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National Trends in Chronic Rhinosinusitis and Inpatient Sinus Surgery in Adults with Cystic Fibrosis

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Abstract

Objective. Given the recent dramatic changes in medical therapy for cystic fibrosis (CF), this study aims to describe temporal changes in chronic rhinosinusitis (CRS) and endoscopic sinus surgery (ESS) rates.

Methods. National Inpatient Sample (2004-2019; weighted estimates for 119,067 pediatric and 202,407 adult patients) was used to analyze adult (age ≥18 years) and pediatric patients with CF with pulmonary manifestations. Comorbid CRS, ESS rates, and extended length of stay (LOS, ≥75th percentile) were analyzed.

Results. The rate of CRS in both pediatric (14.1% vs 21.1%, $P < .001$) and adult (16.5% vs 40.9%, $P < .001$) patients increased. Rate of ESS in pediatric patients with CRS decreased from 25.3% to 3.4% ($P < .001$). A similar decline occurred in adults with CRS (12.3% vs 3.6%, $P < .001$). In multivariate analysis from 2015 to 2019, ESS and extended LOS were associated with admission in the Western United States ($P < .001$). CRS (OR 1.14, $P = .002$) and ESS (OR 1.78, $P = .002$) were independent predictors of extended LOS. Elective admission, primary insurance, race, and hospital teaching/location were significantly associated with ESS and extended LOS ($P < .05$).

Conclusion. Despite the increased prevalence of CRS in adults and pediatric patients with CF, rates of inpatient ESS have declined from 2004 to 2019. Patient and hospital factors affect undergoing ESS in 2015 to 2019. CRS and ESS are associated with extended LOS in recent years.

Keywords

chronic disease, chronic rhinosinusitis, endoscopic sinus surgery, mucocilliary clearance, paranasal sinus disease, quality of life

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Sinus disease in patients with cystic fibrosis (CF) is a source of significant morbidity and decreased quality of life. Thickened epithelial secretions lead to impaired mucociliary clearance, frequent infections, and persistent inflammation. Some studies suggest that nearly 100% of patients with CF (pwCF) have endoscopic evidence of chronic rhinosinusitis (CRS).[1] While saline rinses, topical steroids, dornase alfa, topical antibiotics, and, more recently, CFTR modulators have been shown to reduce hospitalizations due to pulmonary exacerbations, a recent review found that no randomized controlled trials have studied the efficacy of these medications for CF-related CRS.[2,3] Endoscopic sinus surgery (ESS) may be used in patients who have failed medical management, but the indications for ESS are unclear.[1] Care for pwCF is rapidly evolving, which may affect trends in CRS and ESS. A previous study using the Kids Inpatient Database found that rates of CRS have increased in pediatric pwCF over time, while rates of ESS have decreased.[4] This trend has not been described in the aging adult CF population.

CF therapies have changed drastically over the past couple decades, with improvements to infection control, nutritional supplementation, pancreatic enzyme replacement, and lung transplantation.[5] CFTR modulators, which help restore chloride transport, have been especially effective.[6] Survival in pwCF has significantly improved. While previously thought of as a pediatric disease, adults now make up over 50% of pwCF.[5] As more patients are living into adulthood, CF comorbidities are likely increasing.

Little is known about how the prevalence of CRS and ESS have changed with time in adult pwCF. Thus, the aim of this study is to report temporal trends in CRS and ESS in pwCF and characterize differences between patients who underwent ESS and those who did not.

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Methods

Data Collection and Study Population

A longitudinal analysis (2004-2019) was performed on the National Inpatient Sample Database (NIS) from the Agency for Healthcare Research and Quality, which represents the largest all-payer inpatient database in the United States.[7] The NIS currently has data available up to 2020; however, this year was excluded due to potential influence from the COVID-19 pandemic. This study was exempt from review by the Loma Linda University Health Institutional Review Board. International Classification of Disease, Ninth and Tenth Revisions (ICD-9/10) codes were used to extract medical records of adult (age ≥18 years) and pediatric (age <18 years) pwCF with pulmonary manifestations (Supplemental Table S1, available online). As pediatric rates of CRS and ESS have already been described, this group was included for comparison to adults.[4] CRS, other CF comorbidities, and ESS procedure codes were extracted. Admission quarter was dervied from the month of admission: 1st (January-March), 2nd (April-June), 3rd (July-September), and 4th (October-December). Unless otherwise specified, variables are predefined by the NIS which are fully described within their online documentation.[7]

Statistical Analysis

Data were analyzed using the IBM SPSS Complex Samples software, v27. Data reported reflect national estimates using discharge weights. Pearson chi-square was used to compare rates of CRS (%) in pediatric and adult patients by year, with 2004 used as the reference group, and between each other (adult versus pediatric). A similar analysis was performed for rates of ESS (%). As there were multiple comparisons, we opted to define a statistical significance level of $\alpha = 0.01$.

