers are limited. The purpose of this study was to compare objective and subjective treatment burdens, and psychological response in primary caregivers of children born CL/P receiving PSIO to those not receiving PSIO. Treatment load was measured by the duration of treatment and number of appointments. Caregivers’ subjective perception of treatment burden was assessed using a series of visual analogue scale questions. Caregiver psychological response was assessed using the following psychometric tests: Maternal Confidence Questionnaire, Stress Scale for Parents of Cleft Lip and Palate Children, Parenting Stress Index 4th Edition, and Coping Response Inventory. Preliminary pilot data of 8 participants is reported in this dissertation. Objectively assessed treatment load was greater in PSIO, with patients requiring an average of additional 7.3 appointments over 96 days. Caregivers reported that PSIO entailed significant subjective emotional and time burdens, and significantly increased the time burden of overall CL/P treatment at 3 months. No statistically significant differences in caregiver confidence, stress, or coping strategies were detected between PSIO and non-PSIO groups. Findings should be interpreted with caution due to the limited sample size at this time. Review of pilot study data indicates that multi-centre involvement will be required to successfully recruit an adequate sample for complete statistical analysis.
Preface

This dissertation is an original intellectual product of the author, T. Gibson. The project and methods were approved by the University of British Columbia Research Ethics Board [certificate #H14-01903].
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Chapter 1: Introduction

1.1 Embryogenesis of Cleft Lip and Palate

Facial clefts involving the lip and/or palate are congenital craniofacial anomalies that arise secondary to failure of facial process fusion\(^1\). The development of these facial processes is a complex process which begins around 15 days embryonic age with the development of a three-layered embryo (gastrulation) and the notochord – a midline mesodermal structure involved in neural patterning\(^2\). Signaling molecules from the notochord, in particular Bone Morphogenetic Protein-4, prevent the overlying ectoderm from developing into epithelium, and instead lead to a localized ectodermal thickening referred to as the neural plate. The neural plate folds along its length to become the neural tube, which eventually develops into the central nervous system\(^2\). Cells from the fusing edges of the developing neural tube (the neural crests) undergo epithelial-mesenchymal transformation and move into the underlying mesoderm to form multi-potent ectomesenchymal progenitor cells called neural crest cells (NCCs). By the 4\(^{th}\) week of embryonic development, the NCCs have migrated into the developing face, where they contribute significantly to the formation of the facial processes and branchial arches\(^2\).

Major facial processes formed in the 4\(^{th}\) week are the maxillary and mandibular processes, and frontonasal prominence (Figure 1a). The mandibular and maxillary processes form the lower lip and lateral portions of the upper lip respectively, as well as associated bones and musculature (Figure 1c). The frontonasal prominence gives rise to the medial and lateral nasal processes by the 5\(^{th}\) week of development. The medial nasal processes form the philtrum of the upper lip as well as the medial nose, while the lateral nasal processes form the alae of the nose (Figure 1c). The palate is formed anteriorly by an extension of the frontonasal prominence (primary palate), and posteriorly by the palatine processes of the maxillary processes. The palatine processes, or palatal shelves, form during the 6\(^{th}\) week of development (Figure 1d), but do not fuse until they re-orient from their initial vertical position to a horizontal one around the 8\(^{th}\) week of development (Figure 1e-f). After
reorientation, the palatine processes fuse with the primary palate and nasal septum to form the palate. Fusion of the palatine processes begins anteriorly and continues posteriorly into the soft palate.


As previously mentioned, CL/P develop secondary to failure of fusion of processes during facial formation between 4 and 10 weeks embryonic age. Failure of fusion of the maxillary processes, medial nasal processes, and primary palate at 4-6 weeks embryonic age results in clefting of the lip, alveolus, and primary hard palate (anterior to the incisive papilla). Failure of fusion of the palatal shelves of the maxillary processes at 8-10 weeks embryonic age results in clefting of the soft palate and/or secondary hard palate (posterior to incisive
papilla). Clefting of the primary palate is thus a result of the same embryologic mechanism as clefting of the lip, and is generally considered a separate entity from clefting of the soft and secondary hard palates.

1.2 Epidemiology of Cleft Lip and Palate
Facial clefting involving the lip and/or palate is the most common congenital craniofacial anomaly in humans, affecting approximately 1.4 in 1000 live births in Canada, and a similar proportion worldwide. Incidence varies with both ethnicity and gender, as well as by specific clinical presentation.

Cleft lip (CL) and cleft lip with cleft palate (CLP) have been noted to aggregate together in families, and as such cleft lip with or without cleft palate (CL/P) is generally considered single anomaly of variable presentation. Reports of CL/P frequency vary from 3.4-22.9 / 10,000 live births, with a 2:1 male predilection commonly reported. The lowest occurrence is observed in those of African descent (1/2500), followed by Caucasians (1/1000). Higher prevalence have been reported in Asian and Latin populations (1/500). A high prevalence of CL/P (1/525) has also been reported in Canadian First Nations, nearly double that of the non-aboriginal population from the same geographic region.

Isolated cleft palate (CP) is less common than CL/P, affecting 1/2000 live births. A 2:1 female predilection has been reported, and the majority of studies have not detected any ethnic differences. CP is traditionally considered a different diagnostic entity from CL/P, as they aggregate separately in families.

1.3 Etiology of Cleft Lip and Palate
The etiology of cleft lip and palate is complex, with both genetic and environmental risk factors identified. Genetic factors include both polygenetic inheritance and single-gene mutations associated with clefting syndromes. Furthermore, different mutations of the same gene may be associated with polygenetic non-syndromic or single-gene syndromic
presentations. Polygenetic non-syndromic cleft lip and palate has been associated with mutations of IFR6, MAFB, TBX22, BMP4, and chromosome region 8q24; single-gene cleft syndromes include Van der Woude (IFR6 loss of function) and DiGeorge (TBX-1 deletion)3,9

Environmental risk factors associated with non-syndromic cleft lip and palate include maternal zinc deficiency, viral infection, smoking, anticonvulsant medications, and exposure to organic solvents3. Maternal Vitamin A deficiency has also been proposed as a potential risk factor, with a recent case-control study reporting decreased occurrence of isolated cleft palate (CP) in children of mothers with high Vitamin A intake10. Similarly, folate deficiency has been proposed to increase cleft lip and palate risk secondary to a noted decrease in incidence after mandatory fortification was introduced3. Historically, research on this topic has been limited, leading a Cochrane review to conclude that there was inadequate evidence to support a protective effect of folic acid supplementation against cleft lip and palate11. However, research is ongoing, and more recently a large prospective study of over 240,000 women found that 400µg daily folic acid supplementation significantly decreased the occurrence of cleft lip and palate in offspring (OR 0.69, 95% confidence interval 0.55-0.87)12.

1.4 Classification of Cleft Lip and Palate
Cleft lip and palate is classically divided into two categories: cleft lip with or without cleft palate (CL/P), and isolated cleft palate (CP). This division is based on embryologic development and observed familial aggregation as discussed above3,3. CL/P includes clefts of the lip, which may or may not have involvement of the alveolus, primary palate, or secondary palate as well. CP includes only clefts of the secondary hard and soft palates4. Additional classification frequently includes laterality and depth. Clefts of the lip, alveolus, and primary palate may be unilateral or bilateral; rare occurrences of midline clefts are also observed in specific craniofacial syndromes such as frontonasal dysplasia1. Clefting of the secondary hard and soft palates are generally in the midline. Cleft depth in CL/P is
classified as complete if the cleft extends into the nasal floor, and incomplete if the nasal floor is intact. Cleft depth in CP refers to the antero-posterior extent of the cleft, with complete CP indicating a cleft extending from the posterior soft palate to the incisive foramen. Incomplete CP does not extend anteriorly as far as the incisive foramen.

1.5 Clinical Features of Cleft Lip and Palate
The clinical features of cleft lip and palate arise by two distinct mechanisms. First are those that arise as a direct result of the anatomic disruption of the cleft, which are typically notable at birth. In addition to these primary clinical features, the extensive surgical intervention for repair of cleft lip and palate can disrupt growth, leading to additional characteristic clinical features later in life.

1.5.1 Primary Clinical Features
Anatomical disruption as a result of cleft lip and palate characteristically involves alterations to the nose, lip, alveolar arch, and palate. The degree of disruption varies with the location and severity of clefting.

In patients with unilateral cleft lip (Figure 2 below), discontinuity of peri-oral tissues interferes with the normal action of facial muscles, particularly orbicularis oris. Muscle tension results in lateral displacement of the lip segments and associated structures. The nose presents with a depressed alar rim and increased nasal base width on the affected side, while the columella and nasal tip are deviated to the unaffected side as a result of intact muscle insertions and unopposed muscle activity. If involved, the alveolar segments are similarly laterally displaced, with the anterior region of the larger (greater) segment being displaced both laterally and anteriorly, again due to unopposed activity of the unilaterally intact peri-oral musculature. Decreased depth of involvement (incomplete lip clefts) and absence of palatal cleft will decrease the severity of these features.
Patients with bilateral cleft lip present with differing nasal, lip, and alveolar alterations from those with unilateral involvement (Figure 3). As a result of bilateral discontinuity in the peri-oral musculature, both alar rims are depressed and the nasal base is bilaterally increased in width. The nasal tip lacks projection, and the columella is short or absent. With no intact musculature to control it’s position, the pre-maxillary portion of the
alveolar arch is significantly protrusive, and may appear to be attached almost directly to the nasal tip. As with unilateral presentations, decreased depth and lack of palatal involvement will decrease the severity of the anatomical disruption.

