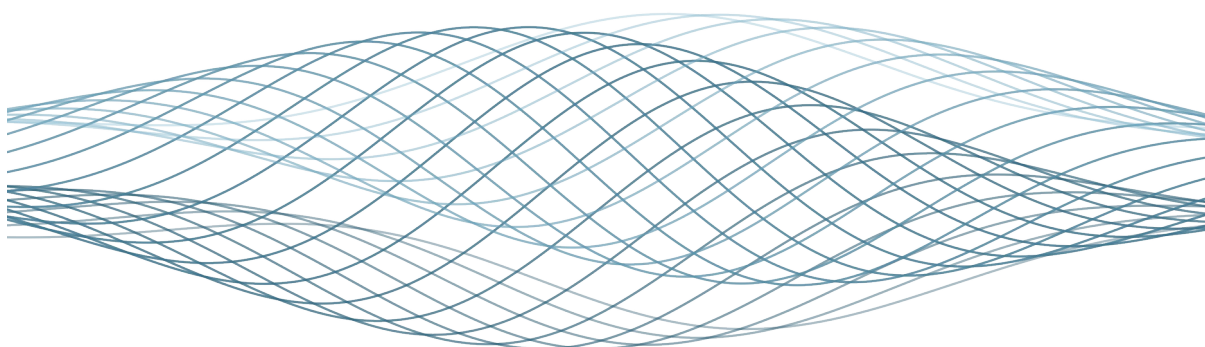


Breathtaking
FUNDRAISING NPC

HEALTH ECONOMICS REPORT

Transforming Cystic Fibrosis Care in South Africa

CFTR Modulator Therapy: Costs, Resource Use and Patient Experiences¹



In collaboration with



Division of Health Economics
School of Public Health



UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

Final report | September 2026

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Document at a glance

Report Title	<i>CFTR Modulator Therapy: Costs, Resource Use and Patient Experiences</i>
For	<i>Breathtaking Fundraising NPC</i>
Setting	<i>South Africa</i>
Timeline	<i>2018-2025</i>
Analysis	<i>Mixed-methods study; Quantitative (before-and-after cost analysis) and Qualitative (thematic synthesis)</i>
Perspective	<i>Medical-scheme payer perspective, complemented by the experiences of people living with cystic fibrosis and caregivers recorded in the Breathtaking beneficiary database</i>
Key Partners	<i>Breathtaking NPC, University of Cape Town, Red Cross War Memorial Children's Hospital, Quantum Health</i>
Status	<i>Final report - September 2026</i>
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1. Executive summary

Cystic fibrosis (CF) is a rare, progressive, life-limiting genetic disorder that places a substantial burden on individuals, families, and healthcare systems. Despite remarkable advances in treatment, access to highly effective Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) modulator therapies, including elexacaftor/tezacaftor/ivacaftor (ETI; e.g., Trikafta, Trixacar), remains severely limited in low- and middle-resource settings because of high prices, patent restrictions, and reimbursement barriers. Trikafta is the originator brand of ETI, while Trixacar is a lower-cost generic version with the same active-ingredient combination. In South Africa, although approximately 85% of people living with CF are eligible for ETI therapy, only about 55% have access to treatment with ETIs (1).

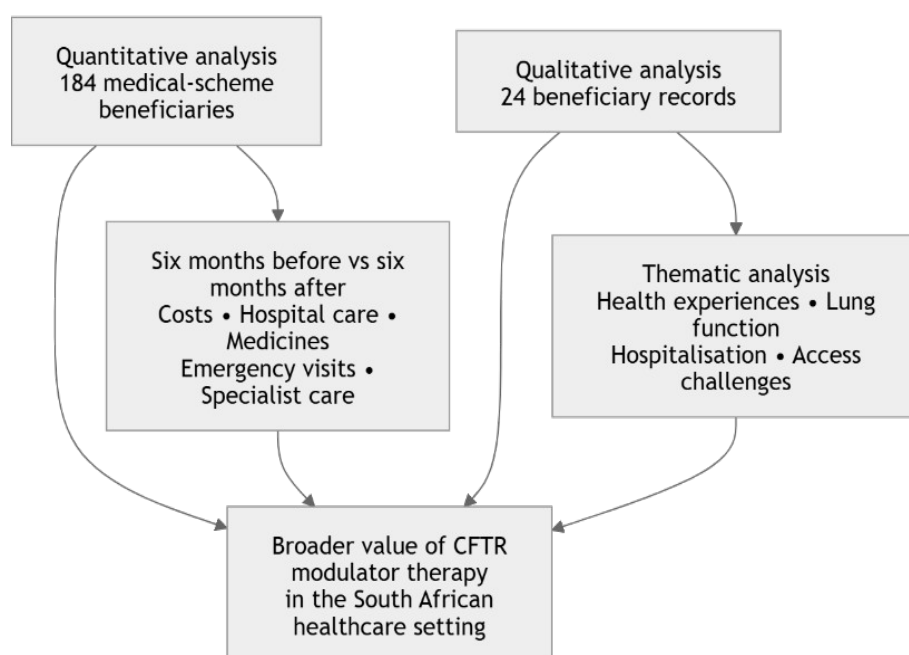
Key message

CFTR modulator therapy has the potential to transform the lives of people living with cystic fibrosis (CF) in South Africa. Our real-world findings suggest that treatment is associated with improved health outcomes and reductions in healthcare utilisation, supporting the need for evidence-informed policies that expand equitable access while ensuring sustainable healthcare financing.

1.1 Why this report matters

This report presents findings from a mixed-methods evaluation of the health and economic impact of CFTR modulator therapy, combining real-world healthcare claims data with patient-reported experiences to generate locally relevant evidence for policymakers, healthcare funders, clinicians, patients with CF and their households, and patient advocacy organisations. The study addresses an important evidence gap by moving beyond clinical efficacy to examine how these therapies influence healthcare utilisation, costs, and patient-reported health improvements in the South African context.

