

# Periodontal disease prevalence and oral hygiene status of adults with cystic fibrosis: A case–control study

Niamh Coffey<sup>1</sup>  | Fiona O'Leary<sup>1</sup> | Francis Burke<sup>1</sup> | Laura Kirwan<sup>2</sup> | Paul O'Regan<sup>2</sup> | Barry Plant<sup>3</sup> | Anthony Roberts<sup>1</sup> | Martina Hayes<sup>4</sup>

<sup>1</sup>Department of Restorative Dentistry, University College Cork, Cork, Ireland

<sup>2</sup>Cystic Fibrosis Registry of Ireland, University College Dublin, Dublin, Ireland

<sup>3</sup>Adult Cystic Fibrosis Unit, Cork University Hospital, Cork, Ireland

<sup>4</sup>Department of Restorative Dentistry, Dublin Dental University Hospital, Dublin, Ireland

## Correspondence

Niamh Coffey, Cork University Dental School and Hospital, Wilton, Cork T12 8EYV, Ireland.  
Email: [niamh.coffey@ucc.ie](mailto:niamh.coffey@ucc.ie)

## Funding information

Cystic Fibrosis Ireland; Health Research Board; CiSA

## Abstract

**Aim:** To investigate the prevalence of gingivitis and periodontitis, and the oral hygiene status of adults with cystic fibrosis (CF) in the Republic of Ireland.

**Materials and Methods:** A case–control study in the form of a clinical examination of 92 adults with a diagnosis of CF was carried out in the adult CF unit in Cork University Hospital. A 40-item questionnaire was used to capture socio-demographic variables and medical and dental information. Two calibrated examiners carried out a periodontal assessment on participants, using the WHO-recommended CPI-modified index, and oral hygiene status was measured using the Greene–Vermillion index. The results were compared with a population-based control group of similar socio-demographic profile.

**Results:** Oral hygiene levels (plaque and calculus) were significantly worse in people with CF, with a median plaque index of 0.83 (interquartile range [IQR] 0.333–1.542) in the CF group compared with 0.5 (IQR 0.167–0.667) in the non-CF group. Calculus index in the CF group was 0.33 (IQR 0.17–0.83) compared with 0.33 (IQR 0.125–0.33) in the non-CF group. However, periodontal disease levels were significantly lower in the CF group. Gingivitis (bleeding on probing  $\geq 10\%$  sites) was seen in 67.4% of the CF group, compared with 83.7% of the non-CF group, OR 0.365 (95% confidence interval [CI] 0.181–0.736), relative risk (RR) 0.779 (95% CI 0.655–0.928). Mild periodontitis (periodontal probing depth [PPD]  $< 5$  mm) was seen in 15.2% of the CF group, compared with 31.5% of the non-CF group, OR 0.390 (CI 0.190–0.800), RR 0.483 (95% CI 0.273–0.852). Severe periodontitis (PPD  $\geq 6$  mm) was seen in 0% of the CF group, compared with 9.8% of the non-CF group. There was a tendency, albeit non-significant, towards reduced periodontitis in PWCF who regularly took antibiotics, particularly azithromycin.

**Conclusions:** In this study, adults with CF had poor oral hygiene practices, with high levels of plaque and calculus. Despite this finding, adults with CF had lower levels of clinical gingivitis and periodontitis than seen in a non-CF control group. Further study is required to examine the causes of this phenomenon.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2024 The Authors. *Journal of Clinical Periodontology* published by John Wiley & Sons Ltd.

**KEYWORDS**

cystic fibrosis, gingivitis, oral hygiene, periodontal diseases

**Clinical Relevance**

*Scientific rationale for study:* There is a lack of studies on the periodontal status of people with cystic fibrosis (PWCF), due to their historically low life expectancy. Knowledge regarding the periodontal status of these individuals is pertinent as they may require dental evaluation prior to solid organ transplantation, and periodontal disease can impact respiratory function, which is already compromised by cystic fibrosis (CF). This study investigated the oral hygiene and prevalence of gingivitis and periodontitis in adults with CF. *Principal findings:* There were relatively high levels of plaque and calculus in PWCF studied. Despite this, they had lower levels of clinical gingivitis and periodontitis. *Practical implications:* PWCF have poorer levels of oral hygiene. Targeted oral hygiene advice should be given to these patients, despite the lack of clinical signs of gingivitis or periodontitis.

**1 | INTRODUCTION**

Cystic fibrosis (CF) is the most common autosomal recessive condition in Caucasian populations, caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which is located on chromosome 7. The main function of the corresponding protein is a cAMP-mediated chloride channel that regulates the ion and water balance across epithelial surfaces (Proesmans et al., 2008). The CFTR gene is expressed throughout the body; therefore, the consequences of mutations can be seen in every organ system, with the greatest effects seen in the respiratory tract, digestive tract, urogenital tract and sweat glands. This can clinically present as obstructed ducts, atrophic epithelia, gland hypertrophy and can ultimately lead to inflammation and fibrosis (Xue et al., 2016).

**1.1 | Epidemiology**

More than 52,000 people in Europe, including approximately 11,000 people in the United Kingdom, have CF (Orenti et al., 2022; Trust, 2022). In the United States, 1 in 2500 Caucasian children are born with CF (Farooq et al., 2020). Ireland has the highest per capita rate of people with cystic fibrosis (PWCF), and approximately 1 in 19 people (Sasaki et al., 2020) are carriers of a mutated gene.

The life expectancy of PWCF has markedly increased; Children born with CF in 1954 had a median life expectancy of 4–5 years, whereas in much of the Western world, the median survival age is now between 44 and 53 years (McBennett et al., 2022).

There is no cure for CF; however, there are a number of treatment modalities available to control symptoms, reduce complications and reduce the severity of different manifestations of CF. These can include physiotherapy, nutritional management, mucus thinners and long-term use of antibiotics, steroid inhalers and pancreatic enzyme replacement therapy (PERT) (CFF, 2020;

NHS, 2020). More recently, there has been CFTR-based therapy with the introduction of CFTR modulators, such as Kaftrio®/ Trikafta® (ivacaftor/tezacaftor/elexacaftor).<sup>1</sup> A combination of these therapies has led to steady improvements in the life expectancy and quality of life in people with CF (Clancy et al., 2019).

There is little research into the oral health of PWCF, as life expectancy was historically low. A recent systematic review into the periodontal and oral hygiene levels of PWCF was inconclusive and found the majority of studies focused exclusively on children with CF (Coffey et al., 2020). Additionally, most of these studies were carried out prior to the advent of CFTR modulators in 2012.

