

Discovering new challenges and biopsychosocial changes in time of CFTR modulators

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**Spanish Cystic Fibrosis Psychology Group of the Spanish Cystic
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The Spanish Group of Psychology for Cystic Fibrosis (GEPS-FQ), formed by workers from the associations that make up the Spanish Federation of Cystic Fibrosis, was born from the interest of unifying, complementing and developing professional knowledge and experience, with the aim of improving prevention and psychological intervention within the Cystic Fibrosis (CF) framework.

Recent medical and pharmacological advances in the therapeutic process of Cystic Fibrosis (CF) have made it possible to extend its effectiveness not only in treating the signs and symptoms associated with this disease, but also in attempting to regulate and even restore the function of the CF-causing CFTR protein (Aspinall, et al. 2022). Since the approval of funding in Spain for the triple modulatory therapy *Elexacaftor-Tezacaftor-Ivacaftor* in November 2021 for people over 12 years of age and from October 2022 for children aged 6-12 years, physical, psychological and social changes have been seen in the lives of people with CF who have been able to access these treatments. In some cases, these changes have been so significant that they have led to a substantial improvement in the quality of life of these people (Aspinall et al., 2022; Heneghan et al., 2022; Regard et al., 2022), even in patients with severely advanced disease, improving enough to be removed from transplant lists (Delgado, 2021).

In general, these treatments are associated with improvements in respiratory symptoms: such as lung function, number of exacerbations, symptoms such as cough and expectoration (Heneghan et al., 2022); nutritional status (Delgado, 2021); emotional experience of the disease through the feeling of hope, normality and independence and openness to establish new and unthinkable social and personal milestones (Aspinall et al., 2022). For all these reasons, they represent a fundamental turning point in the therapeutic approach to CF and open up an immense field for us to explore and analyse the impact of these treatments in all areas for people with CF.

The present study arose from the motivation to observe the effects that medication with CFTR modulators, following the start of treatment with *Kaftrio*[®], had had on the lives of CF patients from the first week of treatment.

The main objective of the study is to find out the changes experienced by patients receiving triple therapy treatment at the physical, psychological, social and treatment levels. Knowing the changes experienced will allow us to know where we should direct our research in the face of new modulators from the field of psychology, that is, how to use the data obtained to develop coping

strategies that allow us to address those aspects that are identified as problematic or worthy of being addressed as a result of the analysis of the results.

Method

Study design and participants

Observational and descriptive data collection was carried out through the creation of a questionnaire aimed at people with CF over 16 years of age belonging to CF Associations in Spain, with the aim of observing the effects experienced by CF patients from the first week of treatment with *Kaftrio*[®] medication.

The inclusion criteria for participation in the study were to be as follows: a person with CF over 16 years of age, to belong to one of the associations of the Spanish Cystic Fibrosis Federation (FEFQ), to have taken *Kaftrio*[®] medication for at least one week at the time of completing the questionnaire, and to have signed the informed consent form for participation in the study. The exclusion criteria included children under 16 years of age, as well as unidentified values or conflicting answers. Participation was voluntary and anonymous.

The initial sample consisted of 67 people, six of whom were excluded from the study because they did not meet the inclusion requirements agreed by the GEPS-FQ. Finally, the sample (represented by *n*) consisted of 61 people with CF, 42 women (69%) and 19 men (31%) (figure 1), aged between 16 and 65 years (figure 2). All of them lived in Spain, in the following autonomous communities: Andalusia, Principality of Asturias, Castilla la Mancha, Community of Valencia, Extremadura, Galicia, Madrid, Region of Murcia and the Basque Country.

It should be noted that not all respondents started taking medication at the same time, so the data obtained corresponds to people who started treatment in a time frame between January 2020 and April 2022.

