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INVITED MEDICAL REVIEW

The impact of orofacial clefts on quality of life and healthcare use and costs

GL Wehby[1], CH Cassell[2]

[1]*Department of Health Management and Policy, College of Public Health, University of Iowa, Iowa City, IA, USA;* [2]*Department of Public Health Sciences, College of Health and Human Services, The University of North Carolina at Charlotte, Charlotte, NC, USA*

Orofacial clefts are common birth defects that may impose a large burden on the health, quality of life, and socioeconomic well-being of affected individuals and families. They also result in significant healthcare use and costs. Understanding the impact of orofacial clefts on these outcomes is important for identifying unmet needs and developing public policies to reduce the burden of orofacial clefts at the individual, family and societal levels. This paper reviews and summarizes the main findings of recent studies that have evaluated the impact of orofacial clefts on these outcomes, with a focus on quality of life, socioeconomic outcomes, long-term health, and healthcare use and costs. Several studies identify an increased burden of orofacial clefts on these outcomes, but some of the findings are inconsistent. A summary of the primary limitations of the studies in this area is presented, along with recommendations and directions for future research.
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Introduction

Orofacial clefts (OFC) are one of the most common birth defects and occur in 1 per 500 to 2,500 births depending on ancestry, geographic residential location, maternal age and prenatal exposures, and socioeconomic status (SES) (Mossey and Little, 2002; Clark *et al*, 2003; Durning *et al*, 2007). Recent studies suggest that orofacial clefts are one of the most prevalent birth defects in the US, with more than 6,500 born in 2001 (Centers for Disease Control and Prevention (CDC), 2006). OFC occur in three main types: cleft lip only (CL), cleft lip with palate (CLP), and cleft palate only (CP). More than 60% of cases with OFC have CL or CLP (Centers for Disease Control and Prevention (CDC), 2006). The majority of cases with cleft lip with/without cleft palate (CL/P) are non-syndromic (NS) (Jones, 1988; Marazita, 2002), occurring without recognized syndromes or other major birth defects and developmental disabilities (Murray, 2002).

Several treatments including surgery, speech therapy, dental care and psychological support are available for OFC. However, OFC impose a large psychosocial and economic burden on affected families and society (Berk and Marazita, 2002), and are associated with several health problems and complications early in life such as problems with feeding or ear infections (Nackashi *et al*, 2002), which can result in significant morbidity risks and also increased mortality risks, especially in less developed settings, where early systematic pediatric care may not be commonly accessible (Wehby *et al*, 2006a). OFC may also reduce quality of life throughout the life span. Several of the effects of OFC may extend through adulthood resulting in increased mortality and morbidity (Christensen and Mortensen, 2002; Christensen *et al*, 2004). Despite the prevalence of OFC, a paucity of information exists on the quality of life, long-term health and healthcare use and costs of affected individuals and families. Understanding the effects of OFC on the well-being of affected individuals and families and identifying healthcare needs are critical for making changes in healthcare practices and public policies to improve the health outcomes of affected individuals and families and to reduce the burden of OFC at the individual, family and societal levels.

The primary goal of this paper is to review the recent research on health-related quality of life (HRQL), socioeconomic outcomes, health outcomes, and healthcare service utilization and costs. A secondary objective is to identify primary research gaps and potential study designs to address these gaps. This effort is complementary to other recent efforts, such as the Centers for Disease Control and Prevention (CDC) panel on identifying research priorities in OFC research (Yazdy *et al*, 2007).

Correspondence: George L. Wehby, Department of Health Management and Policy, College of Public Health, University of Iowa, E204, GH, Iowa City, IA 52242, USA. Tel: 319 384 5133, Fax: 319 384 5125, E-mail: george-wehby@uiowa.edu
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Review of health-related quality of life research on individuals with orofacial clefts

A few studies on the effects of OFC on HRQL among children, adolescents and adults have been conducted. These studies have provided important preliminary insights into the relationship between OFC and HRQL. However, some of the study findings were inconsistent partly because of differences between studies with regard to patient populations, HRQL measures and study designs. Differences in HRQL measures were because of instruments employed, which ranged from HRQL instruments/questionnaires [such as the Pediatric Quality of Life Inventory (Varni *et al*, 2001; Damiano *et al*, 2007) or the Child's Perceptions Questionnaire (Jokovic *et al*, 2002, 2004; Wogelius *et al*, 2009)] to utility-based methods such as the visual analog scales (Wehby *et al*, 2006b), as well as the groups whose preferences/perspectives for HRQL of OFC were measured, such as parents, patients, and health professionals. Studies also employed different designs, such as inclusion or exclusion of a control group of unaffected individuals. A common limitation of some studies was the reliance on small and convenience samples, primarily because of the challenges of identifying large and population-level samples of affected and unaffected individuals for such studies. Further, the majority of studies focused on assessing the effects of OFC on HRQL, but very few studies attempted to identify the factors that mediate the effects of OFC on HRQL. The most recent studies on HRQL of individuals with OFC are briefly summarized below.