Figure 3 - Complete Bilateral Cleft Lip and Palate (Clinical images courtesy of Dr Paul Pocock, used with permission)

1.5.2 Clinical Features Secondary to Treatment

In a landmark study of adolescents and adults with unoperated CL/P, Mars and Houston demonstrated that many characteristic features of adults with CL/P were best attributed to surgical intervention rather than the cleft itself. They investigated cephalometric measurements and dental malocclusion in Sri Lankan males over 13 years of age who were born with CL/P, but never received surgical intervention. When comparing to non-cleft controls and CL/P patients who had received surgical repair, it was determined that
the unoperated CL/P subjects had grown similarly to the non-cleft control, while the operated group of CL/P subjects presented with significant maxillary growth restriction, particularly those patients who had received palatal surgeries. As the majority of patients encountered in a clinical setting will have had surgical repair, it can be expected that most adolescent CL/P patients encountered will present with maxillary hypoplasia, as well as associated dental malocclusions including anterior and posterior crossbites and Class III buccal relationship. In addition, missing and malformed teeth are frequently encountered both adjacent to the cleft site, and at other sites. Missing or malformed teeth in the region of the cleft may be developmental anomalies, or secondary to surgical intervention.

1.6 Treatment of Cleft Lip and Palate

Treatment for cleft lip and palate is complex and prolonged. Surgical correction of the anatomical and dental anomalies alone may extend from shortly after birth into adulthood (Figure 4). Complete treatment involves an extensive range of health care professionals, including maxillofacial and plastic surgeons, pediatric dentists, orthodontists, prosthodontists, pediatricians, otolaryngologists, audiologists, speech-language pathologists, counselors, social workers, and nurses. Due to the complexity of treatment, it is strongly recommended that treatment be provided in a hospital setting by a specialized inter-disciplinary team.
Orthodontic treatment for CL/P (Figure 5) involves multiple phases throughout adolescence and adulthood. Prior to alveolar bone grafting around age 9, orthodontic treatment is initiated to expand the alveolar arch and align teeth away from the cleft site – this provides surgical access for bone grafting, as well as corrects the transverse maxillary constriction which develops secondary to surgical repair\(^1\). Some practitioners also advocated growth modification treatment such as a reverse-pull headgear during this treatment phase; however, the long-term benefits of this treatment are still unclear\(^{17-19}\) and research is ongoing. In the teenage years, conventional complete orthodontic treatment is conducted to provide a functional and aesthetic occlusion. For patients with relatively minor maxillary hypoplasia, only orthodontic treatment is required, whereas for patients presenting with more significant maxillary hypoplasia, orthognathic surgery may be indicated\(^20\). Orthognathic surgery is generally delayed until growth completion to prevent post-surgical growth from causing relapse of the surgical correction\(^{21}\).
1.6.1 Pre-Surgical Infant Orthopedic Treatment for Cleft Lip and Palate

An additional period where orthodontic treatment may be involved is shortly after birth, prior to lip surgery. Treatments provided at this age are better referred to as “orthopedic” as there are no teeth erupted, with treatment instead focusing on the movement of bony segments and surrounding soft tissues.

1.6.1.1 Types of Pre-Surgical Infant Orthopedics

Numerous methods and appliances for ‘pre-surgical infant orthopedics’ (PSIO) have been reported over the past four to five decades\textsuperscript{22}. In general, three broad categories of PSIO may be outlined: lip taping, traditional infant orthopedics, and nasoalveolar molding.
Figure 6 - Lip Taping. The pictured patient has conventional lip tape in place during fitting of an additional PSIO appliance (clinical image courtesy of Dr Paul Pocock, used with permission).

Lip taping involves the placement of adhesive tape across the lip cleft. The tension applied by the adhesive tape mimics the action of the orbicularis oris muscle, leading to a decrease in cleft size, decrease in nasal base width, and retraction of the protrusive premaxillary alveolus\textsuperscript{23,24}. Lip taping is an alternative to lip adhesion, a surgical procedure in which deep lip tissues in the cleft site are repaired prior to definitive lip repair in order to produce a similar molding action to that described above\textsuperscript{25}. 
Figure 7 - Traditional Infant Orthopedic Appliance. Activation to approximate alveolar segments may be performed by addition (blue) and removal (green) of acrylic, or by active components such as wire frameworks or expansion screws (not pictured).

One of the most extensively investigated PSIO methods, traditional infant orthopedics (TIO) utilizes an intraoral acrylic plate to move the displaced alveolar segments to the appropriate position and width. Alveolar movement is accomplished by the addition and removal of acrylic from the plate (Figure 6), or by the incorporation of active components such as wire frameworks, expansion screws, or hinge arms, such as in the once commonly used Latham appliance. Historically these appliances have been retained by surgically inserted pins, though it is now common for appliances to be retained by commercially available denture adhesives and extra-oral tape.
Figure 8 - Nasoalveolar Molding Appliance. Top: appliance for treatment of bilateral CL/P consisting of acrylic plate and bilateral nasal stents. Bottom: appliance in place, retained by elastics and tape; nasal stents extend extraorally and into the nose to apply pressure to the collapsed alar rims (clinical images courtesy of Dr Paul Pocock, used with permission).
Most recently developed, nasoalveolar molding (NAM) is based on the principle of cartilage plasticity. High levels of maternal estrogen present in neonatal circulation have been proposed to maintain hyaluronic acid content in infant cartilage for 3 to 4 months after birth, producing a more plastic (permanently deformable) cartilage\textsuperscript{28,29}. This neonatal cartilage plasticity was originally used in the correction of ear morphology\textsuperscript{28,30}. NAM combines the objectives of lip taping and TIO with nasal stents intended to correct nasal morphology by reshaping the nasal cartilages. Specifically, the nasal stents are placed on the cleft side(s) and apply anteriorly directed pressure from inside the nostril. Treatment goals for the nasal stent include production of alar rim convexity and nasal tip projection, and correction of columellar deviation\textsuperscript{22}.

1.6.1.2 Effectiveness of Pre-Surgical Infant Orthopedics

Despite the existence of PSIO techniques for nearly 50 years, evidence on the effectiveness of various techniques is limited\textsuperscript{22,31}. Because of the prolonged course of treatment for CL/P, long-term outcome measures are desirable when investigating different treatment methods. Unfortunately, the number of different interventions that a single patient may receive over the course of treatment makes the investigation of any single treatment challenging. Furthermore, different methods may be used at each stage of treatment, further complicating analysis. Illustratively, a 2001 study of European cleft centres determined that 194 different treatment protocols were used in the 201 treatment centres investigated\textsuperscript{32}.

1.6.1.2.1 Traditional Infant Orthopedics

On account of its relatively early development, TIO benefits from a stronger body of evidence than other methods of PSIO discussed above. Both randomized prospective trials and systematic reviews have been published investigating the effectiveness of TIO at long-term follow-up, and are reviewed below.
Dutchcleft is a multicentre clinical trial investigating the effectiveness of TIO. Patients enrolled in this study were randomized to TIO or no PSIO, with 20-25 UCLP patients per group depending on the publication. Patients were followed longitudinally for a wide range of outcomes. This investigation concluded TIO offered no significant benefits in feeding and infant weight gain up to 24 weeks\textsuperscript{33} nor motherhood satisfaction up to 14 months\textsuperscript{34}. Furthermore, TIO did not prevent maxillary arch collapse\textsuperscript{35,36}, nor improve cephalometric skeletal relationships or dental malocclusion at 4 and 6 years\textsuperscript{37-39}. TIO did offer some benefit in speech development; specifically, consonant development and expressive language were improved at age 2.5-3 years compared to the patients who did not receive PSIO\textsuperscript{40-42}. However, no differences were detected at 6 years, leading the authors to conclude that TIO offered no long-term benefit in speech development. TIO also produced a temporary improvement in subjectively rated facial aesthetics at age 4, with difference no longer detectable to lay observers at age 6\textsuperscript{41}. Overall, the Dutchcleft project concluded that the benefits of TIO were minimal and transient in nature, leading to the discontinuation of TIO in all three treatment centres in the Netherlands\textsuperscript{15}.

Eurocleft, another multicentre longitudinal study of 5 European centres, investigated long-term outcomes in 127 patients with UCLP up to age 17\textsuperscript{32}. Unlike Dutchcleft, participants in Eurocleft were not randomized to treatment groups, and some data was obtained retrospectively. Consequently, the authors were unable to attribute outcomes to specific interventions. However, it was noted that the amount of treatment a patient received was not correlated with improved outcomes. In fact, the two centres using PSIO were noted to have the worst long-term results for dental occlusion and skeletal cephalometric relationship\textsuperscript{32,44-48}.