1.2 Study overview

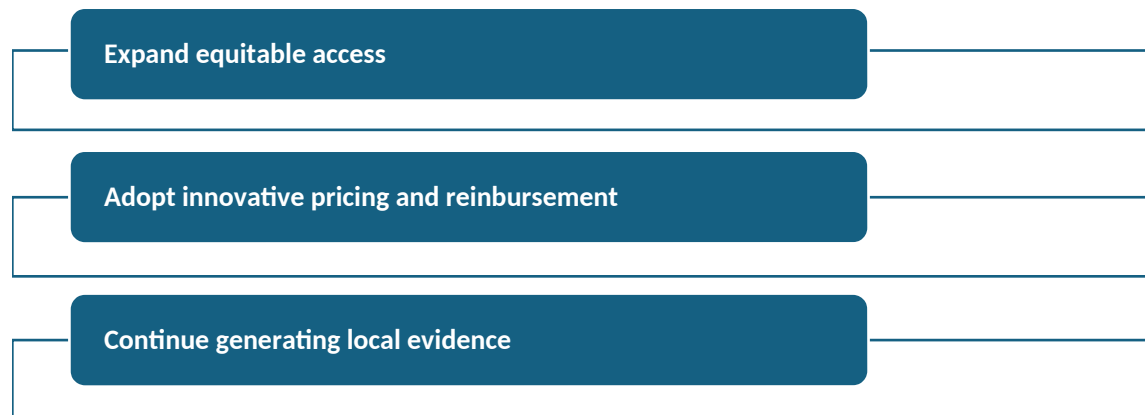


1.3 Key findings

- *CFTR modulator therapy (Trikafta) was associated with substantial reductions in healthcare use and costs. Excluding the cost of Trikafta, mean healthcare expenditure decreased significantly by approximately R75,000 per patient, a 35% reduction during the six months following treatment initiation.*
- *The greatest reductions were observed in hospital care. Hospital admissions reduced by approximately 21%, hospital days by 31%, and total hospitalisation costs decreased from R4.97 million to R3.02 million, representing savings of approximately R1.95 million in six months, indicating that improved disease control may reduce the need for costly inpatient care.*
- *Use of other healthcare resources also declined. Following treatment initiation, antibiotic courses decreased by 22%, overall, medication use by 14%, health-professional service claims by 26%, and procedures by 11%.*
- *CF Patient/ caregiver experiences supported the quantitative findings. Among 21 analysable narratives, 43% described improved overall health and 19% reported improved lung function. Individual accounts also described fewer hospitalisations and improved sweat-test results.*
- *Health benefits did not guarantee sustainable access. Families reported fundraising, borrowing money, arranging international medicine collection and stretching available supplies through reduced or alternate-day dosing. These barriers persisted even among patients with medical aid and are likely to be greater for people relying solely on public-sector care.*

1.4 Policy highlights

The challenge is not whether CFTR modulators work, but how to make them accessible, affordable and sustainable for all eligible patients in South Africa.



Equitable access requires policy decisions that consider not only the cost of CFTR modulators, but also potential savings from avoided healthcare use and patient-reported health improvements. Negotiated pricing, risk-sharing, and structured outcome monitoring could support sustainable access, while continued data collection will enable full economic evaluations that guide resource allocation.

2. Background

2.1 A rare disease with disproportionate burden

Cystic fibrosis (CF) is an inherited autosomal recessive disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator gene, which reduce chloride and bicarbonate transport across epithelial surfaces and affect multiple organ systems, most notably the lungs and digestive tract (2). Although CF has traditionally been regarded as a disease affecting predominantly high-income countries, growing evidence suggests that it remains substantially underdiagnosed in many low- and middle-income countries (LMICs) (3). The South African Cystic Fibrosis Registry recorded 505 confirmed patients across 17 treatment centres by the end of 2023, of whom approximately 85% were eligible for CFTR modulator therapy based on their genotype (1). However, these figures likely underestimate the true burden due to delayed diagnosis, limited awareness, and unequal access to specialised care.

2.2 Transforming care, not access

South Africa's therapeutic landscape for CF has evolved rapidly in recent years, but access to transformative treatment has not kept pace.

The introduction of Cystic Fibrosis Transmembrane Conductance Regulator modulators (CFTRm) has fundamentally changed the treatment landscape by targeting the underlying genetic defect rather than managing symptoms alone. ETI has demonstrated substantial improvements in lung function, quality of life, and survival, and has become the international standard of care for most people living with CF. Studies have also shown reductions in pulmonary exacerbations, hospital admissions, treatment burden, and improved lived experiences following initiation of therapy (4-6).

Despite these advances, access to CFTRm remains one of the greatest challenges facing people living with CF in South Africa. High medicine prices, patent protection, limited reimbursement, and regulatory barriers have restricted access to this life-changing therapy, creating significant inequities in treatment. Before the originator product became available in South Africa in 2024, many patients who could afford treatment travelled internationally to obtain generic ETI at their own expense, highlighting profound disparities in access. Access to CFTR modulator therapy has expanded in South Africa, with approximately half of eligible patients, primarily those with comprehensive private medical insurance, now receiving treatment. Nevertheless, the rest cannot access these therapies, particularly patients reliant on the public healthcare sector, where routine access remains unavailable.

2.3 Building the case for equitable access

Policy question: Could wider access to CFTR modulator therapy reduce the long-term cost of CF care in South Africa?

Although the clinical effectiveness of ETI is well established, important questions remain about its long-term impact on healthcare utilisation and overall cost of care. Due to the limited access to this therapy in South Africa, the management of CF relies on lifelong symptomatic treatment, often requiring multiple daily therapies such as inhaled hypertonic saline, recombinant human deoxyribonuclease (rhDNase), bronchodilators, inhaled and oral corticosteroids, antibiotics, proton pump inhibitors, nutritional support, oxygen therapy, non-invasive ventilation, and,

where clinically indicated, surgical interventions such as gastrostomy. While these interventions improve survival and disease management, they contribute to a substantial lifelong treatment burden and ongoing healthcare expenditure.

From a health economics perspective, a key unanswered question is whether the high acquisition cost of CFTRm therapy may be partially offset by reduced use of these chronic therapies and other healthcare resources. Improved disease control could reduce hospital admissions, use of supportive medications, outpatient consultations, and other costly healthcare services, while improving patients' quality of life and reducing treatment burden. However, evidence on these potential downstream benefits remains limited in South Africa.

3. Generating the evidence

3.1 Building the evidence through collaboration

Generating real-world evidence for rare diseases requires close collaboration between patient advocacy organisations, clinicians, researchers, and data partners. Breathtaking Fundraising NPC identified the need, and a multidisciplinary partnership was formed. The partnership combined expertise in clinical care, health economics, epidemiology, patient advocacy, and data analytics to evaluate the impact of ETI from both the healthcare system and patient perspectives. After conceptualising the study, the team developed a detailed research protocol defining the study design, data sources, health economic and statistical analyses, qualitative approach, data management, and ethical considerations. The protocol was reviewed, and the UCT Human Research Ethics Committee (HREC ref. 941/2025) approved it before data access and analysis commenced.

