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Academic Outcomes in Children with Orofacial Clefts

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Academic Outcomes in Children with Orofacial Clefts

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Bachelor of Arts

University of Virginia

2008

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Abstract

Academic Outcomes in Children with Orofacial Clefts

By Jessica Knight

Background: Previous research has measured differences in IQ or standardized test scores between children with and without orofacial clefts (OFC), but little is known about other academic outcomes in this population. This study examines parent-reported letter grades, grade retention, and school days missed among school-aged children with and without OFC, using a statewide, population-based sample.

Methods: In 2007-2008, questionnaires were mailed to a random sample of 504 mothers of children with OFC born 1996-2002 (ages 5-12) identified by the NC birth defects registry (case mothers). A random sample of 504 mothers of children without birth defects born 1996-2002 was selected from NC birth certificates (control mothers). The questionnaire included Likert-scale, closed-, and open-ended questions from validated quality of life instruments. Domains included demographics, outcomes, and quality of life. Univariate and bivariate analysis and multivariable logistic regression were used to compare mother reported educational outcomes between children with and without OFC. Among children with OFC, outcomes were compared by cleft type and between children with isolated and non-isolated OFC. Univariate and bivariate analysis also evaluated the maternal-report of selected medical conditions related to academic outcomes.

Results: About thirty percent (N=150) of eligible case mothers and 27.6% (N=139) of eligible control mothers responded. Case mothers reported more developmental delay/ physical impairment, speech impairment, hearing problems and behavioral/ conduct problems among their children than control mothers. No significant differences were found with letter grades and grade retention among children with and without OFC or by cleft type among children with OFC. Children with OFC missed significantly more school days than unaffected children. Children with non-isolated OFC were significantly more likely to repeat a grade than those with isolated OFC.

Conclusions: Despite more mothers reporting behavioral and developmental problems in children with isolated OFC, these children appear to perform similarly in school to their peers who do not have birth defects. However, children with non-isolated OFC may benefit from additional interventions to avoid repeating a grade in school. Further studies should investigate the specific impacts of the presence of these co-morbidities on children with OFC in relation to their services needs and academic success.

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Introduction

Children with oroficial clefts (OFC), a type of birth defect, have increased rates of hearing problems, frequent ear infections, difficulties with language and reading skills, learning disability, and intellectual disability compared to children without this birth defect (1-16). Research suggests that children with OFC also have higher rates of behavioral problems, attention-deficit hyperactivity disorder (ADHD), anxiety and depression than children without birth defects, but these results are not as definitive (13, 17-22). Finally, children with OFC are often victims of stigmatization due to facial disfiguration or speech impairment (23). These problems often culminate in difficulties, such as missed school days and lower grades, for school-aged children. Children with OFC have been shown to score lower on standardized tests, use more special education services and repeat grades in school more often than their unaffected peers (1, 13, 16). However, the research on how these children perform in academic settings is limited by: clinic-based, convenience samples; lack of comparison groups in some studies; and limited comparison of different cleft types. Therefore, the aim of this population-based case-control study is to compare academic outcomes in elementary school-age children with OFC (cases) to children without a major birth defect (controls). The academic outcomes to be assessed are: letter grades, grade retention, and number of school days missed. The implications of this study should help advise parents about expectations for their child's success in school, and guide healthcare professionals in planning for early intervention, special education and special needs services for children with OFC. In addition, results from this study could help school professionals with program planning and development for children with special needs, such as children with OFC. Studies on outcomes of children with OFC, such as this one, were recently seen as public health research priorities by experts convened by the Centers for Disease Control and Prevention (24)

Background/ Literature review

Impact and Description of Orofacial Clefts

Birth defects are structural anomalies formed before birth that can affect any part of the body. They are the leading cause of infant death in the United States, accounting for approximately twenty percent of deaths before the age of one (25). Orofacial clefts (OFC) are among the most common forms of major birth defects. These birth defects occur when the mouth or lip do not form properly and include infants born with a cleft lip only, cleft palate only, or cleft lip and cleft palate. It has been estimated that each year in this country, 4,437 infants are born with cleft lip with or without cleft palate, and another 2,651 infants are born with cleft palate alone (26). Specifically in North Carolina, about 180 infants are born with OFC each year (27). Racial differences exist in children with OFC, with the highest prevalences occurring in American Indians, followed by Asian/Pacific Islanders, whites, and finally blacks (28, 29).

The etiology of OFC is largely unknown (31). Studies have shown that smoking during pregnancy is a risk factor for giving birth to a child with OFC, and that genetics also play a role in this association by making some infants more susceptible to the effects of smoking (30, 31). Young maternal age has also been associated with increased risk of having a child born with OFC (29, 32).

Orofacial clefts (OFC) can be classified as an isolated or non-isolated OFC. Non-isolated OFC occurs in children who have at least one other major birth defect, associated syndrome or sequence. Only 30% of all children with OFC have a non-isolated OFC, but this proportion is higher among children with cleft palate only. It is commonly thought that cleft palate alone occurs from a different etiologic process than cleft lip with or without cleft palate (31).

Management and treatment for OFC oftern involves multiple surgeries, specialized services like speech and language services and early intervention. Children with OFC also require specialized dental and orthodontic treatment. All types of OFC can affect the infant's ability to eat and drink and may hinder their speech development throughout childhood and adolescence (31). Childrenwith OFC also continue to have increased difficulties compared to unaffected children including speech and language difficulties, problems with hearing, learning disorders, other co-morbidities and stigmatization. More research is being done to clarify these differences between children with and without OFC, but these studies originated with the evaluation of intellect in children with OFC.

Cognitive Function in Children with OFC

Intellectual differences between children with OFC and children without this birth defect were initially studied in the 1960s. Leonard Goodstein conducted one of the original comparison studies by administering the Wechsler Intelligence Scale for Children (WISC), a standardized test of intelligence, to 105 children with OFC and 95 matched control children ranging in age from 5 to 16 years old. The control group, only specified as community volunteers, were matched by child's age, sex, birth order, family size, rural or urban residence, socioeconomic status, and religious affiliation. The mean scores for the Verbal IQ, Performance IQ, and Full scale IQ were all found to be significantly lower in the OFC group than the control group. However, the distribution of the Full IQ scores for the OFC group was not significantly different from the expected distribution of scores. Children with OFC had the lowest mean score and largest difference in score from the controls on the Verbal IQ. Among children with OFC, the scores on both the Verbal and Performance IQ were lowest among children with cleft palate only compared to children with cleft lip only and cleft lip and palate (6).

These findings, that the intelligence of children with OFC is within normal ranges but that it is typically lower than children without OFC, have since been replicated in many other studies (5, 7, 11, 33-36). One study, conducted in 1978, of children 2 to 33 months of age found that the group of 24 children with OFC, from a plastic surgery clinic in Texas, scored lower on all developmental measures than 24 children without OFC or other major medical or developmental problems, from a well-clinic. The children with OFC scored especially low on the language scores from the Receptive Expressive Emergent Language Scale (REEL) (37). These findings were reiterated in a recent study of children with cleft lip and palate and without other risk factors for developmental delay from a cleft lip and palate registry in Canada, which assessed cognition using the standardized Bayley Scales of Infant Development (BSID) at 12 and 24 months of age. Their scores were compared to healthy children, without risk factors for developmental delay, matched to the children with OFC on sex, race, SES, and birth order (7). These studies showed that even at this early stage in life, the children with OFC scored significantly lower than the control group. In another clinic-based study, which used the Bayley Scales of Infant Development (BSID), researchers administered the BSID to children with OFC up to 24 months of age. The authors showed that scores on the Mental Scale decreased in the OFC group as the children got older with 45% moving to a lower score classification from a younger age to an older age (35). Another study compared 26 sets of siblings, one with a cleft palate without or without cleft lip and one without an OFC. It found that the sibling with OFC had significantly lower scores than the sibling without OFC on the measures of verbal intelligence and comprehension but not in performance IQ or perceptual organization. Here, verbal cognition was measured using the Peabody Picture Vocabulary Test (PPVT), WISC verbal IQ, and a verbal comprehension factor(38). As shown above, the literature is fairly

conclusive that children with OFC tend to have lower IQs than children without this birth defect or other developmental disorders, especially in the area of verbal cognition. Nevertheless, most children with OFC still have overall IQs in the normal ranges.

The relationship between intelligence scores and cleft type has not been conclusive in previous studies. Several studies did not find a difference between children with cleft palate only and children with cleft lip with or without cleft palate as seen in Goodstein's study and other studies described above (6, 34, 39, 40). One such study, conducted on a sample of children from a craniofacial center in St. Louis, that did not find a significant difference between cleft types on any of the mean test scores, found instead that the interaction between cleft type and gender may play an important role in the relationship between intelligence and cleft type. The results showed males with cleft lip with or without cleft palate scored higher than females with cleft lip with or without cleft palate, and females with cleft palate only scored higher than males with cleft palate only (9). Females with cleft lip with or without cleft palate and males with cleft palate only are also less prevalent than males with cleft palate with or without cleft palate and females with cleft palate only. These less prevelant genders for each cleft type also appear to have more major anomalies in addition to the OFC(41).

Other studies have specifically assessed the impact of additional anomalies in children with OFC. One such study compared intelligence between four groups: children with isolated cleft lip and palate, children with non-isolated cleft lip and palate, children with isolated cleft palate only, and children with non-isolated cleft palate only. It used various Wechsler Intelligence Scales according to the age of the study participant (ranging from 4 to over 16 years old). In the verbal IQ scores, those with non-isolated cleft palate only had the lowest mean score (90.55), and it was significantly lower than the mean score for the isolated cleft palate only group

(101.28). The cleft lip and palate groups showed the same trend but the difference in scores was not significant. In the performance IQ scores and full scale IQ scores, the same trend was also seen. For all IQ scores, the highest mean scores were in the isolated cleft lip and palate group, then the isolated cleft palate only group, the non-isolated cleft lip and palate group, and finally the non-isolated cleft palate only group (10). These findings are supported in another study of 18 month-old Dutch children using scores on a Dutch version of the Bayley Scales of Infant Development (BSID) (39).

Researchers are not as certain as to what causes these slight cognitive deficits. One line of reasoning follows the thought that development problems of the face are closely related to development problems of the brain (42). Evidence for cognitive differences has been seen in neuro-imaging studies that have found certain brain anomalies in individuals with OFC (12, 20, 43, 44). In one study, a specific midline brain anomaly had a higher rate of occurrence and greater severity in adults with isolated OFC than healthy controls. This particular anomaly is not solely present in individuals with OFC, but is more common in people with other neurodevelopmental disorders as well. Furthermore, the severity of this anomaly was inversely correlated with IQ scores, but only in the OFC group (43). More general differences have also been found between the brain structure of children with OFC and children with no major medical, neurological, or psychiatric illness or learning disability. These differences include smaller intracranial volume, total gray and white mater, cerebral volume and cerebellar volume, after controlling for body size, in the children with OFC (12). More research is needed in this area, but these findings may indicate that some differences in intellect are attributable to brain developmental differences occurring prenatally along with the OFC itself.