Another multicentre study, Americleft retrospectively investigated the growth, malocclusion, and aesthetic outcomes in adolescence for 169 consecutively treated UCL/P patients from 5 treatment centres\textsuperscript{49}. As with Eurocleft, the retrospective non-randomized design of this study generally prevented the attribution of outcomes to
specific treatments. The results of the Americleft study are in agreement with those of Eurocleft: increased treatment protocol complexity was associated with poorer long-term outcomes; in particular, it was noted that early surgical intervention in the form of early alveolar bone grafting had significant adverse effects on growth and occlusion in adolescence\textsuperscript{49-53}.

Recently, a systematic review of controlled trials investigating PSIO outcome at a minimum of 6 year follow-up was published\textsuperscript{54}. Twelve controlled trials with adequate follow-up were included, the majority of which were from the Dutchcleft project. Unsurprisingly, the authors reached the same conclusions regarding the effectiveness of TIO as discussed above – no long-term significant improvements in motherhood satisfaction, feeding, speech, nasolabial appearance, occlusion, facial growth, or maxillary arch dimensions were detected\textsuperscript{54}. One study that met the inclusion criteria of this review reported a significant benefit in nasal symmetry in patients who received nasoalveolar molding (NAM)\textsuperscript{55}, and will be discussed subsequently.

### 1.6.1.2.2 Nasoalveolar Molding

As a more recently developed technique, NAM does not have the level of evidence available in the investigation of TIO. As of their 2011 review, Uzel and Alparslan\textsuperscript{54} were only able to identify one controlled trial on the effects of NAM at a follow-up of greater than 6 years\textsuperscript{55}. This study was a retrospective comparison of 25 consecutive UCLP patients; 15 who received NAM and 10 who received no PSIO. In comparing six anthropomorphc measures of nasal symmetry at age 9, two blinded examiners found a statistically significant 3.5-10\% increase in symmetry with NAM. The clinical and subjective significance of this improvement is unknown\textsuperscript{55}.

In comparing NAM directly to TIO, one large case control study is available\textsuperscript{56}. Bennun and colleagues compared nasal tip protrusion, columellar length, and nasal width in UCLP patients at 6 years of age\textsuperscript{56}. The study sample consisted of 46 patients who received
NAM, 47 who received TIO, and 48 non-cleft controls. The authors found that patients who received NAM had greater nasal tip protrusion and columellar length than those receiving TIO, with the NAM group achieving comparable nasal tip protrusion and columellar length to the non-cleft control subjects. However, subjects in both NAM and TIO groups had wider nasal base widths when compared to non-cleft controls.

Anthropomorphic measurements are appealing in research design as they offer both ease of measurement and amenability to conventional statistical analysis. However, statistically significant improvements in these measures are not necessarily indicative of clinically significant or self-perceived improvements in aesthetics. A recent Master’s thesis from the University of Toronto addressed this limitation by comparing subjective nasolabial aesthetics at age 4-6 years in 149 UCLP patients who had received TIO, NAM, or no PSIO. Aesthetic outcome was assessed on frontal and lateral facial photographs cropped to include only the nasolabial region. A panel of six orthodontists and one orthodontic resident rated nasolabial aesthetics using the Asher-McDade scale, a five-point ordinal assessment of nasolabial profile, nasal symmetry, nasal form, and vermillion border. Overall, few significant differences were noted, and variation within the samples was large. However, vermillion border aesthetic scores were significantly higher in patients who received NAM than those who received TIO, and in both groups compared to no PSIO.

Another proposed benefit of NAM is a reduction in the number of secondary or revision surgeries to improve the nasolabial aesthetics after initial lip repair. Lee and colleagues published the first report on this topic, comparing the frequency of nasal revision surgery in a small sample of 26 patients bilateral CLP, with half receiving NAM and half no PSIO. By age 9 years, all 13 patients who had received no PSIO required surgical nasal revision, while none of the group who were treated with NAM required such revision. More recently, a large retrospective study of 275 consecutively treated unilateral and bilateral CLP patients treated at New York University was published. By age 14, 21% of patients
with unilateral CLP who had not received NAM required nasal revision surgeries, compared to 3% of those who had received NAM; the difference was statistically significant. Similarly, 7% of bilateral CLP patients receiving NAM required nasal revision surgeries, compared to 40% of those not receiving NAM. However, this difference was not statistically significant, likely due the small sample of bilateral CLP patients in this study\textsuperscript{60}.

At present, the available evidence supports a decrease in the number of surgical interventions required in patients receiving NAM, and a possible benefit in nasolabial aesthetics. Some authors have proposed that these benefits do not outweigh the cost of NAM, particularly with regards to the number of appointments involved, and the potential stress to parents of children with CL/P\textsuperscript{31}.

1.6.1.3 Burden of Pre-Surgical Infant Orthopedics

Despite the proposal that the burden of PSIO treatment outweighs its benefits, relatively little research has been conducted investigating the cost and treatment burden of PSIO. Retrospective data from the University of Toronto determined that PSIO treatment required an average of 6.6 additional visits for TIO or 9.9 visits for NAM over 112 and 127 days respectively\textsuperscript{57}. In addition to these visits, caregivers are required to place and adjust PSIO appliances and tapes daily, particularly for NAM. To date, no research has assessed the time-related burden for primary caregivers during the provision of this treatment.

In addition to the time requirements of PSIO, the financial cost to both caregivers and medical providers should be considered. Despite the substantial potential cost to caregivers (who can be expected to incur the cost of missed work and travel to frequent appointments), research is limited\textsuperscript{61}. No studies were identified which assessed the financial cost of PSIO for caregivers. The cost of NAM to medical providers is $4500 to $6500 USD per patient, though by age 14 NAM has been found to save $491 to $2381 USD per patient because of decreased surgical revisions\textsuperscript{60}. 
A final point of contention regarding the burden of PSIO treatment is its effect on caregiver stress and psychological well-being. Some authors have proposed that the objectively measured burden discussed above results in increased stress for caregivers\textsuperscript{31}. Conversely, proponents of PSIO have suggested that caregivers feel that they are helping with treatment, and subsequently experience reduced anxiety, a sense of empowerment, and develop positive coping strategies\textsuperscript{22}.

The effect PSIO on caregiver stress and coping is important for both parent and child. In a longitudinal study of caregivers and children with craniofacial anomalies, increased parental stress at 1 year of age was correlated with childhood behavioral problems at 3 years\textsuperscript{62}. Furthermore, cross-sectional psychometric data from families of CL/P children has demonstrated that poor parental coping is associated with psychological distress, which has an adverse impact on family function\textsuperscript{63,64}. At the time our study was designed, a review of literature could not locate any publications directly assessing the effect of PSIO on caregiver psychological well-being. More recently, the first report from a longitudinal qualitative study on this topic was published\textsuperscript{65}. Sischo and colleagues conducted semi-structured interviews with 68 consecutive caregivers of children with CL/P receiving NAM at 4 treatment centres in the United States\textsuperscript{65}. Interviews were conducted at several time points (1 week after NAM initiation, after completion of NAM and prior to lip surgery, and at follow-up 1 year after lip repair). The researchers concluded that caregivers initially felt apprehension regarding the demands of NAM, but later reported increased self-esteem and feelings of empowerment despite the treatment burden. Although this study provides some support that NAM promotes a positive psychological response in caregivers, due to the lack of a control group it is not possible to determine if comparable changes also occur in caregivers whose children are treated without NAM. Furthermore, the sample investigated was self-selected, as it included only caregivers who chose to proceed with NAM, and did not include the 12\% of caregivers who attempted NAM but discontinued treatment prior to completion. Thus, further research allowing comparison between
caregivers of children both receiving PSIO and those being treated without PSIO is required.

1.7 Research Justification
At present, pre-surgical infant orthopedics is utilized in over one third of large cleft and craniofacial treatment centres in the United States. Despite its relatively common usage, little is known about the treatment burden and its psychological effect on caregivers. As outlined above, limited evidence suggests both an increased burden, and possible psychological benefits to caregivers such as decreased stress. No publications to date have compared caregivers of children receiving or not receiving PSIO with respect to their perception of treatment burden, nor the psychological effect of treatment burden.

1.8 Study Objectives and Hypotheses
The goals of this study are to:

1. Objectively compare the treatment load of PSIO and non-PSIO treatments for cleft lip with or without cleft palate.
2. Compare caregivers’ subjective perception of treatment burden for PSIO and non-PSIO treatment of cleft lip with or without cleft palate.
3. Compare caregiver stress, confidence, and coping response to PSIO and non-PSIO treatment of cleft lip with or without cleft palate.

The following null hypotheses will be tested:

Null Hypothesis 1 ($H_0^1$): objectively assessed treatment load, as measured by number of appointments and treatment duration, will not differ between PSIO and non-PSIO treatment for cleft lip with or without cleft palate

Null Hypothesis 2 ($H_0^2$): the subjective treatment burden reported by caregivers will not differ between PSIO and non-PSIO treatment for cleft lip with or without cleft palate
Null Hypothesis 3 ($H_0^3$): caregiver stress, confidence, and coping strategies will not differ between PSIO and non-PSIO treatment for cleft lip with or without cleft palate
Chapter 2: Methodology

2.1 Study Design
This pilot study consists of a case series of consenting caregivers of patients treated at BC Children’s Hospital (BCCH) for repair of cleft lip with or without cleft palate. Due to ethical and practical considerations, treatment groups (PSIO, no-PSIO) were not be assigned by the study, but continued to be assigned by the clinician and treatment centre.

