BMJ Open Respiratory Research

Understanding beliefs about elexacaftor-tezacaftor-ivacaftor therapy in adults living with cystic fibrosis

Catherine O'Leary,[1] Alec Vinh,[2] Mari Lea-Davies ,[1] John Weinman,[3] Rob Horne,[4] Jamie Duckers [1]

To cite: O'Leary C, Vinh A, Lea-Davies M, *et al*. Understanding beliefs about elexacaftor-tezacaftor-ivacaftor therapy in adults living with cystic fibrosis. *BMJ Open Respir Res* 2025;**12**:e002546. doi:10.1136/bmjresp-2024-002546

Received 3 May 2024
Accepted 12 March 2025

[1]Respiratory Medicine, Cardiff and Vale University Health Board, Cardiff, UK
[2]Cardiff University, Cardiff, UK
[3]King's College London, London, UK
[4]University College London, London, UK

Correspondence to
Dr Jamie Duckers;
jamie.duckers@wales.nhs.uk

ABSTRACT

Background A person's beliefs about treatment influence their engagement and adherence to that treatment. The Necessity-Concerns Framework suggests that adherence is influenced by a person's judgement of their own need for treatment (necessity beliefs) and concerns about the potential adverse consequences of taking the treatment. This study was conducted to explore the Necessity-Concerns Framework for elexacaftor-tezacaftor-ivacaftor (ETI) therapy (Kaftrio) in adults with cystic fibrosis (CF).

Methods A total of 64 adults with CF were maintained on ETI therapy as part of their routine CF care, and completed the Beliefs about Medicines Questionnaire. Patient demographics, lung function, body mass index and quality of life using the Cystic Fibrosis Questionnaire Revised were collected as part of routine clinical care. Duration of ETI therapy along with medicines possession ratio was recorded.

Results Patients reported strong beliefs about the necessity of ETI therapy. The majority of patients (78%) reported low concerns about ETI therapy while 22% of patients reported high concerns. A small number of patients (n=4) had concerns which were stronger than their beliefs about necessity.

Discussion Patients reported strong beliefs in the necessity of ETI therapy. Although concerns were lower, a significant proportion of the sample had strong concerns about their ETI therapy. By being aware of people with CF's necessity and concerns beliefs around ETI therapy clinical teams will be better armed to engage them in treatment decisions and support optimal adherence.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Understanding a patient's beliefs about the necessity and concerns of treatment can help us predict those in whom poor adherence may be an issue.

WHAT THIS STUDY ADDS

⇒ In this study, the majority of cystic fibrosis patients had beliefs that elexacaftor-tezacaftor-ivacaftor (ETI) therapy is more beneficial than costly. Concerns outweighed beliefs about the benefits in a small number of patients.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We have identified that a small number of patients have concerns about ETI therapy that outweigh beliefs about necessity. These findings can help us target those patients by addressing concerns, providing education and engaging them in treatment decisions to support optimal adherence.

INTRODUCTION

Cystic fibrosis (CF) transmembrane conductor regulator (CFTR) modulator therapies target specific defects in CFTR protein function caused by gene mutation and have revolutionised CF management. Currently, four CFTR modulators (ivacaftor, ivacaftor/lumacaftor (Orkambi), tezacaftor/ivacaftor (symkevi) and elexacaftor/tezacaftor/ivacaftor (ETI: Kaftrio or Trikafta)) are approved for the treatment of CF. ETI therapy was granted a formal licence and became available in the UK for people with CF aged over 12 years in August 2020. By this time, people with CF across the UK were keen to start the therapy.