Table 1. Project partners and contributions

Partner	Role in the Study
Breathtaking Fundraising NPC	Convened the multidisciplinary team, provided strategic oversight, patient advocacy, stakeholder engagement, report design and formatting, and study access to the CF patient registry.
Division of Health Economics, University of Cape Town (UCT)	Project coordination and study design, health economics analysis, interpretation of findings, and drafting the project blog, report and journal manuscript.
Quantium Health	Analytical partner responsible for providing secure access to de-identified health claims data and supporting data extraction and analysis.
Clinical Collaborators	Provided clinical expertise on cystic fibrosis management, interpretation of findings, and contextualisation of the results for South African practice.

3.2 Purpose and scope

To generate locally relevant evidence to support advocacy and policy discussions on equitable access to highly effective therapies for people living with CF.

Recognising that healthcare decisions require evidence beyond clinical trial efficacy, the study combined quantitative health economics analysis with qualitative patient-reported experiences to provide a comprehensive assessment of the value of CFTR modulator therapy within the South African context. By integrating healthcare utilisation, direct medical costs, and lived experiences, the study provides a more holistic understanding of how these therapies influence both health outcomes and health system resource use.

The study addressed two key objectives in line with our purpose:

Quantitative

To evaluate changes in healthcare utilisation and direct medical costs before and after initiation of CFTR modulator therapy from the perspective of a South African private healthcare funder.

Qualitative

To explore the experiences of patients and caregivers following treatment initiation, including perceived changes in health, treatment burden, and quality of life.

3.3 Our approach

The quantitative component employed a before-and-after cost analysis, comparing healthcare utilisation and direct medical costs during the six months before and six months after CFTRm treatment initiation among 184 eligible patients receiving CFTRm therapy. Healthcare utilisation included hospital admissions, emergency department visits, ICU admissions, specialist consultations, medication utilisation, and overall healthcare expenditure. All expenditure figures are presented in South African rand (ZAR). The qualitative component involved a thematic exploration of 24 patients'/caregivers' perceptions of overall health status after initiating a CFTRm, focusing on changes in respiratory health, daily functioning, treatment burden, and overall quality of life. A single researcher coded de-identified patient and caregiver narratives in Microsoft Excel using an inductive qualitative content analysis approach. The researcher developed descriptive codes from the responses and grouped them into emergent themes rather than specifying them in advance. No formal inter-rater assessment was conducted; however, the coding framework and emerging themes were reviewed and refined in consultation with another member of the research team.

Combining both approaches allowed the research team to evaluate not only whether healthcare utilisation changed following treatment, but also how those changes translated into meaningful improvements in the lives of people living with cystic fibrosis.

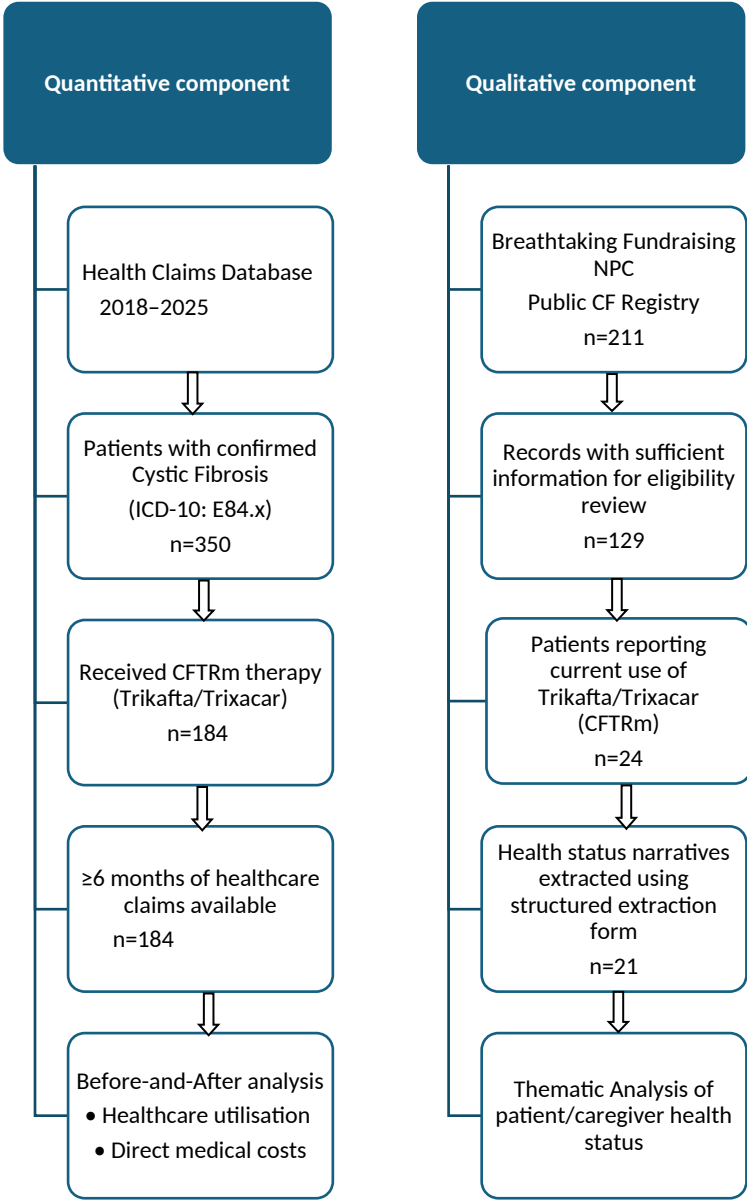
3.4 The data behind the findings

Identifying an appropriate data source on healthcare utilisation and costs was a major challenge. This challenge was further compounded by the unavailability of CFTRm therapy in the South African public healthcare sector. As a result, our options were limited to private insurers. After establishing the necessary partnership and data-sharing agreements, the study's quantitative analysis formally began with a project kick-off meeting in April 2026, which included the research team and our data analytics partner.

