

# **Dental Utilization for Medicaid-Enrolled Children with Cystic Fibrosis**

Elise Watson Sarvas

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Committee:

Donald L. Chi

Colleen E. Huebner

Johan K. Aps

JoAnna M. Scott

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Department of Health Services

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Elise Watson Sarvas

University of Washington

Abstract

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Elise Watson Sarvas

Chair of the Supervisory Committee:

Donald L. Chi, DDS, PhD

Department of Pediatric Dentistry and Department of Health Services

**Background:** Despite a highly cariogenic diet and frequent use of inhaled xerostomia-inducing medications, children with CF are believed to be at a lower risk for dental caries (tooth decay) compared to other children. A potential protective factor is increased use of preventive dental care, but not studies to date have examined dental use for children with CF. This goal of this study was to compare dental care use for Medicaid-enrolled children with and without CF.

**Methodology:** Iowa Medicaid data from 2012 were analyzed for children age 3 –17 years who were enrolled in Medicaid for at least 11 months (N = 156,268). Poisson regression models were used to compare utilization rates for any dental care and also for specific categories of dental care (diagnostic, preventive, routine restorative, and complex restorative).

**Results:** The study included 85 children with CF (0.05%). Overall, 66.8% of study children utilized dental care. Children with CF were significantly less likely to use any dental care than children without CF after

adjusting for confounders (incident rate ratio: 0.819, 95% CI: 0.80–0.84,  $p < 0.001$ ). Among children who utilized any dental care, children with CF were more likely to have used diagnostic and preventive care and less likely to have used restorative care than children without CF, but these differences were not statistically significant.

Conclusions: Medicaid-enrolled children with CF are less likely to use dental care than children without CF. These findings suggest that greater use of dental care is an unlikely explanation for lower caries rates among children with CF

Keywords: cystic fibrosis, dental utilization, Medicaid-enrolled children, dental health services

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## **Dedication**

To Jeff

## **Introduction**

Cystic fibrosis (CF) is the most common lethal genetic disease in Whites and is caused by a mutation to the Cystic Fibrosis Transmembrane Regulator (CFTR) gene which results in abnormal transport of chloride and sodium across cell membranes. Most morbidity and mortality results from fatal progressive lung disease resulting from thick mucosal obstructions and subsequent infections (1).

## **Characteristics of Cystic Fibrosis**

### **Mutations and pathophysiology**

CF is caused by mutations to the 230 kb gene on chromosome 7 that encodes a 1480 amino acid polypeptide called the Cystic Fibrosis Transmembrane Regulator (CFTR) (2). Since 1989 when the location of the gene was identified by positional cloning, more than 1700 specific mutations have been discovered (3,4). The most common mutation is the  $\Delta F508$  found in 86.8% of patients with one or two mutations followed by the G542X (4.6%), G551D (4.4%), R117H (2.7%), N1303K (2.5%), W1282X (2.4%), R553X (1.8%) and 621+1G->T (1.7%) mutations (5). A patient must have two defective copies of the CFTR gene in order to have the disease, though the mutations in each copy do not need to be the same.

The CFTR is a cAMP-regulated chloride and thiocyanate transporter found on epithelial cell membranes that also serves as a regulatory protein for other conductances (6). Clinically, a defective CFTR results in deranged transport of chloride and other ions across membranes and manifests itself in increased chloride content of sweat gland secretions and thickened, viscous secretions in the lungs, pancreas, liver, and intestines (7). The CF genotype is of therapeutic importance because there is one drug, ivacaftor (trade name Kalydeco™), which was approved by the Food and Drug Administration in January 2012 to treat the underlying defective CFTR protein in the G551D mutation. In response to this success and the marked improvement of patients taking this medication, future CF drug therapies aim to address genotype specific proteins.

## Epidemiology and diagnosis

Of the 70,000 individuals worldwide who have CF, approximately 30,000 live in the United States (US) (8). The mean prevalence in the US is 0.797/10,000 which is similar to the mean prevalence of 0.737/10,000 calculated for 27 European Union (EU) countries (9). More accurate counts of individuals with CF worldwide are expected in the future as newborn screening improves and as individuals are consolidated into national treatment centers and registries.

The incidence of CF in a population varies by race, but the majority (94.1% in the US) of individuals with CF are white. The prevalence of CF among Whites is 1:3,200, in Hispanics 1:7,000, in African Americans 1:15,000 and in Asian Americans 1:31,000 (5,6). While previously considered only a disease of Whites, other races are experiencing an increase in number of CF cases. The percentage of individuals with CF in the US who identified as African American increased from 3.3% to 4.5% from 1992 – 2012 and the percentage that identified as Hispanic increased from 4.1% to 7.7% during the same time period (5).

Previous screening for CF relied on observations of the clinical manifestations of the disease such as frequent lung infections, abnormally salty skin and failure to thrive in children and adolescents. In the newborn period, presence of a meconium ileus shortly after birth due to reduced fecal water content, served as a reliable screening tool (10). Today almost 60% of individuals with CF are diagnosed by newborn screening panels as early diagnosis is thought to improve outcomes for survival (5). Currently all 50 states and the District of Columbia screen for CF at birth by determining the immunoreactive trypsinogen (IRT) concentrations on dried blood spots collected from the heel on a Guthrie card as part of the National Newborn Screening protocol. If the IRT is abnormally high, a second test is done from dried blood spots a few weeks later. Follow up quantitative pilocarpine iontophoresis or a “sweat test” to determine if there are elevated chloride concentrations in sweat excretions and genetic testing confirm the diagnosis (11).

