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Original Research

Discontinuation of supportive therapies in people with cystic fibrosis treated with elexacaftor/tezacaftor/ivacaftor – A patient-reported outcomes' study

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ABSTRACT

Background: With the introduction of elexacaftor/tezacaftor/ivacaftor (ETI), there has been significant impact on the health and quality of life of people with cystic fibrosis, raising questions about the need for ongoing supportive therapies. This study examines patient-reported outcomes related to ETI and its influence on supportive therapy adherence.

Methods: An anonymized cross-sectional survey was conducted among 1589 members of the German Cystic Fibrosis Association to assess treatment burden, and quality of life before and during ETI treatment, focusing on adherence and factors affecting the continuation of supportive therapies.

Results: Of the 406 respondents (effective response rate 25.5 %), 276 were receiving ETI. Analysis showed increased quality of life and decreased symptoms, with a majority reporting reduced or absent cough (93 %) and sputum (91 %) following ETI treatment. The desire to reduce therapy burden was high, with 80.4 % reporting a prior or present reduction of supportive therapies, particularly of mucoactive inhalations and antibiotics. Age was a significant factor in therapy adherence, with higher adherence in adolescents than adults. Improved quality of life and better lung function correlated with greater adherence to antibiotic inhalations, while better lung function increased the likelihood of reducing mucoactive therapies.

Conclusions: Many people with CF are reducing supportive therapies despite the absence of clear guidelines. Decision-making is influenced by factors such as the desire to lessen therapy burden, reduced symptom severity, and maximizing therapeutic effects. The study highlights the need for comprehensive recommendations and calls for further research to understand the factors involved in therapy adherence and reduction.

Abbreviations:

pwCF	Person/people with CF
ETI	elexacaftor/tezacaftor/ivacaftor
PRO	Patient-reported outcomes

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CFQ-R	Cystic Fibrosis Questionnaire-Revised
QoL	quality of life
ppFEV1	percent predicted Forced Expiratory Volume in 1 s
pwCF-ETI	pwCF receiving modulator therapy

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pwCF-nomt	pwCF not receiving modulator therapy
PERT	pancreatic enzyme replacement
CFRD)	CF-related diabetes
GI	gastrointestinal

1. Introduction

Cystic fibrosis (CF) is a multisystemic, life-limiting, autosomal recessive genetic disease, affecting more than 100,000 people worldwide. Mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene cause clinical manifestations including respiratory, hepatic, pancreatic, and gastrointestinal symptoms. Pulmonary disease is the major cause of morbidity and mortality [1,2].

The discovery of novel therapies that directly target the CFTR defect led to a fundamental change in therapy options for people with cystic fibrosis (pwCF) [3]. These CFTR modulator drugs have the capability to enhance CFTR activity by rectifying the folding and trafficking of the dysfunctional protein (correctors) or augmenting the probability of the channel being open (potentiators) [4]. A triple combination therapy comprising **e**lexacaftor, **t**ezacaftor and **i**vacaftor (ETI) was approved 5 years ago for the treatment of pwCF and at least one *F508del* variant in *CFTR* [5,6]. Numerous clinical trials have since demonstrated the effectiveness of ETI in improving lung function, nutritional status, as well as relieving respiratory and gastrointestinal symptoms [7,8].

Patient-reported outcomes (PROs) can provide valuable patient-centred, real-world insights into risks and benefits of a drug, improve patient-clinician communication and the clinicians' awareness of patient's symptoms [9,10]. In the context of CF, the Cystic Fibrosis Questionnaire-Revised (CFQ-R), is the predominant tool utilized for investigating patient perspectives. It has been employed to assess the impact of ETI on pwCF many times in the past [5,6]. Other than the CFQ-R, very few patient-directed surveys on the perception of symptom changes, treatment burden and quality of life have been conducted in the years since ETI approval.

Treatment burden due to daily treatment regimens in pwCF is generally high, with considerable time and effort dedicated each day to therapy strategies [11]. Hence, minimizing therapy burden is becoming a key aspect of the advantages that new CF drugs can offer. In fact, reduction of treatment burden was identified as the number one priority in CF research topics in a survey conducted in 2018 [12], while Cameron et al. even reported that pwCF would be willing to trade key objectives such as extended life expectancy or increased lung function in exchange for a reduction in treatment time or burden [13]. Since the emergence of modulator therapies and their unparalleled alleviative effect on signs and symptoms of CF, it comes as no surprise that the question arises if continuation of the time-consuming pre-existing therapies is still necessary. First short-term studies suggest that reduction of inhaled hypertonic saline and dornase alfa are non-inferior to continued therapy [14,15]. Necessary long-term studies are currently underway [16,17]. However, since ETI can only restore CFTR function to about 50 % of wild-type [18] (depending on the underlying genotype) and potential long-term negative effects of supportive therapy de-escalation have not been investigated yet, exercising caution when reducing supportive therapies remains important. Still, despite the current lack of consensus on this topic, a reduction in the use of supportive therapies was reported in several studies [19–21], making the establishment of guidelines and recommendations on this topic even more essential. Currently, the extent to which pwCF are reducing supportive therapies, in collaboration with their physicians or independently, remains unknown and would provide a valuable source of information for physicians to counsel pwCF accordingly.

Therefore, the aim of this study was to investigate if and to what extent pwCF are reducing supportive therapies after ETI initiation and to identify the factors involved, including patient-reported symptom changes and treatment burden.

2. Materials and methods

2.1. Ethics approval

The study was approved by the Ethical Committee of the Medical Faculty of Leipzig University (177/22-ek). All members of the German Cystic Fibrosis Association have given written informed consent to being contacted for research purposes. All survey participants consented to anonymous and confidential participation; refusal or withdrawal resulted in exclusion from the survey.

2.2. Survey design

A 17-item cross-sectional survey was designed and divided into two subsections (Suppl. Table S1). The first covered questions regarding general aspects, therapy burden and different dimensions of wellbeing (treatment burden, quality of life (QoL), physical capacity and capacity to handle everyday tasks), rated on a scale from 1 (severe burden/very poor) to 5 (no burden/very good). The second subsection was modulator-therapy-specific and was therefore only accessible for participants receiving CFTR modulator therapy. Participants rated the effect of the modulator on symptoms and supportive therapy on a 6-point scale. For comparability, the subsequent analysis included only pwCF receiving ETI (n = 276).

To preserve anonymity, no identifying data such as genotype or precise age was enquired. An option not to respond was offered in the majority of questions. Wherever applied, percentages refer to the total (*n*) of participants that answered the question.

2.3. Inclusion criteria and distribution

The questionnaire was created in German using the cloud-based software SoSci Survey [22], which was kindly made available to the German Cystic Fibrosis Association Mukoviszidose e.V. The link was distributed via email by the Mukoviszidose e.V. on July 19th, 2022 to 1589 members of the German Cystic Fibrosis Association: 825 parents of adolescents with CF and 764 adult pwCF. Parents of children younger than 12 years were excluded. A reminder for participation in the survey was sent out on August 18th, and the questionnaire was closed for accession on September 11th, 2022.

2.4. Statistical analysis

Descriptive statistics are given as counts and percentages. In addition, the distribution of the reported change in symptoms were visualized as Likert plot. The change in usage of different supportive therapies was assessed using univariable logistic regression models with sex, age, QoL, percent predicted Forced Expiratory Volume in 1 s (ppFEV1), therapy burden, and ETI's effect on the different symptoms. Effects are reported as odds ratios and 95 %-confidence intervals. A posthoc list of all possible group comparisons were created according to Tukey's Honest Significant Difference method. In addition, we visualized the resulting proportions.