These studies on cognitive differences in children with OFC are important because they not only show that children with OFC tend to score lower on IQ tests then unaffected children, but they show that there is a pattern to these cognitive differences. First, children with OFC score lowest on measures of verbal IQ. Furthermore, children with non-isolated OFC have lower average IQ scores than children with isolated OFC. Finally, there may be some interaction between cleft type and gender resulting in males with cleft palate only and females with cleft lip and cleft palate having lower average IQ scores. These patterns are essential for craniofacial teams to keep in mind when evaluating children with OFC. They are also important in regards to academic achievement because of the importance of intelligence in school performance. However, intelligence is not the only factor that determines academic success, so other abilities must be addressed both individually and in conjunction with intelligence.

Language and Reading in Children with OFC

As shown in several of the studies above, children with OFC have been shown to perform poorest on measures of verbal cognition. Children with OFC also tend to score lower than children without OFC on various measures of reading, including single word and non-word reading, comprehension, fluency, and repetition, and on measures of writing ability (4, 8). Therefore, it may be that verbal cognition affects these other abilities or that difficulty in these other areas affects verbal cognition.

Mostly, it is thought that there is a higher prevalence of reading disability among children with OFC compared to unaffected children. One study, conducted in 1988 on a clinic-based sample, found that in children with cleft lip and palate or cleft palate only, over all ages assessed (6 - 13 years old), 35% had moderate reading disability and another 17% had severe

reading disability. The rates were higher among the 6 to 7 year olds and reading disability rates decreased with age. By the oldest age group, 10 to 13 year olds, children with cleft lip and palate had levels of reading disability close to that in the general population, 8.6%, but children with cleft palate only still had a much higher percentage, 33.3% (14).

It has also been suggested that there are other differences in patterns of deficits related to reading disability between cleft lip and palate and cleft palate only. That is, children with cleft palate only have shown lower language association and auditory short-term memory, lower reading comprehension, and more sight word errors which suggest more overall language deficiency in these children compared to children with cleft lip and palate (45). One prospective study, from a U.S. craniofacial center in 2010, did not see a difference in reading scores between children with and without OFC, but the language scores were slightly lower for the children with cleft lip and palate and cleft palate only. However, this finding differs from most studies and may be due to differences in the severity of the OFC and other clinical features of the sample that were not considered (46).

Also affecting language and reading abilities is the fact that children born with OFC are at a higher risk for frequent ear infections, hearing difficulties and speech problems than unaffected children (4, 7, 34). Middle-ear effusion occurs in almost all children with OFC at one point during the early years of life so that the placement of a tube is necessary to aid in drainage. The lack of drainage can impede conductive hearing and lead to frequent ear infections. If this problem is left untreated, these hearing problems can also affect the child's speech and language development (7, 47-51). Children with OFC are almost four times more likely to receive services for a speech or language disorder than children without birth defects (16).

Many studies have looked into the relationship between cognition, language, reading, hearing and speech in children with OFC. One clinic-based U.S. study from 1970 found no relationship between speech, hearing sensitivity, and standardized test scores for children with OFC from a clinic-based sample (5). However, other studies have used more specific measures of each of these abilities to assess their associations in children with OFC and have come to different conclusions (7, 34, 37). In one such study, from Minnesota published in 1998, the children with cleft palate with or without cleft lip acquired words on average three months slower than the children without OFC. The children with OFC also had lower vocabularies and lower mean lengths of utterance (MLU), but when hearing ability and velopharyngeal function were controlled, these differences were no longer present (34). Other studies have shown that hearing loss is significantly correlated with numerous measures of development including BSID scores and language abilities (7, 37). A positive correlation was also shown between BSID scores and language measures so that hearing, language and development seem to be connected. (7). This relationship was found in another U.S. study, conducted in 2011, where a positive correlation was found between early reading and speech and between reading and language scores within the children with OFC, but was not found in the comparison group of children without OFC (2). On measures of conversational skills, studies have shown that preschoolers with cleft lip and palate are less assertive and more likely to make maintaining utterances but less likely to make topic extending ones (3, 52). Furthermore, findings have suggested that children with OFC and poorer articulation are less likely to be assertive in dialog (52). Less of a difference in conversational skills was seen between school-aged children with and without OFC than between these groups at the younger preschool age (3).

In an attempt to tease out the temporality of these relationships, one Australian study, published in 2003, compared language and speech outcomes between children with OFC who had early expressive language delays and those with normal early language development. The first assessments were made at age two to categorize the children, and then they were retested at age three. Therefore, there was only a year of development observed, and most of the children in the delayed group received some sort of intervention service. At age three, those in the delayed group scored significantly lower on mean length utterance scores and most measures of speech ability (53). This study is important because it reveals that among children with OFC, some are affected more severely than others in the areas of speech and language. Furthermore, children with language difficulties early in life appear to have continued problems as they get older, and therefore would likely benefit from early identification and intervention. Reading and language skills are especially essential components in preschool and early elementary school where these skills are being developed.

Impact of Other Co-morbidities

Children with OFC also have higher rates of a number of other disabilities and developmental problems that may affect academic achievement, such as intellectual disability (15, 17, 18). In a clinic-based study, conducted in 1993, researchers found approximately 10% of children with OFC diagnosed with intellectual disability compared to only 1% in the general population (15, 54). Furthermore, children with cleft palate only were approximately twice as likely to have intellectual disability as children with cleft lip only or cleft lip and palate, and about half of the children with OFC and intellectual disability had a non-isolated OFC. Children with OFC and intellectual disability have been typically viewed as a separate subset of children with OFC, and typically have not been assessed in studies of academic achievement because

intellectual disability can influence academic outcomes; however, they are important to consider in the special education needs of children with OFC (15).

Inattention and hyperactivity have also been assessed in children with OFC. Anecdotally, attention-deficit hyperactivity disorder (ADHD) has been suggested to occur more frequently in children with OFC for years, but the findings in studies have been conflicting (19, 22, 55). In a clinic-based study of siblings conducted in 2002, 9.8% of the children (6-11 years old) with isolated OFC and no other developmental or medical disabilities were diagnosed with ADHD. This was not significantly different than the prevalence of ADHD in the comparison group of siblings with no birth defects or other disabilities, but there were only 14 siblings in the study (19). Thus, this study was biased by using a very small sample size and convenience sample. In a larger, population-based study conducted in 2012, 20.3% of children with OFC (6-12 years old) were above the standardized 90^{th} percentile in measured levels of inattention and hyperactivity. This was much greater than the 4.4% in the children with OFC 2-5 years old and the 10% expected in the general population (55). However, there has been some question as to whether some of these children are incorrectly diagnosed with ADHD instead of a learning disability because children with undiagnosed learning disabilities may become bored and exhibit behaviors characterized with ADHD (22). There have also been various hypotheses to the cause of ADHD in children with OFC. These include differences in the brain structure of these children, stigmatization leading toward behaviors of inattention and hyperactivity, and new evidence that exposure to general anesthesia before the age of 2 years old increases the risk for ADHD (20, 55, 56).

Other behavioral problems have also been identified at higher rates in children with OFC than children without OFC. These consist of externalizing behavior problems, which include

conduct problems and impulsivity, and internalizing behavior problems. Internalizing behavior problems include anxiety, depression, and shyness, and are often measured by the Behavior Problem Checklist (18). A longitudinal study of children with OFC (4-12 years old) conducted in 1997 in the US, found that boys and girls with OFC had higher mean scores of internalizing behavior problems than children without OFC from previous cross-sectional studies (13, 21, 57, 58). The scores increased with age for both boys and girls, but the difference in scores between girls with OFC and girls in the comparison group also increased with age. Boys with OFC had higher mean scores on externalized behavior problems at ages 6 and 7, but then they dropped to below the mean scores of the comparison group. Girls with OFC had similar scores in externalized behavior problems to the comparison group at younger ages, but then girls with OFC had increasingly higher scores starting around age 10 (21). Another study conducted in the US in 1997 found that children with OFC at 9 years old had higher levels of internalizing behavior if they had fewer speech problems, and at 12 years old had higher levels of internalizing behavior with greater facial disfigurement, which appears to be conflicting (59). Speech impairment and facial appearance have also been associated with low self-esteem, depression, and anxiety in other studies (55, 60). By cleft type, children with cleft palate only have shown to have higher levels of anxiety and depression than children with cleft lip with or without cleft palate and normative data, which can lead children to be distracted in school or desire to leave school completely (60).

Stigmatization

Despite some uncertainty on the effect of stigmatization on behavioral problems in children in with OFC, stigmatization from speech impairments and facial appearance is frequently reported by children with OFC and their parents and has been shown to play an

important role in the quality of life of children with OFC (23, 61, 62). Forms of stigmatization include teasing and bullying and other more subtle forms, such as questions about the child's face and judgment from others (61, 63). Children with OFC have also been shown to experience more intrusive and controlling mother-child interactions than the interaction between mothers and children without birth defects. This may be the case because the mother is trying to compensate for any developmental delays in the child (64). Teachers and parents also tend to have lower expectations, especially of intelligence, of children with OFC (63). High percentages of children with OFC, 15-20% of children with cleft lip without or without cleft palate, have reported being unsatisfied with their facial appearance (65). All of these may contribute to low self-esteem, low competitiveness, and behavioral problems, and therefore contribute to low academic achievement (57, 60).

Academic Success and Outcomes in Children with OFC

As stated above, numerous studies have been conducted on intelligence, language abilities, reading, speech, hearing, and other disabilities in children with OFC. Most of these studies have only assessed one or a couple of these factors, which is necessary to draw clearer conclusions about the effects of each factor. However, often many of these factors along with issues that arise from multiple corrective surgeries, stigmatization, and behavioral inhibition, all act on the child, affecting his or her academic success. These factors logically culminate in the school setting where social, behavioral and intellectual abilities are all important. Few studies have focused specifically on academic outcomes, and they have not been able to assess the impact of all of these important components together.

One study conducted in 1976 assessing academic outcomes compared the success of 44 children with cleft palate with or without cleft lip to 44 controls, children randomly sampled from a local public school, based on scores from the Iowa Tests of Basic Skills (ITBS). The control children were matched on sex, age, grade, SES and IQ. A significant difference was found in the ITBS scores with the children without OFC having a mean score over one point higher than the children with OFC (6.90 and 5.82 respectively). Furthermore, the sample only included children with no or mild hearing and speech problems, making the groups more homogenous, which was a strength of this study. Because the study controlled for the characteristics listed above (e.g. sex, age, grade, SES and IQ), it offers that the remaining difference between the groups lies in achievement. The authors discussed that this may result from inhibition in the children with OFC and represent lower confidence and competitiveness in these children due to teasing from peers (13).

One study conducted in 2008 using the Metropolitan Atlanta Congenital Defects Program data and linkage to special education files, evaluated special education services used by children with OFC as compared to children without a major birth defect. In a population-based sample, 25.9% of the children with OFC received special education services for at least one year between 3 and 10 years of age. This was significantly different than the 8.0% of children without a major birth defect who had received the same services. The children with isolated cleft lip had the lowest percentage of children who received services compared to the other cleft types. Speech and language services were the most common services used by children with OFC. However, with these services excluded, children with OFC were still 2.4 times more likely to receive services than the children without a major birth defect; this estimate did not adjust for other characteristics. Children with OFC also entered special education services at a younger age on

average than the unaffected children (16). This earlier usage of special education services may be partly due to increased evaluation of children with OFC compared to children without OFC.