CF can be diagnosed at any age, but most are diagnosed before age 2. As newborn screenings have improved, the median age of diagnosis dropped from 6 months in 1992 to 4 months in 2012. There were 920 new diagnoses of CF in 2012 in the US, but this number may be lower than anticipated due to data adjustments by the CF Foundation's Patient Registry (5).

### Age and sex characteristics

The life expectancy for individuals with CF has increased significantly in recent decades. A child born with CF in the 1950s could not expect to make it to elementary school, but by 1992, the predicted mean survival was 29.4 years (95% CI: 28.2 – 30.8). In 2012 the predicted mean survival for an individual with CF was 41.1 years (95% CI: 37.4 – 43.1) (5). About half of individuals with CF in the US are over the age of 18.

Because CF is an autosomal mutation, CF affects equal numbers of males and females at birth. A sex difference however has been described in terms of patient survival. Despite similar baseline levels of coughing and wheezing, chest radiographic severity scores measured in the first 10 years, and age at first acquisition of *Pseudomonas aeruginosa*, males tend to live longer than females (12). A proposed explanation for this is that in studies of CF registries in the US and UK, males were referred earlier for diagnostic sweat testing than females, thus leading to an earlier diagnosis and treatment (13). The reason for early referral was attributed to a variety of social and physiologic factors including more severe hallmark symptoms in males.

In a 2012 study of available EU databases, males made up 53% of total number of individuals with CF overall and significantly outnumbered females in all age groups. This historical trend was attributed to earlier screening for males and reaffirmed recommendations that strongly support universal newborn screening programs so life-prolonging treatment may be initiated as soon as possible (14). In the US, the percentage of individuals with CF who are male has steadily declined from 53.9% in

1992 to 51.7% in 2012 (5). It is unknown if early treatment for all individuals will close this gap as data regarding life expectancy do not yet exist for cohorts of individuals born under the now almost ubiquitous newborn screening programs.

### Medical Management

Current guidelines in the US and EU recommend that patients with CF meet with their medical management team every three months (four times a year) for maintenance sessions as well as additional visits as needed for management and/or treatment of recurrent infections. Maintenance visits allow for continuous lung function testing, attenuation of daily and weekly medications and dosing schedules, nutritional monitoring and overall health assessment. Adherence to these guidelines by clinics have been associated with better CF health metrics such as improved BMI and increased Forced Expiratory Volume (FEV1) scores (15,16).

There is no cure for CF. Its progression is marked by periods of stable health with intermittent periods of pulmonary exacerbations that are treated in specialized CF centers. There are 110 centers in the US accredited by the Cystic Fibrosis Foundation. Located at teaching and community hospitals, these centers have been praised by the National Institutes of Health as an ideal model for which to manage chronic diseases and the dramatic increase in life expectancy for individuals with CF is primarily attributable to them. A multidisciplinary team that in addition to physicians and nurses may include physiotherapists, nutritionists, social workers, genetic counselors, pharmacists, psychologists and infectious disease specialists housed at each center provides maintenance and acute infection support.

### Clinical significance of CF on various organ systems

Among the phenotypic signs and symptoms of CF, those affecting the lungs are the most damaging. The inability to clear thickened mucous, its colonization by pathogenic bacteria and

subsequent stimulation of more obstructing mucous is a cyclically destructive process that proceeds to atelectasis, bronchiectasis and ultimately death (17). The prevalence of certain fauna of the infected CF respiratory tract changes as the patient ages, most notably from *S. aureus* in the early course of the disease and *P. aeruginosa* at a later stage (18).

Early respiratory symptoms associated with CF vary between individuals and by mutation and range from productive coughs, wheezing and hyperinflation of the lungs to signs of obstructive airway disease. The thick, mucous secretions are difficult to clear and soon become colonized with a classic array of microorganisms such as *Staphylococcus aureus*, *Haemophilus influenza*, *Pseudomonas aeruginosa* and *Burkholderia cepacia* in an age dependent sequence and fungi such as *Candida* and *Aspergillus* (5). Chronic infections lead to a marked neutrophilic inflammatory response and ultimately result in tissue damage, irreversible bronchiectasis and progressive respiratory failure (7,19). There is no known cure for the respiratory manifestations of CF apart from lung transplant. In addition to lung infection, the majority of individuals with CF also experience upper respiratory complications such as sinus disease (20).

The earliest manifestation of CF in the gastrointestinal tract, meconium ileus, is usually pathognomonic for the disease. The viscid meconium and poor intestinal mobility cause a blocked ileum in 10-20% of individuals with CF and may require surgical intervention (21). As the individual with CF gets older, viscid fecal material may continue to potentially obstruct the terminal ileus and proximal colon in a condition known as distal intestinal obstruction syndrome (DIOS). Treatment includes oral rehydration in combination with laxatives (22).

Pancreatic insufficiency is common among individuals with CF and is the main cause of poor growth, malnutrition and failure to thrive (23). Due to their inability to absorb necessary micro and macronutrients, individuals with CF often take supplemental pancreatic enzymes and drastically increase their caloric intake (24). Even with extra supplementation, many individuals with CF remain

chronically low in serum vitamin D levels either as a result of underlying complications and oxidative stress that increases the body's need or a poorly understood interaction between the CFTR and vitamin D transporters in the intestinal cells (25,26). A systematic review reported that supplemental vitamin D reduced the risk of dental decay 47%, and that this association was strongest in young children (27). Individuals with CF may therefore be at greater risk for dental decay because of their chronically low vitamin D serum levels, even when it is supplemented for in their diet.