Health-related quality of life in children with orofacial clefts

In the US, Damiano *et al* (2007) measured maternal perceptions of child's HRQL in a sample of children 2–12 years old with OFC from Iowa. The authors found that HRQL decreased significantly with the presence of severe speech problems, and that older children with CP had lower HRQL compared with children with CLP. However, the study included no control group of unaffected children. Kramer *et al* (2008) found no significant effects of the cleft type on child and parent-reported HRQL in a sample of children with OFC aged 5–6 years from Germany. The authors found that parental ratings of the child's HRQL were lower than the child's ratings. The children's rating on the physical well-being domain decreased with the number of surgeries, but increased with the number of siblings.

Wogelius *et al* (2009) found no significant differences in HRQL in a small sample of children with OFC and children without OFC aged 8–14 years from Denmark. Other studies found decreased quality of life of adolescents with congenital and acquired facial malformations compared with unaffected adolescents as well as frequent reporting of stigmatization experiences (Topolski *et al*, 2005; Strauss *et al*, 2007). Quality of life decreased with the individuals' perceptions of increasing severity of facial malformations (Patrick *et al*, 2007). However, these studies included other congenital anomalies besides OFC.

Health-related quality of life in adults with orofacial clefts

Sinko *et al* (2005) found lower HRQL among a sample of Chinese adults with repaired CLP aged 18–30 years, who wanted to receive more treatment compared with those who did not. Further, the study found that CLP impacted emotional and social functioning. Marcusson *et al* (2001) evaluated the HRQL in a sample of adults with CLP and unaffected adults from Sweden. The authors reported significantly lower HRQL in the affected sample compared with the unaffected sample. The study found higher HRQL among adults who were more satisfied with their facial appearance (Marcusson *et al*, 2002).

Oosterkamp *et al* (2007) evaluated the HRQL of a small sample of affected adults with bilateral CLP and unaffected adults from the Netherlands and found no significant differences in HRQL scores between the two groups, but higher HRQL among adults who were satisfied with their appearance.

Health professionals' perspective on health-related quality of life of orofacial clefts

Most studies of HRQL of OFC measured the preferences of affected individuals and parents. Variations in the HRQL preferences of patients, parents and health professionals were reported in the previous studies (Saigal *et al*, 1999). Differences in the HRQL preferences of patients with craniofacial conditions and their parents have also been reported (Wilson-Genderson *et al*, 2007). Wehby *et al* (2006b) measured the perceptions of health professionals involved in providing craniofacial care to patients with OFC in the US of the overall impact of OFC on quality of life of affected individuals, using a visual analog scale (VAS) method. The HRQL scores were solicited on a scale between 0 for the lowest quality of life possible and 1 for the highest quality of life possible. The study found that health professionals perceived a low effect of NS CL and NS CLP on HRQL. Study results suggested that professionals perceived a decreasing burden of OFC on HRQL with age of affected individuals, perhaps because of a larger emphasis on the surgical and medical treatments early in life than the long-term health and psychosocial effects (Wehby *et al*, 2006b).

The study did not assess the preferences of patients or parents. Given that the professionals', patients', and families' perceptions of the impact of OFC on HRQL may vary, a direct comparison by measuring the HRQL preferences of patients and parents using the VAS method becomes an important question for future research to address.

Impact of OFC on socioeconomic and psychosocial outcomes

A few studies have assessed the effects of OFC on the socioeconomic and psychosocial outcomes of affected individuals and families. These studies have provided important insights into the psychosocial and socioeconomic burden of OFC. However, similar to the studies on HRQL, these studies were significantly limited by

small and convenience samples and descriptive analyses that are subject to significant confounding factors, such as family-level and individual-level socioeconomic factors that may relate to both OFC and the studied outcomes.

Socioeconomic outcomes
Kramer *et al* (2007) did not find that OFC increased the financial burden of 130 families of children with OFC aged 6–24 months in Germany, but found that CP increased the family financial burden compared with CL or CLP. On the contrary, Kramer *et al* (2008) found no differences in the financial impact of OFC by cleft type in another sample of families of 5–6 years old affected children.

In Norway, Ramstad *et al* (1995) found overall no significant differences in employment and education of adults with CLP 20–35 years old compared with unaffected adults, but reported lower income, lower marriage rates, and older age at marriage among the affected sample. Marcusson *et al* (2001) reported reduced economic performance among affected adults with OFC compared with unaffected adults.