Finally, researchers evaluated the rate of learning disability, grade retention, and standardized achievement test scores among 168 children with OFC (6 - 18 years old). Overall, 46% of the children were categorized as having a learning disability. When stratified by cleft type, this rate was as large as 79% among males with cleft palate only. Twenty-seven percent of the children had repeated a grade, and this was also highest among males with cleft palate only (38%). Approximately 50% of the children had scored below the 25th percentile on standardized achievement tests (either the Iowa Test of Basic Skills or the California Achievement Test) (1). Therefore, this study illustrates that children with OFC not only have poorer academic outcomes and that services for these children appear to be needed, but also that the academic success of children with OFC varies by cleft type and gender.

Summary, Importance, and Limitations of Previous Studies

All of the studies described above lead to the general conclusion that children with OFC tend to have more cognitive, developmental, behavioral and academic difficulties than children not affected by OFC. However, it is still unclear what the magnitude and effect of these difficulties are and their relationship to each other. Also, as demonstrated above, there is little research on the impact of all of these characteristics on educational outcomes in children with OFC. In 2006, the Centers for Disease Control and Prevention held a workshop of cleft and craniofacial experts to prioritize areas of public health research on OFC. One of the areas given importance was quality of life for children with OFC, which included educational outcomes among other factors, such as reading interventions, access to an interdisciplinary team,

psychological outcomes, timing and type of surgery, adherence to care guidelines, family out-of-pocket costs, and the effects on caregivers (24). Therefore, further studies are required in these areas.

Along with limited research, the studies that are available have numerous limitations. One such limitation is the frequent recruitment of children with OFC from clinical settings instead of population-based samples. Clinic-based samples may be biased by including children who require more care and are from urban areas and of higher socioeconomic status. Furthermore, the children with OFC often differed in case definition in the previous studies. Frequently, those with non-isolated OFC were excluded, but not always. Depending on the outcome of interest, children with hearing deficits or other known conditions that may hinder development may also have been excluded. These differences in exclusion criteria may also apply to the comparison group. The definition of the comparison group varied throughout the previous studies, ranging from children without craniofacial anomalies to more strict criteria, such as no birth defects or no other known developmental conditions. In both groups of children, children with intellectual disability were usually excluded to make the groups of children more homogenous. Furthermore, many previous studies did not include an unaffected comparison group and instead compared different types of OFC or compared the affected children to standardized scores. These differences between studies may also be complicated by different categorization of cleft types. Specifically, in some studies children with cleft lip with or without cleft palate were grouped together, whereas, other studies differentiated between children with cleft lip only, cleft lip with cleft palate and cleft palate only. Consistency in inclusion criteria and case definitions is important so that comparisons and summary estimates can be made

between and across studies. However, this is difficult with children with OFC where sample sizes are often small and limited to readily accessible data.

Specific Aims

To address the previous study limitations and gaps in academic outcomes research in children with OFC, the purpose of this study was to evaluate the academic success of children with OFC compared to children without a major birth defect (controls), using a population-based, state-wide sample. A secondary objective was to examine academic success among children with OFC by the three cleft types (cleft lip only, cleft palate only, and cleft lip with cleft palate) and by the presence of other birth defects (non-isolated OFC) compared to isolated OFC (diagnosis of OFC only). The specific research questions of interest were:

1. Do children with OFC differ from children without birth defects on measures of academic outcomes defined as letter grades, grade retention and school days missed?
2. Among children with OFC, do these same academic outcomes differ by each of the three cleft types and by non-isolated and isolated OFC?
3. What are the odds of receiving below average letter grades (≤ C's), repeating a grade and missing more days of school among children with OFC compared to children without a major birth defect after controlling for certain maternal and child characteristics?
4. Among children with OFC, what are the odds of receiving below average letter grades (≤ C's), repeating a grade and missing more days of school by each of the three cleft types and by non-isolated and isolated OFC?

We hypothesized that children with OFC would have lower letter grades, higher rates of grade retention, and would miss more school days than children without a major birth defect.

We also hypothesized that children with non-isolated OFC would have poorer academic outcomes than children with isolated OFC, and that children with cleft lip and palate and cleft palate only would have poorer academic outcomes than children with cleft lip only. Furthermore, we thought these trends would persist after adjustment for maternal and child characteristics.

Methods

Study Sample

This study was conducted on a population-based, state-wide sample of cases, children with OFC, and controls, children without a major birth defect. A random sample of parents of children with OFC born 1996-2002, ages 5-12 years old, were identified by the North Carolina Birth Defects Monitoring Program (NCBDMP) (n = 504). This registry, started in 1987, is a population-based, statewide birth defects surveillance system that gathers information from all hospitals, except military hospitals, in the state of North Carolina. It ascertains information on all live-born infants, fetal deaths at or after 20 weeks gestation, and pregnancy terminations with one or more major birth defects diagnosed in the first year of life whose mothers are North Carolina residents. For the infants identified as having a major birth defect, the registry collects information from health services databases, Medicaid paid claim information, and vital statistics data (66). For this study, infants with OFC were identified by the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes or the British Pediatric Association (BPA) coding system.

A random sample of parents of children without a major birth defect born during the same time period was selected from North Carolina birth certificates (n = 504). Parents were excluded from both groups whose children had died at any point, whose children were born out of state or if the parents were unable to speak or read English or Spanish.

Questionnaire

Between May 2007 and April 2008, mailed questionnaires were sent to both groups of parents. The survey included Likert-scale, closed- and open-ended questions from validated quality of life instruments (67-72). Domains included demographics, outcomes, family life,

dental health, experience of diagnosis, and other quality of life aspects. Survey responses were linked with birth certificate data for the unaffected children and to the North Carolina Birth Defects Monitoring Program (North Carolina birth defects registry) information for children with OFC.

Exposure variable

The OFC diagnosis was made by using ICD-9-CM and BPA codes for OFC (749.000 - 749.290) which included the cleft type: cleft lip only, cleft lip and palate, or cleft palate only. The ICD-9-CM and BPA codes for birth defects were also used by the North Carolina Birth Defects Monitoring Program to determine the presence of another birth defect.

Outcome variables

The measures of academic outcomes were obtained from maternal-report in the questionnaire. The academic outcomes were measured by overall letter grades, grade retention and number of school days missed in the past 12 months. Along with the choices of mostly A's to mostly F's, mothers were able to choose "not in school" or "other" for their child's letter grades in the most recent grading period. If the respondent selected "other", a space was available for the parent to specify their answer. Those children indicated as "not in school" were excluded from evaluation of this outcome because letter grades could not be discerned. However, answers of "other" were individually evaluated to assess whether the mother's response could be reassigned to a letter grade category. Children with answers that could not fit the categories, for example, "child received S for satisfactory in kindergarten", also were excluded for this outcome. For the bivariate and regression analysis, the grade categories were combined to form a dichotomous variable. The response of mostly A's and B's were grouped

together because these are typically considered above average and then mostly C's, D's, and F's were grouped together as these grades are usually considered average or below average.

Grade retention was initially a dichotomous variable that represented whether the child had repeated any grades since kindergarten (yes/ no). The only other response option for the mother was "don't know". The question of how many days of school the child had missed in the past 12 months allowed the mother to fill in the number of days missed or to chose "not in school". As before, children with "not in school" were excluded from the analysis of this outcome because they did not have a response that could be evaluated. The number of days missed was dichotomized for further analysis by creating a variable indicating 5 or fewer days (1 school week or less) missed compared to more than 5 days of school (more than 1 school week) missed.

Children were included in this study regardless of type of school they were enrolled. Therefore, some school types may not give grades on the A through F grading scale, but as long as the child was in a school, they could still repeat a grade and be absent from school. Therefore, it was decided that children excluded from one outcome were allowed to be included in the other two academic outcomes if they had response values that could be included. Therefore, the total number of children included for the analysis of each outcome (i.e., denominator) was different.

Covariates

The sources of maternal and child variables of interest that were used in this study are shown in Table 1. If the variable could be obtained from the questionnaire and vital statistics/ NCBDMP, then the concordance of these responses was evaluated. Due to a lower than expected concordance rate for gender among the children in the control group, it became clear that some mothers may have answered the questionnaires for a different child in the family than

the one intended by the researchers. Because we wanted to use information that would match the child for which the mother reported the academic outcomes, it was decided that the questionnaire values would be used for variables, where the questionnaire and vital statistics/ NCBDMP data were available, including child's race, child's age, and maternal age. If responses in the questionnaire were missing or illogical, then values were imputed from vital statistics/ NCBDMP data.

Maternal age at birth of the child was used instead of maternal age at survey because the first is more meaningful in the academic success of that child. Because the children range in age from 5 to 12 years old, a mother who is 35 years old at the survey would be 30 at the birth of the 5 year old but only 23 at the birth of a 12 year old. A 23 year old mother and 30 year old mother would likely be different in education, income, marital status, and other characteristics that would affect the academic success of their child.

The socioeconomic status (SES) variable was created from the mother's education level, the household income level, and the child's primary insurance. Each of these variables was dichotomized into low and high (low: mother's education ≤ high school degree, household income < $25,000, the child has public or no insurance). The number of these three variables classified as "low" was totaled to give an SES score from 0 - 3 with 0 representing the highest SES and 3 the lowest. This method was derived from another study involving children with orofacial clefts and academic outcomes, and the categorizations were evaluated using a correlation matrix (55).

Additional medical conditions

The presence of other medical conditions was also obtained from mother-report on the questionnaire. The questions used to ascertain this information are validated, standardized

questions used in the National Survey of Children with Special Health Care Needs to collect information on co-morbidities. The wording of these questions was as follows: "Has a doctor or medical professional ever told you that your child has_____". There was a separate question for each of the following conditions: hearing problems, speech problems, 3 or more ear infections in the past year, vision problems not corrected by glasses or contacts, attention-deficit disorder/ attention-deficit hyperactive disorder (ADD/ ADHD), behavioral/conduct problems, anxiety/depression, developmental delay/physical impairment, shyness, and intellectual disability. Vision problems were not assessed in this analysis because there is no previous evidence that these should occur differently between children with OFC and those unaffected children.

Descriptive Statistical Analysis

Any child whose parent reported a diagnosis of intellectual disability was excluded from all analysis for better homogeneity in the sample and comparability to other studies (N = 9). Descriptive analyses were performed comparing maternal and child characteristics of children in the sample with OFC to the children in the sample without a major birth defect.

Descriptive analysis was also conducted for the selected medical conditions. The percentage of children with each of the other medical conditions was compared between children with OFC and children without a major birth defect, between children with isolated and non-isolated OFC and among the three OFC types. In evaluating the role of other medical conditions in affecting children's academic success, it was unclear whether some of these may be an intermediate between the OFC and the academic outcomes or result from an unknown perinatal factor that is also associated with the OFC (alternative DAGs in appendix, Figure A and B). These included hearing problems, frequent ear infections, and developmental delay/ physical

impairment. Therefore, to evaluate the effect of these conditions, additional analysis was conducted for each outcome comparing children with OFC to those without a birth defect stratifying on each of these three conditions. Analysis of speech problems, behavioral and conduct problems, ADD/ ADHD, shyness, and anxiety/ depression was restricted to descriptive comparisons, and they were not controlled for in further analyses because it was hypothesized that these are intermediates between OFC and academic outcomes. For example, the presence of an OFC may cause a child to be teased, which can lead to depression or anxiety, which can also lead to the child being less competitive and willing to try in school, which can lead to poorer academic outcomes.

Bivariate Statistical Analyses

Bivariate analyses were conducted comparing the percentages of children with each of the maternal and child characteristics between children with OFC and unaffected children. The percent of children with each academic outcome was compared between children with OFC and unaffected children, and between children with isolated OFC and unaffected children. The academic outcomes were also compared between children with isolated and non-isolated OFC and among the three cleft types. These analyses were performed using chi-squared tests, Fisher's exact tests, and t-tests to calculate p-values.