The role of periodontal bacteria in the pathogenesis of respiratory infections is a phenomenon that has been a focus of investigation, with studies linking periodontal pathogens (e.g. *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*) to respiratory infections such as pneumonia and lung abscesses (Gomes-Filho et al., 2014; Scannapieco & Ho, 2001; Scannapieco & Mylotte, 1996). A recent study has shown that subgingival microbial diversity is significantly associated with reduced respiratory function, measured by % predicted FEV<sub>1</sub> (Winning et al., 2023). Furthermore, *Pseudomonas aeruginosa*, a pathogenic bacteria that can cause chronic and significant infection in PWCF, has been recovered from subgingival plaque samples in PWCF, suggesting that the oral cavity is a potential reservoir of such organisms (Caldas et al., 2015). As pulmonary infections are the primary cause of morbidity and mortality in PWCF (Lipuma, 2010), it is important to diagnose and treat periodontal disease as early as possible in this cohort of patients.

The aim of this study was to assess periodontal health status and oral hygiene levels in a cohort of adults living in Ireland with CF and to compare the results with a control group from the general Irish population.

<sup>1</sup>Kaftrio/Trikafta are registered trademarks of Vertex Pharmaceuticals Incorporated, Boston, MA, USA.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design

A case-control study was carried out in accordance with the World Medical Association Declaration of Helsinki. Each participant received a patient information leaflet to ensure they understood the objectives of the study and written informed consent was obtained. Patients were seen during the COVID-19 pandemic, between September 2020 and October 2022. The study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting case-control studies (von Elm et al., 2008).

### 2.2 | Study population

The study participants were recruited from the Adult Cystic Fibrosis Unit ( $n = 180$ ) at Cork University Hospital. In order to recruit as many participants as possible, every patient who attended for medical review during the study period was invited to participate.

A population-based control group was recruited by advertisements in locations around Cork city and through social media channels. A phone call with a clinical dental nurse was carried out prior to enrolment in the study, to confirm that there was no known family history of CF and to explain the process of the study.

The inclusion criteria for the study group were as follows:

- Adults ( $\geq 18$  years) with a diagnosis of CF.
- Living in the Republic of Ireland.

The exclusion criteria for the study group were as follows:

- People below the age of 18 years.

The inclusion criteria for the control group were as follows:

- Adults ( $\geq 18$  years), with a similar age and gender profile to the case group.
- Living in the Republic of Ireland.

The exclusion criteria for the control group were as follows:

- People below the age of 18 years.
- People with a family history of CF.

The research questions were 'Are adults who have cystic fibrosis at higher risk of gingivitis and periodontitis than adults without cystic fibrosis?' 'Do adults with cystic fibrosis have greater levels of plaque and calculus than adults without cystic fibrosis?'

### 2.3 | Data collection

A 40-item questionnaire, which gathered medical and dental information, as well as information about diet and social background, was distributed to participants. The oral examination was carried out by two qualified dentists (N.C. and F.O.) who had previously been calibrated ( $\kappa = 0.94$ ) against a gold standard examiner using new patient volunteers attending for assessment at Cork University Dental School and Hospital.

#### 2.3.1 | Clinical parameters and indices

The periodontal condition was recorded using the CPI-modified index, as described in the WHO Oral Health Surveys (WHO, 2013). This consisted of the following measurements, which were taken using a WHO probe at six sites around each tooth present:

1. Full mouth bleeding score by assigning a binary score to each tooth (1 for bleeding present, 0 for absent).
2. Presence of periodontal pocket (0 = no pocket present; 1 = mild pocketing of 4–5 mm; 2 = severe pocketing of  $\geq 6$  mm).

Oral hygiene status was recorded using the Oral Hygiene Index of Greene–Vermillion (1960), in accordance with the WHO criteria for epidemiological studies. This involves splitting the mouth into sextants and examining each of them for:

1. Debris/soft plaque/staining.
2. Calculus.

Each sextant is given a score between 0 and 3, which are added together, and the total is divided by the number of sextants scored.

#### 2.3.2 | Diagnoses of gingivitis and periodontitis

The diagnosis of gingivitis in this study is based on the diagnosis defined by the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions, that is,  $\geq 10\%$  bleeding sites with probing depths  $\leq 3$  mm (Chapple et al., 2018).

Pocket scores were determined based on the CPI-modified index; accordingly, mild-moderate periodontitis was diagnosed in this study when probing depths were 4–5 mm and severe periodontitis was diagnosed when pocket depths  $\geq 6$  mm. As radiographic assessment was not carried out in this study, grading of periodontitis progression was not included.

#### 2.3.3 | Lung function measurements

Lung function was measured by the CF specialist nurses in the adult CF unit on the same day as the dental examination. The maximum forced expiratory volume in 1 second (FEV<sub>1</sub>) was measured in litres, and this was converted to percent predicted forced FEV<sub>1</sub> (ppFEV<sub>1</sub>)

using the Global Lung Function Initiative (Cooper et al., 2017). Lung disease is categorized according to an individual's  $ppFEV_1$ :  $ppFEV_1 < 40\%$  is severe,  $40\%–69\%$  is moderate and  $\geq 70\%$  is mild or normal (Cystic Fibrosis Registry of Ireland, 2023).

## 2.4 | Data analysis

Demographic and dental health characteristic data are summarized, and the CF and non-CF groups are compared using the chi-squared test for categorical variables and a Wilcoxon rank sum test for age. Periodontal disease status categories were compared between the groups using chi-squared tests. Where there were fewer than five subjects in a category, Fisher's exact test was used in place of a chi-squared test. The effect of age on periodontal condition was assessed by fitting a binomial regression model to the periodontal disease variable, including CF status and age in the model. Plaque score and calculus score are discrete numeric variables and are summarized as medians with interquartile range (IQR), and the CF and non-CF groups are compared using a Wilcoxon rank sum test. Further analysis was conducted on the CF group using chi-squared tests and negative binomial regression models to assess the impact of medication use (PERT, CFTR modulator therapy and antibiotic/azithromycin) and CF-related diabetes status on periodontal disease and oral hygiene indices. Confounding factors, such as smoking and diabetic status, were accounted for. All tests were performed at significance level  $\alpha = .05$ , and statistical analysis was implemented using R (version 4.2.0).

## 3 | RESULTS

### 3.1 | Characteristics of the study population

A total of 92 PWCF for the case group and 92 individuals for the control group were recruited (Table 1). The case group was comprised of 54 men and 38 women, with a median age of 31 years (IQR 25–35.75). The control group was comprised of 43 men and 49 women, with a median age of 27 years (IQR 23–33). Smoking levels were low in both groups (1.1% in the CF group, 7.6% in the non-CF group) and the two groups were similar in terms of alcohol consumption (76.1% alcohol drinkers in the CF group, 74.7% in the non-CF group). There was no significant difference between the groups for gender, education, smoking and alcohol levels. There was a significant difference in median age, with the non-CF group having a lower median age than the CF group; however, there was a large overlap between the two groups (Appendix 1).