As a CF service, we were aware of the anticipation for this treatment from people living with CF and their families, and how it was viewed as potentially 'life changing'. As it became available to our patients, we were interested in exploring our patients' perceptions and beliefs about ETI therapy. This is important as an individual's beliefs about a treatment influence treatment engagement and adherence. Although it is too early to establish whether adherence rates to ETI in our population will be suboptimal, there is evidence that adherence to other CFTR modulator therapies is not 100%[1 2] and may decline with time on the treatment.[3]

By examining an individual's beliefs about their medication, researchers have demonstrated that those with high concerns and low beliefs about the necessity of a treatment are more likely to adhere poorly, while conversely

those with low concerns and strong necessity beliefs are more likely to have higher levels of adherence.[4]

In CF populations, Bucks *et al*[5] found adherence to chest physiotherapy in adolescents with CF was related to this trade-off between beliefs about the necessity of chest physiotherapy and beliefs about potential adverse effects. Similarly, Goodfellow *et al*[6] found the necessity beliefs of adolescents with CF and their parents towards vitamin supplements were related to poor adherence. The researchers speculate that these beliefs are related to a lack of understanding about the importance of vitamins given their wide availability over the counter and in supermarkets.

However, there have been no studies examining the beliefs of people living with CF about the necessity of or concerns about CFTR modulator therapy. This study was conducted to explore the Necessity-Concerns Framework for ETI therapy (Kaftrio) in adults with CF.

METHODS

Over a 6-week period, 65 consecutive adult patients attending annual review appointments who had commenced ETI therapy were asked to complete a Beliefs about Medicines Questionnaire (BMQ).[7] Patients who met the inclusion/exclusion criteria (N=65) were sent a letter prior to their clinic appointment informing them about the service evaluation project. Inclusion criteria included individuals receiving regular clinical care from the All-Wales Adult CF Centre at University Hospital Llandough, 18 years of age and older, commenced on ETI therapy, sufficiently fluent in English to read and understand the information sheets, give verbal consent and complete the questionnaire. Exclusion criteria included any patient who was acutely unwell/currently experiencing an acute exacerbation.

Over a 6-week period between March 2021 and April 2021, 65 consecutive adult patients attending annual review appointments who had commenced ETI therapy were asked to complete a BMQ[7] during their clinic appointment. 64 of those approached agreed to take part and verbal consent was provided. Data was collated by the authors. Demographics, most recent forced expiratory volume in 1 s (FEV_1%), body mass index (BMI) and Cystic Fibrosis Questionnaire Revised (CFQ-R) quality of life domain scores which are routinely collected as part of clinical care were recorded. The medicines possession ratio (MPR) for ETI was calculated using the time interval between homecare deliveries. MPR=days of treatment received/days of treatment prescribed.

Data analysis was performed using SPSS (SPSS Chicago) V.27. Analyses included χ^2 and Pearson's correlation. A $p<0.05$ was considered significant.

Demographics, most recent FEV_1%, BMI and CFQR quality of life domain scores which are routinely collected as part of clinical care were recorded. The MPR for ETI was calculated using the time interval between homecare deliveries. MPR=days of treatment received/days of treatment prescribed.

Mean time between commencing therapy with ETI and completing the BMQ questionnaire was 120 days (SD 40; range 40–360 days).

Patient and public involvement

There was no patient or public involvement in the design or conduct of the study.

Beliefs about Medicines Questionnaire

The BMQ assesses individuals' cognitive representations of medicine.[7] It consists of two sections: the BMQ-General and the BMQ-Specific. The BMQ-General comprises 8 items measuring beliefs regarding the harm of medicines in general and their overuse by clinicians. The BMQ-Specific comprises 10 items with two components measuring beliefs about the *necessity* of prescribed medication and *concerns* including side-effects, disruption to life and dependency. The BMQ-Specific was adapted to assess beliefs regarding ETI.

Items are presented with a 5-point Likert scale from 'strongly agree' to 'strongly disagree'. Necessity and concern scores range from 5 to 25, with a high score indicating either strong concern or strong beliefs about necessity. The BMQ-Specific necessity-concerns differential was calculated for ETI by subtracting the BMQ-Specific concerns score from the BMQ Specific necessity score.[7] Individuals were categorised into the following groups: greater cost, greater benefit, costs and benefits equal. Patients were also categorised into attitudinal groups by splitting necessity and concern scores at the midpoint value (≥13).