Multivariable Regression Statistical Analyses

Logistic regression models were developed for each of the three academic outcomes. Models were first assessed for each outcome with the exposure variable as children with or without OFC. First, all children with OFC were compared to the control children, and then the group was condensed to only children with isolated OFC and compared to the control children for better comparability to previous studies. Models were then analyzed for each academic

outcome among the children with OFC, measuring the effect of isolated compared to non-isolated OFC and the three OFC types. For all models, demographic and birth characteristics were initially included as potential confounders if thought *a priori* that they were associated with academic success and would be different between children with OFC and those without birth defects. The adjusted logistic regression models for each of the three academic outcomes included the following potential confounders: gender, child's race, child's age, preterm birth, SES, marital status, and mom's age at child's birth. Backward elimination was used to determine the most appropriate and parsimonious final models for each estimate of interest.

Analyses were conducted using SAS software 9.3 (SAS Institute, Cary, NC). This study was approved by the Institutional Review Boards of the North Carolina Division of Public Health and Emory University.

Results

Response Rate and Study Sample Demographics

From the 1008 questionnaires that were mailed, 289 were completed and returned for an overall response rate of 28.7%. Among the 289 completed questionnaires, 150 were received from mothers of children with OFC and 139 from mothers of children without a major birth defect, response rates of 29.8% and 27.6% respectively. Using information from the North Carolina vital statistics, non-responders were significantly more likely to be non-Hispanic black and be born to younger mothers than children whose mothers responded to the survey. All other demographics were similar between responders and non-responders of the survey.

A total of nine children (8 children with OFC, 1 unaffected child) were excluded because the mother reported the child having a diagnosis of intellectual disability. The final sample size for analysis was 142 children with OFC and 138 unaffected children.

Maternal and Child Characteristics

Selected maternal and child characteristics were compared for children with OFC and children without a major birth defect (Table 2a and 2b). Overall, the children were mostly non-Hispanic white, of higher socioeconomic status, and had married mothers. All of the questionnaires returned for the unaffected children were completed by the biologic mother while 96.5% of the questionnaires for children with OFC were completed by the biologic mother. Children with OFC were significantly more likely to be male, non-Hispanic white, born with low birth weight, be younger in age, and have younger mothers at the time of their birth than children without a major birth defect. Some of these results were not surprising given that children with OFC are more likely to be born non-Hispanic white, low birth weight and to younger mothers

than unaffected children. Cleft lip and palate was the most frequent diagnosis among the children with OFC (n = 59, 41.6%), followed by children with cleft palate only (n = 48, 33.8%), and finally cleft lip only (n = 35, 24.7%). Among all of the children with OFC, 78.9% were classified as an isolated OFC, which was slightly higher than in previous studies in which only about seventy percent of children with OFC had an isolated OFC.

The same maternal and child characteristics were compared between children with isolated OFC only and the unaffected children because these groups were also compared on the academic outcomes and these two groups have been used in previous studies to help control for other confounding factors that are more commonly found with the presence of other birth defects. The only meaningful differences comparing all children with OFC to children with isolated OFC were that less children with isolated OFC were born preterm and with low birth weight than the total group of children with OFC. For low birth weight, there was no longer a significant difference between children with isolated OFC and the unaffected children.

Academic Outcomes: Children with OFC and Unaffected Children

The maternal report of the three academic outcomes (letter grades, grade retention and school days missed) were compared between the children with OFC and the children without a major birth defect (Table 3a). Only 109 (79.0%) of the unaffected children and 93 (65.5%) of the children with OFC had maternal responses to the question about the child's letter grades that were usable for this analysis. The remainder of children did not have usable responses because the mother indicated that the child was not in school (5.8% of unaffected children, 12.0% of children with OFC), specified that the child did not receive letter grades at all or on this scale (13.8% of unaffected children, 18.3% of children with OFC), or were missing (1.4% of

unaffected children, 4.2% of children with OFC). For both grade retention and school days missed, 129 (93.5%) unaffected children and 126 (88.7%) children with OFC had usable responses. Maternal responses not usable for number of school days missed were the indication that the child was not in school or a missing response, and the responses not usable for grade retention were "did not know" or a missing response.

Overall, most mothers reported that their child received mostly A's or B's (64.6%), had not repeated any grades (82.1%), and did not miss over a week (> 5 days) of school (61.4%). Among children with OFC that reported letter grades, 14.0% reported receiving mostly C's and D's, compared to only 7.3% of children without a major birth defect. Among children with OFC whose mother reported on grade retention, 11.1% of mothers reported their child repeating a grade compared to 8.5% children without a major birth defect. Neither of these comparisons was statistically significant (Table 3a). Among children with OFC that had responses for school days missed, 40.5% of children missed more than a week of school compared to only 25.4% of the unaffected children, which was statistically significant.

Maternal report of the three academic outcomes was compared between the unaffected children and the children with isolated OFC (Table 3a). The results for letter grades and school days missed were not different from the results of the comparison with all children with OFC above. Among children with isolated OFC, only 7.8% had repeated a grade which was slightly less than the percentage for all children with OFC (11.1%) and the unaffected children (8.5%).

Academic Outcomes: Children with OFC by Presence of Another Birth Defect and by Cleft Type

Among children with OFC, the academic outcomes were compared between children with non-isolated OFC and isolated OFC, and each of the three cleft types (Table 3b). Children

with non-isolated OFC had a significantly higher proportion of children repeat a grade than children with isolated OFC, 26.1% and 7.8%, respectively. There was no significant difference between children with isolated OFC and non-isolated OFC on letter grades and school days missed. Among children with non-isolated OFC whose mother reported a letter grade, 14.3% of children received mostly C's and D's compared to 13.9% among children with isolated OFC. Approximately 10% more children with non-isolated OFC missed more than a week of school than children with isolated OFC, 48.2% children with non-isolated OFC and 38.4% children with isolated OFC (Table 3b).

Among the three cleft types, there was little difference in maternal report of letter grades obtained in school. Maternal report of mostly C's or D's occurred in 15.0% of children with cleft lip only, 13.9% of children with cleft lip and palate, and 13.5% of children with cleft palate only among those who had reported a letter grade. Grade retention was also similar by cleft type. Children with cleft lip and palate had the most maternal report of repeating a grade (13.5%) compared to children with cleft palate only (9.5%) and children with cleft lip only (9.4%). There was a significant difference between the three cleft types on the number of school days missed. Children with cleft lip only and cleft lip and palate were very similar with 46.7% and 49.1% respectively missing more than a week of school. Only 25.6% of the children with cleft palate only missed more than a week of school (Table 3b).

Results for the Selected Medical Conditions

Many mothers in both groups of children reported more than one medical condition for their child, and therefore some children are included in Tables 4a and 4b multiple times. Children with OFC had significantly more of the following conditions than unaffected children:

behavioral and conduct problems (10.7% children with OFC, 2.9% controls), developmental delay/physical impairment (23.4% children with OFC, 5.8% controls), hearing problems (37.6% children with OFC, 8.0% controls), speech problems (31.4% children with OFC, 8.0% controls), and 3 or more ear infections in the past 12 months (20.6% children with OFC, 2.9% controls). When only children with isolated OFC were compared to children without a major birth defect, there was no longer a significant difference in behavioral and conduct problems only (Table 4a).

Children with non-isolated OFC had significantly more developmental delay/physical impairment (46.7%) and speech problems (66.7%) than children with isolated OFC, 17.1% and 22.5% respectively (Table 4b). The number of children with developmental delay/ physical impairment, hearing and speech problems varied significantly by the three cleft types. Among children with cleft palate only, 36.2% of mothers reported developmental delay or physical impairment compared to about 17% of mothers with children with both cleft lip only and cleft lip and palate. Children with cleft lip and palate and cleft palate only had higher rates of hearing and speech problems compared to children with cleft lip only (hearing: 47.5% children with cleft lip and palate, 42.6% children with cleft palate only, 14.3% children with cleft lip only; speech: 37.3% children with cleft lip and palate, 44.7% children with cleft palate only, 5.7% children with cleft lip only) (Table 4b).

Multivariable Analysis Regression Results: Children with OFC compared to Children without a Major Birth Defect

The crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated comparing all children with OFC to unaffected children and comparing children with isolated OFC to unaffected children for each of the academic outcomes (Figures 1 – 3). For

these comparisons, the children without a major birth defect served as the reference group. Only SES was significant for the multivariate model for the letter grades outcomes, SES and child's age were significant for grade retention, and only child's age was significant for school days missed. For simplification and because SES and child's age each were important for two of the outcomes, all of the reported estimates adjusted for only SES and child's age in the final models (see appendix Table A1 for comparison of fully adjusted models to the final models used).

When adjusted for SES and child's age, children with OFC were 2.5 times more likely to receive mostly C's or D's than children without a major birth defect (95% CI: 0.9-7.0), which was only slightly higher than the crude odds ratio of 2.1 (95% CI: 0.8-5.2) (Figure 1). Controlling for SES and child's age, children with isolated OFC were 2.8 times more likely to receive C's and D's than unaffected children (95% CI: 0.9-8.3) (Figure 1).

The adjusted odds ratio for repeating a grade comparing all children with OFC to unaffected children was 1.4 (95% CI: 0.6-3.6) (Figure 2). Children with isolated OFC were 20% less likely to repeat a grade than the unaffected children, but these results were not significant (adj. OR: 0.8, 95% CI: 0.3-2.4) (Figure 2).

All children with OFC and only those with isolated OFC were about two times more likely to miss more than a week of school than the unaffected children before adjusting for SES and child's age (Figure 3). The adjusted ORs were similar between all the children with OFC (adj. OR: 1.7, 95% CI: 0.9-3.0) and only the children with isolated OFC (adj. OR: 1.6, 95% CI: 0.9-3.0). The adjusted ORs were slightly lower than the crude estimates and were no longer statistically significant.

Multivariable Regression Results: Children with Isolated OFC Compared to Children with Non-isolated OFC

Crude and adjusted odds ratios and 95% confidence intervals were also calculated among children with OFC for each of the academic outcomes. Children with non-isolated OFC were compared to children with isolated OFC (reference group), and children with cleft lip and palate and with cleft palate only were compared to children with cleft lip only (reference group).

For these comparisons, the most parsimonious models differed for each of the academic outcomes. Gender, SES, marital status, and child's age were significant in the models for letter grades. Preterm birth, SES, and child's age were significant in the models for grade retention. Child's race, preterm birth, marital status, and SES were significant in the models for school days missed (see appendix Table A2 for comparison of fully adjusted models to the most parsimonious).

After adjusting for these significant variables, children with non-isolated OFC were 2.5 times more likely than children with isolated OFC to receive mostly C's or D's, which was not statistically significant. No significant difference was seen for letter grades by cleft type either (children with cleft palate only were 20% more likely to receive C's and D's and children with cleft lip and palate were 20% less likely to receive C's and D's than children with cleft lip only). Children with non-isolated OFC were 8.5 times more likely to repeat a grade compared children with isolated OFC. This estimate had a wide 95% confidence interval, 1.7 - 42.8, but did not include the null value and thus was significant. Children were similar in grade retention by cleft type with children with cleft palate only 30% less likely and children with cleft lip and palate were 20% less likely than to repeat a grade than children with cleft lip only. Children with non-

isolated OFC had about the same likelihood of missing over a week of school than children with isolated OFC (adj OR = 1.2, 95% CI: 0.4 - 3.7). Children with cleft lip and palate and with cleft palate only were 30% and 70% respectively less likely to miss more than a week of school than children with cleft lip only, but these were not significant (adj. ORs: 0.7, 0.3 respectively; 95% CI: 0.2 - 1.9, 0.1 - 1.0 respectively). The confidence intervals were very wide for all of these models due to small sample size. The full results of this analysis are shown in the appendix (Table B).