#### 3.1.1 | Oral hygiene

The CF group brushed less frequently than the non-CF group, with 24.7% of the CF group brushing less than twice daily compared with only 7.6% of the control group. Interdental cleaning rates were

also lower in the CF group, with 51.7% 'never' using inter-dental cleaning aids, compared with 13% of the control group. More PWCF (20.2% vs. 2.2% controls) were unsure whether their toothpaste contained fluoride. There was no statistical difference between the regularity of dental attendance and the time since last dental visit. There was a significant difference between the groups, regarding the reasons for dental attendance, with the CF group attending less regularly for check-ups (56.2%, compared with 72.8% of the non-CF group), and the CF group attending more frequently for issues such as 'needing treatment' or pain.

#### 3.1.2 | Gingival bleeding and periodontitis

Gingival bleeding in  $\geq 10\%$  of sites was observed in 65.2% of the CF group, compared with 83.7% of the non-CF group, with a statistically significant  $p$ -value of .01, relative risk (RR) 0.92 (95% confidence interval [CI] 0.81–1.04).

Similarly, there were lower levels of moderate (15.2%) and severe (0%) periodontitis compared with the non-CF group (31.5% and 9.8% respectively); (moderate periodontitis RR 0.54 [95% CI 0.32–0.90]). These results are shown in Table 2.

#### 3.1.3 | Oral hygiene index

Assessment of the oral hygiene status showed that there was a significant difference in the plaque and calculus scores of the two groups, with plaque and calculus levels being significantly higher in the CF group (Table 3, Figure 1).

#### 3.1.4 | Systemic health factors

Chi-squared tests and negative binomial regression models were fitted to examine the effects of PERT, CFTR modulator use and antibiotic/azithromycin use, as well as diabetic status, and age group on all the above parameters, that is, plaque score, calculus score, gingival bleeding, mild periodontitis. (As there were no cases of severe periodontitis in the CF group, this was not examined.) A Kruskal–Wallis test was performed to investigate the presence of an association between  $ppFEV_1$  and periodontal parameters. When  $n < 5$  for any of the groups, Fisher's exact test was performed. There was no significant effect of PERT, CFTR modulator therapy, antibiotic or azithromycin use on the oral health outcomes (Table 4).

##### Diabetes

There were a total of 88 patients in the CF group whose diabetic status was known, 18 of whom had CF-related diabetes.

Gingival bleeding levels were higher in PWCF with diabetes, but mild periodontitis levels were lower in PWCF with diabetes; the latter link is statistically significant ( $p$ -value = .0216).

These results are shown in Table 4.

**TABLE 1** Characteristics of study participants.

Characteristics			CF group, n (%)	Non-CF group, n (%)	p-Value*
Demographics	Gender	Male	54 (58.7%)	43 (46.7%)	.238
		Female	38 (41.3%)	49 (53.3%)	
	Median age		31 (IQR 25–35.75)	27 (IQR 23–33)	<b>.043*</b>
Socioeconomics	Education	Primary	1 (1.2%)	2 (2.2%)	.889
		Did not complete second level	2 (2.2%)	2 (2.2%)	
		Second level	25 (29.1%)	23 (25%)	
		Third level	58 (67.4%)	65 (70.7%)	
Personal habits	Current smoker	Yes	1 (1.1%)	7 (7.6%)	.078
		No	88 (98.9%)	85 (92.4%)	
	Units of alcohol per week	None	24 (33.3%)	31 (34.4%)	.581
Less than 5		30 (41.7%)	44 (48.9%)		
5–10		15 (20.8%)	13 (14.4%)		
More than 10		3 (4.2%)	2 (2.2%)		
Oral hygiene habits	Interdental cleaning	Daily	8 (9.0%)	38 (41.3%)	<b>&lt;.001*</b>
		Occasionally	36 (39.3%)	42 (45.7%)	
		Never	48 (51.7%)	12 (13.0%)	
	Toothbrushing	Twice a day or more	67 (72.3%)	85 (92.4%)	<b>.003*</b>
		Once a day or less	22 (24.7%)	7 (7.6%)	
	Fluoride containing	Yes	73 (79.8%)	88 (95.7%)	<b>&lt;.05*</b>
		No	0 (0%)	2 (2.2%)	
		Don't know	19 (20.2%)	2 (2.2%)	
Mouthwash	Daily use	20 (21.6%)	19 (20.7%)	.936	
	Occasional use	37 (39.8%)	35 (38.0%)		
	Never	36 (38.6%)	38 (41.3%)		
Use of dental service	Has own general dentist	Yes	73 (79.8%)	69 (75%)	.555
		No	19 (20.2%)	23 (25%)	
	Reason for seeking dental services	Check-up at least once a year	44 (48.3%)	53 (57.6%)	<b>.029*</b>
Check-up at least twice a year		7 (7.9%)	14 (15.2%)		
'When I feel I need treatment'		14 (15.7%)	15 (16.3%)		
Pain/problem		16 (16.9%)	8 (8.7%)		
'I never go to the dentist'		10 (11.2%)	2 (2.2%)		
	Last dental attendance	Less than 1 year	44 (49.4%)	58 (63.0%)	.076
1–3 years ago		21 (23.6%)	21 (22.8%)		
3+ years		24 (27.0%)	13 (14.1%)		

Abbreviations: CF, cystic fibrosis; IQR, interquartile range.

\*Statistical significance with  $p$ -value  $<.05$  when measured using a chi-squared test (in bold).

#### Lung function and periodontal condition

Regression models found no statistical difference in the mean of  $ppFEV_1$  in the presence of mild periodontitis ( $p$ -value = .4461). Mean  $ppFEV_1$  is lower in people with mild periodontitis, 73.32% versus 77.64%, but is not statistically significant, [Appendix 2, Figure A1](#).

Similarly, although  $ppFEV_1$  was lower in people with higher levels of calculus, the difference was not found to be statistically significant ( $p$ -value .30), [Appendix 2, Figure A2](#).

There was no correlation between  $ppFEV_1$  and plaque levels ( $R^2 = .0166$ ), or gingivitis levels ( $R^2 = .0009$ ).

#### Age and periodontal condition

A binomial regression model was fitted and we found a significant interaction between CF status and age group in their effect on gingivitis;  $p$ -value = .044. The risk of having gingivitis increases with the patient's age for the non-CF control group. For the CF group, the risk increases up to the age of 29 years, with a decline in risk for the 30- to 34-year age category (Figure 2). The odds of having mild periodontitis were higher in the non-CF group, and this increased with age. The increase in mild periodontitis rates was consistent across the two CF status groups (Figure 3).

Periodontal status	CF group, n (%)	Non-CF group, n (%)	p-Value*
Healthy periodontium (PPD ≤ 3 mm)	78 (84.7%)	54 (58.6%)	<b>.003*</b>
Moderate periodontitis (PPD 4–5 mm)	14 (15.2%)	29 (31.5%)	<b>.015*</b>
Severe periodontitis (PPD ≥ 6 mm)	0 (0%)	9 (9.8%)	<b>.003*</b>

Abbreviation: PPD, periodontal probing depth.

\*Statistical significance with p-value <.05 (in bold).