Improvements in care of individuals with CF have led to dramatic decreases in mortality rate and many are living into their fifth and sixth decades of life (5). As life expectancy increases, insufficient exocrine secretions are manifesting as pancreatitis and cystic fibrosis related diabetes (CFRD) more frequently (28). Hepatobiliary disease is also becoming more common with increased life expectancy. Bile, like other exocrine secretions is thickened and can obstruct the intrahepatic bile ducts progressing to periportal fibrosis and eventually cirrhosis (29). Clinical signs and symptoms may take years to manifest and include complications such as gastrointestinal hemorrhage, ascites, fatigue, weight loss, anorexia, jaundice and portal hypertension (30).

#### Bacterial colonization and antibiotic therapy

The most common and usually earliest pathogen colonizing infants and children (under 11 years) is *S. aureus*, an anaerobic Gram-positive cocci bacterium (5,31). The prevalence of individuals with CF who test positive for Methicillin resistant *S. aureus* (MRSA) increased from 7.3% in 2001 to 25.9% in 2011 (5). Management of patients includes routine cultures of respiratory sputum to guide antibiotic selection every three months to monitor and anticipate antibiotic coverage, especially during acute pulmonary exacerbations. Oral antibiotic treatment for *S. aureus* include penicillin derivatives (e.g. dicloxacillin, methicillin or amoxicillin-clavulanate), first generation cephalosporins (e.g. cephalexin), macrolides, trimethoprim-sulfamethoxazole or doxycycline. Trimethoprim-sulfamethoxazole, doxycycline

or an oral linezolid can be taken orally when MRSA is present. Intravenous antibiotics given during acute pulmonary exacerbations include cefazolin or nafcillin and vancomycin if there is MRSA.

The incidence of *P. aeruginosa* colonization increases with age, especially after 11 years, and it has been isolated from almost 80% of US adults with CF (5). This aerobic, Gram-negative, cocci bacterium causes a more damaging inflammatory response in young children when it infects the lower airway (31). Treatment usually includes two classes of antibiotics to prevent resistance, capitalizing on synergistic effects and target both mucoid and non-mucoid strains. Oral ciprofloxacin has been shown to be effective in some cases, but IV antibiotics are more effective in cases of acute pulmonary exacerbation. Typical regimens pair tobramycin, an aminoglycoside, with an antipseudomonal semisynthetic penicillin (e.g., piperacillin-tazobactam), an extended third generation cephalosporin (e.g. ceftazidime, cefepime), a carbapenem (e.g. imipenem-cilastatin or meropenem) or less frequently with a monobactam aztreonam.

A variety of chronic antibiotic regimens have been tested empirically for the treatment of CF-related infections, but this contributes to antibiotic resistance and may potentiate unwanted side effects so the practice is not currently recommended. A recent Cochrane review reported on the exception to this may be azithromycin, which after continuous use for six months showed an improvement in respiratory function and a decrease in *S. aureus* cultures. Macrolides such as azithromycin do not show any direct killing of *P. aeruginosa*, but may reduce its activity (18).

### **Cystic Fibrosis and Oral Health**

Children with special health care needs are at a greater risk for dental caries due to a variety of systemic and environmental factors (32,33). Individuals with CF however do not seem to have a higher caries prevalence than similar general or special healthcare needs populations despite the high cariogenic diet requirements to maintain their overall health (34,35) . Possible explanations include

long-term antibiotic use, pancreatic enzyme replacement therapy, increased salivary buffering capacity and an increased patient awareness of microbiota (17,35–38). The risk factors for dental caries for children with CF can be categorized as physiologic (i.e. defects to oral hard tissues; salivary characteristics; comorbid factors) or behavioral (i.e. antibiotic use, diet, toothbrushing with fluoride toothpaste, preventive dental care use).

### Caries prevalence

Studies on CF caries prevalence have relied on variable control populations to varying outcomes. Most studies report a significantly lower prevalence of caries in CF populations when compared to healthy matched controls (36,39–43) and also with healthy siblings (39,44). Lower prevalence of caries in CF populations have also been reported when compared to other individuals with chronic respiratory conditions (45). Comparing the caries experience between children with CF and with other children with special health care needs does not take into account the multifactorial process of the disease and conclusions may not be reliable. An early study with 63 children with CF showed a tendency for their caries prevalence to be lower than that of an undefined cohort of physically handicapped children (46). Two later studies however showed a higher dmft score for Norwegian preschoolers with CF than for both other disabled Norwegian preschoolers and disabled Norwegian school aged-children (47,48). A small study of Polish children showed similarly high caries rate in both individuals with CF and healthy individuals in 23 matched pairs (49).

### Caries prevalence reported by age

A 2013 systematic review of the oral health literature for individuals with CF concluded that the discrepancies in reported caries experience may reflect an underlying age-based subgroup bias (50). When the reported caries prevalence was reported for primary teeth, individuals with CF

consistently had significantly lower caries prevalence than their healthy controls (36,41,44,51,52) except in one study where caries experience was high for both individuals with CF and without CF (49). In a study where individuals with CF were matched with similar subjects with chronic respiratory disease, there was no significant difference in dmft (45).

Caries prevalence in the mixed dentition of children with CF was more variable in its relationship to matched controls. In a study of 63 individuals with CF and their healthy siblings from New England, 7.0-9.9 year old individuals with CF (n = 22) had a significantly lower dmft/s and DMFT/S, but in the 10-11.9 year age group of individuals with CF (n = 21) the difference in dmft/s was not significant while the DMFT/S remained significant (44). A study of 86 individuals with CF and their healthy matched controls from Minnesota reported that individuals with CF in the mixed dentition and mean chronologic age of 9.8 (n = 27) had significantly lower mean dental caries (51). In Northern Ireland a study of 118 individuals with CF and their healthy, presumably heterozygous siblings, reported a lower, but non-significant difference in mean caries prevalence in the mixed dentition of 11-15 year olds (n = 35) (36,52). A population of 131 individuals with CF and healthy matched non-sibling controls from the same center in Northern Ireland later reported a similar pattern of lower DMFT/S in the mixed dentition (n = 79) that was also non-significant (41). In a study of 74 individuals with CF who were matched with other individuals with chronic respiratory diseases, dmft and DMFT in the early mixed dentitions (n = 18) was lower, but not significantly different (45).