We evaluated the representativeness of the cohort by calculating standardized mean differences (SMDs) compared to data from the German CF Registry, as far as it was openly available [23]. Differences were interpreted as follows: ≤ 0.1 as negligible, ≤ 0.2 as minor, ≤ 0.3 as moderate, and >0.3 as noticeable. This approach allowed us to quantify how closely the study cohort reflected the broader CF population.

Proportions were compared by applying proportion tests. All analyses were carried out using R Statistical Software (v4.1.1) [24]. The significance level was set to $\alpha = 0.05$.

3. Results

3.1. Participants

406 participants completed the survey, 400 of which gave informed consent for further evaluation. Effective response rate was 25.5 %, limiting generalizability to the broader CF population. Participants' basic characteristics are listed in Table 1. 304 (76 %) of them had previously received or were receiving modulator therapy (ETI or other) at the time of participation. The vast majority (n = 276, 91 %) were taking ETI. Of the 276 pwCF receiving ETI, 212 (77 %) had not previously received modulator therapy. More than half of the participants receiving ETI were taking it for a duration of >2 years (52 %).

Comparison with the German Cystic Fibrosis Registry regarding sample representativeness showed that differences were negligible for the age groups 12–18 (SMD 0.09) and 31–40 (SMD 0.05), moderate for 18–30 (underrepresented, SMD 0.30), and noticeable for >40 (overrepresented, SMD 0.35). Regarding sex distribution, women were moderately overrepresented in our cohort at 58 % (SMD 0.20) compared to 48.1 % in the registry.

3.2. Treatment burden

Treatment burden and wish for reduction of supportive therapies were evaluated amongst pwCF receiving ETI therapy (pwCF-ETI) and pwCF not receiving modulator therapy (pwCF-nomt) (Fig. 1A and B).

PwCF-nomt reported more often to have a strong therapy burden compared to pwCF-ETI (18.8 % vs 6.5 %, $p < 0.001$), while both groups reported similar levels of severe burden (3.3 % vs. 3.1 %). PwCF ETI reported significantly more often that they were not burdened at all by their regimen (17.8 % vs. 6.2 %, $p = 0.006$, Fig. 1A).

Most pwCF preferred to maintain their current supportive therapy, although a notable portion expressed interest in reducing it. There were varying preferences between pwCF-ETI and pwCF-nomt. PwCF-nomt wished for regimen intensification more often than pwCF-ETI across all therapy components (Fig. 1B).

3.3. Effect of ETI

There were big improvements in all categories of life after ETI initiation (e.g. Quality of Life, physical fitness and everyday tasks, Suppl. Fig. S1 and S2), while almost half (48.2 %) of pwCF reported not having any adverse events (Suppl. Fig. S3).

Table 1
Characteristics as reported by the pwCF; data is presented as *n* (%), whereas *n* constitutes the amount of pwCF who answered the question.

Age *(n = 400)*	
<18 years of age	84 (21 %)
18–30 years of age	83 (21 %)
31–40 years of age	105 (26 %)
>40 years of age	128 (32 %)
Sex *(n = 399)*	
Male	168 (42 %)
Female	231 (58 %)
Occupation *(n = 392)*	
Employed	164 (42 %)
Not in employment (e.g. unable to work, parental leave, …)	120 (30 %)
Student	108 (28 %)
Lung function *(n = 392)*	
Not reduced (FEV1 >80 %)	177 (45 %)
Reduced (FEV1 50–80 %)	144 (37 %)
Notably reduced (FEV1 30 %–50 %)	59 (15 %)
Strongly reduced (FEV1 <30 %)	12 (3 %)
pwCF and modulator therapy *(n = 400)*	
Receiving CFTR modulator	304 (76 %)
Of which receiving ETI	276 (91 %)
Time since administration of ETI *(n = 270)*	
<12 months	44 (16 %)
>1 year	86 (32 %)
>2 years	130 (48 %)
>3 years	10 (4 %)

3.4. Change in supportive therapies during ETI treatment

Symptom reduction was most pronounced for cough and sputum (93 % and 91 %, respectively) amongst pwCF receiving ETI, while bowel symptoms were more often reported as unchanged or even increased (Fig. 2A).

222 out of the 276 pwCF on ETI (80.4 %) stated to have reduced their supportive therapies presently or in the past. All studied therapies showed some degree of reduction among pwCF, with mucoactive inhalations and systemic antibiotics demonstrating a more than 50 % decrease. Inhaled antibiotics, physiotherapy, and high-calorie foods were reduced by approximately a third, whereas insulin and pancreatic enzymes were reduced by only 14.4 % and 11.7 %, respectively (Fig. 2B).

After ETI initiation, 59.6 % of pwCF reported that intravenous antibiotics were no longer needed, followed by 55.2 % of pwCF reporting fewer inpatient treatments, whereas only 2.8 % deemed pancreatic enzyme replacements superfluous (Suppl. Fig. S4).

A logistic regression analysis was used to analyse the relationship between symptom improvement and treatment reduction in pwCF receiving ETI (Fig. 3).

A tendency (significant or not) towards therapy adjustments was observed for the following coherences: a) pwCF with reduced cough were less likely to see a reduction in antibiotic inhalations but more likely to experience a decrease in systemic antibiotics and mucoactive inhalations; b) pwCF with reduced bacterial pathogens in the airways were more likely to have reduced antibiotic inhalations and systemic antibiotics; c) pwCF with reduced sputum production were found to be more likely to experience a reduction in mucoactive inhalations but less likely to see a decrease in antibiotic inhalations.

Age: The odds of reducing antibiotic inhalation were lowest in 12-17-year-olds (21 %), increasing to 32 % in 18-30-year-olds and 49 % in 30-40-year-olds, the latter being significantly different from the youngest age group (OR = 3.8, $p = 0.004$). For patients older than 40, the rate dropped to 41 % (Fig. 4D). A similar pattern was found for systemic antibiotics (Fig. 4G), while we found no age trend for mucoactive inhalations (Fig. 4A).

FEV1: The group size of pwCF with ppFEV1 <30 % was too small to draw valid conclusions (n = 10). PwCF with a ppFEV1 above 50 % were significantly more likely to reduce mucoactive inhalations than those with a ppFEV1 of 30–50 % (Fig. 4B). PwCF with a ppFEV1 above 80 % were significantly less likely to reduce antibiotic inhalations than all other groups (Fig. 4E). For systemic antibiotics, there was no significant difference between the groups. (Fig. 4H).

QoL: We found increasing QoL associated with a decreasing reduction probability for antibiotic inhalation. Consequently, pwCF with a perceived very good QoL were less likely to reduce antibiotic inhalations than those with bad or intermediate QoL (Fig. 4F). No consistent association was observed for mucoactive inhalations (Fig. 4C) or systematic antibiotics (Fig. 4I).

There was no significant difference in the probabilities of reducing supportive therapies between male and female pwCF (Suppl. Fig. S5, top panel). Therapy burden was significant only for systemic antibiotics, with the likelihood of systemic antibiotic reduction decreasing as therapy burden increased. (Suppl. Fig. S5, bottom panel).