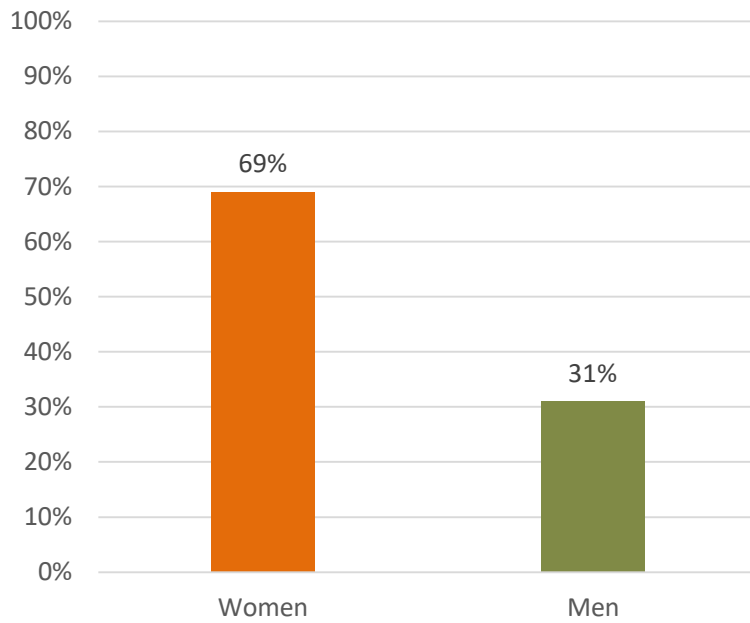


Figure 1. Gender of participants

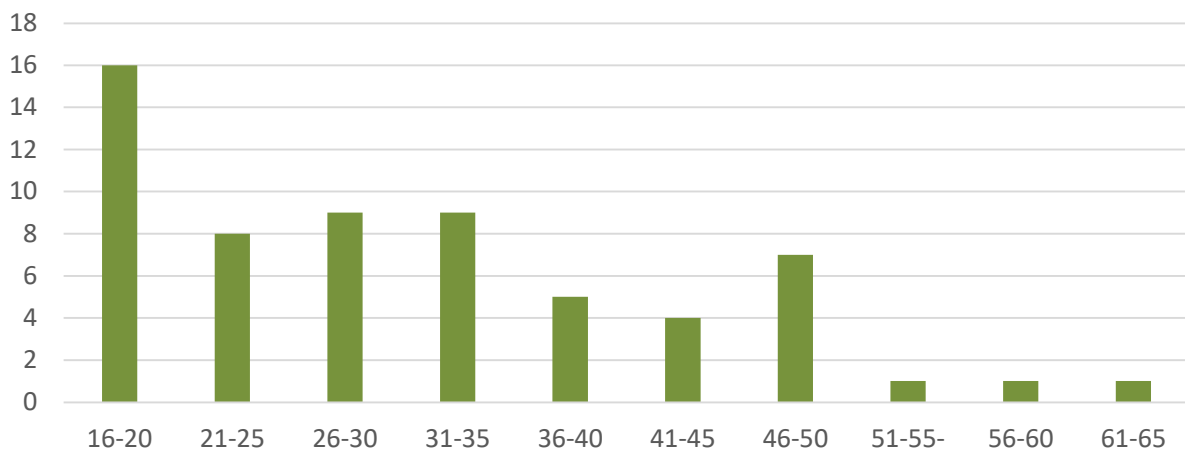


Figure 2. Age of participants

Questionnaire

To collect the information, an anonymous and confidential "ad hoc" digital questionnaire was developed and presented under the title "*Kaftrio*[®] and me". The tool collected, in addition to demographic data, 30 questions that were grouped into four factors: a) physical aspects, b) psychological aspects, c) social aspects and d) treatment-related aspects.

The factor "physical aspects" was composed of 12 items related to the following variables: changes in mucus, cough, taste, sleep, skin, appetite, energy level, changes in activity and difficulties associated with such changes.

The factor "psychological aspects" included 8 items related to the following variables: Changes in basic emotions, joy, fear, anger, sadness, as well as levels of uncertainty, coping and other perceived emotional changes.

The factor "social aspects" included 3 items related to the variables: changes in family and/or social communication, changes at work level.

The factor "treatments" collected 7 items related to the variables: Start of treatment, changes in treatment, taking other modulators and testimonials.

The questions were formulated in a combined form, using Likert-type scales from 0 to 10 and open-ended questions to collect personal experiences, which were then categorised into 3 groups (less, equal or more) for statistical analysis.

Procedure

In the first phase, the study design and the development of the questionnaire were carried out. These were carried out by the GEPS-FQ through videoconference meetings.

The Google Form was then transferred to CF Associations for dissemination to partners via email and/or mailing lists.

Data analyses were performed using descriptive statistics, referring to categorical variables in terms of percentage and frequency analyses.

Results

The results extracted in relation to the frequency of the participants' responses are presented below. Each of the dimensions included in the questionnaire are analysed separately.

I. Physical factor

To the question "Did you notice any changes during the first week?" (figure 3) 80.33% (n=49) of the sample reported noticing changes, while only 19.67% (n=12) did not notice any changes.

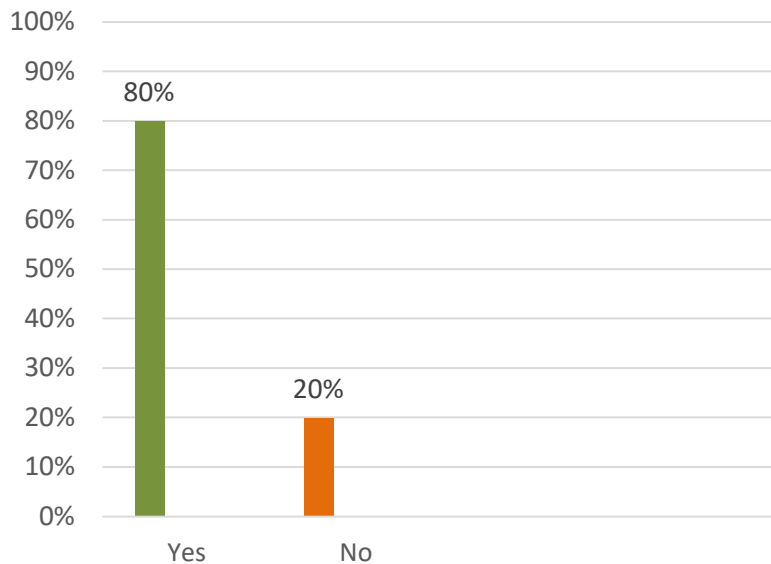


Figure 3. Changes during the first week of starting Kaftrio®.

In terms of the changes experienced, the use of open-ended questions allowed the participants' experiences to be captured:



"I started to cough up very dark coloured sputum, I felt it was less difficult to cough it up when doing physiotherapy".

Adult with CF, 20 years old



"Incredible increase in lung function within hours of first ingestion. Improved fatigue, increased vitality and much less expectoration. It's been like starting to breathe in a way I didn't know how.

Adult with CF, 29 years old

In addition, information was collected on the **typology of changes** experienced by the study participants. Thus, participants perceived desirable, undesirable, mixed or no change. Figure 4 shows that 51% (n=31) of respondents reported *desirable changes* since starting treatment with Kaftrio®, 10% (n=6) reported *undesirable changes*, 3% (n=2) reported both types of changes, and 36% (n=22) reported no change.