As individuals with CF age, many transition into adult clinic settings, which can make it difficult to include them in pediatric dental studies. The oldest age of study subjects with CF included in caries prevalence reporting studies was 24.2 years (51). When the reported caries prevalence was reported for permanent teeth, whether by age or specifically the DMFT/S designation, individuals with CF consistently had significantly lower caries prevalence than their healthy controls (36,42,44,52) except in one study where caries rate was high for both individuals with and without CF (49). In a study where

individuals with CF were matched with similar subjects with chronic respiratory disease they experienced non-significantly lower DMFT (45).

The systematic review concluded that while the current paradigm presented in pediatric dentistry prescribes that all individuals with CF are at low risk for dental caries, this might only really be true for younger children with CF and adolescents with CF may have a higher caries burden (50).

### **CFTR-Related Risk Factors for Dental Caries**

#### Tooth discoloration

Certain types of tooth discoloration, depending on etiology, may increase the risk for dental caries either through inherent weakening of the enamel layer or as an iatrogenic result of subsequent esthetic repair or masking of the staining.

Tooth discoloration was among the earliest reports on the unique dentition of individuals with CF in the literature. Discoloration is a broad term used to describe abnormal tooth color and can be intrinsic or extrinsic to the tooth or both. Intrinsic discoloration of a tooth can trace its etiology to disruptions in the development of the dentin and/or enamel matrix during tooth formation or trauma. Developmental disturbances are usually caused by medications like tetracycline and its derivatives that irreversibly bind to calcium in the developing tooth bud and the severity of discoloration depends on the dose received during development, length of the exposure and the stage and degree of tooth mineralization (46,53). Supra-optimal fluoride can also cause internal mottling or discoloration of teeth when the exposure happens during development. Trauma to teeth can cause physiologic changes in the nerve and vascular supply of teeth that can change how light is reflected through teeth, making them appear grey or brown. Extrinsic discoloration can have multiple different etiologies that usually happen after tooth development including stain acquired by foods or medicines (e.g. clorehexidine), behaviors (e.g. smoking), and poor oral hygiene (e.g. plaque, chromogenic bacteria accumulation). As a person

ages, the outer enamel layer becomes thinner through abrasion resulting in yellower looking teeth. Enamel defects from stresses and injuries during development of the outer enamel matrix may create micro and macro surface discrepancies in an otherwise smooth surface which can be discolored and/or pick up stain from the environment. Injuries can also occur after tooth formation and may result in small enamel fractures that can hold staining.

Intrinsic enamel defects in individuals with CF were among the earliest reported dental abnormalities documented and often result in tooth discoloration. Initial reports of enamel hypoplasia in individuals with CF during the tetracycline use era are inconclusive because of additional factors that may cause tooth discoloration (history of trauma, preceding deciduous tooth abscess) and rates (5% versus 1% in healthy sibling controls) were nonsignificant (44). Primosch described enamel defects as falling into the category of hypoplasia or hypomineralization depending on the clinical presentation. Enamel defects, especially in the permanent incisors, have been broadly described as ranging from hypoplasia to hypomineralization depending on the clinical presentation and have a reported prevalence ranging from 28.4% to 56% (42,44,45,54,55).

Enamel defects may be another sequela of the disrupted ion transport in CFTR mutations. Murine models suggest that the altered *cftr* gene expression in ameloblasts is the likely etiology of enamel defects (56). CFTR knockout mice enamel had decreased calcium and calcium-to-phosphorus ratios compared to wild type mice which parallels studies in human teeth that showed decreased calcium, but normal phosphorus levels (57). Follow up histologic studies in mice and human fetal jaws have confirmed that the *cftr* gene is expressed in maturation stage ameloblasts and is critical for the completion of enamel mineralization (58).

## Salivary glands and saliva

Disturbances in CFTR gene expression manifest in the salivary glands of individuals with CF and include clinical observations of hypertrophy (44) and histologic signs of abnormal parenchymal structure, especially in the almost exclusively mucous sublingual gland (17). The saliva of individuals with CF has been described as having higher concentrations of phosphate and calcium than control subjects (39,59) which may explain reports of higher pH and better buffering capacity (36,52) leading to a decrease in the caries process. Murine models however have given contradictory results on pH and buffering capacity (60). Possibly due to an increase of soluble ions in saliva, individuals with CF have been observed to have higher rates of calculus (41,59,61), but surprisingly less gingivitis (39,40,46) than controls.

Murine models have conversely shown a lower pH in submandibular gland saliva, suggesting that the CFTR gene may disrupt bicarbonate secretion mechanisms (60). This low pH and disrupted buffering capacity lead to an increase in number and severity of carious lesions in the  $\Delta F508$  mice when compared with their wild type littermates.