The quantitative analysis used de-identified health claims and reimbursement data from a major South African private insurer that represents a notable share of the country's private medical scheme market. This data provides detailed information on healthcare utilisation, including hospital admissions, medication utilisation, ICU services, specialist consultations, emergency care, pathology, radiology, and associated healthcare costs. To complement the quantitative findings, we obtained patient-reported narratives from the Breathtaking Fundraising NPC Public Cystic Fibrosis Registry. This registry captures the lived experiences of people with cystic fibrosis and their caregivers, providing valuable insights into the broader impact of

CFTRm therapy that healthcare data do not routinely capture. A thematic analysis of de-identified responses explored perceived changes after initiating ETIs (Trikafta or Trixacar). Integrating these patient perspectives with healthcare claims data enabled the study to assess not only changes in healthcare utilisation and costs but also whether these translated into meaningful improvements in patients' everyday lives.

Figure 1: Inclusion and eligibility criteria



4. The economic story: what changed after CFTRm therapy initiation?

Average healthcare costs decreased by R75,130 per patient over six months, representing a 35.3% reduction compared with the six months before treatment initiation ($p < 0.001$), excluding the cost of Trikafta.

The findings tell an important economic story. Introducing Trikafta substantially increased total healthcare expenditure due to the medicine's high cost. However, once the cost of Trikafta itself was excluded, expenditure on other healthcare post-CFTRm therapy fell significantly. This reduction was due to fewer antibiotic claims, hospitalisations, emergency department visits, procedures and selected specialist services.

4.1 Notable reduction in downstream healthcare costs

When the cost of Trikafta was included, average total healthcare claims increased substantially, from approximately R212,919 per patient before treatment to R1.23 million after treatment. This increase was expected given the high cost of CFTRm therapy and should not, in isolation, be interpreted as evidence of increased disease-related healthcare utilisation. A different picture emerged when Trikafta expenditure was separated from other healthcare costs. Average healthcare costs decreased from R212,919 to R137,789 per patient during the six months after treatment initiation, a 35% reduction of approximately R75,130 per patient. This reduction was statistically significant ($p < 0.001$).

Table 2. Healthcare expenditure before and after Trikafta initiation

Cost per patient (ZAR)	6 months before	6 months after	Change per patient	Change (%)
Total amount claimed including Trikafta	212,919	1,231,125	1,018,205	+478.2%
Total amount claimed excluding Trikafta	212,919	137,789	-75,130	-35.3%
Total amount paid including Trikafta	200,003	339,514	139,512	+69.8%
Total amount paid excluding Trikafta	200,003	127,817	-72,186	-36.1%

Paired two-sample t-test; $n = 184$. All four before-and-after differences were statistically significant (two-tailed $p < 0.001$).

The cost of Trikafta remains the central affordability challenge, but this alone does not capture its full health-system impact. South Africa's CF population is small relative to the prevalence of the major conditions that constitute the country's quadruple burden of disease. Therefore, the relevant policy question is not simply whether Trikafta is expensive, but what value could be generated from treating a small eligible population and how that treatment should be financed. Our findings show a 35.3% reduction in healthcare expenditure (R75,130 per patient) within six months, excluding the cost of Trikafta. These reductions have an important opportunity cost dimension, as eliminating no longer required services can free up scarce health system capacity

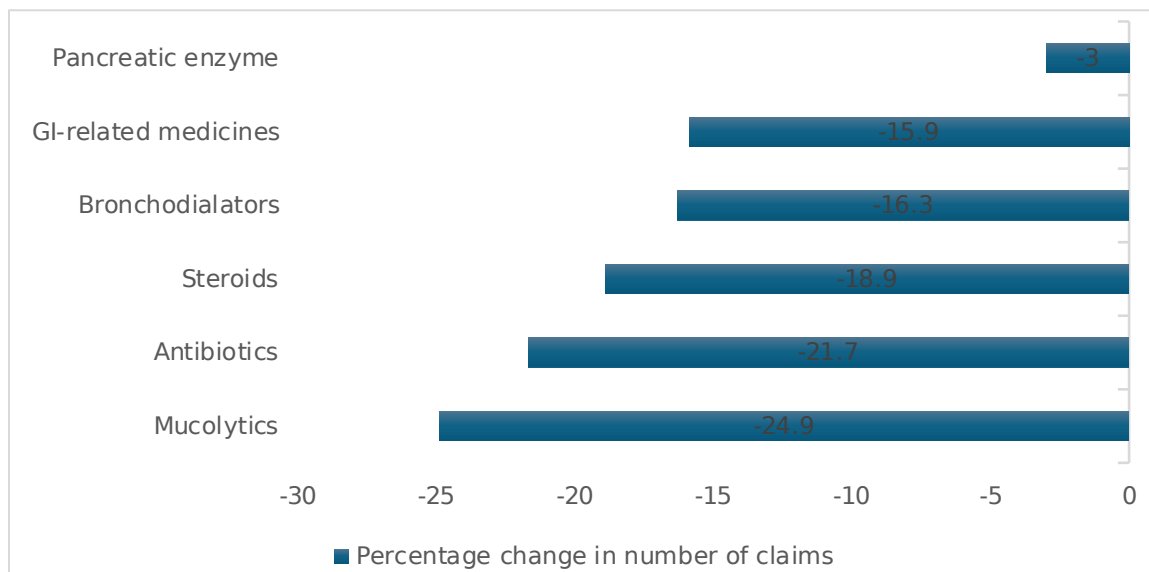
for other patients. Although the current analysis cannot demonstrate that downstream savings will ultimately offset the acquisition cost of Trikafta, the six-month follow-up period may not capture its full economic impact. Healthcare utilisation shortly after treatment initiation may remain influenced by complications and care needs established before ETI initiation; therefore, longer-term reductions in costs and resource use may be underestimated. These findings strengthen the case for longer-term evaluation alongside mechanisms to improve affordability.

In a resource-constrained health system, the policy challenge is therefore to find a price and financing mechanism that enables the substantial health benefits of CFTRm therapy to be realised without displacing higher-value care elsewhere in the health system.

4.2 Reduced reliance on antibiotics and other supportive medicines

Changes in medication use provide an important indication of whether CFTRm therapy altered the ongoing management burden of CF. Across the cohort, antibiotic claims decreased from 1,182 in the six months before treatment to 925 after treatment, a 21.7% reduction. The mean number of antibiotic courses per patient fell from 6.4 to 5.0, representing approximately 1.4 fewer courses over six months ($p < 0.001$). This was accompanied by a reduction in total antibiotic expenditure from approximately R4.72 million to R3.30 million, representing a saving of approximately R1.42 million (30.0%). The reduction extended beyond antibiotics: overall medication claims decreased by approximately 13.6%, with fewer claims for mucolytics, steroids, bronchodilators, gastrointestinal medications, and pancreatic enzyme replacement therapy. Notably, expenditure on mucolytics fell by approximately R1.02 million (19.3%), while bronchodilator and steroid expenditure declined by approximately R61,823 (14.7%) and R46,982 (30.9%), respectively. Reduced use of supportive medicines contributes to the broader downstream healthcare savings observed after CFTRm initiation.