Predictors of undergoing ESS in adults with CF and CRS and having an extended length of stay (eLOS) in adults with CF from October 2015 to 2019, which corresponds to ICD-10 diagnostic and procedure codes, were evaluated using binary logistic regression. eLOS was defined as ≥75th percentile. Least-square difference post hoc testing was used.

Results

Incidence of CF with Pulmonary Manifestations

An estimated total of 119,067 pediatric patients and 202,407 adult patients with CF with pulmonary manifestations were admitted from 2004 to 2019 (**Figure 1**). Most primary admission diagnosis codes were related to pulmonary pathology (Supplemental Table S2, available online). The top 5 ICD-9 and ICD-10 codes constituted an unweighted 69.4% of the primary diagnosis codes. Nine out of 10 codes were related to pulmonary manifestations with CF or coded as pulmonary infections. There was more variation in the pediatric population from 2004 to 2010. During this period, the lowest and peak incidences were 92.3 in 2004 and 167.4 per 100,000 admissions in 2010, respectively. This declined in subsequent years to 121.07 per 100,000 admissions in 2019. In adults, incidence from 2004 to 2019 increased by 52%, from 30.8 to 46.8 per 100,000 admissions.

Rate of CRS

We next examined the rate of CRS by identifying patients with CRS addressed as a diagnosis within the admission.

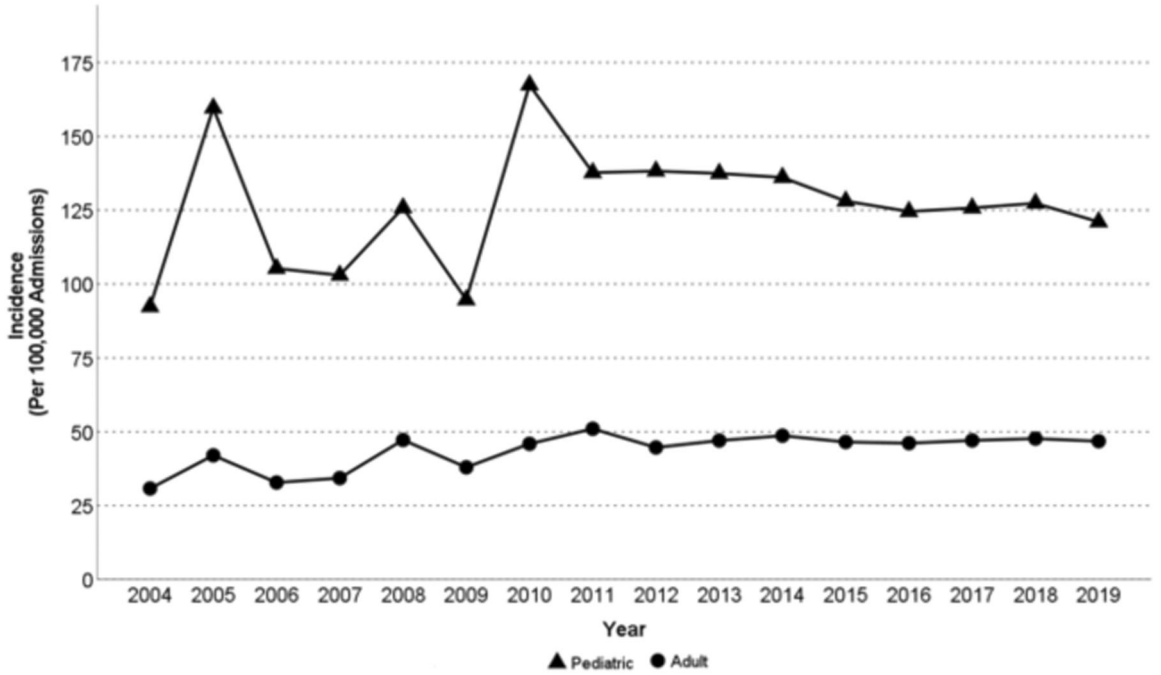

Figure 1. Incidence of cystic fibrosis with pulmonary manifestations in adult and pediatric patients; 2004 to 2019.

The rate of CRS in pediatric patients in 2004 was 14.1% which increased to 21.1% by 2019 (**Table 1**; $P < .001$). The increase in CRS appeared earlier in adults. By 2007, the rate of CRS increased from 16.5% to 22.8% ($P < .001$). The rate of CRS continued to increase to 40.9% in 2019 ($P < .001\%$). While the rates of CRS between pediatric and adult patients were similar around 2004, the adult rate saw a steeper increase and was nearly twice the pediatric rate by the late 2010s.