4. Discussion

Whether or not pwCF have been reducing supportive therapies while taking ETI and the safety of such reductions is a subject of ongoing research. Studies addressing this issue reported that short-term reductions in supportive therapy are non-inferior to continued therapy in

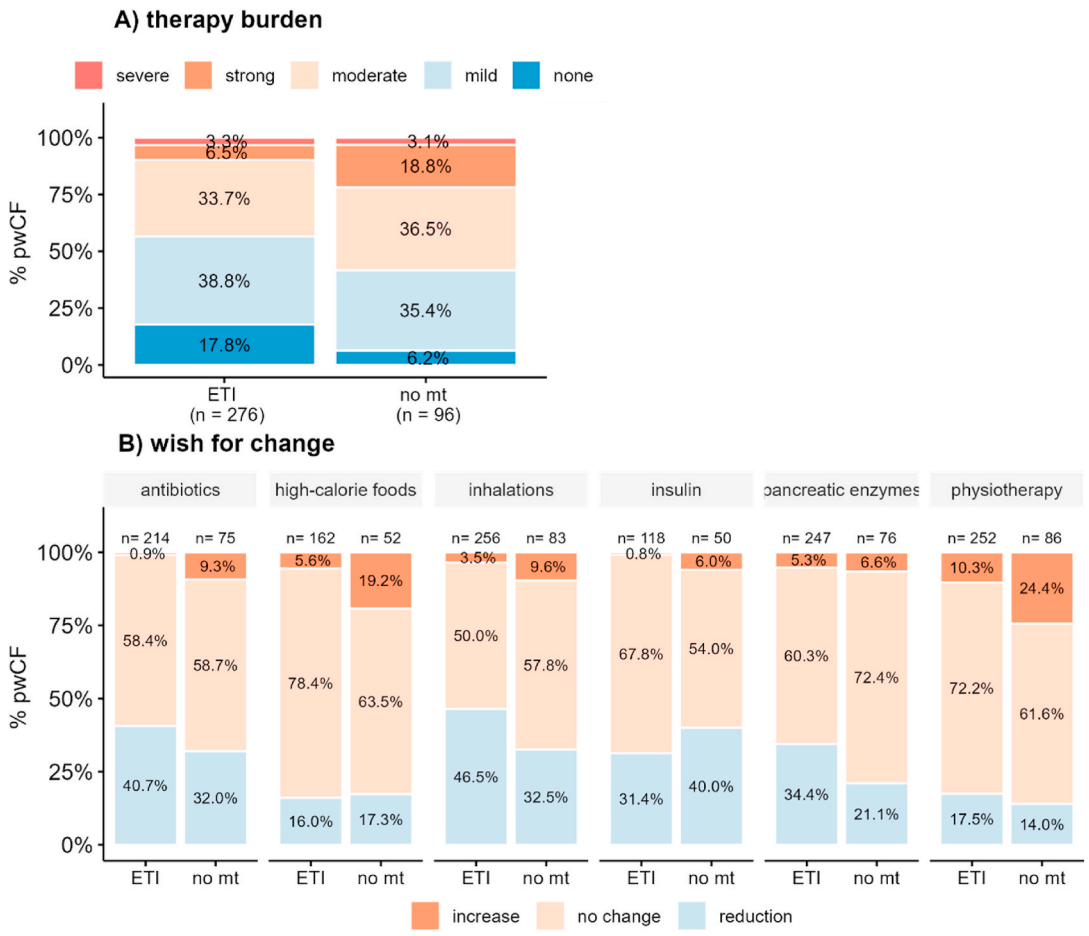

Fig. 1. Self-reported treatment burden and wish for change of conventional therapies; **A** therapy burden between pwCF-ETI & pwCF-nomt ranging from none to severe; **B** wish for change in pwCF-ETI & pwCF-nomt regarding supportive therapies (antibiotics (both inhaled and systemic), high-calorie foods, mucoactive inhalations, insulin, pancreatic enzyme replacements & physiotherapy) ranging from wish for reduction to wish for increase of the respective component; n refers to the number of pwCF who answered the question; ETI = receiving ETI Therapy, no mt = not receiving modulator therapy.

terms of maintaining pulmonary stability [14,15], while pwCF are already reported to reduce their supportive therapies in other studies [19–21]. However, since a methodological bias cannot be ruled out in these studies, and to capture the therapy changes made by pwCF as accurately as possible, we conducted an anonymized survey on patient-reported outcomes, to our knowledge, for the first time.

As shown earlier [25], an increase in treatments results in a greater treatment burden, and in our study, this burden was generally higher in pwCF-nomt. This is consistent with an actual reduction of supportive therapies and with previous reports of time savings for airway clearance upon ETI initiation [26]. Similarly, reducing inhaled therapies, antibiotic intake and pancreatic enzyme replacement (PERT) were areas where pwCF most wished for a reduction. This aligns with the findings of Davies et al., who identified these three aspects as among the top five most burdensome components for pwCF. [27]. Interestingly, insulin therapy, taken for CF-related diabetes (CFRD) by up to 32.6 % of pwCF in Europe [28], was perceived in our survey as more burdensome by pwCF without modulator therapy than pwCF receiving ETI, in line with reports of ETI being associated with improved glucose regulation [29]. A considerable number of pwCF not receiving ETI treatment expressed a preference for increasing supportive therapies, particularly physiotherapy and high-calorie foods. This desire may be attributed to the higher disease burden in this group. QoL, physical performance and ability to perform everyday tasks all improved with ETI treatment, confirming previous reports[30–32].

In our study, pwCF receiving ETI therapy reported very little adverse events. Notably, there were reports of worsening symptoms related to sleep and concentration. This is consistent with recent studies that highlighted that sleep difficulties have newly arisen in children with CF, ranging from 10 % [33] to as high as 49 % [34]. Additionally, the latter study reported that 33 % of children developed attention-deficit hyperactivity disorder, and 2 % reported difficulty concentrating. Similar results were reported in 7.1 % of adult pwCF by Spoletini et al. [35].

The primary focus of our survey was to determine whether pwCF are reducing supportive therapies under ETI treatment. The study design did not reveal whether these reductions were made on physicians' recommendations or autonomously. However, since prior research shows patients often withhold information from doctors due to fear of judgment [36], we believed an anonymous survey would encourage more honest responses and reduce bias. Discontinuation of supportive therapies was reported by the majority of pwCF and for all therapies enquired, with a clear trend of primarily reducing their mucoactive therapies. This aligns with study results indicating a decrease in prescription refills for dornase alfa and hypertonic saline in the period following ETI initiation [20,21]. Interestingly, some pwCF reported reducing their use of antidiabetic therapies and PERT, albeit fewer than pwCF reducing mucoactive therapies. Despite the widely held view that modulator therapy usually cannot restore pancreatic function, some reports show evidence of reversibility of exocrine pancreatic insufficiency following ivacaftor treatment [37] and even following ETI treatment [38], as well as a decrease in refilled prescriptions for PERT medication [20,21]. Endocrine pancreatic function seems to improve with the advance of ETI as well [39,40], although the underlying mechanisms are not yet fully understood.