Potential further analysis would include stratifying the comparisons by the presence of hearing problems and then by developmental delay/physical impairment. However, in this study there were too few observations to obtain reliable estimates from that level of stratification.

Discussion

This study found that all children with OFC were 2.5 times more likely to receive lower letter grades, 1.4 times more likely to repeat a grade level, and 1.7 times more likely to miss over a week of school than children without a major birth defect after adjusting for SES and child's age. However, none of these differences were statistically significant. When only children with isolated OFC were compared instead, the association between these children and unaffected children was not meaningfully different from the association between all children with OFC and unaffected children for letter grades or school days missed (adjusted ORs: 2.8 and 1.6; 95% CIs: 0.9-8.3 and 0.9-3.0, respectively). Comparing only the children with isolated OFC to the unaffected children did cause the adjusted odds ratio for grade retention to change from 1.4 to 0.8, which was still not a large change. Because neither estimate was statistically significant, this does not change the interpretation that children with OFC were found to be similar to children with no major birth defect on grade retention.

Children with non-isolated OFC were not statistically different from children with isolated OFC on letter grades or number of school days missed. However, children with non-isolated OFC were over eight times more likely to repeat a grade than children with isolated OFC. Given this, it is reasonable that including children with non-isolated OFC did not meaningfully change the estimate for letter grades or school days missed. It is also reasonable that including children with non-isolated OFC increased the estimate of children with OFC repeating a grade level. It likely did not alter the interpretation of the estimate for grade retention because this estimate was already close to the null value and the confidence intervals were wide.

There was little difference seen in academic success among the three cleft types, and because of small numbers the confidence intervals quickly became wide for this analysis. Thus,

these results must be interpreted with caution. There was some indication that children with cleft lip and palate and cleft palate only may be slightly less likely to repeat a grade than children with cleft lip only, and children with cleft palate only were 70% less likely to miss over a week of school compared to children with cleft lip only.

The results of this study did not show as severe academic deficits among children with OFC as has been shown in previous studies (1, 13). In this study, only 7.8% of children with isolated OFC and 26.1% of children with non-isolated OFC had repeated a grade. This level for children with isolated OFC is much less than the 27% found in a previous study conducted in 1998 that included only children with isolated OFC (1). Part of this difference may be due to the clinic-based sample design of the previous study, which only included children with cleft palate only or cleft lip and palate. Therefore, these children receiving care at the clinic may have had more severe problems than the population-based sample used in our study. This may also be why the percentage found previously is more similar to that in the children with non-isolated OFC in our study. Furthermore, this previous study evaluated children ranging from ages 6-18 years old, whereas our study only examined children 5-12 years old. It is reasonable that children may be more likely to repeat a grade level as they get older.

The children in both groups of this study also reported missing less days of school than a previous study showed for fourth through sixth graders using the National Survey for Children with Special Health Care Needs. This study compared children with long-term health problems leading to ongoing use of medical services or functional limitations to other children in the school who did not test positive in the screener. Although this study did not use a sample of strictly children with OFC, children with this birth defect would have been included in the children with long-term health problems. School absences were also ascertained from parent-

report. In this study the average number of school days missed in a year was 8.5 for the unaffected children and 10.5 for the children with special health care needs. In our study, only about one fourth of the unaffected children reported missing greater than five days, and even among the children with OFC, less than half reported greater than five days of school missed. One possible explanation for this may be that parents who participated in our study were those who's children were more active and successful in school, or are healthier overall. Alternatively, there may be other differences in the underlying characteristics of the samples of these two studies.

Previous studies also indicated that children with non-isolated OFC would perform worse academically than children with isolated OFC (10, 39). In this study, letter grades and school days missed did not show a similar trend, but children with non-isolated OFC were much more likely to repeat a grade level. It appears inconsistent that children with non-isolated OFC would have such a high level of grade retention, but then receive similar letter grades to children with isolated OFC. Part of the explanation may lie in the number of observations that were usable for letter grades in this study compared to grade retention. Among children with non-isolated OFC, only 47.6% had reported a letter grade comparable to the scale analyzed compared to 70.5% among the children with isolated OFC. Furthermore, 76.7% of children with non-isolated OFC reported on grade retention. This may indicate that those children with the most severe problems had been integrated into a regular school system, but then repeated a grade and were moved to home-school or specialty programs. Typically, other studies have excluded children with non-isolated OFC to maintain a more homogeneous sample. However, the findings from our study may suggest that children with non-isolated OFC can be included in future studies without

compromising the validity of estimates. However, as seen even with this study among the three academic outcomes, this inclusion may depend on the outcome in question.

This reasoning applied to the results seen in children with non-isolated and isolated OFC may also apply to the three cleft types. Other studies have indicated that children with cleft palate tend to have more difficulties than children with cleft lip only, but in this study there was little difference between the cleft types (6, 34, 39, 40). Furthermore, the difference that was seen indicated that children with cleft lip only were more likely to repeat a grade and miss more school than children with cleft lip and palate and cleft palate only. As seen above, this may be partly due to those children with cleft lip and palate and cleft palate only with the most severe problems not having usable values for the academic outcomes or not participating in the study.

Limitations of Study

One limitation of using the North Carolina Birth Defects Monitoring Program was that it does not ascertain information of laterality of the OFC. This may be important if children with bilateral OFC have different academic success than those with an unilateral OFC. In previous research, most studies were also not able to assess laterality, and therefore there is scarce research on the effect of laterality on academic outcomes. Additionally, this birth defect registry documents non-isolated OFC by the diagnosis of another major birth defect in addition to the OFC. However, the definition of non-isolated OFC also includes children with OFC for which the cleft diagnosis is part of a syndrome or sequence. Therefore, it is possible that some of the children in our study were misclassified as having an isolated OFC if they had an associated syndrome or sequence. This was likely not problematic because it was the presence of additional birth defects that is of most concern in children with non-isolated OFC, but if there was large

misclassification, then this might explain why less of a difference was observed between children with isolated and non-isolated OFC than expected.

As shown, the problem of unusable observations is a limitation of this study. The nature of the questions on academic success led to a large number of observations that could not be used if the parent reported that their child was not in school or did not receive traditional letter grades in school. The largest reason for this problem seemed to be that the youngest children were still in preschool or kindergarten and did not yet receive letter grades. However, there were also older children who could not be assessed for certain academic outcomes due to enrollment in alternative schooling, such as private school, Montessori schools or home-school. Furthermore, for these children it is unknown if they are in these schools because of previous difficulties or by parental choice.

The questions were also limiting because the academic outcomes had to be measured through maternal-report. With maternal-report instead of school records there is more chance for misclassification of the academic outcome. This may be especially problematic because previous studies have suggested that parents of children with OFC may have lower academic expectations of their children which could lead to differential misclassification (63). That is, mothers of children with OFC may report lower grades for their children whereas mothers of the unaffected group would not. This would seem to bias the results away from the null. Because no significant differences were seen in this study, this is likely not a large concern.

Further limitations include no information on the types of schools the children attended in regards to public or private or home-school unless the mother specifically indicated this in an open response question. Information was not available on special education and intervention

services utilized by any of the children, which is problematic because children that have received services may have different academic success than children who have not received services, especially among the children with OFC. In addition, no indication was given as to why the child repeated a grade, if this was reported. Therefore, it is unknown whether the child repeated a grade because he or she failed academically or was held back a year for medical or behavioral problems. This does not alter the estimate of children who have repeated a grade, but may alter the interpretation and implications of the findings. Finally, we could not discern how many days of school were missed due to the child being sick, having medical appointments, being on vacation or due to other reasons unrelated to having an OFC. Therefore, the number of days of school missed may be high for some children only because of a long family vacation, and the interpretation of schools days missed must be interpreted cautiously.

Another large limitation was the low response rate (28.7% overall). This not only limits the sample size, but also has the potential to create a biased sample if responders and nonresponders differed on measures that effect the academic outcomes but were not evaluated. Although the respondents did tend to be slightly different in race and age than those who did not respond, the study sample is still demographically similar to the population of North Carolina and therefore still seems reasonable to consider as population-based. Nevertheless, the small sample size did prevent some of the desired stratifications from being conducted. In this study, current contact information could not be found for much of the original sample which accounted for much of the response rate. Therefore, future studies may consider working with local craniofacial centers to obtain more current contact information. This study offered a $20 incentive to families that returned the questionnaire, but increased incentives may increase the response rate of families that are reached. Furthermore, studies that link birth certificate and

birth defect registry information with school records would alleiviate several of the limitations above. Specifically, by linking with school records, current contact information would be available, school records could be compared to parent report for better accuracy of outcomes, school records would include some information on special education placement, and the type of school would be known.

Most importantly, the small sample size prevented the evaluation of the role of the additional medical conditions in this analysis beyond a descriptive assessment. Hearing problems and developmental delay were statistically different between children without a major birth defect and children with OFC and among children with the three types of OFC, and developemental delay were significantly different between children with isolated and non-isolated OFC. Although few differences were found for academic outcomes, it would still be important to evaluate what, if any, role these conditions played in this association. It is interesting to note that these two conditions do not follow the same trend among children with OFC by the different types of OFC and presence of another birth defect. Developmental delay/ physical impairment is much higher in children with non-isolated OFC than in children with isolated OFC, but the percentage of children with hearing problems is much more similar between the two groups. Furthermore, children with cleft palate reported much higher rates of developmental delay than children with cleft lip with or without palate, but children with cleft lip and palate reported the highest rates of hearing problems. Therefore, it is difficult to hypothesize what overall effect these conditions may have had on the academic outcomes.

Another important factor that was not fully evaluated in this study is the effect of stigmatization. The questionnaire did include several questions on teasing and bullying, but they were not assessed in the evaluation because of the likelihood that stigmatization is an intervening

variable between the presence of OFC and academic success and due to the small sample size. Nevertheless, bivariate analysis of these questions indicated that children with OFC were not significantly different from children without a major birth defect in how often they were bullied (see appendix Table C1). However, children with OFC did report being teased about their facial appearance more often than unaffected children (8.8% of children with OFC vs. 3.0% of unaffected children reported being teased at least sometimes - see appendix Table C1). Also, 13.0% of children with OFC compared to 5.0% of unaffected children felt unwelcome because of their facial appearance at least sometimes (see appendix Table C1). Therefore, although mothers of children with OFC did not report more frequent bullying and the majority of children reported never or almost never being teased or feeling unwelcome, children with OFC were still exposed at higher rates to these increased subtle acts of stigmatization which still may affect self-esteem and confidence. As expected, compared to mothers of children with cleft palate only, mothers of children with cleft lip with or without cleft palate reported more: bullying (6.1% children with cleft lip only and 10.2% children with cleft lip and palate vs. 2.1% children with cleft palate only were bullied two or more times); teasing (14.7% and 17.2% vs. 6.4% respectively were teased at least sometimes); and feelings of unwelcome because of their facial appearance (6.3% and 16.1% vs. 2.1% indicated at least sometimes). This difference in levels of stigmatization may partially explain why children with cleft palate only were found to have better academic outcomes than expected compared to the other two cleft types.