Rate of Sinus Surgery

While CRS rates increased over time, the ESS rates declined in both adult and pediatric patients (**Table 2**). While the initial rate of ESS in pediatric patients was twice that of adult patients, there was no longer a significant difference by the late 2010s (2019; 3.38 vs 3.63%, $P = .842$). Together, these data suggest that both adult and pediatric pwCF are more likely to have CRS but are less likely to undergo inpatient ESS.

Predictors of Sinus Surgery in Adults with CF and CRS

Next, we performed a binary logistic regression to determine demographic factors associated with inpatient sinus surgery in adults with CF and CRS (**Table 3**). Because the rate of inpatient sinus surgery had declined significantly over time, we only analyzed data from October 2015 to 2019, which corresponds to ICD-10 coding schema. The surgical and nonsurgical groups did not differ in age (30.2 vs 29.8 years, $P = .462$) and gender (61.1% vs 56.6% female, $P = .449$). The race distribution was significantly different between groups ($P < .001$), though the absolute differences were relatively small. Patient income was not different ($P = .439$). Other CF comorbidities did not differ either.

Nearly all admissions occurred at urban teaching hospitals. All surgical cases occurred at urban teaching hospitals, whereas all rural and urban nonteaching admissions were managed nonoperatively. This made hospital location and teaching status significantly different between groups ($P < .001$). Patients who underwent sinus surgery were significantly more likely to be admitted electively (49.5% vs 17.9%, OR 3.95, $P < .001$). Surgical patients were also more likely to have Medicare (29.5% vs 22.7%) and less likely to have Medicaid (22.1% vs 26.2%) or private insurance (43.2% vs 45.2%). Admission quarter, patient location, and hospital size were not different.

There was a significant difference in regional distribution of surgical versus nonsurgical admissions ($P < .001$). Most surgical cases occurred in the Western United States (56.8%) as opposed to the 25.7% of nonoperative cases in the West. Surgical admissions were less likely to be from the Northeast (6.3% vs 10.9%), Midwest (14.7% vs 27.8%), or South (22.1% vs 35.6%) when compared to non-surgical admissions. Most cases of adult CF with CRS originated from the Midwest (n = 5170) or the South (n = 6620). Fewer cases were from the West (n = 4970) and Northeast (n = 2030).

Predictors of Extended Length of Stay in Adults with CF

Multivariate binary logistic regression was also performed to identify predictors for eLOS (≥75th percentile, 14 days) in adult pwCF from October 2015 to 2019 (Table **4**). The

Table 1. Rate of CRS in Adult and Pediatric Patients with CF, 2004 to 2019

	Pediatric		Adult		
	Rate of CRS (%, 95% CI)	*P* value[a]	Rate of CRS (%, 95% CI)	*P* value[a]	*P* value[b]
2004	14.1 (12.2, 15.9)	ref	16.5 (14.8, 18.1)	ref	.057
2005	18.7 (17.1, 20.3)	<.001*	17.2 (15.8, 18.6)	.548	.159
2006	14.3 (12.4, 16.2)	.847	17.8 (16.2, 19.5)	.263	.006*
2007	20.6 (18.5, 22.7)	<.001*	22.8 (21.1, 24.6)	<.001*	.114
2008	14.9 (13.2, 16.7)	.514	19.9 (18.5, 21.3)	.002*	<.001*
2009	15.8 (13.7, 17.9)	.225	22.1 (20.5, 23.7)	<.001*	<.001*
2010	19.7 (18.0, 21.4)	<.001*	28.5 (26.9, 30.2)	<.001*	<.001*
2011	16.2 (14.4, 18.0)	.108	25.1 (23.6, 26.5)	<.001*	<.001*
2012	18.7 (16.6, 20.8)	.001*	27.5 (25.7, 29.3)	<.001*	<.001*
2013	19.2 (17.2, 21.1)	<.001*	31.6 (29.9, 33.4)	<.001*	<.001*
2014	20.8 (18.7, 22.8)	<.001*	29.3 (27.6, 30.9)	<.001*	<.001*
2015	22.3 (20.1, 24.5)	<.001*	33.1 (31.3, 34.8)	<.001*	<.001*
2016	23.4 (21.1, 25.6)	<.001*	37.0 (35.3, 38.8)	<.001*	<.001*
2017	23.0 (20.8, 25.3)	<.001*	39.0 (37.2, 40.8)	<.001*	<.001*
2018	21.4 (19.2, 23.6)	<.001*	42.7 (40.9, 44.5)	<.001*	<.001*
2019	21.1 (18.9, 23.4)	<.001*	40.9 (39.1, 42.7)	<.001*	<.001*

*$P < 0.01$; pediatric versus adult for each given year.
[a]Rate of CRS in pediatric or adults, versus 2004.
[b]Rate of CRS by year, pediatric versus adults.