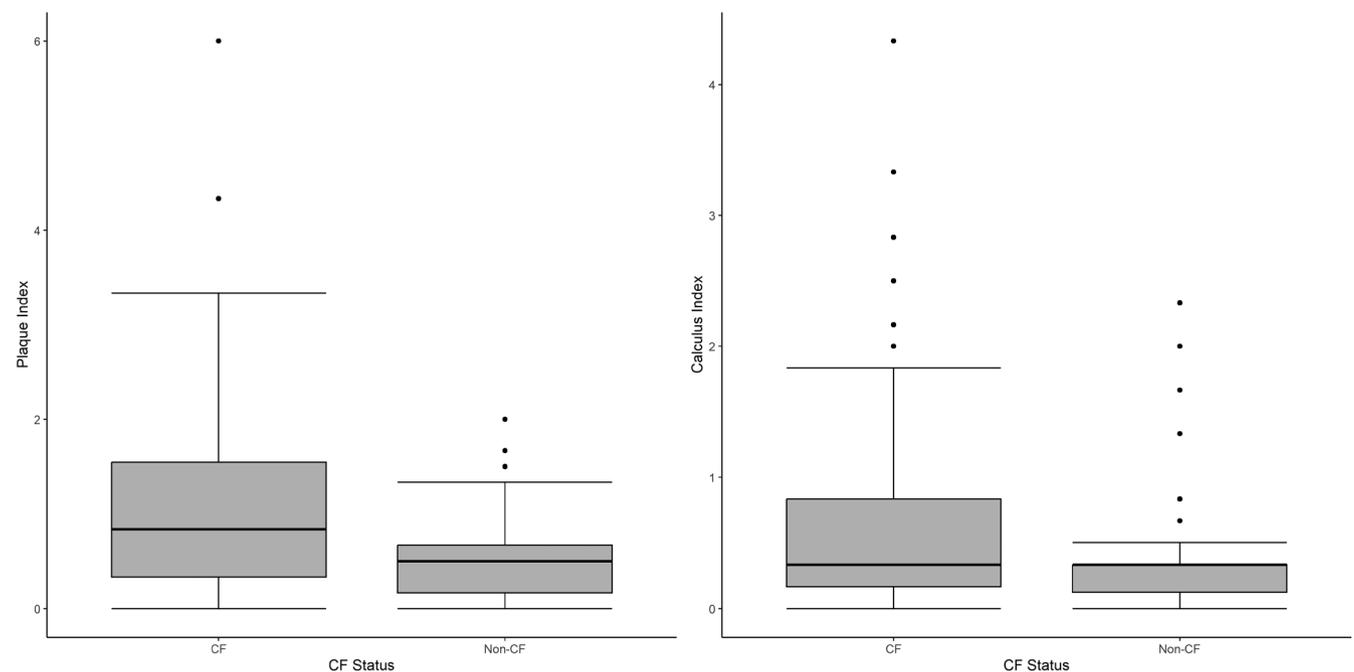
**TABLE 2** Periodontal disease levels in the cystic fibrosis (CF) versus non-CF group.

Parameter	CF group		Non-CF group		p-Value
	Median	IQR	Median	IQR	
Plaque score	0.83	0.333–1.542	0.5	0.167–0.667	<b>.002*</b>
Calculus score	0.33	0.17–0.83	0.33	0.125–0.33	<b>.012*</b>

Abbreviations: CF, cystic fibrosis; IQR, interquartile range.

\*Statistical significance with p-value <.05 (in bold).

**TABLE 3** Mean oral hygiene index of the two groups.



**FIGURE 1** Plaque and calculus indices of the two groups. CF, cystic fibrosis.

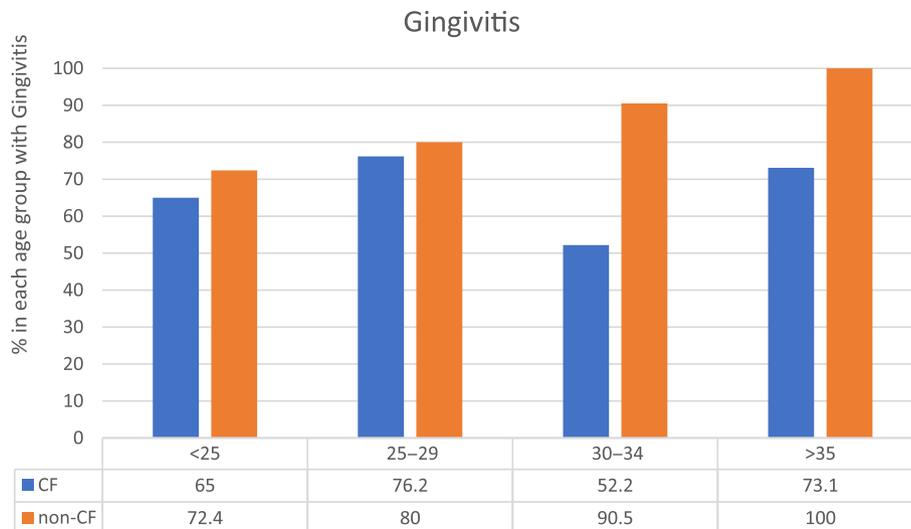
**TABLE 4** Analysis of the effect of medications and systemic health factors on gingivitis, periodontitis, plaque and calculus levels.

Variable	% gingivitis	% mild periodontitis	Plaque/debris score	Calculus score
On PERT (n = 65)	68% (n = 44)	18% (n = 12)	0.67 (IQR 0.33–1.67)	0.33 (IQR 0.17–0.83)
Not on PERT (n = 19)	78% (n = 15)	11% (n = 2)	0.67 (IQR 0.5–0.96)	0.33 (IQR 0.17–1.13)
CFTR (n = 62)	71% (n = 44)	14.5% (n = 9)	0.75 (IQR 0.17–1.67)	0.33 (IQR 0.17–0.83)
No CFTR (n = 21)	71% (n = 15)	23.8% (n = 5)	0.83 (IQR 0.67–1.5)	0.33 (IQR 0.33–1)
Antibiotic (n = 64)	68.8% (n = 44)	15.6% (n = 10)	0.67 (IQR 0.33–1.67)	0.33 (IQR 0.67–0.83)
No antibiotic (n = 18)	83.3% (n = 15)	23.5% (n = 4)	0.83 (IQR 0.67–1.67)	0.33 (IQR 0.33–1.33)
AZT (n = 55)	65.5% (n = 36)	12.7% (n = 7)	0.67 (IQR 0.67–1.58)*	0.33 (IQR 0–0.83)*
No AZT (n = 26)	85% (n = 22)	27% (n = 7)	0.83 (IQR 0.67–1.67)*	0.5 (IQR 0.33–1.13)*
Diabetic (n = 18)	77.8% (n = 14)	<b>0%* (n = 0)</b>	-	-
Not diabetic (n = 70)	64.3% (n = 45)	<b>20%* (n = 14)</b>	-	-

