Table 1 (abstract 46):
Lipid profile measurements (means) before and after patients were started on highly effective modulator therapy and mean difference. Results of paired t-tests are displayed.

Table 1. Measurements before and after modulator initiation				
	Pre-HEMT[e], mean	**Post-HEMT**, mean	**Difference**, mean (95%CI[f])	**p value**
TC[a] (mg/dL) n = 41	153.1	169.9	16.8 (5.55, 30.0)	0.0043
HDL[b] (mg/dL) n = 39	54	53.2	-0.821(-6.24, 4.61)	0.76
LDL[c] (mg/dL) n = 36	73.4	91.2	17.9 (9.27, 26.5)	0.0002
TC/HDL n = 40	3.07	3.47	0.395 (0.0728, 0.716)	0.016
BMI[d] (kg/m^2) n = 41	25.1	26.1	1.00 (0.460, 1.54)	0.00062

a. TC = total cholesterol, b. HDL = high density lipoprotein, c. LDL = low density lipoprotein d. BMI = body mass index, e. HEMT = highly effective modulator therapy, f. CI = confidence interval

Conclusions: Our results are limited by their retrospective nature, variable time between lipid assessments and exposure to HEMT, but in this small sample, the increases in TC, TC/HDL ratio, and LDL may be clinically meaningful because higher values were associated with greater CVD risk. HDL, a cardioprotective lipid, did not change. If confirmed in larger, more tightly controlled studies, this could mean that long-term exposure to HEMT increases CVD risk. This knowledge may influence health screening practices. When combined with other CVD risk factors, lipid-lowering therapy may be considered for some PwCF on HEMT.

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Longitudinal assessment of health-related quality of life and clinical outcomes in children and adolescents with cystic fibrosis in Australia

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Background: The Australian Cystic Fibrosis Data Registry (ACFDR) collects data from more than 3,500 people with cystic fibrosis (CF). The registry does not capture health-related quality of life (HRQOL) measures. HRQOL is an important outcome, influencing decisions regarding the efficacy and value of health interventions in clinical settings. The aim of this study was to assess and compare child-reported HRQOL and evaluate relationship with clinical outcomes by analyzing 10 years of patient-reported outcome measures collected at one ACFDR contributing center.

Methods: Children and adolescents aged 6 to 18 described their HRQOL using the Cystic Fibrosis Questionnaire-Revised (CFQ-R) between 2010 and 2020. Eight HRQOL domains were assessed: respiratory, physical, emotional, body, digestive, treatment burden, emotion, social. Demographic and diagnostic data, as well as information on body mass index (BMI) and forced expiratory volume in 1 second (FEV_1), of study participants were extracted from the ACFDR. Descriptive analysis was used to describe the study population. Spearman rank correlation was calculated for CFQ-R domains, BMI, and FEV_1. $P < 0.05$ was considered to be significant.

Results: Forty-seven children and adolescents completed at least one CFQ-R between 2010 and 2020: 23 (48.9%) female; 40 (85%) aged 6 to 13, and 22 (46.8%) F508del homozygous. A Spearman rho correlation test demonstrated a strong relationship between FEV_1 and CFQ-R body domain ($r = 0.328$, $p = 0.004$) in girls. A significant negative relationship between FEV_1 and CFQ-R treatment body domain ($r = -0.262$, $p = 0.005$) was observed in boys. A strong positive relationship was also observed between BMI and CFQ-R physical domain ($r = 0.243$, $p = 0.009$ in boys only) and the CFQ-R eating domain ($r = 0.372$, $p < 0.001$ in boys; $r = 0.342$, $p = 0.003$ in girls). Additional analyses and associations between HRQOL scores stratified according to age group and sex will be presented at the conference.

Conclusions: The initial findings of our study are consistent with those in the literature, suggesting that the CFQ-R is a meaningful clinical endpoint to evaluate clinical interventions in children. By incorporating the CFQ-R into the ACFDR, this study will provide a patient perspective for clinicians and policy makers, enhancing the treatment and management of children and adolescents with CF.

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Longitudinal outcomes of adults and children with cystic fibrosis during the COVID-19 pandemic

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Background: The onset of the COVID-19 pandemic was associated with restricted community movement, including limited access to health care facilities, resulting in a change in clinical service delivery to people with cystic fibrosis (CF). The aim of this study was to determine clinical outcomes of Australian adults and children with CF in the 12 months after the onset of the COVID-19 pandemic.

Methods: This longitudinal cohort study used prospectively entered national registry data. Primary outcomes were 12-month change in percentage predicted forced expiratory volume in one second (FEV_1pp), body mass index (BMI) in adults, and BMI z-scores in children. A piecewise linear mixed-effects model was used to determine trends in outcomes in the 24 months before and 12 months after the onset of the pandemic. Comparative analysis of hospitalization and service delivery data before and after the onset of the pandemic was conducted.

Results: Data were available for 3,662 individuals (median age 19.6, range 0–82). Overall registry data completeness was 95%. When trends in outcomes before and after pandemic onset were compared; FEV_1pp went from a mean annual change of –0.13% (95% CI, –0.39 to 0.13) to a mean improvement of 1.73% (95% CI, 1.29–2.17). Annual mean annual change in

BMI improved from 0.01 kg/m^2 (95% CI, −0.07–0.09 kg/m^2) to 0.33 kg/m^2 (95% CI, 0.23–0.43 kg/m^2). There was no change in BMI z-scores. Number of hospitalizations decreased from 2,656 to 1,957 ($p < 0.01$). Virtual outpatient consultations increased from 8% of toal outpatient consultations before pandemic onset to 47% during the pandemic. There was an increase in average number of consultations per patient from a median of 4 (interquartile range 2–5) to 5 (interquartile range 3–6) ($p < 0.01$).

