MONASH
University

AUSTRALIAN CYSTIC FIBROSIS DATA REGISTRY

2023

ANNUAL REPORT

Data Extract Period

The data contained in this report was extracted from the ACFDR on 19 April 2024, and pertains to data related to patient events from 1 January to 31 December 2023. As the registry does not capture data in real time, there can be a lag between the occurrence of an event and its capture in the ACFDR.

Abbreviations

ACFDR	Australian Cystic Fibrosis Data Registry
BAL	Broncho Alveolar Lavage
BMI	Body Mass Index
CF	Cystic Fibrosis
CFA	Cystic Fibrosis Australia
CFRD	Cystic Fibrosis Related Diabetes
CFTR	Cystic Fibrosis Transmembrane Conductance Regulator
ETI	Elexacaftor/tezacaftor/ivacaftor
FEV	Forced Expiratory Volume
FEV1 pp	Percent predicted Forced Expiratory Volume (litres) in 1 second
GLI	Global Lung Initiative
IV	Intravenous
MRSA	Methicillin–resistant *Staphylococcus aureus*
NTM	Nontuberculous Mycobacteria
PBS	Pharmaceutical Benefits Scheme
pwCF	People with Cystic Fibrosis

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Susannah Ahern, Ahmad Reza Pourghaderi, Rasa Ruseckaite, Marisa Caruso, John Liman, Peter Wark, Andre Schultz and Jo Armstrong, on behalf of the ACFDR. The ACFDR Registry Annual Report, 2023. School of Public Health and Preventive Medicine, Monash University, July 2024, Report No 25.

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CYSTIC FIBROSIS Australia

MONASH University

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FROM THE CYSTIC FIBROSIS AUSTRALIA CEO

It is with great optimism that we present the 2023 Australian Cystic Fibrosis Data Registry (ACFDR) Annual Report. This year's report highlights the remarkable progress and inspiring outcomes achieved within the cystic fibrosis (CF) community, underscoring the collective efforts of healthcare professionals, researchers, patients, and their families.

The advancements in the treatment and management of CF are truly transformative. Most notably, we are witnessing increasingly improved outcomes for most individuals living with CF. Life expectancy continues to rise, and quality of life is enhancing significantly. This is a testament to the efficacy of new therapeutic interventions and the specialist care that patients are receiving today. It is heartening to observe that these medical breakthroughs are translating into tangible benefits for those living with CF.

A particularly encouraging trend in this year's data is once again the significantly reduced number of hospitalisations among CF patients. This decline not only reflects the better management of the disease but also points to a broader, systemic improvement in healthcare delivery and patient adherence to treatment regimens. Reduced hospital stays mean less disruption to daily life, allowing individuals with CF to lead more fulfilling and productive lives.

Another uplifting development is the increasing number of pregnancies among women with CF. This milestone signifies a profound shift in the outlook for people with CF, who are now more able to pursue life milestones previously considered unattainable. Congratulations to all of the new CF parents!

As we celebrate these achievements, we remain steadfast in our hope and determination that all individuals with CF will one day experience the full spectrum of benefits from the advancements we are beginning to see. The future holds great promise, and we are committed to ensuring that everyone has a full and healthy life. By continuing to support research, improving access to cutting-edge treatments, and fostering a robust, compassionate community, we can make this hope a reality.

My sincere thanks to everyone who has committed their support to the registry including the team at Monash University, the ACFDR Steering Committee Members, the team at Cystic Fibrosis Australia and those who have assisted with funding this critical work of the ACFDR.

Together, we look forward to a future where CF is no longer a limiting factor in the lives of those affected, but merely a part of their remarkable journey.

Dr Jo Armstrong
Chief Executive Officer,
Cystic Fibrosis Australia

CYSTIC FIBROSIS Australia

FROM THE MONASH UNIVERSITY ACFDR LEAD

On behalf of the team at the School of Public Health and Preventive Medicine that manages the Australian Cystic Fibrosis Data Registry, I am pleased to present the 2023 Annual Report. Comprising information regarding the characteristics and outcomes of people with CF from twenty-three CF centres across Australia, the latest data relates to 3,798 people with CF in Australia, an additional 68 from 2022.

