



School of Psychology

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**The Psychosocial Impact of CFTR Modulator Therapies:
A Qualitative Meta-Synthesis, and A Qualitative Exploration
of The Experiences of Adults with Cystic Fibrosis unable to
benefit from Triple Combination Therapy**

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Preface

Cystic Fibrosis (CF) is a life limiting genetic condition characterised by the accumulation of mucus in various parts of the body, mainly impacting the lungs. Historically, treatment options for people with CF were focused solely on managing symptoms. However, the past decade has seen the development of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) modulator therapies, which address the underlying cause of CF. Since 2012, four CFTR modulators have been introduced for use. The most recent, a triple combination therapy of Elexacaftor, Tezacaftor and Ivacaftor (ETI) released in 2019 in the USA and 2020 in the UK, targets the mutation present in most people with CF, making it beneficial for approximately 90% of the CF population.

The current thesis consists of two separate papers. The systematic review aimed to integrate the existing qualitative studies on the psychosocial experiences of people with CF receiving any of the four approved CFTR modulator therapies. A systematic review protocol was developed to search for relevant qualitative studies across five databases. Following guidelines for conducting systematic reviews, nine studies were found that met the inclusion criteria and were quality assessed. Thematic synthesis was used to integrate the findings, resulting in five analytical themes and eight descriptive subthemes.

The first theme 'living a life less defined by CF', highlighted how CFTR modulator therapies have transformed the lives of people with CF. These treatments have enabled them to envision a future without the previous limitations of CF, allowing for new opportunities due to better health and longer life expectancy. The second theme 'double edged sword of CFTR modulator therapies', captured both the positive and negative impact of these treatments, with some participants discontinuing modulator therapies due to side

effects. The third theme, 'complex emotional landscape' explored the mixed emotions of feeling happy and relief for oneself while experiencing sadness for those without access to CFTR modulators. It also addressed feelings of grief, loss, survivors' guilt, anxiety, and uncertainty about the long-term efficacy of modulator therapies. The fourth theme, 'navigating changes in identity', described the process of adapting to a new sense of self beyond being defined solely by CF. Some participants experienced a loss of identity previously defined by CF, while others embraced a 'normal identity' following improved health status. The final theme, 'CF care in the CFTR modulator therapy era', included the challenges and opportunities presented by these new treatments. Concerns about reproductive health, weight management, and CF-related lifestyle factors were highlighted, along with a call for increased psychological support.

The second part of the thesis aimed to explore the experiences of adults with CF who cannot benefit from ETI due to genetic factors. Research on this topic is limited, as most emerging literature has focused on the experiences of those who can benefit from CFTR modulator therapies. Seven adults participated, with interviews lasting between 35 and 70 minutes, and were conducted through MS Teams. The methodological approach used was Interpretative Phenomenological Analysis (IPA) as it is well suited for exploring how participants make sense of their experiences. In IPA, the researcher interprets how participants make sense of their experiences, and so, the researcher kept a reflective journal and attempted to reduce the risk of any personal biases influencing data interpretation.

Four main themes with six subthemes emerged from the analysis. The first theme, 'feeling forgotten', highlighted the challenges of being in a minority group and feeling overlooked or left behind. The second theme, 'conflicted emotions', explored the emotional

impact of comparing one's situation with those who can benefit from ETI, and whilst feeling happy for others who can benefit from ETI, they experienced disappointment for themselves. The third theme, 'fragility of hope', illustrated how many of the participants' were initially hopeful before the release of ETI, then lost hope upon realising that they could not benefit from it. Despite this, some found a renewed sense of hope for future treatments, while others remained cautiously hopeful, concerned that their declining health might prevent them from benefitting from new drugs. The final theme, 'remaining on the old CF trajectory', detailed the ongoing challenges of living with CF, highlighting the significance of ETI and the coping strategies participants use to navigate these difficulties.

Both the systematic review and the empirical study contribute to our understanding of the diverse experiences within the CF community in this new era of CFTR modulators. They highlight the positive impact of CFTR modulator therapies on the lives of many people with CF, while also drawing attention to the unique struggles of both those who can and cannot access these medications. Both the review and empirical study offer novel unique insights which have implications for clinical practice, service development and future research. Ultimately, this thesis highlights the need for a holistic approach to CF care that addresses both medical and psychosocial aspects, ensuring that all individuals with CF receive the support they need to navigate their unique journeys.

The Psychosocial Impact of CFTR Modulator Therapies: A Qualitative Meta-Synthesis.

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Appendix A.

Abstract

Purpose

Cystic Fibrosis is a life limiting genetic condition affecting multiple organs in the body. Previously, treatment options for CF only managed symptoms. Over the last decade, new medications, known as Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) modulator therapies have been developed which address the underlying cause of CF. The current systematic review aims to synthesise the currently limited qualitative studies on the psychosocial experiences of taking CFTR modulators.

Methods

Searches were run on five databases to identify qualitative studies focusing on the psychosocial experiences of people with CF taking CFTR modulator therapies. PRISMA guidance was followed, and nine articles were identified for inclusion. The quality of each article was appraised. Thematic synthesis was then conducted to generate themes.

Results

Five analytical themes emerged: 'living a life less defined by CF', 'double edged sword of CFTR modulator therapies', 'complex emotional landscape', 'navigating changes in identity', and 'CF care in the CFTR modulator therapy era'.

Conclusion

CFTR modulator therapies can bring about improvements in physical and mental health outcomes. However, individuals taking CFTR modulators also navigate various challenges such as changes in identity. Services should ensure to address psychosocial

aspects arising from the use of CFTR modulators. Practical strategies to support people with CF taking CFTR modulator therapies and areas for future research are discussed.

Keywords

Cystic Fibrosis, CFTR modulator therapies, Qualitative research, Thematic Synthesis, Systematic Review

Introduction

Cystic Fibrosis and the role of the CFTR protein

Cystic Fibrosis (CF) is a life limiting genetic disorder and affects people from various racial and ethnic backgrounds (Taylor-Cousar, 2020). However, it predominantly impacts individuals of European descent (Cutting, 2015). CF is caused by mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein, which is vital for the transport of salt and water across the body's organs (Bell et al., 2020). More than 2000 mutations in the CFTR gene have been identified, with over 300 mutations known to cause CF (Clancy et al., 2019; Taylor-Cousar et al., 2023). These CFTR gene mutations are categorised into six classes (see Table 1).

The identification of the CFTR gene in the late 1980s sparked a wave of fundamental research, creating a new hope for curative treatment (Bell et al., 2020). Sequencing the CFTR gene has paved the way for the development of small molecule therapies that address the underlying cause of CF, known as CFTR modulator therapies (Middleton et al., 2019). Exploring the experiences of people with CF taking CFTR modulators represents a new area in CF research; hence, this study aims to synthesise the limited research on this topic.

Table 1*Classes of CFTR gene mutations (Zaher et al., 2021)*

Type of mutation	Type of CFTR mutation	Percentage of people with CF who have at least 1 mutation
Normal	CFTR protein is created and moves to the cell surface, allowing the transfer of chloride and water	N/A
Class I	No functional CFTR protein is created	22%
Class II	CFTR protein is created but misfolds, keeping it from moving to the cell surface. This is called a trafficking defect.	88%
Class III	CFTR protein is created and moves to the cell surface, but the channel gate does not open. This is called a defective channel regulation.	6%
Class IV	CFTR protein is created and moves to the cell surface, but the channel function is faulty. This is called decreased channel conductance	6%
Class V	Normal CFTR protein is created and moves correctly to the cell surface but not enough amount of the protein. This is called reduced synthesis of CFTR	5%
Class VI	CFTR protein is created but it does not work properly at the cell membrane. This is called decreased CFTR stability.	5%

Cystic Fibrosis Symptoms

CFTR mutations result in the formation of thick and sticky mucus in various organs, resulting in pulmonary, gastrointestinal, pancreatic, and reproductive system diseases (Zaher et al., 2021). Although CF affects multiple organs, the cycle of inflammation and infection mainly impacts the lungs, and recurrent pulmonary exacerbations are the main cause of illness and death (Fraser-Pitt & O'Neil, 2015; Petrocheilou et al., 2022). People with CF often face a significant treatment burden to manage their health, including taking oral medications, sometimes up to 70 tablets daily, engaging in airway clearance therapies and regular exercise, and adhering to a specialised high calorie diet (Earlam, 2022; Talwalkar et al., 2017; Almulhem et al., 2022). Moreover, acute pulmonary exacerbations and disease progression expose people with CF to painful and potentially distressing medical procedures (Quittner et al., 2014). Recent research by O'Leary et al. (2022) highlights the prevalence of childhood trauma associated with CF, often stemming from undergoing painful and frightening medical procedures.

Regarding the psychological impact of CF, a psychological screening study with data from both Europe and the USA revealed that adolescents and adults with CF, as well as their caregivers, experience significantly higher rates of depression compared to findings from the general population (Quittner et al., 2014). People with CF also face social challenges such as limited interaction with other people with CF due to risk of cross infection (Saiman et al., 2014; Quittner et al., 2016). Additionally, frequent coughing can have negative social implications such as others perceiving it as contagious (Pakhale et al., 2014; Quittner et al., 2016). Managing CF also involves navigating challenges related to disclosing their condition and dealing with stigmatisation, which are both factors that can hinder treatment

compliance (Sawicki et al., 2015; Quittner et al., 2016). Addressing the psychosocial wellbeing of people with CF is therefore important.

Evolution of Cystic Fibrosis Treatment

The treatment landscape for CF has evolved significantly from symptom management to the development of CFTR modulator therapies that target the root cause of CF (Proesmans et al., 2008; Cuevas-Ocana et al., 2020; Taylor-Cousar et al., 2023; Middleton et al., 2019). Presently, there are four approved oral therapies that improve CFTR function (Zemanick & Accurso, 2019; Bell et al., 2020). The first CFTR modulator therapy, Ivacaftor (IVA), sold under the brand name Kalydeco received approval in 2012 but was only available to a small percentage of people with CF because it only targets people with one of the class III mutations (Dwight & Marshall, 2021; Hine et al., 2022; Desai et al., 2022; Rogers et al., 2020; Despotes & Donaldson 2022). Later in 2015 and 2018, two combination therapies, Lumacaftor/Ivacaftor (LUM/IVA), brand name Orkambi and Tezacaftor/Ivacaftor (TEZ/IVA), brand names Symkevi or Symdeco, were also approved. The most recent addition, a triple combination therapy, gained approval in 2019 in the USA and 2020 in the UK. This therapy comprises of Elexacaftor/Tezacaftor/Ivacaftor (ETI), marketed under the brand names Kaftrio or Trikafta. ETI is suitable for a broader spectrum of mutation profiles, including the most common CF mutation, Delta F508: Class II Mutation found in nearly 90% of people with CF (Guo et al., 2022; Taylor-Cousar et al., 2023; Middleton et al., 2019). Consequently, approximately 90% of people with CF are expected to benefit from ETI, overcoming the limitations of earlier CFTR modulator therapies (Pittman & Ferkol, 2015; Hine et al., 2022; Dwight & Marshall, 2021).

Physiological Impact of CFTR Modulator Therapies

Recent advancement in CFTR modulators have led to significant improvements for people with CF, such as improved lung function, higher body mass index, reduced frequency of pulmonary exacerbations and overall better quality of life (Keating et al., 2018). These treatments not only address current symptoms but also hold promise in potentially preventing complications such as bronchiectasis, diabetes and other associated health problems (Tümmler, 2023). Evidence from the CF Foundation (based in the USA) and the UK CF patient registries indicates that people with CF treated with IVA had lower rates of CF related complications, including CF related diabetes, hepatobiliary complications, bone or joint issues, and depression, compared to untreated matched controls (Bessonova et al., 2018). Moreover, across paediatric and adult populations, all approved modulators have contributed to weight gain (Despotes & Donaldson, 2022). A review summarising French real-world studies revealed improved lung function, improved nutritional status, reduced sweat chloride concentration, decreased hospitalisation rates, and less intravenous (IV) medication use, comparable to data from CF registries in the USA and UK (Regard et al., 2022). It is worth noting that improved nutritional status has been linked with reduced pulmonary exacerbations and better lung function (Shepherd et al., 1986; Bailey et al., 2022).

However, despite the positive impact of CFTR modulators, they have not been without side effects, with responses varying among individuals (Heijerman et al., 2019; Allen et al 2023). A systematic review of 54 studies summarising real world adverse events related to the available CFTR modulators reported a wide range of physical side effects, some of which led to treatment discontinuation (Dagenais et al., 2020). These side effects include

pulmonary exacerbations, haemoptysis, nausea, vomiting, abdominal pain, constipation, headaches, rash, diarrhoea, increased blood pressure, chest tightness, hair loss, fatigue, and blurred vision (Dagenais et al., 2020). A retrospective analysis of children with CF who started ETI between 2020 and 2023 identified side effects such as rash, mild elevation of creatine kinase and alkaline phosphatase levels, headaches, and fatigue (Olivier et al., 2023), which were comparable with those reported in studies involving adults.

Psychological impact of CFTR modulators

While a mixed methods study of 245 participants starting ETI highlighted improved quality of life and the pursuit of new life goals (Martin et al., 2021), there are emerging indications of negative cognitive and emotional changes in people taking modulator therapies (Finlay et al., 2022). Worsening of depression or anxiety were reported after initiation of LUM/IVA in two case reports (Graarup et al., 2017; Talwalkar et al., 2017), as well as new onset depression and suicide attempts in adolescents beginning ETI (Arslan et al., 2023). One large prospective cohort study noted cases where individuals discontinued LUM/IVA due to depression (Burgel et al., 2020), and one person in each of two smaller cohort studies reported anxiety as the cause of discontinuation (Sergeev et al., 2020; Mckinzie et al., 2017).

Additionally, cognitive side effects like fogginess, slurred speech, word finding difficulties and memory issues have been reported after commencing TEZ/IVA (Heo et al., 2022). Neuropsychiatric adverse events such as visual hallucinations, depersonalisation, and brain fog have been reported after initiation of TEZ/IVA (Dagenais et al., 2020; Perez et al., 2019). Case reports have further described worsening depression, and sleep disturbances with hypnopompic hallucinations and passive suicidal ideation after starting ETI (Dagenais et

al., 2020; Tindell et al., 2020). With the increasing use of CFTR modulators, it is vital to understand the psychosocial impacts experienced by people with CF on these medications.

Rationale and aim of the review

To our knowledge, there has not yet been a systematic review of qualitative studies that considers the psychosocial impact of CFTR modulator therapies. This review aims to synthesise the evidence from this emerging area of research to provide a comprehensive understanding of the psychosocial impact of CFTR modulators. The findings of this review hold the potential to be valuable in informing healthcare service delivery by providing insights and knowledge about personal experiences to both healthcare providers and people with CF, thereby benefitting multidisciplinary clinical teams (often including psychologists) in fully supporting individuals with CF.

In summary, this systematic review aims to:

- a) Systematically search for the available qualitative studies that explore the experiences of people with CF taking any of the available CFTR modulators and assess the quality of these studies.
- b) Synthesise the limited evidence from these emerging studies to gain a comprehensive understanding of the psychosocial impact of CFTR modulators.
- c) Offer valuable insights by drawing from the synthesised experiences of people with CF to inform service design and delivery.

Method

Protocol

The protocol for this review was registered on the international prospective register PROSPERO (reference: CRD42023408986).

Search Strategy

The PICO framework (Population, Phenomenon of Interest, Context, see table 2) was used to formulate the research question and determine the search terms used in the thematic synthesis. PICO is a framework suitable for conducting systematic reviews of qualitative research as noted by Hosseini et al. (2024).

Table 2

PICO applied to the Review Question

Characteristic of PICO	PICO characteristics applied to review question
Population	People with CF taking CFTR modulator therapies
Phenomenon of Interest	Psychosocial experiences
Context	Any

After formulating the research question, the following search terms were identified: ("CFTR modulator*" OR Ivacaftor OR Lumacaftor OR Tezacaftor OR Elexacaftor OR "Cystic Fibrosis Transmembrane Regulator Modulator*" OR "cystic fibrosis transmembrane conductance regulator modulator*" OR Kaftrio OR Trikafta) AND (Wellbeing OR psychological OR emotional OR "mental health" OR psychosocial OR "quality of life" OR experience OR perspective) AND (Interpretative phenomenological analysis" OR "grounded theory" OR "thematic analysis" OR "content analysis" OR "phenomenological approach" OR

"constructivist epistemological framework" OR "semi-structured" OR semistructured OR unstructured OR informal OR indepth OR indepth OR "face-to-face" OR structured OR interview* OR discussion* OR questionnaire* OR "focus group" OR qualitative OR ethnograph* OR "field work" OR fieldwork).

Studies were identified by searching five databases (Scopus, PsycINFO, CINAHL, MEDLINE and Web of Science) with the last search being conducted in February 2024. Unpublished studies were sought via grey literature websites Overton and ProQuest. Stork, a website that provides alerts for new research was also utilised. The search strategy utilised a combination of keywords and subject heading/indexed terms, combined using Boolean operators. The search strategy was tailored according to each database. Additionally, citations and reference lists were also reviewed from the eligible studies to ensure the search criteria were sufficient and that no studies were missed.

Search Criteria

A set of inclusion and exclusion criteria was established to direct the manual search of database findings (refer to Table 3). The primary researcher conducted the searches and identified the studies included in the review. Subsequent discussion took place with the research supervisors to resolve any uncertainties regarding whether a study met the criteria. All chosen studies were reviewed and approved by research supervisors.

Table 3*Study inclusion and exclusion criteria*

Inclusion Criteria	Exclusion Criteria
People of all age groups with Cystic Fibrosis receiving CFTR modulator therapies	Studies not reporting the use of CFTR modulators or on the experiences of people with CF who cannot benefit from CFTR modulator therapies.
Qualitative studies on the direct experiences of individuals themselves (excluding those of parents', carers', or healthcare professionals')	Third person accounts e.g., case reports from professionals without detailed quotes
Studies reporting on psychosocial factors following initiation of CFTR modulator therapies	Studies that report solely on the physiological impact of CFTR modulator therapies, such as their impact on lung function
Studies that include quantitative elements, such as mixed-method studies, but only using the qualitative data	Studies not based on empirical findings or studies that have not included participant quotes
Full text manuscript available in English	Non-English publications

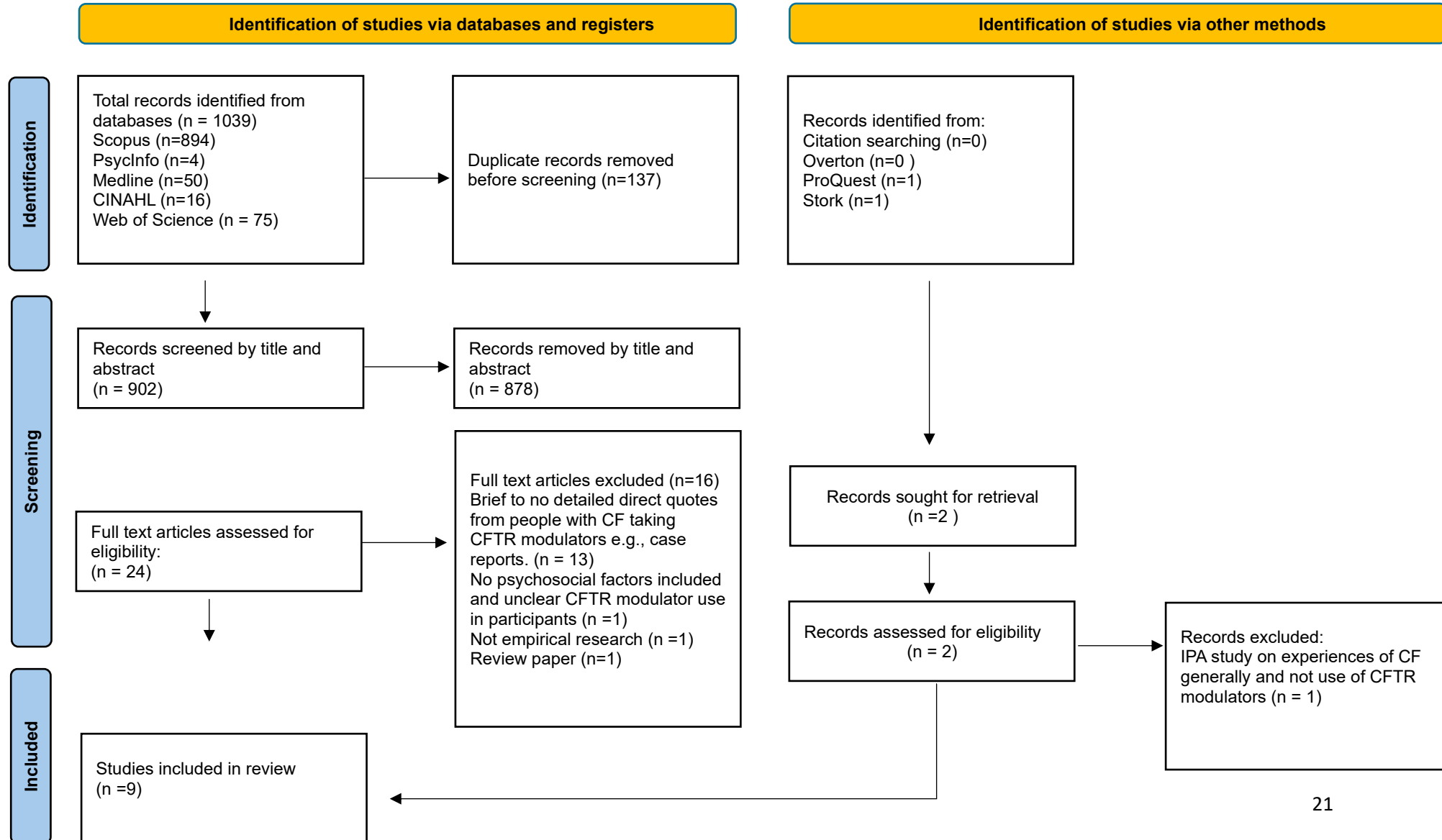
Search Outcome

The search strategy initially identified 1039 studies, which was narrowed down to 902 after removing duplicates. The titles and abstracts were screened against the eligibility criteria by the primary researcher (MM). Of the 902 studies, 25% (n=225) were screened by a doctoral postgraduate researcher. Any disagreements were resolved through discussion and mutual consensus [0.99 kappa] indicating almost perfect agreement. This process returned 24 studies that required full-text screening against the review criteria, and a further 16 were rejected. Again, 25% (n=6) of the 24 studies requiring full text screening were

screened by the same doctoral postgraduate researcher, and any disagreements were resolved through discussion and mutual consensus [0.92 kappa] indicating almost perfect agreement. One study was retrieved from a new paper alert from Stork. See Prisma diagram in Figure 1.

Figure 1

PRISMA flow diagram summarising the screening process (Page et al., 2021: an updated guideline for reporting systematic reviews)



Data Extraction

Data extraction captured relevant data and study characteristics including authors, aims, country setting, sample, type of CFTR modulator therapy, method of data collection and method of analysis. The final nine included studies were all published from 2020 onwards, which highlighted the newness of CFTR modulator therapies and qualitative studies in this area. There were 67 participants who were receiving one of the four approved CFTR modulators. Four studies also interviewed clinicians, caregivers of people with CF taking CFTR modulators and those who were not eligible due to genetic factors or had no access to CFTR modulators in their countries. Only quotes from people with CF taking CFTR modulators were included in this review. Two studies involving just one participant were included as they nevertheless provide insight into this relatively new topic. Only one study explored the experiences of children and young people. Three studies were conducted in the UK, five in the USA, one study recruited participants from the UK, USA, Germany, Ireland and Australia. The ages of the participants across the included studies ranged from 12 to 51 years old. For more details on the included studies in the current review and thematic synthesis, please see Table 4.

Table 4*Data extracted from each study*

Authors	Aim	Country Setting	Sample	CFTR Modulators	Method of Data Collection	Method of Analysis
Almulhem et al. (2022)	To explore the opinions of children with CF, their parents/carers and healthcare professionals (HCPs) on the impact of ETI, airway clearance techniques (ACTs) and nebulised treatments	UK	10 participants <ul style="list-style-type: none"> • age = 12-18 • 7 females and 3 males • ethnicity - not stated 	ETI (n=10)	Semi Structured Interviews	Inductive Thematic Analysis
Aspinall et al. (2022)	To explore the effect physiological changes have on an individual's perception of reality and to what extent the modulator has changed their life beyond just the physical aspects.	UK	12 participants <ul style="list-style-type: none"> • age = 28.1 ± 6.4 years • 10 females and 2 males • ethnicity – not stated 	ETI (n=12)	Semi Structured Interviews	Qualitative content analysis
Kauser et al. (2022)	To explore the psychosocial challenges faced in adulthood life by this relatively new adult CF population and to understand and explore attitudes and experiences of mindfulness and self-compassion	UK	20 participants <ul style="list-style-type: none"> • age = mean 37 • 11 female and 9 males • ethnicity - Caucasian 	Symkevi (n= 4) Kalydeco =(n= 2) Orkambi = (n=1) No CFTR Modulators = (n=13)	Semi Structured Interview	Thematic Analysis

Keyte et al. (2023)	To explore how modulator therapies (or the prospect of modulator therapies) have affected individuals' lives, encompassing both physical and psychological wellbeing	UK (15) USA (2) Ireland (1) Germany (1) Australia (1)	20 participants <ul style="list-style-type: none"> • age = 22-51 • 12 females and 8 males • ethnicity – not stated 	ETI = (n=17) Discontinued ETI (n=1) Not eligible for ETI (n=1) No access to ETI (n=1)	Semi Structured Interviews	Thematic Analysis
Ladores and Polen. (2021)	To explore the experiences of a woman successfully treated with ETI who subsequently encountered unanticipated internal turmoil.	USA	1 participant <ul style="list-style-type: none"> • age = 29 • female • ethnicity – not stated 	ETI	Semi Structured Interview	Thematic Analysis
Ladores et al. (2020)	To describe the experiences of a woman with CF who had two unexpected pregnancies while on lumacaftor/ivacaftor.	USA	1 participant <ul style="list-style-type: none"> • age = 29 • female • ethnicity – Caucasian 	Lumacaftor/Ivacaftor	Telephone Interview	Thematic Analysis
Landess et al. (2024)	To explore patient, caregiver, and clinician perceptions of modulators and influence on decisions about starting CFTR modulators	USA	28 participants (9 adults taking CFTR modulators) <ul style="list-style-type: none"> • age = 20-61 • ethnicity – not stated 	Varied modulators, not stated (n=8) Not eligible due to genotype (n=1)	Semi Structured Interviews	Not specified but provide details of analysis such as coding responses and developing themes

Page et al. (2022)	To explore whether there is a relationship between using CFTR-modulator drugs and the psychological and social aspects of the lives of individuals with CF, including: career, relationships, family planning and psychological functioning	USA	8 participants <ul style="list-style-type: none"> • age = 24-32 • 4 females and 4 males • ethnicity – not stated 	Tezacaftor/Ivacaftor = 7 Lumacaftor/Ivacaftor = 1	Semi Structured Interviews	Grounded Theory
Vall (2022)	To better understand how living with CF impacts development and identity	USA	5 participants <ul style="list-style-type: none"> • age = 21 -25 • 4 females and 1 male • ethnicity – 4 Caucasian and 1 Middle Eastern 	ETI (n=4) Not Eligible = (n=1)	Semi Structured Interviews	Narrative Inquiry Framework

Quality assessment

The primary researcher used the Critical Appraisal Skills Programme (CASP, 2018) tool to assess the quality of the research studies used in the current review. The CASP tool consists of 10 questions which serve to evaluate the strengths and limitations of qualitative research methodologies (Long et al., 2020). The first two questions enable an additional eligibility screening, while the subsequent eight assess the study's credibility and relevance. These questions consider the research aims, research design, recruitment strategy, data collection method, reflexivity of the researchers in interpreting the data, research ethics, data analysis and how valuable the findings are. The CASP tool is tailored for use with health-related research and was therefore deemed appropriate for this review's context (Long et al., 2020). To facilitate interpretation, a three-point scoring system (0, 0.5, or 1) developed by Feder et al. (2006) was applied to each study evaluated with CASP.