Psychosocial outcomes
Several studies related to the impact of OFC on the psychosocial status of affected individuals have been conducted. Several studies have reported psychological challenges among children, adolescents and young adults with OFC (Kapp-Simon *et al*, 1992; Kapp-Simon and McGuire, 1997; Hunt *et al*, 2006; Brand *et al*, 2009). Speech problems and concerns about esthetics are thought to contribute to these challenges (Thomas *et al*, 1997; Hunt *et al*, 2005, 2006; Patrick *et al*, 2007). Some studies have also found increased social anxiety among affected adults, although findings have varied between studies (Berk *et al*, 2001; Cheung *et al*, 2007). Christensen *et al* (2004) reported a higher mortality rate as a result of suicide among individuals with OFC in Denmark compared with unaffected individuals.

Impact of orofacial clefts on long-term health

Understanding the effects of OFC and other craniofacial conditions on long-term health outcomes is important for quantifying the health burden and improving service delivery and healthcare policies for affected populations. However, much remains unknown about the effects of OFC on individual and family long-term health outcomes and on healthcare needs. To date, only a few studies have examined long-term health outcomes, such as survival and occurrence of chronic diseases. One inherent limitation in conducting such studies has been the limited access to appropriate data sources and health registries that provide data individuals with OFC throughout life and provide large population-level random samples of unaffected individuals.

Several studies using the Danish health registries have assessed long-term health outcomes of OFC. Christensen *et al* (2004) found increased mortality risks for both males and females with OFC. Bille *et al* (2005) found increased risks of breast and brain cancer among females with OFC and CP, respectively, and increased risk of lung cancer among males with CLP, all compared with unaffected individuals. Further, Christensen and Mortensen (2002) found higher risks of hospital admission because of mental health complications among adults with CP and CL/P, compared with unaffected adults. These studies strongly suggest that OFC imposes a large burden on the health of affected individuals throughout the life span.

Healthcare service utilization and costs of children with orofacial clefts

In the US, several studies have examined health service utilization and costs among children with and without special healthcare needs using national datasets including the Medical Expenditure Panel Survey and the National Survey of Children with Special Healthcare Needs. The HCUP includes all payers of health services and is the largest collection of longitudinal healthcare data in the US (Russo and Elixhauser, 2007). However, these studies did not examine children with birth defects, including OFC, and did not verify the condition or diagnosis. Until recently, only a few studies had been conducted on health service use and costs of children with birth defects, including OFC. This section summarizes the current studies on health service use and costs of children with OFC in the US.

Several cost perspectives exist, including the healthcare system, which includes direct costs, and societal perspective, which includes all costs, for example, caregiver costs and out-of-pocket expenses. Another viewpoint is the payer perspective, such as public and private health insurance, which measures costs with payments to providers. Depending on which perspective one is using, costs, charges, or expenditures are the appropriate measure of effect.

Because costs and expenditures are often used as a proxy for healthcare service utilization and are usually the most salient issues in terms of service delivery, program planning and policy development, this section focuses primarily on costs and expenditures of children with OFC and briefly mentions health service utilization. Differences in the results of these studies are attributable to using different: payers; definitions for healthcare service categories; ages; and units of analysis, such as hospital discharge (hospital stay) compared with an individual.

Studies conducted by Waitzman (1996), Waitzman *et al* (1992, 1994) and Harris and James (1997) are the most comprehensive studies conducted on costs of birth defects, which included costs of OFC; however, they are now outdated. A major strength was that the authors estimated costs from the healthcare and the societal perspective and employed several major data sources to determine costs. Costs associated with mortality, morbidity, lost productivity, and developmental services and medical costs were included in the analysis. Despite the strengths of these studies, they did not provide information by cleft type or NS or syndromic status.

Several other studies have examined the healthcare costs of children with OFC. However, these studies suffered from several limitations, including small sample size, sample and treatment selection biases, examination of charges, and not controlling for other confounding factors such as age and malformation type (Berk and Marazita, 2002; Snowden *et al*, 2003).

Four studies were recently conducted on hospitalizations and hospital costs of children with birth defects, which included OFC. Using the HCUP data, Russo and Elixhauser (2007) evaluated the hospital stays and costs of children of varying ages with OFC who had hospitalizations and costs for the year 2004. In this study, total hospital charges were converted to costs using HCUP cost-to-charge ratios. These were based on hospital accounting reports from the US Centers for Medicare and Medicaid Services (Russo and Elixhauser, 2007). The authors found that for children with NS CP, the total number of hospital stays was 2900 per 100 000 affected children. In comparison, children with CL/P had a total of 4900 hospital stays (Russo and Elixhauser, 2007). Russo and Elixhauser (2007) found that in 2004, the aggregate hospitalization cost for CL and CLP was about $11.6 million more compared with the aggregate costs of CP (Russo and Elixhauser, 2007).