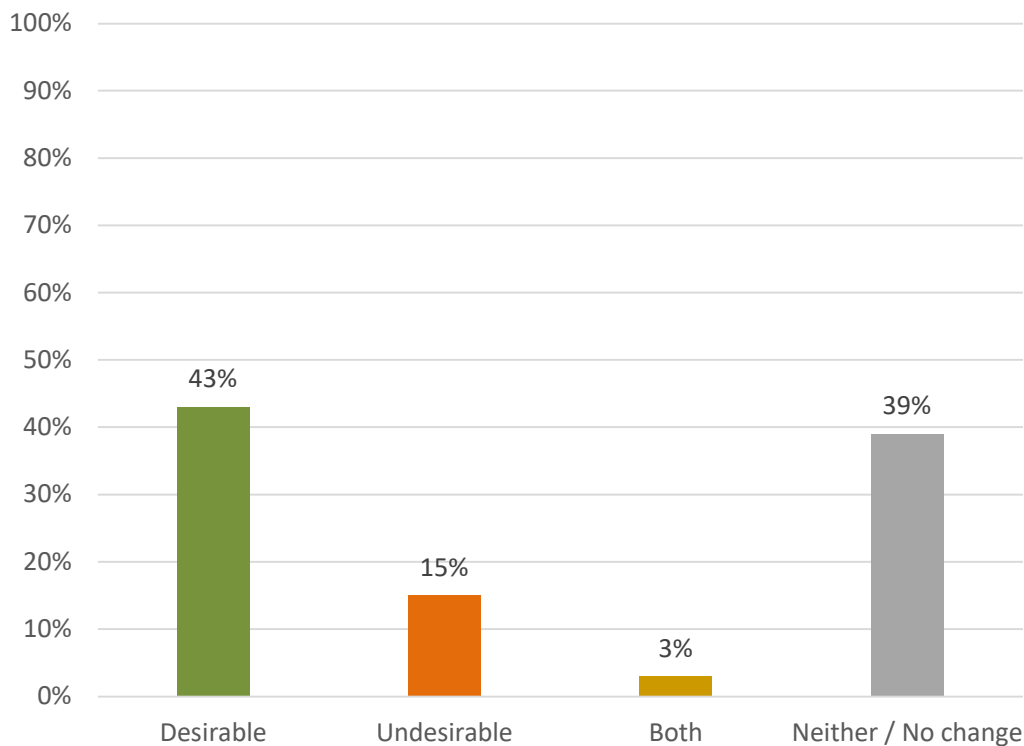


Figure 4. Desirable and undesirable changes of participants

Among the changes described as **desirable** are weight gain, less fatigue, more energy, more vitality, less coughing, less exhaustion with physiotherapy, more physical strength, agility, slightly increased oxygen saturation, more muscle mass, stronger hair perception, no sinus pain, better digestion, regular periods, thinner bodily fluids, softer skin, being able to sleep lying down, and increased chest circumference.

Conversely, perceived **undesirable** changes include a change in voice pitch, hair loss, allergic reactions, skin side effects (dryness and flaking), and abdominal distension.

The 3% who reported **mixed** changes described experiencing less fatigue and found it easier to gain muscle strength (desirable changes), and experiencing skin side effects and allergic reactions (undesirable changes).

In addition, this study also records changes in physical symptoms such as cough or mucus, changes in taste or appetite, sleep and energy level, assessing whether these changes are perceived

to have increased, decreased or, on the contrary, remained the same as before starting triple therapy treatment.

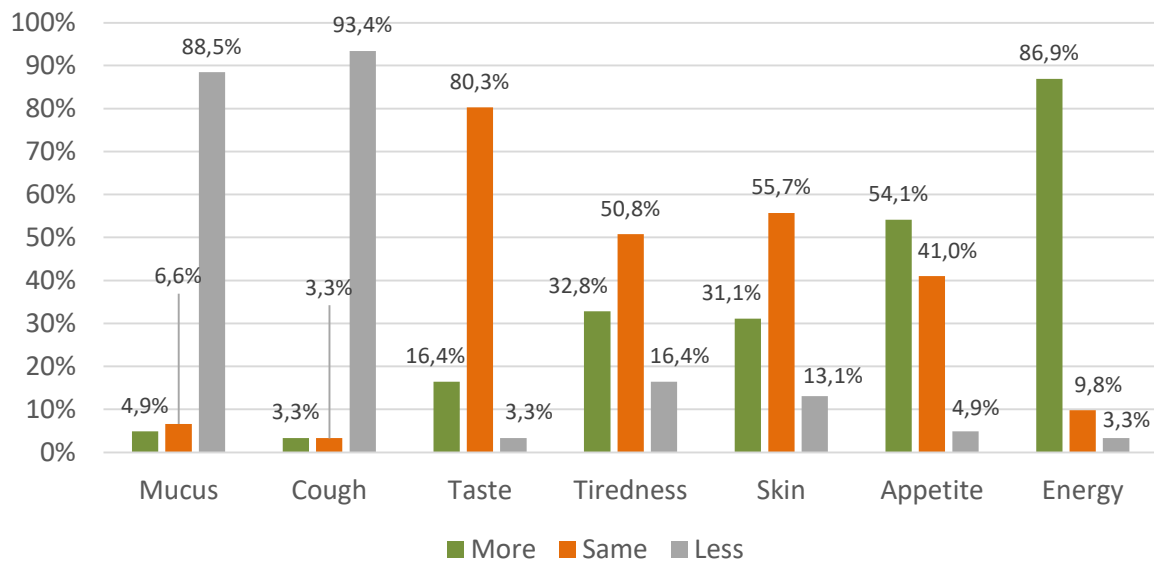


Figure 5. Participants' physical changes since taking Kaftrio®.

Figure 5 shows a marked decrease in symptoms associated with mucus and cough. Regarding **mucus**, 88.5% of the sample (n=54) reported that they had less mucus since the start of treatment; 6.6% (n=4) reported having the same mucus as before and only 4.9% (n=3) reported having much more mucus. A similar situation occurred with **coughing**: 93.4% of participants (n=57) reported coughing less than before, 3.3% (n=2) reported coughing more, and 3.3% (n=2) reported having no change or remaining the same as before.

Changes in taste, sleep and skin are similar: most participants had not experienced any changes, and only a minority reported feeling worse than before. This is especially notable in the case of **taste**, where 80.3% of the sample (n=49) reported no change, while 16.4% (n=10) reported more or stronger taste than before, and only 3.3% (n=2) reported a decrease in their sense of taste. In terms of **sleep**, 50.8% of participants (n=31) reported sleeping as usual, 32.8% (n=20) reported sleeping much more than before, and 16.4% (n=10) reported sleeping a little less. In terms of **skin changes**, 55.7% (n=34) said they perceived their skin as usual, 31.1% (n=19) did experience some skin changes, and 13.1% (n=8) had experienced fewer skin problems or changes.

