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Impact of elexacaftor/tezacaftor/ivacaftor on depression and anxiety in cystic fibrosis

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Abstract

Background: Cystic fibrosis (CF) is associated with worsening of depression and anxiety symptoms. Elexacaftor/tezacaftor/ivacaftor (Trikafta®), a cystic fibrosis transmembrane regulator (CFTR) modulator approved in 2019, significantly improves lung function, decreases pulmonary exacerbations, and improves quality of life. Studies are needed to evaluate the effects of Trikafta on symptoms of anxiety and depression.

Research Question: Do adults with CF report a change in depression and anxiety symptoms after Trikafta initiation?

Study Design and Methods: A retrospective chart review was conducted of patients with CF ($n = 127$) receiving care from January 2015 through February 2022. Data collected included demographics, annual PHQ-9 and GAD-7 scores, FEV1 percent predicted at each visit, BMI, consistency and timeline of Trikafta use, mental health diagnoses, counseling/psychotherapy use, psychiatric medication use, prescriber of psychiatric medications, number of psychiatric emergency department visits and psychiatric hospital admissions, and sleep disturbances.

Results: Of the 127 patients screened for eligibility, 100 patients were included. Data collected yielded 563 PHQ-9, 563 GAD-7, and 560 ppFEV1 data points. No significant changes in average PHQ-9 or GAD-7 scores were found after Trikafta initiation or due to the COVID-19 pandemic. However, 22% of patients initiated or had a change in psychiatric medications, and patients with changes in psychiatric medications had significantly higher PHQ-9 and GAD-7 scores than patients not prescribed psychiatric medications. Trikafta use improved lung function by an average of 5.23% ($p = 8.56e{-}08$). Around a quarter (23%) of all patients reported sleep issues after initiating Trikafta.

Interpretation: No significant changes in average PHQ-9 and GAD-7 scores were found after Trikafta initiation. A quarter of patients required a change in psychiatric medications, and significant differences in depression and anxiety scores were found between patients with a change in psychiatric medications and those not prescribed medication. Twenty-three percent of patients reported a prevalence of sleep issues after Trikafta initiation.

Keywords: anxiety, cystic fibrosis, depression, elexacaftor/tezacaftor/ivacaftor, Trikafta

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Cystic fibrosis (CF) is one of the most common life-limiting genetic diseases, with a prevalence of more than 30,000 patients in the United States.[1] It is caused by an autosomal recessive functional deficiency of the cystic fibrosis transmembrane regulator (CFTR).[2] Almost 2000 CFTR mutations have been identified, with F508del the most common and accounting for more than 80% of patients with CF of Northern European descent.[3] Common CF manifestations include lung disease, inflammation, pancreatitis, and gastrointestinal illness.[1] Patients with CF also have a high prevalence of anxiety and depression. According to an international screening of adolescents and adults with CF, 25% and 35% of the US sample reported depressive and anxiety symptoms, respectively.[2] Depression has been associated with decreased lung function, body mass index

(BMI), and treatment adherence in patients with CF.[2,4,5] The Cystic Fibrosis Foundation and International Committee on Mental Health in Cystic Fibrosis recommend annual depression and anxiety screening using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder Scale-7 (GAD-7).[6]

It is important to understand the psychiatric implications of emerging CF therapies. Elexacaftor/tezacaftor/ivacaftor (Trikafta in the United States, Kaftrio in Europe), a CFTR modulator approved by the US Food and Drug Administration (FDA) in October 2019, is recommended for patients with at least one F508del mutation.[7] Trikafta significantly improves lung function [measured by percent predicted forced expiratory volume in 1 s (ppFEV1), predicted for age, gender, and height], decreases pulmonary exacerbations, improves quality of life, and decreases sweat chloride concentrations.[8,9] Phase III trials indicated it is generally well tolerated with mild adverse events such as cough, nasopharyngeal pain, and upper respiratory infection.[10] Trial participants did not report any psychiatric or sleep disturbances.

However, prior CFTR modulators have been shown to impact anxiety and depression. While patients did not report mental health changes after phase III trials of lumacaftor/ivacaftor, later studies showed associations with increased depression and anxiety symptoms.[11,12] While there were no reported psychiatric adverse events in Trikafta phase II and III trials and little published research on psychiatric implications of Trikafta,[8,10] a case report describes increased depression, anxiety, and sleep paralysis with hypnopompic hallucinations after Trikafta initiation.[13] A recent study also found that in patients whose mental health deteriorated after Trikafta initiation, side effects were ameliorated with a dose adjustment.[14] Therefore, further studies are needed to evaluate the effects of Trikafta on anxiety and depression. This study examined changes in reported symptoms of depression and anxiety in adults with CF after Trikafta initiation.