2.2 Sample and Recruitment
A single primary caregiver for each child born with CL/P and receiving lip repair surgery at BCCH was eligible to participate. Potential participants were identified by the BCCH Plastic Surgery Clinic when they attended pre-surgical consultation for lip repair. Study information was provided to eligible caregivers at this appointment, and informed consent was obtained from those willing to participate. Participants were permitted to consent at any time up to the date of their child's lip surgery. Due to the potential confounding effects of post-surgical care demands, completed questionnaires were required to be returned prior to lip surgery.

2.3 Inclusion Criteria
• One primary caregiver for each child receiving primary lip repair surgery for CL/P during the study period was included.
• Ability to comprehend written English at a 6th Grade level was required to participate.

2.4 Exclusion Criteria
• Caregivers of children who were not followed at BCCH from birth until recruitment were excluded.
• Caregivers of children who had already received surgical lip repair were no longer eligible to participate, as recent surgery could confound the measures being used in this study.
• Caregivers who had confidentially disclosed substance abuse or mental health concerns to the Cleft and Craniofacial Team were excluded.

2.5 Caregiver Questionnaire Design

Data consisted of questionnaires completed by participating caregivers, and treatment reports completed by the patients’ orthodontist (when applicable).

The caregiver questionnaire consisted mainly of psychometric tests assessing stress, confidence, and coping strategies in response to the birth and care requirements of a child born with CL/P. Potential metrics for this study were indentified by reviewing current publications on psychosocial outcomes in parents of children born with congenital anomalies. The compiled list of psychometric tests were then assessed based on the following criteria:

• Metrics must be designed to assess confidence, stress, or coping response.
• As the study questionnaire was expected to be administered to parents of children aged approximately 3 months, included metrics would ideally have validation or sample data available for parents of comparably aged children.
• Included metrics were to demonstrate good internal consistency of subscales and test/re-test reproducibility.

Consideration was also given to the length of time required to complete each metric. After considering the above criteria, four metrics were chosen for inclusion in the caregiver questionnaire.

The Maternal Confidence Questionnaire assesses self-perception and confidence in parenting ability. As no cleft lip/palate specific metric has been published to date in this area, we chose the Maternal Confidence Questionnaire to assess confidence in general
caregiving activities. The MCQ consists of 14 items and uses a 5-point Likert scale ranked from ‘seldom’ to ‘a great deal’ (Appendix A.1). The MCQ is assessed as a total score, as well as three subdomains: knowledge, tasks, and feelings. This tool has been used extensively in healthcare since its publication, and demonstrates excellent subdomain internal consistency (Cronbach’s α 0.82-0.91) and acceptable re-test reliability. Additionally, this metric was previously used at BC Children’s Hospital in a sample of parents of pre-term infants at 1 month of age, offering a relevant comparison group.

One metric was identified which measures stress and anxiety specifically related to the care of a child born with cleft lip/palate. The psychometric testing of the Stress Scale for Parents of Cleft Lip and Palate Children (SSPCL/P) was recently published in Taiwan using an initial 38 questions. Eliminating those items that did not segregate well into common factors (domains) produced a total of 25 questions in four domains: long-term concerns, resource deficiency, family adaptation, and defect management. Scores for total stress and for each subscale are calculated as the mean question score, with Likert scores ranging from 0 for ‘does not apply’ to 4 for ‘always’. The validation for this metric was based on a sample of 184 Chinese speaking caregivers of children from 0-13 years of age, including 88 with children from 0-6 years. Internal consistency of the test’s four subscales was good (Cronbach’s α 0.71-0.84), as was re-test reliability (0.69-0.91). For the purposes of this study, the translation reported in the initial publication was updated (Appendix A.2), mainly to clarify third person and passive voice phrasing.

The Parenting Stress Index 4th Edition (PSI-4) is a proprietary metric produced by Psychological Assessment Resources, Inc. (http://www4.parinc.com). The PSI-4 assesses the effect of parental stress on seven subdomains (competence, attachment, role restriction, depression, spouse/partner relationship, isolation, and health). Participants rate their agreement with a series of statements on a 5-point Likert scale from ‘strongly disagree’ to ‘strongly agree’. The PSI-4 is complementary to the SSPCL/P, as the SSPCL/P directly assesses the stress of caring for a child with CL/P, while the PSI-4 assesses the
effect of stress on a range of general activities and emotions. PSI-4 validation data provided by the company was based on 1056 parents, and demonstrated good internal consistency (Cronbach’s α 0.75-0.87) and re-test reliability (0.69-0.91). Normative data is provided for parents of children less than 1 year of age71. Psychological Assessment Resources do not permit reproduction of their proprietary tests; due to this copyright restriction, it is not possible to include the PSI-4 in this thesis for reference.

The Coping Response Inventory (CRI)72 is a second proprietary metric produced by Psychological Assessment Resources, Inc. (http://www4.parinc.com). The CRI consists of a series of questions asking a participant to rank how frequently they displayed specific behaviors when coping with a recent stressor, using a 4-point Likert scale graded from ‘never’ to ‘frequently’. Coping response is categorized into positive approach-based or negative avoidance-based strategies. Positive coping strategies include logical analysis, positive reappraisal, seeking support, and problem solving. Negative coping strategies include cognitive avoidance, resignation, alternate rewards, and emotional discharge. Higher scores in a subdomain indicate greater reliance on that coping strategy. Validation data provided by the company was based on 1916 participants, and demonstrated acceptable subscale internal consistency (α 0.60-0.74)72. Short-term re-test reproducibility has not been reported. Previous publications have utilized the CRI in samples of CL/P caregivers, providing good comparison samples63,64. Copyright prevents the inclusion of the CRI in this thesis.

In addition to the four metrics outlined above, additional visual analogue scale items were included to assess caregivers’ subjective perception of treatment burden. Six questions were included which asked caregivers to rate both orthodontic and total treatment burden with respect to time, emotional, and financial cost from no burden to extreme, almost unbearable burden (Appendix A.3). Questionnaires were carefully scaled during printing to ensure that all visual analogue items consisted of identical 10 cm lines. Scores for each items were determined by measuring the distance along the line indicated by the
participant. An additional open ended item was also included asking caregivers: ‘If you were to have another child with cleft lip, or cleft lip and palate, would you want them to have the same treatment your child has received?’.

Demographic data was collected from participants, including caregiver role (mother, father, guardian etc.), age, gender, marital status, and education. In addition, clinical CL/P diagnostic information including depth of cleft, laterality, syndromal association, and prenatal diagnosis was obtained.

2.6 Pre-Surgical Treatment Data
For those patients who received PSIO, a report was collected from the treating orthodontist after treatment completion. Data collected included the number of PSIO appointments, duration of PSIO treatment, and if treatment was completed successfully or discontinued. Because practitioners may have different definitions of specific PSIO methods, we requested the orthodontists to indicate all appliances used from a list, rather than requesting what treatment method was used (Appendix A.4).

2.7 Data Collection
BCCH research associates collected all caregiver questionnaire data and forwarded the de-identified, uniquely coded surveys to the research team by secure electronic transfer. When applicable, the research associates contacted treating orthodontists to obtain the pre-surgical treatment data. This treatment data was also de-identified and coded to match the corresponding caregiver survey before being forwarded to the research team.

All data were entered into a password protected Excel spreadsheet on a password-protected computer with medical record storage grade encryption. Response data entered was only identified by unique code; no personal identifiers were included. A master list identifying participants by unique code was kept in a locked cabinet by the research associates at BCCH.
2.8 Sample Size Calculation

Power calculations were conducted for the caregiver questionnaire using existing validation data including population means, standard deviations, and clinically relevant differences for each metric and its subdomains. The Type I error was set at 0.05, and the desired power at 0.80. The required sample size to achieve at least 80% power for all questionnaire metrics was determined to be 126 participants (63 PSIO, 63 non-PSIO). At the time of study design, no data were available on the birth rate of children with CL/P at BCCH. Hospital staff estimated that approximately one patient with CL/P was born per week at BCCH. Based on this estimate it was determined that the desired sample could be collected within three years if a 75% response rate could be obtained.

2.9 Data Analysis

To assess our primary outcomes, caregivers were grouped by whether their child received or did not receive PSIO treatment prior to lip surgery. Differences in objectively assessed treatment load were assessed as the number of appointments and duration of PSIO treatment. Subjective caregiver experience of burden was assessed by comparing visual analogue item scores between PSIO and no-PSIO treatment groups. Caregiver confidence, stress, and coping were assessed by comparing scores on the MCQ, SSPCL/P, PSI-4, CRI metrics and their subdomains. Three metrics included in this study (MCQ, PSI-4, and CRI) use the summed score of multiple Likert scale items to produce total and subdomain scores. The SSPCL/P is scored as the mean Likert scale response for all questions contributing to the relevant subdomain. Previous publications and validation studies have treated these scores as continuous variables. Therefore, t-tests (or non-parametric equivalent) were selected for investigation of inter-group differences.