Table 2. Rate of ESS in Adult and Pediatric Patients with CF and CRS, 2004 to 2019

	Pediatric		Adult		
	Rate of ESS (%, 95% CI)	*P* value[a]	Rate of ESS (%, 95% CI)	*P* value[a]	*P* value[b]
2004	25.3 (18.9, 31.6)	ref	12.3 (8.7, 15.9)	ref	.001*
2005	22.9 (18.9, 26.8)	.524	9.8 (7.1, 12.5)	.272	<.001*
2006	22.8 (16.7, 28.9)	.581	7.0 (4.4, 9.5)	.016	<.001*
2007	18.2 (13.6, 22.7)	.069	10.8 (8.0, 13.6)	.499	.006*
2008	13.2 (9.0, 17.5)	.002*	6.1 (4.2, 7.9)	.001*	.002*
2009	13.7 (8.7, 18.7)	.006*	9.1 (6.7, 11.5)	.137	.107
2010	15.7 (12.1, 19.3)	.007*	7.4 (5.6, 9.2)	.009*	<.001*
2011	14.8 (10.5, 19.1)	.006*	8.1 (6.2, 9.9)	.026	.005*
2012	13.2 (9.0, 17.5)	.002*	5.5 (3.7, 7.2)	<.001*	.001*
2013	13.5 (9.6, 17.4)	.001*	6.5 (4.9, 8.1)	.001*	.001*
2014	14.6 (10.7, 18.5)	.003*	6.0 (4.4, 7.6)	<.001*	<.001*
2015	8.2 (5.2, 11.2)	<.001*	3.9 (2.6, 5.1)	<.001*	.010
2016	3.5 (1.5, 5.5)	<.001*	1.6 (0.8, 2.3)	<.001*	.082
2017	3.2 (1.3, 5.2)	<.001*	1.5 (0.8, 2.2)	<.001*	.112
2018	4.9 (2.4, 7.4)	<.001*	2.8 (1.8, 3.7)	<.001*	.117
2019	3.4 (1.2, 5.6)	<.001*	3.6 (2.6, 4.7)	<.001*	.842

*$P < .01$; pediatric versus adult for each given year.
[a]Rate of sinus surgery in pediatric or adults, versus 2004.
[b]Rate of sinus surgery by year, pediatric versus adults.

average LOS for the normal LOS and extended LOS groups were 6.64 (95% CI, 6.57, 6.71) and 19.55 (95% CI, 19.13, 19.97), respectively. The average LOS overall was 10.25 (95% CI, 10.09, 10.41). Average age did not differ between the normal LOS and the eLOS groups (30.1 vs 29.9 years, $P = .050$). Patients with an eLOS were more likely to be admitted electively (17.2% vs 13.9%, OR 1.29, $P < 0.001$). They were also less likely to be female (49.7% vs 54.7%, OR 0.80, $P < .001$). Hispanic patients also had higher odds of eLOS compared to White patients (OR 1.25, 95% CI 1.07-1.45).

eLOS was also associated with comorbid CRS, hepatobiliary manifestations of CF, and undergoing sinus surgery. Patients with CRS (42.4% vs 37.9%, OR 1.14, $P = .002$) and hepatobiliary manifestations of CF (42.7% vs 35.2%, OR 1.26, $P < .001$) were more likely to have an eLOS. After controlling for these factors, undergoing sinus surgery still predicted an eLOS (1.6% vs 0.7%, OR 1.78, $P = .002$). No other CF comorbidities were associated with an eLOS.

Insurance status was significantly different between groups ($P < .001$). When compared to patients with Medicare, having Medicaid (OR 0.87, 95% CI 0.78-0.98), private insurance (OR 0.55, 95% CI 0.49-0.61), or other form of primary insurance (OR 0.65, 95% CI 0.52-0.82) had significantly lower odds of having an eLOS. There was no difference between Medicare and self-pay (OR 0.73, 95% CI 0.53-1.00) or no charge (OR 0.93, 95% CI 0.24-3.54). Patient income was not associated with eLOS ($P = .401$).

Hospital factors including bed size ($P < .001$), teaching status and location ($P < .001$), and region ($P < .001$) were also associated with eLOS. Small hospitals had higher odds of eLOS when compared to large hospitals (OR 1.40, 95% CI 1.18-1.66). Rural (OR 0.38, 95% CI 0.26-0.58) and urban nonteaching (OR 0.35, 95% CI 0.25-0.51) hospitals were at lower odds of eLOS when compared to urban teaching hospitals. When compared to hospitals in the West, those in the Northeast (OR 0.81, 95% CI 0.71-0.93), Midwest (OR 0.73, 95% CI 0.65-0.82), and South (OR 0.60, 95% CI 0.54-0.68) had lower odds of eLOS.