While the continued improvement in the clinical parameters and outcomes for people with CF is of most importance from this report, the 2023 data also indicates changes in the monitoring and management of people with CF over time.

Complete genotype information is critical to people with CF as it relates to CFTR modulator eligibility and prescribing. In 2023, over 96% of people with CF in the database have two known CF alleles, compared with 88% just five years ago. Similarly, nearly 80% of people with CF currently in the registry have been on a CFTR modulator, compared with 50% only 4 years ago. Within the last few years we have seen changes in social information such that in 2023, 26% reported completing a university degree, which is higher than the national average.

While the use of telehealth post-COVID continues to decline, it remains a component of a mixed model of clinical care for approximately 40% of adults and 15% of children in 2023. While lung function continues to improve across all age groups, the number of lung function tests being undertaken has declined over the last few years. In 2023, adults had on average 2 lung function tests per annum, and children had less than 3 during the same period. These changes have implications for the methods and type of data collection the CF registry will use in the future.

In 2023 we have made some important and new changes to our reported data. The Annual Report has excluded lung transplant data (relating to 118 current people with CF in the registry) from its activity and outcome information. A new section has also been added relating to clinical variation among CF centres, where we explore variation in four measures across paediatric and adult settings.

I would like to thank the hard work of the ACFDR Steering Committee, the incredibly supportive leadership from the ACFDR Chair and Deputy Chair, Jo Armstrong and the helpful team from CFA, clinicians, researchers and all people with CF who have supported the registry. We are very proud of the incredible resource that is the data registry, and we hope you find the 2023 Annual Report relevant, meaningful and insightful reading.

Professor Susannah Ahern
Head, Clinical Outcomes data Reporting and Research,
School of Public Health and Preventive Medicine,
Monash University

FROM THE REGISTRY DEPUTY CLINICAL LEAD

The ACFDR continues to provide high quality data to track important trends in CF. The 2023 ACFDR Annual Report shows that outcomes for people with CF in Australia continue to improve. Hospital admission rates are decreasing and the need for lung transplantation is reducing too. CF modulator therapy has been a major contributor to improved outcomes, but the improvement is also part of the ongoing trend over decades related to almost constant refinements in CF care by a dedicated CF community that includes the people with CF and their families, clinicians, researchers, nongovernmental organisations (importantly CF Australia and state-based CF organisations), and others.

The data raises important questions at a time when many people with CF on modulator therapy are reconsidering their traditional regular treatments and routines: Is the documented drop-off in number of annual clinics visits a good thing? Perhaps the reduced number of clinic attendances just reflect better health. However, the prevalence of respiratory pathogens declined steeply since 2016 but between 2022 and 2023 the decline has been less marked, and even absent for some pathogens. Can we afford to relax now that most people with CF have access to modulator therapy? The answer is almost certainly “No”. In the current dynamic environment, now more than ever, the ACFDR will be essential for monitoring CF in Australia. To that end the 2023 report now also compares individual CF centres in terms of outcomes and aspects of care provided.

I would like to thank the members of the ACFDR Steering Committee and the team at Monash University for their expertise, hard work and patience, the ever-committed staff at CF centres, and the people with CF who are contributing their data to the registry.

Professor André Schultz
Deputy Clinical Lead,
Australian Cystic Fibrosis Data Registry,
Respiratory Physician Department
of Respiratory Medicine,
Child and Adolescent Health Service, Western Australia

FROM THE REGISTRY CLINICAL LEAD

The 2023 annual ACFDR report continues to provide timely and accurate data that reflects the impacts of living with CF and the outcomes experienced by Australians with CF. The report continues to deliver high quality data, captured from all CF centres and 3,798 Australians living with CF. The report continues to capture a rapid time of change for people with CF and the clinicians that care for them. This remains a story of remarkable success and improving outcomes. The number of people with CF recorded on the ACFDR continues to rise, as does the proportion who are older than 18 years. This reflects the overall improvements in health outcomes, with increasing survival continuing, and no increase in the number needing a lung transplant since 2020. In 2023 we saw another record year in pregnancies for women with CF at 88 reported and this is continuing to rise.