Strengths of Study

The major advantages of this study were that it was a population-based, state-wide sample which included an unaffected comparison group, included children with isolated and non-isolated OFC, and distinguished between all three cleft types (cleft lip, cleft palate, cleft lip

and palate). The population-based, state-wide sample is important to reduce bias in the sample and enhance generalizability. Clinic-based samples may include more severe cases, urban residents and children of higher SES than the general population of children with OFC. By including a random comparison group with no major birth defects, our study could compare the children with OFC to children from the same source population instead of to general population information. This minimizes potential bias from differences in characteristics between the sample population and the population used to calculate the comparison estimates. We were also able to compare children with the three cleft types and children isolated OFC to children with non-isolated OFC. This was important to consider because previous literature showed that children in each of these groups may differ on factors that may affect academics such as cognitive abilities and the presence of other medical conditions. Therefore, summary estimates may not be appropriate to report.

Another strength of the study is that the questionnaire was derived from previously validated instruments (67-72). This minimized misclassification because the questions used have been tested to ensure that they were interpreted correctly by respondents. Finally, use of a birth defects registry is a strength because no other previous study on quality of life had used such a registry. This is important because the registry provides accurate diagnosis information on the cleft type along with linked information on healthcare services, Medicaid paid claims, and vital statistics.

Conclusion

The results of this study indicate that children with OFC may not vary greatly in academic success compared to children without a major birth defect. Additionally, children with OFC may not meaningfully vary in academic success by cleft type as has previously been proposed according to the pattern of cognitive abilities and other medical conditions. From this study it is unclear whether this may indicate that current interventions are successful in preparing children with OFC for school or whether these children were able to succeed on their own. Nevertheless, these results are optimistic for parents of children with OFC who might be worried about their child's academic success.

The presence of an additional birth defect may be the most important factor for determining academic success as seen in higher rates of grade retention, but this effect is unclear from the other academic outcomes assessed. If the presence of an non-isolated OFC is an important factor in some outcomes, then these children may be targeted at a younger age for intervention services, and may benefit from specialized schooling programs. However, it appears that a large group of children with non-isolated OFC can still be successful in school. Therefore, it would be important to identify which additional characteristics determine this success.

Future Studies

Future studies are needed to clarify the relationships between academic outcomes and the different types of OFC along with the presence of other birth defects. These studies should focus on ascertaining more accurate and detailed academic records to evaluate success, and strive for larger sample sizes so that further analyses can be conducted. Additional studies should also

evaluate academic success on older children because many of those in this study did not have meaningful academic values, and older children with OFC may diverge further from their peers without OFC. Specifically, public school standardized test scores are available in third grade in some states and standard letter grades are typically used by this point which may make this the youngest meaningful age to include in academic studies. Optimal studies would also include longitudinal data so that the characteristics that predict academic success could be evaluated.

Some of these aspects are currently being incorporated into a newly funded study by the Centers for Disease Control and Prevention, which is using the North Carolina Birth Defects Monitoring Program to clinically verify OFC diagnoses and collaborating with several cleft and craniofacial centers and teams in North Carolina. This study is also linking medical records, academic records and early intervention records to validate academic outcomes and medical diagnoses of co-occuring conditions such as ADHD. This new study will also link academic records to a parent-completed survey. Findings from this thesis have informed and improved upon the current study in North Carolina by suggesting to include questions on type of school child attends, divide school absentees into those taken for medical reasons and those taken for other reasons, include questions of service usage, and to avoid using children still in preschool or kindergarten. The new study in North Carolina is focusing on academic outcomes, and it will be much more detailed and complete in information obtained.

Public Health Implications

The implications of this study should help advise parents about expectations for their child's success in school, and guide healthcare professionals in planning for early intervention, special education and special needs services for children with OFC. Specifically, this study is

optimistic for parents of children with OFC in that it found that the majority of the children are successful in academic settings. For those that were not as successful, that picture is not as clear for healthcare professionals in regards to planning services. From this study, it is difficult to tease out the predictors of academic success in children with OFC, and future studies should be conducted to address this question.

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Tables

Table 1. Maternal and child characteristic and academic outcome variables and their data source of origin

Variable	Data source(s) of origin	Strategy used if more than one data source
Child's gender	Questionnaire Vital statistics/ NCBDMP	If questionnaire value missing, then imputed value from vital statistics/ NCBDMP; If both sources available but discordenant then open response answers in questionnaire viewed for indication of gender (by using "he" or "she"), if a gender indicated then used the source that matched parent's response, if no indication then used questionnaire
Child's race/ ethnicity	Questionnaire Vital statistics/ NCBDMP	Questionnaire used unless value missing, then value imputed from vital statistics/ NCBDMP
Orofacial cleft diagnosis	NCBDMP	
Presence of additional birth defects	NCBDMP	
Preterm birth	Vital statistics (from gestational age)/ NCBDMP	
Birth weight	Vital statistics/ NCBDMP	
Child's primary insurance	Questionnaire	
Child's age	Questionnaire Vital statistics/ NCBDMP	Questionnaire used unless value missing or not logical, then imputed from vital statistics/ NCBDMP
Respondant's relationship to child	Questionnaire	
Marital status	Questionnaire	
Household income	Questionnaire	
Maternal education	Questionnaire	
Mother's age	Questionnaire Vital statistics/ NCBDMP	Questionnaire used unless value missing, then imputed from birth certificate
Letter grades	Questionnaire	
Grade retention	Questionnaire	
School days missed	Questionnaire	

Table 2a. Selected Maternal and Child Characteristics Compared Between Children with Orofacial Clefts (OFC) (cases) and Children Without a Major Birth Defect (controls)

Variables		Cases (N = 142)		Controls (N= 138)		Overall (N= 280)		p-value*
		N	%	N	%	N	%	
Child								
Gender	Male	93	65.5%	69	50.0%	162	57.9%	**0.009**
	Female	49	34.5%	69	50.0%	118	42.1%	
Race/ ethnicity	Non-Hispanic White	118	83.1%	96	69.6%	214	76.4%	**0.003**
	Non-Hispanic Black	5	3.5%	23	16.7%	28	10.0%	
	Multiracial	7	4.9%	9	6.5%	16	5.7%	
	Other[†]	12	8.5%	10	7.3%	22	7.9%	
Cleft type	Cleft lip only	35	24.7%	-	-	-	-	-
	Cleft lip and palate	59	41.6%	-	-	-	-	
	Cleft palate only	48	33.8%	-	-	-	-	
Other birth defects present	No (isolated)	112	78.9%	-	-	-	-	-
	Yes (non-isolated[‡])	30	21.1%	-	-	-	-	
Preterm birth	< 37 weeks gestation	28	19.7%	16	11.6%	44	15.7%	0.062
	≥ 37 weeks gestation	114	80.3%	122	88.4%	236	84.3%	
Birth weight	Low (<2500 g)	25	17.6%	10	7.3%	35	12.5%	**0.009**
	Normal (≥ 2500 g)	117	82.4%	128	92.8%	245	87.5%	
Primary Insurance	Private	84	59.2%	93	67.4%	177	63.2%	**0.005**
	Public	56	39.4%	35	25.4%	91	32.5%	
	None	1	0.7%	8	5.8%	9	3.2%	
	Missing	1	0.7%	2	1.4%	3	1.1%	

Mother								
Relationship	Biologic mother	137	96.5%	138	100.0%	275	98.2%	0.157
	Other[‡]	2	1.4%	0	0.0%	2	0.7%	
	Missing	3	2.1%	0	0.0%	3	1.1%	
Marital status	Married	110	77.5%	102	73.9%	212	75.7%	0.482
	Other[§]	30	21.1%	34	24.6%	64	22.9%	
	Missing	2	1.4%	2	1.4%	4	1.4%	
Household income	< $25,000	38	26.8%	25	18.1%	63	22.5%	0.178
	≥ $25,000	96	67.6%	108	78.3%	204	72.9%	
	Missing	8	5.6%	5	3.6%	13	4.6%	
Education	High school degree or less	41	28.9%	26	18.8%	67	23.9%	**0.045**
	Some college or more	99	69.7%	111	80.4%	210	75.0%	
	Missing	2	1.4%	1	0.7%	3	1.1%	
		mean	**std dev**	**mean**	**std dev**	**mean**	**std dev**	
Child's age	years old at survey	7.9	2.1	8.6	2.1	8.3	2.1	**0.004**
Mother's age	years old at child's birth	27.2	5.8	28.5	5.6	27.8	5.8	**0.045**

*p-values < 0.05 statistically significant

[†]Other races include American Indian, Alaska native, Asian, Native Hawaiian, Pacific Islander, Hispanic, multi-racial, or other

Non-isolated OFC designates the presence of another birth defect in addition to OFC

[§]Other marital status includes divorce, widowed, separated, never married, and unmarried couple

[‡]Other respondent relationship include biologic father and grandmother

Table 2b. Computed SES Levels Compared Between Children with OFC (Controls) and Unaffected Children (Cases)

	Cases (N = 142)		Controls (N= 138)		Overall (N= 280)		p-value*
SES†	**N**	**%**	**N**	**%**	**N**	**%**	
0 (High)	66	46.5%	82	59.4%	148	52.9%	0.086
1	25	17.6%	25	18.1%	50	17.9%	
2	25	17.6%	12	8.7%	37	13.2%	
3 (Low)	17	12.0%	14	10.1%	31	11.1%	
Missing	9	6.3%	5	3.6%	14	5.0%	

* p-values < 0.05 statistically significant

†SES includes household income, maternal education, and insurance status

Table 3a. Bivariate analysis of the three academic outcomes between all children with OFC and unaffected children and children with isolated OFC and unaffected children

	Controls (N= 138)		All Cases (N = 142)		p - value*	Isolated OFC (N = 112)		p - value*
	N	**%**	**N**	**%**		**N**	**%**	
Letter Grades	109	79.0%	93	65.5%		79	70.5%	
Mostly A's, B's	101	92.7%	80	86.0%	0.1233	68	86.1%	0.1393
Mostly C's, D's	8	7.3%	13	14.0%		11	13.9%	
Not in school	8	5.8%	17	12.0%		12	10.7%	
Excluded†	19	13.8%	26	18.3%		19	17.0%	
Missing	2	1.4%	6	4.2%		2	1.8%	
Grade retention	129	93.5%	126	88.7%		103	92.0%	
Yes	11	8.5%	14	11.1%	0.4878	8	7.8%	0.8338
No	118	91.5%	112	88.9%		95	92.2%	
Missing	9	6.5%	16	11.3%		9	8.0%	
School days missed	129	93.5%	126	88.7%		99	88.4%	
0 - 5	97	74.6%	75	59.5%	**0.0076**	61	59.8%	**0.0276**
> 5	32	25.4%	51	40.5%		38	38.4%	
Not in school	2	1.4%	9	6.3%		7	6.3%	
Missing	7	5.1%	7	4.9%		6	5.4%	

*P-values compare all children with OFC to controls and then children with isolated OFC to controls (significant at $p<0.05$)

†Did not have letter grades compatible with these categories

Table 3b. Bivariate analysis of the three academic outcomes between all children with isolated OFC and non-isolated OFC and among children with the three cleft types (cleft lip only, cleft lip and palate, and cleft palate only)