## **Other CF-Mediated Caries Risk Factors**

### Gastroesophageal reflux disease (GERD)

Chronic gastrointestinal complications are one of the earliest hallmarks of CF in children beginning in the neonatal period starting with meconium ileus and progressing to difficulty with digestion and gastroesophageal reflux disease (GERD) in childhood (62). Mild to moderate acid exposure from GERD has been implicated in exacerbating respiratory disease and is present in young infants, children and adults with CF; its prevalence ranges from 55 – 76% (63,64). Gastroesophageal reflux introduces stomach acid to the oral cavity and depending on its frequency and severity can cause dental injury by eroding dental hard tissues (65). This erosion may lead to a decrease in the integrity of mineral

component of the enamel matrix, predisposing the tooth to dental caries (66). Comparisons between individuals with GERD and their healthy siblings show a significantly higher caries experience in those with diagnosed GERD (67).

### Medications

Individuals with CF routinely inhale antibiotics, hypertonic saline and  $\beta$ -adrenergic receptor agonists to control bacterial disease, increase hydration of airway surface liquid and improve lung function (68,69). The frequent use of inhaled  $\beta$ -adrenergic receptor agonists, such as albuterol, have been linked with decreases in salivary pH and buffering capacity and an increase in caries risk in asthmatic patients (70,71). This may hypothetically present a similar challenge in the chronic use of these drugs in individuals with CF.

In 1967 Swallow et al. reported the tendency for children with permanent tooth discoloration staining to have been prescribed higher amounts of tetracycline, an antibiotic that was routinely part of early CF treatments (46). This study and other empirical observations led to the recommendation that other antibiotics should be used in place of tetracyclines before a child is 8 years old to prevent irreversible permanent tooth discoloration (72). A study of 63 children with CF age 5 – 12 years with previous history of antibiotic use from the northeast United States followed this in 1976 with a report that 57% of the individuals with CF they studied had permanent incisor staining (44). In 35% of these individuals the stain was esthetically disfiguring while none of the healthy control siblings had stained teeth. A similar New York population of 4 – 25 year olds showed staining of the clinical crowns in 30% of individuals with CF while their healthy control siblings showed none, though the author noted that this staining may not be attributed exclusively to tetracycline use as other antibiotics were beginning to be used as substitutes (61). One of the last studies to describe tetracycline staining in individuals with CF reported its prevalence in a Minnesota CF population of 3 to 15 year olds as 24.4%. Of the 86 subjects in

this study, enamel defects were noted in direct correlation with tetracycline staining in five individuals, accounting for 23.8% of the staining cases, (42). The reported prevalence of tooth discoloration in individuals with CF has decreased, presumably because of the guidelines introduced regarding tetracycline usage. Disturbances in tooth mineralization in development because of calcium binding medications may increase caries risk.

### Oral Bacteria and CF

Dental caries has long been known as a transmissible disease associated with *Streptococcus mutans* which is often quantified as MS counts (73,74). Individuals with CF had significantly lower levels of MS defined as  $< 10^5$  colony forming units (CFUs), than their healthy matched CF heterozygous or healthy controls as well as less DMF (75). This is in direct contrast to recent CF murine models that found  $\Delta F508$  mice had more and more serious carious lesions in addition to an almost 20-fold higher number in MS counts when compared to their wild type litter mates (60). It was suggested that in this murine model the acid-producing bacteria has an enhanced ability to colonize dental surfaces and cause dental decay.

### Dietary Risk Factors for Dental Caries

The thick mucus lining the intestinal tract of individuals with CF combined with pancreatic insufficiency makes it difficult to absorb nutrients efficiently from food. Therefore families with children affected by CF are counseled to dramatically increase the frequency and amount of quality caloric intake in order to meet metabolic needs (34,76). In the oral cavity, bacteria of the mutans streptococci group metabolize fermentable carbohydrates that are introduced during food consumption to lactic acid causing the pH of saliva to drop. This drop in pH stimulates bicarbonate production in saliva to act as a buffer and bring the pH back up to a physiologic mean of about 6.3 in about 30 to 60 minutes post-

prandial. If the time between food consumption events is too short, the body does not have time to completely buffer the pH drops and the mean pH remains low enough to potentiate enamel demineralization and cause dental caries. The necessity for the increased frequency of meals and snacks for individuals with CF may increase caries risk in individuals with CF.

### **Importance of Looking at Dental Care Use in Children with CF**

Children with special health care needs are generally at greater risk for dental caries due to a variety of systemic, environmental and behavioral factors (32,33). Individuals with CF however do not appear to have a higher caries prevalence despite a highly cariogenic dietary required to maintain weight (34,35), enamel defects, and higher prevalence of gastroesophageal reflux disease (GERD) (54,62,67). In fact, some studies show children with CF may have lower caries prevalence (77,43,41,52,51). Possible protective factors include long-term antibiotic use, pancreatic enzyme replacement therapy, and increased salivary buffering capacity (35,36,17,37,38). However, extant studies of caries prevalence in individuals with CF are limited by a lack of consistency in control group selection, absence of statistical power calculations, increased risk of bias when using a single examiner, and the lack of longitudinal studies (50).

The American Dental Association (ADA) and the American Academy of Pediatric Dentistry (AAPD) both recommend twice-yearly dental checkups (every six months) with more frequent dental checkups for children at increased risk for caries (78). During dental checkups, dentists assess the patient's oral health, monitors growth and development, evaluate the need for any treatment, and make recommendations to reduce caries risk. The visits often include preventive care like dental cleanings, oral hygiene instruction, dietary counseling, pit-and-fissure sealants, and topical fluoride application. Regular dental checkups are important because preventive care helps reduce risk for caries and also address dental disease early, before disease progresses and becomes more costly to fix (79).