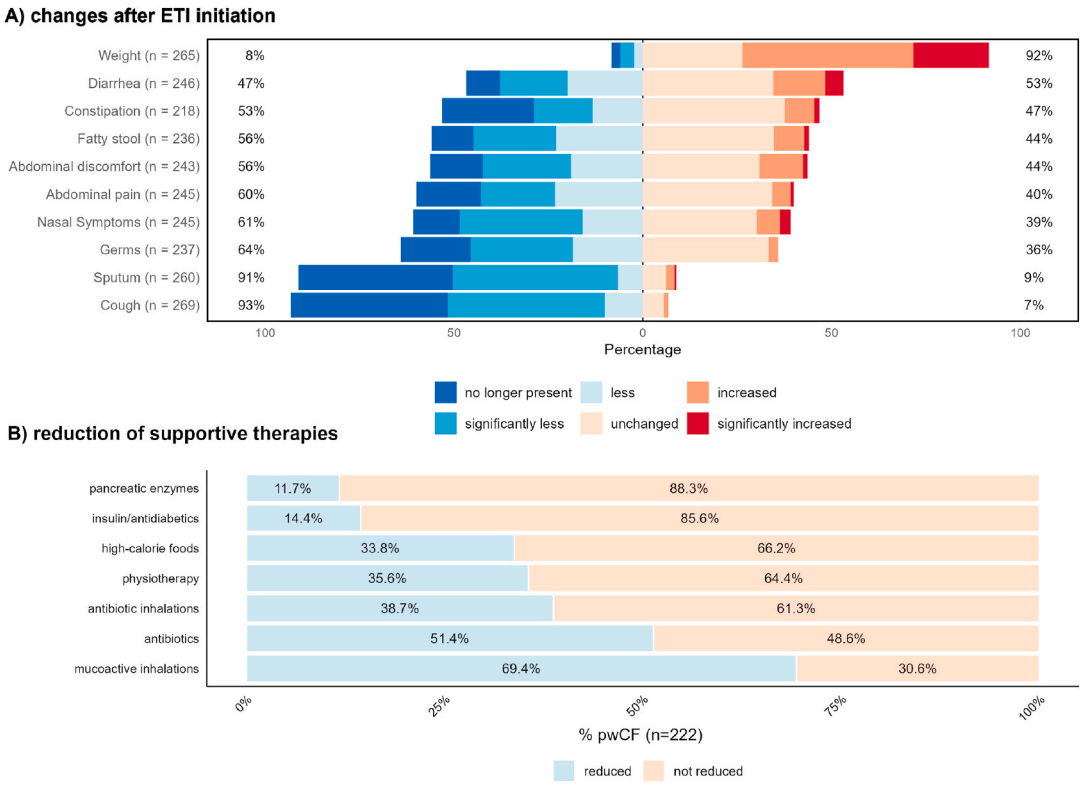

Fig. 2. A Likert plot of self-reported (symptom) changes of pwCF after ETI initiation, ranging from no longer present to significantly increased, n differs depending on how many pwCF answered the question **B** Self-reported reduction of supportive therapies; n = 222 for each treatment - number of pwCF who stated to have reduced supportive therapies in the past 3.5. Therapy reduction based on symptom change.

We aimed to understand the relationship between discontinuing supportive therapies and the degree of reduced symptom severity. While statistically significant associations were few, notable trends emerged: we found that fewer airway pathogens increased the likelihood of reducing both inhaled and systemic antibiotic use, consistent with recent reports on reduced lung infection after ETI initiation [41,42]. Interestingly, in our survey, fewer coughs correlated with continued inhaled-antibiotic therapy, but there was a trend towards reduced systemic antibiotics and mucoactive inhalations. This suggests a commitment to fully eradicating airway pathogens under ETI therapy, sustaining inhaled antibiotics, while reducing treatments for burdensome mucus clearance and acute infections, possibly due to less mucus production and fewer exacerbations [43]. Similar associations were obtained for reduced sputum production. It appears plausible that different motivations drive the reduction or continuation of supportive therapies: 1. the desire to reduce therapy burden (particularly for the most burdensome treatments, inhaled therapies and antibiotic intake), 2. a rational adjustment of therapy dosage or frequency in response to reduced symptom severity, or 3. a commitment to maximizing the therapeutic effects by continuing supportive therapies to amplify the positive impact of ETI symptom alleviation. These motivations might interact and conflict, leading to the observed variance in the relationship between symptom reduction and adherence to supportive therapies.

To further investigate confounding variables for the probability of supportive therapy reduction, we investigated the influence of age, sex, ppFEV1, therapy burden and QoL on answers given. While there was no significant influence of sex on the probability of reducing supportive therapies, age influenced antibiotic use, but not mucoactive inhalations. The strongest trends toward antibiotic use reduction were observed among adults between the ages of 30 and 40, whereas adolescents reported reductions less frequently. Possible explanations for these observations are: 1. Adolescents may still be under the influence of their parents regarding therapy adherence. This is demonstrated by a significantly higher belief in treatment necessity in parents compared to their children aged 11–18 years [44], with recognition of treatment importance as a key driver of therapy adherence [45]. Additionally, therapy adherence has been shown to worsen with age and disease severity [46]. 2. Airway infection with CF-associated pathogens, which necessitates antibiotic treatments, occurs more frequently in older pwCF, indicating a lesser need for antibiotics and a lower therapy burden for adolescents [47]. Indeed, a 2022 observational study on pwCF with advanced lung disease and a median age of 31.1 years showed a 97 % reduction in pulmonary exacerbation rates and subsequent antibiotic use following ETI treatment [48]. Similarly, since ETI's approval in 2020, antibiotic-treated exacerbations per year among older people with CF have dropped significantly from 75-85 % to 25–35 % in Germany. Similar reductions, starting from a lower baseline, are also observed in adolescent pwCF [23]. It is important to note that questions regarding therapy adherence for pwCF under 18 were answered by their parents or guardians, which introduces the potential for biased responses that may not fully reflect the adolescents' perspectives.

Lung function, evaluated using ppFEV1, showed a positive effect on the likelihood of reducing mucoactive inhalations in pwCF and a ppFEV1 $>$ 50 %. This trend may be due to increased confidence from better overall lung function as well as association with lesser mucus production. However, we did not differentiate between mucoactive inhalations, such as hypertonic saline and dornase alfa, leaving it unclear which treatment was reduced earlier or more frequently. Individuals with severely reduced ppFEV1 ($<$30 %) did not significantly differ from other groups in their likelihood of reducing mucoactive inhalations. However, the interpretation is limited by the small sample size (n = 10). It is also possible that other factors such as improvements in QoL, might play a more significant role for this severely affected group. Individuals with ppFEV1 $>$ 80 % were less likely to reduce their antibiotic inhalations compared to other groups. Besides the abovementioned factors regarding younger age in this group, a motivation for complete