Study design and methods

Patient population

A retrospective chart review was conducted of adult patients with CF ($n = 127$) receiving care at University of Virginia (UVA) Adult CF Clinic from January 2015 to February 2022. Inclusion criteria were a diagnosis of CF, prescription of Trikafta for an approved CF mutation or approved for compassionate use (patient with a CF mutation not FDA-approved but patient is seriously ill with limited treatment options), consistent Trikafta use, and at least one PHQ-9 and GAD-7 score before and after Trikafta initiation.

Data extracted

Data collected included demographics (age at 11 October 2021 – onset of data collection, race, sex) and CFTR mutation. History of Trikafta use, ppFEV1, and BMI were measured at each visit and PHQ-9 and GAD-7 scores were collected annually. Mental health data included mental health diagnoses, counseling/psychotherapy use, psychiatric medications, prescriber of psychotropic medications, number of psychiatric emergency department visits and psychiatric admissions, and sleep disturbances.

In accordance with CF care guidelines, patients were screened at least annually for depression and anxiety by the CF team psychologist or social worker using the PHQ-9, a 9-item self-report depression screening tool with score range of 0–27, and the GAD-7, a 7-item self-report anxiety tool with score range of 0–21. For the PHQ-9, a score of 0–4 is 'normal' or minimal depression, 5–9 indicates mild depression, 10–14 indicates moderate depression, 15–19 indicates moderately severe depression, and 20 or more indicates severe depression. Scores 15 and above warrant active treatment (with psychotherapy, medications, or a combination of the two), while scores between 5 and 14 require clinical judgment to determine the necessity of treatment. For the GAD-7, a score of 0–4 indicates minimal anxiety, 5–9 indicates mild anxiety, 10–14 indicates moderate anxiety, and scores greater than 15 indicate severe anxiety. Scores in the mild range usually require monitoring, moderate scores require clinical judgment to determine the need for treatment, and severe scores warrant active treatment.

At our institution, if patients endorsed depression or anxiety symptoms on screeners or during clinic appointments, they were offered psychotherapy and other mental health interventions, and the CF pulmonologist may offer to prescribe an

antidepressant or refer to psychiatry. We also assessed patients' stress, sleep, and other mental health symptoms in addition to the PHQ-9 and GAD-7 questionnaires.

Patients' ppFEV1 and BMI corresponding to the dates of their PHQ-9 and GAD-7 scores were also collected. Patient history of Trikafta use included date of initiation, consistency of use, dosage changes, patient-reported side effects, and in event of drug termination, the reason for termination.

Mental health history data were collected from patient records, records from outside institutions if available, and patient self-report during clinic visits. This included mental health diagnoses, counseling/psychotherapy use, psychiatric medications, psychiatric medication prescriber, and number of psychiatric emergency department visits and psychiatric hospital admissions.

Mental health diagnoses after Trikafta initiation were categorized as: no change, fewer diagnoses, more diagnoses, and no diagnoses. Psychiatric medications after Trikafta initiation were categorized into four groups: no changes; increased dose, medication added, medication change, or multiple medication changes; decreased dose, stopped a medication; don't know (patient received care outside of health system); and not prescribed psychotropics. Psychiatric medication prescriber was grouped into: psychiatrist, primary care provider, CF pulmonologist, other, and not on psychotropics. Psychiatric emergency department visits and psychiatric hospitalizations were reported as the total number of patients experiencing at least one event prior to or during Trikafta use. Sleep issues after Trikafta initiation were categorized as: no sleep difficulties, sleep difficulties, and pre-existing sleep difficulties that continued.

Statistical analyses

Number of weeks past the beginning of COVID-19 was included in analyses due to its potential to significantly affect mental health. The beginning of COVID-19 was set as 15 March 2020, as the World Health Organization declared COVID-19 a pandemic and our health system adopted COVID-19 protocols around that time. The three Black patients and one multiracial patient were combined into a Persons of Color (POC) category.