Finally, increases in appetite and energy are noteworthy. Regarding **appetite**, 54.1% of participants (n=33) said they had more appetite than usual, 41% (n=25) had no change and only 4.9% (n=3) said they had less appetite than before. Similarly for **energy**: while 86.9% (n=53) had noticed an increase in their energy, 9.8% (n=60) did not notice any change and 3.3% (n=2) had seen a decrease in their energy level compared to before starting triple therapy treatment.

Finally, figure 6 shows the changes in **daily activity**: 72% (n=44) reported an increase in their activity, 28% (n=17) reported maintaining their activity, and none reported a decrease in activity since starting treatment.

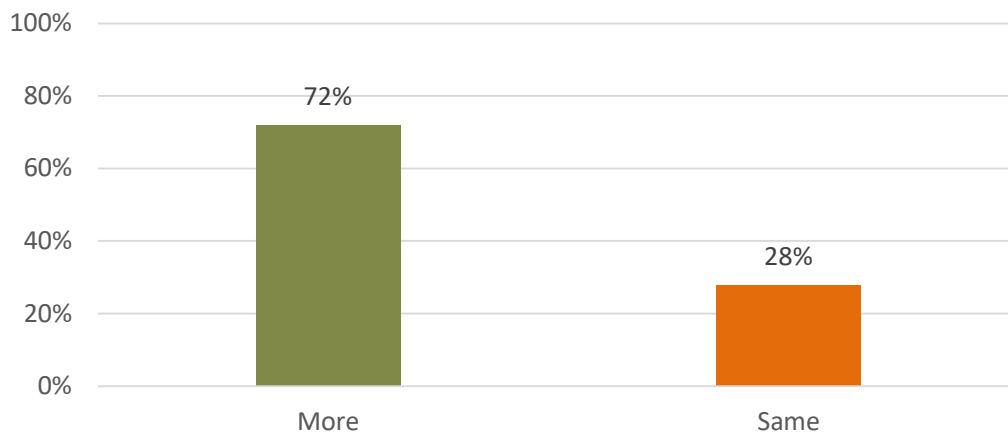


Figure 6. Changes in participant activity

When asked about the activities they had started to do, some people indicated that they had started to do sport, that they had less difficulty climbing stairs or walking and talking at the same time without getting tired. Some of the experiences shared are shown below:



"I've started walking more and going out more in general, instead of spending most of my time at home".

Adult with CF, 25 years old



"I've been encouraged to do some hiking, before I didn't do it because it was too much effort, now it's less difficult, although it's still a big effort for me. On the other hand, I notice that I have more strength in my arms, I can carry more weight without getting tired".

Adult with CF, 36 years old



"I do the same things, but I get less tired and I can do more "non-obligatory" things that I used to skip because I was tired (cooking desserts, cleaning the house more thoroughly, ...)".

Adult with CF, 49 years old

II. Psychological factor

The results show that the initiation of triple therapy treatment is associated with an increase in pleasant emotions and a decrease in unpleasant emotions.

Figure 7, which shows the basic emotions experienced at the start of treatment, shows a notable increase in **happiness** (80.3%, n=49), compared to a decrease in **fear** (61%, n=37), **anger** (75%, n=46) and **sadness** (64%, n=39).

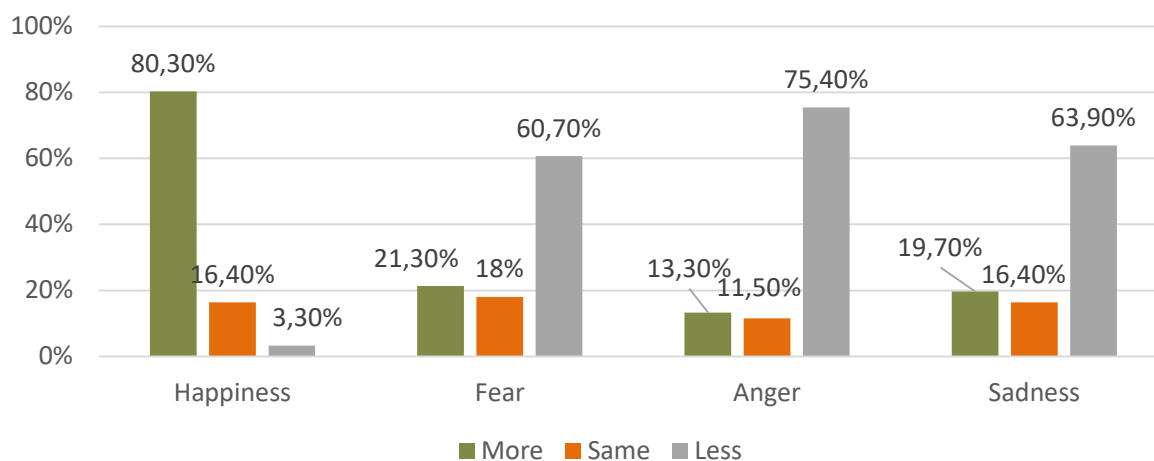


Figure 7. Emotional changes as perceived by participants

In addition, other emotions experienced by the participants were collected and classified according to whether they were experienced as a pleasant emotion, as an unpleasant emotion, or whether both types of emotions were experienced. In Figure 8 we can see that 43% of the sample (n=26) reported experiencing more pleasant emotions compared to 15% (n=9) who reported an increase in unpleasant emotions. Only 3% of the participants (n=2) reported feeling a mixture of both types of emotions. 39% (n=24) did not specify having experienced emotions other than primary emotions.