Using the HCUP 2003 Kids' Inpatient Database (KID) by the Agency for Healthcare Research and Quality, a CDC study found that in 2003, newborns with isolated CP had about 1300 fewer hospitalizations than newborns with CL or CLP (CDC, 2007). The 2003 HCUP KID study examined hospital costs during the newborn period and found that the total hospital charges for CP were about $19 million more than the total hospital charges for CL and CLP, suggesting a higher cost per hospitalization for newborns with CP (CDC, 2007).

The major strength of these two studies was providing updated information on healthcare costs and charges of children with OFC. Yet, these studies suffered from several limitations such as no stratification by presence of other anomalies, no comparison with unaffected children, and the unit of analysis often was the hospital discharge, not the child.

The two most recent studies on health service use expenditures of children with OFC were from a public and private payer respectively. Primary strengths of these studies are that the authors: examined OFC by three different cleft categories and presence of other anomalies; examined different age groups; and compared these results with those of unaffected children (Cassell *et al*, 2008; Boulet *et al*, 2009). The study by Cassell *et al* examined Medicaid healthcare use and expenditures in North Carolina during the first 5 years of life for children with and without OFC. The authors used a statewide, population-based birth defects registry to identify children with OFC born 1995–2002 who were continuously enrolled in Medicaid. The authors compared the results with a random sample of resident Medicaid-enrolled children without OFC born during the same time period. Using paid claims data, the authors examined several healthcare categories for service use and expenditures, including medical, inpatient, outpatient, home health, mental health, well-child care, dental and total healthcare expenditures. The authors found the total Medicaid expenditures for infants with OFC during the first year of life were higher than unaffected infants by about $11 million (Cassell *et al*, 2008). Mean expenditure of a child with syndromic OFC was almost five times that of a child with NS OFC (Cassell *et al*, 2008). In this study, total cumulative Medicaid expenditures over the first five years of life for children with OFC were significantly higher than unaffected children by about $22 million (Cassell *et al*, 2008).

A recent study examined health service use and insurer expenditures of children with and without OFC, ranging in age from birth to 10 years old (Boulet *et al*, 2009). The authors used the 2000–2004 MarketScan® Commercial Claims and Encounters databases (Thomson Medstat; Marketscan Database, Ann Arbor, MI USA), which provides data on healthcare use and expenditures of enrollees in several employer-sponsored plans. For children aged 0–10 years old with and without OFC, the difference in annual mean costs (incremental costs) was $13 405 (eight times higher than unaffected children). Mean costs for an infant with OFC and another major, unrelated defect were 25 times higher than those for an infant without OFC, and five times higher than for infants with an isolated cleft (Boulet *et al*, 2009).

Despite these studies' strengths, they suffered from several weaknesses. In both studies, the authors only examined direct costs and expenditures to the healthcare system. The study by Cassell *et al* (2008) included crude expenditures and estimates may have not been representative of other states because Medicaid reimbursement rates vary between states in the US. In addition, these studies did not include out-of-pocket expenses or caregiver costs (Cassell *et al*, 2008; Boulet *et al*, 2009).

Few data are available to identify determinants of variability in service use and costs, including patient (cleft severity, presence of other conditions), family (socioeconomic and demographic), and area-level (healthcare availability and access) characteristics. These factors are critical because patterns of medical and health-related service use and costs for children with OFC can differ considerably by these factors. Additional studies should examine costs of outpatient care, dental care, speech therapy, and special education, with consistent estimations of out-of-pocket expenses, and caregiver costs to determine the true economic burden of OFC. The American Cleft Palate-Craniofacial Association (ACPA), an international, multidisciplinary organization of healthcare professionals, has formed a Task Force to examine such issues. Currently, very limited information exists on the impact of OFC on indirect costs, such as loss in work productivity, time costs to parents, and effects of siblings' schooling. Understanding patterns of health service use and expenditures can help to target populations in need of services, assess the cost-effectiveness of treatments, and develop policies to improve the cost-effectiveness of and access to healthcare for patients and families with OFC.

Timeliness of and referral to services for children with orofacial clefts

Services and treatment for children with OFC can vary depending on the cleft severity, presence of associated syndromes and/or other birth defects, and the child's age and needs (Nackashi *et al*, 2002). However, some general recommendations exist for services and treatment for children with craniofacial anomalies such as OFC (ACPA, 1993; Canady *et al*, 1998; Nackashi *et al*, 2002; Lynch and Karnell, 2003). These recommendations were originally set forth by the ACPA in 1993 and were amended in 2000 and late 2004 (ACPA, 1993).