Lung function continues to improve across all age groups. Hospitalisations continue to decline, especially in children in the last 12 months. For the first time we now report that less than a third of people with CF are colonised with Pseudomonas Aeruginosa. The number of people with CF receiving modulators continues to increase and in 2023 the sharpest rise was in children, with Trikafta becoming available for children 6 and older. Modulators are now prescribed for 85% of adults and 66% of children 6 years and older. A remarkable achievement with most younger children having commenced in the last 12 months. For the first time we also provide a comparison of important outcomes; lung function, BMI and prescription of CFTR modulators, breaking this down by CF centre. An important objective of the registry is to ensure that everyone with CF receives a similar standard of care and enjoys similar outcomes. Many factors can contribute to variations in outcome, but these comparisons are important to track and to reflect upon.

Serious challenges remain. Sadly 18 people with CF lost their lives and with a median age of only 40 years, that is still too many and too soon. People with CF continue to experience serious chronic disease, despite improvements in many outcomes, with the proportion of people living and newly developing diabetes being unchanged.

The data for key outcomes now does not include people who have had a lung transplant. It is not a reflection on the importance of monitoring, however we have relatively few included in the registry and while they are counted in the numbers, outcomes such as lung function are not comparable to those who have not been transplanted. Further work needs to be done to better serve this important group in the CF community.

Once again, we hope you enjoy reading the report and reflect upon important changes that are occurring in the lives of people with CF in Australia.

Professor Peter Wark
Director of Cystic Fibrosis Service, Respiratory
and Sleep Physician, Alfred Health, Victoria,
Conjoint Professor of Medicine Monash University
School of Translational Medicine,
Adjunct Professor University of Newcastle,
Honorary Senior Staff Specialist Respiratory
and Sleep Medicine John Hunter Hospital,
New South Wales

SUMMARY OF REGISTRY DATA

	2019	2020	2021	2022	2023
PEOPLE WITH CYSTIC FIBROSIS					
Total people with CF in the ACFDR	3,446	3,538	3,616	3,738	3,798
Age (median)	19.6 years	20.2 years	20.6 years	21.1 years	21.7 years
Age (mean)	22.0 years	22.6 years	23.0 years	23.4 years	24.0 years
Adults (≥18 years) number (%);	1,854 (53.8%)	1,965 (55.5%)	2,019 (55.8%)	2,124 (56.8%)	2,212 (58.2%)
Adults: Males %	53.1%	52.8%	52.8%	56.8%	52.5%
CF DIAGNOSIS & GENOTYPING					
Newly diagnosed people with CF	66	74	92	90	68
% New diagnosis <1 year	85.0%	82.4%	82.6%	78.9%	77.9%
% New diagnosis ≥18 years	4.5%	10.8%	12.0%	11.1%	13.2%
Genotyped – one known allele (two alleles)	96.0% (88.0%)	98.4% (92.2%)	98.4% (94.8%)	99.1% (95.9%)	99.2% (96.3%)
% F508del Homozygous	47.0%	47.0%	47.0%	46.0%	46.0%
% F508del Heterozygous	42.0%	43.0%	43.0%	44.0%	44.0%
CLINICAL MEASURES (LUNG FUNCTION & NUTRITION)					
Median FEV1 pp children and adolescents 6 – 17 years	91.0	91.0	93.0	93.2	96.6
Median FEV1 pp adults 18 years and older	71.0	70.0	73.0	75.6	78.6
Median weight for length percentile <2 years	46th	51st	51st	50th	54th
Median BMI percentile children 2 – 17 years	55th	57th	58th	57th	60th
Median BMI adults 18 years and older	23.0	22.9	23.0	23.4	23.9
RESPIRATORY MICROBIOLOGY					
P.aeruginosa (%)	47.8%	41.6%	38.9%	32.7%	22.7%
S.aureus (%)	51.5%	47.1%	47.3%	43.6%	38.1%
Aspergillus spp (%)	22.9%	18.8%	17.5%	13.2%	8.3%
Non-tuberculous mycobacterium (%)	5.9%	6.4%	8.1%	4.2%	2.8%
COMPLICATIONS					
% with CF related Diabetes <12 years	N/A	1.9%	2.2%	2.2%	2.0%
% with CF related Diabetes 12 – 17 years	N/A	17.3%	14.2%	13.6%	11.8%
% with CF related Diabetes 18 – 29 years	N/A	21.5%	23.8%	26.0%	24.5%
% with CF related Diabetes 30+ years	N/A	30.0%	29.9%	29.6%	26.9%
MULTIDISCIPLINARY CARE					
% with Physiotherapy annual review	N/A	N/A	85.7%	83.9%	85.6%
% with Dietician annual review	N/A	N/A	74.7%	76.6%	77.5%
% with Mental Health annual review ≥12 years	N/A	N/A	80.6%	26.8%	23.6%
% with Social review	N/A	N/A	N/A	43.2%	46.2%
% with Gastroenterologist annual review	N/A	N/A	N/A	24.0%	23.8%
% with Endocrinologist annual review	N/A	N/A	N/A	19.5%	19.6%
CFTR MODULATORS					
% taking CFTR modulator – total cohort	37.7	52.6%	55.2%	68.7%	77.9%
% taking CFTR modulator – paediatric	N/A	N/A	N/A	55.6%	68.5%
% taking CFTR modulator – adult	N/A	N/A	N/A	78.7%	84.9%
LUNG TRANSPLANTS AND SURVIVAL					
Bilateral lung transplants	33	15	9	6	9
Deaths (Total CF deaths)	26	18	19	10	18
Median age of death	32.0 years	30.7 years	36.8 years	44.2 years	40.6 years (48.3 TPEX[1])
Survival median (cohort, 5 years)	54.0 years (2014 – 2018)	53.0 years (2015 – 2019)	56.9 years (2016 – 2020)	58.2 years (2017 – 2021)	60.6 years (2018 – 2022)