Figure 2. Changes in medication utilisation (claims) 6 months post CFTRm therapy initiation



Changes are descriptive except for antibiotics ($P < 0.001$)

For people living with CF, treatment burden extends well beyond the cost of a single medication. The observed reductions suggest that CFTRm therapy may reduce the need for supportive medications used to manage the disease. Reduced use of antibiotics, mucolytics, bronchodilators and steroids will lower overall healthcare expenditure and ease the substantial daily treatment burden of patients and families. Reduced antibiotic use also has important implications for antimicrobial resistance.

4.3 Hospital, emergency, procedure, specialist and ICU use²

Hospital care represents an important component of both the clinical and economic burden of CF management. During the six months before CFTRm treatment, the cohort recorded 103 hospitalisations involving 78 patients. In the six months following initiation, this decreased to 81 hospitalisations involving 59 patients. This represented a 21.4% reduction in total hospitalisations and a 24.4% reduction in patients requiring hospital admission. Overall, total hospital days decreased from 714 to 493, representing 221 fewer inpatient days over six months. Consequently, total cohort hospital costs decreased from approximately R4.97 million before treatment to R3.02 million after treatment, representing approximately R1.95 million saved from hospital expenditure.

Avoided hospital care is particularly important when considering the broader value of CFTRm. Fewer admissions and inpatient days free up hospital capacity while reducing both the direct and indirect cost burden associated with acute CF care.

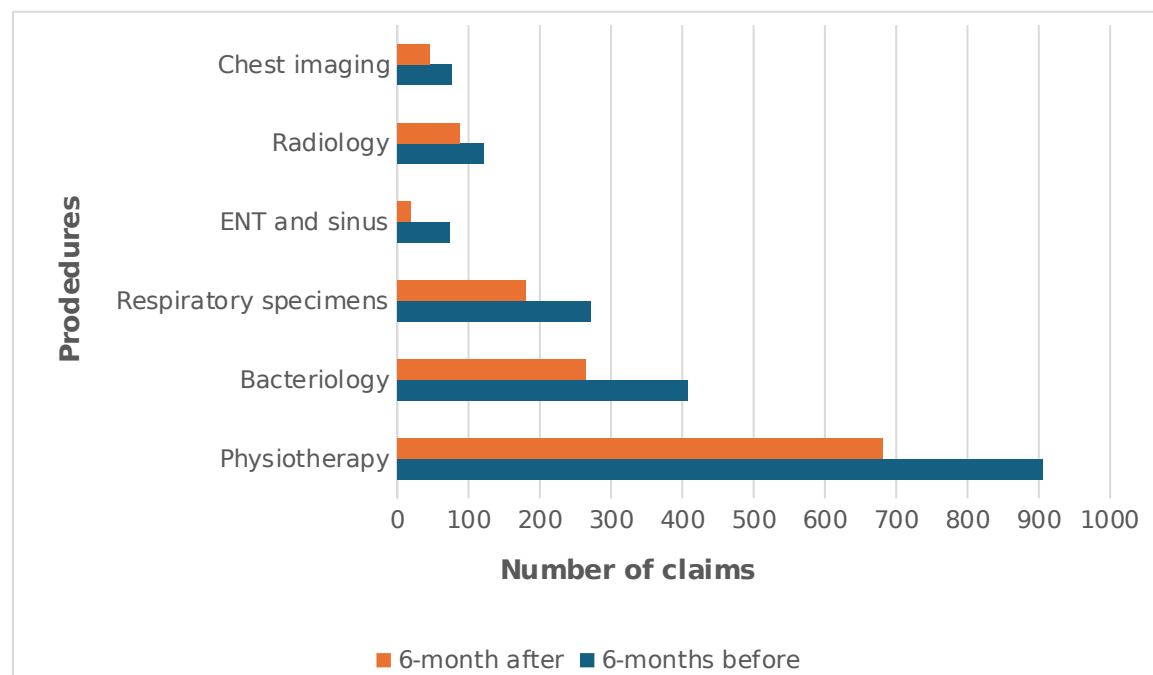
² These findings are interpreted as evidence of an observed change in utilisation and not a confirmed treatment effect.

The same pattern was also evident in emergency department utilisation. Total emergency department visits declined from 52 before treatment to 35 after treatment, a 32.7% reduction, and the number of patients accessing emergency care decreased by 42%. Total cost for emergency department care decreased from R238,376 to R32,854, representing an 86.2% reduction.

Emergency visits represent episodes of unplanned care and may signal periods of treatment instability. The reduction observed after initiation of CFTRm treatment adds to the broader pattern of decreased acute healthcare utilisation. If sustained over time, reductions in emergency and inpatient care could constitute an important component of the downstream economic value associated with effective CF disease management.

Across the cohort, the total number of procedures performed declined by approximately 11% during the six months following Trikafta initiation. This is consistent with the broader pattern of reduced use of downstream healthcare services observed across medications, hospitalisations and emergency care.

Figure 3. Changes in utilisation of procedures six months before and six months after CFTR modulator therapy initiation