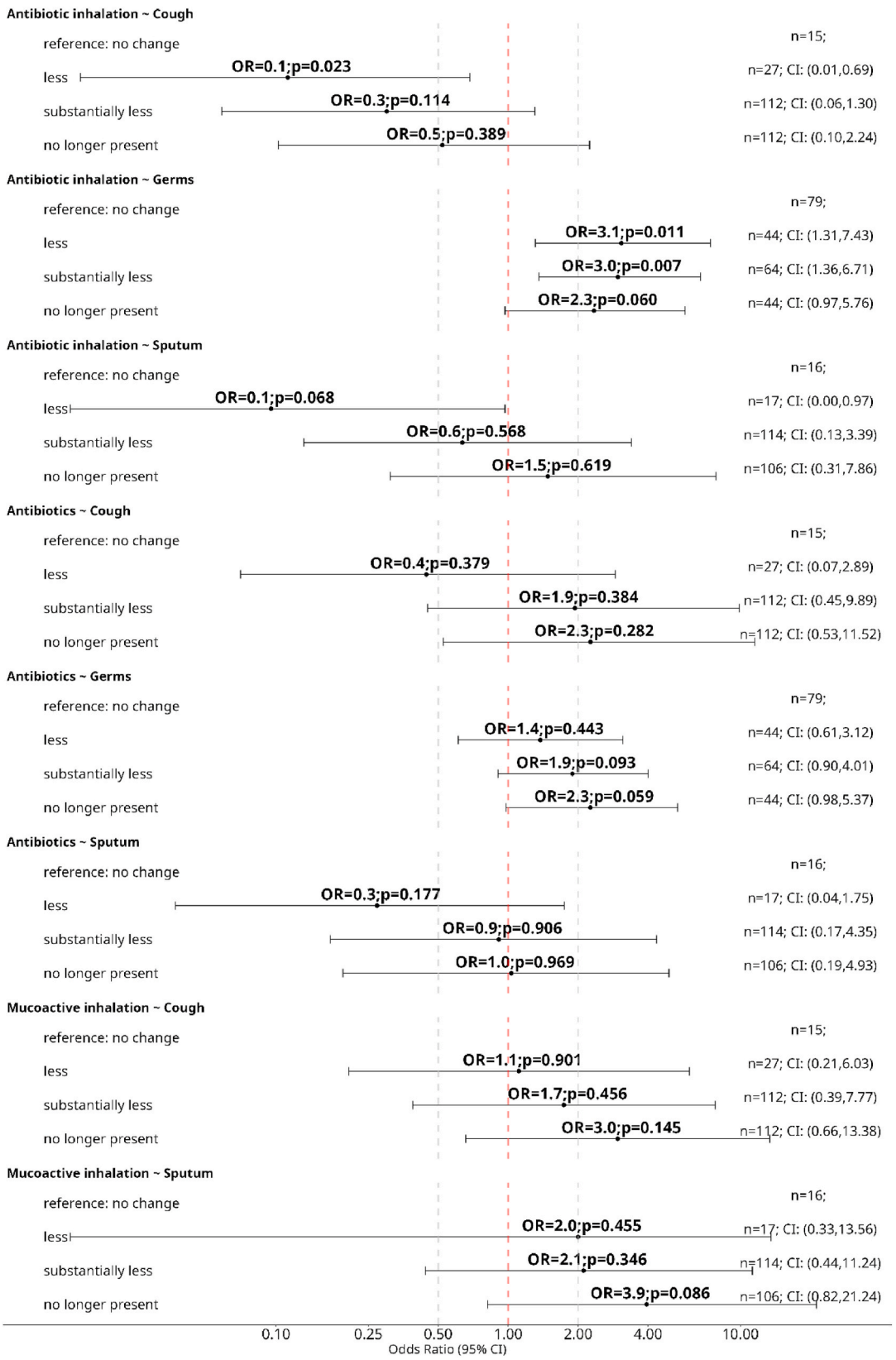

Fig. 3. Logistic regression analysis showing the association between symptom changes and the likelihood to reduce supportive therapies. Shown are odds ratios (OR) and their 95 % confidence interval (CI) as well as group size (n) and p-values. OR < 1 indicates a smaller likelihood to reduce supportive therapies, while OR >1 points towards a tendency to reduce supportive therapies. Dotted red line indicates OR of 1, dotted grey lines indicate ORs of 0.5 and 2 for easier interpretation. Reference group comprises pwCF who indicated no change of the respective symptoms. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

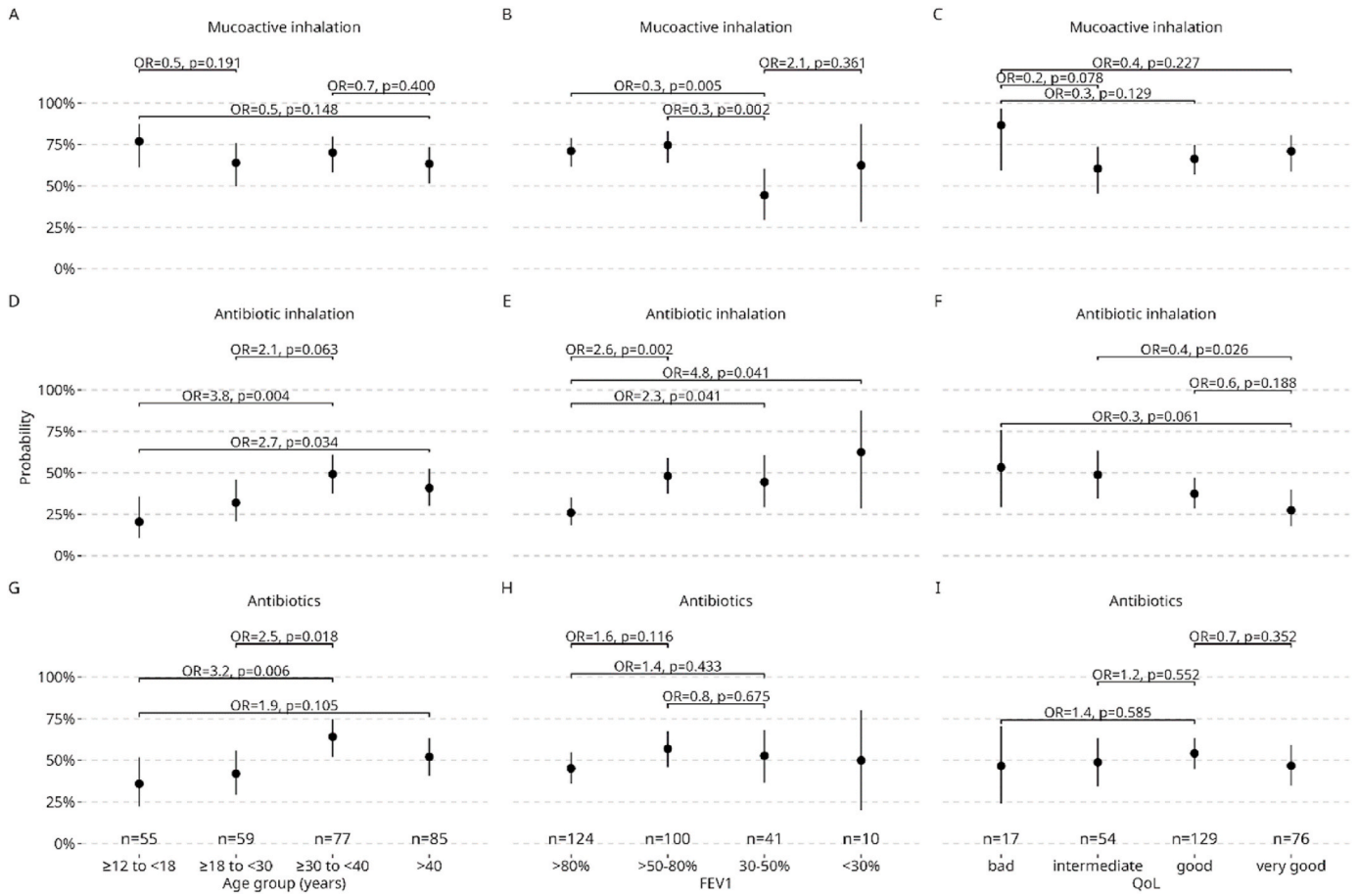

Fig. 4. Effect plots showing group differences regarding age (**A**, **D**, **G**), ppFEV1 (**B**, **E**, **H**) and QoL (**C**, **F**, **I**); ORs for reducing supportive therapies (columns) are added for the three strongest effects, i.e. group comparisons. A complete list of group comparisons including ORs and p-values can be found in Suppl. Table S2; shown are effects on probabilities for therapy reduction of mucoactive inhalations (column 1), antibiotic inhalations (column 2) and systemic antibiotics (column 3), depending on the abovementioned parameters; The three smallest p-values per comparison are indicated in the subplots.

pathogen eradication might motivate them to continue with supportive therapies. Additionally, older pwCF (often those with lower ppFEV1) experience higher rates of structural lung damage, which can limit the effectiveness of inhaled antibiotics due to inhomogeneous particle distribution in the peripheral airways [49], contributing to the decision to reduce inhaled antibiotics and favour systemic ones instead. These findings are supported by reports that pwCF who have better QoL and lower disease burden are less likely to reduce inhaled antibiotics, highlighting a close link between ppFEV1, therapy burden, and QoL.