RESULTS

A total of 64 (25F/39M) completed the BMQ. One patient chose not to complete the questionnaire. Mean age was 30.0 years (SD 9.6; range 17–58), mean FEV_1% predicted was 70.3% (SD 25.9; range 12–117) and mean BMI was 23.0 kg/m^2 (SD 3.5; range 15.6–32.3 kg/m^2). Mean MPR was 92.8% (SD 14.8%). Two patients had an MPR below 80%.

The general characteristics of the participants are provided in table 1.

Table 1 Patient characteristics

	Mean	SD	Range
Age	30.0	9.6	17–58
FEV_1% pred	70.3	25.9	12–117
BMI (kg/m^2)	23.0	3.5	15.6–32.2
Number of medications	17	7	7–56

BMI, body mass index; FEV_1%, forced expiratory volume in 1 s.

Table 2 BMQ scores

	Mean	SD	Range
BMQ necessity	17.2	4.8	6–25
BMQ concerns	9.6	3.6	5–19
BMQ general	15.0	5.0	8–27

BMQ, Beliefs about Medicines Questionnaire.

BMQ score

BMQ scores are presented in table 2.

On the BMQ-Specific, mean necessity score was 17.2 (SD 4.8; range 6–25). Mean necessity score was correlated with FEV_1% (−0.35, p≥0.005) and duration of ETI therapy (0.26, p≥0.04). 50 patients (78%) had a high necessity score (≥13). There was no difference in age or sex between the low and high necessity groups but the high necessity group had a lower mean FEV_1% than the low necessity group (66.9% (25.7) vs 82.4% (23.7)), respectively (p≥0.047).

Mean concerns score was 9.6 (SD 3.6; range 5–19). 50 patients (78%) had a low concerns score (≤13). 10 of 14 patients with high concerns (≥13) were female (p≥0.005). Women were more likely to report that taking ETI therapy worries them (p≥0.028) and to worry about long-term side effects (p≥0.014) than men. The mean concerns score was not correlated with age, FEV_1% or duration of therapy with ETI (p≥0.05).

BMQ necessity-concerns differential scores were calculated; 4 patients had a negative necessity-concern score (greater cost), 3 patients had a zero necessity-concern score (cost and benefits equal) and the other 57 (89%) had a positive necessity-concern score (greater benefit). The mean necessity-concern score was 7.6 (SD 5.9). There was no statistically significant correlation between BMQ necessity-concerns differential and MPR.

Patients were also categorised into attitudinal beliefs based on whether their necessity and concerns score were above the BMQ-Specific midpoint scores (figure 1).

On the BMQ general, mean concerns score was 15.0 (SD 5.0; range 8–27).

Correlation between BMQ and lung function, demographics

The specific necessity score correlated with a higher FEV_1% predicted (−0.53; p≥0.05) and age 0.26 (p≥0.04) but not BMI or MPR. There was a significant relationship between length of time receiving ETI therapy and BMQ-Specific necessity score 0.26 (p≥0.038).

The specific concerns score was not related to age, FEV_1% predicted, BMI or length of time receiving ETI therapy.

There was no correlation between BMQ necessity/concerns differential and age, FEV% pred, BMI, MPR or length of time on ETI therapy.

Correlation between BMQ and CFQ-R

The BMQ-Specific necessity score was significantly correlated with the following CFQ-R domains: physical (−0.28; p≥0.02), emotion (−0.25; p≥0.05) and body (−0.30; p≥0.02). All other results were not significant.

The BMQ-Specific concerns data was negatively correlated with the following CFQ-R domains: vitality (−0.40; p<0.001), emotion (−0.40; p<0.001), eating (−0.36; p≥0.003), health (−0.25; p≥0.04), social (−0.32; p≥0.016) and digestive (−0.39; p≥0.001).