To help assure inter-rater reliability, a doctoral postgraduate researcher completed the CASP qualitative checklist for two studies in the review to mitigate potential bias. There was consensus on the two studies that were reviewed. Each article's appraisal was calculated and summed, resulting in a maximum score of 9 (excluding the last item, appraised against three criteria as detailed in Table 5). A score of 1 indicated extensive justification and explanation of an issue (e.g., thorough reflexive measures implemented to counter biases). A score of 0.5 denoted partial addressing of an issue without adequate elaboration (e.g., explicit acknowledgment of the researchers views and biases but lacking reflection on their influence or mitigation in the study). A score of 0 indicated insufficient justification for a particular issue (e.g., lack of consideration regarding the relationship between the researcher and participants). A 'can't tell' rating on the CASP

was denoted by a question mark and given a score of 0.5. CASP scores for each of the articles included in this review are presented in Table 5.

Table 5

The CASP scores for each of the articles included in the review.

	Articles								
CASP Question	Almulhem et al. (2022)	Aspinall et al. (2022)	Kauser et al. (2022)	Keyte et al. (2022)	Ladores and Polen. (2021)	Ladores et al. (2020)	Landess et al. (2024)	Page et al. (2022)	Vall (2022)
Aims	✓	✓	✓	✓	✓	✓	✓	✓	✓
Methodology	✓	✓	✓	✓	✓	✓	✓	✓	✓
Research Design	✓	✓	✓	✓	✓	✓	✓	✓	✓
Recruitment Strategy	✓	✓	✓	✓	×	×	✓	✓	✓
Data collection	✓	✓	✓	✓	?	?	✓	✓	✓
Reflexivity	×	×	×	✓	×	×	×	?	✓
Ethical Issues	✓	✓	✓	✓	?	?	?	?	✓
Data Analysis	✓	✓	✓	✓	?	?	✓	?	✓
Findings	✓	✓	✓	✓	✓	✓	✓	✓	✓
1. Contribution to the literature	1. ✓	1. ✓	1. ✓	1. ✓	1. ✓	1. ✓	1. ✓	1. ✓	1. ✓
2. Identified further areas for research:	2. ✓	2. ✓	2. ✓	2. ✓	2. ?	2. ?	2. ✓	2. ✓	2. ✓
3. Considered generalisability:	3. ?	3. ✓	3. ?	3. ?	3. ×	3. ×	3. ?	3. ✓	3. ?
Score	8	8	8	9	5.5	5.5	7.5	7.5	9

Thematic Synthesis

The methodology selected to synthesise the findings from the studies identified in the systematic review was thematic synthesis (Thomas & Harden, 2008). Thematic synthesis was chosen as it has a clear and transparent process for synthesising qualitative data in addition to having an interpretative element which produces themes beyond what is reported in the initial studies (Thomas & Harden, 2008).

Thematic synthesis took the form of three stages which overlapped to some degree: a free line-by-line coding of the results section, which included participant quotes and the authors' interpretation, using a table in a Microsoft Word document (see appendix B). After the first study was coded, these codes were used to create a bank of codes and when coding subsequent papers either a code in the bank was used or a new one was created. Following this, the 'free codes' were organised into related areas, resulting in 'descriptive' themes (appendix C) and then the development of 'analytical' themes (see appendix D) (Thomas & Harden, 2008). The themes were derived from the participants narratives, rather than the themes derived from the included studies. Please refer to Table 6 to see which studies contributed to the evidence of each theme.

Table 6

List of themes and subthemes within each study

Analytical and Descriptive Themes	Almulhem et al., 2022	Aspinall et al., 2022	Kauser et al., 2022	Keyte et al., 2023	Ladores and Polen, 2021	Ladores et al., 2020	Landess et al., 2024	Page et al., 2022	Vall 2022
Living a life less defined by CF	✓	✓	✓	✓	✓	✓	✓	✓	✓
<i>Embracing new opportunities</i>	✓	✓	✓	✓	✓	✓	✓	✓	
<i>Hope and optimism</i>	✓	✓	✓	✓			✓	✓	
Double edged sword of CFTR modulators	✓	✓		✓			✓	✓	✓
Complex emotional landscape	✓	✓	✓	✓	✓	✓			
<i>Conflicted emotions</i>		✓		✓				✓	✓
<i>Uncertainty about the long-term efficacy of CFTR modulators</i>	✓	✓		✓	✓				✓
Navigating changes in identity		✓	✓	✓	✓			✓	✓
<i>Conflict between identity and health</i>		✓		✓	✓			✓	✓
<i>Redefinition of self</i>		✓	✓	✓				✓	
CF care in the CFTR modulator therapy era	✓	✓		✓	✓	✓	✓		
<i>Addressing specific concerns</i>	✓	✓	✓	✓	✓	✓	✓		✓
<i>Need for psychological support</i>		✓		✓			✓	✓	

Results

The thematic synthesis of nine studies led to the discovery of five analytical themes. Within these themes, eight subthemes were found.

Theme 1: Living a Life Less Defined by CF

A prevalent theme across all studies was the life changing impact of CFTR modulators, which allowed individuals to envision a life free from the limitations previously imposed by CF. These included improvements in lung function, sleep quality and increased energy levels. Some studies described holistic improvements in their wellbeing as described by a participant in the study by Ladores et al. (2020), "It's like emotionally and physically, for everybody, the quality [of life] has improved...".

Another participant in the study by Keyte et al. (2023) described that "There's not a part of my body that doesn't feel different - muscles, my lungs, my legs; like everything is different." CFTR modulators were also recognised for addressing the root cause of CF rather than merely alleviating symptoms, leading to a more normal and fulfilling life for many, as described by a participant in a study by Kauser et al. (2022) "everyday livings just a lot easier... you sort of know it[modulators] helps with the [...] cause of the problem rather than just the symptoms...so you're actually P feeling a bit more normal...which is all you can ask for"

A contrasting experience was noted in one study by Almulhem et al. (2022), where a participant did not perceive significant improvements in their lung function especially when they compared this to the improvements of others, leading to feelings of disappointment: "I haven't really seen a huge impact. My doctors might say otherwise, but me personally, I think it has not really done that much."

The theme of 'living a life less defined by CF' consists of two subthemes: a) embracing new opportunities and b) hope and optimism.

Subtheme 1a: Embracing New Opportunities

The majority of studies included in this review highlighted how access to CFTR modulator therapies empowered participants to envision the future and embrace increased choices and opportunities. Quotes from participants, such as those from studies by Aspinall et al., (2022) and Kauser et al, (2022), reflected a newfound optimism and confidence about long term plans and aspirations, like retirement savings, pursuing neglected passions such as sports, or starting new ones:

With time extending [due to Kaftrio] it just means you are like, 'oh well maybe I could get that retirement plan... (Aspinall et al., 2022)

. . . I had lost sight of everything that was important to me because I was so poorly . . . I dreamt about it [competing in dressage] but now I am like, come on, you can do it... (Aspinall et al., 2022)

[I] took up paddle boarding...before I never would've done that... (Kauser et al., 2022)

Additionally, participants in two studies (Kauser et al.,2022; Keyte et al., 2023) mentioned returning to education and work, citing the stability provided by CFTR modulators in reducing hospitalisations and exacerbations and thereby enhancing career prospects and financial security:

Because of Kaftrio I'm back at college to retrain [as a marine engineer for the Navy] so that has made a big big difference. I can develop myself a career

Yeah I actually have a lot more hope just to have a career... Because I know a lot of places they don't want to... have this ... empty gap in employment from an employee, you know? (Keyte et al., 2023)

Furthermore, CFTR modulators were associated with the potential to start families as reported by four studies (Page et al., 2022; Keyte et al., 2023; Aspinall et al., 2022; Landess et al., 2024). Participants in these studies expressed hope and confidence in their ability to raise children and face life's challenges due to improved health and a positive outlook on their future, as described by a participant in a study by Page et al. (2022):

I feel like where my health is and where my mind is...and because of the hope that Symdeko® and these new developing drugs have... I could raise a child to at least, you know, young teenage years and they would get enough of me to be able to handle everything that comes with life, you know what I mean?

Subtheme 1b: Hope and Optimism

The theme of 'hope and optimism' was identified by six studies and participants expressed a newfound hope and relief with some noting a shift from perceiving CF as a life limiting illness to embracing life with optimism (Keyte et al., 2023; Page et al., 2022; Aspinall et al., 2022).

I can see a future now... I saw a time of not being there for them[family], whereas now I can't see me not being there [...] it's given me a lot of hope. (Keyte et al., 2023)

...I don't really think that CF is going to be the thing that kills me... I used to think that. But I just don't think that anymore. Like, I just don't think that's my way out, you know? (Page et al., 2022)

A different perspective was provided by a participant in a study by Landess et al. (2024). The participant expressed regret and a sense of lost time due to managing the challenges of CF, stating “[I] wish I’d started a 401K [retirement plan] earlier in life”. Although this participant acknowledged the positive aspect of having a renewed perspective on life and the ability to plan for the future, they also felt a sense of lost time compared to those who have had better health and the opportunity to plan for their future earlier. Other participants in studies by Almulhem et al. (2022), Aspinall et al. (2022), Keyte et al. (2023) and, Ladores et al. (2020) expressed gratitude for medical advancements and conveyed sense of hope for ongoing progress in CF treatments.

Double Edged Sword of Modulator Therapies

Despite the positive health outcomes reported in all the included studies, six studies (Almulhem et al., 2022; Aspinall et al., 2022; Keyte et al., 2023; Landess et al., 2024; Page et al., 2022) noted instances where individuals faced significant physical and mental side effects. In some cases, decisions to discontinue ETI were made due to physical and mental health side effects, as illustrated by one participant in a study by Aspinall et al. (2022):

I was elated. It felt like I didn’t have CF but the headaches started on day one... I did not feel like I was on this planet. I forgot my date of birth and sound sensitivity was crazy, even talking became a struggle . . . I have no regrets—it is easier to live with CF than on Kaftrio.

In contrast, in the same study (Aspinall et al., 2022) highlighted that some participants were willing to endure the side effects of ETI in exchange for the long-term health benefits. This highlighted the dilemma some individuals face in weighing up perceived benefits against negative physical and mental health side effects.

Weight management emerged as a significant theme in four studies (Almulhem et al., 2022; Aspinall et al., 2022; Keyte et al., 2023; Vall 2022), with participants dealing with newfound challenges in maintaining a healthy weight after commencing CFTR modulators. One participant in the study by Almulhem (2022) shared: “Before Kaftrio... you could eat anything you want, because you wouldn’t put weight on. Now, there was a period of time where I was getting really upset, because all of a sudden, I had got a lot of weight on”. For others, the weight gain resulted in significant changes in their body image, self-perception and confidence. Another participant from the study by Aspinall et al. (2022) reported that “My lungs got better but I couldn’t enjoy and reap the benefits because I was putting on all this weight. I was looking at myself and wanting to cry because I was so unhappy in how I looked.”

The transition from being able to eat without concerns about weight gain to facing weight related challenges posed significant behavioural adjustments. For example, one participant in the study by Keyte et al., (2023) expressed “I actually have to watch what I eat now, which is a complete turnaround, and after you’ve done it for all your life, it’s quite a hard thing to take on board”.

Furthermore, Keyte et al. (2023) highlighted how participants reported lacking body awareness after commencing CFTR modulators: “I don’t feel like I can read my body. I felt like I was so in tune with my body [...] I don’t know my own body anymore. It’s a total retrain, and we’ve just got to learn as we go”. Improved health and loss or lack of body awareness also seemed to result in non-adherence to other treatment (there is a need for people with CF taking CFTR modulators to comply with other treatments like nebulisers, whilst taking CFTR modulators) which could negatively impact their physical wellbeing (Keyte

et al., 2023). One participant stated: “I’m a bit less compliant now than I used to be. Orkambi helps me so I can afford to do a little bit less...”

The analysis also touched on one participant’s initial reaction regarding starting CFTR modulators from the study by Landess et al. (2024). They expressed being “... skeptically optimistic”. This reflected broader sentiments within this group about embracing new treatments while navigating uncertainties and potential side effects.

Theme 3: Complex Emotional Landscape

This theme explored the complex emotional landscape experienced by people with CF taking CFTR modulators. Findings from most of the studies included in this review revealed a range of emotions including happiness, sadness, grief, loss, survivors’ guilt, and anxiety. This theme contains two underlying subthemes a) conflicted emotions and b) uncertainty about the long-term efficacy of CFTR modulators.

Subtheme 3a: Conflicted Emotions

The subtheme of conflicted emotions emerged in some studies (Aspinall et al., 2022; Keyte et al., 2023; Page et al., 2022; Vall, 2022), where some participants navigated a mixture of both positive and negative feelings after taking CFTR modulators. One participant in the study by Page et al. (2022) acknowledged a mixture of sadness, happiness, hope and fear, highlighting the ongoing emotional turmoil despite the potential for extended life expectancy offered by CFTR modulators:

I feel happy but sad, if that makes sense? Like, um, my birthday was Monday, so I turned thirty-two and that’s good because like... like CF isn’t really much of a childhood disease anymore... as I get older and closer to that number [CF life expectancy] I get kind of... I do worry... it’s scary sometimes. (Page et al., 2022)

This was echoed by another participant in the study by Keyte et al. (2023), who described that exceeding their anticipated life expectancy had taken a toll on their mental health. These sentiments reflect how the positive emotions are tempered by the harsh realities and the challenges of not allowing one's life to be defined by the life expectancy associated with a CF diagnosis, even with the use of CFTR modulators.

Keyte et al. (2023) found that participants also experienced a sense of grief and loss despite positive health outcomes, mourning the challenges and experiences they had before starting CFTR modulators. One participant in the Keyte et al. (2023) study mentioned that "I was equally happy and sad at the same time, because it was almost like the stages of grief. I was grieving what had happened to me through my whole life, and you have to face it as well". Some studies (Aspinall et al., 2022; Keyte et al., 2023; Vall, 2022) referenced a phenomenon akin to survivors' guilt, concerning those unable to benefit from CFTR modulators.

And like, why is my life not...but some peoples' are. And so, it's kind of it's almost a sense of survivor's guilt... (Vall, 2022)

I had a few days where I was feeling almost like survivors' guilt [...] I was so happy and relieved and at the same time I was also feeling awful because there are so many people that are worse than I'm doing and who need this drug so badly and can't have it. (Keyte et al., 2023)

I've got so much guilt that I can't think about it too much. I have this like, it's not survivors' guilt but something along those lines . . . They [the ineligible] are just watching it all unravel. They [Vertex] have to do something for them. (Aspinall et al., 2022)

Participants in these studies expressed a mixture of emotions, feeling both happiness for their own improved health, and sadness for those who cannot access CFTR modulators. They also acknowledged their own fortune while recognising the ongoing challenges faced by others.

Subtheme 3b: Uncertainties about the Long-Term Efficacy of CFTR Modulators

Despite positive changes reported in daily life, several studies found that many people with CF taking CFTR modulators expressed anxiety and fear about the future and the prospect of losing newfound health benefits leading them to question “Will Trikafta stop working, and will my life go back to the way it was?” (Ladores & Polen, 2021). Concerns about the duration of positive health status and the fear of potential failure contributing to this anxiety were reported. Participants worried about how long their positive health status would last and were concerned about their health deteriorating in the future, raising concerns about its efficacy. One participant from the study by Aspinall et al. (2022) described:

I think my main anxiety comes from the fact that I’ve now been given this opportunity or like dangled carrot of, look what your life could be like, and in the back of my mind is when is it going to go away. All the time.

One study described how participants worries stemmed from a lack of knowledge about the long-term efficacy of ETI, raising concerns about potential health deterioration without warning (Aspinall et al., 2022). This theme paints a picture of individuals navigating a transformed present, while facing uncertainties about the future, highlighting the complex emotional landscape individuals face despite experiencing positive health changes with CFTR modulators.

Theme 4: Navigating Changes in Identity

The theme of 'navigating changes in identity' captured the process of adapting to a new sense of self that goes beyond being solely defined by CF. Within this broader theme, there were two subthemes: a) Conflict between identity and health and b) Redefinition of self.

Subtheme 4a: Conflict between Identity and Health

A recurring theme identified in three studies was the emergence of 'identity crises' following the initiation of ETI. A participant in a study by Aspinall et al. (2022) described:

. . I completely lost my identity. Like, I didn't know who I was or what I am doing or what is going on . . . I felt like my identity was my health and my job and now they are not the same.

Similarly, another participant in a study by Ladores and Polen (2020) shared:

There's so much that stuns you and that you identify with as a person. Your identity is now different [with Trikafta™]. I identified as someone that coughed up green mucus a lot. To not have these things... I am expecting to go back. I keep thinking this is gonna wear off. When is it gonna come back?

Participants in these studies struggled with reconciling their past expectations of life with the newfound possibilities of extended health and wellbeing, leading to uncertainties and concerns about the sustainability of these positive changes. Participants in three studies described an existential crisis intertwined with the loss of their CF identity. A participant

struggled to reconcile their improved health with their former identity as being “chronically ill” (Aspinall et al., 2022; Ladores and Polen, 2021).

Subtheme 4b: Redefinition of Self

Participants in four studies (Aspinall et al., 2022; Kauser et al., 2022; Keyte et al., 2023; Page et al., 2022) highlighted how improved health status was associated with a sense of normality that facilitated the adoption of a ‘normal identity’. As expressed in Kauser et al. (2022), participants found everyday life to be more manageable and felt a shift from viewing CF as defining their identity to understanding it as a health condition among others. Similarly, Page et al. (2022) highlighted the positive impact of CFTR modulators on identity, with a participant feeling confident to disclose their CF status to their employer emphasising that CF was no longer the defining aspect of their identity “I have told my employer I have CF but it’s not like... it’s not my identity, right? It’s not my identity anymore”. This shift signifies a redefinition of self, where CF no longer dominated their sense of identity due to reduced hospitalisations and exacerbations brought by modulators such as ETI.

Theme 5: CF Care in the CFTR Modulator Therapy Era

This theme was identified in the majority of the studies. The theme captured the challenges and opportunities associated with navigating the new realities of new treatments. Within this theme are two subthemes: a) addressing specific concerns and b) need for psychological support.

Subtheme 5a: Addressing Specific Concerns

In one study (Aspinall et al., 2022), participants expressed a need for improved communication and understanding from their clinical teams. A notable disparity was observed between perspectives of people with CF and medical professionals, emphasising

the importance of acknowledging their concerns and viewpoints, particularly regarding issues such as weight gain and body image. Some studies pointed out that clinical teams primarily focused on lung function, potentially leading to a disconnect with the priorities of people with CF (Aspinall et al., 2022):

I told them I was struggling with perception of self. I did not like how I looked, it was damaging my confidence... But when I gained weight on Kaftrio, the only thing they had to say to me was, 'no don't worry, . . . your lung function looks great'. That's not what I needed to hear—I felt lost.

Participants in two studies (Ladores et al., 2020; Keyte et al., 2023) expressed worries regarding fertility issues after commencing modulator therapies. CFTR modulators are bringing to the fore fertility concerns due to improved health and life expectancy, emphasising the need for readily accessible information regarding antibiotic use alongside contraception. Participants stressed the importance of understanding reproductive issues as healthcare providers historically did not have to address these concerns:

...up until recently, there wasn't a need for them [health-care providers] to understand reproductive issues because we weren't living as long to have families. (Ladores et al., 2020)

I got pregnant by accident [...] I was on the pill, so I was being sensible. I have antibiotics I take if my chest is having a flare up. If I take extra antibiotics on top of what I'm normally on, that counteracts contraception [...] if you ask the questions, you'll get the answers, but it should be there available to you. (Keyte et al., 2023)

There was a sense of frustration conveyed along with a desire for information to be easily accessible. Participants wished clinical teams would proactively provide information rather than waiting to be asked for such details.

Participants in one study (Keyte et al., 2023) felt that there were gaps in knowledge regarding CF specific adverse effects related to lifestyle factors like smoking, excessive alcohol consumption and illicit drug use. There was a call for proactive education and awareness to be integrated into CF care to cater to the need of both current and future generations of people with CF.

Subtheme 5b: Need for Psychological Support

A common theme across four studies (Keyte et al., 2023; Aspinall et al., 2022; Landes et al., 2024; Page et al., 2022) identified by participants and the authors in the included studies, was the need for psychological support particularly for individuals struggling with side effects challenges with identity, weight, and anxiety. The need for holistic care that encompasses emotional and psychological wellbeing was highlighted, however, a participant in the study by Aspinall et al. (2022) highlighted hurdles such as lengthy waiting lists for psychological services and limited accessibility:

...[In the past] I called my psychology team nearly in tears, I was really struggling. All they told me was that the waiting list was long and that I would likely not be seen for at least eight weeks . . . if that was someone's cry for help, there is no-one listening.

There was a sense of feeling disregarded and a perception of inadequate support when needed. Another participant in a study by Keyte et al. (2023) expressed a desire for routine psychological support like other healthcare professional encountered during clinic appointments. They mentioned:

I wish it was just as common to see the psychologist in your clinic appointments as it is to see your physio, the dietician [...] when I've really struggled, you kind of don't ask for help even though you want it. So actually, to have it given to you without you needing to ask, would be really helpful

A participant from the study by Aspinall et al. (2022) encapsulated this theme by conveying a feeling of helplessness, stating “the teams need to do more. This is a life changing event that we have just been told to be grateful for and get on with it—I don't know how to get on with it.”

Discussion

The review aimed to explore the psychosocial experiences of people with CF taking any of the four available CFTR modulators. From the analysis, five analytical themes, and eight subthemes emerged. These themes will be discussed below in the context of existing literature.

Living a Life Less Defined by CF

A central theme to arise from the review was that CFTR modulators had a positive impact on participants lives, empowering them to plan for the future, pursue opportunities like work or starting a family, and fostering hope and optimism. Similarly, in a mixed methods study on French participants by Martin et al. (2021), not included in this review due to a lack of direct quotes from participants to support interpretation of findings, also found significant improvements in physical and psychosocial wellbeing after taking ETI. Participants in the Martin et al. (2021) study reported a shift in their quality of life, moving from a future overshadowed by death or lung transplant to setting new goals and planning for the future.

There is strong clinical evidence supporting the benefit of CFTR modulators such as improved lung function and overall quality of life (Bacalhau et al., 2023; Keating et al., 2018), aligning with this review's findings. However, this review uniquely emphasises the subjective experiences of increased normality, fulfilment, and freedom from the constraints of CF, aspects that purely quantitative studies might overlook but are important for clinical relevance.

Double Edged Sword of CFTR Modulator Therapies

The findings from this review emphasised the importance of considering both the positive and negative impact of CFTR modulators. While many participants benefited from improved physical and mental wellbeing, some faced difficult decisions about continuing the medication due to side effects, such as weight gain. Before CFTR modulator therapies, people with CF were supported to maintain a healthy weight with a high calorific diet by their clinical teams (Bailey et al., 2022). Weight gain sometimes hindered participants in this review to enjoy the health benefits such as improved lung function, as some participants experienced distress over changes in body image. A qualitative study on UK CF clinicians revealed a knowledge gap in weight management among healthcare providers, with clinicians being hesitant to bring up topics about weight gain (Snowball et al., 2023). Motivational interviewing has been suggested to improve communication and address these issues (Michalopoulou et al., 2022; Oxley & Webb, 2005; Latchford & Duff, 2013).

Similar issues have been observed in other conditions like Lupus, where weight gain from steroid use can lead to negative body image, reduced medication adherence and in some cases, social withdrawal (Hale et al., 2015; Farinha et al., 2017; Rodrigues et al., 2021; Chambers et al., 2009). While this review did not directly link weight gain to non-adherence, it highlighted that some participants stopped taking modulators due to body image concerns

(Aspinall et al., 2022). A study included in this review (Landess et al., 2024) indicated concerns about side effects affected adherence.

Complex Emotional Landscape

The third theme highlighted the complex emotional landscape of using CFTR modulators, encompassing hope, happiness, grief, sadness, loss, survivors' guilt, and anxiety. Some participants in the studies included described conflicting emotions, such as happiness due to improved health, alongside grief for past difficulties. Some felt survivors' guilt, particularly due to the awareness of others who lack access to modulators like ETI. Survivors guilt refers to the feeling of guilt experienced by individuals who survive a disaster or traumatic event that claimed the lives of others (Hendrin & Haas, 1991). Survivors guilt has been documented previously among people with CF, for example in situations such as surviving when a lung donor did not (Fanos et al., 1991), as well as in other clinical groups, such as lung cancer survivors (Perloff et al., 2019).

The equity theory (Walster et al., 1973) suggests people prefer fair outcomes, which may explain the guilt in people with CF benefiting from CFTR modulator therapies when others cannot. In the Perloff et al. (2019) study with lung cancer patients experiencing survivors' guilt, the authors recommended psychological interventions such as self-compassion interventions and Acceptance Commitment Therapy (ACT), which can target guilt and other drivers of negative mood states. These interventions may be appropriate to consider for use with people taking CFTR modulators. It is also important to consider normalising survivors' guilt in people with CF taking CFTR modulators, as it is common in CF and other conditions.

Participants in this review also expressed anxiety about the future, fearing potential treatment failure and uncertainty about the long-term efficacy of CFTR modulators. These concerns echo findings from the mixed methods study by Martin et al. (2021) and highlight the need for further research on the long-term effectiveness of these therapies. Despite these challenges, there was also a sense of hope, with participants expressing gratitude and optimism for continued advancements in CF treatments and equitable access for all people with CF.