1. TPEX: The median age at death (excluding those who underwent lung transplantation) is 48.3 years

1.

COMBINED DATA

1. COMBINED DATA

1.1 OVERVIEW

Cystic fibrosis (CF) is a recessively inherited genetic condition, a multisystem disorder associated with reduced life expectancy, mostly due to respiratory failure. This report highlights the epidemiological and clinical characteristics of children and adults with CF that are captured in the Australian Cystic Fibrosis Data Registry (ACFDR), as of 31 December 2023.

The ACFDR collects data from pwCF from the time of their diagnosis and throughout their life, or until they have undergone a lung transplant, when many pwCF are discharged from CF-centre care. Most pwCF are cared for by specialist clinicians and teams in public hospital CF Centres. These centres may be associated with paediatric health services, adult health services or both. As per the 2022 Report, the ACFDR 2023 Report is structured in three sections in recognition that the experience of living with CF changes over time as do the treatments and outcomes. The sections are:

1. Combined data for both children and adolescents and adults with CF, particularly with trends over time.
2. Data on the diagnosis and management of children and adolescents with CF.
3. Data on the diagnosis and management of adults with CF.

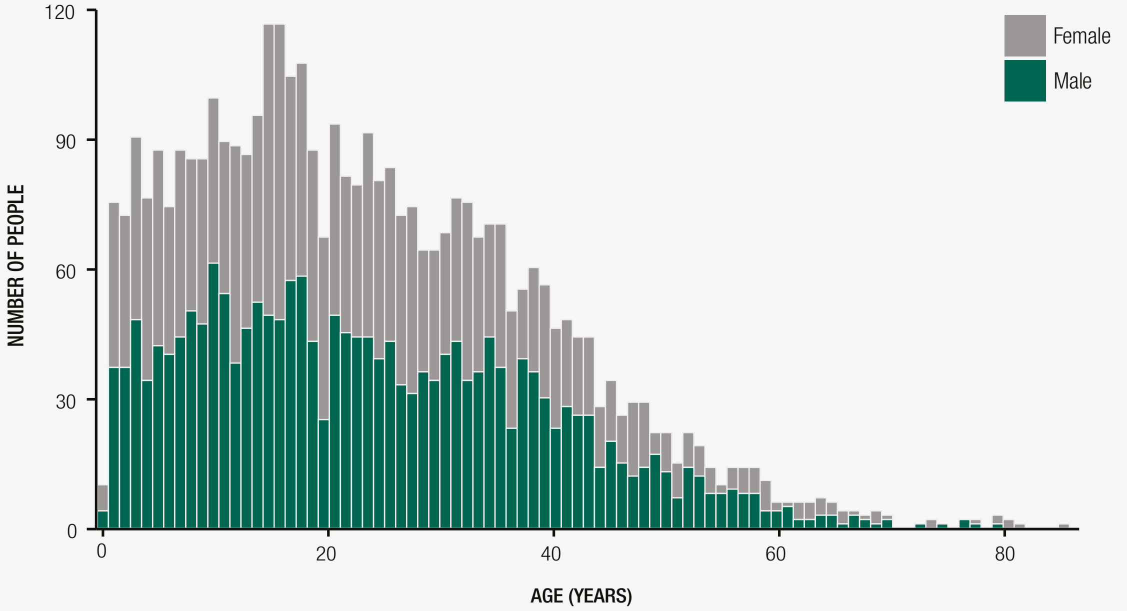
For the first time in the ACFDR Report, we are following international registry reporting practice to **only include data from lung transplant recipients in the following sections — Demographics, Diagnostic and Genotype Information.** This is so that information regarding clinical care and outcomes reflects the majority of pwCF who have **not** had a lung transplant. **Survival analyses will be presented in relation to pwCF with and without transplants separately.** As of 31 December 2023, there were **118 pwCF** (114 adults and 4 children/adolescents with CF) who underwent a lung transplant.

1.2 DEMOGRAPHICS

Age and Sex of People with CF in the Registry

As of 31 December, 2023, the ACFDR held records of **3,798 people with CF; 2,212 adults** (18+ years) and **1,586 children and adolescents** (0 – 17 years) (Figure 1.1).