To date, only one study has examined the timeliness of such services in accordance with the ACPA recommendations (Cassell and Meyer, 2008; Cassell *et al*, in press). This study was a retrospective study of North Carolina resident children with OFC born 1995–2002 who were continuously enrolled in Medicaid. The authors used North Carolina vital statistics, birth defects registry, and Medicaid enrollment and paid claims to examine the mean age at which surgery occurred and factors associated with timely cleft surgery among children with OFC. Using the 2000 ACPA guidelines, the authors found 78.1% of children with OFC had surgery within 18 months. The primary strengths of this study were using several data sources, including a birth defects registry, to provide information on the timeliness of services by maternal (age, race/ethnicity, and education), child (cleft type and presence of other anomalies) and system (service type, residential location, receipt of maternity care coordination) factors associated with such services. The primary limitations of this study were that the results were from one state and a public payer (Cassell and Meyer, 2008; Cassell *et al*, in press).

One factor that can affect receipt of services, thereby affecting health service use and costs among children with OFC, is referral to services. Only three studies have examined referral to services among children with OFC (White, 1981; Williams *et al*, 2003; Cassell *et al*, 2007).

These studies found that identification and referral to services of children with OFC, especially to craniofacial centers and teams, were significantly associated with location of residence, cleft type, presence of other birth defects, presence of other malformations in the family, and receipt of maternity care coordination services (White, 1981; Williams *et al*, 2003; Cassell *et al*, 2007).

As a result of the paucity of data on the identification and referral of children with OFC and other craniofacial anomalies to services, additional research is warranted to improve the timeliness of services and thereby quality of life and health outcomes for affected children.

Recommendations and conclusions

The above sections summarized the findings and limitations of studies of the impact of OFC on individual and family quality of life, socioeconomics, health outcomes, and healthcare use and costs. The primary limitations for conducting large-scale well-designed studies in this area have been the limited access to and availability of large datasets that include measures of these outcomes for the OFC population and of comparison samples of unaffected individuals. The high cost of identifying large samples of affected individuals and conducting large-scale prospective surveys to collect such data has been the main limitation. However, efforts to overcome these data shortages and expand the scale and scope of these studies are increasing.

A unique registry system that provides a strong venue for many of these studies, especially those focused on long-term health, healthcare use, and socioeconomic outcomes is the Danish Health Registry System (Christensen and Mortensen, 2002; Christensen *et al*, 2004; Bille *et al*, 2005). This data system includes a set of registries that include individual-level data on healthcare and prescription drug use, demographics, and socioeconomic characteristics for the entire population and allows for a random selection of large control samples, which provide an important methodological strength (Christensen and Mortensen, 2002; Christensen *et al*, 2004; Bille *et al*, 2005). This system has allowed several important studies of long-term outcomes of OFC and is also enabling further ongoing studies to identify the long-term effects of OFC on health, healthcare utilization, prescription drug use and socioeconomic outcomes. The population-based data allow for consistent and generalizable estimations of such effects in large and representative samples.

A need exists for evaluating the impact of OFC on HRQL of affected individuals and families throughout the lifespan, using large population-based samples, robust HRQL measures, and multiple perspectives, including the societal perspective. The societal perspective is needed for cost-effectiveness analyses of healthcare treatments (Gold *et al*, 1996). Further, it is important to employ both multi-domain survey instruments of HRQL, as well as methods that obtain HRQL values and utility scores, which are needed for cost-effectiveness analysis (Gold *et al*, 1996).

It is also extremely important to further understand the long-term effects of OFC on individual and family socioeconomic well-being. Some studies have identified increased risks of OFC with low socioeconomic status (Clark *et al*, 2003; Durning *et al*, 2007; Yang *et al*, 2008). Given that minimal changes occur in family socioeconomic status over time, baseline family socioeconomic status (prior to the birth of the child) may confound the assessment of the impact of OFC on long-term socioeconomic and financial outcomes. Therefore, studies investigating the impact of OFC on socioeconomic and financial outcomes should account for the family socioeconomic characteristics prior to the birth of the child. This also applies to studies of other outcomes that are influenced by baseline family socioeconomic characteristics, such as health outcomes, healthcare use and psychosocial outcomes.

Other important factors that should be accounted for in studies of OFC are maternal and parental preferences for risk taking and health. Maternal health behaviors such as smoking, alcohol use and multivitamin use affect OFC risks (Romitti *et al*, 1999; Johnson and Little,

2008; Shi *et al*, 2008). Health behaviors are a function of maternal preferences for health and risk taking and for child health, which likely influence other OFC related outcomes, such as healthcare use and costs. Therefore, it is important to account for these preferences, which may confound the relationship between OFC and quality of life, socioeconomic, psychosocial, health and healthcare outcomes. Measuring maternal preferences for risk taking and health through assessment of relevant maternal health behaviors during pregnancy and accounting for these in studies of OFC outcomes are important for obtaining consistent estimates. Further, as the genetic risk factors of OFC are identified, genetic instrumental variable studies can be applied using these genetic variants as instruments for OFC when assessing their effects on quality of life, socioeconomic, healthcare and other outcomes to account for unobserved confounders (Wehby *et al*, 2008).