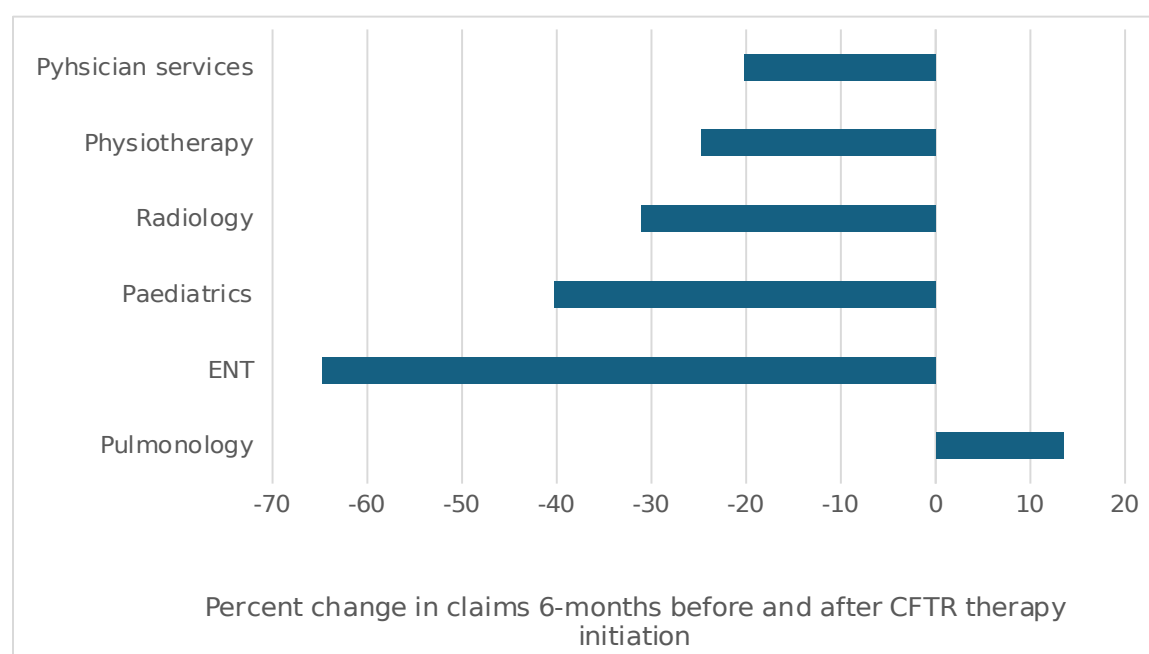


Lower expenditure on health professional services was also observed in the six-month post-treatment period. Across all professional services assessed, total cohort cost declined by approximately R2.87 million. The total number of claims for these services also decreased by 498 claims. Ear, nose and throat (ENT)-related claims fell from approximately R696,000 before treatment to R112,000 after treatment, while physician service costs decreased from approximately R1.83 million to R563,000. Expenditure on radiologists declined from approximately R1.22 million to R601,000; on paediatric services, from R1.58 million to R896,000; and on physiotherapy, from R1.40 million to R1.03 million. Not all services

declined. Some categories, including general practitioner, pulmonology, dietetic, biokinetics and occupational therapy services, showed increases in utilisation and cost. The increased use of pulmonology services after ETI initiation may reflect the lung-function monitoring required to assess treatment response, rather than worsening health. These suggest that CFTRm therapy may reshape rather than uniformly reduce healthcare use, potentially shifting care away from most intensive services while maintaining other forms of routine care.

ICU utilisation was low in both periods and admissions were unchanged, with three ICU admissions recorded in both the six months before and after CFTR modulator initiation. Total ICU days increased slightly from 7 to 8 days, while average ICU stay increased from 2.3 to 2.7 days. Despite this, total ICU costs decreased from R299,234 to R200,133, a 33.1% reduction, while the average cost per ICU admission fell from approximately R99,745 to R66,711.

Figure 4. Percentage change in professional services utilisation during the six months after CFTRm therapy initiation compared with the six months before treatment.



Negative values indicate reduced utilisation; positive values indicate increased utilisation. Changes are descriptive before-and-after comparisons.

4.4 From economic evidence to equitable access

The quantitative before-and-after analysis does not establish that healthcare savings offset the full cost of CFTR modulator therapy; rather, it demonstrates a possible association between treatment initiation and reductions in healthcare expenditure and service utilisation during the subsequent six months.

Excluding Trikafta, average healthcare expenditure fell from R212,919 to R137,789 per patient, a 35.3% reduction (R75,130; $p < 0.001$). Antibiotic use also declined significantly, while descriptive analyses showed fewer hospitalisations, hospital days, emergency visits, procedures and use of several specialist services. Although not every outcome reached

statistical significance, the consistency of these changes suggests that effective CFTRm therapy may reduce reliance on resource-intensive downstream care. These findings are relevant to equitable access, as CFTRm therapy is not routinely available to eligible patients in South Africa's public sector; the benefits observed in this privately insured cohort remain largely inaccessible to patients whose treatment depends on public financing. Expanding access could generate benefits beyond individual patients: avoided hospital days, emergency care, procedures, and specialist services represent opportunity costs because scarce health-system capacity freed from CF care can be used to treat other patients. However, these potential benefits must be weighed against competing priorities within South Africa's resource-constrained health system.

The principal barrier remains the cost of CFTR therapy, in our case, Trikafta. The cost of Trikafta substantially increased overall expenditure despite reductions elsewhere in the care pathway. The findings therefore do not demonstrate that six-month downstream savings offset the cost of Trikafta, nor should they be interpreted as establishing cost-effectiveness. For public-sector adoption, reimbursement would likely require substantial price reductions, along with mechanisms such as confidential price negotiation, risk-sharing and pooled procurement. Importantly, the international market for CFTR modulator therapy is beginning to change. Recent peer-reviewed evidence from Argentina (7) indicates that generic ETIs can produce clinical improvements comparable to those of the originator product (Trikafta). One such newly developed generic is Triko, a lower-cost generic ETI manufactured in Bangladesh, reported in 2026 to be available at substantially lower prices than the originator therapy (8, 9). The emergence of such lower-cost generic alternatives creates an opportunity to explore their clinical, regulatory and economic suitability within the South African context. Evaluating these alternatives, alongside appropriate pricing, procurement and reimbursement mechanisms, could help bridge the current access gap, providing a potential path towards more equitable CFTRm therapy.

5. Beyond healthcare costs: the patient and caregiver experience³

The qualitative analysis included twenty-four de-identified records from patients or their caregivers who reported using Trixacar or Trikafta. Twenty-three respondents reported having medical aid, while one did not. CFTR modulator treatment duration varied across these patients. Eighteen respondents (75.0%) reported using Trixacar or Trikafta for at least 6 months. The remaining records represented more recent treatment initiation, ranging from 1 to 8 weeks (approximately 54 days). Of these, two records contained no narrative health information, while one record contained an unclear response that could not be meaningfully interpreted and was treated as missing data. We reviewed 21 narrative descriptions of the CF patient's current health status or relevant clinical history, provided by the patients themselves or their caregivers, to identify recurring themes in health changes following treatment initiation. Each narrative contained at least one explicitly coded theme, and themes were not mutually exclusive.