We ran three linear mixed models to assess the impact of Trikafta on ppFEV1, PHQ-9, and GAD-7. Each model incorporated all 100 included patients and several observations per patient; total $n = 560$ for ppFEV1 and 563 for PHQ-9 and GAD-7. The ppFEV1 model assessed lung function on a given date using whether the patient was on Trikafta at that time, the number of weeks after the start of the COVID-19 pandemic, and a random effect for each patient. Age and sex were not included in the model as ppFEV1 is already predicted for a given age and gender. The PHQ-9 and GAD-7 models explained score on a given date by whether the patient was on Trikafta at that time, the number of weeks after the start of the COVID-19 pandemic, ppFEV1 at the time the score was taken, age, sex, race, psychiatric medications, and a random effect of patient. Data were analyzed using R software.[15]

This study was approved by UVA's Institutional Review Board for Health Sciences Research (#23337) and followed procedures with ethical standards.

Results

Timing of Trikafta and COVID-19

There was diverse distribution of data across Trikafta initiation dates and the start of COVID-19 (563 total time points from 100 patients). There were 337 time points for patients not on Trikafta before COVID ($n = 94$, 1–7 observations each), 47 for patients on Trikafta before COVID ($n = 39$, 1–4 observations each), 14 for patients not on Trikafta after COVID ($n = 10$, 1–2 observations each), and 164 for patients on Trikafta after COVID ($n = 95$, 1–3 observations each). This allowed teasing apart effects of Trikafta and effects of COVID.

Baseline demographics and characteristics

Baseline demographics and patient characteristics are presented in Table 1. Twenty-seven patients were excluded (1 deceased, 13 inconsistent use or discontinuation of Trikafta, and 13 missing PHQ-9 or GAD-7 scores). The sample of 100 included patients was 96% White, 4% Black/biracial/multiracial, and 52% male. PHQ-9 and GAD-7 scores had a median of 3 but with wide ranges (0–26 and 0–21, respectively).

Table 1. Patient demographics: $N = 100$.

Demographics	
Male sex (*n*)	52
Age (mean ± SD)	35.3 ± 11.3
Race	
White (*n*)	96
Black, biracial, or multiracial (*n*)	4
PHQ-9 score (median, range)	3 (0–26)
GAD-7 score (median, range)	3 (0–21)
Mental health diagnoses after initiating Trikafta	
More diagnoses (*n*)	5
Fewer diagnoses (*n*)	2
No changes (*n*)	50
No diagnoses (*n*)	43
Psychiatric medication after initiating Trikafta	
No changes (*n*)	15
Increased dosage, added medication, switched medication, multiple medication changes (*n*)	22
Decreased or stopped medication (*n*)	4
Not prescribed medication (*n*)	55
Unsure[a] (*n*)	4
Prescriber of psychiatric medications[b]	
Psychiatrist (*n*)	14
Primary care provider (*n*)	8
Pulmonologist (*n*)	22
Other (*n*)	5
No prescribed psychotropics (*n*)	55
Sleep difficulties after initiating Trikafta	
No sleep difficulties (*n*)	47
Sleep difficulties (*n*)	23
Pre-existing difficulties that continued (*n*)	30
Psychiatric emergency department visit	
Before starting Trikafta (*n*)	2
During Trikafta (*n*)	4
Psychiatric hospitalization	
Before starting Trikafta (*n*)	2
During Trikafta (*n*)	2

GAD-7, Generalized Anxiety Disorder Scale-7; PHQ-9, Patient Health Questionnaire 9; SD, standard deviation.
[a]Four patients received psychiatric care outside University of Virginia and may not have reported all medication changes.
[b]Four patients had two prescribers for psychiatric mediations. All prescribers were included in the counts of psychiatric medication prescriber.

Patient characteristics before and during Trikafta use are shown in Table 2.

Five patients received new mental health diagnoses while on Trikafta and two had diagnoses revoked. After initiating Trikafta, 22 patients increased psychotropic medication dosage, added a new medication, switched a medication, or had multiple psychiatric medication changes. Characteristics of these patients are shown in Table 3. Four decreased psychotropic dosage or stopped a medication. Around a quarter ($n=23$) reported new sleep issues and 30 had pre-existing sleep issues that continued (Table 1). Two patients discontinued Trikafta permanently due to significant insomnia, anxiety, and depression symptoms.