Several important questions remain unanswered in terms of the effects of OFC on healthcare use and costs. Further understanding of health service use and costs of affected individuals over the lifespan is warranted. Estimating out-of-pocket, caregiver costs and indirect costs, including lost productivity, among affected individual and families using reliable methods and large scale datasets is needed. Moreover, a great need exists for examining the sources of variation in the type, quantity, and quality of health services provided to affected individuals and families and for estimating the cost-effectiveness of alternative treatment plans in order to identify ways to improve access of affected individuals to appropriate and cost-effective care. In addition, a need exists for further understanding of the role and effectiveness of integrated systems of care for individuals with OFC that involve craniofacial centers and teams, medical homes, dental, speech, and mental health services. The role of health insurance in access to such systems is also an important component to examine further. Further research on the healthcare referral patterns of children and adults with OFC and other craniofacial anomalies is warranted to improve referral and timeliness of services and thereby quality of life and health outcomes of affected individuals.

In conclusion, several studies suggest an impact of OFC on the quality of life, socioeconomic and psychosocial well-being, long-term health, healthcare use and costs for affected individuals and families. However, the primary limitation of most of these studies has been the reliance on small and unrepresentative samples with limited measures on several important outcomes and confounding variables. This in part has been because of the unavailability and lack of access to large-scale datasets that provide rich data for such questions. Therefore, a tremendous need exists for expanding the collaborations between various birth defect registries, craniofacial care providers, and researchers to identify data needs, improve data collection systems, and build consortia that provide access and opportunities to further examine the impact of OFC on multiple outcomes throughout the lifespan.

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Both authors wrote the paper.

References

American Cleft Palate-Craniofacial Association (ACPA) (1993). Parameters for evaluation and treatment of patients with cleft lip/palate or other craniofacial anomalies. *Cleft Palate Craniofac J* **30**(Suppl.)**:** S1–S16.

Berk NW, Marazita ML (2002). Costs of cleft lip and palate: personal and societal implications. In: Wyszynski DF, ed. *Cleft lip and palate: from origin to treatment*. Oxford University Press: New York, pp. 458–467.

Berk NW, Cooper ME, Liu YE, Marazita ML (2001). Social anxiety in Chinese adults with oral-facial clefts. *Cleft Palate Craniofac J* **38:** 126–133.

Bille C, Winther JF, Bautz A, Murray JC, Olsen J, Christensen K (2005). Cancer risk in persons with oral cleft – a population-based study of 8,093 cases. *Am J Epidemiol* **161:** 1047–1055.

Boulet SL, Grosse SD, Honein MA, Correa-Villasenor A (2009). Children with orofacial clefts: health care use and costs among a privately insured population. *Public Health Rep* **124:** 447–453.

Brand S, Blechschmidt A, Müller A *et al* (2009). Psychosocial functioning and sleep patterns in children and adolescents with cleft lip and palate (CLP) compared with healthy controls. *Cleft Palate Craniofac J* **46:** 124–135.

Canady J, Karnell M, Marsh J (1998). *Cleft lip and cleft palate: the first four years [brochure/book]*. Cleft Palate Foundation: Chapel Hill.

Cassell CH, Meyer RE. (2008). Timeliness of services during the first two years of life among medicaid-eligible children with orofacial clefts in North Carolina, 1995–2002, No. 157. North Carolina State Center for Health Statistics Studies: North Carolina. Available at: http://www.schs.state.nc.us/SCHS/pdf/SCHS157.pdf [accessed on 20 March 2009].

Cassell CH, Meyer RE, Farel AM (2007). Predictors of referral to the North Carolina Child Service Coordination Program among infants with orofacial clefts. *Cleft Palate Craniofac J* **44:** 45–51.

Cassell CH, Meyer R, Daniels J (2008). Health care expenditures among Medicaid enrolled children with and without orofacial clefts in North Carolina, 1995–2002. *Birth Defects Res A Clin Mol Teratol* **82:** 785–794.

Cassell CH, Daniels J, Meyer RE (in press). Timeliness of primary cleft lip/palate surgery among children with orofacial clefts in North Carolina, 1995–2002. *Cleft Palate Craniofac J*

CDC (2007). Hospital stays, hospital charges, and in-hospital deaths among infants with selected birth defects – United States, 2003. *MMWR Morb Mortal Wkly Rep* **56:**25–29.

Centers for Disease Control and Prevention (CDC) (2006). Improved national prevalence estimates for 18 selected major birth defects – United States, 1999–2001. *MMWR Morb Mortal Wkly Rep* **54:**1301–1305.

Cheung LK, Loh JS, Ho SM (2007). Psychological profile of Chinese with cleft lip and palate deformities. *Cleft Palate Craniofac J* **44:** 79–86.

Christensen K, Mortensen PB (2002). Facial clefting and psychiatric diseases: a follow-up of the Danish 1936–1987 facial cleft cohort. *Cleft Palate Craniofac J* **39:** 392–396.