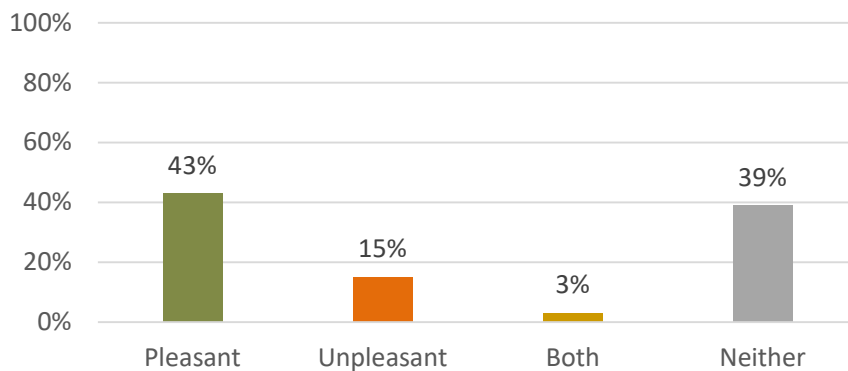


Figure 8. Participants' other emotions

The **pleasant** emotions that respondents reported experiencing were: euphoria, participation, joy, comfort, happiness, hope, relief, desire to do things and take on the world, patience, fulfilment, satisfaction, peace, tranquillity and optimism. In contrast, the emotions that were experienced as **unpleasant** were anxiety, sadness, nervousness, anguish, fear, disappointment, feeling overwhelmed and frustration. Those who reported experiencing a mixture of emotions reported happiness as pleasant, and frustration and fear as unpleasant.



"I have the feeling of being satisfied with what I do because now I can do more things".

Adult with CF, 24 years old

"I really want to do things and take on the world".

Adult with CF, 31 years old



"A lot of sadness, anxiety and a constant urge to cry".

Adult with CF, 30 years old

"I was a bit disappointed at some point, I thought I was going to get much better. Maybe my expectations were too high, having heard that other patients have come off the transplant list.

Adult with CF, 36 years old

Another psychological aspect observed in this study was the perceived change in the level of **uncertainty**, with a decrease in almost half of the sample. Figure 9 shows that 49% of the sample (n=30)

perceived less uncertainty than before, while 32.7% (n=20) reported experiencing more uncertainty than usual, and only 18% (n=11) reported no change.

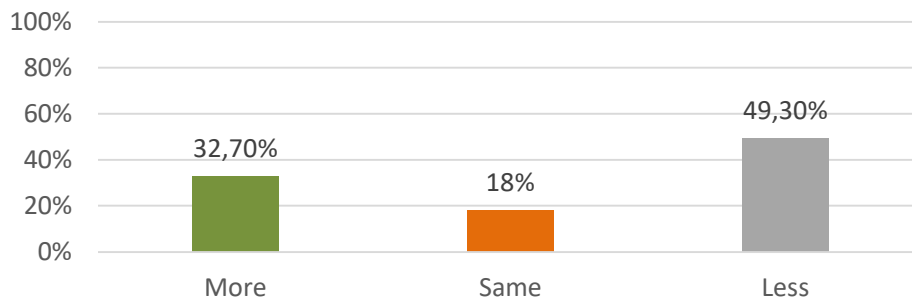


Figure 9. Changes in participants' uncertainty

Finally, table 1 shows the psychological impact of all the changes experienced in the various areas after starting treatment with *Kaftrio*[®]. Thirty-nine people reported feeling better about themselves, 35 indicated that they had become aware of the change in their state of health and 33 reported an improvement in their mood.

Item	<i>n</i>
I have become aware of my current health status vs. before taking <i>Kaftrio</i> [®] .	35
I feel better about myself	39
I feel safer	28
It has improved my mood	33
I have begun to question aspects of my life that I have not done before.	27
Another	6
No answer	1

Table 1. Psychological consequences of the changes experienced as a result of treatment with *Kaftrio*[®].

Notably, some of the participants added the following items to the above:

- ” ”
“ “ *“Before taking Kaftrio[®] I felt fine, but now I feel as if I don't have any illness and it's a great feeling.*

Adult with CF, 36 years old.
- ” ”
“ “ *“I've been off work for a long time, but since I've started taking Kaftrio[®] I think I'm able to go back to work.*

Adult with CF, 47 years old.

”
“

"The disease doesn't make my day-to-day life as difficult as it used to be".

Adult with CF, 39 years old.

”
“

"I feel less fear, more calm and more inner peace", adult with CF, 45 years old.

Adult with CF, 45 years old.

III. Social factor

The social factor collects information on changes in communication and at the work level.

Figure 10 shows the changes experienced in **communication at the family and/or social level**, where we can see that having started this new treatment was not associated with a decrease in communication. On the contrary, 31% (n=19) of the sample reported having experienced an increase in such communication, compared to 69% (n=42) who reported not having noticed any change in this respect.