Discussion

This study examined a large cohort of adult and pediatric patients hospitalized for CF with pulmonary manifestations identified from 16 years of the NIS. Rates of pediatric hospitalization were more variable, possibly because pediatric patients are not reported as consistently within the NIS. However, there was a steady increase in adult hospitalizations over the study period, consistent with a prior study utilizing the NIS from 2003 to 2013 to examine overall CF hospitalizations (**Figure 1**).[8] Similarly, rates of CRS increased in both groups (**Table 1**). The increase observed in the pediatric population aligns with the results from a prior study conducted using the Kids Inpatient Database.[4] Rates of CRS from the most recent year analyzed in this study (2019) compared to rates from the CF Foundation 2022 Patient Registry Annual Report were slightly higher for children (21% vs 17%) and lower for adults (41% vs 51%).[9] The lower rates in adults may be explained by underreporting; previous studies show that even though up to 100% of patients may show evidence of CRS on imaging, only 20% of patients report symptoms.[1,10]

Table 3. Multivariate Binary Logistic Regression of ESS in Adult Patients with CF and CRS, 2015Q3 to 2019

	No ESS (n = 18,315)	ESS (n = 475)	Odds ratio (95% CI)	*P* value
Age (years)	29.7 (29.3, 30.0)	30.2 (28.0, 32.5)	0.99 (0.97, 1.01)	.462
Admission quarter				.869
1st	4470 (24.4%)	130 (27.4%)	ref	
2nd	4120 (22.5%)	110 (23.2%)	0.88 (0.48, 1.61)	
3rd	4400 (24.0%)	100 (21.1%)	0.80 (0.43, 1.49)	
4th	5320 (29.1%)	135 (28.4%)	0.80 (0.45, 1.43)	
Elective admission	3275 (17.9%)	230 (49.5%)	3.95 (2.60, 6.00)	<.001*
Sex				.449
Male	7950 (43.4%)	185 (38.9%)	ref	
Female	10,360 (56.6%)	290 (61.1%)	1.18 (0.77, 1.83)	
Primary payer				<.001*
Medicare	4155 (22.7%)	140 (29.5%)	ref	
Medicaid	4800 (26.2%)	150 (22.1%)	0.56 (0.30, 1.07)	
Private Insurance	8280 (45.2%)	205 (43.2%)	0.64 (0.37, 1.10)	
Self-pay	350 (1.9%)	15 (3.2%)	1.36 (0.38, 4.91)	
No charge	15 (0.1%)	---[a]	---[b]	
Other	705 (3.9%)	---[a]	0.24 (0.05, 1.04)	
Patient location				.418
Large metropolitan areas with at least 1 million residents	9535 (52.1%)	220 (46.3%)	ref	
Small metropolitan areas with less than 1 million residents	5680 (31.1%)	185 (38.9%)	1.45 (0.86, 2.45)	
Micropolitan counties	1655 (9.1%)	50 (10.5%)	1.40 (0.63, 3.12)	
Not metropolitan or micropolitan counties	1415 (7.7%)	20 (4.2%)	0.79 (0.27, 2.38)	
Race				<.001*
White	15,540 (87.5%)	400 (86%)	ref	
Black	600 (3.4%)	10 (2.2%)[a]	0.87 (0.20, 3.83)	
Hispanic	1180 (6.6%)	45 (9.7%)	1.47 (0.64, 3.39)	
Asian or Pacific Islander	65 (0.4%)	---[a]	---[b]	
Native American	85 (0.5%)	---[a]	---[b]	
Other	285 (1.6%)	---[a]	1.47 (0.34, 6.31)	
Income quartile				.439
1st	3895 (21.5%)	70 (14.7%)	ref	
2nd	4350 (24.0%)	135 (28.4%)	1.68 (0.85, 3.29)	
3rd	5190 (28.7%)	150 (31.6%)	1.36 (0.70, 2.66)	
4th	4660 (25.8%)	120 (25.3%)	1.14 (0.52, 2.53)	
Hospital bed size				.882
Small	510 (2.8%)	--- [a]	0.61 (0.09, 4.30)	
Medium	1935 (10.6%)	35 (7.4%)	1.01 (0.43, 2.37)	
Large	15,870 (86.7%)	435 (91.6%)	ref	
Hospital teaching/location				<.001*
Rural	45 (0.2%)	---[a]	---[b]	
Urban nonteaching	85 (0.5%)	---[a]	---[b]	
Urban teaching	18,185 (99.3%)	475 (100%)	ref	
Hospital region				<.001*
Northeast	2000 (10.9%)	30 (6.3%)	0.28 (0.11, 0.72)	
Midwest	5100 (27.8%)	70 (14.7%)	0.24 (0.12, 0.46)	
South	6515 (35.6%)	105 (22.1%)	0.32 (0.19, 0.54)	
West	4700 (25.7%)	270 (56.8%)	ref	
CF Gastrointestinal	4005 (21.9%)	120 (25.3%)	1.38 (0.82, 2.30)	.221
CF Unspecified	310 (1.7%)	---[a]	0.80 (0.10, 6.10)	.825
CF Hepatobiliary	8610 (47%)	285 (60%)	1.29 (0.81, 2.05)	.288
Lung Transplant	310 (1.7%)	---[a]	---[b]	.799

