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**Impact of repeated non-treatment on long-term lung function**

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**Background:** Previous findings from the Epidemiologic Study of Cystic Fibrosis (ESCF) indicated that more-consistent treatment of declines in forced expiratory volume in 1 second (FEV<sub>1</sub>) of 10% or greater from baseline in people with CF (PwCF) was associated with better pulmonary outcomes, yet more than one-third of declines were not treated. Data are lacking from a more recent cohort and regarding the effect of repeated untreated declines. Our objective was to determine the prevalence of untreated lung function decline in a pediatric cohort and evaluate the impact of repeated nontreated decline on the probability of percentage predicted FEV<sub>1</sub> (FEV<sub>1</sub>pp) recovery to 100% of baseline.

**Methods:** We included PwCF aged 6 to 17 followed in the Cystic Fibrosis Foundation Patient Registry between 2016 and 2019. Baseline FEV<sub>1</sub>pp was the average of the highest three FEV<sub>1</sub>pp recorded during a period of stability spanning 30 to 365 days. We assessed relative decreases in FEV<sub>1</sub>pp from baseline between 2017 and 2018. Participants must have had three or more relative declines of at least 5% within a 12-month window and have had a follow-up FEV<sub>1</sub>pp in 2019 to determine whether they had returned to baseline. Treatment within 28 days of decline was categorized as any (intravenous antibiotics, oral or inhaled antibiotics (non-intravenous antibiotics)) versus no antibiotic treatment. We defined our exposure of repeated nontreatment as 50% or more decline events not treated using any antibiotic therapy. Alternate definitions of repeated nontreatment were tested in sensitivity analyses.

**Results:** Four thousand eighty-eight children were reported to have three or more declines of more than 5% in a 12-month window between 2017 and 2018. We identified 2,826 (69.1%) who experienced repeated nontreatment and 1,262 (30.9%) with more than 50% of their decline events having received any antibiotic therapy within 28 days. Children who experienced repeated nontreatment had a median (interquartile range) baseline age of 11.6 years (9.2, 14.7) and baseline FEV<sub>1</sub>pp of 96.7% (85.4, 106.0). The group for whom at least half of their declines were treated had a median age (IQR) of 13.5 years (10.1, 15.8 years) and baseline FEV<sub>1</sub>pp of 85.9% (72.7%, 96.8%). Of the children who experienced repeated non-treatment, 35.5% returned to 100% or more of their baseline, compared with 59.7% of the children who received more frequent antibiotic treatment.

**Conclusions:** We found that a substantial proportion of pediatric PwCF with multiple declines of at least 5% are not being treated with antibiotic therapy, especially those with high baseline FEV<sub>1</sub>pp. Children who experienced repeated nontreatment were younger and had more than a 10% higher baseline FEV<sub>1</sub>pp than those who were more frequently treated with antibiotic therapy, and two-thirds did not return to baseline by the end of 2019. Next steps include modeling FEV<sub>1</sub>pp to evaluate whether repeated nontreatment is associated with accelerated decline in lung function.

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**Gingivitis in children with cystic fibrosis**

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**Background:** The close links between the oral cavity and respiratory tract increase the potential risk of micro-aspiration of oral bacteria. Thus, it is critical to determine whether children with cystic fibrosis (CF) are at risk of oral disease. CF-related comorbidities such as diabetes, as well as systemic inflammation due to frequent lung infections and continued use of dry-mouth-inducing inhaled treatments, are potential risk factors for gingivitis

(gum inflammation) [1,2]. Despite these risk factors, the current literature suggests that children with CF are at lower risk of gingivitis than those without because of chronic use of antibiotics to treat lung infections [3–5], but this literature is outdated (1977–2009) and does not account for potential confounders in the association between CF and gingivitis. Thus, the goal of this study was to compare the prevalence of gingivitis in children with and without CF.

**Methods:** This was a cross-sectional study comparing the risk of gingivitis in children with CF with the risk in those without CF with other special health care needs aged 7 to 17. We recruited children with CF from a single pediatric CF clinic in Seattle, Washington (n = 69) and non-CF controls from Medicaid enrollment files in Washington State (n = 89). Gingivitis was defined as bleeding in 10% or more of examined gingival sites. We used logistic regression to compare the prevalence of gingivitis between the two groups and adjusted for age, sex, race, antibiotic use, and dental insurance type as potential confounders.

**Results:** Children with CF were slightly younger (11.3 ± 3.1 vs 12.4 ± 2.8, p = 0.02), more likely to be white (93% vs 42%, p < 0.001), and less likely to have Medicaid insurance only (32% vs 84%, p < 0.001). Sixty-eight percent of children with CF and 40% of non-CF controls had gingivitis. Children with CF had significantly higher odds of gingivitis than non-CF controls (OR 3.1, 95% CI, 1.6–6.1; p < 0.001). This remained significant after adjusting for potential confounders (OR 4.7, 95% CI, 1.9, 11.9; p = 0.001).

**Conclusions:** In contrast to previous studies, our study showed greater likelihood of gingivitis in children with CF than in non-CF controls. Ensuring optimal oral health for children with CF is critical to maintain overall health and quality of life.

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**Effect of SARS-CoV-2 on long-term physical and mental health symptoms in people with cystic fibrosis and their caregivers**

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**Background:** SARS-CoV-2 affects people long after the acute infection has resolved, with 30% to 50% of the general population reporting persistent