Current guidelines and research take a cautious approach to reducing supportive therapies during ETI treatment and highlight the need for further research. Gramegna et al., in a recent Delphi consensus, recommend individualized decisions with regular monitoring, noting that inhaled antibiotics should generally not be discontinued in a majority of pwCF [50]. Similarly, the ECFS standards for the care of pwCF emphasize careful assessment and suggest that therapy reduction may be considered only when high-quality evidence supports it, with clear criteria for resuming treatment [51]. In this context, our results provide further insights into current therapy adherence among pwCF in Germany, but it does not address the clinical consequences of therapy reduction, which should be evaluated in future studies. Accordingly, our study does not aim to make recommendations regarding the continuation or discontinuation of supportive therapies, and it does not imply that such recommendations should be included in future guidelines. It is important to keep in mind, that discontinuation of supportive therapies may carry significant risks. In clinical studies, ETI treatment restored CFTR activity partially—41.8 % in F508del heterozygotes and 45.9 % in homozygotes [18]—yet disease symptoms are still expected with CFTR function in this range [52,53]. In real-world settings, functional restoration may differ. Furthermore, while ETI improves mucus plugging, it does not normalize it, and structural lung damage such as bronchiectasis persists [54,55]. Consequently, an increase in pulmonary exacerbations, bacterial infections, inflammation, and bronchiectasis is conceivable if supportive therapies are reduced, warranting further investigation. Studies with ivacaftor in G551D patients showed that *Pseudomonas aeruginosa* density initially decreased but rebounded within one year, with persistent infection [56]. Similar patterns have been observed in ETI-treated pwCF [57], indicating that discontinuation of inhaled or systemic antibiotics may increase the risk of lung infections. The updated ECFS guidelines highlight that respiratory physiotherapy remains essential even in the era of CFTR modulators [51]. Reducing or discontinuing such therapies could negatively affect airway clearance and exercise capacity.

This study has several important limitations to consider. First, the cross-sectional design captures responses at a single time point, precluding temporal inferences between ETI initiation and changes in supportive therapy use. It also cannot rule out reverse causality or confounding factors such as baseline symptom severity, regional differences in healthcare access, or fluctuations in service availability during the COVID-19 pandemic, so causal interpretations remain speculative. Future prospective cohort or nested case-control studies are needed to confirm these patterns. Second, the survey was conducted exclusively among members of the German Cystic Fibrosis Association, potentially introducing selection bias related to socioeconomic status,

education, digital access, or engagement with patient organizations. Participants with greater health literacy or proactive disease management may be overrepresented, and demographic characteristics, baseline health status, and therapy availability can vary across regions, limiting generalizability to other CF populations and healthcare systems. Third, our study cohort showed some differences compared to the broader CF population in the German Cystic Fibrosis Registry. In particular, young adults aged 18–30 were slightly underrepresented, participants over 40 were overrepresented, and women were moderately overrepresented. These discrepancies may reflect differential engagement with patient organizations or survey participation and should be considered when interpreting our findings. Consequently, the generalizability of our results to the overall CF population, particularly in certain age groups or in males, may be limited. Finally, proxy responses for adolescents aged 12–18 may not fully capture their perspectives, and self-reported data are subject to recall bias, particularly for pre-ETI therapy use. Variability in interpretation of survey questions and Likert scales may affect accuracy, and the modest sample size with uneven outcome distributions limits multivariable analyses and statistical power to detect subtle associations.

In conclusion, our survey results not only confirm previous findings on the positive effects of ETI on symptoms and QoL, but also reveal that a substantial number of pwCF are already reducing their supportive therapies despite the absence of guidelines on how to do so safely. We suggest that decisions regarding the (dis-)continuation of supportive therapies are influenced by multiple factors beyond physicians' recommendations, including the desire to reduce therapy burden, the wish to improve health, and responses to alleviated symptoms. These sometimes conflicting motivations underscore the need for further studies to better understand these factors. In line with current guidelines [50], we think it best to develop comprehensive recommendations for both individuals with CF and their healthcare providers, guiding them toward optimal, individualized therapy approaches.

CRediT authorship contribution statement

S. Ahting: Conceptualization, Software, Formal analysis, Writing – original draft, Data curation, Visualization. **M. Vogel:** Software, Formal analysis, Writing – review & editing, Data curation, Visualization. **B. Wollschläger:** Formal analysis, Conceptualization, Writing – review & editing, Methodology. **C. Henn:** Conceptualization, Writing – review & editing, Resources. **C. Ludwig:** Data curation, Writing – review & editing. **U. Issa:** Data curation, Writing – review & editing. **A.-L. Strehlow:** Resources, Methodology, Writing – review & editing, Conceptualization, Software. **M. vom Hove:** Data curation, Writing – review & editing, Resources. **J. Hentschel:** Formal analysis, Supervision, Data curation, Project administration, Writing – review & editing, Investigation, Validation. **F. Prenzel:** Conceptualization, Methodology, Validation, Investigation, Supervision, Data curation, Project administration, Writing – review & editing.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT in order to improve language and readability of the work. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: FP received personal fees from Sanofi Aventis, Allergopharma, Stallergenes Greer, Vertex Pharmaceuticals, Takeda Pharma, and ALK-Abelló outside of the submitted work. MvH received personal fees from Vertex Pharmaceuticals. BW received personal fees from Vertex Pharmaceuticals outside of the submitted work.

All other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2025.108464.

Supplementary materials

Supplementary material associated with this article can be found, in the online version.

References

[1] J. Guo, A. Garratt, A. Hill, Worldwide rates of diagnosis and effective treatment for cystic fibrosis, J. Cyst. Fibros. 21 (3) (2022) 456–462, https://doi.org/10.1016/j.jcf.2022.01.009.
[2] F. Ratjen, S.C. Bell, S.M. Rowe, C.H. Goss, A.L. Quittner, A. Bush, Cystic fibrosis, Nat. Rev. Dis. Primers 1 (2015) 15010, https://doi.org/10.1038/nrdp.2015.10.
[3] M. Lopes-Pacheco, N. Pedemonte, G. Veit, Discovery of CFTR modulators for the treatment of cystic fibrosis, Expet Opin. Drug Discov. 16 (8) (2021) 897–913, https://doi.org/10.1080/17460441.2021.1912732.
[4] M. Lopes-Pacheco, CFTR modulators: the changing face of cystic fibrosis in the era of precision medicine, Front. Pharmacol. 10 (2019) 1662, https://doi.org/10.3389/fphar.2019.01662.
[5] H.G.M. Heijerman, E.F. McKone, D.G. Downey, E. van Braeckel, S.M. Rowe, E. Tullis, et al., Efficacy and safety of the elexacaftor plus tezacaftor plus ivacaftor combination regimen in people with cystic fibrosis homozygous for the F508del mutation: a double-blind, randomised, phase 3 trial, Lancet 394 (10212) (2019) 1940–1948, https://doi.org/10.1016/S0140-6736(19)32597-8.
[6] P.G. Middleton, M.A. Mall, P. Dřevínek, L.C. Lands, E.F. McKone, D. Polineni, et al., Elexacaftor-tezacaftor-ivacaftor for cystic fibrosis with a single Phe508del allele, N. Engl. J. Med. 381 (19) (2019) 1809–1819, https://doi.org/10.1056/NEJMoa1908639.
[7] M. Bacalhau, M. Camargo, G.A.V. Magalhães-Ghiotto, S. Drumond, C.H. M. Castelletti, M. Lopes-Pacheco, Elexacaftor-tezacaftor-ivacaftor: a life-changing triple combination of CFTR modulator drugs for cystic fibrosis, Pharmaceuticals 16 (3) (2023), https://doi.org/10.3390/ph16030410.
[8] N. Kapouni, M. Moustaki, K. Douros, I. Loukou, Efficacy and safety of elexacaftor-tezacaftor-ivacaftor in the treatment of cystic fibrosis: a systematic review, Children 10 (3) (2023), https://doi.org/10.3390/children10030554.
[9] G. Kotronoulas, N. Kearney, R. Maguire, A. Harrow, D. Di Domenico, S. Croy, et al., What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials, J. Clin. Oncol. 32 (14) (2014) 1480–1501, https://doi.org/10.1200/JCO.2013.53.5948.
[10] E. Basch, L. Barbera, C.L. Kerrigan, G. Velikova, Implementation of Patient-Reported Outcomes in Routine Medical Care, vol. 38, Am Soc Clin Oncol Educ Book, 2018, pp. 122–134, https://doi.org/10.1200/EDBK_200383.
[11] G.S. Sawicki, D.E. Sellers, W.M. Robinson, High treatment burden in adults with cystic fibrosis: challenges to disease self-management, J. Cyst. Fibros. 8 (2) (2009) 91–96, https://doi.org/10.1016/j.jcf.2008.09.007.
[12] N.J. Rowbotham, S. Smith, P.A. Leighton, O.C. Rayner, K. Gathercole, Z.C. Elliott, et al., The top 10 research priorities in cystic fibrosis developed by a partnership between people with CF and healthcare providers, Thorax 73 (4) (2018) 388–390, https://doi.org/10.1136/thoraxjnl-2017-210473.