Table 2. Patient characteristics before initiating and during Trikafta use: $N = 100$.[a]

	Before (mean ± SD)	During (mean ± SD)
ppFEV1	67.0 ± 21.5	73.1 ± 24.1
BMI	24.5 ± 4.6	25.9 ± 4.8
PHQ-9 score	4.99 ± 4.65	5.07 ± 4.84
GAD-7 score	4.34 ± 4.34	4.54 ± 4.47

BMI, body mass index; GAD-7, Generalized Anxiety Disorder Scale-7; PHQ-9, Patient Health Questionnaire 9; SD, standard deviation.
[a]Multiple observations for each patient before and during Trikafta were averaged.

Lung function

The linear mixed model explained patients' ppFEV1 by whether or not the patient was on Trikafta at that time, weeks post start of COVID-19, and a random effect for each patient. This model included all 100 patients and 560 total data points. The average lung function not on Trikafta at the start of COVID-19 was 67.56%. Trikafta use improved lung function by an average of 5.23% ($p = 8.56e{-}08$). Weeks past start of COVID-19 had no significant effect on lung function.

PHQ-9

PHQ-9 scores on a given date were explained by whether or not the patient was on Trikafta at the time, weeks post start of COVID-19, ppFEV1, age, sex, race, psychiatric medications, and random effect for each patient. Trikafta and COVID-19's effects on PHQ-9 scores were not statistically significant (Table 4). Of note, POC had scores

Table 3. Characteristics of patients who increased medication dosage, added a medication, switched a medication, or had multiple medication changes: $N = 22$.

	Increased dosage	Added medication	Switched medication	Multiple changes
n	6	9	3	4
Average age	30.8	29.2	34.3	35.9
Male sex	3	4	0	0
Race	5 White 1 POC[a]	8 White 1 POC[a]	3 White	4 White
Average pre-Trikafta PHQ-9	9.18	6.14	4.27	11.34
Average post-Trikafta PHQ-9	8.00	7.89	6.92	7.03
Average Pre-Trikafta GAD-7	5.00	5.75	4.37	10.45
Average post-Trikafta GAD-7	4.96	9.68	10.08	5.63
Average pre-Trikafta ppFEV1	67.97	70.08	81.50	61.86
Average post-Trikafta ppFEV1	73.69	79.48	92.50	62.00

GAD-7, Generalized Anxiety Disorder Scale-7; PHQ-9, Patient Health Questionnaire 9.
[a]POC = Persons of color (Black, biracial, or multiracial).

Table 4. Effect of Trikafta, COVID, PPFEV1, age, sex, race, and psychiatric medications on PHQ-9 and GAD-7.

	Estimate	Standard error	df	*t* statistic	*p* value
PHQ-9					
(Intercept)[a]	6.911	2.071	168.5	3.337	0.001
On Trikafta (Y)	−0.059	0.488	484.2	−0.122	0.903
Weeks past COVID-19	0.000	0.003	480.5	−0.127	0.899
ppFEV1	−0.015	0.016	281.9	−0.945	0.345
Age	−0.015	0.038	102.3	−0.384	0.702
Sex (Male)	−1.056	0.836	93.2	−1.264	0.209
Race (POC)	3.862	2.257	110.4	1.711	0.089
Psych meds (Increase)	4.180	0.927	85.5	4.509	2.06e-05
Psych meds (Decrease)	8.158	1.866	93.6	4.372	3.19e-05
Psych meds (No changes)	1.801	1.059	85.6	1.700	0.092
GAD-7					
(Intercept)[a]	6.312	1.948	168.8	3.241	0.001
On Trikafta (Y)	−0.140	0.466	485.6	−0.300	0.764
Weeks past COVID-19	0.001	0.002	482.3	0.703	0.482
ppFEV1	0.005	0.015	275.7	0.348	0.728
Age	−0.047	0.036	103.2	−1.313	0.192
Sex (Male)	−1.179	0.781	94.2	−1.509	0.134
Race (POC)	4.078	2.113	112.0	1.930	0.056
Psych meds (Increase)	3.535	0.916	85.9	3.855	2.22e-4
Psych meds (Decrease)	6.334	1.842	93.5	3.438	8.70e-4
Psych meds (No changes)	1.715	1.047	86.0	1.637	0.105

GAD-7, Generalized Anxiety Disorder Scale-7; PHQ-9, Patient Health Questionnaire 9; POC, persons of color.
[a]The intercept represents the reference category for categorical variables or a 0 value for continuous variables, that is, an observation of a patient not on Trikafta, at 0 weeks past COVID, with ppFEV1 of 0, age of 0, White race, female sex, and not prescribed psychiatric medications. Each line of the table represents the statistical difference of that category level to the reference level (categorical variables) or the effect of a one-unit increase in the variable (continuous variables).