Navigating Changes in Identity

Theme four encapsulated how CFTR modulator therapies affected individuals' sense of identity. 'Illness identity' is a term used to describe the distinct ways in which chronic illness can be integrated into a patient's identity (Charmaz, 1995). Some participants included in this review experienced a loss of identity after starting ETI, feeling like they had drifted from the familiar path defined by CF.

Other research has highlighted the potential relevance of identity in CF, and how this might link to health-related behaviours. For example, a systematic review by Harrigan et al. (2024) found that self-efficacy, self-esteem and self-identity (dimensions of self-concept) were positively linked to better treatment adherence and psychosocial health in people with CF; recommending that clinicians consider these factors in treatment management. Relatedly, Leventhal's Common-Sense Model (CSM) of Self-Regulation, which suggests that perceptions of illness influence health behaviours (Hagger & Orbell, 2022), may also be a relevant framework for supporting people with CF negotiating changes to their identity after commencing CFTR modulator therapies.

In the current review, within the 'navigating changes in identity' theme, some participants reported reclaiming aspects of their lives previously overshadowed by CF, experiencing a shift towards a "normal" identity after starting ETI. Prior studies have shown that while most individuals with CF disclose their condition to prospective employers (Demars et al., 2011), they also fear not being hired on these grounds (Lowton, 2004). This review found that with improved health and fewer hospitalisations after starting CFTR modulators, some individuals were less afraid to disclose their CF diagnosis to employers.

CF Care in the CFTR modulator Therapy Era

The final theme shone light on both the challenges and opportunities for people with CF taking CFTR modulators and healthcare professionals (HCPs) alike. Specifically, the introduction of CFTR modulators represents a significant shift in CF care, leading to the need for re-education, both for people with CF and HCPs. Some gaps in knowledge included weight management, fertility issues and CF specific adverse effects of lifestyle factors.

Some participants in the current review experienced a discrepancy between their priorities and those of HCPs, particularly regarding issues such as weight gain and body image (Aspinall et al., 2022). Such discrepancies have been highlighted as clinically relevant in other physical health populations like Lupus, where in a mixed methods study, Sloan et al. (2022) reported that patients and physician priorities differed significantly. Given the evolving dietary needs in CF, shared decision making, a principle which draws on person centred care (Elwyn et al., 2012) is important. This framework emphasises informing patients about their options and helping them make decisions based on their preferences (Elwyn et al., 2012). The European Cystic Fibrosis Society (ECFS) also recommends clear communication and shared decision making in CF care (Southern et al., 2024).

The findings within this final theme also support the need for collaborative efforts and improved communication in addressing the needs of people with CF, including the provision of information and support without them having to request it. Moreover, the theme highlighted a need for psychological support, but obstacles such as long waiting lists and the need to request support hindered access. Integrating Psychologists into multidisciplinary CF care teams has been recognised as essential (Bathgate et al., 2023; NICE, 2017; CF Trust, 2011). Guidelines in the UK (National Institute for Health and Care Excellence and the CF Standards of Care) and consensus documents recommend including clinical psychologists in CF care teams for early detection and management of psychosocial issues (NICE, 2017; CF Trust, 2011; Dayasiri et al., 2021; Conway et al., 2014; Phillips et al., 2016), but access to these services can be limited in some countries.

Strengths and Limitations

One of the strengths of this review is that it is the first to synthesise the psychosocial experiences of people with CF taking CFTR modulator therapies, in studies that covered a range of demographics in terms of age, gender, type of modulator used, and country. The comprehensive search strategy employed aimed to capture all relevant literature, and the review was conducted systematically. Additionally, the rigorous screening for eligibility and data extraction, performed by the primary researcher and a doctoral postgraduate researcher, reduced the risk of bias and error. The overall quality rating for the body of evidence included in the review was good. However, a limitation of this review stems from the limited research available on psychosocial factors, resulting in some studies lacking rich, detailed participant quotations.

Regarding the quality of the reviewed studies, only two out of nine studies met criteria for reflexivity, which is important in qualitative research to ensure transparency and awareness of the author's biases (Ide & Bedoe, 2023). Additionally, some studies did not provide detailed explanations of the recruitment process (n=2) data collection (n=2), analysis methods (n=3) and ethical considerations (n=4). Although some studies were highly rated, their contribution to the overall themes was limited. Efforts were also made to ensure that the lower quality studies did not disproportionately impact upon the themes generated.

Only one study within the current review explored the experiences of children and young people taking CFTR modulators, and thus there was insufficient scope for drawing out possible differences in adult and child experiences. Thus, there may be further information specifically regarding young people that the current review has not identified. Additionally, all the included studies were conducted in Western countries, therefore, the experiences of people taking CFTR modulators from different countries, particularly those with higher levels of economic deprivation and lower resourced health services, may be different from the ones identified in the current review.

Among the studies included, two were case studies involving only one participant each. These studies were included due to the detailed quotes that provided valuable insight into some of the experiences of individuals taking CFTR modulators. However, caution should be taken in the interpretation of findings, recognising that not all participants encountered the same challenges or benefits. Nonetheless, efforts have been made to address this by presenting the number of studies reporting each theme.

Clinical and Research Implications

The results of this review highlighted the need for a comprehensive understanding of the psychosocial experiences after commencing CFTR modulator therapies. The finding that CFTR modulators have both positive and negative impacts for some people with CF would suggest that clinical teams should adopt a person-centred approach to treatment decision making, considering both the benefits and potential drawbacks. Clinical teams could offer information and support on important aspects highlighted in this review such as reproductive health, weight management, CF specific adverse effects of lifestyle factors, anxiety and uncertainty about the long-term efficacy of CFTR modulator therapies. This support could also include helping people with CF explore new opportunities such as participating in activities like sports, finding employment and planning for retirement. Furthermore, clinical teams could consider undergoing ongoing training to adapt to the changing landscape of CF care introduced by CFTR modulator therapies.

Services could also consider improving access to psychological support to help people with CF navigate the emotional complexities associated with CFTR modulator therapies. Psychologists could help advocate for people with CF by sharing their priorities and concerns and help facilitate shared decision making and improved communication within the team. Psychologists could also consider approaches such as Compassion-Focused Therapy (CFT) and Acceptance and Commitment Therapy (ACT) to address psychological challenges reported in this review such as survivors guilt and offer support to help individuals navigate changes in their self-perception. Additionally, psychologists could provide training to other healthcare professionals in techniques such as Motivational Interviewing, particularly around sensitive topics like weight management.

Despite the usefulness of this review in directing important areas of clinical practice, consideration of the themes from this review indicates several gaps in the literature worthy of future study. Future research should seek to: investigate the long-term psychosocial impact of CFTR modulators, expanding research to include diverse populations from non-Western countries and varying socioeconomic backgrounds; focus on gaps in knowledge about reproductive health, body image and lifestyle factors; and research the development of tailored psychological interventions and effective shared decision-making strategies is important in CF populations. Additionally, understanding CFTR modulators' impact on illness identity and improving access to psychological support in CF care settings are key areas for further study.

Conclusions

In conclusion, this study offers the first systematic review on the psychosocial experiences of people with CF taking CFTR modulators. Although current research is limited, the findings highlight how these treatments can bring about improvements for both physical and mental health outcomes. However, individuals also navigate various challenges including anxiety, uncertainty about the future, grief, survivors' guilt, and changes in identity and body image. A range of practical strategies are suggested to address the psychosocial implications of CFTR modulators, emphasising the importance of comprehensive care approaches that integrate both medical and psychological support.

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A Qualitative Exploration of The Experiences of Adults with Cystic Fibrosis unable to benefit from Triple Combination Therapy

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Abstract

Objectives

Cystic Fibrosis (CF) is a genetic condition, that causes a build-up of thick and sticky mucus in various organs, such as the lungs and digestive system. Treatment options for people with CF have undergone significant changes in recent years. Elexacaftor-Tezacaftor-Ivacaftor (ETI), the latest and most highly effective modulator therapy among four approved modulator therapies, has been beneficial for people with CF who have the most common genetic mutation. However, there has been limited research into the experiences of people with CF who are not able to benefit from ETI due to genetic factors. This study aimed to explore the experiences of these people and how they make sense of being in this situation.

Design

Data were collected from seven adult participants through semi-structured interviews.

Methods

Participants were purposively sampled from CF charities, online CF support groups, various social media platforms and one UK NHS CF Service, and were interviewed about their experiences. Interviews were transcribed verbatim and analysed using Interpretative Phenomenological Analysis (IPA). A reflexive diary was maintained throughout the research process.

Results

The analysis revealed four experiential themes. The first theme, *'feeling forgotten'*, highlighted the challenges of being in a minority group and feeling forgotten, overlooked, or

left behind. The second theme, *'conflicted emotions'*, explored the emotional impact of comparing one's situation with those who can benefit from ETI. The third theme, *'fragility of hope'*, captured the journey of hope experienced by participants, from hopefulness before the release of ETI, losing hope at finding out that they cannot benefit from ETI, and a renewed sense of hope for future treatments for their cohort. The final theme, *'remaining on the old CF trajectory'*, details the ongoing challenges of having CF, highlighting the significance of ETI and the coping strategies participants employ to navigate challenging circumstances.

Conclusion

This study suggests that having CF, but not being able to benefit from ETI, has considerable impact. This novel study has several implications, including offering information to people with CF not able to benefit from ETI insights into ongoing trials and research, potentially alleviating their sense of being forgotten.

Keywords

Cystic Fibrosis, ETI, Triple Combination Therapy, Interpretative Phenomenological Analysis

Introduction

Cystic Fibrosis and Advancements in Treatment

Cystic Fibrosis (CF) is a genetic condition that is caused by a mutation in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Malfunctioning CFTR protein disrupts the movement of salt and water in various organs leading to a build-up of thick and sticky mucus in areas such as the lungs, intestines, and pancreas (Hisert et al., 2023; Hine et al., 2022). It is unclear how many people have CF globally. Guo et al. (2022) estimated that approximately 162,428 people live with CF across 94 countries, using data from patient registries. However, it is worth noting that patient registries may be lacking in low-middle income countries (Guo et al., 2022).

CFTR mutations can cause diverse health issues, such as persistent coughing, recurring chest infections, pancreatic insufficiency, difficulties gaining weight and other related conditions such as bone diseases, CF-related diabetes, male infertility, and liver problems (Chen et al., 2021; Bell et al., 2020). Consequently, managing CF requires a complex treatment regimen involving airway clearance methods, long term nebulised antibiotics and mucolytics, pancreatic enzymes, intravenous antibiotics, and oral antibiotics over extended periods of time (Goldbeck et al., 2014; Davies et al., 2020). Studies have indicated that anxiety and depression are more prevalent amongst people with CF than within the general population (Cruz et al., 2009), with prevalence ranging from 2-3 times higher (Quittner et al., 2014).

Previously, available treatments for CF primarily addressed the symptoms and related complications associated with CF, rather than targeting specific genes. However, significant progress has been made in the last decade with the development of CFTR modulator

therapies which target the root cause of CF (Zemanick & Accurso, 2019; Bell et al., 2020). There are currently four approved CFTR modulator therapies, with the most recent being a triple combination of three different compounds, Elexacaftor, Tezacaftor and Ivacaftor (ETI) also known by its brand names Kaftrio or Trikafta. For this study, this modulator therapy will be referred to by its generic term 'ETI'. ETI has been authorised for use in healthcare systems in many medium-high income countries such as the USA in 2019 and the UK in 2020 (Hine et al., 2020; Bierlaagh et al., 2021). ETI targets the most common CF mutation, potentially benefiting approximately 90% of people within the CF population (Hine et al., 2020). Whilst there is growing research on the physical and psychological benefits of ETI, little is known about the experiences of people with CF who cannot benefit from ETI due to genetic factors. The current study focuses on the experiences of this group.

Experiences of those Suitable for ETI: The 90%

Since the release of ETI, there has been an emergence of qualitative research exploring the experiences of people with CF benefiting from this modulator therapy. Keyte et al. (2023), Aspinall et al. (2022), Almulhem et al. (2022), and Page et al. (2022) collectively reported positive outcomes such as improved physical wellbeing, quality of life, lung function, weight gain, and an increased sense of control, optimism, and hope for the future in some participants. These studies also highlighted participants' newfound abilities to engage in activities that they could not previously and hopes to reach new milestones, like parenthood and retirement. Participants in these studies also reported the negative impact of CFTR modulators, including adverse mental and physical side effects, feelings of loss or the need to redefine one's identity, heightened anxiety and distress following health changes, a perceived lack of understanding from their clinical teams and feelings of

survivors' guilt about benefiting from ETI (Aspinall et al., 2022; Dagenais et al., 2020; Talwalkar et al., 2017; Keyte et al., 2023).

Experiences of those Not Suitable for ETI: The 10%

Various factors contribute to why certain people with CF cannot benefit from ETI. These include having rare mutations, intolerance to the drug, limited access due to costs, age-related restrictions (as ETI is presently approved for individuals aged 2 years and above in the UK, but is likely to be different in other countries) (CF Trust, 2023), and exclusion post-lung transplant as modulators are not recommended for this population (Desai et al., 2022; Fajac & Sermet, 2021; CF Trust, 2022).

Only two studies have investigated the experiences of people with CF who are not able to benefit from ETI. Firstly, Kramer-Galinkoff et al. (2022) conducted a survey, distributed through social media, and emailed to people with CF not benefitting from ETI, which revealed mixed feelings. Whilst most were happy for those benefiting from ETI, they expressed a strong desire to experience similar improvements, resulting in feelings of being overlooked alongside negative self-comparisons with those benefiting from ETI. Secondly, a qualitative study using thematic analysis has been conducted in Italy to explore the experiences of this group. Participants in the study by Milo et al. (2023) expressed conflicting emotions about their declining health and feelings of happiness when observing others' successes. They described a sudden shift from hope and enthusiasm prior to the release of ETI, to disappointment when they found out that the type of mutation they had did not meet the criteria for ETI. They also felt a lack of hope for the future while simultaneously holding onto a renewed sense of hope in relation to ongoing medical research (Milo et al., 2023). However, since this study focused on a younger Italian demographic, exploring

perspectives of older individuals with CF beyond this group could offer new insights.

Additionally, understanding how people with CF who are not able to benefit from ETI re-interpret and find meaning in their situation, remains an important area for further investigation.

Research Aims

The focus of this study is on adults with CF who cannot benefit from ETI due to genetic factors. This study seeks to understand how these individuals' make sense of this situation. This understanding will be important for ensuring clinical practice meets the needs of these individuals.

In summary, the study aims:

- a) To understand the psychosocial impact of not being suitable for ETI due to genetic factors and to gain insight into the meaning adults make of their situation.
- b) To understand how people with CF not suitable for ETI due to genetic factors feel they could be better supported and identify the specific needs they have from services.

Methods

Study Design

Interpretative Phenomenological Analysis (IPA) was chosen as the methodology for this study as it seeks to understand individual participants' experiences by exploring how they make sense of significant life experiences (Smith et al., 2021). The theoretical framework for IPA integrates phenomenology, hermeneutics, and idiographic approaches (Spiers et al., 2016; Smith et al., 2009; Smith et al., 2021).

Participants

The emphasis within IPA research is on using a purposive homogenous sample rather than a random or representative sampling method (Smith et al., 2009). The sample was purposive, consisting of seven adults with CF unable to benefit from ETI due to genetic factors. Participants were eligible if they were: over 18; unable to benefit from ETI due to genetic factors; sufficiently fluent in English to take part, and sufficiently well physically and mentally to participate in an interview lasting 60-90 minutes, with breaks as needed. Participants who were acutely unwell or experiencing an acute exacerbation were excluded. Seven participants, consisting of four males and three females took part in the study. To ensure anonymity, participants were assigned gender neutral pseudonyms and referred to with gender-neutral pronouns. The participants' lung function ranged from 34% to 86% FEV1. Participants were aged 19 - 61, with a mean age of 40.6 years old. Data has been aggregated to protect participants from identification.

Ethical considerations and approval

Ethical approval for the study was gained from Cardiff University School of Research Ethics Committee [EC.23.02.07.6723RA2] (see Appendix E) and from a UK NHS Health Board Research and Development Department (see Appendix F).

Recruitment

Participant recruitment took place through two streams. For the first recruitment stream, participants were recruited through CF charities, online CF support groups and various social media platforms using poster advertisements (see Appendix G). This recruitment method relied on potential participants responding via email or scanning the QR code on the poster to leave their contact details for the researcher to get in touch with them (see Appendix H for consent to contact form). Upon contact, the researcher completed an eligibility screen and provided the participant a copy of the participant information sheet (see Appendix I). Participants were given an opportunity to ask questions before arranging a date and time for the interview.

For the second recruitment stream, the Principal Investigator (PI), who was a Clinical Psychologist, along with Research Specialist Nurses within a UK NHS CF Service identified potentially suitable patients from their clinical databases. Suitable patients were then approached and provided with the specific participant information sheet for this recruitment stream (see Appendix J). Participants had the option to either fill out the consent to contact form by scanning the QR code on the participant information sheet or have their contact information provided to the researcher by the PI and Research Specialist Nurses with their consent. Subsequently, the researcher used the provided contact information to address any

questions and schedule the research interview. Recruitment was conducted from March 2023 to May 2024.

Data Collection Method

Semi structured interviews were conducted by the researcher online via Teams, lasting between 35 and 70 minutes. At the start of each interview, the researcher provided a brief introduction to the study and provided an opportunity to clarify any questions. Participants were directed to an online consent form accessed via Qualtrics before the interview (Appendix K Recruitment Stream 1 and Appendix L Recruitment Stream 2). The researcher reminded participants that their participation was voluntary, that they were free to withdraw at any time and explained confidentiality. The potentially sensitive nature of the research topic was acknowledged, and participants were advised that they did not have to answer any questions they did not wish to. They were also told that they could take a break during the interview if necessary. Socio demographic information such as age, gender, lung function and location were also gathered to situate the sample. The interviews were conducted according to the schedule in Appendix M.

Table 1

Summary of interview questions

Interview Questions
1. Can you tell me about your experience of not being able to benefit from ETI?
2. Are you able to say a bit about what it feels like to not be suitable for receiving ETI?
3. What has life been like for you since you found out?
4. What does being unable to benefit from ETI mean for you?
5. Has this made a difference on how you view your life or things that are important to you?
6. How do you see yourself in the future?
7. Is there anything else that you feel is important that you have not yet had the opportunity to say?

The schedule was developed in consultation with the existing literature, discussions among the research team, and staff and service users at the CF Trust. Although not strictly followed, the schedule served as a guide for participants to prioritise and share what they considered to be central to their experience of not benefiting from ETI due to genetic factors. The style of the interview was inductive, fostering reflection and exploration. Where needed, the researcher probed for more detailed information to gain deeper insights into the participants perspective.

At the end of the interview, a debrief session was given, and although none of the participants expressed distress during the interview, they were signposted to relevant sources of support if needed (see Appendix N for Recruitment Stream 1 and Appendix O for Recruitment Stream 2). Additionally, as a token of appreciation for their participation, all participants were given a £10 voucher. The researcher also sought additional supervision when necessary to manage the emotional impact of engaging with participants' narratives.

Data Analysis Procedures

All interviews were audio recorded via Teams or on a password protected iPad, with participants' permission. Six interviews were transcribed verbatim by the primary researcher and one audio recording was submitted to a professional transcription service. A confidentiality agreement was signed (please see appendix P). Once a transcript was produced, the audio recording was deleted, person identifiable information removed, and the transcript was saved on the primary researchers' encrypted one drive account. Following this, data were analysed using the IPA procedure as outlined by Smith et al. (2021) and Smith et al. (2009). Initially, the researcher read the transcripts multiple times or re-listened to the audio recordings. The researcher then made exploratory notes, commenting on the

participants' descriptions, language, and conceptual elements, particularly focussing on overall concepts or psychological aspects (Smith et al., 2021).

Following these exploratory notes, the researcher constructed experiential statements that highlighted the key features from the transcript. Examples of analysed transcripts are included in Appendix Q. The next step involved identifying connections across experiential statements within each transcript, grouping some statements together and noting overarching concepts. These statements were cross referenced in the transcript to ensure they were grounded in the participants' specific words (Smith et al., 2021). A table of these statements was then generated. Each cluster of experiential statements was termed as the participants 'Personal Experiential Theme', please see Appendix R (Smith et al., 2021).

Once all the seven transcripts were analysed, the researcher then looked for patterns of similarity and differences across participants' 'Personal Experiential Themes' generating a set of 'Group Experiential Themes' (Smith et al., 2021). Another table was created to display the overall 'Group Experiential Themes' and subthemes (see Appendix S). The analysis continued into the writing up process, revealing patterns of convergence and divergence (Smith & Osborn, 2007).

Reflexivity

In IPA, there is a double hermeneutic process, in which the participant seeks to make sense of their own experiences, while the researcher aims to make sense of that sense-making (Smith, 2011). As a result, reflexivity, which is the process of being aware and bringing to light how the researcher influences the research process, is an essential part of IPA (Peat et al., 2019). The researcher kept a reflexive diary throughout the research process, documenting thoughts, reflections, making connections, and discussing these in supervision

(see Appendix T for an example). For instance, after engaging with interviews, the researcher was moved by the experiences shared by those who participated, and their gratitude for the research. Discussing this in supervision was helpful for acknowledging that despite being a researcher, emotive topics like these can impact the researcher.

Results

From the analysis of seven transcripts, four themes emerged. What follows is a detailed description of each 'Group Experiential Theme', supported by quotes from participants. Words that have been omitted from quotes are indicated by ellipses '...' and words added to enhance clarity and understanding for the reader are in square brackets '[]'. It is worth noting that participants referred to ETI by its brand names Kaftrio and Trikafta. Contributions of participants to each theme are shown in Appendix U.

Theme 1: Feeling Forgotten

A significant theme highlighted in participants' descriptions of their experiences was 'feeling forgotten', which was expressed in several ways. With the release of ETI gaining a significant amount of media coverage, all but two participant stated feelings of being 'forgotten', 'overlooked' or 'left behind'.

...and all the stuff in the media is focused on Trikafta Trikafta, and we sort of get a bit forgotten about all those who can't benefit... (Bailey)

...we are sort of left out of discussion when we talk about, you know, a cure for CF or a better medication for it [CF]... (Sam)

Jamie highlighted discussions about those who cannot benefit from ETI as an afterthought, which further emphasises feelings of being overlooked. This was linked to an increase in

feelings of frustration, possibly due to the expectation that research presenters should have a better understanding of inclusivity in their practice.

...like a final note at the end of a presentation is, of course we know that this doesn't apply to everyone, and there are a few people that don't benefit from this, its things like that that just add to the frustration sometimes ... (Jamie)

Jamie further highlighted gaps in services such as 'theratyping', which matches medications to specific types of mutations (Clancy et al., 2019; Graeber & Mall., 2023). The absence of established systems and support added to the challenges faced by those who do not benefit from ETI. This further increased a feeling of being forgotten, overlooked, frustrated and undervalued.

...It's [lack of services and information] just another thing that you don't have access to. It's just, it's an annoyance, it's a frustration... (Jamie)

Two participants did not express feeling forgotten, perhaps, due to reportedly being in a better health position than the other five participants. They stated:

To be honest, my – my health tends to be quite – I am quite healthy with CF, you know, all things considered. (Frankie)

... I'm not suffering with Cystic Fibrosis on a chronic basis...I'm lucky... (Ashley)

Ashley's use of the word 'chronic' may be referring to the chronicity of their 'suffering' rather than CF itself which is chronic.

'Us and them' Comparisons

Visibility on social media and TV shows prompted four participants to compare themselves with those who can benefit from ETI, leading to feelings of being forgotten, a sense of missing out which seemed to enhance their struggle.

...when the 'this changed my life' stories came into social media at the same time that I started being ill, I just felt like it's something I didn't want to hear about. So I blocked certain keywords on all of my profiles. Anything to do with [CF] or Kaftrio...
(Jamie)

Social media served as a reminder that other people's lives were improving whilst theirs was not. For Jamie, witnessing the improvement in others' lives while theirs was deteriorating seemed to engender feelings of sadness, loss and an overwhelming sense that they could only cope by avoiding CF or ETI related information. There was also a sense of disbelief at the improvements they had heard about. For Bailey, there was a significant contrast between their life and the life of the individuals benefiting from ETI that they saw on a TV show:

...Oh my gosh! Like, is she kidding? She doesn't have to do this anymore...Oh why me? Like the amount of hours I spend a day doing a nebulizer. Imagine just not having to do that anymore and just taking 3 pills in the morning or whatever and just going on with my day like a normal human. That just seems sort of incomprehensible to me... (Bailey)

Here, the participant on the show appears to experience a reduced treatment burden, a sense of normality and freedom from CF-related constraints. Although Bailey did not

explicitly mention feeling resentful, there is a sense that they might have these feelings as they compare their need for three nebulisers to what they perceive as the ease of other treatments. There's also a mix of disbelief, amazement, and frustration conveyed through phrases like "oh my gosh" "is she kidding" and "incomprehensible", which highlight the stark contrast in their treatment or CF experiences. Bailey's questioning of "why me" implies a sense of unfairness and injustice, feeling that others benefit from something they cannot. Three participants expressed indifference towards ETI, considering it secondary to other concerns. They conveyed that ETI held no significance for them, reflecting acceptance and a focus on moving forward.

Lack of Consideration in Research Priorities

Four participants also highlighted feeling forgotten in discussions about research priorities. Participants highlighted issues around funding and feeling like research efforts would not be directed to a minority group:

...who on Earth is waking up one day going. Oh, let me decide to research it [a drug that can benefit people with CF not able to benefit from ETI]. I mean, why wouldn't someone want to join the team that's researching Trikafta that they probably make a lot more money... (Bailey)

These feelings of being overlooked in research priorities due to funding were also connected to feelings of not being seen as worthy or seeing themselves as a poor investment. This further highlights a sense of being excluded or undervalued, as if they are not considered worthy or important enough to justify the allocation of funds. Although the participants didn't express explicit anger, there was an underlying sense that these emotions may have been present, given the perceived injustice and unfairness of the situation.

Variable Effort from Healthcare Professionals (HCPs)

All participants highlighted having positive and supportive relationships with their CF teams. However, not all interactions with HCPs were positive, for example:

...I'll do anything that helps you know people like me, but ... from the other side, from the NHS, from the medical professionals [there's] just not seeing the same [effort] that's just heartbreaking you know... (Sam)

Participants in the current study conveyed a sense of being forgotten, frustration and disappointment due to what they perceived as insufficient information, insensitivity, and a lack of commitment from HCPs. They conveyed a willingness to participate and contribute to studies or trials but feel disheartened by what they see as a lack of reciprocal effort from HCPs or services. Describing the experience as “heartbreaking” suggests a strong emotional reaction to feeling that their efforts are not met with the same level of acknowledgment or reciprocity.

Theme 2: Conflicting Emotions

This theme focusses on the conflicting emotions that arose for participants when reflecting on their situation and others' who can benefit from ETI.