FIGURE 1.1: ACFDR 2023: PEOPLE WITH CF IN AUSTRALIA BY AGE AND SEX



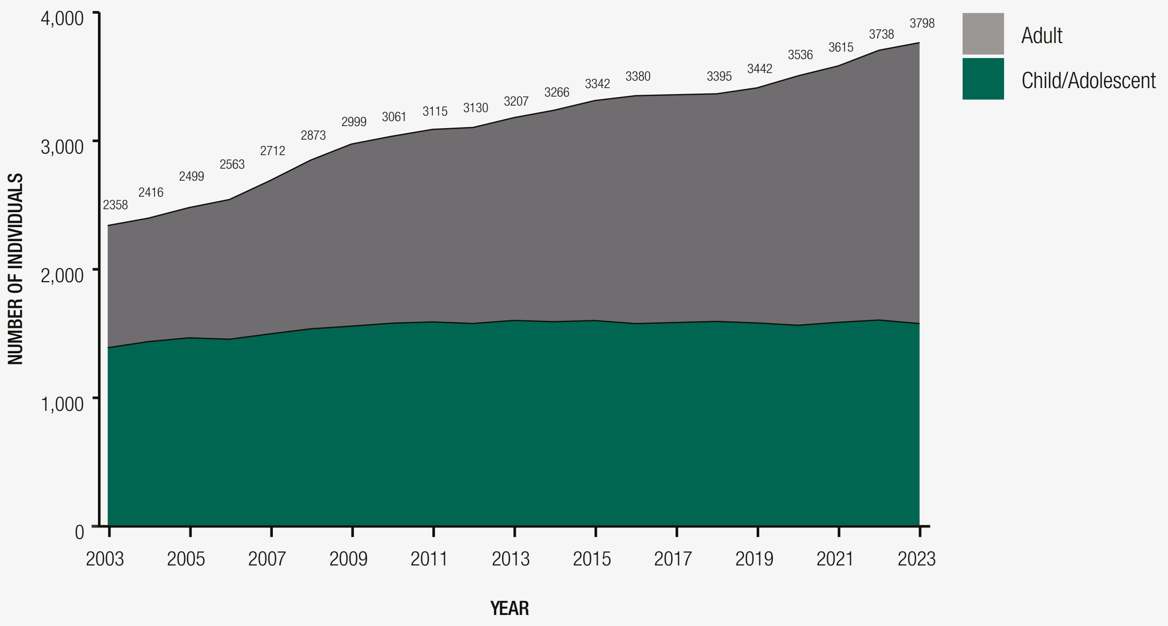
N = 3,798 people

As of 31 December 2023, the proportion of males in the ACFDR was 52.5% and females were 47.5%. The largest age grouping for pwCF is those aged 18 – 29 years which comprises 25.3% of pwCF, followed by pwCF aged 30 – 39 years (16.8%) and adolescents (16.4%) (Table 1.1).

TABLE 1.1: ACFDR 2023: PEOPLE WITH CF BY AGE AND SEX

Age	Female	Male	Total
<2	52.8% (67)	47.2% (60)	127
2 – 5	50.9% (164)	49.1% (158)	322
6 – 11	42.5% (219)	57.5% (296)	515
12 – 17	51.6% (321)	48.4% (301)	622
18 – 29	50.0% (480)	50.0% (480)	960
30 – 39	44.1% (281)	55.9% (356)	637
≥40	44.2% (272)	55.8% (343)	615
Total	47.5% (1,804)	52.5% (1,994)	3,798

FIGURE 1.2: ACFDR 2003 – 2023: PAEDIATRIC VS ADULTS PROPORTION



Note: Population size in 2017 was estimated based on the populations in years 2016 and 2018

The median age of pwCF continues to increase (Figure 1.2). In 2023, the proportion of the registry population who were adult was 58.2%, compared with 56.8% in 2022. In 2023, the median age of the CF population was 21.7 years, with a mean age of 24.0 years. The median age for males at 22.2 years (21.5 years in 2022) remained higher than that for females at 21 years in 2022 (20.5 years in 2022).

Geographical Distribution of People with CF in Australia

Figure 1.3 shows the number of pwCF who received clinical care within each jurisdiction in 2023, as well as the proportion of these who were children/adolescents and adults. New South Wales provided care to the most pwCF, followed by Queensland, Victoria, Western Australia, South Australia, Tasmania and the Australian Capital Territory.