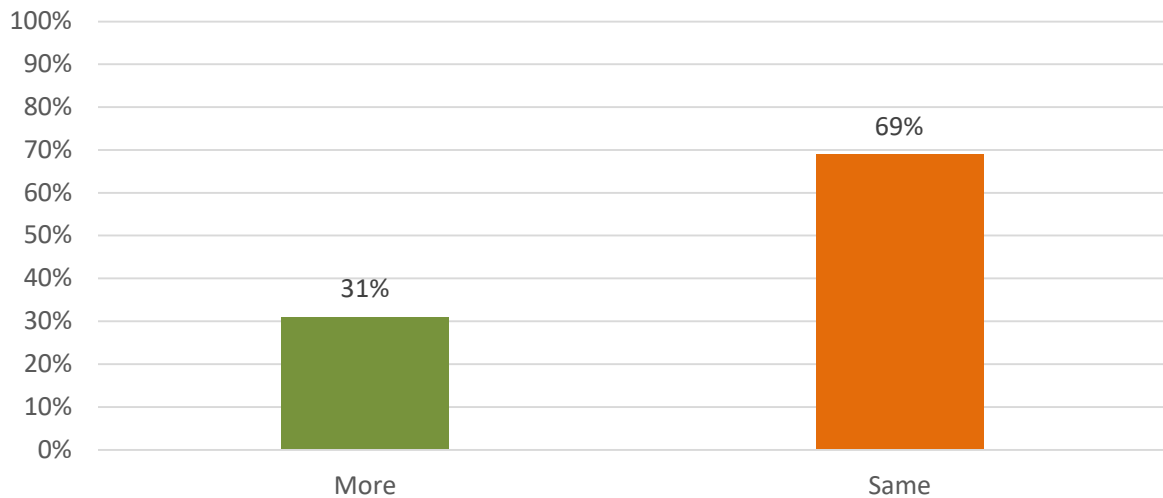


Figure 10. Changes in participants' family and social communication

Regarding the changes experienced in the **work environment** (see figure 11), it is worth highlighting the improvement in their work situation experienced by 44% (n=27) of the sample. On the other hand, more than half of the participants indicated that their employment situation was the

same as before the start of treatment (54%, n=33), and only one person (2%) indicated that their employment situation had worsened.

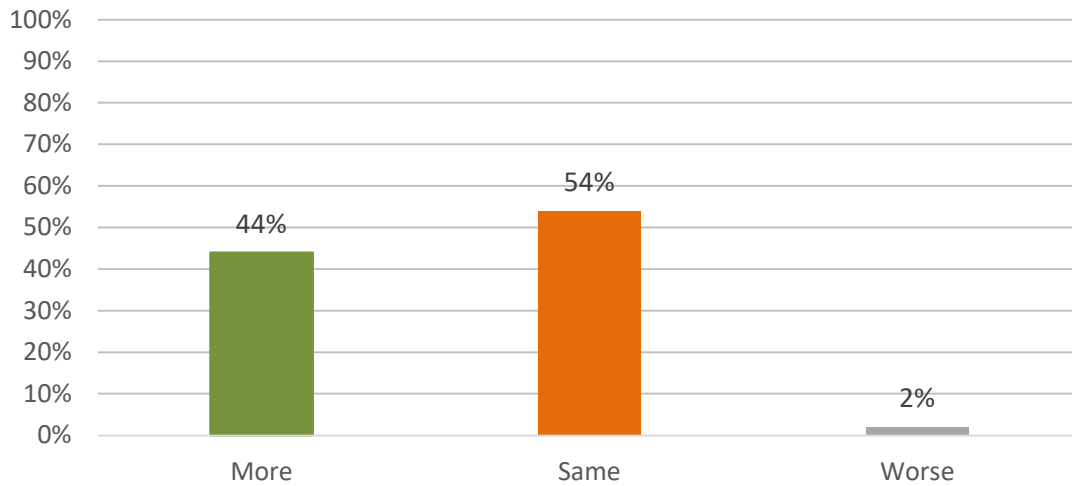


Figure 11. Participants' job changes

IV. Treatment factor

62% of the sample indicated that they had not taken any modulators previously, compared to 38% who had taken them.

Focusing on *Kaftrio*[®] intake, when asked about perceived changes in the performance of usual treatments (figure 12), 21% (n=13) of the sample reported less involvement in treatments, 49% (n=30) had made no changes and continued to do the same as usual, and 30% (n=18) reported a higher degree of involvement.

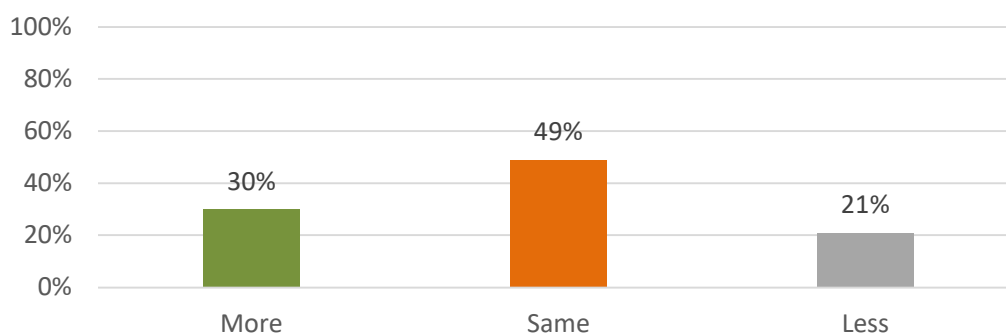


Figure 12. Changes in participants' treatments

In addition, 85% reported no difficulties since starting triple therapy treatment, compared to 15% who reported experiencing some difficulties as a result of the treatment, including mainly difficulties with physiotherapy and expectoration (due to the absence of mucus), as well as constipation, sleep problems or allergic reactions.

Finally, some people shared their experience of taking *Kaftrio*[®], which, on a generalised level, reflects all the results presented above:



"Very good, I feel like a normal person again. I finally feel like I'm worth more."

Adult with CF, 20 years old.



"It has changed my life both physically and mentally. I don't think about things so much because the drug gives me security. I can live a more normal life, more relaxed and enjoy myself without fear."

Adult with CF, 25 years old.



"Kaftrio[®] has changed my life, it has given me back the hope of doing many things in the future as well as allowing me to live without thinking about the number of antibiotics I will need, to count the days left before I get sick, to organise my life according to the calculation of relapses... In short, it has given me back LIFE."

Adult with CF, 19 years old.



"A wonder, to feel like a "normal" person climbing the stairs without getting tired"

Adult with CF, 35 years old.



The improvement in symptoms and increase in lung function means you have to look at life in a different way. I have always tried to lead my life in the "most normal" way possible but CF is always there limiting every step you want to take. With Kaftrio® I feel that these limitations will disappear, although some will remain (in the end, at almost 30 years old, it is inevitable) but above all, I will not suffer the same deterioration from CF that I would have without this medication".

Adult with CF, 29 years old.



"The experience is going very well, although the fear of having to stop and go back to the way I was before sometimes makes me anxious.

Adult with CF, 32 years old.