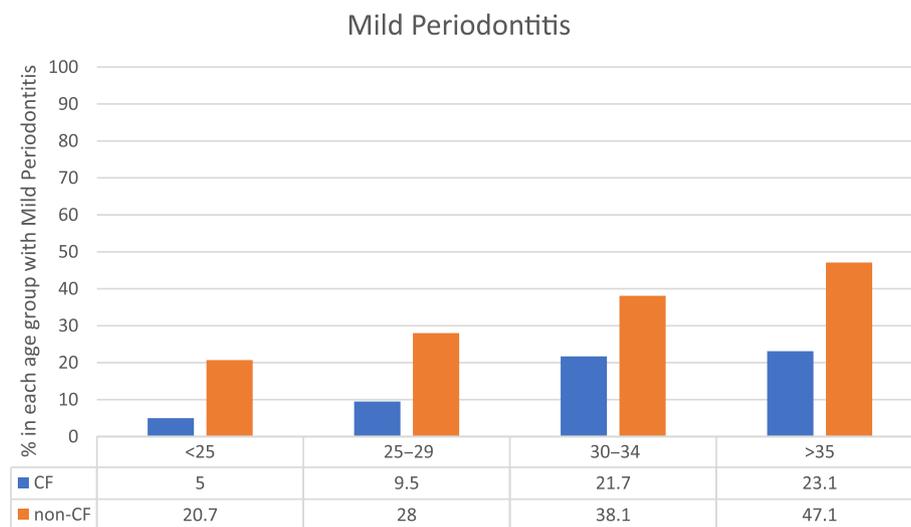
Abbreviations: AZT, azithromycin; CFTR, cystic fibrosis transmembrane conductance regulator; IQR, interquartile range; PERT, pancreatic enzyme replacement therapy.

\*Statistical significance where p-value <.05 when a binomial regression model was fitted (in bold).

**FIGURE 2** Prevalence of gingivitis by age group in the cystic fibrosis (CF) and non-CF groups.



**FIGURE 3** Prevalence of mild periodontitis by age group in the cystic fibrosis (CF) and non-CF groups.



## 4 | DISCUSSION

To date, this is the largest study globally assessing the periodontal health and oral hygiene habits of adults with CF. The strengths of this study are the large sample size of this group, given the rare nature of this condition; the use of standardized indices that makes the study reproducible in different populations; and the use of a non-CF control group.

Plaque levels were higher in the CF group in this study, in contrast to lower or similar levels of plaque seen in other studies (Blacharsh, 1977; Dabrowska et al., 2006; Peker et al., 2014). This study found higher levels of calculus in adults with CF; higher levels of calculus were also seen in the cohort of CF children examined by Kinirons (1989) and Blacharch (1977), and Narang et al. (2003) noted a non-statistically significant increase in calculus in PWCF. However, this pattern was not seen in other studies (Aps et al., 2002a, 2002b; Ferrazzano et al., 2009; Peker et al., 2014). Therefore, it would be interesting to investigate the presence of differences between the different study populations, for example, CF treatment modalities, CF genotypes, that may have led to these differing results.

This study found that, despite greater amounts of plaque and calculus, PWCF had lower levels of gingivitis and periodontitis when compared with a control group. This is similar to findings in a recent study (Pawlaczyk-Kamienska et al., 2019), which found that despite the widespread presence of bacterial dental deposits in 22 adult CF patients, none displayed clinical symptoms of periodontal disease. Similarly, Aps et al. (2002a) found that despite similar levels of dental plaque and calculus, the CF group (which included children) had significantly fewer gingival bleeding sites. This is an interesting finding as, generally speaking, plaque accumulation will increase the risk of development of periodontal diseases such as gingivitis (Löe et al., 1965). The main question raised by this study is: Why does this progression to clinical gingivitis or periodontitis not occur in PWCF?

One hypothesis is that people with CF have better oral hygiene than people without (Abu-Zahra et al., 2019; Narang et al., 2003). However, this has not been shown to be true in this cohort of patients. These authors hypothesize that the long-term use of broad-spectrum antibiotics, known to be taken by at least 70% of this cohort of CF patients, may decrease the bacterial load in the mouth,

thereby decreasing the potential for periodontal disease progression. Azithromycin, which is taken by at least 60% of this study group, has well-defined anti-inflammatory characteristics (Banjanac et al., 2012), which may help to reduce the levels of clinical gingivitis and periodontitis. However, there was no statistical difference in clinical parameters or oral hygiene indices between those who regularly take antibiotics and those who do not. Although the use of antibiotics does not fully explain the decrease in clinical signs of periodontal disease seen in PWCF, there does appear to be a clear tendency to reduced periodontal severity in these patients. Other factors, such as PERT and CFTR modulator use, as well as diabetic status, did not shed any further light on the lower levels of periodontal disease.

In the paper by Aps et al. (2002b), it was suggested that there may be 'as-yet unidentified intrinsic salivary mechanisms' conferring a protective effect onto the periodontium. It has been almost 20 years since the study by Aps, and the mechanism (if any) has not been identified. Therefore, it would be beneficial for further research to take plaque and salivary samples from PWCF in order to investigate the oral microbiome of this cohort.

It has been shown that PWCF may find it more difficult to carry out oral hygiene practices such as cleaning their teeth due to tiredness/lack of energy caused by the condition (Coffey et al., 2022). This is reflected in this group by their lower levels of toothbrushing and interdental cleaning, which has resulted in greater levels of plaque and calculus accumulation. However, as they do not exhibit signs of clinical disease normally seen, such as bleeding and pocketing, there is a risk that this group may become complacent regarding their oral health. Further evidence of this can be seen in the high proportion of PWCF in our study who only attend the dentist when they have pain/a problem. It should be stressed to PWCF that their gingiva and dental biofilm may harbour potentially pathogenic microorganisms, which may induce or exacerbate lung disease, even if they do not notice clinical symptoms such as bleeding, and therefore they should endeavour to reduce the bacterial load in the mouth through proper oral hygiene regimes. It was interesting to note that higher levels of calculus and the presence of mild periodontitis are associated with poorer lung function tests, although the difference was not statistically significant.

A limitation is that it was a single-centre study. It would be beneficial to carry out a multi-centre study in order to compare this group with CF patients who do not have the same treatment regimen, or who may have had poorer access to medical treatment. It would have been beneficial to carry out an a priori power calculation; however, this was not possible due to the lack of studies in this area. As this was a single-centre study of a rare disease, the aim was to be as close to a consensus as possible for this centre, and a coverage rate of 55.5% was achieved from this centre.