Table 3. Themes identified from narratives on health following Trixacar/Trikafta use

Theme	Description	Records (n)	Frequency (%)
Improved overall health	General descriptions of better health or wellbeing after treatment initiation, such as “much improved”, “doing well” or “a big improvement”	9	42.9%
Improved lung function	Explicitly reported improvements in lung-function measurements or respiratory health	4	19.0%
Reduced hospitalisation	Reported reduction in the frequency of hospital admissions after treatment initiation	1	4.8%
Improved sweat-test results	Reported reduction in sweat chloride following treatment initiation	1	4.8%
Ongoing health challenges	Descriptions of persistent or severe illness, including poor health, oxygen use, recent intensive care admission or declining health	4	19.0%
Other/contextual responses	Information on treatment initiation or duration, clinical history, comorbidities, baseline lung function, reduced dosing or access difficulties, without an explicit description of improvement or deterioration	7	33.3%

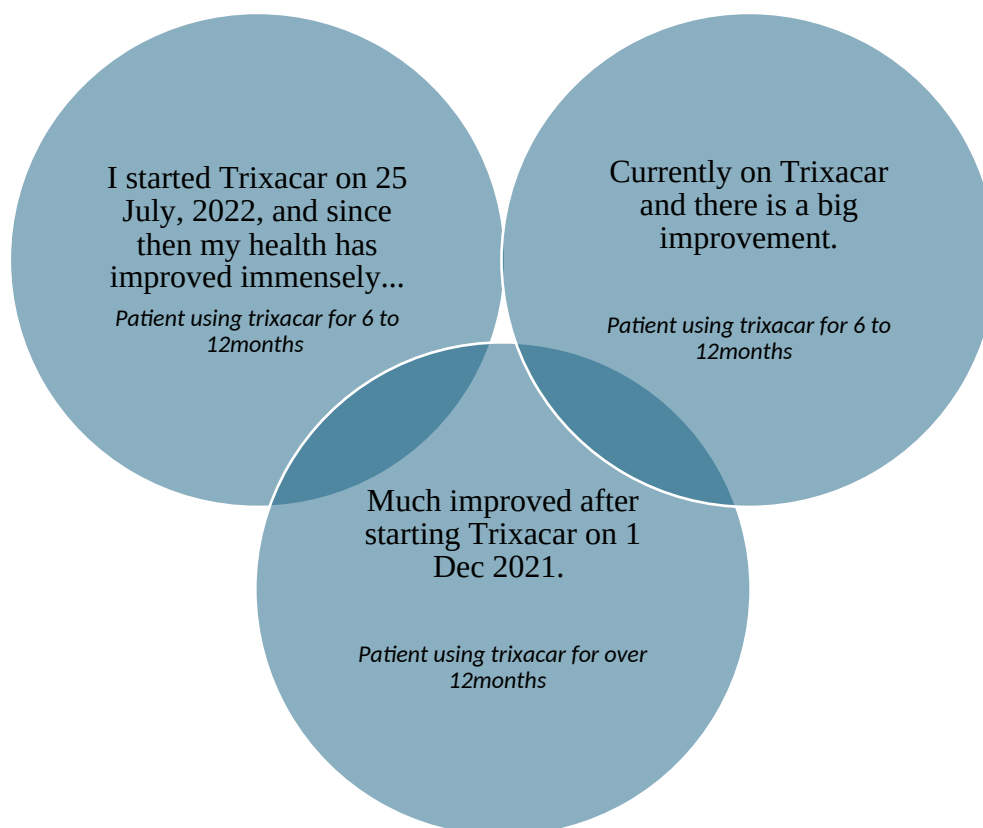
Themes were not mutually exclusive; therefore, one narrative could contribute to more than one theme and percentages do not sum to 100%.

³ Findings reflect changes explicitly reported in narratives collected at varying stages of treatment, with some providing limited before-and-after information; therefore, they represent reported experiences and cannot establish causality.

5.1 Improved overall health

Improved overall health was the most frequently identified theme, appearing in over 40% of the analysed narratives. Patients or caregivers used expressions such as “*much improved*”, “*doing well*”, “*good*”, “*healthy*” and “*a big improvement*” to describe health after starting CFTRm therapy. These suggest that patients perceived the effects of treatment as extending beyond a single clinical outcome. The descriptions point towards broader improvements in general wellbeing and day-to-day health. For people living with cystic fibrosis, such changes may reflect fewer respiratory symptoms, improved energy, greater physical functioning, reduced treatment burden, and an improved ability to participate in normal daily activities.

Figure 5. Illustrative narratives of perceived treatment-related health improvement



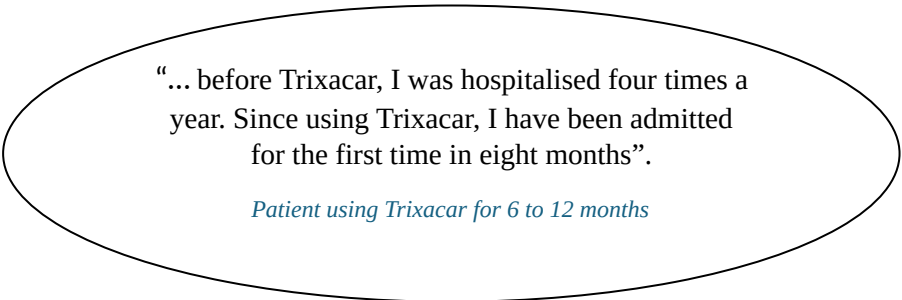
This theme's prominence matters for policy. Treatment effectiveness is often assessed using measures of clinical outcomes alone. Although these outcomes remain essential, these findings indicate that the value of CFTRm treatment may also be experienced through broader improvements that matter to CF patients and their households.

5.2 Improved lung function and sweat test results

Improved lung function was identified in 4 individual narratives, representing 19% of the analysed records. Some narratives included specific lung function values; one patient reported

that lung function “...increased from 31% to 57% after starting Trixacar”. Another narrative described “...an improvement from values in the 80% range to 106% and 90 to 23 for lung function and sweat test, respectively, after starting Trikafta”. A further record “...attributed a current lung-function value of 65% to CFTR modulator therapy”. These findings are consistent with the expected clinical effect of highly effective CFTRm therapy, which targets the underlying defect responsible for cystic fibrosis rather than only managing its downstream symptoms. Improvements in lung function may translate into fewer respiratory exacerbations and a reduced need for intensive supportive care. However, the lung function and sweat test values stated above were self-reported. Information on the measurement date, testing method, baseline clinical condition, and duration of treatment before the test was unknown.