Counts may not add to the total column count due to missing data for each individual variable. Estimated national counts (%) or mean (95% CI) are reported.
[a]Counts less than 10 are not published in accordance with the National Inpatient Sample publication requirements.
[b]Odds ratio not provided as one of the counts was zero.
*$P < .05$.

Table 4. Multivariate Binary Logistic Regression of Extended Length of Stay (≥75th Percentile) in Adult Patients with CF, 2015Q4 to 2019

	Normal LOS (n = 47,530)	Extended LOS (n = 18,475)	Odds ratio (95% CI)	*P* value
Length of Stay (days)	6.64 (6.57, 6.71)	19.55 (19.13, 19.97)		
Age (years)	30.1 (29.9, 30.4)	29.9 (29.5, 30.3)	1.00 (0.99, 1.00)	.050
Admission quarter				.696
1st	12,420 (26.1%)	4750 (25.7%)	ref	
2nd	10,550 (22.2%)	4115 (22.3%)	1.02 (0.91, 1.15)	
3rd	10,735 (22.6%)	4370 (23.7%)	1.07 (0.95, 1.20)	
4th	13,890 (29.2%)	5230 (28.3%)	1.01 (0.91, 1.13)	
Elective admission	6620 (13.9%)	3180 (17.2%)	1.29 (1.15, 1.44)	<.001*
Sex				<.001*
Male	21,555 (45.3%)	9290 (50.3%)	ref	
Female	26,040 (54.7%)	9180 (49.7%)	0.80 (0.73, 0.86)	
Primary payer				<.001*
Medicare	10,930 (23.0%)	5315 (28.8%)	ref	
Medicaid	12,715 (26.7%)	5910 (32.0%)	0.87 (0.78, 0.98)	
Private Insurance	21,435 (45.1%)	6275 (34.0%)	0.55 (0.49, 0.61)	
Self-pay	810 (1.7%)	280 (1.5%)	0.73 (0.53, 1.00)	
No charge	30 (0.1%)	15 (0.1%)	0.93 (0.24, 3.54)	
Other	1660 (3.5%)	665 (3.6%)	0.65 (0.52, 0.82)	
Patient location				.035
Large metropolitan areas with at least 1 million residents	23,690 (49.9%)	8675 (47.1%)	ref	
Small metropolitan areas with less than 1 million residents	15,430 (32.5%)	6295 (34.2%)	1.092 (0.99, 1.20)	
Micropolitan counties	4675 (9.8%)	2025 (11.0%)	1.22 (1.05, 1.42)	
Not metropolitan or micropolitan counties	3680 (7.8%)	1420 (7.7%)	1.01 (0.85, 1.19)	
Race				.027
White	39,380 (86.1%)	14,805 (83.9%)	ref	
Black	2010 (4.4%)	850 (4.8%)	1.12 (0.93, 1.37)	
Hispanic	3055 (6.7%)	1545 (8.8%)	1.25 (1.07, 1.45)	
Asian or Pacific Islander	240 (0.5%)	85 (0.5%)	0.96 (0.54, 1.72)	
Native American	175 (0.4%)	90 (0.5%)	1.36 (0.74, 2.51)	
Other	900 (2.0%)	275 (1.6%)	0.77 (0.56, 1.07)	
Income quartile				.401
1st	10,895 (23.2%)	4395 (24.2%)	ref	
2nd	12,340 (26.2%)	4935 (27.1%)	0.99 (0.89, 1.11)	
3rd	12,575 (26.7%)	5055 (27.8%)	1.01 (0.90, 1.14)	
4th	11,215 (23.8%)	3810 (20.9%)	0.93 (0.80, 1.05)	
Hospital bed size				<.001*
Small	2985 (6.3%)	1245 (6.7%)	1.40 (1.18, 1.66)	
Medium	2470 (13.4%)	2470 (13.4%)	1.13 (1.00, 1.27)	
Large	38,250 (80.3%)	14,760 (79.9%)	ref	
Hospital teaching/location				<.001*
Rural	935 (2.0%)	160 (0.9%)	0.38 (0.26, 0.58)	
Urban nonteaching	1385 (2.9%)	225 (1.2%)	0.35 (0.25, 0.51)	
Urban teaching	45,285 (95.1%)	18,090 (97.9%)	ref	
Hospital region				<.001*
Northeast	8055 (16.9%)	3030 (16.4%)	0.81 (0.71, 0.93)	
Midwest	12,675 (26.6%)	4770 (25.8%)	0.73 (0.65, 0.82)	
South	17,825 (37.4%)	5720 (31.0%)	0.60 (0.54, 0.68)	
West	9050 (19.0%)	4955 (26.8%)	ref	
CRS	18,035 (37.9%)	7825 (42.4%)	1.14 (1.05, 1.25)	.002*