...I'm very happy for those who can [benefit from ETI]... but then it also creates this level of disappointment that, yes, it's been great for them, but it's not something that I can benefit from... (Sam)

Sam highlights contrasting emotions of happiness for others and disappointment for themselves. Disappointment stems from realising that ETI is something they cannot benefit

from, highlighting a longing and desire for something they cannot have. Jamie echoed this sentiment:

...I was as happy for them as anyone could be, but it's then when the 'this changed my life' stories came into social media at the same time that I started being ill, I just felt like it's something I didn't want to hear about... (Jamie)

These feelings of jealousy, along with emotions like excitement and happiness, were also shared by Bailey:

... when I found out it wouldn't work, it was just sort of... felt like another setback in a way...but obviously it's mixed with feelings of incredible excitement for those who could benefit. But I obviously, selfishly wanted to be able to benefit as well... (Bailey)

The use of the word "another setback" illustrate the multiple challenges that come with CF, with not benefitting from ETI being an additional difficulty. In contrast, Alex expressed happiness and stated not feeling bitter or anger over ETI benefiting others but did indicate sadness about not having something similar to benefit from.

...I'm just kinda glad that there is something for the younger people, you know, or anybody... I'm not bitter. I'm not angry, I'm a little sad that there isn't something that I could have a go at, but it's no more than that... (Alex)

Unlike the experiences shared by other participants, two participants primarily conveyed positive emotions regarding the benefits of ETI for others. They stated:

...And for me, it's absolutely brilliant news. And I'm very buoyant about that. And I'm very happy and happy about it...I think it's fantastic (Ashley)

...I've got friends who have a child with CF, who has the Kaftrio drug, and they've said it's life-changing for them, which is great at the end of the day. (Frankie)

The more positive responses of this participant may be linked to their relatively better health status. However, Frankie and Alex did acknowledge that they may have felt differently if their situation was different.

You know, it's – I think it's – if I was ill all the time, I think I'd probably have a different outlook on it[ETI] and I think it would affect me a lot more. (Frankie)

...as things [health] get worse...I will maybe feel a little bit more angry or anxious...

(Alex)

This theme highlights the nuances present even within a small subgroup like the 10% who cannot benefit from ETI. The conflicting emotions they experience seemed to be influenced by their individual health situations. Nevertheless, they all acknowledged a longing and a desire to experience the benefits that others were experiencing.

Theme 3: Fragility of Hope

Hopeful experiences were intertwined throughout various participant accounts and reported by all seven participants. While five participants initially harboured hope upon ETI's release, believing they could benefit, discovering their rare mutations took the hope away.

...it was a bit disappointing...I've always been told that...there's always that gene therapy going on and one day it's going to be available... I've always had that hope in my back of my mind...then to be sort of told that I'm not eligible for it [ETI]... (Charlie)

Bailey further discussed a recurring pattern and the familiarity of things not working out, followed by the disappointment of not being able to benefit from something that benefits most of the CF population.

...But I feel like nothing ever really seems to happen or to work. And then finally, this thing did work. But then of course, there's a catch. And it didn't work for me. And I just sort of felt like, oh, this is so typical. (Bailey)

It seems that Bailey began with little hope or scepticism about a successful drug but the surprise that ETI did work initially brought a sense of hope, followed by disappointment and the loss of hope that it would not work for them.

Other participants expressed concerns about their current health status, which might not allow them to benefit from new drugs.

And I just keep hoping that maybe they will find something that I can have a go at before it gets to the point where maybe I wouldn't get any benefit. (Alex)

Three participants emphasised the importance of maintaining hope but expressed concerns about declining health or possibility of death, which might lead to missing out on opportunities to benefit from new medications.

Hope Enduring

Although participants mentioned experiencing a loss of hope, they also shared instances where they still had hope. All participants recognised the value of this research and were grateful for the opportunity to talk about their experiences. Additionally, two participants mentioned how this research had instilled hope.

...and then I stumbled upon this study for CF. And I thought, you know, this shines a light on people like me who have been, you know, left out of the discussion... (Sam)

This research appears to have not only made this participant feel acknowledged and provided an opportunity for their voice to be heard, but also instilled a sense of hope that they were not overlooked. This feeling was also expressed by another participant who, upon questioning if anyone would research rare mutations, shared:

...but then I mean, you've given me hope because I thought who on Earth would want to know about the psychological impacts of someone that can't benefit from Trikatfa. So, you know, thank you again for doing this. (Bailey)

These extracts demonstrated how research has the power to instil hope in marginalised groups who may find themselves in situations of hopelessness. Additionally, all seven participants expressed a shared belief that the introduction of ETI had sparked hope for upcoming treatments:

...I thought, you know, the fact that we have this [ETI], I was optimistic to some extent that we have been able to research this, this miracle of a drug and going forward, we might even come up with something that does help people with rare mutations... (Sam)

Sam acknowledged the CF community's prolonged anticipation for a drug like ETI, noting that the wait had been extended for them due to their inability to benefit from ETI. Despite this, they remain optimistic and hopeful for the future, expressing a strong belief in the development of a new drug for individuals with rare mutations. Another participant

expressed similar feelings of hope while also voicing concerns about what it means in terms of research priorities:

...Yeah, I think a little bit of both, but I think definitely Trikafta has given hope... but at the same time, it's also, in a sense, made me concerned that all the research will now be focused on that mutation. But, I still do hold out hope because you know, if it can happen for some people, why not me? (Bailey)

Theme 4: Remaining on the Old CF Trajectory

A notable aspect of the experiences of individuals with CF who cannot benefit from ETI was the feeling that they remained on the old CF trajectory. While all participants described continuing on their existing journey, there were subtle differences in their narratives. Bailey mentioned that those taking ETI no longer had to be concerned about their health:

...yeah, I think since Trikafta it's definitely made it more apparent that I'm still on the old track of CF disease progression where people get worse, not better. (Bailey)

This extract recognises the positive trajectory for individuals who can benefit from ETI, highlighting the contrast that made it clearer that Bailey was still experiencing the old course of CF disease progression, with the certainty of health decline.

Another participant draws a sharp comparison between the lives of individuals with rare mutations and those who cannot benefit from ETI:

...It is literally a life changing thing for those who can benefit from it. And it's ... quite literally a downgrade in those, well, not a downgrade, but for those who can't

benefit from it, they have to, you know, continue with all their treatments and still have a not-so-great quality of life... (Sam)

Again, this extract emphasises feelings of being left behind, and highlights the impact of not benefiting from ETI, resulting in diminished quality of life. There's a palpable sense of unfairness and injustice conveyed through terms like "downgrade". Being in this situation also has the potential to influence one's sense of identity regarding deserving treatments or not.

Two participants reflected on their health declining whilst seeing others' health improving, and a sense of "cruel timing" seeing others improve whilst they remain on the old CF trajectory:

...like it's really cruel timing in the way it's worked out that the majority of people with CF are now having a better life and CF isn't affecting them as much as it was. At the same time the exact opposites happened to me... (Jamie)

...because no matter how much I fight this illness. How much I get out of bed and do my physio and clear my lungs...I'm not really feeling the benefit of it anymore... (Charlie)

Here, Charlie suggests that their efforts are insufficient, leading to feelings of helplessness and an urgent desire for something beneficial as the current therapies do not appear to provide the needed help. Another participant recognised the urgency stemming from declining health and the absence of current options for improvement:

...but my CF my lung damage is quite severe now, it's progressing, so I'm not sure again how much if I did get the option it would actually change that now. (Alex)

This extract emphasises the certainty of health declining and the uncertainty of a new drug that could help with this decline of health, a feeling echoed in other participants' narratives.

Two participants expressed feelings of unfairness and injustice due to their experience of following the old trajectory of CF. This shifted their perspective from seeing themselves as part of the group unable to benefit from ETI to simply being individuals living with CF. Bailey expressed feelings of unfairness using a metaphor involving a deck of cards:

... I feel like in general just being dealt like the cystic fibrosis hand (laughs) if it was a deck of cards, I didn't get [...] dealt the best deck. Or the best hand... (Bailey)

This metaphor may suggest the unfairness of life and the added difficulties that accompany not benefiting from ETI, on top of the challenges of having CF. Jamie also echoed this feeling employing a metaphor involving bingo:

...If I played CF bingo, I'd win, so I'm having [list of health difficulties]. It's like everything's come all at once. In the modulator drugs ... you take them and they circulated through your body... so it benefits all of the areas of CF in your body. It's not just your lungs... (Jamie)

This metaphor was used to highlight a heightened awareness of the severity of CF, encompassing all the associated challenges despite initially experiencing a healthier CF life. Whilst all the participants acknowledged to an extent that they were on the old path of CF disease progression, the distinguishing factor now is that they can compare their situation with others who are receiving benefits from ETI, making their situation worse.

Distraction and positivity as a coping mechanism

Various coping strategies were integrated into the narratives of different participants. Distraction and maintaining positivity emerged as common coping mechanism for some participants. Jamie, Alex and Frankie highlighted that:

...I try not to think about the fact that it's not working, that I don't have that benefit that other people have and try and distract myself by looking at things that I can do to potentially change that... (Jamie)

...I just sort of shake myself and just sort of think...there's always people that I'm close to that unfortunately... that are struggling more and I think just put it into context where you are you know and if you're not well...do something proactive. (Alex)

... it [ETI] did give me a little bit of a kick up the bum to look after myself a little bit more, I think. (Frankie)

In this instance, these participants seem to engage in perspective taking; there is a sense of empathy and compassion towards others, and they advocate taking proactive steps to address one's health and wellbeing. There's a notable sense of empowerment and agency in taking control of their life. There is a feeling of embracing the current situation and discovering happiness and satisfaction in the present moment. Despite facing health challenges, there is a sense of appreciation and fulfilment, along with the deliberate decision to enjoy their day-to-day life. All participants expressed a sense of positivity as a coping strategy.

... I'm generally a positive person. I don't dwell on like negativity for too long...especially with CF, you can't you'll have good days, and you'll have bad days. Mostly you'll have bad days. (Bailey)

...but you know that there's no point wishing for something that I know isn't there? Because all you're doing is setting yourself up to have more pain than you know have enough pain in my life. So, you know it's more about enjoying the day. (Alex)

In terms of Kaftrio, I've moved on from it totally because I know it's something that I can't take. You know, there's no point, once again, there's no point dwelling on it. (Frankie)

There's an awareness of negative events occurring, yet there's also a tendency to avoid dwelling on them. Other participants also emphasised the importance of maintaining a sense of positivity or optimism as a coping strategy.

...I'm very blessed and I always try and stay optimistic. And I know I'm a lot healthier than, you know, a lot of people in the world. (Bailey)

Finding solace in comparing their health to others and perceiving themselves as "healthier" seems to contribute to their coping mechanism as well.

I always just seem to have quite a positive outlook on life in general. I think that obviously, having CF, I think you have to a little bit, otherwise every time you're ill it's going to get you down a bit more. (Frankie)

...You have to live life to your fullest, you know? And that's what I try to do most the time. But it's just that you always have this thing in the back of your mind that ...

you'd always ... have to struggle and you just don't know ... how and if ever it would ...change... (Sam)

There is a notable sense of positivity and resilience in persisting despite challenges of CF and not experiencing benefits from ETI. However, it appears that for Sam, it is not always possible to maintain this mindset successfully, as the thought of not benefiting from ETI often lingers in their mind.

Discussion

The current study is the first study employing an IPA methodology to explore the experiences of adults with CF who cannot benefit from ETI due to genetic factors. The study identified four main themes, including 'feeling forgotten', 'conflicting emotions', 'the fragility of hope', and 'remaining on the old CF trajectory'. This group has often been referred to as the "10%" (Desai et al., 2022), however, the current study offered a much-needed nuanced perspective of the experiences that exist within this group.

While all participants shared in the inability to benefit from ETI due to genetic factors, their individual situations varied. Some were relatively healthier, some learned upon the ETI's release that their mutations had been misidentified, placing them in the "10%", some had late CF diagnoses and were grateful for the 'good years' they had, while others experienced health deterioration post ETI release. Despite feeling forgotten, grappling with a range of emotions, and recognising that they had remained on the old path of CF disease progression, all participants acknowledged the transformative potential of ETI and held on to hope that there might be new treatments that help them in the future.

The first theme, 'feeling forgotten' emerged as a prominent experience among participants, aligning with findings from Kramer-Galinkoff et al. (2022), who conducted a survey with people with CF and their families, about their experiences of not being able to benefit from ETI. While their survey included open-ended questions, it was limited in their ability to capture in depth information of participants' experiences which this study provides. Additionally, the Kramer-Galinkoff. (2022) study combined the experiences of individuals with CF and their caregiver's, potentially limiting the specific experiences of those with CF who cannot benefit from ETI.

This study extends previous research by capturing nuanced emotions interlinked with feeling forgotten, such as disappointment and frustration. The feelings of disappointment and frustration reported in the current study were also reported by Milo et al. (2023) in a qualitative study exploring the experiences of people with CF who cannot benefit from ETI. The current study extends their findings, as the use of IPA provided the opportunity for an in-depth exploration of participants experiences. For example, some participants in the current study expressed feeling forgotten, disappointed, and frustrated particularly when encountering success stories on social media, television and in discussions about CF treatments. They felt overlooked in research priorities due to funding issues, leading to a perception of being seen as a poor investment. This sense of unworthiness, fuelled by a lack of research funding, echoes concerns raised by Landess et al. (2024) in a qualitative study primarily involving individuals who can take CFTR modulators, with one participant who couldn't benefit from ETI reported fear that less prevalent mutations would attract less research interest.

The theme of 'feeling forgotten' highlighted issues of access to life changing treatments like ETI as seen in recent UK controversies, where the National Institute for Health and Care Excellence (NICE) acknowledged the benefits of ETI but deemed their costs too high for use within the UK National Health Service (NHS) (Brendbekken & Bhopal, 2024; Wise, 2023; CF Trust, 2023). One participant in the current study recounted being denied access to trial ETI due to cost, increasing feelings of being overlooked and undervalued. This mirrors issues seen with expensive cancer drugs for the treatment of renal cancer and metastatic melanomas (Jackson, 2010; Siddiqui & Rajkumar, 2012).

One participant in the current study felt that being in the minority group without access to drugs like ETI made their challenges more pronounced compared to those benefiting from ETI, who, despite ongoing challenges, experience a better quality of life. This highlighted a profound sense of being left behind and highlights the need for increased funding and advocacy for this group. Their experiences also raise important questions about the value placed on their lives and the persistent feelings of being forgotten and unworthy in health economic decisions (Brendbekken & Bhopal, 2023; Wise, 2023).

Despite feeling forgotten, participants expressed a strong desire to be involved in research and trials for treatments, aligning with Kramer-Galinkoff et al. (2022). However, this study uncovered deeper themes not previously captured by previous research, revealing varied experiences regarding information about ETI and new treatments. Some participants in the current study felt that HCPs did not provide adequate information about ETI upon its release and lacked commitment to updating them on new trials. Three participants in the current study reported being informed about new trials, while others who felt information

was lacking experienced a sense of having to seek out information themselves, contributing to feelings of being forgotten and powerlessness.

The second theme of this study ‘conflicted emotions’ revealed a complex mixture of emotions among people with CF who cannot benefit from ETI. Participants in the current study expressed happiness and excitement for those who could benefit, alongside disappointment, sadness, feeling overwhelmed, and a strong desire to experience similar benefits themselves. These emotions were intertwined with a sense of hope. This contrasts with studies on those who can benefit from ETI, who often feel happy for themselves but sad for those who cannot (Keyte et al., 2023; Page et al., 2022; Aspinall et al., 2022)

These conflicting emotions expressed by people with CF highlighted the close-knit nature of the CF community, marked by empathy for those who cannot benefit by those who can, and happiness for those who can benefit from ETI by those who cannot. However, this also suggests potential divisions because of ETI. One participant in the current study noted that media focus on ETI risked overshadowing the needs of those who cannot benefit, while another reported avoiding any stimuli. Although not explicitly reported in this study, such experiences could potentially lead to resentment towards those who benefit from ETI.

The third theme, ‘the fragility of hope’, captured the fluctuating sense of hope experienced by people with CF who cannot benefit from ETI due to genetic factors. While hope was a constant in their lives, participants initially felt hopeful about ETI’s release, only to quickly lose that hope upon discovering their genetic mutations excluded them from its benefits. This led to feelings of disappointment and disbelief, with one participant questioning “*why me?*” Despite this, participant found a renewed, yet cautious, sense of hope for new treatments, as some worried about the time it takes for new drugs to progress

from development to trials to release, considering their health concerns. This mixed sentiment aligns with previous research on people with CF who cannot benefit from ETI (Milo et al., 2023). The use of IPA methodology in this study was particularly effective in capturing the nuanced fluctuations of hope, and the detailed, personal transitions in participants' experiences.

The final theme revealed that participants felt that they had remained on the old CF trajectory, facing worsening health typical of CF. They recognised the significant impact ETI could have on their overall wellbeing if they were eligible to receive it. Participants also expressed a sense of unfairness and injustice regarding the continued burden of their current treatments with limited efficacy. Participants in the current study employed coping strategies such as distraction, avoidance, optimism and maintaining a positive attitude. Participants in the current study employed coping strategies such as distraction, avoidance, optimism and maintaining a positive attitude. White et al. (2018) reviewed existing literature on coping with chronic illness and proposed a framework for clinicians. The framework included internal factors such as personal habits, individual differences and preferences, values and belief and emotional factors, as well as external resources such as social support and therapeutic interventions. White et al. (2018) emphasised the importance of both internal and external factors in promoting positive adjustment and coping. For instance, social support from family, friends and interactions with others who cannot benefit from ETI can help alleviate feelings of isolation, being left behind, or unworthiness reported by participants in the current study. Moreover, psychological interventions could assist people with CF who are not able to benefit from ETI by offering strategies to manage, regulate and express emotions, as suppressing or avoiding emotional responses have been linked to poor coping outcomes (De Ridder et al., 2008).

Study Strengths and Limitations

The study methodology, IPA, enabled a nuanced account of the experiences of a small and under-researched target group to be examined in depth. This approach allowed the participants in the current study to have their voices heard more profoundly than in previous research that have used other methodologies. Through detailed interviews and iterative interpretative analysis, the study did not just describe participants' experiences, but critically interpreted and explored underlying meanings. While previous studies have examined the experiences of this group, they lacked this level of analysis and interpretation, marking a unique contribution to the existing literature. Information was gathered through semi structured interviews, allowing the researcher to follow different lines of inquiry as they naturally arose. The seven participants represented various geographical locations within the UK and Australia, providing a broader perspective than studies that focused on a single locality, such as Milo et al. (2023), which centred on an Italian demographic.

The current study faced limitations, primarily the small sample size of seven participants. Despite challenges in recruiting, the sample size met the minimum criteria for an IPA study. Smith and Osborn (2007) argue that smaller numbers are suitable for the detailed and interpretative analysis, essential to IPA. Another limitation of the study is that most of the participants were from the UK, with one from Australia, and although generalisability is not the aim of an IPA study this potentially limits the applicability of findings beyond these regions, particularly to those in medium-low-income countries. Additionally, the study did not include views from those unable to benefit from ETI due to other factors like lung transplant or limited access in their countries.

Moreover, the lack of demographic details such as ethnicity might make it harder for some readers to determine the relevance of the results to their clinical populations. Future studies should address this issue, especially given that a higher percentage of people who cannot benefit from ETI are from ethnic minority groups (Desai et al., 2022). Another limitation was the inclusion of a participant who had rare genes but had not confirmed eligibility status with their CF team; however, their input on the lack of information provided by their healthcare teams was deemed valuable.

Clinical and Research Implications

Participants in this study generally reported positive relationships with their CF healthcare teams, but also expressed disappointment over gaps in service provision and information about ETI, new clinical trials and new research. They emphasised that better communication could help them feel more acknowledged and included. One participant in the current study, for instance, did not feel like part of the “forgotten few” due to their active participation and awareness of ongoing developments for people who cannot benefit from ETI. HCPs should consider acknowledging the specific struggles faced by people with CF not able to benefit from ETI, ensuring that they do not feel ‘forgotten’. They should communicate the reasons for ETI ineligibility clearly and empathetically, acknowledging the patient’s disappointment and other emotions. Clinicians should also provide updates on ongoing research and potential future therapies which can help mitigate feelings of hopelessness. There is also a potential role for service users’ involvement such as those who are not able to benefit from ETI to offer peer support which can provide a sense of community and validation, reducing feelings of being forgotten and unworthiness.

Given the different emotions experienced by participants in this study, such as hopelessness, feeling forgotten, undervalued, and powerless, it seems important that people with CF not suitable for ETI are offered psychological support where possible. In the wider CF literature, psychological support has been shown to be helpful (Havermans & Duff, 2020; Havermans & Staab, 2016). Interventions such as Acceptance and Commitment Therapy (ACT) and mindfulness exercises could help manage conflicting emotions arising from not being able to benefit from ETI, and can help people with CF manage any underlying feelings of anger and resentment or concerns about declining health, fostering a greater sense of present moment and acceptance (Kausser et al, 2022; Havermans & Duff, 2020).

Participants in the current study who cannot benefit from ETI due to genetic factors raised concerns about media portrayals of CF and ETI potentially leading to misconceptions and diverting funding away from research that could benefit them. Participants in the current study called for fair and equitable access to effective treatments for all people with CF. This suggests that there could be a role for CF charities to work with the media and ensure balanced portrayals that include the experiences of those not eligible for ETI, thereby, highlighting ongoing challenges and the need for continued research. This could involve featuring diverse patient stories and advocating for inclusive research and funding approaches. Future research could explore the experiences of those unable to benefit from ETI due to factors beyond genetics. Additionally, engaging service users in setting research priorities and involving them in advocacy efforts could ensure that the most pressing unmet needs are addressed.

Conclusion

This research explored the experiences of adults with CF who cannot benefit from ETI due to genetic factors. Participants in the current study shared rich, emotive, and personal stories that hold significant value for HCPs, therapists, researchers, pharmaceutical companies, and government organisations. Participants accounts highlight the profound impact of not benefiting from ETI, particularly feeling forgotten and undervalued, yet holding on to hope. Understanding these perspectives can guide the development of more inclusive and effective support systems and treatments.

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Appendices

Appendix A: Journal Guidelines for British Journal of Health Psychology

1. SUBMISSION

Authors should kindly note that submission implies that the content has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium.

New submissions should be made via the [Research Exchange submission portal](#). Should your manuscript proceed to the revision stage, you will be directed to make your revisions via the same submission portal. You may check the status of your submission at anytime by logging on to submission.wiley.com and clicking the “My Submissions” button. For technical help with the submission system, please review our FAQs or contact submissionhelp@wiley.com.

All papers published in the *British Journal of Health Psychology* are eligible for Panel A: Psychology, Psychiatry and Neuroscience in the Research Excellence Framework (REF).

Data protection:

By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including, when necessary, sharing with the publisher (Wiley) and partners for production and publication. The publication and the publisher recognize the importance of protecting the personal information collected from users in the operation of these services, and have practices in place to ensure that steps are taken to maintain the security, integrity, and privacy of the personal data collected and processed. You can learn more at <https://authorservices.wiley.com/statements/data-protection-policy.html>.

Preprint policy:

This journal will consider for review articles previously available as preprints. Authors may also post the submitted version of a manuscript to a preprint server at any time. Authors are requested to update any pre-publication versions with a link to the final published article.

2. AIMS AND SCOPE

The British Journal of Health Psychology publishes original research on all aspects of psychology related to health, health-related behaviour and illness across the lifespan including:

- experimental and clinical research on aetiology
- management of acute and chronic illness
- responses to ill-health
- health-related behaviour change and maintenance
- screening and medical procedures
- psychosocial mediators and moderators of health-related behaviours

- influence of emotion on health and health-related behaviours
- psychosocial processes relevant to disease outcomes
- psychological interventions in health and disease
- emotional and behavioural responses to ill health, screening and medical procedures
- psychological aspects of prevention

Papers must make a clear potential contribution to health psychology theory, knowledge and/or practice and employ rigorous research design and methodology..

We do not typically publish cross-sectional studies or those using only student populations unless there is a strong rationale for doing so.

Papers describing intervention development (without also presenting an analysis of the outcomes of the intervention) will usually only be considered if they make a contribution to health psychology theory, knowledge and/or practice beyond the specific intervention context.

3. MANUSCRIPT CATEGORIES

The types of paper invited are:

- papers reporting original empirical investigations, using quantitative, qualitative or mixed methods;
- theoretical papers which report analyses of theories in health psychology;
- review papers, which should provide systematic overviews, evaluations and interpretations of research in a given field of health psychology (narrative reviews will only be considered for editorials or important theoretical discourses);
- methodological papers dealing with methodological issues of particular relevance to health psychology;
- we particularly welcome papers reporting effectiveness (for example, Randomised Controlled Trials) and process evaluations of interventions in clinical and non-clinical populations.

Authors who are interested in submitting papers that do not fit into these categories are advised to contact the editors who would be very happy to discuss the potential submission.

Papers describing quantitative research (including reviews with quantitative analyses) should be no more than 5000 words (excluding the abstract, reference list, tables and figures). Papers describing qualitative or mixed methods research (including reviews with qualitative analyses) should be no more than 6000 words (including quotes, whether in the text or in tables, but excluding the abstract, tables, figures and references). In exceptional cases the Editor retains discretion to publish papers beyond this length where the clear and concise expression of the scientific content requires greater length (e.g., explanation of a new theory or a substantially new method). Authors must contact the Editor prior to submission in such a case.

All systematic reviews must be pre-registered and an anonymous link to the pre-registration must be provided in the main document, so that it is available to reviewers. Systematic reviews without pre-registration details will be returned to the authors at submission.

Please refer to the separate guidelines for [Registered Reports](#).

4. PREPARING THE SUBMISSION

Open Research initiatives.

Recognizing the importance of research transparency and data sharing to cumulative research, *British Journal of Health Psychology* encourages the following Open Research practices.

Sharing of data, materials, research instruments and their accessibility. *British Journal of Health Psychology* encourages authors to share the data, materials, research instruments, and other artifacts supporting the results in their study by archiving them in an appropriate public repository. Qualifying public, open-access repositories are committed to preserving data, materials, and/or registered analysis plans and keeping them publicly accessible via the web into perpetuity. Examples include the Open Science Framework (OSF) and the various Dataverse networks. Hundreds of other qualifying data/materials repositories are listed at the Registry of Research Data Repositories (<http://www.re3data.org>). Personal websites and most departmental websites do not qualify as repositories.

Free Format Submission

British Journal of Health Psychology now offers free format submission for a simplified and streamlined submission process.