2.10 Participant Safety

Patients and their families receiving treatment at the BCCH Cleft and Craniofacial Clinic are routinely followed by an interdisciplinary team including counselors and social
workers. Despite having ready access to emotional support and mental health specialists, we felt it important to ensure prompt access to care for any study participants who were determined to be experiencing significant mental or emotional distress at the time of study participation. Three methods of referral for additional professional support were included in the study protocol:

1. The introductory letter given to participants explained that if they found any questions distressing, they could stop answering at any time. Participants were invited to speak confidentially with the research associate to be directed to the appropriate support services if they desired.

2. Included with caregiver questionnaires was a check-box item that could be ticked to indicate that the participant wished to receive additional follow-up with Cleft and Craniofacial Team support services.

3. Any participants scoring greater than one standard deviation above normal on the PSI-4 Depression subscale would receive follow-up from Cleft and Craniofacial Team support services. This threshold was based on the company’s recommendation that this should be considered a clinical significant score, and thus could indicate clinical depression in the participant.
Chapter 3: Results

3.1 Recruitment
Data collection began November 18th, 2014 and is still ongoing. This dissertation includes pilot data for all participants through March 18th, 2016. During this period, 21 patients with CL/P received lip repair at BCCH. Of these, 8 (38%) participated in this study. Reasons for non-participation in the remaining 13 (62%) were: 1 (8%) ineligible due to English language requirements, 5 (38.5%) declined to participate, 5 (38.5%) missed study recruitment by research associates, and 2 (15%) consented but failed to complete questionnaire prior to lip surgery.

3.2 Caregiver Demographics and Geography
Participating caregivers were from a highly uniform demographic population. All participants completing the study materials indicated that they were the patients’ mothers. Mean maternal age at the time of data collection was 30.25 ± 4.53 years. All participants indicated married or common law marital status. The majority indicated they had some university of college education (7/8), with three completing Bachelor’s degrees. Geographic home location of participants relative to treatment centre (BCCH) was bi-modally distributed with five participants living locally (20.0 ± 13.9 km) and 3 living remotely (640.3 ± 118.7 km). Comparison data from non-participating caregivers is unavailable due to ethical restrictions in research design.

3.3 Patient Diagnosis
Patients in this study presented with a range of CL/P diagnoses. Half (4/8) were diagnosed with cleft lip, and half with cleft lip and palate. Unilateral involvement (6/8) was more common than bilateral involvement, and incomplete cleft depth (6/8) was more common than complete. No patients presented with known clefting syndromes, though two patients were still undergoing investigations for possible syndromal association at the time of
participation. Over half of the participating caregivers (5/8) were aware of their child’s cleft prior to birth.

### 3.4 Pre-Surgical Treatment

Four patients received lip repair surgery with no PSIO prior to surgery. The remaining four patients received PSIO from two different orthodontists. Three patients received PSIO using an acrylic intraoral appliance with nasal stent and lip taping (NAM) while one received a nasal stent and lip taping without intra-oral appliance. The duration of PSIO treatment was 6 to 10 appointments (7.3 ± 1.9 visits) over an average of 96.0 days (SD 25.7 days). Patients in both groups consistently underwent lip repair surgery at 3 months of age.

### 3.5 Parental Stress, Burden, and Coping Response

At this time, the small sample size precludes inferential statistical analyses. Descriptive outcome data for all participants and treatment groups will be presented with basic statistical testing. Due to the small sample size, all methods of PSIO were combined as one group. Caution is advised in the interpretation of statistical testing at this time due to the small sample size.

#### 3.5.1 Caregiver Confidence

Caregiver confidence as assessed by the Maternal Confidence Questionnaire (MCQ) is presented in Table 1 below. Overall confidence in this small sample was high compared with published normal ranges\(^6^7\). Furthermore, the average total MCQ score in this sample (61.38 ± 4.14) was greater than that reported in a previous study investigating caregivers of premature infants at the same centre (MCQ 50.4 ± 9.8)\(^6^9\). While no statistically significant differences between the PSIO and no-PSIO treatment groups were found, there was a trend for caregivers in the PSIO group to believe they were better able to understand and respond to their child’s mood and feelings than caregivers who did not participate in PSIO.
Table 1 – Sample and Treatment Group Scores: Maternal Confidence Questionnaire

<table>
<thead>
<tr>
<th></th>
<th>Total Sample Mean (SD)</th>
<th>No PSIO Mean (SD)</th>
<th>PSIO Mean (SD)</th>
<th>Treatment Group Differences Mean (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge</td>
<td>25.75 (1.67)</td>
<td>25.25 (1.26)</td>
<td>26.25 (2.06)</td>
<td>-1.00 (-3.96, 1.96)</td>
<td>0.439</td>
</tr>
<tr>
<td>Tasks</td>
<td>14.38 (1.19)</td>
<td>14.50 (1.00)</td>
<td>14.25 (1.50)</td>
<td>0.25 (-1.96, 2.46)</td>
<td>0.791</td>
</tr>
<tr>
<td>Feelings</td>
<td>21.25 (1.99)</td>
<td>20.25 (2.06)</td>
<td>22.25 (1.50)</td>
<td>-2.00 (-5.12, 1.12)</td>
<td>0.168</td>
</tr>
<tr>
<td>MCQ Total</td>
<td>61.38 (4.14)</td>
<td>60.00 (3.92)</td>
<td>62.75 (4.43)</td>
<td>-2.75 (-9.98, 4.48)</td>
<td>0.388</td>
</tr>
</tbody>
</table>

3.5.2 Caregiver Stress

Adverse effects of parental stress were assessed with the PSI-4 (Table 2), and stress caused by caring for a child with CL/P with the SSPCL/P (Table 3).

The adverse effects of parental stress, as assessed by the PSI-4 did not differ significantly from the company’s published normal reference. The total stress score and all subdomain scores were within the 45th-55th percentile scores of published normative data for parents with children younger than 1 year of age71. This may indicate a generally normal stress profile for caregivers participating in this study. No statistically significant inter-group difference were noted when comparing PSIO and no-PSIO, though a non-significant trend was noted in the depression subdomain. Preliminary data show that parents of infants who did not receive PSIO tended to report greater depressive feelings related to caring for their child. No caregivers in either group reported depressive feelings significant enough to require additional referral as per the study protocol, nor did any participants request additional follow-up.
Stress associated with concerns specific to caring for a child with CL/P was assessed using the SSPCL/P. As a relatively new metric, appropriate reference data for comparison is currently limited. No significant differences between PSIO and no-PSIO groups were found, though a non-significant trend was noted with the PSIO group reporting more concerns related to management of the cleft defect, resource deficiency, and greater overall stress.
Table 3 - Sample and Treatment Group Scores: Stress Scale for Parents of CL/P Children (SSPCL/P)

<table>
<thead>
<tr>
<th></th>
<th>Total Sample</th>
<th>No PSIO</th>
<th>PSIO</th>
<th>Treatment Group Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (95% CI)</td>
</tr>
<tr>
<td><strong>Long-Term Concerns</strong></td>
<td>1.66 (0.29)</td>
<td>1.63 (0.26)</td>
<td>1.70 (0.36)</td>
<td>-0.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-0.62, 0.47)</td>
</tr>
<tr>
<td><strong>Resources</strong></td>
<td>1.31 (0.30)</td>
<td>1.17 (0.13)</td>
<td>1.46 (0.37)</td>
<td>-0.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-0.77, 0.19)</td>
</tr>
<tr>
<td><strong>Family Adaptation</strong></td>
<td>1.50 (0.65)</td>
<td>1.44 (0.43)</td>
<td>1.56 (0.90)</td>
<td>-0.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-1.34, 1.09)</td>
</tr>
<tr>
<td><strong>Defect Management</strong></td>
<td>1.17 (0.76)</td>
<td>0.75 (0.42)</td>
<td>1.59 (0.83)</td>
<td>-0.84</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-1.98, 0.31)</td>
</tr>
<tr>
<td><strong>Overall Stress</strong></td>
<td>1.35 (0.49)</td>
<td>1.12 (0.32)</td>
<td>1.57 (0.57)</td>
<td>-0.46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-1.26, 0.35)</td>
</tr>
</tbody>
</table>

3.5.3 Caregiver Coping

Coping response in the study sample, as assessed by the CRI, demonstrated greater use of positive (approach) coping than negative (avoidant) coping strategies (Table 4). When compared to the normal scoring profile provided by the manufacturer, the sample population exhibited a generally average coping pattern. Logical analysis, positive reappraisal, seeking guidance, problem solving, cognitive avoidance, acceptance/resignation, and seeking alternative reward coping strategy mean scores were within the 50th-55th percentiles of normative data. Emotional discharge was relied upon marginally more commonly in this sample compared to the normative data (60th percentile). No statistically significant differences in coping response were found between treatment groups.
Table 4 - Sample and Treatment Group Scores: Coping Response Inventory