	Isolated OFC (N = 112)		Non-isolated OFC (N=30)		p - value*	Cleft lip only (N= 35)		Cleft lip and palate (N=59)		Cleft palate only (N = 48)		p - value*
	N	%	N	%		N	%	N	%	N	%	
Letter Grades	79	70.5%	14	46.7%		20	57.1%	36	61.0%	37	77.1%	
Mostly A's, B's	68	86.1%	12	85.7%	1.000	17	85.0%	31	86.1%	32	86.5%	1.000
Mostly C's, D's	11	13.9%	2	14.3%		3	15.0%	5	13.9%	5	13.5%	
Not in school	12	10.7%	5	16.7%		6	17.1%	6	10.2%	5	10.4%	
Excluded[†]	19	17.0%	7	23.3%		8	22.9%	15	25.4%	3	6.3%	
Missing	2	1.8%	4	13.3%		1	2.9%	2	3.4%	3	6.3%	
Grade retention	103	92.0%	23	76.7%		32	91.4%	52	88.1%	42	87.5%	
Yes	8	7.8%	6	26.1%	**0.022**	3	9.4%	7	13.5%	4	9.5%	0.821
No	95	92.2%	17	73.9%		29	90.6%	45	86.5%	38	90.5%	
Mssing	9	8.0%	7	23.3%		3	8.6%	7	11.9%	6	12.5%	
School days missed	99	88.4%	27	90.0%		30	85.7%	53	89.8%	43	89.6%	
0 - 5	61	61.6%	14	51.9%	0.384	16	53.3%	27	50.9%	32	74.4%	**0.048**
> 5	38	38.4%	13	48.2%		14	46.7%	26	49.1%	11	25.6%	
Not in school	2	1.4%	2	6.7%		4	11.4%	4	6.8%	1	2.1%	
Missing	7	5.1%	1	3.3%		1	2.9%	2	3.4%	4	8.3%	

*P-values compare all children with isolated OFC and non-isolated OFC and then children with the three cleft types (significant at $p<0.05$)

[†]Did not have letter grades compatible with these categories

Table 4a. Bivariate analysis of the selected medical conditions between all children with orofacial clefts (OFC) and unaffected children (controls) and children with isolated OFC and unaffected children

		Controls (N= 138)		All Cases (N = 142)		Isolated OFC (N = 112)	
	Medical Conditions	**N**	**%**	**N**	**%**	**N**	**%**
Behavioral problems	ADD or ADHD	14	10.3%	21	15.0%	14	12.7%
	Depression or anxiety	7	5.1%	8	5.7%	4	3.6%
	Behavioral or conduct problems	4	2.9%	15 *	10.7%	9	8.1%
	Problem with shyness	3	2.2%	6	4.3%	3	2.7%
Developmental/ physical problems	Developmental delay or physical impairments	8	5.8%	33 †	23.4%	19 †	17.1%
Hearing/ speech problems							
	Hearing problems	11	8.0%	53 †	37.6%	39 †	35.1%
	Speech problem	11	8.0%	45 †	31.4%	25	22.5%
	>= 3 ear infections in past 12 months	4	2.9%	29	20.6%	†19	17.1%

* $p < 0.05$ (level of significance)

† $p < 0.01$

Either p-value symbol in the all OFC column compare children with all OFC to controls, in the isolated OFC column compare children with isolated OFC to controls

Table 4b. Bivariate analysis of the selected medical conditions between children with isolated OFC and non-isolated OFC, and among the three cleft types (cleft lip only, cleft lip and palate, and cleft palate only)

		Isolated OFC (N = 112)		Non-isolated OFC (N=30)		Cleft lip only (N= 35)		Cleft lip and palate (N=59)		Cleft palate only (N = 48)	
	Medical Conditions	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Behavioral problems	ADD or ADHD	14	12.7%	7	23.3%	5	14.7%	8	13.6%	8	17.0%
	Depression or anxiety	4	3.6%	4	13.3%	2	5.7%	6	10.3%	0	0.0%
	Behavioral or conduct problems	9	8.1%	6	20.7%	5	14.3%	7	11.9%	3	6.5%
	Problem with shyness	3	2.7%	3	10.0%	0	0.0%	5	8.5%	1	2.1%
Developmental/ physical problems	Developmental delay or physical impairments	† 19	17.1%	† 14	46.7%	* 6	17.1%	10	17.0%	17	36.2%
Hearing/ speech problems	Hearing problems	† 39	35.1%	† 14	46.7%	† 5	14.3%	28	47.5%	20	42.6%
	Speech problem	† 25	22.5%	† 20	66.7%	† 2	5.7%	22	37.3%	21	44.7%
	>= 3 ear infections in past 12 months	† 19	17.1%	10	33.3%	4	11.4%	14	23.7%	11	23.4%

* $p < 0.05$ (level of significance)

† $p < 0.01$

Either p-value symbol in the non-isolated OFC column compare children with non-isolated OFC to children with isolated OFC, and in the cleft lip only column compares all 3 cleft types (cleft lip only, cleft lip and palate, and cleft palate only)

Figures

Figure 1. Odd ratios and 95% confidence intervals from the logistic regression model for receiving mostly C's or D's comparing all children with OFC to unaffected children (controls) and comparing children with isolated OFC to unaffected children

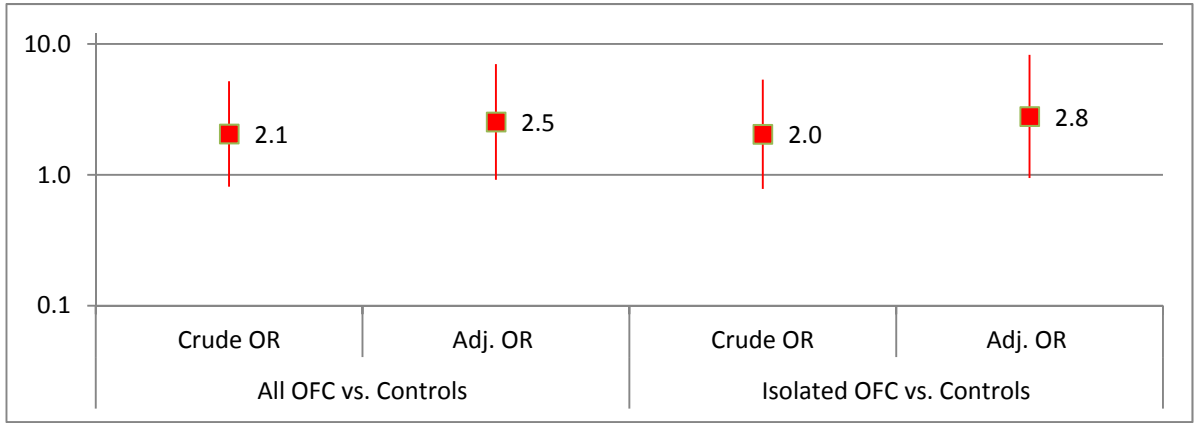


Figure 2. Odd ratios and 95% confidence intervals from the logistic regression model for repeating any grade comparing all children with OFC to unaffected children (controls) and comparing children with isolated OFC to unaffected children

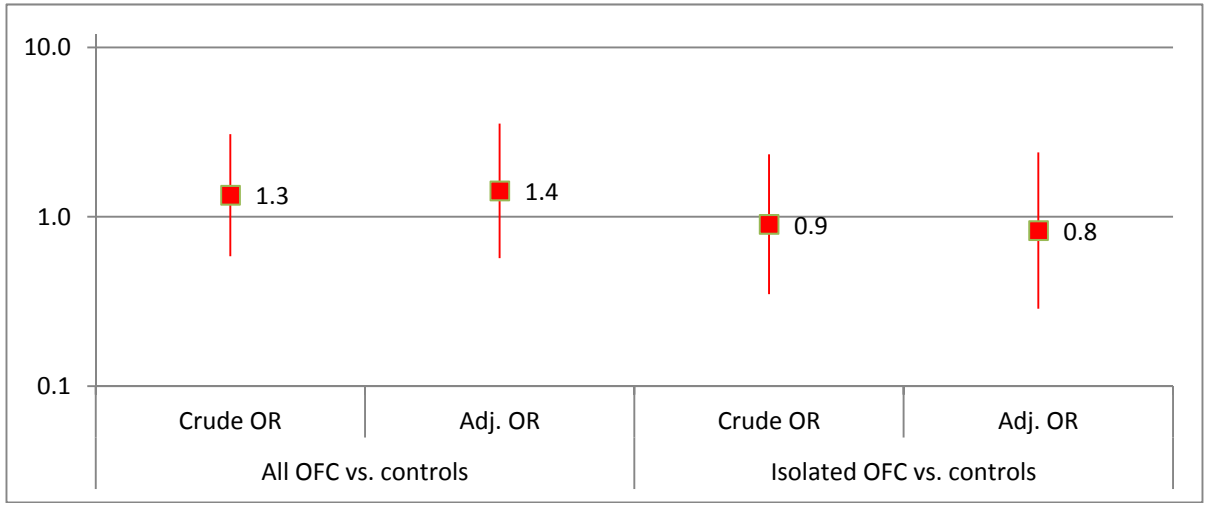
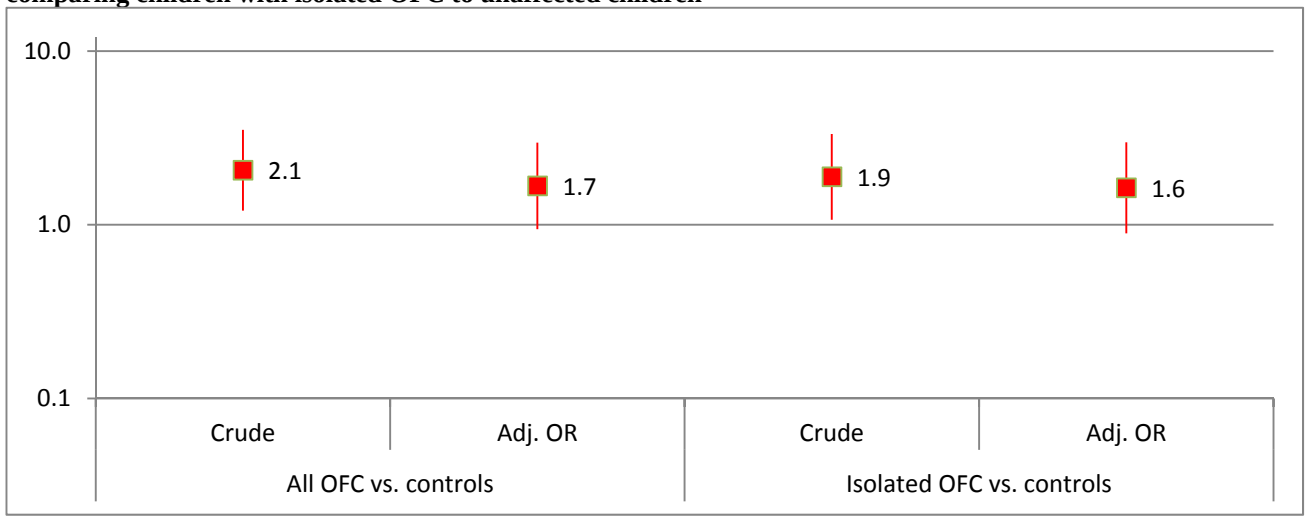


Figure 3. Odd ratios and 95% confidence intervals from the logistic regression model for missing more than 5 days of school (> 1 school week), comparing all children with OFC to unaffected children (controls) and comparing children with isolated OFC to unaffected children



Appendix

Alternative Directed Acyclic Graphs (DAGs) using a simplified example of hearing problems to demonstrate the 2 possible pathways relating to the additional medical conditions leading from the presence of OFCs to poor academic outcomes.