5.3 Reduced hospitalisation



“... before Trixacar, I was hospitalised four times a year. Since using Trixacar, I have been admitted for the first time in eight months”.

Patient using Trixacar for 6 to 12 months

Although this finding was based on a single narrative, it illustrates the potential effect of CFTR modulator therapy on the frequency of inpatient care. For patients and families, avoiding a hospital admission may reduce disruption to schooling, employment, caregiving and family life. For the health system, fewer days spent in hospital may represent improved productivity and reduce hospitalisation expenditure.

This finding is consistent with quantitative analyses showing reductions in hospital admissions, hospital days, and hospital-related expenditure following initiation of Trikafta. The two sources of evidence are not equivalent, but their convergence strengthens the evidence that CFTRm use may reduce acute healthcare needs for some CF patients.

5.4 Ongoing health challenges

Four coded narratives indicated ongoing or severe health challenges, including descriptions such as “sick”, “not good”, being on oxygen following a recent intensive care admission, and experiencing declining health alongside bronchiectasis. These accounts demonstrate that experiences were not uniformly positive and that disease burden persisted for some individuals despite reported use of CFTRm. Although the underlying causes of the self-reported health challenges were not established, they may reflect advanced CF, delayed treatment initiation, or interruptions in access to CFTR modulator therapy.

5.5 Improved health but fragile access

The reported health experiences were accompanied by evidence that access to treatment remained financially and logistically fragile. Several narratives described taking reduced or alternate-day doses to extend the duration of their available medication. For example, *one*

narrative reported taking Trixacar every other day, while another reported using a reduced dose of donated Trikafta. These accounts suggest that some patients may modify prescribed treatment schedules because they cannot reliably secure the next supply. This highlights an important distinction between having access at one point in time and having reliable, continuous access. Even among a sample in which almost all CF patients had medical aid, narratives still signified substantial out-of-pocket costs. Medical-aid membership should consequently not be treated as a sufficient indicator of financial protection or effective access to CFTRm therapy. This finding strengthens the case for advocating for equitable access to CFTRm for all eligible people living with cystic fibrosis in South Africa. If families with medical-aid coverage experience considerable financial difficulty maintaining treatment, these barriers are likely to be even greater for patients and families who rely solely on the resource-constrained public health system. Equitable access policies are therefore essential to prevent treatment availability from being determined by insurance status, household income, fundraising capacity or access to international medicine-collection networks.

6. Final note

6.1 Putting the findings together

The quantitative and qualitative findings provide complementary perspectives on the real-world value of CFTR modulator therapy. The before-and-after analysis shows how healthcare costs and resource use changed after initiating Trikafta, while the thematic exploration illustrates how people living with cystic fibrosis and their caregivers perceive these changes. Key quantitative findings show that, excluding the cost of CFTRm therapy (Trikafta), mean healthcare expenditure decreased by approximately R75,000 per patient, hospitalisation costs decreased by 39%, and antibiotic courses decreased by 22%. These findings suggest that improved disease control may reduce the need for recurrent and resource-intensive care. The qualitative findings provide context for these reductions. The self-reported narratives described improvements in overall health and lung function, fewer hospitalisations, and improved sweat-test results. These experiences are directionally consistent with the reductions observed in hospital care, antibiotic use and other healthcare services. Policy decisions should move beyond considering the price of Trikafta alone and assess treatment value across hospitalisations, antibiotic and medication use, quality of life, productivity and caregiver burden.

6.2 Limitations

While this report presents important real-world evidence on the health and economic impact of CFTR modulator therapy in South Africa, several limitations should be considered when interpreting the findings. The quantitative analysis was conducted from the perspective of a single private healthcare funder, capturing direct medical costs and healthcare utilisation reflected in reimbursed claims; consequently, the findings may not be generalisable to South Africa's public sector, and may not represent the experiences of people with CF covered by other medical schemes. Claims data provide limited clinical information on factors that could influence healthcare utilisation. The self-controlled before-and-after design, although it captures health utilisation and costs before and after CFTR modulator therapy, lacked an untreated comparator group, so the observed changes cannot be attributed solely to CFTR modulator therapy. In addition, if CFTR modulator therapy was initiated during periods of clinical instability or unusually high healthcare use, regression to the mean may partly explain the subsequent reductions observed, particularly without an untreated comparator group. Given the relatively recent introduction and uptake of CFTRm (Trikafta) in South Africa, the available follow-up period was limited; however, a longer observation period would have helped assess whether the observed reductions in healthcare utilisation and costs are sustained over time. The qualitative analysis was based on secondary, de-identified responses from the Breathtaking Fundraising NPC Public CF Registry rather than interviews conducted specifically for this study. Consequently, researchers could not probe responses, clarify statements, or explore emerging themes in greater depth. Convenience sampling and inclusion of patients with available information who were receiving Trixacar/Trikafta may introduce selection bias and may not represent the experiences of all people living with CF in South Africa, particularly those without access to CFTR modulators. Nevertheless, these patient and caregiver perspectives provide important complementary context for interpreting the healthcare utilisation and cost findings.

6.3 Moving forward

This report provides important South African real-world evidence on the health and economic impact of CFTR modulator therapy. In the six months following treatment initiation, healthcare expenditure excluding Trikafta decreased significantly, alongside significant reductions in antibiotic use and descriptive reductions in hospitalisations, hospital days, emergency care, procedures, and several specialist services. Patient and caregiver experiences complement this economic evidence, with reported improvements in overall health, lung function, hospitalisation and sweat-test results. While these findings do not demonstrate that downstream savings offset the acquisition cost of Trikafta or establish causality, they show that the value of CFTRm therapy extends beyond the medicine's price and should be considered across the full pathway of CF care.

Moving forward, the priority is to translate this evidence into affordable and equitable access, particularly for eligible patients currently reliant on the public health sector. Policy options should include negotiated pricing and reimbursement arrangements, exploration of lower-cost generic ETI alternatives, and structured monitoring of treatment outcomes and resource use. Continued data collection with longer follow-up will be essential to determine whether observed reductions in healthcare utilisation and costs are sustained. Future research should build on this study by conducting a full economic evaluation and budget impact analysis that incorporates longer-term costs, clinical outcomes, and patient-reported outcomes. Together, these approaches can help establish the price, financing and implementation conditions under which CFTR modulator therapy could be made both sustainable for the health system and accessible to all eligible South Africans living with CF.

7. References

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