Christensen K, Juel K, Herskind AM, Murray JC (2004). Long term follow up study of survival associated with cleft lip and palate at birth. *Br Med J* **328:** 1405–1408.

Clark JD, Mossey PA, Sharp L, Little J (2003). Socioeconomic status and orofacial clefts in Scotland, 1989 to 1998. *Cleft Palate Craniofac J* **40:** 481–485.

Damiano P, Tyler M, Romitti P *et al* (2007). Health-related quality of life among preadolescent children with oral clefts. *Pediatrics* **120:** e283–e290.

Durning P, Chestnutt IG, Morgan MZ, Lester NJ (2007). The relationship between orofacial clefts and material deprivation in wales. *Cleft Palate Craniofac J* **44:** 203–207.

Gold MR, Siegel JE, Russell LB, Weinstein MC (eds) (1996). *Cost-effectiveness in health and medicine*. Oxford University Press: New York.

Harris JA, James L (1997). State-by-state cost of birth defects – 1992. *Teratology* **56:** 11–16.

Hunt O, Burden D, Hepper P, Johnston C (2005). The psychosocial effects of cleft lip and palate: a systematic review. *Eur J Orthod* **27:** 274–285.

Hunt O, Burden D, Hepper P, Stevenson M, Johnston C (2006). Self-reports of psychosocial functioning among children and young adults with cleft lip and palate. *Cleft Palate Craniofac J* **43:** 598–605.

Johnson CY, Little J (2008). Folate intake, markers of folate status and oral clefts: is the evidence converging? *Int J Epidemiol* **37:** 1041–1058.

Jokovic A, Locker D, Stephens M, Kenny D, Tompson B, Guyatt G (2002). Validity and reliability of a questionnaire for measuring child oral-health-related quality of life. *J Dent Res* **81:** 459–463.

Jokovic A, Locker D, Tompson B, Guyatt G (2004). Questionnaire for measuring oral health-related quality of life in eight- to ten-year-old children. *Pediatr Dent* **26:** 512–518.

Jones MC (1988). Etiology of facial clefts: prospective evaluation of 428 patients. *Cleft Palate J* **25:** 16–20.

Kapp-Simon KA, McGuire DE (1997). Observed social interaction patterns in adolescents with and without craniofacial conditions. *Cleft Palate Craniofac J* **34:** 380–384.

Kapp-Simon KA, Simon DJ, Kristovich S (1992). Self-perception, social skills, adjustment, and inhibition in young adolescents with craniofacial anomalies. *Cleft Palate Craniofac J* **29:** 352–356.

Kramer FJ, Baethge C, Sinikovic B, Schliephake H (2007). An analysis of quality of life in 130 families having small children with cleft lip/palate using the impact on family scale. *Int J Oral Maxillofac Surg* **36:** 1146–1152.

Kramer FJ, Gruber R, Fialka F, Sinikovic B, Schliephake H (2008). Quality of life and family functioning in children with nonsyndromic orofacial clefts at preschool ages. *J Craniofac Surg* **19:** 580–587.

Lynch JI, Karnell MP (2003). *Cleft lip and palate: the school-aged child [booklet]*. Cleft Palate Foundation: Chapel Hill.

Marazita ML (2002). Segregation analysis. In: Wyszynski DF, ed. *Cleft lip and palate: from origin to treatment*. Oxford University Press: New York, NY, pp. 222–233.

Marcusson A, Akerlind I, Paulin G (2001). Quality of life in adults with repaired complete cleft lip and palate. *Cleft Palate Craniofac J* **38:** 379–385.

Marcusson A, Paulin G, Ostrup L (2002). Facial appearance in adults who had cleft lip and palate treated in childhood. *Scand J Plast Reconstr Surg Hand Surg* **36:** 16–23.

Mossey PA, Little J (2002). Epidemiology of oral clefts: an international perspective. In: Wyszynski D, ed. *Cleft lip and palate: from origin to treatment*. New York, NY: Oxford University Press: Oxford, pp. 127–144.

Murray JC (2002). Gene/environment causes of cleft lip and/or palate. *Clin Genet* **61:** 248–256.

Nackashi A, Dedlow Rosellen E, Dixon-Wood V (2002). Health care for children with cleft lip and palate: comprehensive services, and infant feeding. In: Wyszynski DF, ed. *Cleft lip and palate from origin to treatment*. New York, NY: Oxford University Press, pp. 127–158.

Oosterkamp BC, Dijkstra PU, Remmelink HJ *et al* (2007). Satisfaction with treatment outcome in bilateral cleft lip and palate patients. *Int J Oral Maxillofac Surg* **36:** 890–895.

Patrick DL, Topolski TD, Edwards TC *et al* (2007). Measuring the quality of life of youth with facial differences. *Cleft Palate Craniofac J* **44:** 538–547.