Medicaid-enrolled children are known to encounter barriers to preventive dental care, especially compared to privately-insured children (80). However, a recent study found that Medicaid-enrolled children with chronic conditions were significantly more likely to use dental care than other Medicaid-enrolled children (81). Additionally, use of dental care by Medicaid-enrolled children with chronic respiratory conditions was found to be higher when compared with other Medicaid-enrolled children with chronic conditions (82). In regards to children with CF, dental checkups may be a factor that is protective against caries. The rationale for this is that soon after a CF diagnosis is made, families are introduced to the health care system and are advised to make regular medical care visits (16). In the course of these visits, caregivers and children may become more aware of healthcare services available and be more accustomed to interacting with healthcare providers leading to greater likelihood of dental visits. However, to date, no studies have assessed dental care use for Medicaid-enrolled children with CF.

This study was designed to test two hypotheses: 1) Medicaid-enrolled children with CF are more likely to use dental care than children without CF and 2) Among Medicaid-enrolled children who utilize dental care, children with CF are more likely to use diagnostic and preventive care and less likely to use restorative care than children without CF.

## **Methods**

### **Study Setting**

The 2010 Iowa census data showed a total of population 688,838 children between the ages of 3 and 17, of whom 51.3% were male. In the 2012 July 1<sup>st</sup> population estimate of 607,992 total Iowan children between the ages of 3 and 17, there were 122,194 children age 3 – 5 years (20.1%); 283,296 children age 6 – 12 years (46.6%); and 202,502 children age 13 – 17 years (33.3%). In this age range, Iowa census data reported that 89.4% of children were White, 4.4% were African-American, 8.6% were

Hispanic/Multi-Hispanic and 6.2% were classified as other (Asian American, American Indian and Native American, Native Hawaiian and Pacific Islander or two or more races).

The Iowa Medicaid program, administered by the Iowa Medicaid Enterprise, a division of the Iowa Department of Human Services, provides medical and dental insurance coverage for eligible children under age of 21 years. Covered dental care services include diagnostic, preventive and restorative care. Cystic Fibrosis Foundation (CFF) data indicate that there were approximately 190 Medicaid-enrolled individuals with CF who lived in Iowa in 2012. About half of these individuals are children under age 18 years. Iowa Medicaid is based on a fee-for-service model in which dentists are paid for services rendered. In 2012, children from families with incomes below 100% of the Federal Poverty Level (FPL) were eligible for Iowa Medicaid. In 2012, there was an expansion to include children from families between 100% and 133% of the FPL (83). Three accredited CF centers are located in the Iowa: Blank Children's CF Center in Des Moines; Mary Greeley Hospital's McFarland Clinic in Ames; and the University of Iowa's Pediatric and Adult CF clinics in Iowa City.

### Study Population

The study population consisted of Medicaid-enrolled children age 3– 17 years. Child's age was assessed on January 1, 2012. Children under 3 years were excluded because dental use for younger children is very low, indicating that factors related to dental use are different for this younger subgroup. Consistent with previous studies, children who were enrolled in Medicaid less than 11 months were excluded. This criterion is based on methods developed by the National Committee for Quality Assurance. The final dataset included a total of 156,268 Medicaid-enrolled children. The study was approved by the University of Iowa Institutional Review Board (IRB).

## Data

Iowa Medicaid administrative enrollment and claims files were obtained under an agreement with the Iowa Department of Human Services. All recipient level data were de-identified to ensure patient confidentiality. The Medicaid enrollment files included the child's unique identification number, gender, date of birth, race/ethnicity, county code, zip code and the number of months enrolled in Medicaid. The Medicaid claims files included medical diagnoses based on International Statistical Classification of Diseases and Related Health Problems (ICD-9-CM) codes and dental claims based on Code on Dental Procedures and Nomenclature (CDT). The child's unique identification number was used to link claims and enrollment files.

The unique provider identification number was linked to provider enrollment data including location of practice. The type of dental provider seen by children with CF was assessed by first merging the provider location codes for children who used dental care with a separate file of Medicaid providers from Iowa. Providers were either contacted by phone or their practice website was used to determine their dental training. In cases where there was ambiguity, a phone call to the practice was always made. Practices or clinics for which there were multiple providers with varying levels of training (i.e. a mixture of pediatric and general dentists) were coded as "unknown".

## Study Variables

The independent variable in our study was the child's CF status. A child was classified as having CF if he or she has any of the following ICD-9-CM codes in the medical claims files: 277.00, 277.01, 277.02, 277.03 or 277.09. All other children were classified as not having CF.

The main dependent variable in our study was whether a child utilized any dental care in 2012, defined as the presence of any dental claim (84). In addition, we created four variables to represent different types of dental care using previously published criteria (84). Diagnostic care (e.g. examinations,

radiographs) was defined as CDT codes ranging from D0110 – D0340. Preventive care (e.g. topical fluoride placement, pit-and-fissure sealants) was defined as CDT codes ranging from D1110 – D1351. Routine restorative care (e.g. fillings) was defined as CDT codes ranging from D2140 – D2394. Complex restorative care (e.g. root canals, crowns, extractions) was defined as CDT codes ranging from D2930 – D2750.

There were three additional study variables: age, gender and race. Age was analyzed as a continuous variable and also as a categorical variable (3 – 5 years, 6 – 12 years and 13 – 17 years) categories corresponding to the stages of primary, mixed and permanent dentitions, respectively. Parent-reported race was classified as White, Black, American Indian, Asian, Hispanic, Pacific Islander, Multi-Hispanic, Multi-Race, and Missing. To address problems with sparse data, it was decided to collapse the categories of Hispanic and Multi-Hispanic together to form “Hispanic/Multi-Hispanic.” In addition, the categories of American Indian, Asian, Pacific Islander and Multi-Race were combined into “Other”. The final race categories were: White, Black, Hispanic/Multi-Hispanic, Other and Unknown.