<table>
<thead>
<tr>
<th></th>
<th>Total Sample</th>
<th>No PSIO</th>
<th>PSIO</th>
<th>Treatment Group Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (95% CI)</td>
</tr>
<tr>
<td>Logical Analysis</td>
<td>10.38 (1.85)</td>
<td>9.75 (1.50)</td>
<td>11.00 (2.16)</td>
<td>-1.25 (-4.47, 1.97)</td>
</tr>
<tr>
<td>Positive Reappraisal</td>
<td>13.13 (2.10)</td>
<td>12.75 (2.87)</td>
<td>13.50 (1.29)</td>
<td>-0.75 (-4.60, 3.10)</td>
</tr>
<tr>
<td>Seeking Guidance</td>
<td>10.25 (2.82)</td>
<td>10.50 (2.38)</td>
<td>10.00 (3.56)</td>
<td>0.50 (-4.74, 5.74)</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>13.38 (2.67)</td>
<td>13.25 (3.30)</td>
<td>13.50 (2.38)</td>
<td>-0.25 (-5.23, 4.73)</td>
</tr>
<tr>
<td>Approach Coping</td>
<td>47.13 (5.89)</td>
<td>46.25 (5.38)</td>
<td>48.00 (7.07)</td>
<td>-1.75 (-12.62, 9.12)</td>
</tr>
<tr>
<td>Cognitive Avoidance</td>
<td>6.13 (3.64)</td>
<td>5.50 (4.20)</td>
<td>6.75 (3.50)</td>
<td>-1.25 (-7.94, 5.44)</td>
</tr>
<tr>
<td>Acceptance/Resignation</td>
<td>7.13 (3.36)</td>
<td>7.25 (4.50)</td>
<td>7.00 (2.45)</td>
<td>0.25 (-6.02, 6.52)</td>
</tr>
<tr>
<td>Alternative Rewards</td>
<td>6.63 (4.69)</td>
<td>4.75 (5.68)</td>
<td>8.50 (3.11)</td>
<td>-3.75 (-11.67, 4.17)</td>
</tr>
<tr>
<td>Emotional Discharge</td>
<td>7.00 (2.73)</td>
<td>7.25 (3.78)</td>
<td>6.75 (1.71)</td>
<td>0.50 (-4.57, 5.57)</td>
</tr>
<tr>
<td>Avoidance Coping</td>
<td>26.88 (9.80)</td>
<td>24.75 (13.96)</td>
<td>29.00 (4.16)</td>
<td>-4.25 (-22.07, 13.57)</td>
</tr>
</tbody>
</table>

3.5.4 Visual Analogue Items

Visual analogue items were included to assess the subjective severity of caregiver burden. The group receiving PSIO treatment reported financial, emotional, and time burden related to treatment ‘provided by an orthodontist’, with statistically significant differences in emotional (p=0.024) and time burden (p=0.007) when compared to the group that did not receive PSIO (Table 5). The group that did not receive PSIO treatment (ie: no treatment from an orthodontist) reported no financial or time burden due to orthodontic treatment. One participant in the no-PSIO group did report a modest emotional burden from orthodontic treatment.
### Table 5 - Visual Analogue Scale Outcomes for Orthodontic Treatment Burden

<table>
<thead>
<tr>
<th>Orthodontic Burden</th>
<th>Total Sample Mean (SD)</th>
<th>No PSIO Mean (SD)</th>
<th>PSIO Mean (SD)</th>
<th>Treatment Group Differences Mean (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financial</td>
<td>11.56 (24.51)</td>
<td>0.00 (0.00)</td>
<td>23.13 (32.34)</td>
<td>-23.13 (-62.69, 16.44)</td>
<td>0.203</td>
</tr>
<tr>
<td>Emotional</td>
<td>30.56 (30.80)</td>
<td>8.25 (16.50)</td>
<td>52.88 (24.77)</td>
<td>-44.63 (-81.04, -8.21)</td>
<td>0.024</td>
</tr>
<tr>
<td>Time</td>
<td>25.50 (31.88)</td>
<td>0.00 (0.00)</td>
<td>51.00 (25.26)</td>
<td>-51.00 (-81.90, -20.10)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Differences in total treatment burden (Table 6) were also noted between treatment groups, with the PSIO group again tending to report greater subjective burden. The differences in perceived total treatment burden between groups was statistically significant for time (p=0.029), but not for financial (p=0.122) or emotional (p=0.328) burdens.

### Table 6 - Visual Analogue Scale Outcomes for Total Treatment Burden

<table>
<thead>
<tr>
<th>Treatment Burden</th>
<th>Total Sample Mean (SD)</th>
<th>No PSIO Mean (SD)</th>
<th>PSIO Mean (SD)</th>
<th>Treatment Group Differences Mean (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financial</td>
<td>17.75 (16.91)</td>
<td>8.38 (9.74)</td>
<td>27.13 (18.39)</td>
<td>-18.75 (-44.21, 6.71)</td>
<td>0.122</td>
</tr>
<tr>
<td>Emotional</td>
<td>37.56 (20.97)</td>
<td>29.75 (24.80)</td>
<td>45.38 (15.75)</td>
<td>-15.63 (-51.57, 20.32)</td>
<td>0.328</td>
</tr>
<tr>
<td>Time</td>
<td>30.31 (23.84)</td>
<td>13.38 (9.16)</td>
<td>47.25 (21.86)</td>
<td>-33.88 (-62.87, -4.88)</td>
<td>0.029</td>
</tr>
</tbody>
</table>

Despite the moderate treatment burden reported by participants, the majority (6/8) indicated that they would request the same treatment method in the future if they had another child born with CL/P. One subject in the PSIO group reported that they were unsure if they would pursue the same treatment, as they felt the treatment was difficult to cope with for both themselves and their child. Conversely, one patient in the no-PSIO group reported dissatisfaction with the treatment received in their remote community,
indicating that if they were to have another child with CL/P they would prefer to relocate closer to the treatment centre.
Chapter 4: Discussion

4.1 Objective Assessment of Treatment Load

Treatment load for pre-surgical infant orthopedic treatment was assessed in this study by the duration of treatment and number of appointments. Patients receiving PSIO treatment attended 7.3 more appointments (p < 0.001) over a treatment period of 96 days on average when compared to those not receiving PSIO. This is marginally less than a previous report which found NAM required an additional average 9.9 visits over 127 days\textsuperscript{57}. This difference may be explained by treatment group differences between the studies: Singer\textsuperscript{57} included only NAM, while our PSIO group included both children who received NAM and other methods such as nasal stenting with lip taping. Furthermore, NAM treatment in the Singer study was provided at a hospital centre, whereas PSIO in this study was provided in private practice.

It should be considered that the number of appointments required for PSIO is only one factor in the total treatment load. For example, PSIO has been shown to influence the requirement for additional surgeries in the teenage years. In a large retrospective cohort study, Patel and colleagues reported that NAM decreased the average number of nasal surgeries required by age 14, and proposed that this decrease in surgical intervention may be considered a reduced treatment load\textsuperscript{60}. Additionally, other measures of treatment load such as financial cost need to be considered. In comparing the cost of NAM compared to surgical costs, NAM has been shown to save the treating hospital an average of $491 for UCLP patients, and $2381 for BCLP patients\textsuperscript{60}. For a publically funded medical system such as that in British Columbia, reducing the financial burden of treatment on the hospital is a significant consideration.

Within the limitations outlined above, we can conclude from our preliminary data that null hypothesis 1 may be rejected. PSIO treatment was found to have a significantly greater objectively assessed treatment load in the short term, as measured by treatment
duration and number of appointments. Additional studies to determine if these differences persist in the long-term would be of benefit.

4.2 Subjective Assessment of Burden of Care
The second objective of this study was to compare the subjective perception of burden between caregivers from the two treatment groups. Subjective burden was assessed using visual analogue scale ratings for both ‘orthodontic’ (PSIO) treatment and total treatment, with specific consideration given to financial, emotional, and time burden to caregivers.

When asked to consider specifically treatment provided by their orthodontist, the no-PSIO caregivers reported no financial or time burden, as would be expected. One participant in the no-PSIO group reported an emotional burden from orthodontic treatment. It is possible that this is an erroneous result due to misunderstanding in completing the question. Alternatively, this participant may have been seen for orthodontic consultation and declined PSIO – a potentially difficult decision that may have lead to the emotional burden reported. Participants in the PSIO group identified significantly greater orthodontic emotional and time burden than those in the no-PSIO group. Differences in orthodontic financial burden did not differ significantly between treatment groups, possibly because treatment fees are covered by the public medical system.

Treatment in PSIO and no-PSIO groups differed only in the ‘orthodontic’ component of treatment – all other treatments within the study period were generally similar between the groups, apart from some individual variation related to patient treatment needs. Thus, comparing the burden of the entire treatment between these groups can be considered an exploration of the change in burden as a result of the orthodontic PSIO treatment. Caregivers of children receiving PSIO reported 2-3 times greater mean visual analogue scores for overall treatment burden in all categories: financial, emotional, and time. Despite these large differences, only overall treatment time burden differences were statistically significant, possibly due to the small sample size. At this time, our preliminary
results allow a limited rejection null hypothesis 2: caregivers of children receiving PSIO perceived a greater treatment burden, particularly with respect to the time requirements of treatment.