FIGURE 1.3: ACFDR 2023: DISTRIBUTION BY STATE AND TERRITORY WHERE CARE WAS PROVIDED

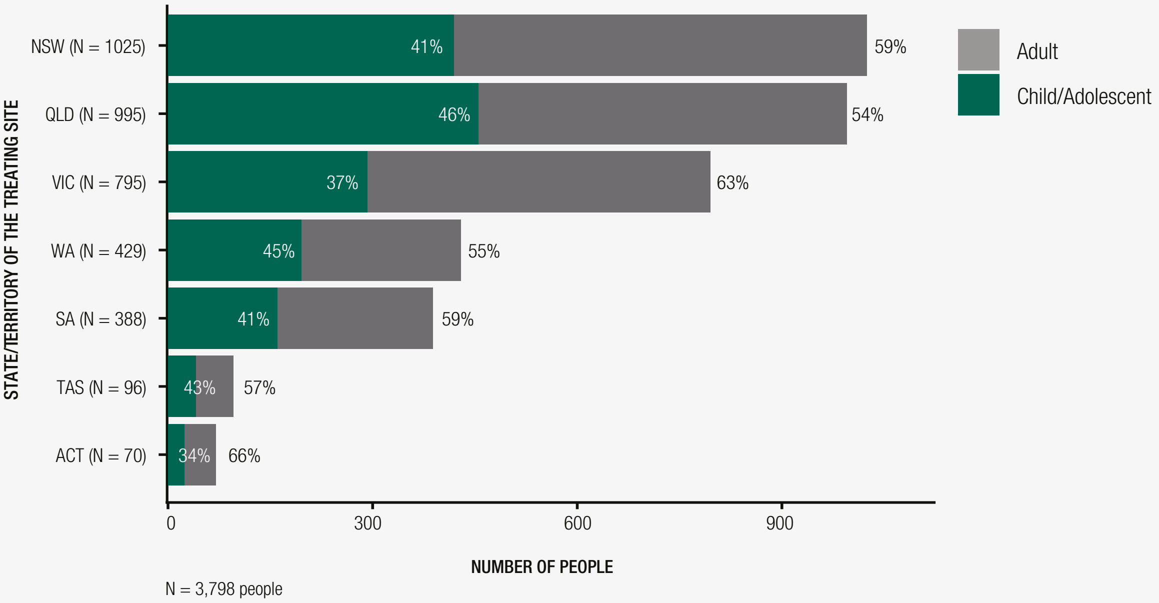


Figure 1.4 shows the jurisdictions where pwCF lived in 2023 (or the most recent prior year), derived from postcode information collected by the registry. New South Wales had the highest number and proportion (1,105/29.3% of residing pwCF), followed by Queensland (927/24.6%), Victoria (768/20.3%), Western Australia (431/11.4%), South Australia (393/9.9%), the Australian Capital Territory (58/1.5%) and the Northern Territory (16/0.4%). Twenty-three pwCF (0.6%) did not have their postcode reported. Table 1.1a shows the proportion of adult and paediatric pwCF residing in each jurisdiction.

FIGURE 1.4: ACFDR 2023: DISTRIBUTION BY PATIENT RESIDENCE

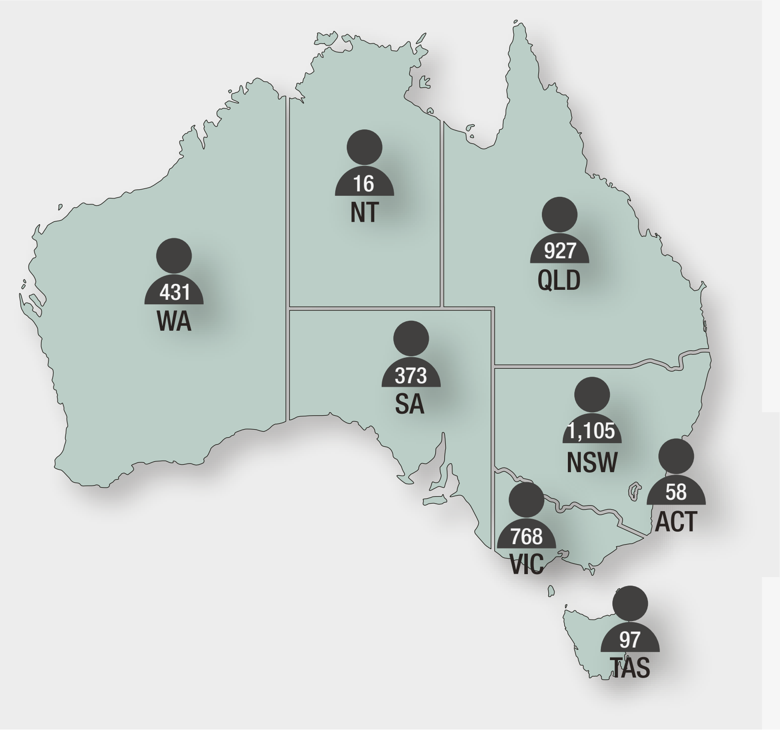


TABLE 1.1A: ACFDR 2023: DISTRIBUTION OF RESIDENTIAL JURISDICTIONS

Residential jurisdiction	Adult	Paediatric	Total
ACT	72.4%	27.6%	100.0% (58)
NSW	58.3%	41.7%	100.0% (1,105)
NT	37.5%	62.5%	100.0% (16)
QLD	54.6%	45.4%	100.0% (927)
SA	59.0%	41.0%	100.0% (373)
TAS	56.7%	43.3%	100.0% (97)
VIC	63.0%	37.0%	100.0% (768)
WA	55.0%	45.0%	100.0% (431)
Total	58.1% (2,194)	41.9% (1,581)	100.0% (3,775)

1.3 DIAGNOSTIC AND GENOTYPE INFORMATION

Diagnostic Information

New Diagnoses

The number of new diagnoses of pwCF notified to the registry in 2023 was **68,** including 53 people diagnosed at less than one year of age. New diagnoses in 2023 also included those aged 1 – 17 years (6 cases), and over 18 (9 cases). There were no new cases where the diagnosis date was unknown (Table 1.2).