Conclusions: In the 12 months after the onset of the COVID-19 pandemic, improvement was observed in the clinical outcomes of people with CF and the model of care delivery changed from the pre-pandemic period. Health care teams must consider how best to deliver care in light of improved outcomes observed during the COVID-19 pandemic.

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Medication adherence and lung function changes with elexacaftor/tezacaftor/ivacaftor treatment

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Background: Introduction of triple combination therapy (TCT) with elexacaftor/tezacaftor/ivacaftor improves clinical measures in many people with cystic fibrosis (PwCF). Anecdotally, many PwCF respond to improved clinical status by reducing adherence to routine CF care, including inhaled medications, but the extent to which this occurs and clinical consequences of reduced adherence are unknown.

Methods: To address this question, we identified all PwCF undergoing CFTR modulator therapy from our pharmacy database. Medication adherence measured according to medication possession ratio (actual months filled/prescribed months) for modulators and inhaled medications hypertonic saline (HTS) and dornase alpha were assessed and compared with clinical outcome measures.

Results: Three hundred eleven PwCF had three or more CFTR modulator prescriptions filled from November 2016 to August 2021, of whom 235 had three or more fills for TCT. Medication adherence was high across all modulators (0.99 ± 0.10 for ivacaftor alone, 0.98 ± 0.09 for lumacaftor/ivacaftor, 0.97 ± 0.11 for tezacaftor/ivacaftor, 1.02 ± 0.20 for TCT). Lung function values were available for 156 PwCF before and after TCT initiation, demonstrating the expected increase in percentage predicted forced expiratory volume in 1 minute (FEV_1pp) values with treatment (76.2 ± 24.6 vs 84.1 ± 24.8, $p < 0.003$), although rate of change in FEV_1 per year remained negative after modulator therapy, with a trend toward a more-negative slope after treatment initiation (−0.7 ± 5.1 vs −1.5 ± 6.1, $p = 0.15$). Adherence to HTS and dornase also declined after TCT initiation within the group as a whole (negative slope in medication possession ratio with time) and was most evident in those who regularly filled these prescriptions through our pharmacy (n = 46 and n = 37, respectively), in whom adherence was greater than 80% and steady over time before TCT but fell to 69% and 73%, respectively, with a negative slope over time after TCT (Figure 1). Adherence to pancreatic enzymes (n = 52) followed a similar pattern, although changes in adherence to HTS or dornase after modulator therapy were not associated with lung function or changes in lung function over time.

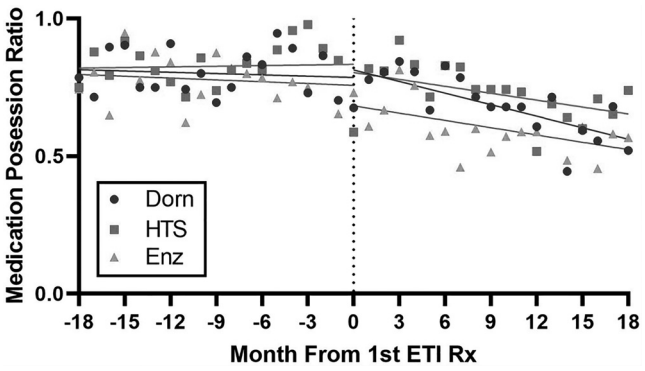

Figure 1. Medication possession ratio for dornase (Dorn), hypertonic saline (HTS), and pancreatic enzymes (Enz) relative to time before and after first prescription for elexacaftor/tezacaftor/ivacaftor (ETI)

Conclusions: In this real-world study, PwCF undergoing TCT were strongly adherent to modulator therapy, with substantial gains in lung function but continued decline in lung function over time. Although continued lung function decline on TCT could reflect the observed decrease in adherence to inhaled CF therapies, we did not observe a direct correlation between lung function and adherence. Further study will be needed to determine whether declines in lung function after TCT are sustained or reflect short-term changes in approach to CF care with highly effective modulator treatment.

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Multi-center cohort study exploring the impact of the first U.K. COVID-19 lockdown on nebulizer use in adults with cystic fibrosis in the CFHealthHub learning health system

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Background: Promoting adherence to preventative inhaled therapy in cystic fibrosis (CF) is challenging despite a clear association with better outcomes. Motivation to maintain adherence is one aspect of the complex process required for sustained behavior change. Fear is recognized as an acute motivator, and the COVID-19 pandemic created a significant fear stimulus, especially in people with underlying respiratory disease. The objective of this study was to explore changes in nebulizer use in response to the COVID-19 pandemic.

Methods: This 16-center cohort study involved more than 60% of adult CF centers in England through the CFHealthHub learning health system. CFHealthHub was established in 2015 to help promote adherence to nebulized therapy. It provides people with CF and their clinicians objective usage information through nebulizers with real-time electronic data capture capability. We explored the association between the first U.K. national lockdown (March 23, 2020, to May 28, 2020) and nebulizer use, using the mixed-effect multilevel model adjusted for potential confounders including age (fitted as a nonlinear term), sex, and deprivation index.

Results: We included 581 adults with CF participating in CFHealthHub between September 1, 2019, and August 21, 2020. Mean age was 34; 49% participants were female. The range of mean weekly nebulizations per patient increased from 9 to 12 to 12 to 14 in the week after the first U.K. national lockdown before decreasing to 11 to 12 throughout the rest of the study period (Figure 1). The association between lockdown and nebulizer