### Statistical Analyses

Univariate descriptive statistics were generated to describe the overall study population. The proportion of children with CF and the proportions of children who utilized dental care were calculated. Bivariate descriptive statistics were then generated to compare the CF and non-CF study groups. Chi-square tests were used to analyze differences between CF and non-CF categorical age, race, and gender. Two sample t-tests (equal variances assumed) were used to analyze differences between CF and non-CF mean age. Modified Poisson regression models (with robust standard error) were used to estimate the incidence rate ratio of dental care use for children with and without CF. There were two confounders: age and race. Age, measured as a continuous variable, was a statistical confounder associated with both CF status and dental use. Cystic fibrosis is a genetic disorder and disproportionately affects Whites (9).

Race is also associated with dental care utilization (85). Poisson regression models were run both unadjusted and adjusted for the confounders. Statistical analyses were completed using Stata/MP Version 13.1. The significance level was set to 0.05 *a priori*.

## **Results**

### Descriptive Statistics

The study included 85 children with CF (0.05%) and 156,183 children without a CF diagnosis (99.95%). The majority of children were male (51.4%), White (43.8%) and the average age was 9.50 years ( $\pm 4.13$  years) (Table 1).

### Bivariate statistics

Children with CF were significantly younger than children without CF ( $8.6 \pm 4.1$  years vs.  $9.5 \pm 4.1$  years;  $p = 0.004$ ). There was no significant difference in the proportion of males and females in the CF and non-CF groups (44.7% vs. 51.4%;  $p = 0.22$ ). A significantly larger proportion of children with CF were White than children without CF (63.5% vs. 47.8%;  $p < 0.001$ ) (Table 1).

### Dental Care Use

The majority of children had at least one dental visit in 2012 (66.8%). A significantly lower proportion of children with CF used dental care than children without CF (50.6% vs. 69.7%;  $p < 0.001$ ). There were no significant differences between children with and without CF for use of diagnostic care ( $p = 0.177$ ), preventive care ( $p = 0.201$ ), routine restorative care ( $p = 0.100$ ), or complex restorative care ( $p = 0.935$ ) (Table 1).

### Multiple Variable Regression Models

In the unadjusted model, children with CF were 0.20 times less likely to have used any dental care (IRR 0.80; 95% CI: (0.78 – 0.81);  $p < 0.001$ ) than children without CF. After adjusting for race and age, children with CF were 0.18 times less likely to have used any dental care when adjusting for race and age (IRR 0.82; (0.80 – 0.84);  $p < 0.001$ ). Among who utilized dental care, there were no statistically significant differences in the types of services utilized by CF status (Table 2).

### **Discussion**

This study was conducted to compare dental care use for Medicaid-enrolled children with CF compared to Medicaid-enrolled children without CF. It was hypothesized that children with CF would be more likely to use dental care than children without CF because of their extensive and repeated use of other health services. Contrary to the hypothesis, the data indicate that children with CF were significantly less likely to use dental care than children without CF. Among those who utilized dental care, there were no significant differences in the use of specific types of dental care (diagnostic, preventive, routine restorative and complex restorative) for children with and without CF.

There are three possible explanations for why the study hypothesis, that Medicaid-enrolled children with CF would be more likely to use dental care than Medicaid-enrolled children without CF, was not supported. First, children with CF and their families are frequent visitors to health providers and increased use of health care related to CF care may lead to fewer resources to devote to dental care (16). Second, children with CF are hospitalized for long periods of time, particularly when symptoms associated with CF are exacerbated, which may interfere with scheduling regular dental appointments (68). And finally, children with CF may view CF clinics as their “medical home” because of their frequent visits to them. At these clinics they may not be receiving adequate oral health risk assessments and

recommendations for establishing dental homes that they would have otherwise received during well-child visits to a primary care physician (86).

This study also compared use of different types of dental care for Medicaid-enrolled children by CF status. It was hypothesized that children with CF would be more likely to use diagnostic and preventive care and less likely to use restorative care than children without CF. When children with CF did use dental care, they used diagnostic and preventive care at slightly higher rates, although not significantly higher. Given that children with CF are at a high risk for dental caries and reported caries prevalence in this population have been inconsistent, it is important that children with CF have access to diagnostic and preventive care services to mitigate known caries risk factors that affect children with CF. It was also found that children with CF utilized restorative care at slightly lower rates than children without CF, but these differences were not significant. In a post hoc analysis, use of specific types of restorative procedures (e.g., fillings, stainless steel crowns, root canals, extractions) was similar between children with and without CF. Collectively, these findings indicate that dental utilization patterns for specific types of dental care are similar for Medicaid-enrolled children with and without CF.

The present study's findings have clinical relevance for medical and dental providers who care for patients with CF. Children with CF receive the majority of their health care services from their CF team, which includes physicians, nurses, and nutritionists. Because individuals with CF are susceptible to respiratory infections, preventing caries and dental infections is important to ensuring optimal systemic health for patients with CF. CF teams should perform regular oral health screenings, learn how to recognize early signs of dental disease, and educate families about the importance of oral health, including regular dental checkups. This could be accomplished by 1) discussing the need for optimal oral health and establishment of a dental home, 2) referring children with CF to dentists and coordinating care if needed, and 3) bundling preventive dental visits with CF team visits in the hospital setting if dental care facilities exist. The Medicaid data indicated that the majority of children with CF were seen

by general dentists. Of the 43 children with CF who utilized any dental care in 2012, 19 were seen by only by a general dentist (44.2%). Ten of the children with CF were seen only by a pediatric dentist (23.3%) and two were seen in a university setting, most likely by a pediatric dentist or pediatric dental resident (4.7%). The type of dental providers for 3 of the children with CF could not be assessed (7.0%) and 9 children with CF had claims made by multiple types of providers (20.9%). Currently only select post-graduate dental programs like general practice residencies (GPRs) or pediatric dental residencies offer extensive training in treating children with special health care needs. Dental schools should therefore include education on the unique oral health care needs of patients with CF at the pre-doctoral level as well as clinical rotations that expose dental students to the medical complexities associated with the treatment of CF. Training should include instruction on the unique dental risk factors that present in patients with CF as well as the need for vigilant monitoring to ensure access to dental care, despite some evidence suggesting that individuals with CF are at lower risk for dental caries.