DISCUSSION

The results of this study indicate that the majority of CF patients (78%) had strong perceptions of the necessity of ETI therapy. This is not surprising given the highly publicised and anticipated nature of this medication. Patients

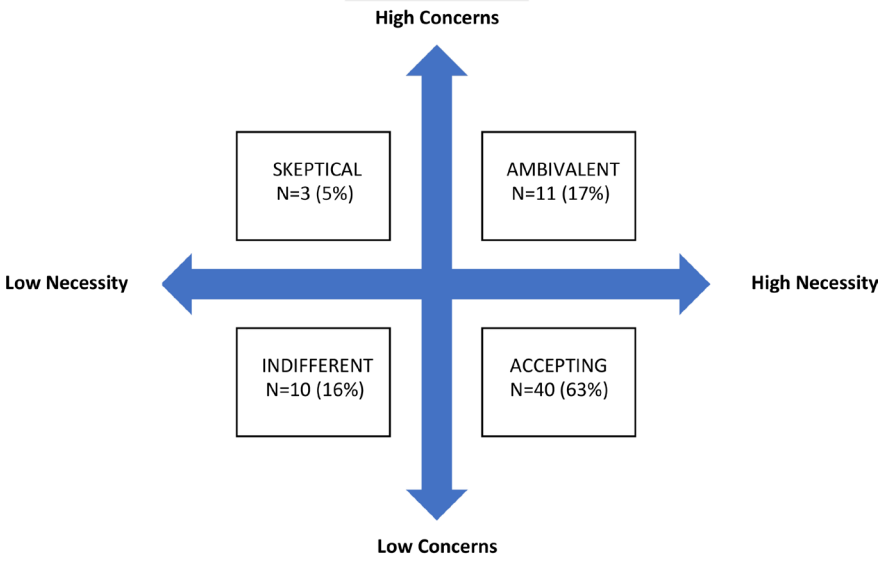

Figure 1 Percentage of patients in each attitudinal group defined by beliefs about elexacaftor-tezacaftor-ivacaftor therapy.

who were older, had a lower lung function and poorer physical functioning had higher beliefs in the necessity of it for their health. From previous meta-analyses in long-term conditions[8] stronger perceptions of the necessity of treatment were associated with higher adherence so we might expect good levels of adherence in our population to ETI therapy.

Women were more likely to report concerns than men, as were those with lower scores on several quality of life domains including digestive and eating, suggesting there may be more worries about starting a CFTR modulator if there are also gastrointestinal problems.

Using the Necessity-Concerns Framework, these results indicate that the majority of CF patients had expectations that ETI therapy would give them more benefits than costs. Concerns outweighed beliefs about benefits in a small number of patients. Although most patients were convinced about their personal need for ETI treatment (n=50/78%), a number still had strong concerns (n=14/22%). The attitudinal analysis illustrated in figure 1 provides evidence of a necessity concerns dilemma where patient ideas about treatment are nuanced and complex with personal necessity beliefs tempered by strong concerns about the negative consequences of a treatment. Ambivalence between necessity and concerns creates a difficult balancing act for many patients.

The length of time on ETI therapy was related to stronger necessity beliefs and, while previous studies have illustrated adherence rates to CFTR modulators as being higher than other treatments,[1] we remain cautious about the potential problem of adherence as those with lower MPR of their CFTR therapy had increased rate of FEV_1 decline.[3] Although CFTR modulators have revolutionised CF care, it is with a significant drug acquisition cost and non-adherence is often a hidden problem.

Our study reveals that there is a proportion of people with CF who have strong concerns about ETI therapy and who may need support with it. According to previous research, these individuals are at risk of poor adherence.[4] Over time, an individual's support needs and adherence rates may vary and, as these beliefs are often held implicitly and may not be disclosed spontaneously in clinic, we recommend intermittently monitoring the perceptions about ETI therapy. Evidence suggests inaccurate beliefs about treatment are modifiable through engagement in psychological therapy resulting in improved outcomes.[9] Where concerns are valid understanding beliefs can help teams collaborate with the individual to provide the best possible care. This may involve addressing concerns, providing appropriate information and support to treat or manage side effects and helping the patient make informed choices and decisions about their treatments. Taking account of patients' necessity beliefs and concerns could enhance the quality of ETI prescribing by helping clinical care teams to engage people living with CF in treatment decisions and discuss concerns to help support optimal adherence to ETI therapy.