3.86 points higher than White patients, but this effect did not reach significance ($p = 0.089$). Compared with patients not prescribed psychiatric medications, patients with an increase (increased dosage, added a medication, switched medications, or multiple changes) had scores 4.18 points higher ($p = 0.00002$) and patients who decreased or stopped medications had scores 8.16 points higher ($p = 0.00003$).

GAD-7

GAD-7 scores on a given date were explained by whether or not the patient was on Trikafta, weeks post start of COVID-19, ppFEV1, age, sex, race, psychiatric medications, and random effect of each person. Neither Trikafta nor COVID-19's effects on GAD-7 scores were significant (Table 4). Compared with White patients, POC had scores 4.08 points higher, which almost reached

significance ($p = 0.056$). Compared with patients not prescribed psychiatric medications, patients with an increase in medications (increased dosage, added a medication, switched medications, or multiple changes) had scores 3.53 points higher (0.0002) and patients who decreased or stopped medications had scores 6.33 points higher ($p = 0.0008$).

Discussion

Trikafta use was associated with improvements in ppFEV1, reinforcing its efficacy. Although no significant changes were found in average PHQ-9 or GAD-7 scores after Trikafta initiation, 5% of patients received a new mental health diagnosis and 22% increased psychotropic dosage, added a new psychotropic, switched psychotropics, or had multiple changes. Therefore, it is possible Trikafta impacts mood and anxiety, but changes were mitigated by psychiatric medication. It is also possible Trikafta affects absorption or effectiveness of psychiatric medications. Factors that may have contributed to lack of significant change in scores include early symptom identification through routine mental health screening, access to mental health services through CF team, and proactive and effective management of psychiatric symptoms through psychotropics and psychotherapy. Moreover, 22% of patients were prescribed psychotropics by their pulmonologist and psychiatric symptoms were likely assessed and monitored at CF appointments. In addition, there are limitations to use of screeners as patient symptoms are only measured at one time point and may have improved by time of screening. These are important findings and CF providers need to be aware of and monitor for changes in depression or anxiety after Trikafta initiation. Side effects of anxiety or depression can be detrimental to a patient and may impact adherence or desire to take Trikafta. Such symptoms can also impact treatment prognosis and depression is associated with decreased lung function, BMI, and treatment adherence in patients with CF.[2,4,5]

While there were no significant changes in scores overall, 26% of patients with a change in psychiatric medication (increase or decrease) had significantly higher PHQ-9 and GAD-7 scores compared with those not prescribed medication. It is notable that patients who both increased and decreased medications had significantly higher scores, and this is an area to explore in future research. It is possible that patients with a medication increase needed additional dose adjustments or were screened before medication benefits were reached. For patients who decreased medications, it is possible they decreased dosage due to unwanted side effects, desire to reduce amount of medications, or a change in desire to engage in psychopharmacological treatment. It is also possible these patients' screening scores were even higher prior to dose change or that they chose to address mood and anxiety with non-pharmacological methods. These patient groups need careful monitoring by CF providers and may need additional mental health treatment. If a patient's depression or anxiety continues to worsen despite treatment, a Trikafta dose change may be considered. In a recent study, patients who reported mental health deterioration after starting Trikafta experienced symptom improvement after dosage adjustment.[14]

Of note, 2 of the 100 patients discontinued Trikafta permanently after reporting significant insomnia, anxiety, and depression. However, these patients had elevated PHQ-9 and GAD-7 scores before initiation of Trikafta. It is possible that patients with existing anxiety and depression are more likely to be cautious of starting novel therapies, including Trikafta. Furthermore, starting a new therapy can be a stressor in itself and those with less psychological reserve may be more likely to experience a negative impact. Patients with elevated PHQ-9 and GAD-7 scores prior to Trikafta initiation require careful monitoring.

The ability to access or afford Trikafta may also impact self-reported mood and anxiety symptoms. Many of our patients had difficulties with insurance approval and the ability to consistently afford Trikafta, and there were several occurrences of inability to access Trikafta during hospital admission. Many patients experienced at least one incidence of inability to refill prescriptions on time due to insurance coverage lapses, and some went for weeks to months without Trikafta due to these barriers (they were excluded from this study). Several even considered discontinuing Trikafta due to access difficulties. These factors can be stressful and may impact mood or anxiety symptoms.