Further research is required to determine if the differences in financial and emotional burden between the groups will also be observed in studies including larger samples.

4.3 Caregiver Stress, Confidence, and Coping

Thus far we have considered the objective treatment load, and the subjective perception of the burden experienced by primary caregivers of children with CL/P. Our third objective was to compare differences in caregiver response to treatment burden between PSIO and no-PSIO groups. Specifically, we were interested in caregiver stress, confidence, and coping strategies.

As a result of the small sample size collected to date in this study, only a limited interpretation of the preliminary data is feasible. Caregiver confidence in this sample was greater than previous reports using the Maternal Confidence Questionnaire (MCQ). General population scores on this metric typically range from 51-59\(^6\), and a previous study conducted at BCCH found a mean MCQ score of 50.4 in mothers of preterm infants\(^6\). In the present study, the mean total MCQ score for participants was 61.38 ± 4.14, indicating that caregivers had a relatively high confidence in their ability to meet the needs of their child. One possible explanation for the high caregiver confidence reported in this study is the frequent follow-up that caregiver and child received from the cleft and craniofacial treatment team. Frequent interactions with physicians, nurses, counselors, and other health care professionals may assist in developing caregiver skill and confidence. PSIO treatment was not found to have a statistically significant effect on total caregiver confidence, though a non-significant trend was noted in the feelings subdomain, with the PSIO group reporting greater confidence in understanding and responding to their child’s mood (p=0.168).
Adverse effects of parental stress on daily life were assessed in this study using the Parenting Stress Index 4th Edition (PSI-4), and did not differ substantially from available normative data for parents of children less than 1 year of age\(^7\). The PSI-4 has been used previously in CL/P research, providing the opportunity to compare our results with those of previous studies. Andrews-Casal and colleagues used the Parenting Stress Index in their investigation on the effect of family history of CL/P\(^7\). In this study, both mothers and fathers of children with CL/P were assessed, and were stratified by the presence or absence of a family history of CL/P. In all groups assessed, the Parent Domain total score of the PSI was between 100 to 105 – similar to both the normative data 50th percentile score, and the sample mean of 111.63 ± 20.81 in our present study. Similarly, in a longitudinal study of parents of children born with craniofacial anomalies, parental stress between birth and 24 months of age did not differ significantly from normative data\(^6\). Interestingly, although mean PSI scores did not differ from normative data, the authors noted a non-normal distribution with a skew to increased stress severity in their sample compared to normative data\(^6\). At this time our sample size is insufficient to further investigate this possibility.

Parental stress assessments using the PSI-4 have also previously been reported in other age groups. A case-control study comparing 93 parents of children with CL/P at 2 years of age to 124 controls found that the CL/P and control groups did not differ significantly in PSI-4 scores, and that scores in both groups (111.25 ± 25.62 and 111.02 ± 24.49) were comparable to normative data\(^7\). The relative consistency of PSI-4 scores observed in various studies, and their similarity to normative data may have two possible explanations. Firstly, it is conceivable that the general stress of caring for a young infant is already relatively high, and that additional stressors such as health concerns contribute proportionally small increases in total stress. Alternatively, it is possible that despite the good psychometric profile of this metric, it is still unable to assess the complex emotions involved in having a child with CL/P. This potential limitation of psychometric tests in the
CL/P population has been suggested previously, with some authors proposing that qualitative studies are the most appropriate method to investigate parental emotion and stress. Unfortunately, qualitative interview studies can be challenging and time consuming to conduct, and at this time are relatively scarce in this field.

Parental stress was also assessed in this study using the Stress Scale for Parents with Cleft Lip and/or Palate Children (SSPCL/P). This metric investigates stress specifically related to caring for a child with CL/P, and as such may have some advantages over generic stress metrics such as the PSI-4. To date, only the initial psychometric validation study on the SSPCL/P has been reported. Lei et al. assessed the SSPCL/P on Chinese-speaking parents of children with CL/P aged 0 to 13 years in Taiwan, and validated the subscales of the SSPCL/P by factor analysis. Comparison data from the 184 parents is available from this study; however, caution is indicated as the population investigated differs significantly from ours. Furthermore, the original SSPCL/P was administered in Chinese, and translated to English only for publication purposes. It is also important to consider that the metric was further modified for our study – we altered any phrasing in the English translation that might have been confusing for participants (Appendix A.2). The current small sample size precludes us from conducting a factor analysis and validating the English version of this scale at this time.

Comparing SSPCL/P scores in our study sample to validation data demonstrated no difference in overall stress. Differences in the subdomain stress pattern were noted, with our sample reporting greater stress related to family adaptation, and less stress related to treatment procedures. Due to the limitations discussed above, it is not possible at this time to determine if these differences are due to population differences, treatment rendered, or translation of the metric to English. No statistically significant differences in parental stress were found between the PSIO and no-PSIO groups. However, non-significant trends were noted with parents in the PSIO group reporting greater overall stress, and greater stress specific to CL/P defect management and resource deficiency. Despite this increase in CL/P
specific stress, the PSIO group did not report any increase in adverse effects of stress as assessed by the PSI-4, and actually reported a decrease in depressive symptoms. These differences should be interpreted with caution due to the small sample size at present; however, these differences may support the hypothesis that the challenges of PSIO treatment promote positive adaptation and coping in caregivers. Alternatively, because treatment groups could not be randomly assigned in this study, it is possible that the PSIO treatment group is a self-selecting population of positive coping caregivers. Because PSIO treatment is initiated within days to weeks of birth, it was deemed unfeasible to obtain baseline measurements in this study prior to treatment. As such, it is not possible to determine if treatment group differences were pre-existing.

Finally, caregiver coping response was assessed using the Coping Response Inventory (CRI)72. Two recent publications have used the CRI in CL/P populations. Baker and colleagues investigated coping strategies in 103 parents of children with CL/P aged 0 to 18 years in the United Kingdom63. Similar to our study, they found that approach-based coping was more commonly utilized than avoidant coping, with CRI scores of 38.28 ± 12.54 and 22.71 ± 11.06 respectively63. Our sample reported greater use of approach coping (47.13 ± 5.89), and similar reliance on avoidance coping (26.88 ± 9.80). Further subdomain scoring was not reported by the authors. A second study from Mashhad, Iran reported CRI scores in parents of children with CL/P aged 8 to 18 years64. Reliance on approach coping (44.70 ± 12.49) was again greater than avoidant coping (32.94 ± 7.97), with this sample reporting greater reliance on avoidant coping when compared to both our sample and that reported by Baker et al. Differences in CRI scores between these two studies and ours may be a result of study location, or differing age of participants. Further studies assessing coping response in parents of infants and young children with CL/P would likely be of benefit. Finally, in comparing coping response between PSIO and no-PSIO treatment groups, no statistically significant differences were detected.
At present, we cannot reject null hypothesis 3 because no statistically significant differences in caregiver stress, confidence, or coping response were detected between PSIO and no-PSIO groups. Non-significant trends may suggest possible differences including greater confidence, decreased depressive symptoms, and greater concern over defect management and resource deficiency in caregivers of children receiving PSIO. Further data collection is required to achieve adequate power for the chosen metrics.

4.4 Study Limitations

The most significant limitation of this study at present is the small sample size. During study design, it was anticipated that this thesis would consist of a pilot report of preliminary data. At the time, it was estimated that approximately one child with CL/P was born per week at BC Children’s Hospital (BCCH). If a high response rate of 75% could be obtained, we anticipated that the available 17 months of data collection would produce nearly half of the desired 126 participant sample. Unfortunately, only 8 participants were collected during this time. A significant contributor to the difference in expected and actual participants was the birth rate of children with CL/P at BCCH. Recently, a chart review of all BCCH CL/P patients was conducted as part of a Doctoral thesis at the University of British Columbia. This review found that incidence of CL/P at BCCH was both far lower than initially estimated, and highly variable from year to year. As can be seen in Figure 8, the average number of CL/P patients treated at BCCH each year is less than half of the estimate used in designing this study. This discrepancy between estimated and actual birth rates illustrates the importance of accurate occurrence rates when designing prospective studies, particularly when the population of interest has a relatively rare condition such as cleft lip and palate. Future prospective studies in this population would benefit from accurate incidence data during study design to ensure that data collection can be accomplished with a feasible study duration.
Another limitation of the present study is the low recruitment rate. Of the 21 potential participants during the data collection period, 5 declined to participate – potentially comparable to our desired response rate of 75%. However, an additional 3 subjects were excluded due to English language requirements or failure to complete the caregiver questionnaire prior to lip surgery. Furthermore, 5 families were missed by our recruiters and were never approached to participate in the study. Ultimately, the participation rate for our preliminary data collection period was 38% - significantly less than desired. Similar participation rates of 29-34% have been previously reported in questionnaire studies of parents of children with CL/P⁶³,⁷⁶.

In addition to limiting statistical interpretation of the results, our small sample size may be non-representative of the study population. As with any self-selecting sample, it is possible that non-participants differ systematically from participants. For example, caregivers who felt especially overwhelmed may have declined to participate due to the 30 to 60 minutes
required to complete the questionnaire. We attempted to minimize this selection bias by explaining to all caregivers that sharing any feelings of being overwhelmed through this study could help us improve support in the future. Additionally, we attempted to provide flexibility to participants. Questionnaires could be completed at routine appointments, where hospital staff were available to assist in caregiving duties during study participation, or taken home to be completed at a more convenient time.