[13] R.A. Cameron, D. Office, J. Matthews, M. Rowley, J. Abbott, N.J. Simmonds, et al., Treatment preference among people with cystic fibrosis: the importance of reducing treatment burden, Chest 162 (6) (2022) 1241–1254, https://doi.org/10.1016/j.chest.2022.07.008.

[14] N. Mayer-Hamblett, F. Ratjen, R. Russell, S.H. Donaldson, K.A. Riekert, G. S. Sawicki, et al., Discontinuation versus continuation of hypertonic saline or dornase alfa in modulator treated people with cystic fibrosis (SIMPLIFY): results from two parallel, multicentre, open-label, randomised, controlled, non-inferiority trials, Lancet Respir. Med. 11 (4) (2023) 329–340, https://doi.org/10.1016/S2213-2600(22)00434-9.

[15] E.L. Guenther, K.S. McCoy, M. Eisner, S. Bai, C.J. Nemastil, K.J. Novak, et al., Impact of chronic medication de-escalation in patients with cystic fibrosis taking elexacaftor, tezacaftor, ivacaftor: a retrospective review, J. Cyst. Fibros. (2023), https://doi.org/10.1016/j.jcf.2023.03.018.

[16] CF STORM, Available from: https://www.cfstorm.org.uk/.

[17] HERO-2, Available from: https://apps.cff.org/trials/finder/details/646/HERO-2?_ga=2.166495741.21884570.1689935875-658564453.1609879192.

[18] S.Y. Graeber, C. Vitzthum, S.T. Pallenberg, L. Naehrlich, M. Stahl, A. Rohrbach, et al., Effects of elexacaftor/tezacaftor/ivacaftor therapy on CFTR function in patients with cystic fibrosis and one or two F508del alleles, Am. J. Respir. Crit. Care Med. 205 (5) (2022) 540–549, https://doi.org/10.1164/rccm.202110-2249OC.

[19] D.P. Nichols, A.C. Paynter, S.L. Heltshe, S.H. Donaldson, C.A. Frederick, S. D. Freedman, et al., Clinical effectiveness of elexacaftor/tezacaftor/ivacaftor in people with cystic fibrosis: a clinical trial, Am. J. Respir. Crit. Care Med. 205 (5) (2022) 529–539, https://doi.org/10.1164/rccm.202108-1986OC.

[20] J.T. Song, S. Desai, A.N. Franciosi, R.V.E. Dagenais, B.S. Quon, Research letter: the impact of elexacaftor/tezacaftor/ivacaftor on adherence to nebulized maintenance therapies in people with cystic fibrosis, J. Cyst. Fibros. 21 (6) (2022) 1080–1081, https://doi.org/10.1016/j.jcf.2022.05.005.

[21] R de Vuyst, C.W. Kam, C.J. McKinzie, C.R. Esther, Medication utilization and lung function changes after initiation of treatment with elexacaftor/tezacaftor/ivacaftor, Pediatr. Pulmonol. (2024), https://doi.org/10.1002/ppul.27018.

[22] D.J. Leiner, Sosci Survey, 2019. Version 3.1.06.

[23] L. Nährlich, M. Burkhart, J. Wosniok, German Cystic Fibrosis Registry: Annual Report 2023 2024, vol. 26, 2024.

[24] R Core Team, R: a Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria, 2025.

[25] R. Altabee, S.B. Carr, J. Abbott, R. Cameron, D. Office, J. Matthews, et al., Exploring the nature of perceived treatment burden: a study to compare treatment burden measures in adults with cystic fibrosis version 1; peer review: 2 approved, NIHR Open Res 2 (2022) 36, https://doi.org/10.3310/nihropenres.13260.1.

[26] C. Blardone, S. Gambazza, A. Mariani, R. Galgani, A. Brivio, R.M. Nobili, et al., Perceived burden of respiratory physiotherapy in people with cystic fibrosis taking elexacaftor-tezacaftor-ivacaftor combination: a 1-year observational study, Ther. Adv. Respir. Dis. 18 (2024) 17534666241235054, https://doi.org/10.1177/17534666241235054.

[27] G. Davies, N.J. Rowbotham, S. Smith, Z.C. Elliot, K. Gathercole, O. Rayner, et al., Characterising burden of treatment in cystic fibrosis to identify priority areas for clinical trials, J. Cyst. Fibros. 19 (3) (2020) 499–502, https://doi.org/10.1016/j.jcf.2019.10.025.

[28] H.V. Olesen, P. Drevinek, V.A. Gulmans, E. Hatziagorou, A. Jung, M. Mei-Zahav, et al., Cystic fibrosis related diabetes in Europe: prevalence, risk factors and outcome; Olesen et al, J. Cyst. Fibros. 19 (2) (2020) 321–327, https://doi.org/10.1016/j.jcf.2019.10.009.

[29] M. Salazar-Barragan, D.R. Taub, The effects of elexacaftor, tezacaftor, and ivacaftor (ETI) on blood glucose in patients with cystic fibrosis: a systematic review, Cureus 15 (7) (2023) e41697, https://doi.org/10.7759/cureus.41697.

[30] R. Kos, A.H. Neerincx, D.W. Fenn, P. Brinkman, R. Lub, S.E.M. Vonk, et al., Real-life efficacy and safety of elexacaftor/tezacaftor/ivacaftor on severe cystic fibrosis lung disease patients, Pharmacol Res Perspect 10 (6) (2022) e01015, https://doi.org/10.1002/prp2.1015.

[31] W. Gruber, F. Stehling, C. Blosch, S. Dillenhoefer, M. Olivier, F. Brinkmann, et al., Longitudinal changes in habitual physical activity in adult people with cystic fibrosis in the presence or absence of treatment with elexacaftor/tezacaftor/ivacaftor, Front Sports Act Living 6 (2024) 1284878, https://doi.org/10.3389/fspor.2024.1284878.

[32] L. Piehler, R. Thalemann, C. Lehmann, S. Thee, J. Röhmel, Z. Syunyaeva, et al., Effects of elexacaftor/tezacaftor/ivacaftor therapy on mental health of patients with cystic fibrosis, Front. Pharmacol. 14 (2023) 1179208, https://doi.org/10.3389/fphar.2023.1179208.

[33] H. Pham, M. Vandeleur, R.M. Mainzer, S. Ranganathan, Mental health, sleep, and respiratory health after initiating elexacaftor/tezacaftor/ivacaftor treatment in children with cystic fibrosis, Pediatr. Pulmonol. (2024), https://doi.org/10.1002/ppul.27100.

[34] I. Sermet-Gaudelus, S. Benaboud, S. Bui, T. Bihouée, S. Gautier, Behavioural and sleep issues after initiation of elexacaftor-tezacaftor-ivacaftor in preschool-age children with cystic fibrosis, Lancet 404 (10448) (2024) 117–120, https://doi.org/10.1016/S0140-6736(24)01134-6.

[35] G. Spoletini, L. Gillgrass, K. Pollard, N. Shaw, E. Williams, C. Etherington, et al., Dose adjustments of elexacaftor/tezacaftor/ivacaftor in response to mental health side effects in adults with cystic fibrosis, J. Cyst. Fibros. 21 (6) (2022) 1061–1065, https://doi.org/10.1016/j.jcf.2022.05.001.