Before you submit, you will need:

- Your manuscript: this can be a single file including text, figures, and tables, or separate files – whichever you prefer (if you do submit separate files, we encourage you to also include your figures within the main document to make it easier for editors and reviewers to read your manuscript, but this is not compulsory). All required sections should be contained in your manuscript, including abstract, introduction, methods, results, and conclusions. Figures and tables should have legends. References may be submitted in any style or format, as long as it is consistent throughout the manuscript. If the manuscript, figures or tables are difficult for you to read, they will also be difficult for the editors and reviewers. If your manuscript is difficult to read, the editorial office may send it back to you for revision.
- The title page of the manuscript, including a data availability statement and your co-author details with affiliations. (*Why is this important? We need to keep all co-authors informed of the outcome of the peer review process.*) You may like to use [this template](#) for your title page.

Important: the journal operates a double-anonymous peer review policy. Please anonymise your manuscript and prepare a separate title page containing author

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To submit, login at <https://wiley.atyponrex.com/journal/BJHP> and create a new submission. Follow the submission steps as required and submit the manuscript.

If you are invited to revise your manuscript after peer review, the journal will also request the revised manuscript to be formatted according to journal requirements as described below.

Revised Manuscript Submission

Contributions must be typed in double spacing. All sheets must be numbered.

Cover letters are not mandatory; however, they may be supplied at the author's discretion. They should be pasted into the 'Comments' box in Editorial Manager.

Parts of the Manuscript

The manuscript should be submitted in separate files: title page; statement of contribution; main text file; figures/tables; supporting information.

Title Page

You may like to use [this template](#) for your title page. The title page should contain:

- A short informative title containing the major key words. The title should not contain abbreviations (see Wiley's [best practice SEO tips](#));
- A short running title of less than 40 characters;
- The full names of the authors;
- The author's institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- Abstract;
- Keywords;
- Data availability statement (see [Data Sharing and Data Accessibility Policy](#));
- Acknowledgments.

Author Contributions

For all articles, the journal mandates the CRediT (Contribution Roles Taxonomy)—more information is available on our [Author Services](#) site.

Abstract

For articles containing original scientific research, a structured abstract of up to 250 words should be included with the headings: Objectives, Design, Methods, Results, Conclusions. Review articles should use these headings: Purpose, Methods, Results, Conclusions. As the abstract is often the most widely visible part of your paper, it is important that it conveys succinctly all the most important features of your study. You can save words by writing short, direct sentences. Helpful hints about writing the conclusions to abstracts can be found [here](#).

Keywords

Please provide appropriate keywords.

Acknowledgements

Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

Statement of Contribution

All authors are required to provide a clear summary of ‘what is already known on this subject?’ and ‘what does this study add?’. Authors should identify existing research knowledge relating to the specific research question and give a summary of the new knowledge added by your study. Under each of these headings, please provide 2-3 (maximum) clear outcome statements (not process statements of what the paper does); the statements for ‘what does this study add?’ should be presented as bullet points of no more than 100 characters each.

Main Text File

As papers are double-anonymous peer reviewed, the main text file should not include any information that might identify the authors.

Manuscripts can be uploaded either as a single document (containing the main text, tables and figures), or with figures and tables provided as separate files. Should your manuscript reach revision stage, figures and tables must be provided as separate files. The main manuscript file can be submitted in Microsoft Word (.doc or .docx) or LaTeX (.tex) format.

If submitting your manuscript file in LaTeX format via Research Exchange, select the file designation “Main Document – LaTeX .tex File” on upload. When submitting a LaTeX Main Document, you must also provide a PDF version of the manuscript for Peer Review. Please upload this file as “Main Document - LaTeX PDF.” All supporting files that are referred to in the LaTeX Main Document should be uploaded as a “LaTeX Supplementary File.”

LaTeX Guidelines for Post-Acceptance:

Please check that you have supplied the following files for typesetting post-acceptance:

- PDF of the finalized source manuscript files compiled without any errors.
- The LaTeX source code files (text, figure captions, and tables, preferably in a single file), BibTeX files (if used), any associated packages/files along with all other files needed for compiling without any errors. This is particularly important if authors

have used any LaTeX style or class files, bibliography files (.bbl, .bst, .blg) or packages apart from those used in the NJD LaTeX Template class file.

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- Abstract structured (intro/methods/results/conclusion);
- Up to seven keywords;
- Main body: formatted as introduction, materials & methods, results, discussion, conclusion;
- References;
- Tables (each table complete with title and footnotes);
- Figure legends: Legends should be supplied as a complete list in the text. Figures should be uploaded as separate files (see below)
- Statement of Contribution.

Supporting information should be supplied as separate files. Tables and figures can be included at the end of the main document or attached as separate files but they must be mentioned in the text.

- The main text file should not include any information that might identify the authors. Please do not mention the authors' names or affiliations and always refer to any previous work in the third person.
- The journal uses British spelling; however, authors may submit using either option, as spelling of accepted papers is converted during the production process.

References

This journal uses APA reference style; as the journal offers Free Format submission, however, this is for information only and you do not need to format the references in your article. This will instead be taken care of by the typesetter.

Tables

Tables should be self-contained and complement, not duplicate, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, ¶, should be used (in that order) and *, **, *** should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

Figures

Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted.

[Click here](#) for the basic figure requirements for figures submitted with manuscripts for initial peer review, as well as the more detailed post-acceptance figure requirements.

Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

Supporting Information

Supporting information is information that is not essential to the article, but provides greater depth and background. It is hosted online and appears without editing or typesetting. It may include tables, figures, videos, datasets, etc. [Click here](#) for Wiley's FAQs on supporting information.

Note: if data, scripts, or other artefacts used to generate the analyses presented in the paper are available via a publicly available data repository, authors should include a reference to the location of the material within their paper.

General Style Points

For guidelines on editorial style, please consult the [APA Publication Manual](#) published by the American Psychological Association. The following points provide general advice on formatting and style.

- **Language:** Authors must avoid the use of sexist or any other discriminatory language.
- **Abbreviations:** In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Initially, use the word in full, followed by the abbreviation in parentheses. Thereafter use the abbreviation only.
- **Units of measurement:** Measurements should be given in SI or SI-derived units. Visit the [Bureau International des Poids et Mesures \(BIPM\) website](#) for more information about SI units.
- **Effect size:** In normal circumstances, effect size should be incorporated.
- **Numbers:** numbers under 10 are spelt out, except for: measurements with a unit (8mmol/l); age (6 weeks old), or lists with other numbers (11 dogs, 9 cats, 4 gerbils).

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5. EDITORIAL POLICIES AND ETHICAL CONSIDERATIONS

Peer Review and Acceptance

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Appendix B: Line by Line Coding

Example from Almulhem et al. (2022).

Extract from Almulhem et al. (2022)	Line by line coding
<p>'Kaftrio changed my life' Most participants emphasised the changes in their lifestyle after starting ETI and they compared this with the time before they were taking it: 'Well, it doesn't affect me anymore'. As this young man indicated when asked about the difference he experienced after ETI, he described how the symptoms he had experienced had disappeared. He felt that CF does not affect his health any longer. The majority of cwCF interviewed felt that their respiratory symptoms, such as cough and shortness of breath, had reduced and that their lung function had improved.</p> <p>For example, Anna said: 'I would say that it has made my lungs feel better. It's been less coughing overnight, which I appreciate ... and less mucus which I appreciate'. Being more active and awake, having more energy, not being tired and sleeping well were all frequently described. Maggie spoke about her health after ETI: 'I'd say a bit because it's made me a lot better, more awake ... I was really tired before and I'd have like nine hours of sleep and still be tired and just like I need another nap. Now it's like I can wake up and just have a day and then sleep at the end instead of needing breaks during the day. Which is nice.</p> <p>This subtheme focused on the psychological impact reported by children and their families. Many participants reported a positive change in their outlook towards their lives. Several children relayed how as long as they could remember they had experienced symptoms and that now they felt incredibly well comparatively. This healthy feeling meant for the first time they looked optimistically to the future. Rose talked about her feelings before and after ETI: for such a very, very long time CF felt like a really untreatable thing, and everything you're doing feels like you're just trying to prolong something that like prolong a life that might not be as high a quality as a lot of people's. But the Kaftrio has really been the first proper step towards an effective treatment, that actually does something more than necessarily prolonging ... you feel more like other people and you feel more like you are healthy, even if you aren't necessarily better properly.</p>	<p>Lifecchanging impact</p> <p>Comparing then and now</p> <p>Not affected by CF since taking ETI</p> <p>Disappearance of CF symptoms</p> <p>Improved respiratory symptoms.</p> <p>Gratitude expressed for improvements.</p> <p>Feeling energetic</p> <p>Sleeping improved</p> <p>Positive feelings towards improvement</p> <p>Feeling incredibly well</p> <p>Optimistic about the future</p> <p>Comparing lives pre and post ETI</p> <p>Optimistic for the future</p> <p>CF felt untreatable (sense of things being impossible)</p> <p>ETI step towards effective treatment</p>

<p>Some cwCF expressed disappointment and frustration that they had not experienced as much benefit as some other people had. Several children had compared results with others who shared experiences on social media. For example, Ruby talked about her lung function and how she felt about not seeing the huge impact that she had been expecting I don't think there has been a huge impact. It's probably in the 80s now, which is still good. It's really good, but the difference, probably. I know some people who—well, I don't say I know, I mean like on social media and stuff—that has gone from 30 to 90, like it has been incredible. Yes. I haven't seen a huge impact from the lung function side ... I think there are people who it has impacted their life and made a huge difference, and I think that's amazing for them. For me, personally, yes, sports, for example, amazing. But apart from that, I haven't really seen a huge impact. My doctors might say otherwise, but me personally, I think it has not really done that much. The first theme, 'Kaftrio changed my life', highlights the physical and mental improvement reported by cwCF and their families and its influence on their day to day lives. The next theme that developed from the analysis related to treatment burden.</p>	<p>ETI more than life prolonging Disappointment and frustration when comparing to others</p> <p>Comparing with others taking ETI</p> <p>Acknowledgement of improvement</p> <p>Disappointed at not seeing same improvement</p> <p>Amazed at the improvement of others</p> <p>Disparity between what they think and what clinicians might think regarding lung function</p> <p>Lung function good but not good enough</p>
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Example from Keyte et al. (2023)

Extract from Aspinall et al. (2020)	Line by line coding
<p>Unpleasant side effects were something that many individuals within the study were willing to live with, given the trade-off for long-term health benefits. However, others worried that the potential side effects would mean that they had to discontinue Kaftrio. Similarly, all participants were wary of the effect that Kaftrio had on their liver, with the worry that potential increases in liver enzymes would result in their team removing access to modulator therapy. Laura, who had CF-related liver disease, noted that Kaftrio had elicited major positive changes to her pulmonary health, but she was concerned that this might only be short-lived should her liver status change: “Back in 2020, around June, my liver disease became fatal and failed . . . after being on it [Kaftrio] for a couple of weeks . . . my liver function rose . . . for me it was very stressful . . . The liver</p>	<p>Weighing options</p> <p>Living with side effects vs living without Kaftrio</p> <p>Worries about impact of Kaftrio on Liver function</p> <p>Worries about stopping to take Kaftrio</p>

<p>thing is never going to get better, that's always going to be there. I have got the fear that . . . because your liver function can just go up, I get scared in case they stop you . . . would I revert back to how I was and everything that has improved be ripped away from me?" Accordingly, as many participants had seen the positive changes that Kaftrio had on their day-to-day life, a number of participants lived in fear of Kaftrio subsequently being removed due to other health complications. For many, returning to a life pre-Kaftrio was now unimaginable, with Ben describing: "I think my main anxiety comes from the fact that I've now been given this opportunity or like dangled carrot of, look what your life could be like, and in the back of my mind is when is it going to go away. All the time." These feelings were echoed by Marin: ". . .</p> <p>It's all riding on it [Kaftrio] now . . . there's no other alternatives . . . and if it stops working, where do you go, even in your head with that?" As a result, a sense of uncertainty around the future was something that the majority of individuals reported, regardless of their overall experience. These participants stated that the lack of available knowledge regarding the long-term efficacy of Kaftrio raised concerns that their health may start to deteriorate without warning. For older individuals, such as Katie and Marin, they referred to Kaftrio as their 'last chance', and Marin expressed a desire for additional understanding as to how their health may hypothetically look in the short-term future: "What happens if I go back to where I was [pre-Kaftrio]? This was the be all and end all, this was supposed to solve all my problems and if this doesn't work then what? I have had to speak with a psychologist... It is [the worry] more the idea of what happens when this goes away—how long is that going to be there? Nobody knows." Many described CF as a proverbial rollercoaster, with emotional highs and lows. The participants were accustomed to "looking over their shoulder" for negative health outcomes to present themselves, and Kaftrio was suggested to represent for some a scenario that was almost too good to be true and "something that never happens to us [CF individuals]". As such, individuals consistently professed they were "not allowing themselves to get carried away".</p> <p>Loss of Identity For some, modulator therapy resulted in an "identity crisis" and a feeling of being overwhelmed. Four individuals noted an understanding as to the path in which their life was following pre-therapy; however, the prospect of an extended life left a lot of unanswered questions and thoughts regarding both short- and long-term goals. Individuals spoke about how their CF has always been 'road mapped' out, whereas, since Kaftrio, the road was unclear. Ben spoke about his struggles of having to alter his perception of self: ". . . this is</p>	<p>Worries about reverting to life pre Kaftrio</p> <p>Fear of Kaftrio being stopped</p> <p>Tasting a life with Kaftrio brings worries about reverting back</p> <p>Back of my mind might refer to thinking about it all the time</p> <p>Kaftrio seen as the only hope</p> <p>Uncertainty about the future</p> <p>Lack of knowledge on Kaftrio</p> <p>Fear of health deteriorating suddenly</p> <p>Kaftrio seen as last chance</p> <p>Role of psychologist in discussing these worries</p> <p>A sense of Kaftrio being too good to be true</p> <p>Worries Kaftrio would be taken away</p> <p>Loss of identity post Kaftrio</p> <p>Prospect of extended life led to unanswered questions</p> <p>Uncertain of what life looks like post Kaftrio</p> <p>Certainty of life pre Kaftrio</p>
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<p>how I summed it up. I completely lost my identity. Like, I didn't know who I was or what I am doing or what is going on . . . I felt like my identity was my health and my job and now they are not the same." Indeed, the concept of a loss of identity highlights that, for some, Kaftrio may represent a period of trauma in which individuals find it hard to manage or conceptualise their new health status. For two participants, the issues lay in having to disassociate with the person they were and the life they were used to when the future remained so uncertain. Overall, the perceived negative impacts of Kaftrio found within this sample were mainly focused on the side effects, having the taste of a 'normal' life cruelly removed, and fear and uncertainty regarding a drug in its infancy, which left the participants unable to let themselves become "too carried away".</p>	<p>Loss of identity</p> <p>Difficulties conceptualising new health status</p> <p>Negative impact of Kaftrio (side effects, discontinuation, uncertainty and worries, loss of identity)</p>
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Example from Ladores et al., (2020)

Extract from Ladores et al. (2020)	Line by line coding
<p>Ana began taking LUMA/IVA 7 months after getting married and became pregnant 2 weeks after starting the drug. Ana shared the positive changes that she noticed after starting LUMA/IVA: "I was definitely less congested lung-wise just a few days after." She went on to add that, "I had a feeling that also means that the mucus that I had covering my cervix also thinned out." Once Ana became pregnant, she spoke to her CF care team about her pregnancy and described their reactions: "There was one or two doctors who had warned me previously that they didn't support pregnancy in CF patients because it's dangerous." Despite the initial negative reception to her pregnancy announcement, Ana eventually found support from her health-care providers. When her first son was approximately 7 months old, Ana was placed on intravenous antibiotics for a CF exacerbation. She described how the LUMA/IVA and being on the antibiotics resulted in her second unanticipated pregnancy: "It [antibiotic] caused me to ovulate twice. It threw off my ovulation so much [that] I got pregnant the month after I was in the hospital." She shared that the second pregnancy was an even bigger surprise compared to the first. However, with the shock also came anxiety: "The danger of being pregnant hit me more ... having a child already and knowing [that] something could happen to me and [I may have to] leave him." Lastly, Ana spoke about the changing needs of women with CF: "I don't think that, up until recently, there was a need for them [health-care providers] to understand reproductive issues because we weren't living as long to have families."</p>	<p>Improvement in physical health</p> <p>Became pregnant post Lumacaftor/Ivacaftor</p> <p>Doctors not in support of pregnancy in CF with CFTR modulators</p> <p>Support from HCPs later received</p> <p>Antibiotics and LUM/IVA led to second pregnancy</p> <p>Second pregnancy shock and anxiety – potentially due to being unwell and already having another child</p> <p>Was this the danger the doctors had originally warned her about</p>

	Changing needs of women in new CFTR mod era
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Appendix C: Example of the development of descriptive themes from initial codes

Descriptive Themes	Initial codes
<p>Negative impact of CFTR modulator therapies – both physical and mental</p> <p>Side effects and challenges</p> <p>Weighing up decisions to continue or discontinue.</p> <p>Potential for improved health leading to non-adherence of treatments</p> <p>Lack or loss of body awareness</p>	<ul style="list-style-type: none"> - Improved health make it hard to recognise exacerbations (Keyte et al., 2023) - Retraining reading ones body (Keyte et al., 2023) - Fear that lack of body awareness might have detrimental impact on health (Keyte et al., 2023) - Potential of Kaftrio leading to non adherence for other treatments (Keyte et al., 2023) - Death and future anxiety after taking Trikafta (Vall, 2022) - Concerns with weight gain (Vall, 2022) - Side effects with Orkambi (Page et al.,2022) - Negative perceptions of Kaftrio/ Side effects (Aspinall et al., 2022) - Discontinuation of CFTR modulators (Aspinall et al., 2022) - Negative physiological and psychological side effects (Aspinall et al., 2022) - Weighing decisions to stop taking CFTR modulators (Aspinall et al., 2022) - Shift in emotions from elated to negative side effects (Aspinall et a., 2022) - Negative impact of Kaftrio (side effects, discontinuation, uncertainty and worries, loss of identity) (Aspinall et al., 2022) - Concerns about side effects (Landess et al., 2024)

	<ul style="list-style-type: none"> - “Should be happy” – sense of how she should feel but isn’t feeling that way due to side effects (Keyte et al., 2023) -
<p>Impact of CFTR modulator therapies on identity- loss of identity/redefining identity</p> <p>Changes in identity</p> <p>Conflict between good health and loss of identity</p> <p>Embracing a new identity or redefining their identity</p> <p>Embracing their identity as someone having CF due to less CF constraints post modulators</p> <p>Normality as a new identity</p>	<ul style="list-style-type: none"> - Kalydeco impacted positively on confidence and identity (Kausar et al., 2022) - Symkevi impacted positively on identity (Kausar et al., 2022) - Symkevi led to normal identity (Kausar et al., 2022) - Change in identity and change in support from other people with CF (Keyte et al., 2023) - Loss of CF identity (Vall, 2022; Ladores and Polen, 2021; Aspinall et al., 2022) - Conflict between identity and health - Change in identity – CF not defining their lives (Page et al., 2022) - Previously viewed CF as sole identity (Page et al., 2022) - Modulators changed how they viewed themselves (Page et al., 2022) - Existential crisis (Ladores and Polen, 2021) - Post Trikafta looked different to life before Trikafta (Ladores and Polen, 2021) - A sense of change on what was previously normal (Aspinall et al., 2022) - New illness narrative (Aspinall et al., 2022) - Certainty of life pre Kaftrio (Aspinall et al. 2022) - Difficulties conceptualising new health status (Aspinall et al., 2022) - Feeling lost on Kaftrio (Aspinall et al., 2022) - Lack of support from HCPs regarding identity issues (Aspinall et al., 2022)
Experiences of survivor’s guilt	<ul style="list-style-type: none"> - Survivors guilt (Keyte et al., 2023; Vall, 2022)

<p>Survivors guilt felt when comparing to those who cannot take modulators</p> <p>Survivors guilt mixed with other emotions</p>	<ul style="list-style-type: none"> - Survivors guilt mixed with happiness, relief and feeling awful for others (Keyte et al., 2023)
<p>Conflicting or mixed emotions</p> <p>Complex emotions around grief, loss and trauma from lives before modulators</p> <p>Message of hope for those who cannot benefit from modulators</p>	<ul style="list-style-type: none"> - Conflicting emotions (Keyte et al, 2022; Vall, 2022) - Happy for self, sad for others (Keyte et al., 2023) - Happy and relieved for self and feeling awful for others (Keyte et al., 2023) - Experiences of hope (Kauser et al., 2022; Keyte et al., 2023; Page et al., 2022; Aspinall et al., 2022) - Hopefulness and scepticism (Landess et al., 2024) - Grieving for past lives and processing trauma of it (Keyte et al., 2023) - Survivors guilt and hope for the 10% (Aspinall et al., 2022; Vall 2022)
<p>Anxiety about health deteriorating</p> <p>Anxiety about the long-term efficacy of modulators</p> <p>Anxiety about reverting to life pre modulators</p> <p>Anxiety about reaching CF life expectancy</p> <p>Anxiety about ETI being taken away</p> <p>Anxiety around lack of information on modulators</p> <p>Anxiety whilst experiencing positive health outcomes</p>	<ul style="list-style-type: none"> - Worries about long term efficacy of Kaftrio (Aspinall et al., 2022) - Worries, anxiety, uncertainty about future health deteriorating (Aspinall et al., 2022; Keyte et al., 2023;) - Anxiety regarding long term efficacy (Keyte et al., 2023) - Apprehension due to new gained health status (Keyte et al., 2023) - Fear of increased health and lung function failing (Keyte et al., 2023) - Worries around life expectancy (Page et al., 2022; Keyte et al., 2023) - Worries that Trikafta will stop working (Ladores and Polen, 2021) - Worries and fears of going back to life pre Kaftrio (Page et al., 2022) - Worries about going back and losing benefits of Kaftrio (Page et al., 2022) - Concerns about side effects and uncertainties (Landes et al., 2024) - Skepticism from newness of ETI (Landess et al., 2024) - Worries about impact of Kaftrio on Liver function (Aspinall et al., 2022)

	<ul style="list-style-type: none"> - Worries about stopping to take Kaftrio (Aspinall et al., 2022) - Worries about reverting to life pre Kaftrio (Aspinall et al., 2022) - Fear of Kaftrio being stopped (Aspinall et al., 2022) - Tasting a life with Kaftrio brings worries about reverting back (Aspinall et al., 2022) - Back of my mind might refer to thinking about it all the time (Aspinall et al., 2022) - Uncertainty about the future (Aspinall et al., 2022) - Fear of health deteriorating suddenly (Aspinall et al., 2022) - Worries Kaftrio would be taken away (Aspinall et al., 2022) - Prospect of extended life led to unanswered questions (Aspinall et al., 2022)
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Appendix D: Example of Development of Analytical Themes from Descriptive Themes

Analytical Themes	Subthemes	Descriptive Themes
Complex emotional landscape	<p><i>Conflicted emotions</i></p> <p><i>Uncertainty about long-term efficacy of CFTR modulators</i></p>	<p>Experiences of survivor’s guilt</p> <p>Survivors guilt when comparing to those who cannot take modulators.</p> <p>Survivors guilt mixed with other emotions</p> <p>Conflicting or mixed emotions</p> <p>Complex emotions around grief, loss and trauma from lives before modulators</p> <p>Message of hope for those who cannot benefit from modulators</p> <p>Anxiety about health deteriorating</p>

		<p>Anxiety about the long-term efficacy of modulators</p> <p>Anxiety about reverting to life pre modulators</p> <p>Anxiety about reaching CF life expectancy</p> <p>Anxiety about ETI being taken away</p> <p>Anxiety around lack of information on modulators</p> <p>Complex emotions of anxiety whilst experiencing positive health outcomes</p>
<p>Navigating changes in identity</p>	<p><i>Conflict between identity and health</i></p> <p><i>Redefinition of self</i></p>	<p>Impact of CFTR modulator therapies on identity- loss of identity/redefining identity</p> <p>Changes in identity</p> <p>Conflict between good health and loss of identity</p> <p>Embracing a new identity or redefining their identity</p> <p>Embracing their identity as someone having CF due to less CF constraints post modulators</p> <p>Normality as a new identity</p>

Appendix E: Cardiff University Ethical Approval Confirmation Email

Ethics Feedback - EC.23.02.07.6723RA2 psychethics <psychethics@cardiff.ac.uk>

Thu 07/12/2023 14:16

To: Mulongwe Mwelwa [REDACTED]

Cc: [REDACTED]

Dear Mulongwe,

The Ethics Committee has considered the amendment to your PG project proposal: An exploration of the experiences of adults with Cystic Fibrosis unable to benefit from triple combination therapy, using Interpretative Phenomenological Analysis (EC.23.02.07.6723RA2).

Your amended project proposal has received a **Favourable Opinion** based on the information described in the proforma and supporting documentation.

Additional approvals

This letter provides an ethical opinion only. You must not start your research project until all appropriate approvals are in place.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met:

- Please note that if any changes are made to the above project, then you must notify the Ethics Committee.
- Please use the EC reference number on all future correspondence.
- The Committee must be informed of any unexpected ethical issues or unexpected adverse events that arise during the research project.
- The Committee must be informed when your research project has ended. This notification should be made to psychethics@cardiff.ac.uk within three months of research project completion. All data will be retained/processed/destroyed in line with University policy.

Amendments

Any substantial amendments to proposal previously reviewed by the Committee must be submitted to the Committee via psychethics@cardiff.ac.uk for consideration using the PSYCH amendment form and cannot be implemented until the Committee has confirmed it is satisfied with the proposed amendments.

Complaints/Appeals

If you are dissatisfied with the decision made by the Committee, please contact psychethics@cardiff.ac.uk in the first instance to discuss your complaint. If this discussion does not resolve the issue, you are entitled to refer the matter to the Head of School for further consideration.

The Head of School may refer the matter to the Open Research Integrity and Ethics Committee (ORIEC), where this is appropriate.

Please be advised that ORIEC will not normally interfere with a decision of the Committee and is concerned only with the general principles of natural justice, reasonableness and fairness of the decision.

The Committee reminds you that it is your responsibility to conduct your research project to the highest ethical standards and to keep all ethical issues arising from your research project under regular review.

You are expected to comply with Cardiff University's policies, procedures and guidance at all times, including, but not limited to, its [Policy on the Ethical Conduct of Research involving Human Participants, Human Material or Human Data](#) and our [Research Integrity and Governance Code of Practice](#).

Kind regards,



School of Psychology Research Ethics Committee

The 2023/4 list of Full proposal deadlines and [Ethics - Home \(sharepoint.com\)](#)

Appendix F: UK NHS Health Board R&D Approval Form and Email

1.0 Title of project

A Qualitative Exploration of The Experiences of Adults with Cystic Fibrosis unable to benefit from Triple Combination Therapy

2.0 Aim of project (the main reason for undertaking the project):

The aim of the study focuses on exploring the experiences of adults with Cystic Fibrosis (CF) who are not able to benefit from Kaftrio due to genetic factors. This group is often overlooked in research studies, as the focus is primarily on those who can benefit from CFTR modulators.