Over 50% of Medicaid-enrolled children with CF did not utilize dental care in 2012. Future research should examine the barriers to dental care for children with CF, particularly those children who do not seek dental care regularly. These families could be surveyed to identify specific barriers to care that might help improve access to dental care. In addition to dental care use, future work should identify other oral health related behaviors in children with CF that are related to caries risk, including dietary factors and fluoride exposure. This information can inform not only the dental teams on how to best provide care and manage caries risk in patients with CF, it can also aid the CF team in determining how to best link these children with an oral health care provider. In addition, comprehensive studies should be conducted to assess caries prevalence and the various factors that contribute to caries risk in individuals with CF.

Until now, most studies on the oral health of individuals with CF have focused on caries prevalence and other oral manifestations of the disease; however these studies have inherent bias

because they rely on families and children who present to academic medical centers. This study adds to the literature by focusing on the population of Medicaid-enrolled children with CF. However, there are three main limitations. First, the outcome measured focused on dental utilization, which does not give an indication of existing dental needs. In other words, children who utilized dental care may still have existing unmet dental care needs. Future research needs to include both dental care utilization and clinical oral health measures to assess the extent to which use leads to lower levels of unmet need. Second, the study assessed dental use in one year. The 2012 Medicaid expansion to increase coverage of families to 133% of the FPL may have influenced the study findings. Longitudinal studies across multiple years should be conducted to validate the current findings. Third, the present study focused on children enrolled in Medicaid and did not include privately or non-insured children with CF. Medicaid-enrolled children with chronic respiratory conditions have been found to use dental care at a higher rate, which conflicts with current findings (82). Future studies should assess dental care use for children with CF across various types of dental insurance.

## **Conclusion**

Dental care utilization rates for Medicaid-enrolled children with and without CF in Iowa were compared to determine if differential use of dental care might be a potential explanation to support some studies suggesting lower caries risk for individuals with CF. Contrary to the original hypothesis, Medicaid-enrolled children with CF were significantly less likely to use dental care than Medicaid-enrolled children without CF. Additional research is needed to fully understand the factors that are implicated in dental caries risk in children and adolescents with CF. This information is needed to ensure that all individuals with CF have an opportunity for optimal oral health over the life course.

## Tables

**Table 1: Demographics: of Children Ages 3 – 17 Years enrolled in Iowa Medicaid for 11 or 12 months in 2012**

	<b>Total (N = 156,268)</b>	<b>CF (N = 85)</b>	<b>Non-CF (N = 156,183)</b>	<b>p-value*</b>
	N (%)	N (%)	N (%)	
<b>Gender</b>				0.215
Male	80,363 (51.4)	38 (44.7)	80,325 (51.4)	
Female	75,905 (48.6)	47 (55.3)	75,858 (48.6)	
<b>Categorical Age (years)</b>				0.210
3 – 5	40,605 (26.0)	29 (34.1)	40,576 (26.0)	
6 – 12	77,092 (49.3)	39 (45.9)	77,053 (49.3)	
13 – 17	38,571 (24.7)	17 (20.0)	38,554 (24.7)	
<b>Race</b>				0.005
White	68,470 (43.8)	54 (63.5)	68,416 (43.8)	
Black	10,253 (6.6)	3 (3.5)	10,250 (6.6)	
Hispanic/Multi-Hispanic	16,369 (10.5)	6 (7.1)	16,363 (10.5)	
Other	5,881 (3.8))	0 (0)	5,881 (3.8)	
Missing	55,295 (35.4)	22 (25.9)	55,273 (35.4)	
<b>Dental care utilization</b>				
Any dental care	104,452 (66.8)	43 (50.6)	104,409 (69.7)	< 0.001
Diagnostic	104,451 (66.8)	42 (49.4)	104,409 (66.9)	0.177
Preventive	102,759 (65.8)	41 (48.2)	102,718 (65.8)	0.201
Routine Restorative	30,607 (19.6)	5 (5.9)	30,602 (19.6)	0.100
Complex Restorative	18,720 (12.0)	6 (7.1)	18,714 (12.0)	0.935

\*Calculated using a Chi-square test

**Table 2: Types of dental care utilization**

	<b>IRR Unadjusted (95% CI)</b>	<b>p-value</b>	<b>IRR Adjusted for race and age (95% CI)</b>	<b>p-value</b>
<b>Any dental care</b>	0.797 (0.78 – 0.81)	< 0.01	0.819 (0.80 – 0.84)	< 0.001
<b>Type of dental care</b>				
<b>Diagnostic</b>	1.21 (0.92 – 1.60)	0.17	1.21 (0.89 – 1.64)	0.225
<b>Preventive</b>	1.20 (0.91 – 1.60)	0.20	1.19 (0.88 – 1.63)	0.264
<b>Routine Restorative</b>	0.49 (0.21 – 1.18)	0.11	0.50 (0.19 – 1.34)	0.165
<b>Complex Restorative</b>	0.97 (0.44 – 2.13)	0.94	0.82 (0.31 – 2.16)	0.684

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