While this is a large study when compared with other CF studies, when sub-group analysis is carried out, the numbers are small and therefore it is difficult to draw many conclusions with confidence. Therefore, a larger multi-centre study would again be useful. The fact that there is a statistically significant age difference between the two groups is also a limitation; this was due to the fact that recruitment

was severely hampered by the COVID-19 pandemic. Despite this, there is a large overlap in the age groups, shown in Appendix 1. Another limitation is the use of the CPI-based approach in the clinical diagnosis of the participants. The authors recognize that characterizing the periodontal status based on the current classification for periodontal disease based on the 2017 World Workshop (Caton et al., 2018) would have been more appropriate; however, the dental assessment was not undertaken in a dental setting, and due to COVID-19 and time constraints, a more detailed periodontal charting was not possible. A further limitation is that PWCF were seen in the CF unit, and consequently it was not possible for examiners to be blinded.

This is an important study as it provides a comprehensive insight into the periodontal health and oral hygiene habits of PWCF. As mentioned previously, this is a group of medically vulnerable patients who are at higher risk of respiratory infections, which can sometimes be due to the aspiration of periodontal pathogens. Further research is needed to establish the composition of the oral microbiome in these patients, as it may be necessary for them to significantly improve their level of oral hygiene, especially if it is found that the increased levels of plaque identified contain disease-promoting pathobionts. This research could focus on the prevalence of pathobionts (e.g., *P. gingivalis* and *Treponema denticola*), whole-genome sequencing, and prevalence and levels of biomolecules, such as cytokines and matrix metalloproteinases. It would be important to focus not only on the presence or absence of inflammation-promoting bacteria but also on the level of dysbiosis in the oral environment, as both dysbiosis and inflammation are contributory factors in the pathogenesis of periodontitis in susceptible individuals (Lamont et al., 2018).

## 5 | CONCLUSION

In this study, PWCF had poor oral hygiene practices, with high levels of plaque and calculus. Despite this finding, adults with CF had lower levels of clinical gingivitis and periodontitis than seen in a non-CF control group. Further study is required to explore this phenomenon.

### AUTHOR CONTRIBUTIONS

**Niamh Coffey:** Data collection and curation; formal analysis; investigation; methodology; writing—original draft; writing—review and editing. **Fiona O'Leary:** Data collection and curation; investigation; methodology. **Francis Burke:** Writing—review and editing; supervision. **Laura Kirwan:** Statistical support. **Paul O'Regan:** Statistical support. **Barry Plant:** Conceptualization; writing—review and editing; supervision. **Anthony Roberts:** Writing—review and editing; supervision. **Martina Hayes:** Conceptualization; methodology; writing—review and editing; supervision; funding acquisition; project administration.

### ACKNOWLEDGEMENT

Open access funding provided by IReL.

**FUNDING INFORMATION**

This study received funding from Cystic Fibrosis Ireland, the Health Research Board (Ireland) and CISA funding from University College Cork.

**CONFLICT OF INTEREST STATEMENT**

The authors declare no conflicts of interest.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**ETHICS STATEMENT**

Ethical approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals (ECM 03/2022 PUB).

**ORCID**

Niamh Coffey  <https://orcid.org/0000-0001-9421-5392>

**REFERENCES**

- Abu-Zahra, R., Antos, N. J., Kump, T., & Angelopoulou, M. V. (2019). Oral health of cystic fibrosis patients at a north american center: A pilot study. *Medicina Oral, Patologia Oral y Cirugía Bucal*, 24(3), e379–e384. <https://doi.org/10.4317/medoral.22756>
- Aps, J. K., Van Maele, G. O., & Martens, L. C. (2002a). Oral hygiene habits and oral health in cystic fibrosis. *European Journal of Paediatric Dentistry*, 3(4), 181–187.
- Aps, J. K., Van Maele, G. O., & Martens, L. C. (2002b). Caries experience and oral cleanliness in cystic fibrosis homozygotes and heterozygotes. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*, 93(5), 560–563. <https://doi.org/10.1067/moe.2002.121280>
- Banjanac, M., Munić Kos, V., Nujčić, K., Vrančić, M., Belamarić, D., Crnković, S., Hlevnjak, M., & Eraković Haber, V. (2012). Anti-inflammatory mechanism of action of azithromycin in LPS-stimulated J774A.1 cells. *Pharmacological Research*, 66(4), 357–362. <https://doi.org/10.1016/j.phrs.2012.06.011>
- Blacharsh, C. (1977). Dental aspects of patients with cystic fibrosis: A preliminary clinical study. *Journal of the American Dental Association* (1939), 95(1), 106–110.
- Caldas, R. R., Le Gall, F., Revert, K., Rault, G., Virmaux, M., Gouriou, S., Héry-Arnaud, G., Barbier, G., & Boisramé, S. (2015). Pseudomonas aeruginosa and periodontal pathogens in the oral cavity and lungs of cystic fibrosis patients: A case-control study. *Journal of Clinical Microbiology*, 53(6), 1898–1907. <https://doi.org/10.1128/jcm.00368-15>
- Caton, J. G., Armitage, G., Berglundh, T., Chapple, I. L. C., Jepsen, S., Kornman, K. S., Mealey, B. L., Papapanou, P. N., Sanz, M., & Tonetti, M. S. (2018). A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification. *Journal of Clinical Periodontology*, 45-(Suppl. 20), S1–s8. <https://doi.org/10.1111/jcpe.12935>
- CFF. (2020). *CF: Treatment and therapies*. Cystic Fibrosis Foundation. Retrieved February 27, 2020, from <https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Medications/Antibiotics/>
- Chapple, I. L. C., Mealey, B. L., Van Dyke, T. E., Bartold, P. M., Dommisch, H., Eickholz, P., Geisinger, M. L., Genco, R. J., Glogauer, M., Goldstein, M., Griffin, T. J., Holmstrup, P., Johnson, G. K., Kapila, Y., Lang, N. P., Meyle, J., Murakami, S., Plemons, J., Romito, G. A., ... Yoshie, H. (2018). Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Periodontology*, 89(S1), S74–S84. <https://doi.org/10.1002/JPER.17-0719>
- Clancy, J. P., Cotton, C. U., Donaldson, S. H., Solomon, G. M., VanDevanter, D. R., Boyle, M. P., Gentsch, M., Nick, J. A., Illek, B., Wallenburg, J. C., Sorscher, E. J., Amaral, M. D., Beekman, J. M., Naren, A. P., Bridges, R. J., Thomas, P. J., Cutting, G., Rowe, S., Durmowicz, A. G., ... Tuggle, K. L. (2019). CFTR modulator therotyping: Current status, gaps and future directions. *Journal of Cystic Fibrosis*, 18(1), 22–34. <https://doi.org/10.1016/j.jcf.2018.05.004>
- Coffey, N., O'Leary, F., Burke, F., Plant, B., Roberts, A., & Hayes, M. (2022). Self-reported dental attendance, oral hygiene habits and dietary habits of adults with cystic fibrosis in the Republic of Ireland. *Special Care in Dentistry*, 43, 401–408. <https://doi.org/10.1111/scd.12773>
- Coffey, N., O'Leary, F., Burke, F., Roberts, A., & Hayes, M. (2020). Periodontal and oral health status of people with cystic fibrosis: A systematic review. *Journal of Dentistry*, 103, 103509. <https://doi.org/10.1016/j.jdent.2020.103509>
- Cooper, B. G., Stocks, J., Hall, G. L., Culver, B., Steenbruggen, I., Carter, K. W., Thompson, B. R., Graham, B. L., Miller, M. R., Ruppel, G., Henderson, J., Fragoso, C. A. V., & Stanojevic, S. (2017). The Global Lung Function Initiative (GLI) Network: Bringing the world's respiratory reference values together. *Breathe*, 13(3), e56–e64. <https://doi.org/10.1183/20734735.012717>
- Cystic Fibrosis Registry of Ireland. (2023). *2021 annual report*, CF Registry of Ireland. [https://pub.flowpaper.com/docs/https://cfri.ie/wp-content/uploads/2023/01/CFRI\\_2021\\_Annual\\_Report.pdf](https://pub.flowpaper.com/docs/https://cfri.ie/wp-content/uploads/2023/01/CFRI_2021_Annual_Report.pdf)
- Dabrowska, E., Błahuszczyńska, K., Minarowska, A., Kaczmarski, M., Niedźwiecka-Andrzejewicz, I., & Stokowska, W. (2006). Assessment of dental status and oral hygiene in the study population of cystic fibrosis patients in the Podlasie province. *Advances in Medical Sciences*, 51-(Suppl. 1), 100–103.
- Farooq, F., Mogayzel, P. J., Lanzkron, S., Haywood, C., & Strouse, J. J. (2020). Comparison of US federal and foundation funding of research for sickle cell disease and cystic fibrosis and factors associated with research productivity. *JAMA Network Open*, 3(3), e201737. <https://doi.org/10.1001/jamanetworkopen.2020.1737>
- Ferrazzano, G. F., Orlando, S., Sangianantoni, G., Cantile, T., & Ingenito, A. (2009). Dental and periodontal health status in children affected by cystic fibrosis in a southern Italian region. *European Journal of Paediatric Dentistry*, 10(2), 65–68.
- Gomes-Filho, I. S., Leitão de Oliveira, T. F., Seixas da Cruz, S., de Santana Passos-Soares, J., Trindade, S. C., Oliveira, M. T., Souza-Machado, A., Cruz, Á. A., Barreto, M. L., & Seymour, G. J. (2014). Influence of periodontitis in the development of nosocomial pneumonia: A case control study. *Journal of Periodontology*, 85(5), e82–e90. <https://doi.org/10.1902/jop.2013.130369>
- Kinirons, M. J. (1989). Dental health of patients suffering from cystic fibrosis in Northern Ireland. *Community Dental Health*, 6(2), 113–120.
- Lamont, R. J., Koo, H., & Hajishengallis, G. (2018). The oral microbiota: Dynamic communities and host interactions. *Nature Reviews Microbiology*, 16, 745–759. <https://doi.org/10.1038/s41579-018-0089-x>
- Lipuma, J. J. (2010). The changing microbial epidemiology in cystic fibrosis. *Clinical Microbiology Reviews*, 23(2), 299–323. <https://doi.org/10.1128/cmr.00068-09>
- Löe, H., Theilade, E., & Jensen, S. B. (1965). Experimental gingivitis in man. *The Journal of Periodontology*, 36(3), 177–187.
- McBennett, K. A., Davis, P. B., & Konstan, M. W. (2022). Increasing life expectancy in cystic fibrosis: Advances and challenges. *Pediatric Pulmonology*, 57 Suppl 1(Suppl. 1), S5–s12. <https://doi.org/10.1002/ppul.25733>
- Narang, A., Maguire, A., Nunn, J. H., & Bush, A. (2003). Oral health and related factors in cystic fibrosis and other chronic respiratory disorders. *Archives of Disease in Childhood*, 88(8), 702–707. <https://doi.org/10.1136/adc.88.8.702>