3.0 Objectives: Please detail the objectives in terms which will allow for later evaluation

The objectives of this study include:

1. To give voice to this group of adults with CF unable to benefit from Kaftrio due to genetic factors, by conducting an in-depth exploration of their lived experiences and gaining a deeper understanding of how they make sense of being in this situation.
2. This research may also identify coping mechanisms and strategies employed by patients in this group, offering insights into their resilience.
3. The findings from this research may also enhance clinicians' ability to share information with patients in this group and their families in a clinically sensitive manner.
4. This research may also highlight existing support systems available to this group and identify areas where improvements or additional resources may be needed.
5. To contribute to the limited pool of knowledge on this topic and provide valuable insights into their experiences.

Ultimately, we hope that the research findings will help develop clinical practice guidelines informed by their opinions and views on their experiences.

Subsequent evaluations may assess the impact of the proposed recommendations.

4.0 Proposed Start Date

Anticipated End Date

5.0 Personnel Information

**Name of Project
Leader**

[REDACTED]

Job title

Principal Investigator
Consultant Clinical Psychologist

email: phone

[REDACTED]

Directorate/Division

[REDACTED]

Other Staff involved in the project

Name/Designation	Email / phone number
Mulongwe Mwelwa (Trainee Clinical Psychologist)	[REDACTED]
[REDACTED]	[REDACTED]
Dr Steven Stirk (Field/External Supervisor)	[REDACTED]
Dr Victoria Samuel (Secondary/Academic Supervisor)	[REDACTED]

6.0 Methodology: Describe briefly the project design e.g. population, method of selecting participants, data collection and analysis methodology.

A qualitative approach is considered appropriate for the research aims as it will enable rich and detailed exploration of the experiences of adults with CF who are unable to benefit from triple combination therapy due to genetic factors.

Participant Sample

Participants will be recruited from [REDACTED]. In keeping with IPA, a purposive homogenous sampling method will be employed in this study. Considering the qualitative nature of the study and the requirement for a comprehensive exploration of each individual's experience, a sample size of 6-8 participants is deemed appropriate.

Inclusion Criteria

- Individuals will be 18 years of age and older, not able to benefit from Kaftrio due to genetic factors.

[REDACTED] Individuals who receive regular clinical care from [REDACTED]

- Sufficiently fluent in English to read and understand the information sheets, give informed consent and to participate in the interview.
- Sufficiently well clinically to take part in an interview lasting 60-90 minutes (with breaks as necessary)
- *As a contingency, staff caring for these patients will be invited to take part.*

Exclusion criteria

- Acutely unwell/currently experiencing an acute exacerbation.

Method of selecting participants

The Principal Investigator (PI) involved in the CF services will apply the predetermined inclusion and exclusion criteria to their respective clinical databases. The PI will utilise their professional judgment to assess the physical and emotional wellbeing of potential participants and determine whether their involvement in the study is unlikely to have any significant adverse effects.

At this stage, the clinicians will provide eligible individuals with a copy of the Participant Information Sheet. The information in the participant information sheet will offer an opportunity to contact the researcher directly for any clarifications or to express their interest in participating by completing the Consent to be Contacted form. A QR code has been included on the participant information sheet for potential participants to complete the form. Subsequently, the researcher will use the provided contact information on the consent to be contacted form to address any queries the participant may have and schedule the research interview if applicable.

Prior to completing the consent form, the participant information sheet will be reviewed again with the participant to address any additional questions. If the participant agrees to proceed, the researcher will direct the participant to the online consent form accessed via Qualtrics for both face-to-face and online interviews.

Poster advertisements will also be utilised.

Note: Recruitment efforts are currently underway through various platforms including social media and the CF Charities (School of Psychology Ethics Approval received for this). Data obtained through this route will be kept separate from service evaluation work. Although this is a study that will have a broader participant pool, it will be helpful for service evaluation because it will enhance our understanding and knowledge.

Data collection

Semi-structured interviews will be conducted, with an expected duration of approximately 60-90 minutes. These interviews will be held face to face or remotely via Teams/Zoom.

To facilitate data transcription and analysis, audio recordings of the interviews will be made using an iPad. Participants will be informed about the recording process and will have provided informed consent when agreeing to participate in the research. In cases where transcription services are utilised, the transcriber will be provided with detailed instructions on how to conduct the transcription, including the removal of any identifying information, and a confidentiality agreement will be signed. Sufficient funding is available to cover the cost of transcription services.

Data Storage and Management

The interviews will be recording using a Cardiff University owned iPad protected with a password. The audio files will be stored on the encrypted Cardiff University One Drive account belonging to Mulongwe Mwelwa, using pseudonyms as file names. Afterward, the audio files will be deleted from the iPad.

To ensure anonymity, the audio recording will be transcribed using gender neutral pseudonyms. The researcher will listen to the audio recordings, and a member of the transcription service may also listen to them when typing up the interviews, both bound by confidentiality agreements.

The transcribed files will be stored on the lead researchers Cardiff University OneDrive account. All data will be held by Cardiff University and retained for a minimum of 15 years following the publication of any findings. Data handling will comply with the Data Protection Act (2018), the General Data Protection Regulation (2018), and Cardiff University's data handling and management policies. Personally identifiable data will be stored securely and separately from the rest of the research data, with access limited to the research team. Regulatory authorities may have access to data for monitoring and auditing purposes but on a limited basis.

Once the transcription process is complete, all audio recordings will be deleted. Except for the participants name on the consent form which will be stored separately from other personally identifiable data, all personally identifiable data will be deleted at the project's end. De-identified research data will be retained for 15 years after the study's completion, in accordance with Cardiff University's data retention policy. Raw data will be retained throughout the retention period.

Analysis

Data will be analysed using Interpretative phenomenological analysis (IPA) to explore how participants make meaning of their life experiences. Flexible guidelines will be drawn upon and adapted accordingly (Pietkiewicz & Smith, 2014). This may include:

1. Multiple reading and note making (or re-listening to audio recordings). This allows for full immersion in the data and may lead to new insights. This process also encourages researcher reflexivity. Notes may include comments about content, language, context and emotional responses.
2. Transforming notes into emerging themes. This process encourages psychological conceptualization, whilst simultaneously ensuring the themes are still rooted in the specific detail of the participant's description.
3. Seeking relationships and clustering themes. This may lead to the development of superordinate themes and sub-themes when writing up a narrative account of the study.

7.0 Service User involvement:

Consultations have been conducted with service users and staff via focus groups from the [REDACTED] (26/10/2022) and the CF Trust (08/11/2022) to engage in discussions and gather feedback on the projects aims, and relevant documentation such as participation information sheets, debrief forms, and interview questions. Additionally, participants may be approached through a field link to seek their input on the research themes that will emerge during the analysis phase.

8.0 Please identify other services which might be affected by this piece of work (e.g. other departments in the UHB, other professional groups)

N/A

9.0 Expected outcome

Training Restructuring of service Protocol/Guideline Patient Information

NICE guideline compliance Other Please specify The results will be written up as part of a thesis for the South Wales Doctoral Programme in Clinical Psychology and may be published in academic journals and presented at conferences.

10.0 Action Plan

Please list the people who will be involved in the development and implementation of the Action Plan

Mulongwe Mwelwa
 [REDACTED]
 [REDACTED]
 Dr Victoria Samuel
 Dr Steve Stirk
 [REDACTED]

11.0 Dissemination of the project report

Please state how it is proposed to disseminate the results of the work

Publication/Peer Review Journal Directorate meeting Divisional Meeting Audit / Quality and Safety? meeting
 Neighbourhood meeting LSB Meeting

Electronically via email/intranet Other Please specify If possible, Mulongwe will present the findings of the study to the staff team.

12.0 Statement by Project leader

I agree to carry out the project as set out in this plan

I confirm that I have read the UHB Data Protection guidance issued by the UHB and agree to ensure that all data for this project will be collected, collated and stored in accordance with the principles outlined in this guidance.

I agree to ensure that a copy of the findings and recommendations are submitted to the Assistant Director of Innovation and Improvement upon project completion.

Signature



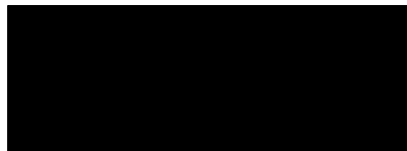
Name (PRINT)



13.0 Statement of Support

 Cystic Fibrosis Service Manager support this application.

Signature



Name
(PRINT)



Date

10.10.2023

[REDACTED] via AMaT <no-reply@amat.co.uk>

Wed 25/10/2023 14:31

To: Mulongwe Mwelwa <[REDACTED]>

External email to Cardiff University - Take care when replying/opening attachments or links.

Nid ebost mewnol o Brifysgol Caerdydd yw hwn - Cymerwch ofal wrth ateb/agor atodiadau neu ddolenni.

Clinical audit - Approval confirmation

Hi MULONGWE,

The audit facilitator has approved a clinical audit, which can be accessed in YOUR AUDITS within the Clinical Audit & Improvement section on the AMaT system.

Audit code: Cystic Fibrosis/SE/2023-24/02

Audit title: An exploration of the experiences of adults with Cystic Fibrosis unable to benefit from triple combination therapy, using Interpretative Phenomenological Analysis

Speciality: Cystic Fibrosis

Lead participant: MULONGWE MWELWA

Date approved: 25/10/2023

Approved by: Alison Shor

Audit Facilitator name: Sara Vernon

Audit Lead name: Debbie Jones

Audit lead approval comment: None provided

Audit facilitator approval comments:

None provided

Your role in this audit: Lead participant

This notification is sent to: Facilitator, Audit lead, Lead Participants, Participants and Mentor.

Please follow this link to view this audit: [Click here to view this audit](#)

Best regards,

Alison Shor

Appendix G: Study Recruitment Poster



RESEARCH IN CYSTIC FIBROSIS: THE 10%

Do you have cystic fibrosis and are unable to benefit from triple combination therapy such as Kaftrio due to genetics?

Are you currently aged 18 years or older?

If **YES** to **BOTH** of the above, you are invited to take part in a Cardiff University study!

What is the study about?

There is limited research on the experiences of people with cystic fibrosis unable to benefit from Kaftrio due to having rare genes. The study aims to develop an understanding of their experiences, and we hope that this will inform clinical practice and research.

The study will involve taking part in an audio-recorded interview either online or face-face.

The interview will last between 60 – 90 minutes.

For more details and an information sheet, please contact Mulongwe Mwelwa (Lead Researcher)


mwelwam@cardiff.ac.uk

or scan the QR code to leave your contact details and the researcher will contact you.




This study has been approved by the School of Psychology Research Ethics Committee at Cardiff University on 23/02/2023

Appendix H: Consent to Contact Form



School of Psychology



Study: An exploration of the experiences of adults with Cystic Fibrosis unable to benefit from triple combination therapy, using Interpretative Phenomenological Analysis

Researcher: Mulongwe Mwelwa

If you would be interested in taking part in the study, please complete your details below:

Name:

Address:

Phone:

Email:

Accessed from: https://cardiffunipsych.eu.qualtrics.com/jfe/form/SV_bJVAt1943PVCA86 on 01/06/2024

Appendix I: Participant Information Sheet (Recruitment Stream 1)



PARTICIPANT INFORMATION SHEET

Title: A Qualitative Exploration of The Experiences of Adults with Cystic Fibrosis unable to benefit from Triple Combination Therapy

You are being invited to take part in a Cardiff University research project. Before you decide whether or not to take part, it is important for you to understand why the research is being undertaken and what it will involve.

This document will provide you with more information about the research and participation process. Please take time to read the following information carefully and discuss it with others if you wish. If you have any questions, please feel free to contact any of the researchers (details below).

Thank you for reading this!

What is the purpose of this research project?

This study aims to expand the currently limited understanding of the experiences of people with Cystic Fibrosis unable to benefit from triple combination therapies because of genetic factors. The hope is that the research is valuable, shaping both clinical practice and research. This research project is being conducted as part of Mulongwe Mwelwa's (Lead Researcher) Doctorate qualification in Clinical Psychology (DClinPsy) at Cardiff University.

Why have I been invited to take part?

You have been invited to take part for two reasons:

1. Because the research project requires information from adults who have CF
2. Because you are currently not able to benefit from triple combination therapy due to underlying genetic mutations.

We aim to invite 6-8 people to take part and we would be grateful if you would help with this study.

Do I have to take part?

Your participation in this research study is entirely voluntary and it is up to you to decide whether or not to take part. If you decide to take part, we will discuss the research study with you and ask you to sign a consent form. If you decide not to take part, you do not have to explain your reasons and it will not affect your legal rights. Also, your decision to take part or not to take part will not affect the care that you receive.

If you change your mind, you are free to withdraw from the research at any time. If you choose to leave the study, we will need to keep any data you have provided up until the point you chose to leave the study and it may be included in the final analysis. As is the case for all participants, you will not be identified in any publications or presentations about the study. However, some quotations from your interview might be included in the published findings in a non-identifiable way.

What will taking part involve?

This is an interview-based study which will take place online using i.e., Teams or Zoom, or Face to Face where you will meet with the researcher in your own/family member's home or if you prefer, at a university site or at your local cystic fibrosis centre.

Before the interview, the researcher will go through this information sheet with you and ask you to complete a consent form and you will be able to ask any questions you may have. During the interview you will be invited by the researcher to share your experiences, this will last between 60 – 90 minutes. The interviews will be audio recorded on a password protected iPad which is locked away when not in use. The audio recording will then be saved onto the lead researchers encrypted Cardiff University One Drive account and will be subsequently deleted within a week after transcription. We will ask you to provide consent for this recording which would be held anonymously.

No person identifiable information will be included in the interview transcript. This means that any information that can be traced back to you will be removed at point of transcription. If transcription services are used, a detailed description on how this is to be conducted will be provided to the transcriber and a confidentiality agreement signed.

Following your interview after the researcher has analysed data from all the interviews, you may also be contacted again by the researcher to ask if you would like to meet so that the researcher can talk to you about the overall findings of the study. This meeting would take place via Teams or Zoom. Participation in any future meeting is also voluntary and you do not have to take part if you don't want to.

Will I be paid for taking part?

You will not be paid for taking part in the study. A £10 voucher will be given as a "thank you" for participation.

What are the possible benefits of taking part?

It is hoped that taking part in the research will be beneficial to you. It may provide you with a space to reflect on your experiences and could develop our understanding of the experiences of adults with CF unable to benefit from modulator therapies due to underlying genetic mutations. We also hope that participation in this research will inform and shape clinical practice and encourage researchers to develop treatments that will be beneficial for everyone living with CF.

What are the possible risks of taking part?

Some people find it difficult or upsetting to answer questions about the experiences they have had. If you do get upset, the researcher will be sympathetic and supportive. You can take a break or stop the interview altogether. The researcher will make sure there is time at the end of the interview to provide support and advice if this is needed. Should you feel affected by any issues raised during the interview, the researcher will provide you with information on support systems such as:

- CF Trust Helpline [Helpline | Cystic Fibrosis Trust](#)
- C.A.L.L Helpline [C.A.L.L. Helpline \(Community Advice & Listening Line\) - Public Health Wales \(nhs.wales\)](#)
- Samaritans [Contact Us | Samaritans](#)
- Your Cystic Fibrosis Service i.e., CF clinical psychologist and other clinicians
- And other International Mental Health and Wellbeing Helplines

Will my taking part in this research project be kept confidential?

All of your information will remain confidential and be anonymised (unidentifiable). Participants will be recruited in South Wales and internationally online which will help minimise the risk of identifying any individuals involved in the study. The interview will be audio recorded to allow the researchers to type up (transcribe) the interview, and the transcription will then be held securely within Cardiff University and analysed by the researchers.

Direct quotes may be used for academic submissions and research publications and given this all attempts to remove identifiable information will be made. Please see the additional information below regarding how your information will be handled, under the GDPR legislation and in line with Cardiff University data governance and records management policy.

Confidentiality will be maintained throughout the interview. If there are any concerns regarding risk to you or others, the research team will aim to notify you of the need to break confidentiality to keep you and others safe.

What will happen to my Personal Data?

Cardiff University is the Data Controller and is committed to respecting and protecting your personal data in accordance with your expectations and Data Protection legislation. Further information about Data Protection, including: your rights, the legal basis under which Cardiff University processes your personal data for research, Cardiff University's Data Protection Policy, how to contact the Cardiff University Data Protection Officer, how to contact the Information Commissioner's Office may be found at <https://www.cardiff.ac.uk/public-information/policies-and-procedures/dataprotection>.

The University's Data Protection Officer can be contacted at: inforequest@cardiff.ac.uk.

Cardiff University will keep identifiable information about you for a minimum period of 15 years after the study has finished. The legal basis we will rely upon to collect and store your information is public task. The only people in Cardiff University who will have access to information that identifies you will be people who need to contact you about the study or to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

What happens to the data at the end of the research project?

The interviews will be audio recorded, using a password protected iPad. The audio files will be saved using pseudonyms as file names and will only be stored on the researchers encrypted Cardiff University OneDrive account. They will then be deleted from the iPad.

The audio files will subsequently be transcribed, again using pseudonyms to ensure anonymity. These files will be stored on the lead researcher's Cardiff University OneDrive account. All data will be stored with Cardiff University and retained for a minimum period of 15 years after the publication of any findings from this data.

You can find out more on what happens to the data at the end of the research project on: [Records management policy and retention schedules - Public information - Cardiff University](#)

What will happen to the results of the research project?

The study results will be written up as part of Mulongwe's doctoral thesis and may be published in academic journals, presented at conferences and used in training. All results will remain anonymous, and participants will not be identified in any report, publication, or presentation.

What if there is a problem?

If at any point during the research you wish to make a complaint or wish to speak to someone independent of the study, you can contact the School of Psychology Ethics Committee (SREC) Secretary:

Secretary of Ethics Committee
School of Psychology
Cardiff University
Park Place
CF10 3AT
Email: psychethics@cardiff.ac.uk
Tel: +44 (0) 02920870707

Who is organising and funding this research project?

The research project is not funded. It is being undertaken by Mulongwe Mwelwa, a trainee clinical psychologist who will be supervised by Dr Victoria Samuel (South Wales Doctoral Programme in

Clinical Psychology), Dr Chris Hobson (South Wales Doctoral Programme in Clinical Psychology), Dr Steven Stirk ([REDACTED] [REDACTED]) Feel free to use the provided contact details below should you have any questions.

Who has reviewed this research project?

This research project has been reviewed and given a favourable ethical opinion by the School of Psychology Research Ethics Committee at Cardiff University on Date: (23/02/2023)

Further information and contact details

Should you have any questions relating to this research project, you may contact the study team:

Key Contacts	
<p>Lead Researcher/Primary Contact: Mulongwe Mwelwa South Wales Clinical Psychology Doctoral Programme 11th Floor, Tower Building 70 Park Place Cardiff CF10 3AT Email: [REDACTED] Tel: [REDACTED] (Mon – Fri 9am-5pm)</p>	
<p>Chief Investigator/Academic Supervisors Dr Victoria Samuel and Dr Chris Hobson South Wales Clinical Psychology Doctoral Programme 11th Floor, Tower Building 70 Park Place Cardiff CF10 3AT Email: [REDACTED] Email: [REDACTED]</p>	<p>Principal Investigator at [REDACTED] Site/Field Supervisors Dr Steven Stirk [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] Email: [REDACTED] Email: [REDACTED]</p>

Thank you for expressing an interest to take part in this research project.

Appendix J: Participant Information Sheet (Recruitment Stream 2)



PARTICIPANT INFORMATION SHEET

Title: A Qualitative Exploration of The Experiences of Adults with Cystic Fibrosis unable to benefit from Triple Combination Therapy

You are being invited to take part in a Cardiff University research project. Before you decide whether or not to take part, it is important for you to understand why the research is being undertaken and what it will involve.

This document will provide you with more information about the research and participation process. Please take time to read the following information carefully and discuss it with others if you wish. If you have any questions, please feel free to contact any of the researchers (details below).

Thank you for reading this!

What is the purpose of this research project?

This study aims to expand the currently limited understanding of the experiences of people with Cystic Fibrosis unable to benefit from triple combination therapies because of genetic factors. The hope is that the research is valuable, shaping both clinical practice and research. This research project is being conducted as part of Mulongwe Mwelwa's (Lead Researcher) Doctorate qualification in Clinical Psychology (DClinPsy) at Cardiff University.

Why have I been invited to take part?

You have been invited to take part for two reasons:

1. Because the research project requires information from adults who have CF
2. Because you are currently not able to benefit from triple combination therapy due to underlying genetic mutations.

We aim to invite 6-8 people to take part and we would be grateful if you would help with this study.

Do I have to take part?

Your participation in this research study is entirely voluntary and it is up to you to decide whether or not to take part. If you decide to take part, we will discuss the research study with you and ask you to sign a consent form. If you decide not to take part, you do not have to explain your reasons and it will not affect your legal rights. Also, your decision to take part or not to take part will not affect the care that you receive.

If you change your mind, you are free to withdraw from the research at any time. If you choose to leave the study, we will need to keep any data you have provided up until the point you chose to leave the study and it may be included in the final analysis. As is the case for all participants, you will not be identified in any publications or presentations about the study. However, some quotations from your interview might be included in the published findings in a non-identifiable way.

What will taking part involve?

This is an interview-based study which will take place online using i.e., Teams or Zoom, or Face to Face where you will meet with the researcher in your own/family member's home or if you prefer, at a university site or at your local cystic fibrosis centre.

Before the interview, the researcher will go through this information sheet with you and ask you to complete a consent form and you will be able to ask any questions you may have. During the interview you will be invited by the researcher to share your experiences, this will last between 60 – 90 minutes. The interviews will be audio recorded on a password protected iPad which is locked away when not in use. The audio recording will then be saved onto the lead researchers encrypted Cardiff University One Drive account and will be subsequently deleted within a week after transcription. We will ask you to provide consent for this recording which would be held anonymously.

No person identifiable information will be included in the interview transcript. This means that any information that can be traced back to you will be removed at point of transcription. If transcription services are used, a detailed description on how this is to be conducted will be provided to the transcriber and a confidentiality agreement signed.

Following your interview after the researcher has analysed data from all the interviews, you may also be contacted again by the researcher to ask if you would like to meet so that the researcher can talk to you about the overall findings of the study. This meeting would take place via Teams or Zoom. Participation in any future meeting is also voluntary and you do not have to take part if you don't want to.

Will I be paid for taking part?

You will not be paid for taking part in the study. A £10 voucher will be given as a "thank you" for participation.

What are the possible benefits of taking part?

It is hoped that taking part in the research will be beneficial to you. It may provide you with a space to reflect on your experiences and could develop our understanding of the experiences of adults with CF unable to benefit from modulator therapies due to underlying genetic mutations. We also hope that participation in this research will inform and shape clinical practice and encourage researchers to develop treatments that will be beneficial for everyone living with CF.

What are the possible risks of taking part?

Some people find it difficult or upsetting to answer questions about the experiences they have had. If you do get upset, the researcher will be sympathetic and supportive. You can take a break or stop the interview altogether. The researcher will make sure there is time at the end of the interview to provide support and advice if this is needed. Should you feel affected by any issues raised during the interview, the researcher will provide you with information on support systems such as:

- CF Trust Helpline [Helpline | Cystic Fibrosis Trust](#)
- C.A.L.L Helpline [C.A.L.L. Helpline \(Community Advice & Listening Line\) - Public Health Wales \(nhs.wales\)](#)
- Samaritans [Contact Us | Samaritans](#)
- You are encouraged to contact your Cystic Fibrosis Service i.e., psychology team and the wider clinical team

- And other Mental Health and Wellbeing Helplines

By consenting to take part in the study, you will also be consenting for the researcher to contact the psychology team and the wider clinical team at the Cystic Fibrosis Service, University Hospital Llandough in cases where they are concerned about **significant psychological distress**. This will be discussed directly with you before contacting the team except in the case of an emergency.

Will my taking part in this research project be kept confidential?

All of your information will remain confidential and be anonymised (unidentifiable). Participants will be recruited in South Wales and internationally online which will help minimise the risk of identifying any individuals involved in the study. The interview will be audio recorded to allow the researchers to type up (transcribe) the interview, and the transcription will then be held securely within Cardiff University and analysed by the researchers.

Direct quotes may be used for academic submissions and research publications and given this all attempts to remove identifiable information will be made. Please see the additional information below regarding how your information will be handled, under the GDPR legislation and in line with Cardiff University data governance and records management policy.

Confidentiality will be maintained throughout the interview. If there are any concerns regarding risk to you or others, the research team will aim to notify you of the need to break confidentiality to keep you and others safe.

What will happen to my Personal Data?

Cardiff University is the Data Controller and is committed to respecting and protecting your personal data in accordance with your expectations and Data Protection legislation. Further information about Data Protection, including: your rights, the legal basis under which Cardiff University processes your personal data for research, Cardiff University's Data Protection Policy, how to contact the Cardiff University Data Protection Officer, how to contact the Information Commissioner's Office may be found at <https://www.cardiff.ac.uk/public-information/policies-and-procedures/dataprotection>.

The University's Data Protection Officer can be contacted at: inforequest@cardiff.ac.uk.

Cardiff University will keep identifiable information about you for a minimum period of 15 years after the study has finished. The legal basis we will rely upon to collect and store your information is public task. The only people in Cardiff University who will have access to information that identifies you will be people who need to contact you about the study or to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

What happens to the data at the end of the research project?

The interviews will be audio recorded, using a password protected iPad. The audio files will be saved using pseudonyms as file names and will only be stored on the researchers encrypted Cardiff University OneDrive account. They will then be deleted from the iPad.

The audio files will subsequently be transcribed, again using pseudonyms to ensure anonymity. These files will be stored on the lead researcher's Cardiff University OneDrive account. All data will be stored with Cardiff University and retained for a minimum period of 15 years after the publication of any findings from this data.

You can find out more on what happens to the data at the end of the research project on: [Records management policy and retention schedules - Public information - Cardiff University](#)

What will happen to the results of the research project?

The study results will be written up as part of Mulongwe's doctoral thesis and may be published in academic journals, presented at conferences and used in training. All results will remain anonymous, and participants will not be identified in any report, publication, or presentation.

What if there is a problem?

If at any point during the research you wish to make a complaint or wish to speak to someone independent of the study, you can contact the School of Psychology Ethics Committee (SREC) Secretary:

Secretary of Ethics Committee
School of Psychology
Cardiff University
Park Place
CF10 3AT
Email: psychethics@cardiff.ac.uk
Tel: +44 (0) 02920870707

Who is organising and funding this research project?

The research project is not funded. It is being undertaken by Mulongwe Mwelwa, a trainee clinical psychologist who will be supervised by Dr Victoria Samuel (South Wales Doctoral Programme in Clinical Psychology), Dr Chris Hobson (South Wales Doctoral Programme in Clinical Psychology), Dr Steven Stirk [REDACTED] and [REDACTED]. Feel free to use the provided contact details below should you have any questions.