This study has potential limitations. Our sample size was small and single centre and as such may not reflect the diversity and opinions of the wider UK CF population. In future research, it will be important to assess adherence to ETI therapy in relation to beliefs and perceptions in a larger, more diverse population. Although MPR was estimated, in such populations this may not be a valid measure of adherence. It would be useful to have a more objective measure of adherence and to examine this and beliefs after patients have had the opportunity to take ETI therapy for a longer period of time. In the current study, many people had been prescribed ETI for only a few weeks and so it had not established routines. This study therefore only provided a snapshot of patient beliefs soon after starting ETI therapy. It will be useful to see how beliefs about the usefulness and negative impacts of ETI therapy change over time as people establish routines and gain experience of the medicine.

CONCLUSION

Patients reported strong beliefs in the necessity of ETI therapy. Although the majority of participants reported low concerns, a significant proportion of the sample had high or strong concerns about their ETI therapy. Awareness of necessity and concerns beliefs around ETI therapy will better enable clinical teams to engage people with CF in treatment decisions and support optimal adherence.

X Catherine O'Leary @DrCatherine_OL

Contributors CO'L: conceptualisation, data curation, formal analysis, writing reviewing and editing. AV: data curation, writing. ML-D: data curation, writing. JW: conceptualisation, writing, reviewing editing. RH: conceptualisation, reviewing and editing. JD: conceptualisation, data curation, formal analysis, writing, review and editing. JD is the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants but Cardiff and Vale University Health Board deemed this work a service evaluation and ethical approval was not required. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

ORCID iDs
Mari Lea-Davies http://orcid.org/0000-0003-1731-1203
Jamie Duckers http://orcid.org/0000-0003-3004-279X

REFERENCES

1 Mehta Z, Kamal KM, Miller R, *et al*. Adherence to cystic fibrosis transmembrane conductance regulator (CFTR) modulators:

analysis of a national specialty pharmacy database. *J Drug Assess* 2021;10:62–7.
2 Siracusa CM, Ryan J, Burns L, *et al*. Electronic monitoring reveals highly variable adherence patterns in patients prescribed ivacaftor. *J Cyst Fibros* 2015;14:621–6.
3 Mitchell RM, Jones AM, Stocking K, *et al*. Longitudinal effects of ivacaftor and medicine possession ratio in people with the *Gly551Asp* mutation: a 5-year study. *Thorax* 2021;76:874–9.
4 Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999;47:555–67.
5 Bucks RS, Hawkins K, Skinner TC, *et al*. Adherence to treatment in adolescents with cystic fibrosis: the role of illness perceptions and treatment beliefs. *J Pediatr Psychol* 2009;34:893–902.
6 Goodfellow NA, Hawwa AF, Reid AJ, *et al*. Adherence to treatment in children and adolescents with cystic fibrosis: a cross-sectional, multi-method study investigating the influence of beliefs about treatment and parental depressive symptoms. *BMC Pulm Med* 2015;15:43.
7 Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health* 1999;14:1–24.
8 Horne R, Chapman SCE, Parham R, *et al*. Understanding Patients' Adherence-Related Beliefs about Medicines Prescribed for Long-Term Conditions: A Meta-Analytic Review of the Necessity-Concerns Framework. *PLoS ONE* 2013;8:e80633.
9 Hale ED, Treharne GJ, Kitas GD. The Common-Sense Model of self-regulation of health and illness: how can we use it to understand and respond to our patients' needs? *Rheumatology (Sunnyvale)* 2007;46:904–6.