Importantly, there were no significant changes in PHQ-9 and GAD-7 scores following onset of COVID-19. The stability of patient scores and

mental health screening process during COVID-19 is described in Bruschwein *et al.*[16] This finding may be somewhat surprising, given the general impact of COVID-19 on society. A review on occurrence of mental health problems during COVID-19 suggested a psychiatric epidemic co-occurring with the COVID-19 pandemic, as people reported a higher burden of mental health problems.[17] However, our finding is consistent with Ciprandi *et al.*[18] that people with CF had similar or lower rates of psychological distress compared with the general population during COVID-19. It may be possible that patients with CF are better able to cope with COVID-19-related stress due to experiencing coping with a chronic health condition. In addition, it may be possible that CF providers closely monitored patients' mental health after the onset of COVID-19 and offered resources, providing early detection and treatment of mental health concerns. Our clinic made a rapid transition to telehealth and patient care was not interrupted by COVID-19 (described in List *et al.*[19]), which may have contributed to score stability. As Trikafta's FDA approval and the start of COVID-19 occurred within a few months, efforts by CF centers to identify and address mental health issues (whether due to Trikafta or COVID-19) may have mitigated any significant changes in scores and thus impacted our findings.

While sleep difficulties or disturbances related to CF have been observed,[20] there is limited research on effects of Trikafta on sleep. A case report describes sleep paralysis after Trikafta,[13] but there is little evidence overall of sleep disturbance after Trikafta and it was not reported as a side effect during initial trials.[10] In this study, 23% of patients reported sleep issues after initiation of Trikafta and an additional 30% reported pre-existing sleep issues that continued after initiation. This suggests sleep disturbances may occur more frequently than expected after Trikafta initiation and should be carefully screened for and monitored. Dosage changes may need to be considered for patients who experience significant sleep issues but wish to continue Trikafta. Given over half of patients reported new or ongoing sleep difficulties after Trikafta initiation and sleep issues were a factor in two patients discontinuing Trikafta, interventions to assess and treat sleep issues should be included in CF care and referrals made to sleep providers when appropriate.

POC had higher PHQ-9 and GAD-7 scores compared with White patients, though not statistically significant. However, these results are based on 4 out of 100 patients, and a larger sample would likely reach significance. This could reflect the difficulties of being a POC within healthcare systems and with CF. Articles have highlighted racism and implicit bias within healthcare, where Black patients receive lower quality of care compared with White counterparts independent of sociodemographic factors.[21–23] There is also evidence that POC with CF are less likely to be eligible for CFTR modulators.[24] This has been met with a push to improve screening options for Black patients, as they have higher frequencies of different CF mutations.[25,26] In addition, many people still believe CF to be a diagnosis for White patients and POC with CF may feel isolated.

A strength of this study is the diversity of observations for patients before and during Trikafta use and before and after the beginning of COVID-19. By incorporating 563 time points from 100 patients into statistical models, we were able to separate the influence of Trikafta from COVID-19. Study limitations include a potential lack of mental health data for the four patients who received mental health care outside of UVA, a retrospective and single-center design, and relative homogeneity of study participants.

Interpretation

No significant change was found in PHQ-9 and GAD-7 scores in patients with CF after initiating Trikafta or after the onset of COVID-19. Trikafta use was associated with improvements in ppFEV1. However, a quarter of patients had a change in psychiatric medications and significant differences in scores were found between these patients and those not prescribed medication. There is also a potential for new sleep disturbances after Trikafta initiation. Further research is required to better understand implications of Trikafta on patients' mental health and psychiatric medication use, especially for POC, and to examine the effect of Trikafta on sleep.

Prior Abstract Presentation

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Declarations

Ethics approval and consent to participate

This study was approved by our institution's IRB; consent not applicable.

Consent for publication

Not applicable.

Author contributions

Lijia Zhang: Conceptualization; Data curation; Investigation; Methodology; Visualization; Writing – original draft; Writing – review & editing.

Dana Albon: Supervision; Writing – original draft; Writing – review & editing.

Marieke Jones: Formal analysis; Software; Visualization; Writing – review & editing.

Heather Bruschwein: Conceptualization; Supervision; Writing – original draft; Writing – review & editing.

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