Who has reviewed this research project?

This research project has been reviewed and given a favourable ethical opinion by the School of Psychology Research Ethics Committee at Cardiff University on Date: (07/12/2023). This Research has also received approval from [REDACTED] (Cystic Fibrosis Service Manager at the [REDACTED] [REDACTED], [REDACTED]) on 10/10/2023 and [REDACTED] Quality Improvement Department on 25/10/2023.

Further information and contact details

Should you have any questions relating to this research project, you may contact the study team:

Key Contacts
<p>Lead Researcher/Primary Contact: Mulongwe Mwelwa South Wales Clinical Psychology Doctoral Programme 11th Floor, Tower Building 70 Park Place Cardiff CF10 3AT Email: [REDACTED] Tel: [REDACTED]</p>

Chief Investigator/Academic Supervisors

Dr Victoria Samuel
Dr Chris Hobson
South Wales Clinical Psychology Doctoral
Programme
11th Floor, Tower Building
70 Park Place
Cardiff
CF10 3AT

Email: [Redacted]

Email: [Redacted]

Principal Investigator at [Redacted] Site/Field Supervisors

Dr Steven Stirk

[Redacted]

Email: [Redacted]

Email: [Redacted]

Thank you for expressing an interest to take part in this research project. If you decide to participate, please complete the Consent to Contact Form by scanning the QR code below.



CONSENT FORM

Title of research project: A Qualitative Exploration of The Experiences of Adults with Cystic Fibrosis unable to benefit from Triple Combination Therapy

Name of Chief Investigator: Dr Victoria Samuel

Name of Researcher: Mulongwe Mwelwa

I confirm that I have read and understood the information sheet dated 21st October (version 1.5) for the above research project. I have had the opportunity to ask questions and have had these answered satisfactorily.

Yes

No

I understand that my participation is voluntary, and I am free to withdraw at any time without giving a reason and without any adverse consequences. I understand that if I withdraw, information about me that has already been obtained may be kept by Cardiff University.

Yes

No

I understand that the information I provide during the interview will be fully anonymised and held securely within Cardiff University at the end of the research project.

Yes

No

I consent to being audio recorded for the purposes of the research project and I understand how it will be used in the research.

Yes

No

I understand that anonymised excerpts and/or verbatim quotes from my interview may be used as part of the research publication. I understand that attempts will be made to protect my anonymity, by allocating me a pseudonym (fictitious name) and removing any personal information that could be identifiable.

Yes

No

I consent to the processing of my personal information i.e., name, age and gender for the purposes explained to me. I understand that such information will be held in accordance with all applicable data protection legislation and in strict confidence unless disclosure is required by law or professional obligation.

Yes

No

I give permission for the researchers to signpost me to relevant sources of support where they have concerns about significant psychological distress.

Yes

No

I agree to take part in this research project.

Yes

No

Please sign and date:

Name of participant
(Please Print)

Date

Signature

THANK YOU FOR PARTICIPATING IN OUR RESEARCH

Accessed from: https://cardiffunipsych.eu.qualtrics.com/jfe/form/SV_6mp5dBTuXeayr5k on
[01/06/2024](#)

Appendix L: Consent Form (Recruitment Stream 2)

CF SERVICE CONSENT FORM

Title of research project: A Qualitative Exploration of The Experiences of Adults with Cystic Fibrosis unable to benefit from Triple Combination Therapy

Name of Chief Investigator: Dr Victoria Samuel

Name of Researcher: Mulongwe Mwelwa

I confirm that I have read and understood the information sheet dated 28th October 2023 (version 1.0) for the above research project. I have had the opportunity to ask questions and have had these answered satisfactorily.

Yes

No

I understand that my participation is voluntary, and I am free to withdraw at any time without giving a reason and without any adverse consequences. I understand that if I withdraw, information about me that has already been obtained may be kept by Cardiff University.

Yes

No

I understand that the information I provide during the interview will be fully anonymised and held securely within Cardiff University at the end of the research project.

Yes

No

I consent to being audio recorded for the purposes of the research project and I understand how it will be used in the research.

Yes

No

I understand that anonymised excerpts and/or verbatim quotes from my interview may be used as part of the research publication. I understand that attempts will be made to protect

my anonymity, by allocating me a pseudonym (fictitious name) and removing any personal information that could be identifiable.

Yes

No

I consent to the processing of my personal information i.e., name, age and gender for the purposes explained to me. I understand that such information will be held in accordance with all applicable data protection legislation and in strict confidence unless disclosure is required by law or professional obligation.

Yes

No

I give permission for the researchers to contact the psychology team and the wider clinical team of my local cystic fibrosis service in cases where they have concerns about significant psychological distress.

Yes

No

I agree to take part in this research project.

Yes

No

Please complete:

Name of Participant: _____

Date: _____

Please sign: _____

**THANK YOU FOR PARTICIPATING IN OUR RESEARCH
YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.**

Accessed from: https://cardiffunipsych.eu.qualtrics.com/jfe/form/SV_eYfyK6fAPG6VG6i on 01/06/2024

Appendix M: Interview Schedule

Instruction to participants:

Thank you for taking part in the study. The study will involve asking questions about your experiences of not being able to benefit from ETI and how you make sense of being in this situation.

Ice Breaker Question: To begin with, what were your first thoughts when you were asked to take part in this research project?

Broad/Main Question:

- 1) Can you tell me about your experience of not being able to benefit from ETI?
Possible prompts:
 - What was it like when you first found out about the release of ETI?
 - What were your hopes, expectations or fears?
 - What was the process of finding out that you were not able to benefit from ETI?
- 2) Are you able to say a bit about what it feels like to not be suitable for receiving ETI?
Prompt:
 - How did you feel when you found out? How do you feel now?
- 3) What has life been like for you since you found out?
- 4) What does being unable to benefit from ETI mean for you?
Prompts:
 - What are the differences between a good day and a bad day?
 - What helps you cope?
- 5) Has this made a difference on how you view your life or things that are important to you?
Prompts:
 - Relationships – CF Teams, other pwCF, partner, family, friends, work colleagues? Career? Hobbies/Interests?
 - How do you think other people see you? (CF Teams, other pwCF, partner, family, friends, work colleagues)
- 6) How do you see yourself in the future?
Prompts:
 - Do you see yourself differently now than before you found out? In what way?
 - Has this changed the way you think or feel about yourself?
 - What are your thoughts and feelings about future treatments for your cohort?
- 7) Is there anything else that you feel is important that you have not yet had the opportunity to say?

Appendix N: Participant Debrief (Recruitment Stream 1)

PARTICIPANT DEBRIEF FORM

Thank you for taking part in this study. The aim of the study was to explore the experiences of adults with cystic fibrosis (CF) unable to benefit from triple combination therapies due to underlying genetic mutations. We would like to thank you for sharing your experiences. The information you shared with us today will further our understanding and inform clinical practice and research.

Once all the data has been collected and analysed, the results will be written up as part of a thesis for the South Wales Doctoral Programme in Clinical Psychology and may be published in academic journals, presented at conferences, and used in training. As explained previously, all the results will remain anonymous, and you will not be identified in any report, publication, or presentation.

It's possible that talking about your experience may have raised some difficult feelings or thoughts. If you have been affected by any issues raised in the interview and would like further support, please consider any options in the attached document.

If you wish to raise a concern, or complain about the project, please contact Mulongwe Mwelwa, using the contact details below. If we cannot resolve your concerns or problems, then Cardiff University Research Ethics has a complaints procedure: Please contact the School of Psychology Ethics Committee (SREC) secretary:

Secretary of Ethics Committee
School of Psychology
Cardiff University
Park Place
CF10 3AT
Email: psychethics@cardiff.ac.uk
Tel: +44 (0) 02920870707

We hope that you have found the experience positive. We would like to give you a voucher as a thank you for your participation. Thank you once again.

Yours Sincerely

Mulongwe Mwelwa

Trainee Clinical Psychologist

Key Contacts:
Lead Researcher/Primary Contact: Mulongwe Mwelwa South Wales Clinical Psychology Doctoral Programme 11 th Floor, Tower Building 70 Park Place Cardiff CF10 3AT Email: [REDACTED] Tel: [REDACTED]

Support Information

Urgent Support

Call 999 (UK and Ireland), 911 (US, Canada and Philippines), 107 (South Africa), 111 (New Zealand), 000 (Australia) and 112 (India) or visit your local Accident and Emergency department

UK Helplines

CF Trust Helpline (Available Monday to Friday 10am to 4pm)

Telephone: 0300 373 1000 or 020 3795 2184

(Monday to Friday 10am -4pm)

Email: Helpline@cysticfibrosis.org.uk

Website: <https://www.cysticfibrosis.org.uk/the-work-we-do/support-available/helpline>

Samaritans (Available 24/7)

Telephone: 116 123

Email: jo@samaritans.org

Website: <https://www.samaritans.org>

Community Advice and Listening Line (C.A.L.L) Helpline: Wales Only Helpline (Available 24/7)

Telephone: 0800 132 737

Text: 81066

Website: <https://www.callhelpline.org.uk>

SANELine (Available 4.30pm -10.30pm everyday)

Telephone: 0300 304 7000

Website: <https://www.sane.org.uk/how-we-help/emotional-support/saneline-services>

United States Helplines and Services

Cystic Fibrosis Foundation

844-COMPASS (844-266-7277)

Email: compass@cff.org

Website: <https://www.cff.org/support#contact-us>

National Alliance on Mental Illness [NAMI Helpline](#): 1-800-950-6264 or text NAMI to 741741

[Crisis Support Services](#) national helpline: 800-273-8255

[SAMHSA's National Helpline](#) (substance abuse and mental health): 800-662-HELP (800662-4357)

[988 Suicide and Crisis Lifeline](#): 988 or [Lifeline Chat](#)

South Africa Helplines

Lifeline counselling: National: 0861 322 322, Johannesburg: 011 728-1331, Alexandra: 011 443 3555, Soweto: 067 019 0845 or 074 129 6960

South African Federation for Mental Health (SAFMH) offers a helpdesk and information on mental health services: +27 (0) 11 781 1852

New Zealand Helplines and Services

Cystic Fibrosis New Zealand

Website: <https://www.cfnz.org.nz/life-with-cf/mental-health-and-wellbeing/>

Healthline for general health advice and information: 0800 611 116

Need to Talk? 1737 to speak with a trained counsellor or peer support worker: Call or text 1737

Samaritans: 0800 726 666

Lifeline 24/7 Helpline: 0800 543 354

Philippines Helplines

Philippine Mental Health Association (PMHA): +63 2 921 4958

In Touch Philippines free and anonymous 24/7 crisis line: +63 2 8893 7603, +63 917 800 1123, or +63 922 893 8944

Ireland Helplines and Services

Cystic Fibrosis Ireland

Website: <https://www.cfireland.ie/contact>

Email: info@cfireland.ie

Call: 014962433

Grow mental health support: 1890 474 474

Shine supporting people affected by mental ill health: 01 541 3715 Crisis Text Line: Text HELLO to 50808

Australia Helplines

Health direct 24-hour health advice: 1800 022 222

Sane Australia counselling support for mental health issues: 1800 187 263 Lifeline: 13 11 14

Canada Helplines and Services

Cystic Fibrosis Canada

Email: helpline@cysticfibrosis.ca

Website: <https://www.cysticfibrosis.ca/>

Wellness Together Canada mental health and substance use support: 1-866-585-0445 or text WELLNESS to 741741

Crisis Services Canada Suicide Prevention Service: 1-833-456-4566

India Helplines

Mann Talks to speak with a trained mental health professional: +91-8686139139
Samaritans Mumbai helpline for those who are stressed, distressed, depressed, or suicidal: +91 84229 84528, +91 84229 84529, or +91 84229 84530
The MINDS Foundation for those experiencing mental health problems: 18005-477-200

Hong Kong Helpline
Samaritans 24/7 HOTLINE 2896 0000

International
Befrienders Worldwide: You can find a list of helplines around the world on their website.
<https://befrienders.org/find-support-now/samaritans-uk/?> Centres include:

Livslinien: Call 70201201 (from 11:00 – 04:00am, daily)
Email: jkt@livslinien.dk

Community Help Service (CHS) Belgium.
Call 026484014
Email: office@chsbelgium.org

Samaritans in the Republic of Ireland:
Call 116 123
Email: Ireland@samaritans.ie (24/7)

SOS Help: Call 0146214646 (15:00 – 23:00 daily)

Crisis Text Line: Text HOME TO:
741741 (US)
686868 (Canada)
85258 (UK)
50808 (Ireland)
Crisis Text Line | Text HOME To 741741 free, 24/7 Crisis Counselling

International Association for Suicide Prevention
Website: <https://findahelpline.com/i/iasp>

Appendix O: Participant Debrief (Recruitment Stream 2)

PARTICIPANT DEBRIEF FORM

Thank you for taking part in this study. The aim of the study was to explore the experiences of adults with cystic fibrosis (CF) unable to benefit from triple combination therapies due to underlying genetic mutations. We would like to thank you for sharing your experiences. The information you shared with us today will further our understanding and inform clinical practice and research.

Once all the data has been collected and analysed, the results will be written up as part of a thesis for the South Wales Doctoral Programme in Clinical Psychology and may be published in academic journals, presented at conferences, and used in training. As explained previously, all the results will remain anonymous, and you will not be identified in any report, publication, or presentation.

It's possible that talking about your experience may have raised some difficult feelings or thoughts. If you have been affected by any issues raised in the interview and would like further support, please contact your Clinical Psychologist or other Clinicians in your Cystic Fibrosis Service or consider any options in the attached document.

If you wish to raise a concern, or complain about the project, please contact Mulongwe Mwelwa, using the contact details below. If we cannot resolve your concerns or problems, then Cardiff University Research Ethics has a complaints procedure: Please contact the School of Psychology Ethics Committee (SREC) secretary:

Secretary of Ethics Committee
School of Psychology
Cardiff University
Park Place
CF10 3AT
Email: psychethics@cardiff.ac.uk
Tel: +44 (0) 02920870707

We hope that you have found the experience positive. We would like to give you a voucher as a thank you for your participation. Thank you once again.

Yours Sincerely

Mulongwe Mwelwa

Trainee Clinical Psychologist

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Telephone: 0300 373 1000 or 020 3795 2184

(Monday to Friday 10am -4pm)

Email: Helpline@cysticfibrosis.org.uk

Website: <https://www.cysticfibrosis.org.uk/the-work-we-do/support-available/helpline>

Samaritans (Available 24/7)

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Website: <https://www.samaritans.org>

Community Advice and Listening Line (C.A.L.L) Helpline: Wales Only Helpline (Available 24/7)

Telephone: 0800 132 737

Text: 81066

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SANEline (Available 4.30pm -10.30pm everyday)

Telephone: 0300 304 7000

Website: <https://www.sane.org.uk/how-we-help/emotional-support/saneline-services>

Appendix Q: Sample of interview transcripts with exploratory noting and experiential statements

Example from interview 4

Experiential Statements	Transcript	Exploratory notes
<p>Attempting not to be hopeful to managing expectations</p> <p>Hopeful to benefit from ETI</p> <p>Attempts to not get hopes high with CF</p> <p>Hope was short-lived</p>	<p>I tried not to get [pause] I mean, I was hopeful, but anytime it comes to CF, I always try not to get my hopes up. I think that's just sort of a coping mechanism.</p>	<p>This makes me think that they really struggled with their emotions of trying to articulate that they “tried not to get...” I suppose they meant hopeful, but also admitting that they were indeed “hopeful”.</p> <p>They provide an explanation for this in the context of CF of always not getting hopes up (what does this say about having CF? You can't have hope with CF? are there many disappointments with CF? and did ETI give her permission to have hope? Sadly this was short lived as they described “hope gone quickly”)</p> <p>Managing expectations seems to be seen as a coping mechanism</p>
<p>Not benefiting from ETI added to the setbacks</p>	<p>But yeah, definitely when I found out it wouldn't work, it was. It just sort of felt like another set back in a way.</p>	<p>Impact of not benefiting from ETI was seen as “another set back” (I wonder if they meant that having CF brings many set backs, and this added to the set backs? I get a sense of disappointment at not being able to benefit from ETI</p>
<p>Mixed feelings – excitement for others and disappointment or sad for self</p> <p>Desire or longing to benefit from ETI</p>	<p>But obviously it mixed with feelings of incredible excitement for those who could benefit.</p> <p>But I obviously, selfishly wanted to be able to benefit as well.</p>	<p>Mixed feelings stemming from excitement for those who can benefit</p> <p>The use of “selfishly” implies how much they too wanted to benefit from Trikafta (this adds to the mixture of feelings initially expressed)</p>
<p>Sceptical about success of new drugs</p>	<p>And yeah, it's just sort of a, oh, another sort of, there's always these things that, you know, I hear about all they're</p>	<p>Emphasis on “another” thing not working</p> <p>They describe a recurring pattern and familiarity of things not working</p>

<p>Disappointment at ETI not working for them</p> <p>Repetitive pattern of things not working</p> <p>Hope to hope gone quickly</p>	<p>trying this they're trying this. But I feel like nothing ever really seems to happen or to work. And then finally, this thing did work. But then of course, there's a catch. And it didn't work for me. And I just sort of felt like, oh, this is so typical.</p>	<p>and maybe disappointment might be a thing they felt (this also gives an indication into the research that goes in to developing new drugs) I wondered if they were sceptical about ETI too not working and then “finally this thing did work”</p> <p>The “of course there’s a catch” and this is “so typical” might imply a sense of things being inevitable and play into the recurrent pattern of things not working (again, hopeful to hope gone quickly)</p>
	<p>Interviewer: And when you when you kind of share about this being typical, what what do you mean by that?</p>	
<p>Sense of injustice and unfairness about having CF</p> <p>Sense of health being unfair</p>	<p>Oh, I don't know. I just feel like. Oh yeah, I feel like in general just being dealt like the cystic fibrosis hand (laughs) if it was a deck of cards I didn't get deal dealt the best deck. Or the best hand?</p>	<p>Initial hesitation of “I don’t know” but again they provides an explanation in the context of having CF</p> <p>The use of the phrase “deck of cards” and not being dealt the best deck implies the challenges that come with having CF and additional setbacks from not being able to benefit from ETI (who is handing out the deck of cards? What feelings do they have towards them?)</p>
<p>Positive outlook on life</p> <p>Comparison and seeing self as better than others regarding health</p> <p>Positivity and optimism as coping mechanism?</p>	<p>So yeah, it just sort of. I don't know. I mean, I don't mean to sound like there's so many things that go wrong in my life because I'm very blessed and I always try and stay optimistic. And I know I'm a lot healthier than, you know, a lot of people in the world.</p>	<p>Reflection on the positive things in their life using words like “I’m very blessed” and staying optimistic</p> <p>Reflection on being “healthier” than a lot of people</p> <p>Is this how they cope?</p>
<p>Sense of being robbed of ETI</p>	<p>Yeah, it just sort of, it does feel like, I don't know... Yeah. Another thing that could have</p>	<p>Acknowledgement of importance of ETI as being another thing that would have been “so good” – within reach and taken out of grasp</p>

Acceptance of the situation Hopeful for the future	been so good (laughs) but just yeah. Wasn't meant to be for me [pause] yet. yeah	Again laughter might be hiding difficult emotions "YET" might suggest a sense of hopefulness for the future
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Example from interview 1

Experiential Statements	Transcript	Exploratory notes
Exclusion and a sense of unworthiness Feelings of being forgotten, undeserving, not important or not cared for Desire for inclusion and recognition	Participant: So we are sort of left out of discussion. When we talk about, you know, a cure for CF or a better medication for it, we are left out of the discussion because we're a very small portion of the of the topic, but it is still very important to look at those people because those are still the people who are part of who are part of this group that have been disadvantaged, that do not have.	This is powerful when they say that they are "left out" of discussions that talk about a "cure" for CF (I get a sense of not being worthy of, being forgotten, not deserving, not important, not being cared for) "we're a very small proportion" – it makes me think they might be saying why would they (researchers) research on this small group, almost like they have been made to believe that they are not deserving of it)
Feeling forgotten or left behind	That might have again, as I said, some might have very severe mutations. Some might have not so severe, but really depends on what you have.	A desire for inclusion
Advocacy for the minority group who cannot benefit from ETI	And these are the just people who have been left behind in that discussion.	Emphasises importance of looking at those who cannot benefit from ETI Reference to being "disadvantaged" (again a sense of unfairness, exclusion, injustice, left out)
Advocacy for equitable access to treatments	And I think it's very important that we shine light on that. So after you know that whole thing, as I looked at the study [current study], I was like, OK, this does seem interesting. I should, you know, I should	Emphasis that the non ETI group might have "severe mutations" (feels like they are providing a reason why they are worth looking into and maybe even more important)

Curiosity and gratitude for research	put some time aside to be a part of this.	<p>Provides a balanced view that some might not have a “severe form” (again provides a sense of inclusivity despite how severe, that all people with CF are deserving of a chance to have something like Kaftrio)</p> <p>Emphasis of being “left behind” and the importance of shining a light on this group</p> <p>Study looked “interested” and a desire to be a part of it – sense of gratitude for this research</p> <p>“just see what its about” sense of curiosity</p>
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Appendix R: Sample Personal Experiential Themes

Example from interview 4

	PETs	Experiential Statements
1.	Thoughts and feelings about current research	<ul style="list-style-type: none"> - Phrases used to describe current research ‘refreshing’ to see something regarding the minority group. - Current research made them feel ‘seen, heard and validated’. - This research fostered hope. - Hope that participation in this research will increase research into rare mutations. - Appreciation for opportunity to share. - Expressing gratitude towards this research
2	Feeling forgotten, left behind or overlooked	<ul style="list-style-type: none"> - Feeling forgotten in research priorities - Release of ETI contributed to feeling forgotten (contrast with ETI giving hope as well – conflicted emotions) - Fear of being forgotten in research and funding initiatives - Feeling forgotten in media portrayals of CF (one-sided portrayals of CF)

		<ul style="list-style-type: none"> - Feeling forgotten linked to feelings of unworthiness or unimportant - Too much focus on ETI leading to feelings of being forgotten - Perception that needs of those who cannot benefit from ETI are forgotten - Feeling forgotten by healthcare professionals - Sense of unfairness and injustice linked to feeling forgotten. - Sense of seeing themselves as a poor investment regarding funding for research into the minority group - Doubt and questioning research priorities into rare mutations. - Perceived lack of information from CF teams on rare mutations - Perceived CF teams out of the loop on rare mutations - Feeling less acknowledged or considered in treatment discussions - Feeling out of the loop increases feelings of being forgotten
3	Comparison and media portrayals of people with CF who can benefit from ETI	<ul style="list-style-type: none"> - Comparison increases feelings of being forgotten or left behind - Certainty of others health getting better vs. certainty of their health is getting worse - Contrast in health trajectories – theirs going the opposite way (getting worse) - Disbelief and shock at the improvements of others - Envy of others living an almost ‘normal life’ - Longing for similar improvements and opportunities - Comparison and visibility on social media makes experience worse - Frustration due to misconceptions of ETI by others as curing everyone - Positive perspective of media portrayals of CF pre ETI (linked to increased awareness of CF by general population) - Negative perspective of media portrayals of CF post ETI (linked to sense of being forgotten) - Perception that the media can be a distraction from CF realities - Anger? and frustration at media for showing one sided narratives of CF - Desire for inclusivity in the media and research
4	Experiences of hope	<ul style="list-style-type: none"> - Initially hopeful at the release of ETI

		<ul style="list-style-type: none"> - Lost hope quickly at finding out that they cannot benefit from ETI - Managing expectations and trying not to be hopeful - Hope seems fragile - Choosing to remain hopeful despite disappointment - Hopeful for the future, and for a cure - ETI has given hope for future treatments - Sense of hope that the minority has not been forgotten despite feeling forgotten - Sense of resigned hopefulness - Remaining hopeful and optimistic despite uncertainty about new treatments - Sense of frustration while remaining hopeful
5	Mixed feelings – particularly when comparing self to others who can benefit from ETI	<ul style="list-style-type: none"> - Excitement and happy for others who can benefit from ETI, sad and disappointed for self - Sense of jealousy that they cannot benefit from ETI - Mix of hope and doubt regarding possibility into research for rare mutations

Appendix S: Sample Group Experiential Themes

Group experiential Theme (GET)	Subtheme	Example quotes to support themes
<p><i>Feling forgotten</i></p>	<p><i>Feeling forgotten, left behind or overlooked</i></p>	<ul style="list-style-type: none"> - <i>“I was actually really grateful that ... something like this [current research] had been mentioned because I feel like a lot of the research these days is obviously and all the stuff in the media is focused on Trikafta Trikafta and we sort of get a bit forgotten about all those who can't benefit” (Bailey)</i> - <i>“The forgotten few is something that I've heard other people say... I don't think that relates to me 'cause I don't think it is the case, because ... I read around this and I'm involved in some of it, and I know the work that is going on to look at alternatives” (Jamie)</i> - <i>“... my doctor says it [ETI] doesn't work like that... it [ETI] will not work on you full stop, and it is very expensive, so they can't just, you know, give it out willingly if ..., if it's not going to work.” (Charlie)</i> - <i>“...we are sort of left out of discussion when we talk about, you know, a cure for CF or a better medication for it[CF]...” (Sam)</i> - <i>“Oh, it's just it just sucks to put it frankly, I don't know...that feeling of being left behind so it sort of takes a bit of a mental toll and then physically as well. It's just I think of what my life could be like if I was on it. Yeah, it doesn't even seem real like to think about it sometimes.” (Bailey)</i>
	<p><i>Us and them Comparisons</i></p>	<ul style="list-style-type: none"> - <i>“I suppose ever since Trikafta came out, I've noticed everyone else's [those who can benefit from ETI]... online, people post out their lung function increasing and everything, but obviously for me, that's not been the case. And it hasn't, it hasn't gone down drastically, but I would say I haven't gotten any healthier...” (Jamie)</i> - <i>“You know you might hear stories that they [other people who can benefit from ETI] are able to gain weight now which is nearly impossible. It's very hard for CF patients to gain weight you know.” (Sam)</i>