(*continued*)

Table 4. (continued)

	Normal LOS (n = 47,530)	Extended LOS (n = 18,475)	Odds ratio (95% CI)	*P* value
ESS	330 (0.7%)	300 (1.6%)	1.78 (1.23, 2.59)	.002*
CF Gastrointestinal	8140 (17.1%)	3560 (19.3%)	1.09 (0.98, 1.21)	.101
CF Unspecified	1050 (2.2%)	355 (1.9%)	0.90 (0.68, 1.20)	.479
CF Hepatobiliary	16,770 (35.2%)	7880 (42.7%)	1.26 (1.16, 1.37)	<.001*
Lung Transplant	1005 (2.1%)	380 (2.1%)	1.01 (0.77, 1.34)	.921

Counts may not add to the total column count due to missing data for each individual variable. Estimated national counts (%) or mean (95% CI) are reported.
*$P < .05$.

Within this study, CRS may also be underreported as it may not been a diagnosis directly addressed during the admission. Alternatively, improved CF treatments may lead to a healthier adult CF, decreasing hospital admissions for treatment. Thus, the rates found in this study may be lower since only inpatient CRS was analyzed. While rates of CRS were initially similar between pediatric and adult patients, adults had significantly higher rates every year from 2008 to 2019. This is consistent with the 2022 Patient Registry data, which shows that rates of sinus disease increase with age.[9]

Several factors may have contributed to the increased rates of CRS. Wang et al suggest that there is heightened awareness of CRS, because the paranasal sinuses have been recognized as bacterial reservoirs that can cause pulmonary exacerbations.[4,11] Quality of life measures are also used more frequently in pwCF, which may increase detection of CRS.[4] Furthermore, treatment modalities for CF have improved significantly over the past 2 decades, and the median projected life span in pwCF has increased from 32.7 to 43.6 years for those born between 2002 to 2007 and 2012 to 2017 respectively.[9] This increase in life expectancy means that more patients are likely to develop complications that typically affect older adults. Similar to the increased CRS rates seen in this study, CF-related liver disease also increased in incidence in a previous study analyzing the NIS and Kids databases from 2002 to 2017.[12]

Rates of ESS decreased in both children and adults despite increased CRS rates. While pediatric patients underwent significantly more ESS than adults at the start of the study period, no difference was seen between the groups in more recent years (**Table 2**). Although ESS is considered safe and effective for both children and adults with CF CRS, no clear indications exist for its use.[1] Previous studies have identified predictive factors for undergoing ESS as having severe CFTR mutations, previous ESS, high Lund Mackay CT score, high SNOT-22 (>39), nasal polyposis, and lower forced expiratory volume in 1 second (FEV1) (<68.7%) at presentation.[13,14] ESS has also been shown to decrease graft infection after lung transplant by decreasing the paranasal sinus bacterial burden.[11] A consensus statement from the CF Foundation and a recent evidence-based review suggest that ESS is best suited for patients who have not been adequately treated with medical therapy.[10,15] With the introduction of CFTR modulators, patients may be less likely to fail medical therapy, thus reducing the need for inpatient surgery.

Over the last decade, the percentage of individuals treated with CFTR modulators has increased by over 80%.[9] Several studies have shown that patients treated with CFTR modulators, especially Elexacftor/Tezacftor/Ivacaftor (ETI) therapy, have better measures of sinus health, such as improved CT/MRI and endoscopy findings, reduced bacterial colonization, and improved sinus quality of life measures.[16–23] Recent studies have shown decreased ESS in patients treated with ETI therapy.[24,25] An evidence-based review recommends that surgery should not be performed soon after the initiation of CFTR modulators, as the medications alone may lead to complete resolution of symptoms. Randomized controlled trials are still needed to confirm the efficacy of CFTR modulators for CF-related CRS and research is still needed on the role of surgery in patients treated with CFTR modulators.[3,10] While the dataset used in this study does not allow for direct measurements of CFTR modulator use, the greatest decreases in rates of ESS were seen around 2012 to 2014, which corresponds to when CFTR modulators were introduced (**Table 2**). A similar trend was found in another study, where rates of lung transplants decreased immediately after the introduction of ETI therapy in France.[26]

One limitation of this study is that it only examines inpatient ESS. It is possible that patients may still be undergoing ESS as outpatients. While rates of hospitalizations for CF have been increasing, mortality has been decreasing.[8] Improved medical therapy may mean patients present to the hospital with less severe disease and can be stabilized and discharged for outpatient treatment. A prior study found no difference in outcomes when ESS was performed early compared to when it was delayed, further supporting that ESS can be performed outpatient.[14] To our knowledge, no large-scale, aggregate data exists for outpatient ESS rates in pwCF, though this would be key for future research.