[36] L. Vogel, Why do patients often lie to their doctors? CMAJ (Can. Med. Assoc. J.) 191 (4) (2019) E115 https://doi.org/10.1503/cmaj.109-5705.

[37] D. Munce, M. Lim, K. Akong, Persistent recovery of pancreatic function in patients with cystic fibrosis after ivacaftor, Pediatr. Pulmonol. 55 (12) (2020) 3381–3383, https://doi.org/10.1002/ppul.25065.

[38] N. Stastna, L. Kunovsky, M. Svoboda, E. Pokojova, L. Homola, M. Mala, et al., Improved nutritional outcomes and gastrointestinal symptoms in adult cystic fibrosis patients treated with elexacaftor/tezacaftor/ivacaftor, Dig. Dis. 42 (4) (2024) 361–368, https://doi.org/10.1159/000538606.

[39] K.J. Scully, P. Marchetti, G.S. Sawicki, A. Uluer, M. Cernadas, R.E. Cagnina, et al., The effect of elexacaftor/tezacaftor/ivacaftor (ETI) on glycemia in adults with cystic fibrosis, J. Cyst. Fibros. 21 (2) (2022) 258–263, https://doi.org/10.1016/j.jcf.2021.09.001.

[40] F. Lurquin, M. Buysschaert, V. Preumont, Advances in cystic fibrosis-related diabetes: current status and future directions, Diabetes Metabol. Syndr. 17 (11) (2023) 102899, https://doi.org/10.1016/j.dsx.2023.102899.

[41] A.-M. Dittrich, S. Sieber, L. Naehrlich, M. Burkhart, S. Hafkemeyer, B. Tümmler, Use of elexacaftor/tezacaftor/ivacaftor leads to changes in detection frequencies of Staphylococcus aureus and Pseudomonas aeruginosa dependent on age and lung function in people with cystic fibrosis, Int. J. Infect. Dis. 139 (2024) 124–131, https://doi.org/10.1016/j.ijid.2023.11.013.

[42] L. Schaupp, A. Addante, M. Völler, K. Fentker, A. Kuppe, M. Bardua, et al., Longitudinal effects of elexacaftor/tezacaftor/ivacaftor on sputum viscoelastic properties, airway infection and inflammation in patients with cystic fibrosis, Eur. Respir. J. 62 (2) (2023), https://doi.org/10.1183/13993003.02153-2022.

[43] S. Sutharsan, S. Dillenhoefer, M. Welsner, F. Stehling, F. Brinkmann, M. Burkhart, et al., Impact of elexacaftor/tezacaftor/ivacaftor on lung function, nutritional status, pulmonary exacerbation frequency and sweat chloride in people with cystic fibrosis: real-world evidence from the German CF registry, Lancet Reg Health Eur 32 (2023) 100690, https://doi.org/10.1016/j.lanepe.2023.100690.

[44] N.A. Goodfellow, A.F. Hawwa, A.J. Reid, R. Horne, M.D. Shields, J.C. McElnay, 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. 15 (2015) 43, https://doi.org/10.1186/s12890-015-0038-7.

[45] G.S. Sawicki, K.S. Heller, N. Demars, W.M. Robinson, Motivating adherence among adolescents with cystic fibrosis: youth and parent perspectives, Pediatr. Pulmonol. 50 (2) (2015) 127–136, https://doi.org/10.1002/ppul.23017.

[46] Llorente RP. Arias, C. Bousoño García, J.J. Díaz Martín, Treatment compliance in children and adults with cystic fibrosis, J. Cyst. Fibros. 7 (5) (2008) 359–367, https://doi.org/10.1016/j.jcf.2008.01.003.

[47] B. Coburn, P.W. Wang, J. Diaz Caballero, S.T. Clark, V. Brahma, S. Donaldson, et al., Lung microbiota across age and disease stage in cystic fibrosis, Sci. Rep. 5 (2015) 10241, https://doi.org/10.1038/srep10241.

[48] V. Carnovale, P. Iacotucci, V. Terlizzi, C. Colangelo, L. Ferrillo, A. Pepe, et al., Elexacaftor/tezacaftor/ivacaftor in patients with cystic fibrosis homozygous for the F508del mutation and advanced lung disease: a 48-Week observational study, J. Clin. Med. 11 (4) (2022), https://doi.org/10.3390/jcm11041021.

[49] A.M. Akkerman-Nijland, O.W. Akkerman, F. Grasmeijer, P. Hagedoorn, H. W. Frijlink, B.L. Rottier, et al., The pharmacokinetics of antibiotics in cystic fibrosis, Expert Opin. Drug Metab. Toxicol. 17 (1) (2021) 53–68, https://doi.org/10.1080/17425255.2021.1836157.

[50] A. Gramegna, S. Aliberti, M.A. Calderazzo, R. Casciaro, C. Ceruti, G. Cimino, et al., The impact of elexacaftor/tezacaftor/ivacaftor therapy on the pulmonary management of adults with cystic fibrosis: an expert-based Delphi consensus, Respir. Med. 220 (2023) 107455, https://doi.org/10.1016/j.rmed.2023.107455.

[51] K.W. Southern, C. Addy, S.C. Bell, A. Bevan, U. Borawska, C. Brown, et al., Standards for the care of people with cystic fibrosis; establishing and maintaining health, J. Cyst. Fibros. 23 (1) (2024) 12–28, https://doi.org/10.1016/j.jcf.2023.12.002.

[52] M. Mei-Zahav, A. Orenti, A. Jung, E. Kerem, Variability in disease severity among cystic fibrosis patients carrying residual-function variants: data from the european cystic fibrosis society patient registry, ERJ Open Res 11 (1) (2025), https://doi.org/10.1183/23120541.00587-2024.

[53] F.J. Accurso, F. van Goor, J. Zha, A.J. Stone, Q. Dong, C.L. Ordonez, et al., Sweat chloride as a biomarker of CFTR activity: proof of concept and ivacaftor clinical trial data, J. Cyst. Fibros. 13 (2) (2014) 139–147, https://doi.org/10.1016/j.jcf.2013.09.007.

[54] P. McNally, K. Lester, G. Stone, B. Elnazir, M. Williamson, Cox Des, et al., Improvement in lung clearance index and chest computed tomography scores with elexacaftor/tezacaftor/ivacaftor treatment in people with cystic fibrosis aged 12 years and older - the RECOVER trial, Am. J. Respir. Crit. Care Med. 208 (9) (2023) 917–929, https://doi.org/10.1164/rccm.202308-1317OC.

[55] R. Bec, M. Reynaud-Gaubert, F. Arnaud, R. Naud, N. Dufeu, M. Di Bisceglie, et al., Chest computed tomography improvement in patients with cystic fibrosis treated with elexacaftor-tezacaftor-ivacaftor: early report, Eur. J. Radiol. 154 (2022) 110421, https://doi.org/10.1016/j.ejrad.2022.110421.

[56] S.L. Heltshe, N. Mayer-Hamblett, J.L. Burns, U. Khan, A. Baines, B.W. Ramsey, et al., Pseudomonas aeruginosa in cystic fibrosis patients with G551D-CFTR treated with ivacaftor, Clin. Infect. Dis. 60 (5) (2015) 703–712, https://doi.org/10.1093/cid/ciu944.

[57] C.R. Armbruster, Y.K. Hilliam, A.C. Zemke, S. Atteih, C.W. Marshall, J. Moore, et al., Persistence and evolution of Pseudomonas aeruginosa following initiation of highly effective modulator therapy in cystic fibrosis, mBio 15 (5) (2024) e0051924, https://doi.org/10.1128/mbio.00519-24.