Ramstad T, Ottem E, Shaw WC (1995). Psychosocial adjustment in Norwegian adults who had undergone standardised treatment of complete cleft lip and palate. I. Education, employment and marriage. *Scand J Plast Reconstr Surg Hand Surg* **29:** 251–257.

Romitti PA, Lidral AC, Munger RG, Daack-Hirsch S, Burns TL, Murray JC (1999). Candidate genes for nonsyndromic cleft lip and palate and maternal cigarette smoking and alcohol consumption: evaluation of genotype-environment interactions from a population-based case-control study of orofacial clefts. *Teratology* **59:** 39–50.

Russo CA, Elixhauser A. (2007). *Hospitalizations for birth defects, 2004*. Report No. 24. U.S. Agency for Healthcare Research and Quality: Rockville. Available at: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb24.pdf accessed on 24 January 2007.

Saigal S, Stoskopf BL, Feeny D *et al* (1999). Differences in preferences for neonatal outcomes among health care professionals, parents, and adolescents. *J Am Med Assoc* **281:** 1991–1997.

Shi M, Wehby GL, Murray JC (2008). Review on genetic variants and maternal smoking in the etiology of oral clefts and other birth defects. *Birth Defects Res C* **84:** 16–29.

Sinko K, Jagsch R, Prechtl V, Watzinger F, Hollmann K, Baumann A (2005). Evaluation of esthetic, functional, and quality-of-life outcome in adult cleft lip and palate patients. *Cleft Palate Craniofac J* **42:** 355–361.

Snowden CB, Miller TR, Jensen AF, Lawrence BA (2003). Costs of medically treated craniofacial conditions. *Public Health Rep* **118:** 10–17.

Strauss RP, Ramsey BL, Edwards TC *et al* (2007). Stigma experiences in youth with facial differences: a multi-site study of adolescents and their mothers. *Orthod Craniofac Res*. **10:** 96–103.

Thomas PT, Turner SR, Rumsey N, Dowell T, Sandy JR (1997). Satisfaction with facial appearance among subjects affected by a cleft. *Cleft Palate Craniofac J* **34:** 226–231.

Topolski TD, Edwards TC, Patrick DL (2005). Quality of life: how do adolescents with facial differences compare with other adolescents? *Cleft Palate Craniofac J* **42:** 25–32.

Varni JW, Seid M, Kurtin PS (2001). PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care* **39:** 800–812.

Waitzman NJ (1996). *The cost of birth defects: estimates of the value of prevention*. University Press of America: Lanham.

Waitzman NJ, Romano PS, Sheffler RM, Harris JA (1992). Economic cost of birth defects and cerebral palsy-United States. *MMWR* **44:** 694–699.

Waitzman NJ, Romano PS, Scheffler RM (1994). Estimates of the economic costs of birth defects. *Inquiry* **31:** 188–205.

Wehby GL, Castilla EE, Goco N *et al* (2006a). Description of the methodology used and progress to date in an ongoing pediatric care interventional study of children born with cleft lip and palate in South America. *BMC Pediatr* **6:** 9.

Wehby GL, Ohsfeldt RL, Murray JC (2006b). Health professionals' assessment of health-related quality of life values for oral clefting by age using a visual analogue scale method. *Cleft Palate Craniofac J* **43:** 383–391.

Wehby GL, Ohsfeldt RL, Murray JC (2008). 'Mendelian randomization' equals instrumental variable analysis with genetic instruments. *Stat Med* **27:** 2745–2749.

White RB (1981). Services for children with congenital facial clefts through a state Crippled Children's Service Program. *Cleft Palate J* **18:** 116–121.

Williams CA, Mardon RE, Grove D *et al* (2003). Treatment of oralfacial clefts by state-affiliated craniofacial centers and cleft palate clinics. *Birth Defects Res A Clin Mol Teratol* **67:** 643–646.

Wilson-Genderson M, Broder HL, Phillips C (2007). Concordance between caregiver and child reports of children's oral health-related quality of life. *Community Dent Oral Epidemiol* **35**(Suppl. 1)**:** 32–40.

Wogelius P, Gjorup H, Haubek D, Lopez R, Poulsen S (2009). Development of Danish version of child oral-health-related quality of life questionnaires (CPQ8-10 and CPQ11-14). *BMC Oral Health* **9:** 11.

Yang J, Carmichael SL, Canfield M, Song J, Shaw GM, National Birth Defects Prevention Study (2008). Socioeconomic status in relation to selected birth defects in a large multicentered US case-control study. *Am J Epidemiol* **167:** 145–154.

Yazdy MM, Honein MA, Rasmussen SA, Frias JL (2007). Priorities for future public health research in orofacial clefts. *Cleft Palate Craniofac J* **44:** 351–357.