This study also identified several factors that were predictive of undergoing sinus surgery or having an eLOS

(**Tables 3** and **4**). Hispanic patients had significantly higher odds of having an eLOS compared to Caucasian patients. Hispanic pwCF are at increased risk of early-age *Pseudomonas* colonization when compared to white patients, which is one of the most common pathogens isolated in adult CF CRS.[17,27] Thus, Hispanic patients may present with more severe CRS, requiring an eLOS. Furthermore, patients from minority groups are less likely to be eligible for CFTR modulators based on their CFTR mutations, which may also contribute to racial differences in CRS management.[28]

Regarding insurance status, the proportion of Medicare patients was higher in the surgery group while both Medicare and Medicaid patients were more common in the eLOS group. Studies have shown that pwCF with public insurance have worse pulmonary function tests compared to patients with private insurance.[29,30] Thus, the higher rates of surgery and eLOS for patients with public insurance observed in this study may have been caused by increased disease severity.

There was variability in which comorbidities were predictive of an eLOS: CF-related sinus and hepatobiliary disease were associated with an eLOS, while CF-related gastrointestinal and unspecified disease were not. The unified airway model suggests that disease can spread from the sinuses, worsening pulmonary manifestations of CF.[31] The increased LOS of patients with CRS seen in this study is likely because they had more severe pulmonary exacerbations. Hepatobiliary disease is also a more severe complication of CF, likely explaining why these patients also had an eLOS.[9]

Finally, hospital setting also affected surgery rates and LOS. Surgery and eLOS were more common in urban teaching hospitals and in the West. This may reflect differences in practice preference regionally and by institution. All surgeries occurred at urban teaching institutions, possibly because these institutions had adequate resources for surgical management. A previous study also identified numerous differences in CF disease characteristics between regions. While rates of CRS were not examined, rates of *Pseudomonas* colonization were lower in the West than in the Midwest and South, contrasting the results seen in this study. On the other hand, rates of fungal colonization were higher in the West. Several other demographic and disease factors also varied between regions, which may be responsible for the different practice patterns seen in the West.[32] Studies examining geographic variation specifically of CF-related CRS are needed.

Using the NIS for this study allowed for examination of a large cohort of pwCF CRS. However, several limitations exist within this dataset. The study period examined does not go beyond 2019; ETI therapy, which has proven to be the most successful CFTR modulator treatment, was not approved by the FDA until 2019. Thus, the impact of this medication is not reflected in our results. However, given the precipitous decline in ESS rates observed in this study, the higher efficacy of ETI would likely further make inpatient surgical management less necessary, causing this trend to continue. Only inpatient management of CRS was assessed, which may not be representative of CRS trends overall, but does likely represent changes in the most severe CRS cases. The dataset also does not contain variables on the practice protocols at each institution, which may explain some of the variation seen. Single-institution studies may better capture these granular details but would lack benefits afforded by the large sample size of our study. Future studies should also examine the direct impact of CFTR modulators on CRS and ESS rates. To our knowledge, no national databases currently include data on CFTR modulator use, so large, multi-institutional studies may needed to do this.[10]

Conclusion

Over the past 16 years, rates of CRS have increased in both pediatric and adult pwCF. Conversely, rates of ESS have decreased. These trends may reflect increased awareness of CRS in pwCF. Additionally, the recent improvements in the treatment of CF—namely the introduction of CFTR modulators—have increased life expectancy and improved medical management of sinus disease. Further studies are needed to identify the appropriate indications for ESS, especially within the context of CFTR modulator use.

Author Contributions

Roy W. Qu, study design, data acquisition, statistical analysis, data interpretation, and manuscript preparation; **Nihal Punjabi**, data interpretation and manuscript preparation; **Wilson P. Lao**, data interpretation and manuscript preparation; **Kristin A. Seiberling**, data interpretation and manuscript preparation; **Christopher A. Church**, study design, data interpretation, and manuscript preparation; all authors approve the manuscript and agree to be accountable for all aspects of the work presented herein.

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Supplemental Material

Additional supporting information is available in the online version of the article.

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