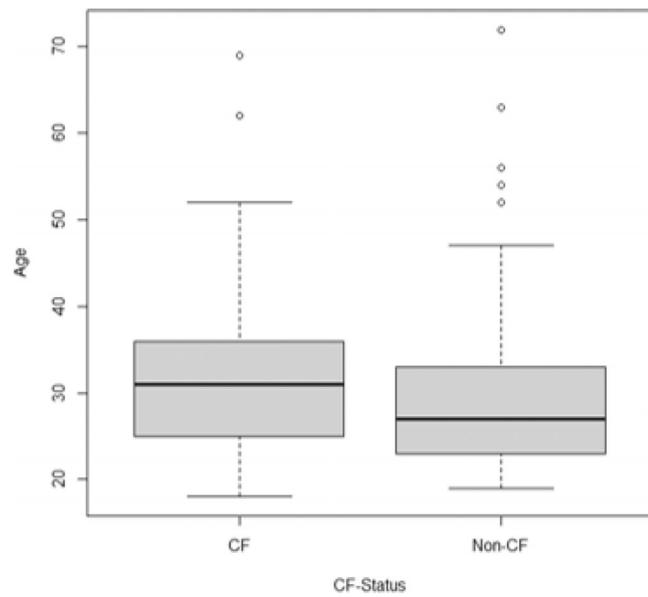
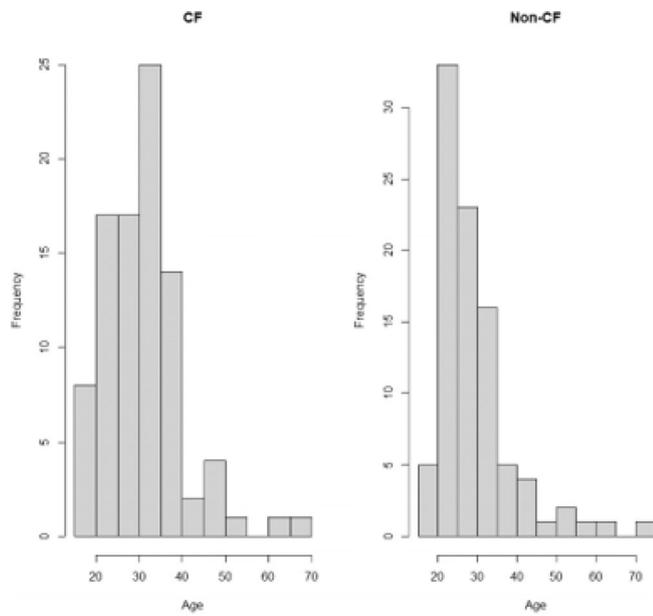
- NHS. (2020). *Treating cystic fibrosis*. Retrieved February 27, 2020, from <https://www.nhsinform.scot/illnesses-and-conditions/lungs-and-airways/cystic-fibrosis#treating-cystic-fibrosis>
- Orenti, A., Zolin, A., Jung, A., van Rens, J., Fox, A., Krasnyk, M., Daneau, G., Hatziagorou, E., Mei-Zahav, M., & Naehrlich, L. (2022). *European Cystic Fibrosis Society Patient Registry annual report 2020*.
- Pawlaczyk-Kamienska, T., Sniatala, R., Batura-Gabryel, H., Borysewicz-Lewicka, M., & Cofta, S. (2019). Periodontal status and subgingival biofilms in cystic fibrosis adults. *Polish Journal of Microbiology*, 68(3), 377–382. <https://doi.org/10.33073/pjm-2019-040>
- Peker, S., Mete, S., Gokdemir, Y., Karadag, B., & Kargul, B. (2014). Related factors of dental caries and molar incisor hypomineralisation in a group of children with cystic fibrosis. *European Archives of Paediatric Dentistry*, 15(4), 275–280. <https://doi.org/10.1007/s40368-014-0112-5>
- Proesmans, M., Vermeulen, F., & De Boeck, K. (2008). What's new in cystic fibrosis? From treating symptoms to correction of the basic defect. *European Journal of Pediatrics*, 167(8), 839–849. <https://doi.org/10.1007/s00431-008-0693-2>
- Sasaki, E., Kostocenko, M., Lang, N., Clark, T., Rogers, M., Muldowney, R., Walsh, O., O'Grady, L., Edge, G., Ward, A., Linnane, B., Borovickova, I., Barton, D. E., & Lynch, S. A. (2020). National Newborn Screening for cystic fibrosis in the Republic of Ireland: Genetic data from the first 6.5 years. *European Journal of Human Genetics*, 28(12), 1669–1674. <https://doi.org/10.1038/s41431-020-0661-5>
- Scannapieco, F. A., & Ho, A. W. (2001). Potential associations between chronic respiratory disease and periodontal disease: Analysis of National Health and Nutrition Examination Survey III. *Journal of Periodontology*, 72(1), 50–56. <https://doi.org/10.1902/jop.2001.72.1.50>
- Scannapieco, F. A., & Mylotte, J. M. (1996). Relationships between periodontal disease and bacterial pneumonia. *Journal of Periodontology*, 67(10S), 1114–1122. <https://doi.org/10.1902/jop.1996.67.10s.1114>
- Trust, C. F. (2022). *UK cystic fibrosis registry annual data report 2021*. <https://www.cysticfibrosis.org.uk/the-work-we-do/uk-cf-registry/reporting-and-resources>
- von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., & Vandenbroucke, J. P. (2008). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Journal of Clinical Epidemiology*, 61(4), 344–349. <https://doi.org/10.1016/j.jclinepi.2007.11.008>
- WHO. (2013). *Oral health surveys: Basic methods*. World Health Organization.
- Winning, L., Moran, G., McClory, M., El Karim, I., Lundy, F. T., Patterson, C. C., Linden, D., Cullen, K. M., Kee, F., & Linden, G. J. (2023). Subgingival microbial diversity and respiratory decline: A cross-sectional study. *Journal of Clinical Periodontology*, 50(7), 921–931. <https://doi.org/10.1111/jcpe.13819>
- Xue, R., Gu, H., Qiu, Y., Guo, Y., Korteweg, C., Huang, J., & Gu, J. (2016). Expression of cystic fibrosis transmembrane conductance regulator in ganglia of human gastrointestinal tract. *Scientific Reports*, 6, 30926. <https://doi.org/10.1038/srep30926>