Discussion and conclusions

While the positive effects that triple therapy has had on increasing quality of life and respiratory function have been described (Aspinall et al., 2022; Heneghan et al., 2022), few studies have explored the effects that this new treatment has had overall on the life of the person with CF. This article is both a qualitative and quantitative survey of the effects of the new medication on CF patients over a short period of time.

There are similarities between our study and that conducted by Aspinall et al. (2022), who, using a qualitative methodology, conducted semi-structured interviews with 12 people with CF receiving triple therapy, concluding that, although the quality of life of these patients had improved, it was not without change. These authors found an increase in positive perceptions related to increased quality of life and lung function; but also the emergence of negative perceptions (related to

side effects, worry about having to stop taking medication and loss of identity), and changes experienced in the relationship with CF teams.

Our study has identified some of the changes that occurred after starting treatment with *hexacaftor-tezacaftor-ivacaftor*, grouping them into four areas: physical, psychological, social and treatment-related.

Physical factor

80.33% of people with CF reported changes during the first week of *elexacaftor-tezacaftor-ivacaftor* treatment. Specifically, there was a marked decrease in mucus and cough, a significant increase in energy and appetite, and improvements in skin and sleep quality. These results are in line with those obtained by other authors, who have also found that, after starting this new treatment, people with CF experience less coughing and shortness of breath, increased energy and appetite, improved sleep quality and duration, and ease in performing daily activities (Aspinall et al., 2022; Regard et al., 2022).

In addition, half of the sample reported experiencing desirable physical changes, which, in addition to a reduction in coughing, tiredness and exhaustion, included weight gain, increased energy and strength, as well as an easier time sleeping lying down, smoother skin, and regular menstruation, among others. As a 29-year-old woman comments: *"I feel more vitality and less tiredness. As I cough less, physiotherapy is also less tiring"*. However, we should not forget the 10% of the sample who report experiencing undesirable changes, such as allergic reactions or side effects. In fact, the occurrence of such undesirable changes or side effects could explain some of the unpleasant emotions experienced by some of the study participants, such as disappointment, anxiety or frustration, as the occurrence of side symptoms has been associated with decreased quality of life, worry and anxiety at the thought of having to stop treatment (Aspinall et al., 2022). This idea is reinforced by the following testimony from one of the study participants:



"In my case, I can summarise that on a psychological level, starting to take Kaftrio® has been like a roller coaster, with peaks of joy and euphoria when I saw that the medication was working so quickly and effectively, but also with peaks of disappointment and sadness when I saw that they had to withdraw it due to allergic reactions, and with plateaus of uncertainty and expectation when they reintroduced the medication again. Now that I seem to have these allergic reactions more or less under control, my concern about Kaftrio® is about some liver-related side effects, so the uncertainty continues until my next blood test.

Adult with CF, 47 years old.

On the other hand, a notable increase in activity has been observed, which could be explained by the increase in energy and the decrease in fatigue. In our study, 72% said that they had started to devote their time to activities that they were previously unable to do or had to stop due to their state of health. These activities they have started to do range from increasing physical exercise and taking up new sports, to doing everyday activities (e.g. walking longer distances, talking while walking, shopping, going out more, climbing stairs, cooking or cleaning). Others report that they continue to do the same activities as before, but without the feeling of constant tiredness. These results suggest that treatment with *elexacaftor-tezacaftor-ivacaftor* has contributed to a feeling of normality, being able to carry out daily activities without the burden and limitations of CF symptoms. These findings are in line with those of Aspinall et al. (2022), who found that treatment with *elexacaftor-tezacaftor-ivacaftor* facilitated a sense of normality based on independence, opportunity and hope. However, with regard to increased physical exercise, we emphasise the importance of channelling this increased energy through the guidance of an exercise professional to avoid injury, so exercise programmes for people with CF are a consideration.

Psychological factor

In our study we measured changes in four of the five basic emotions, finding a considerable increase in happiness and a decrease in sadness, fear, and especially anger.

As in the study by Aspinall et al. (2022), our study shows a positive perception of health status, which is accompanied by more pleasant emotions and feelings such as euphoria, joy, comfort, happiness, excitement, hope, relief, coping, etc., and fewer unpleasant emotions or feelings such as anxiety, sadness, nervousness, anguish, fear, disappointment, feeling overwhelmed or frustration. The feeling of normality, increased energy and the opportunity to resume or start new activities, as well as the decrease in symptoms and limitations associated with CF, could explain the increase in such pleasant feelings and the decrease in more unpleasant ones.

However, we must not forget that these changes do not affect all people equally, so we must take into account that minority of patients who have increased their fear, anger and sadness. As previously mentioned, the increase in these unpleasant emotions could be explained by the presence of secondary symptoms as indicated by 10% of the sample. The occurrence of side effects of triple therapy treatment has been linked to a perceived decrease in quality of life, the possibility of having to discontinue *Kaftrio*[®] treatment, increased anxiety, fear and uncertainty about returning to life *before Kaftrio*[®] (Aspinall et al., 2022). We must also take into account the role of expectations, which in many cases were positive before starting treatment (Almulhem et al., 2022): in our study, some people report that at the start of treatment they expected to improve much more, so the occurrence of such side effects, or the fact of not improving as much as expected, could explain the increase in unpleasant emotions, and even worries related to stopping treatment (Aspinall et al., 2022).

Others report experiencing more anxiety, distress, sadness or nervousness. In addition to the side effects of treatment, this could be explained by aspects such as loss of identity, worries about the future, or the multiple changes experienced in such a short space of time (Aspinall et al., 2022), aspects that have not been explored in this article. In addition, cases have been described in which there has been an increase in anxious and depressive symptomatology after starting treatment with CFTR

modulators (Talwalkar et al., 2017; Zhang et al., 2022), so further research is needed to periodically monitor anxiety and depression, and to assess the psychological impact of starting therapy with a new modulator (Zhang et al., 2022).