Figure A. DAG showing OFCs and hearing problems being caused by a shared parent which may be an unknown pre- or perinatal exposure that affects development of both the ear and mouth areas; in this case, hearing should be controlled for as a proxy for the parent to close the confounding backdoor pathway

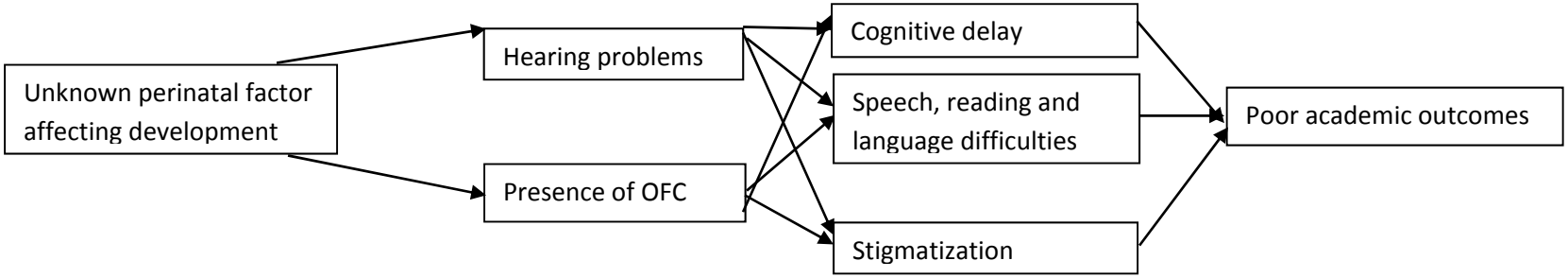


Figure B. DAG showing OFCs as the cause of hearing problems; here hearing should not be controlled for as it is an intermediate on the causal pathway

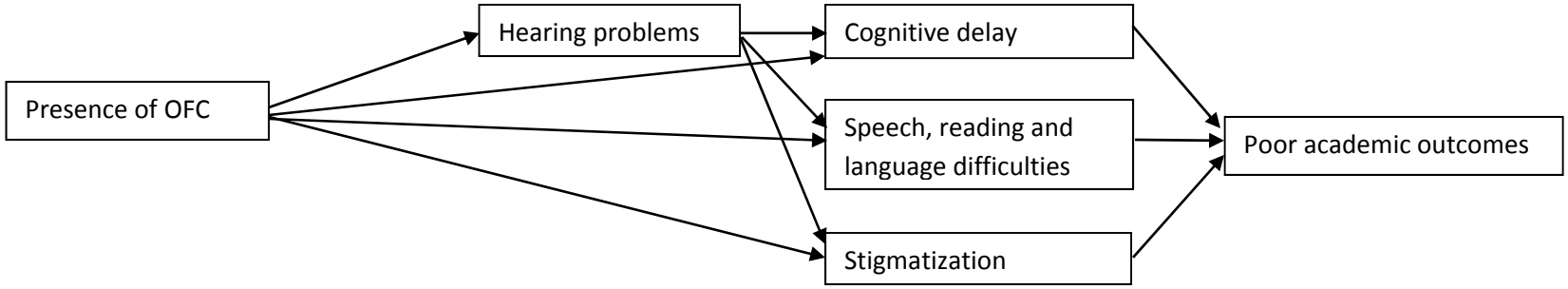


Table A1. Comparison of ORs and 95% CIs of the model with all potential confounders (full model) to the final adjusted model for the academic outcomes comparing children with OFC to unaffected children

	Gold Standard*			Final adjusted**		
	OR	**95% CI**		**OR**	**95% CI**	
Letter Grades (mostly C's or D's)						
All OFC vs. Controls	2.5	0.9	7.4	2.5	0.9	7.0
Isolated OFC vs. Controls	2.7	0.9	8.3	2.8	0.9	8.3
Grade Retention (yes)						
All OFC vs. Controls	1.4	0.5	3.8	1.4	0.6	3.6
Isolated OFC vs. Controls	0.8	0.3	2.5	0.8	0.3	2.4
School days missed (> 5 days)						
All OFC vs. Controls	1.6	0.9	2.9	1.7	0.9	3.0
Isolated OFC vs. Controls	1.6	0.9	3.1	1.6	0.9	3.0

* Gold standard model included: gender, child's race, preterm birth, SES, marital status, child's age, and maternal age

**All adjusted for SES and child's age

Table A2. Comparison of ORs and 95% CIs of the model with all potential confounders (full model) to the final adjusted model for the academic outcomes by presence of another birth defect and cleft type

	Gold Standard			Final adjusted		
	OR	**95% CI**		**OR**	**95% CI**	
Letter Grades (mostly C's or D's)[†]						
Non-isolated vs. Isolated OFC	0.7	0.1	5.2	0.7	0.1	5.2
Cleft lip & palate vs. cleft lip only	0.8	0.1	4.7	0.8	0.1	4.4
Cleft palate only vs. cleft lip only	1.2	0.2	8.1	1.2	0.2	7.2
Grade Retention (yes)[‡]						
Non-isolated vs. Isolated OFC	7.9	1.5	41.2	8.5	1.7	42.8
Cleft lip & palate vs. cleft lip only	0.8	0.1	5.1	0.8	0.1	5.2
Cleft palate only vs. cleft lip only	0.6	0.1	4.3	0.7	0.1	4.5
School days missed (> 5 days)[§]						
Non-isolated vs. Isolated OFC	1.3	0.4	3.8	1.2	0.4	3.7
Cleft lip & palate vs. cleft lip only	0.7	0.2	1.9	0.7	0.2	1.9
Cleft palate only vs. cleft lip only	0.3	0.1	1.0	0.3	0.1	1.0

***** Gold standard model included: gender, child's race, preterm birth, SES, marital status, child's age, and maternal age

[†]Letter grade models adjusted for gender, SES, marital status and child's age

[‡]Grade retention models adjusted for preterm birth, SES, child's age

[§]School days missed models adjusted for child's race, preterm birth, marital status, SES

Table B. Odds ratios (OR) and 95% confidence intervals for logistic regression models for each of the three academic outcomes comparing children with isolate and non-isolated OFC and comparing the three cleft types

	Crude			Adjusted		
	OR	**95% CI**		**OR**	**95% CI**	
Letter Grades (mostly C's or D's)						
Non-isolated vs. Isolated OFC	1.0	0.2	5.2	0.7	0.1	5.2
Cleft lip & palate vs. cleft lip only	0.9	0.2	4.2	0.8	0.1	4.4
Cleft palate only vs. cleft lip only	0.9	0.2	4.3	1.2	0.2	7.2
Grade Retention (yes)						
Non-isolated vs. Isolated OFC	4.2	**1.3**	**13.6**	8.5	**1.7**	**42.8**
Cleft lip & palate vs. cleft lip only	1.5	0.4	6.3	0.8	0.1	5.2
Cleft palate only vs. cleft lip only	1.0	0.2	4.9	0.7	0.1	4.5
School days missed (> 5 days)						
Non-isolated vs. Isolated OFC	1.5	0.6	3.5	1.2	0.4	3.7
Cleft lip & palate vs. cleft lip only	1.0	0.4	2.7	0.7	0.2	1.9
Cleft palate only vs. cleft lip only	0.4	0.1	1.1	0.3	0.1	1.0

Table C1. Comparison of reported stigmatization including teasing, feeling unwelcome because of looks, and being bullied between children with OFC and unaffected children

		All OFC (N=142)		**Controls (N= 138)**		**p value**	**Isolated OFC (N=112)**		**p - value**
		N	%	N	%		**N**	**%**	
Teased about facial appearance	Never or almost never	124	91.2 %	129	97.0 %	**0.044**	97	90.7%	**0.0373**
	Sometimes, fairly or very often	12	8.8%	4	3.0 %		10	9.4%	
	Missing	6	4.2%	5	3.6 %		5	4.5%	
Feels unwelcome because of looks	Never or almost never	121	87.1 %	130	94.9 %	**0.023**	96	86.5%	**0.0206**
	Sometimes, fairly or very often	18	13.0 %	7	5.1 %		15	13.5%	
	Missing	3	2.1%	1	0.7 %		1	0.9%	
Been bulllied in past month	Has not been bullied	120	85.7 %	106	77.4 %	0.183	95	85.6%	0.2594
	Bullied once	11	7.9%	19	13.9 %		10	9.0%	
	Bullied 2-3 times or more	9	6.4%	12	8.8 %		6	5.4%	
	Missing	2	1.4%	1	0.7 %		1	0.9%	

Table C2. Comparison of reported stigmatization including teasing, feeling unwelcome because of looks, and being bullied between children with OFC and unaffected children

		Isolated OFC (N=112)		Non-isolated OFC (N=30)		p-value	Cleft lip only (N= 35)		Cleft lip and palate (N=59)		Cleft palate only (N = 48)		p-value
		N	%	N	%		N	%	N	%	N	%	
Teased about facial appearance	Never or almost never	97	90.7%	25	89.3%	1.000	29	85.3%	48	82.8%	44	93.6%	0.2322
	Sometimes to very often	10	9.4%	3	10.7%		5	14.7%	10	17.2%	3	6.4%	
	Missing	5	4.5%	2	6.7%		1	2.9%	1	1.7%	1	2.1%	
Feels unwelcome because of looks	Never or almost never	96	86.5%	27	93.1%	1.000	30	93.8%	47	83.9%	47	97.9%	**0.0394**
	Sometimes to very often	15	13.5%	2	6.9%		2	6.3%	9	16.1%	1	2.1%	
	Missing	1	0.9%	1	3.3%		3	8.6%	3	5.1%	0	0.0%	
Been bulllied in past month	Has not been bullied	95	85.6%	25	86.2%	0.481	28	84.9%	49	83.1%	43	89.6%	0.557
	Bullied once	10	9.0%	1	3.5%		3	9.1%	4	6.8%	4	8.3%	
	Bullied 2-3 times or more	6	5.4%	3	10.3%		2	6.1%	6	10.2%	1	2.1%	
	Missing	1	0.9%	1	3.3%		2	5.7%	0	0.0%	0	0.0%	

EMORY UNIVERSITY

Institutional Review Board

August 2, 2011

RE: Determination: No IRB Review Required
Title: Parent Perspectives on Cleft and Craniofacial Care, Quality of Life and Outcomes for Children with Orofacial Clefts in North Carolina
PI: Jessica Knight

Dear Ms. Knight,

Thank you for requesting a determination from our office about the above-referenced project. Based on our review of the materials you provided, we have determined that it does not require IRB review because it does not meet the definition(s) of "research" involving "human subjects" or the definition of "clinical investigation" as set forth in Emory policies and procedures and federal rules, if applicable. Specifically, in this project, you will be conducting a secondary analysis of de identified data sets.

This determination could be affected by substantive changes in the study design, subject populations, or identifiability of data. If the project changes in any substantive way, please contact our office for clarification.

Thank you for consulting the IRB.

Sincerely,

Andrea Goosen, MPH
Research Protocol Analyst
This letter has been digitally signed

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