**How to cite this article:** Coffey, N., O'Leary, F., Burke, F., Kirwan, L., O'Regan, P., Plant, B., Roberts, A., & Hayes, M. (2024). Periodontal disease prevalence and oral hygiene status of adults with cystic fibrosis: A case-control study. *Journal of Clinical Periodontology*, 51(5), 571–582. <https://doi.org/10.1111/jcpe.13944>

APPENDIX 1

AGE GROUPS

	Median age	Interquartile range	Min	Max	t Test p-value	Wilcoxon test p-value
CF yes N = 90	31	25–35.75	18	69	.2432	.04366
CF no N = 92	27	23–33	19	72		



APPENDIX 2

LUNG FUNCTION AND PERIODONTAL CONDITION

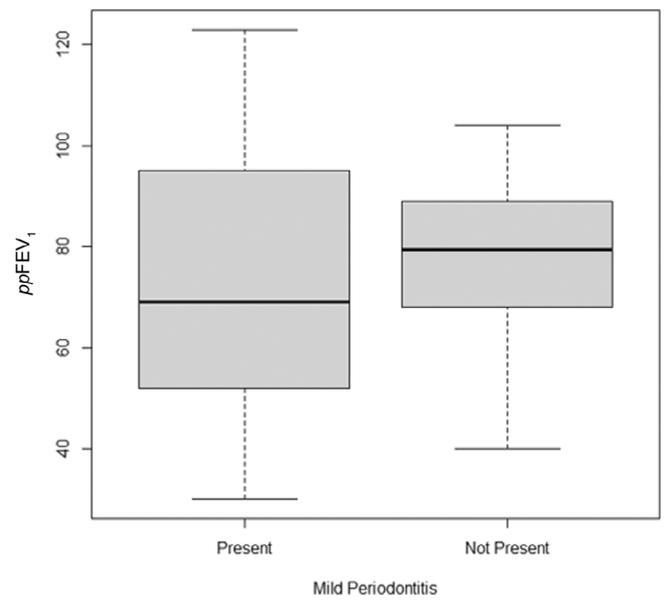
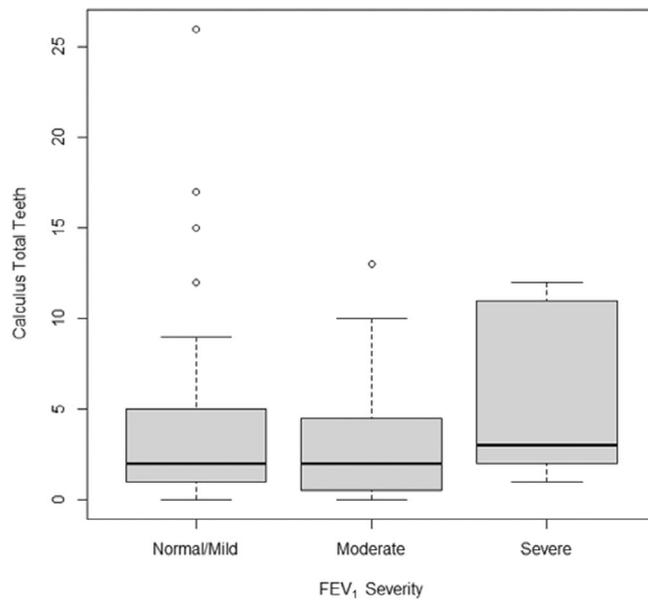


FIGURE A1 ppFEV<sub>1</sub> and mild periodontitis status.



**FIGURE A2**  $ppFEV_1$  categories and calculus levels.