Finally, we highlight the level of uncertainty about the future, which has been maintained or increased in half of the sample. This could be explained by the emergence of concerns related to worsening health, ineffectiveness of treatment, long-term side effects, or future changes in different areas of life (Aspinall et al., 2022), as well as the raising of issues that had not been previously reflected upon.

Social factor

Kaftrio[®] is initiating substantial changes in the lives of individuals at different levels, which is why we wanted to collect information on these changes in social areas, such as family communication and working life. Analysing the social context and its interactions with the disease is necessary if we want to expand our resources to meet and detect new needs, which can hardly be understood from linear assumptions.

The data indicates that almost a third of the sample (31%) have improved their family or social communication. This positive effect of *Kaftrio*[®] on family communication can be interpreted as an increase in the need for communication among family members, as a result of the transition period after starting medication, which requires greater communication to adjust to the new roles and challenges that arise after the improvement in physical condition, to manage and assimilate these changes.

With regard to work, regaining a normal life includes being able to have a working life that guarantees personal development and autonomy, a key element for quality of life. The circular changes that may occur after starting to take modulators will not all occur at the same time. Some of these changes, such as those in the area of work, may require a longer period of time to be established.

Initial data in this area indicate that 44% of the sample have improved their working lives. We hope that as time progresses and the necessary adaptive adjustments are made, these results will increase and people with CF will be able to develop a more normal professional or working life.

Treatment factor

With regard to how taking CFTR modulators has influenced treatments, in this study we explored this factor globally, aiming to capture the subjective experience of changes in the degree to which people felt involved or committed to their treatments, before and after taking CFTR modulators. We might expect that an improvement in physical fitness and a reduction in symptomatology might influence less engagement with treatments overall. Especially for those who experience many benefits, continuing to adhere to symptom-directed treatments can be a major challenge (Allen et al., 2023). However, almost half of the sample, 49%, indicate that there has been no change in their usual treatments when starting *Kaftrio*[®], although this is not necessarily indicative of optimal levels of adherence. Therefore, this question requires further quantitative studies, and it would also be interesting to assess the evolution of adherence since starting treatment with triple therapy.

On the other hand, 30% of participants indicate that they are more committed to their usual treatments than before. We can relate this increased engagement to a greater hope for a healthy future, as well as an increase in energy and mood. Confidence in one's own abilities and the expectation that treatments will improve health are related to self-efficacy. Various studies point to self-efficacy as a powerful indicator of adherence to treatment (Parcel et al., 1994), and it would therefore be interesting to consider this variable in future studies.

With regards to the 21% of the sample indicating that they are less involved than before in their daily care, we wonder whether there has been an adjustment of treatments that has reduced the burden and therefore the need for involvement, or whether these are cases where the effect of modulators is being overestimated and this may be dangerously reducing adherence to treatment. At this time of rapid changes in the CF landscape, there may be changes in intensity or type of treatment

needs, so monitoring of patients should be continuous to identify difficulties and adjust to their needs. As Rowbotham and Daniels (2022) point out, "*Precision medicine is likely to lead to the need for greater precision and individualised management around other maintenance therapies*".

The data collected reflect a variable effect on the degree of treatment engagement that calls for more in-depth studies to tailor interventions to new and emerging needs. Given the rapid changes that are emerging in the context of people with CF, we believe it is important to study how change in treatment-related beliefs, views of self and capabilities, and views of the future are affecting treatment adherence.

This study has a number of limitations. Firstly, it is a descriptive study, a first approach to the challenges of starting therapy with *Kaftrio*[®], motivated by the changes that the authors observed in our patients during clinical practice. The initial idea of a quick exploration motivated by curiosity meant that standardised tests were not used. However, the richness and magnitude of the data obtained, coupled with the challenges and changes involved in starting treatment with CFTR modulators, indicate the need for more comprehensive studies and analysis, incorporating the use of standardised psychometric tests, as well as the study between the different variables discussed here. It would be interesting, as mentioned above, to include the study of the psychological impact initially and over time during treatment with modulators.

On the other hand, the sample shows a broad spectrum in the time elapsed since the start of treatment with *elexacaftor-tezacaftor-ivacaftor*. Future research should be able to differentiate between people in the first months of treatment and those who have been on treatment for longer.

Finally, although the sample can be considered small (61 people compared to the more than 2000 people estimated to have this disease in Spain, according to the Spanish Cystic Fibrosis Registry (Spanish Federation of Cystic Fibrosis, 2018), we consider that participation has been quite positive for three reasons: 1) the sample comes from different autonomous communities of the country, 2) the number of young people who have participated has been high, compared to other studies we have previously conducted from GEPS-FQ, and 3) taking as a reference the low participation that we

generally observe by the CF associative movement, 61 people can be considered an acceptable sample. Therefore, we can conclude that participation in this study and the final sample are positive.

In terms of strengths, this first approach to the problem yields very valuable information regarding the changes experienced by patients at a physical and treatment level, the improvements and limitations experienced at a social level, and how they have experienced these first moments of modulator therapy at an emotional level. Furthermore, the results of this first collection of information indicate that further studies are needed to determine the long-term clinical benefits of this therapy. In this sense, the results obtained have allowed us to identify future lines of research beyond the effects related to the physical symptomatology of CF, highlighting the importance of starting a new therapy with CFTR modulators and the changes associated with it at a psychological level. Finally, it highlights the importance of multidisciplinary care for CF patients, as it has been shown that the changes experienced are biopsychosocial in nature.

Ultimately, treatment with *elxacaftor-tezacaftor-ivacaftor* has shown physical, social and psychological benefits for CF patients to date. The changes observed in our patients during clinical practice and the new challenges they themselves reported to us were the starting point for this descriptive study, which provides an overview of the changes and challenges faced by people with CF receiving this treatment, with results similar to those of other scientific research. The effect of medication generates changes in several areas, so we propose the importance of prior assessments that include comprehensive evaluation of psychological aspects (such as expectations, concerns, presence of psychological symptomatology) before starting treatment with the new modulators.

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