		<ul style="list-style-type: none"> - <i>“When it did become available, I was as happy for them as anyone could be, but it's then when the this changed my life stories came into social media at the same time that I started being ill. I just felt like it's something I didn't want to hear about. So I blocked certain keywords on all of my profiles. Anything to do with [CF] or Kaftrio...” (Jamie)</i> - <i>“And she was saying on the show that she doesn't even do nebulizers anymore...she just has to take the Trikafta pills or whatever. And that's like all she does in a day. And 'cause, I'm sat here doing like three nebulisers a day, I was actually watching the show, doing my nebulizer thinking ‘Oh my gosh. Like, is she kidding?’ She [person on the show] doesn't have to do this anymore. ...Imagine just not having to do that anymore and just taking 3 pills in the morning or whatever and just going on with my day like a ‘normal human’. That just seems sort of incomprehensible to me, I just couldn't believe.” (Bailey)</i> - <i>“...[media] push everything out about Trikafta and it's, you know, they're not gonna be going on the show ‘but this only benefits 80% of the population or something’. So I think there's a lot of misconception. Then we've got the media portrays that everyone was CF is now cured and we don't need to worry about CF anymore. We don't need to donate to CF anymore because they're all fine. They've got this miracle drug and we can move on to the next disease or something like that.” (Bailey)</i> - <i>“It's the way that media portrays Trikafta and the benefits that people will now just believe [pause] CF is sort of cured and we can move on to funding for the next thing. Yeah, so I guess that was my feeling of frustration.” (Bailey).</i> - <i>“... it was, it is obviously really good when CF gets portrayed in the media because more people can learn about it... I used to think for any media attention with CF was good attention, but now I guess there's a little niggle in my mind going maybe that's not the case, maybe too much focus on Trikafta or on everything is making people unaware that there is still some of us left behind” (Bailey)</i> - <i>“it [ETI] was quite well documented in the news from what I remember about this drug, and I had quite a lot of family, friends asking about it, you know, about me</i>
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		<p>having the drug...I remember one time in work...I had one of my managers mention it, that, oh, your life must be, you know, great now you have this drug. And I had to explain to a lot of people that I couldn't have it, and explain as to why I couldn't have it, which was a little bit annoying by the end of it." (Bailey)</p> <ul style="list-style-type: none"> - "I guess the part of the reason I mean I think these drugs are absolutely amazing and I think you know if they don't allow it for like there was talk about these five year olds, I think in the news that they may not allow them to start if they're not already on it. I think that's an absolute travesty because if you can stop children, anybody getting ill apart from the cost it costs the NHS but just for the sake of the person that it should be, it should be used." (Alex) - "Not too much really to be honest. I – I've got – I've got friends who have a child with CF, who has the Kaftrio drug, and they've said it's life-changing for them, which is great at the end of the day. But, in terms of how it's affected me, not really all that much. My health hasn't really – because this was, you know, about four years ago, wasn't it? My health hasn't really deteriorated all that much over the last, you know, over the last four years. So, I haven't really noticed much if I'm being honest with you." (Frankie)
	<p>Lack of consideration in research priorities</p>	<ul style="list-style-type: none"> - "And then I stumbled upon this study for CF and I thought, you know, this shines a light on people like me who have been...you know, left out of the discussion who are not talked about that much because, you know, Trikafta and a lot of these medications [other CFTR modulators] satisfy the vast majority of CF patients. So we are sort of left out of discussion when we talk about, you know, a cure for CF or a better medication for it. We are left out of the discussion because we're a very small portion of the topic, but it is still very important to look at those people because those are still the people who are part of who are part of this group that have been disadvantaged. (Sam) - "It's nice for a presenter, especially if they are part of the clinical world to tell good news stories, to tell how great the advancement of science is... on these occasions. And it's nicer to talk about how well people are doing, how the fact

		<p><i>that lots of women are now having children, which they didn't before and people are living longer and lung function as a whole is better.” (Jamie)</i></p> <ul style="list-style-type: none"> - <i>“A final note at the end of a presentation is of course we know that this doesn't apply to everyone, and there are a few people that don't benefit from this. Its things like that that just add to the frustration sometimes. (Jamie)</i> - <i>“ We need to create more of an awareness in the scientific community about that and just, you know, it's not that hard to look for people. There are people with CF are generally registered globally that they're healthcare professionals and it's easy to find their records. And I think if we had the right mindset for it, if we had the right research orientation for it. We could definitely do extensive research on this sector (Sam)</i> - <i>“...the fact is, research unfortunately is very much money driven. It is very much driven by where the funding is and funding generally does not go to a small minority of people because it's a small percentage of people who are ...I think we need to change the orientation in terms of how research is funded...” (Sam)</i> - <i>“I just think who on Earth is waking up one day going, ‘Oh, let me decide to research it’. I mean, why wouldn't someone want to join the team that's researching Trikafta that they probably make a lot more money...they'd be benefiting more people... (Bailey)</i> - <i>“...rare mutations are going to be the one that are more problematic, right? Because we do have a very good solution for those with D508 [majority mutation], although it's [ETI] not a full form cure, but it's still a very large improvement for those with a rare mutation. We have pretty much nothing, you know. So that's the place I think a lot of CF Funding and resources need to go towards...” (Sam)</i> - <i>“...the thing about corporations is that ... they're very profit driven and if they don't see profit in a sector that they that they don't proceed research on it because they don't see profit in it. So it's very important that not only do we seek out government ...they [government should] push these corporations, maybe help them in funding, maybe help them in in getting the right people for research, and</i>
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		<p><i>maybe getting the right commitment. We need people pushing for this. We need governments pushing for this so that these large corporations do put effort and funding into making something [new drugs]....” (Sam)</i></p>
	<p>Variable effort from Healthcare Professionals (HCPs)</p>	<ul style="list-style-type: none"> - <i>“Its a very, very good relationship I have with them [CF teams]. They're great people, they really are. I couldn't speak highly enough of them. I think it's just one of those things where they maybe either assumed or decided maybe that there's no point in [telling them about their eligibility status or information about ETI], you know this drug is not applicable to and that's that, that's the end of it. (Ashley)</i> - <i>“And so there is an escape balm if you like. There [CF Service] where I can touch base with CF and say look I'm struggling and they will say yeah come in or we need to see you or make an appointment and that's the good thing about it.” (Ashley)</i> - <i>“I guess a bad day would be when I have an infection or I'm just not feeling well and it gets to a point where I just it's just not manageable at home, so I have to call up my CF team. I have to e-mail them or call up them up. And you know, just tell them about it (Sam)</i> - <i>“I can't always hope that they'll [CF Teams] have some new research or clinical trial that, you know, they might be on the lookout to see if there's any clinical trials that they could get me on or if there's any new information. And sometimes when they have to be like, ‘oh, are you on Trikafta?’ it's like, no ... you've known me for so long. How do you not know this... obviously. I mean, they see so many patients, they can't always remember. But then I guess most of the patients are on it [ETI].” (Bailey)</i> - <i>“You just not just cause the amount of effort that you want to put into something you know cause I'm more than happy to be part of studies. I'm more than be happy to be part of trials, you know. I'll, I'll do every anything that helps you know people like me, but it's just to not see that effort. The same effort being, you know, being made from the other side, from the NHS, from the medical</i>

		<p><i>professionals just not seeing the same. That's just heartbreaking you know.” (Sam)</i></p> <ul style="list-style-type: none"> - <i>“...Physios would say, oh, what's your normal lung function? And my response is I don't know...[I feel] frustrated because they should have read my notes and they should know not to ask that stupid question. But on and on a deep level like, I'm not sure what baseline is for me and I'm not sure what normal is now...” (Jamie)</i> - <i>“...I can tell when the doctors who were treating me are looking at my results. You can see that. They realise what a big impact it would make. And you can tell that it bothers them as well...It's hard knowing that I don't have that option.” (Jamie)</i>
	<p>Lack of services and information</p>	<ul style="list-style-type: none"> - <i>“... you hear mention of off label access to the drugs, but there's nothing telling individuals how to get that. And under the very vaguely worded and funding agreement with the ... doctors are permitted to give off label access. But you need documented evidence. That the drugs would work and if your mutation is so rare, how do you get that? And it's taken me a long time. And doing all of the legwork myself to get access to a lab who might be willing to go through theratyping with me, but if there ... was a system where in the UK, under the NHS that would fund theratyping...” (Jamie)</i> - <i>“It's just another thing that you don't have access to it. It's just. It's an annoyance. It's a frustration.” (Jamie)</i> - <i>“In terms of people with rare mutations, I haven't seen much ... in general... I haven't been, you know, offered any [trials] or been informed about any [trials]. So it's just a feeling of just being left out, you know, it's just, it just feels like we're not put in being put into consideration by the NHS.” (Sam)</i> - <i>“These days the problem is obviously like everything else is there's a financial, you know, they [research] needs finance...” (Ashley)</i> - <i>“.. I understand funding can be difficult. I understand that researchers have, you know, their priorities, but these are people, who are sort of, you know, forgotten to this discussion. And I think we do need to direct funding into this because there's quite a few people I believe in the UK and the US who do suffer from this,</i>

		<p><i>who, who have who cannot use Trikafta and who are just, you know, left there..." (Sam)</i></p>
<p>Conflicting emotions</p>		<ul style="list-style-type: none"> - <i>"Yeah I mean, as I said, I was happy, you know, because it is a step in the right direction. We do have people who would benefit greatly for this, you know, and I'm very happy for those who can, you know, because [laughter] I read these happy stories in that Facebook group that I'm in, that people, children, or people who have been receiving this [ETI] and it's just a giant improvement for them and, you know, makes me very happy to read those things. But then it's also creates this level of disappointment that, yes, it's been great for them, but it's not something that I can benefit from... So it is such a great step in the right direction, but not in the direction that would, you know, help me improve my state of living." (Sam)</i> - <i>"When it did become available, I was as happy for them [those who can benefit from ETI] as anyone could be. But it's then when the this changed my life stories came into social media at the same time that I started being ill. I just felt like it's something I didn't want to hear about. So I blocked certain keywords on all of my profiles. Anything to do with [CF] or Kaftrio or any keywords that I can't remember all of them. Any keywords that would surround it because I didn't want to read about it. But at the same time, I was really happy that those people were having the benefit of it." (Jamie)</i> - <i>"...it was disappointing, but then at the same time I was thinking 'you know what, there's something out there now, at least, and it's actually working for people', so I'm happy for those people that is working for 'cause obviously, I'd love that life of having a better lung function and everything, and then it also gives me hope that, you know, there is if they've obviously got this Kaftrio out, there will be something." (Charlie)</i> - <i>"But yeah, definitely when I found out it wouldn't work, it was ... just sort of felt like another setback in a way. But obviously it mixed with feelings of incredible excitement for those who could benefit. But I obviously, selfishly wanted to be able to benefit as well." (Bailey)</i>

		<ul style="list-style-type: none"> - <i>"... It's been a life changer for her [talking about somebody benefiting from Kaftrio] and I'm glad, but you're not gonna get me to say I'm upset or I'm bitter or I'm angry because I'm not." (Alex)</i> - <i>"Yeah, I think it's, I think it's great. I think it's amazing and I think it's long, long overdue in terms of having something that's breakthrough science-based drugs for people who are suffering with chronic cystic fibrosis, which is an awful disease. And for me, it's absolutely brilliant news. And I, and I'm very buoyant about that. And I'm very happy. And happy about it. I'm very supportive of it. I don't, as I said, don't hold it. You know, it's definitely don't hold any grudges. People who can benefit from it, I think it's fantastic." (Ashley)</i> - <i>"Yeah, yeah, because at the end of the day, it's good for him[somebody who can benefit from ETI]. If he – if he can take – if he can take the drug and it's been working great for him, and he's – I think he's about 15/16 years old now and he's on, like, he's doing running, like cross-country running, and he's, you know, he's fit and healthy and it's changed his life. He's not taking as much medication as he used to now, which is great. He's taking less [Creon], and yeah, he's – he's been getting along fine with it, so that's – that – I feel really proud for him, to be honest, quite happy for him." (Frankie)</i> - <i>"I was angry and I was sad as well. And, you know, sometimes those emotions are correlated. Sometimes you are angry and sad. So I was feeling that way at that time because, you know, it's just, I'd never thought I would be wrong. I never thought, you know, something that's in my lab report would ever be wrong. I never expected that. But in the second and third testing, it came out. It was so then it was inevitable that that that is the correct one because they did try." (Sam)</i>
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Fragility of hope	Shades of hope	
		<ul style="list-style-type: none"> - <i>“I’m not gonna lie, it was a bit disappointing. Because. It’s like all my life of having CF. I’ve always been told that, you know, there’s always that gene therapy going on and one day it’s going to be available and you know. And then obviously I’ve always had that hope in my back of my mind as I’ve been, you know, going through my early years of CF and growing up. I’ve always had that thought that soon, you know, hopefully there’ll be something close to a cure and I hope I’m around for that. But then to be sort of told that I’m not eligible for it because ... my mutation’s totally different, not totally different, but it’s different to the common mutations.” (Charlie)</i> - <i>“... it was disappointing. It was a bit because you had started I suppose, when initially it wasn’t through the hospital. I don’t think that I hear I think it was. Obviously there was a lot on the news media and things in general and in healthcare sort of about these new ‘wonder drugs’, ...which they are in fairness, and then when the specifics I suppose became more available, I realized and I questioned obviously when I went up the next time and you know I yeah, I was disappointed.” (Charlie)</i> - <i>“And then, yeah, but then at the same time, I get that feeling of ‘Oh my God, it’s me’, like, I don’t know, it’s just definitely like, oh ... imagine if I just happened to have, like, why do I happen to have this rare mutation? Why does 80% or however many of the population have this? And then I’ve just got this random one, like, how does that? Yeah, I don’t know.” (Bailey)</i> - <i>“... I wasn’t really aware of it initially. I kind of ignored it all. And then because I was too busy living my life. And then when it was more prominent in the newspaper, started reading about it and I did think oh, let’s have a look, then see if it will make a difference. And that’s when I realised that it wouldn’t affect me...” (Jamie)</i> - <i>“And he – he just – he just, like, sort of broke the news to me that it wasn’t available, but they had other things in the pipeline and as soon as they’re available we’ll let you know about them. And one of them being the drug that – the trial that I’m going to be going on now in the next few months...” (Frankie)</i>

	Fluctuating hope	<ul style="list-style-type: none"> - "...anyway at that point, it was very short lived, the oh, I wonder if it will help." (Jamie) - "And then obviously when I spoke to my consultant, I still did, I still, I'm not going to lie, I still have the little bit of hope that maybe she'll actually, if I quite remember the conversation, I think I did. I did even ask her. Actually I did. Yeah. I asked her if I can trial it anyway." (Charlie) - "Yeah, it's a plethora of feeling you feel that way. You mostly feel hopeless cause you know... you believe your entire life that you have this mutation that you know that we finally have a drug for. And now it turns out it can't help you. You know. It turns out it's not for you. So that does make you feel hopeless." (Sam) - "I guess I was very hopeful that it would work for me, but then yeah, quickly realising it wasn't gonna be a part of my life. That's kind of just became very quick, hope gone." (Bailey) - "And yeah, it's just sort of ... oh, another sort of, there's always these things that, you know, I hear about ...they're trying this they're trying this. But I feel like nothing ever really seems to happen or to work. And then finally, this thing did work. But then of course, there's a catch. And it didn't work for me. And I just sort of felt like, oh, this is so typical." (Bailey)
	Hope Enduring	<ul style="list-style-type: none"> - "And then I stumbled upon this study for CF. And I thought, you know, this shines a light on people like me who have been, you know, left out of the discussion who are not talked about that much because, you know, it does Trikafta and a lot of these medications they do satisfy the vast majority of CF patients." (Sam) - "...But then I mean, you've given me hope because I thought who on Earth would want to know about the psychological impacts of someone that can't benefit from Trikafta. So, you know, thank you again for doing this." (Bailey) - "Then I started thinking about, you know, all right, it's out there. They've got something great. There'll be something else, hopefully for us. So yeah." (Charlie) - "Well, I did believe that since we do have this drug and it's been a long way and it's it's taken a long time for us to come up with something like this. I thought, you know, the fact that we have this, I was optimistic to some extent that we have

		<p><i>been able to research this, this miracle of a drug and going forward, we might even come up with something that does help people with rare mutations, you know. But I think we actually can do that. I think with the right amount of funding and the right amount of research, that is something we can achieve.” (Sam)</i></p> <ul style="list-style-type: none"> - <i>“Yeah, I think a little bit of both, but I think definitely Trikafta has given hope... I would say it definitely is given me hope, but at the same time, it's also. In a sense, made me concerned that all the research will now be focused on that mutation. But. I still do hold out hope because you know, if it can happen for some people, why not me?” (Bailey)</i> - <i>“Except, yeah, as I was saying, hope that there's someone out there. Who's decided to research into a random mutation with CF, which seems really far fetched to think about that? Anyone could even be doing that, but. Yeah, I just sort of have to sit back and hope. And yeah, I feel like I can't do anything.” (Bailey)</i> - <i>“But they said after – after that trial, there are going to be new ones coming out as well, which will hopefully – that I'll hopefully be eligible for as well. So, we'll, you know, we'll do this drug trial first, yeah, we'll get on with it, and then there's another one coming out as well that they said, when it's available, you know, they're going to put me forward for it. So, yeah, it's all – all good news coming from that, to be honest. And I'll be more than happy to take as many trials as is needed if – if – if it keeps me healthy, then definitely.” (Frankie)</i>
	<p><i>Cautiously hopeful</i></p>	<ul style="list-style-type: none"> - <i>“So I'm hopeful, to be honest with you. I'm really hopeful that something might be out there, whether I'll be eligible for it just because of my health that's a different situation because this thing that. This new drug that's gonna be trialled soon. Your lung function has to be at a certain level. Mine isn't at that level at the moment, and that's why that's why I'm trying my best, at least maintaining at this level or even try to improve it.” (Charlie)</i> - <i>“And I just keep hoping that maybe they will find something that I can have a go at before it gets to the point where maybe I wouldn't get any benefit.” (Alex)</i>

		<ul style="list-style-type: none">- <i>"I just hope that I don't miss the window for it to become. Something that I can benefit from." (Jamie)</i>- <i>"Yeah, I think it's made me want to focus more on my health. Because I I can't just rely on some miracle drug to come along. So I have tried to sort of, you know, stay more active, although at times it's the mental part, but gets in the way and then I can't really be bothered getting up and exercising. Yeah, I guess it's. I don't know it's. I suppose it's made me. You know, I had conversations with my family. About. No, you know, try not to give up hope. (Bailey)</i>- <i>"It was I tried not to get I mean, I was hopeful, but I went anything. Anytime it comes to CF I always try not to get my hopes up. I think that's just sort of a coping mechanism. (Bailey)</i>
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Remaining on the old CF trajectory

- *“Yeah. No, It's definitely part of Trikafta because I think they don't have that worry anymore.... I feel like they're on the upward trajectory. And then me, I just get worried that I'm going the opposite way and...I think since Trikafta it's definitely made it more apparent that I'm still on the old track of CF disease progression where people get worse, not better. (Bailey).*
- *“...go about their day-to-day life like you know your everyday people. And it's just a revolutionary thing for them and for me not, you know, be to be able to go through that. It's just that for people like me, and for those who have these rare mutations, it just means that they would have not as good of a quality of life as those who do or who are benefiting from it. It is literally a life changing thing for those who can benefit from it. And it's literally and it's quite literally a downgrade in those, well, not a downgrade, but It's for those who can't benefit from it. They have to, you know, continue with all their treatments and still have a not-so-great quality of life.” (Sam)*
- *“Because I'm obviously really happy that their health ... has increased the way it has. Because I've had years of being really well. And being the one that CF hasn't affected. Like it is really cruel timing in the way it's worked out that. The majority of people with CF are now having a better life and CF isn't affecting them as much as it was. At the same time the exact opposites happened to me.” (Jamie)*
- *“Because no matter how much I fight this illness. How much I get out of bed and do my physio and clear my lungs. Spend I spend like 2 1/2, three hours a day just clearing my lungs and then even when I'm trying to keep active walking, try to cycle when the weather's a bit decent and ... I just feel that. I'm not really feeling the benefit of it anymore. (Charlie)*
- *“But ...my lung damage is quite severe now it's progressing, so I'm not sure again how much if I did get the option it would actually change that now. (Alex)*
- *“I'm not chronic, I'm not suffering with Cystic Fibrosis on a chronic basis, you know, and I haven't. I'm lucky that I don't. Having said that, I have had pneumonia in my time, which is really bad, but I compared to that was you know, it's like anything in life.” (Ashley)*

		<ul style="list-style-type: none"> - <i>“Oh, I don't know. I just feel like. Oh yeah, I feel like in general just being dealt like the cystic fibrosis hand (laughs) if it was a deck of cards I didn't get dealt the best deck. Or the best hand? (Bailey)</i> - <i>“If I played CF bingo, I'd win, so I'm having the liver issues [list of conditions]. In the modulator drugs... you take them and they circulated. Through your body, aren't they? Through your blood system, so it it benefits all of the areas of CF in your body. It's not just your lungs. I would I would have that health benefit.” (Jamie)</i> - <i>“You know, it's – I think it's – if I was ill all the time, I think I'd probably have a different outlook on it and I think it would affect me a lot more, but because of my situation where I don't get ill that often, and when I do, I get better quite quickly, it's not – it's not something that I really think about to be honest with you...” (Frankie)</i> - <i>“Umm it [not benefitting from ETI] doesn't really mean anything. You know it if I know. I'm so really sorry cause I know you need different answers but it but it it really it. (Alex)</i> - <i>“It just means that. [Pause] Well, I don't know really because. I've always known that I've had CF. I've always known that my health decline at some point. And. I didn't ever assume that there would be a drug that might work anyway. But then again, I didn't realise that my health would decline now, so. Not being able to access them means that, there isn't a fix for the current decline in health.” (Jamie)</i> - <i>“I think it [not benefitting from ETI] kind of means nothing really.in some respect I nothings changed. Umm, I'm still who I am. I still get on with the way I deal with things on a daily basis and without... without knowing if it can enhance things and make things better. Then if I don't know about it, I just carry on....” (Ashley)</i> - <i>“It's really frustrating because. It's the key to going back to my life. Then maybe. If it was able to improve my health to the extent that it has in some of those stories that I read about. “(Jamie)</i>
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		<p>- <i>“Because at the end of the day, if this drug, you know, is as great as it is and I can’t have it, it was a – I’m going to have to do something because I might end up quite ill in the future and – and, you know, there’s nothing to really help me out. So, I did change my lifestyle a little bit in terms of the amount of alcohol I was consuming, or the amount of, well, smoking, for example. So, I did – it did give me a little bit of a kick up the bum to look after myself a little bit more, I think. But other than that, nothing really I can think of to be honest.” (Frankie)</i></p>
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	<p><i>Distraction and positivity as coping mechanisms</i></p>	<ul style="list-style-type: none"> - <i>“Myself against the drugs so I try not to think about the fact that it's not working, that it that I don't have that benefit that other people have and try and distract myself by looking at things that I can do to potentially change that...” (Jamie)</i> - <i>“I just sort of shake myself and just sort of think well and I try and there there's always people that I'm close to that unfortunately, you know, things can be happening that are worse ...I think just put it into context where you are you know and if you're not well go up and get some treatment and get better and umm, you know, do something proactive.” (Alex)</i> - <i>“I'm generally a positive person. I don't dwell on like negativity for too long I've just done that all my life anyway. So especially with CF ... you'll have good days. And you'll have bad days. Mostly you'll have bad days. (Charlie)</i> - <i>“So yeah, it just sort of. I don't know. I mean, I don't mean to sound like there's so many things that go wrong in my life because I'm very blessed and I always try and stay optimistic. And I know I'm a lot healthier than, you know, a lot of people in the world. (Bailey)</i> - <i>“Oh, right, okay. So, it's – it's – I just – I think – I don't know why I always just seem to have quite a positive outlook on life in general. I think that obviously, having CF, I think you have to a little bit, otherwise every time you're ill it's going to get you down a bit more. So, I think it's just always better to, you know, look forward and, you know, once again, something will come up. And something always does eventually. And that's about it really.” (Frankie)</i> - <i>“Well, I do, you know, try my best to, you know, engage in all things I like and all things that, you know, make me feel happy...You have to live life to your fullest, you know? And that's what I try to do most the time. But it's just that you always have this thing in the back of your mind that you know...”(Sam)</i> - <i>“But you know that there's no point wishing for something that I know isn't there? Because all you're doing is setting yourself up to have more pain than you know have enough pain in my life. So you know it's more about enjoying the day...” (Alex)</i>
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		<p>- <i>“Not at all, to be honest, because I’ve always had the – the – the sort of, the positive outlook. I’ve – I – I don’t really suffer with any sort of being down or any sort of depression, or anything like that. It’s not something that I’ve really had any issue with growing up, or – or now. And I – I – as far as I can remember, I think I’ve always been this way. I’ve never really deviated from – from being happy and just being, just, you know – well, like I am now, to be honest.” (Frankie)</i></p>
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Appendix T: Example of Reflexivity

Reflections after attending the NHS CF Service Focus Group

I was very much aware of how little information I knew about CF. It was helpful to learn more about CF, the different mutations, and new treatments (modulators). It was also helpful to learn that although this group might be small, forming 10% of the CF population, it's diverse with their own specific problems. For example, the experiences of someone not benefiting from ETI would be different for someone whose lung function is better than the other etc.

Reflections after the CF Trust Focus Group

I attended this Focus group after placement, and I was tired. I was grateful that the CF Trust involvement co coordinator planned that they would facilitate the session. I was really moved hearing the stories directly from those who cannot benefit from ETI, and it hit me how difficult (emotionally) doing this project will be, especially now that I have faces to the '10%' unable to benefit from ETI. But also, this focus group motivated me and helped me realise that this is such a worthwhile undertaking for the CF community.

Reflections after interview 1

I was nervous about this interview, and it felt clunky. I could tell that the participant was grateful and passionate about getting their voice heard and raising awareness. They raised concerns around funding, discrimination in work and research priorities. I felt sad about their descriptions of feeling forgotten, and there was a sense of injustice and inequality through a lot of what they were saying. I also got the sense that for them, not benefiting from ETI was just living with CF. I'm not sure if this is their way of coping, but they often used the words 'you' and 'we' and only spoke in the first person on occasion.

Reflection after interview 7

Unlike the other interviews, I wasn't left feeling sad after this interview, I was left feeling very hopeful. I wonder if this is because the participant shared some information about new trials that are commencing for those who cannot benefit from ETI. Throughout all seven interviews, hope, and how it fluctuates, has been a theme that has come up a lot. Whilst some participants told me how this research and ETI gave them hope for the future, I think this research, and particularly this interview also gave me hope for them.

Appendix U: Participant Contributions to Each Theme

Group Experiential Themes and Subthemes	Participants						
	Alex	Frankie	Sam	Charlie	Bailey	Ashley	Jamie
Theme 1: Feeling Forgotten	✓		✓	✓	✓		✓
'Us and them' Comparisons	✓		✓	✓	✓		✓
Lack of consideration in research priorities			✓	✓	✓		
Variable effort from Health care Professionals (HCPs)	✓	✓	✓	✓	✓	✓	✓
Lack of services and information			✓		✓	✓	✓
Theme 2: Conflicting Emotions	✓		✓	✓	✓		✓
Theme 3: Fragility of Hope			✓	✓	✓		✓
Hope Enduring	✓	✓	✓	✓	✓	✓	✓
Theme 4: Remaining on the old CF trajectory	✓	✓	✓	✓	✓	✓	✓
Distraction and positivity as coping mechanisms	✓	✓	✓	✓	✓	✓	✓