Furthermore, the small sample may also be non-representative with respect to CL/P presentation. The most common presentation of CL/P is unilateral, complete involvement. In general, 60% of patients present with complete involvement, and 70% of clefts are unilateral. In our study sample, 75% of patients exhibited unilateral involvement, but only 25% presented with complete cleft depth. It is possible that caregivers of children with more severe cleft presentations were less likely to participate due to increased burden of care or negative emotions. Unfortunately, ethical limitations prevented access to medical charts to determine if there were differences in CL/P presentation between participants and non-participants.

4.5 Study Feasibility and Future Directions
At present, this thesis consists of a pilot study for the full study protocol outlined in the methodology section above. With our current knowledge regarding CL/P birth rate at BCCH and the projected recruitment rate, a better estimate of data collection time is possible. At the present rate of data collection, it would require approximately 22 years to collect the desired sample of 126 participants. If data collection procedures could be improved to ensure that all potential participants were approached, this would be reduced to approximately 17 years, assuming the same response rate. Even with this optimistic improvement, the collection period remains unfeasibly long. It may be concluded from this pilot report that multi-centre involvement will be required to complete this study within a feasible timeframe.
Chapter 5: Conclusion

Pre-surgical infant orthopedic treatment for cleft lip with or without cleft palate requires an average additional 7.3 appointments over 96 days. Caregivers perceive significant time and emotional burdens to this treatment, as well as a significant increase in total treatment time burden when pre-surgical infant orthopedics is employed. Statistical analysis of remaining data was limited by the small pilot sample. Statistically non-significant trends were noted, with caregivers of children who received pre-surgical infant orthopedics reporting increased stress and concerns regarding both management of the cleft and resource deficiencies. These caregivers also tended to report greater confidence in their ability to understand and respond to their child’s mood, and less depressive symptoms. Adverse effects of stress and coping strategies utilized did not differ between treatment groups. These findings lend limited support to the hypothesis that pre-surgical infant orthopedics has beneficial psychological effects on caregivers, despite increased treatment burden. Finally, it was demonstrated that multi-centre involvement will be required to answer the research question posed by the present study.
**Works Cited**


Appendix

Appendix A - Questionnaires and Data Collection Forms
Copies of caregiver questionnaire items and forms for subjective burden of care data collection are included below for reference. Complete metrics including instructions given to participants are provided wherever possible. Copyright protection prevents the inclusion of the Parenting Stress Index, 4th Edition and the Coping Response Inventory.
A.1 Maternal Confidence Questionnaire

The Maternal Confidence Questionnaire (MCQ)\textsuperscript{67} was presented as a single page including instructions and all 14 Likert items in table format.
The following section will ask you questions about how confident you feel in your role as a caregiver. Please mark your response with an ‘X’ in the corresponding box. Please mark only one response for each question.

<table>
<thead>
<tr>
<th></th>
<th>Never 1</th>
<th>Seldom 2</th>
<th>Some 3</th>
<th>Often 4</th>
<th>A great deal 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>I know when my baby wants me to play with him/her.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I know how to take care of my baby better than anyone else.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>When my baby is cranky, I know the reason.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I can tell when my baby is tired and needs sleep.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I know what makes my baby happy.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I can give my baby a bath.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I can feed my baby adequately.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I can hold my baby properly.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I can tell when my baby is sick.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I feel frustrated taking care of my baby.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I would be good at helping others learn to take care of their infants.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Being a parent is demanding and unrewarding.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have all the skills needed to be a good parent.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am satisfied with my role as a parent.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A.2 Stress Scale for Parents of Cleft Lip and Palate Children

The Stress Scale for Parents of Cleft Lip and Palate Children (SSPCL/P\textsuperscript{70}) was presented in table format. Instructions included examples to differentiate “Doesn’t Apply” and “Never” responses.
The following section will ask you questions regarding both current challenges, and your future concerns.

Please circle *only one* response for each question.

Some questions may not be applicable to your child. If you feel a question does not apply, please circle ‘DA’ to indicate that the question does not apply.

### Examples

<table>
<thead>
<tr>
<th>Response</th>
<th>Doesn’t Apply</th>
<th>Never 1</th>
<th>Seldom 2</th>
<th>Often 3</th>
<th>Always 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>My child is uncooperative when treatment is given.</td>
<td>‘DA’</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The response above indicates that the child is never uncooperative during treatment.

This is not the same as a child who has not yet received any treatment. For children who have not yet received treatment, the appropriate response is to circle “DA” under “Doesn’t Apply”:

<table>
<thead>
<tr>
<th>Response</th>
<th>Doesn’t Apply</th>
<th>Never 1</th>
<th>Seldom 2</th>
<th>Often 3</th>
<th>Always 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>My child is uncooperative when treatment is given.</td>
<td>‘DA’</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Note that if “DA” is selected, no number score should be circled. Only one response should be circled for each question.
<table>
<thead>
<tr>
<th>Concern</th>
<th>Doesn’t Apply</th>
<th>Never 1</th>
<th>Seldom 2</th>
<th>Often 3</th>
<th>Always 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am concerned that my child’s cleft lip/palate will contribute to emotional issues (ie: low self-esteem or social exclusion).</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>My child is uncooperative when treatment is given.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am concerned that heredity of cleft lip/palate might lead to hesitation in having another child.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am concerned that feeding my child is difficult.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am concerned that my child might be bullied in school.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>It is inconvenient to go to the hospital regularly because of time constraints.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am concerned about my child’s future (ie: ability to live independently, marriage, employment).</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am concerned that teachers at school or babysitters will be unable or unwilling to take proper care of my child.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am negatively affected when I witness my child receiving treatment.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel I have received enough information about my child’s treatment.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>My child has exhibited significant improvements following treatment.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am concerned that my child may feel alienated by relatives and family friends.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am concerned about what people think of me and my child.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>There is added emotional stress on the family as a result of my child’s condition.</td>
<td>DA</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
A.3 Parenting Stress Index 4th Edition

The Parenting Stress Index 4th Edition is a proprietary metric produced by Psychological Assessment Resources, Inc. Due to copyright restrictions, the PSI-4 cannot be reproduced herein. The PSI-4 can be obtained from Psychological Assessment Resources, Inc. at http://www4.parinc.com/Products/Product.aspx?ProductID=PSI-4
A.4 Coping Response Inventory

The Coping Response Inventory (CRI)\textsuperscript{72} is a proprietary metric produced by Psychological Assessment Resources, Inc. Due to copyright restrictions, the PSI-4 cannot be reproduced herein. The PSI-4 can be obtained from Psychological Assessment Resources, Inc. at: 
http://www4.parinc.com/Products/Product.aspx?ProductID=CRI
A.5  Visual Analogue Questions for Subjective Burden Assessment

Visual analogue items were present together, with a single preceding example. Questionnaires given to participants were carefully scaled during printing to ensure all visual analogue scale lines were 100 mm in length.
The following section will ask you how difficult caring for your child has been. Please indicate your response by marking a vertical line on the scale for each question.

Example:

The overall care for my child since birth has involved a financial burden

Not at all                                          Extremely, Almost Unbearable

The response above indicates that there has been financial burden, but that the burden is relatively minor.

The following questions are regarding the overall care of your child, including medical treatments and daily caregiving activities.

1. The overall care for my child since birth has involved a financial burden

2. The overall care for my child since birth has involved an emotional burden

3. The overall care for my child since birth has involved a time burden
The following questions are regarding orthodontic care, including dental/orthodontic examinations, and any treatment your child has received from an orthodontist.

4. The orthodontic care for my child since birth has involved a financial burden

5. The orthodontic care for my child since birth has involved an emotional burden

6. The orthodontic care for my child since birth has involved a time burden
A.6 Treatment Data Form for Orthodontists

Unique Code (provided by hospital research associate): _____________________

Treating Orthodontist: _________________________________________________

Associated Hospital Treatment Centre: _________________________________

Patient’s Month of Birth (Month, Year): _____________________________

Treatment Start Date: __________________________

Treatment End Date: __________________________

☐ Treatment Completed / Ready for Lip Surgery

☐ Treatment Discontinued

If discontinued, please provide reason: _________________________________

Number of Treatment Visits: ______________

Diagnosis (please check appropriate diagnosis from each grouping):

| ☐ Cleft Lip | ☐ Cleft Lip and Palate |
| ☐ Complete | ☐ Unilateral |
| ☐ Incomplete | ☐ Bilateral |

Treatment (please check all that apply):

☐ No appliances used (consultations, examinations only)

☐ Intraoral appliance

☐ Active components (expansion screws etc.)

☐ Acrylic components

☐ Acrylic not adjusted, or adjusted for comfort only

☐ Acrylic adjusted with the goal of moving alveolar segments

☐ Lip taping

☐ Nasal stent

☐ Attached to intraoral appliance

☐ Attached extra-orally with tape

☐ Other (please describe) ____________________________________________