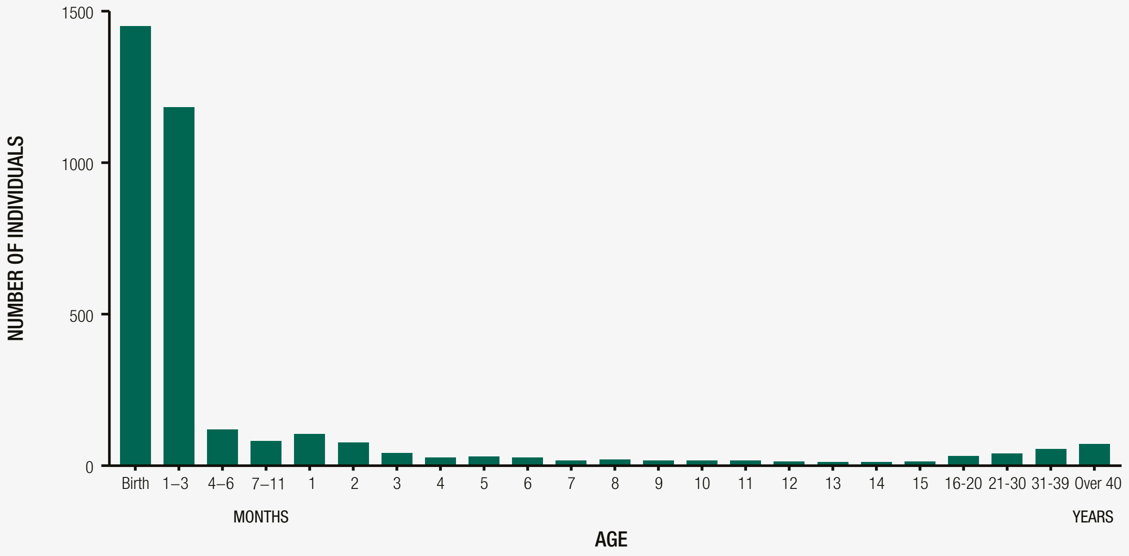
TABLE 1.2: ACFDR 2023: AGE OF NEW DIAGNOSES IN 2023

Age	N (%)
<1	53 (77.9%)
1 – 17	6 (8.8%)
18+	9 (13.2%)
Total	68

Age of Diagnosis for Registry Population

The age of CF diagnosis has been captured in the registry for 90.2% of the total registry cohort (Figure 1.5). Of these, 42.3% were diagnosed between birth and 1 month, 34.5% diagnosed between 1 – 3 months, and a further 5.7% between 4 – 11 months. A total of 82.5% were diagnosed within the first year of life, 5.1% of pwCF were diagnosed as adults, with 71.3% of adult diagnoses occurring at 30 years or older.

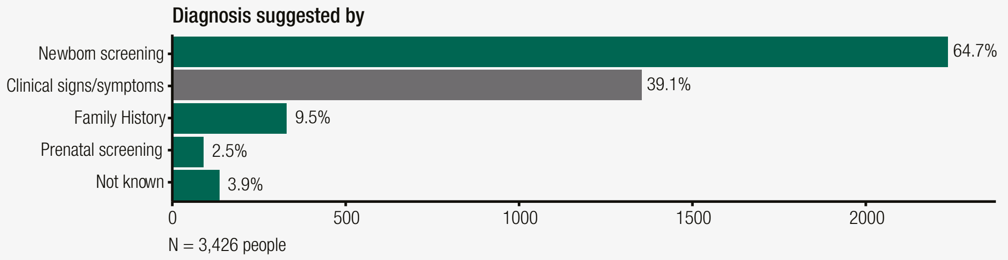
FIGURE 1.5: ACFDR 2023: AGE AT CF DIAGNOSIS

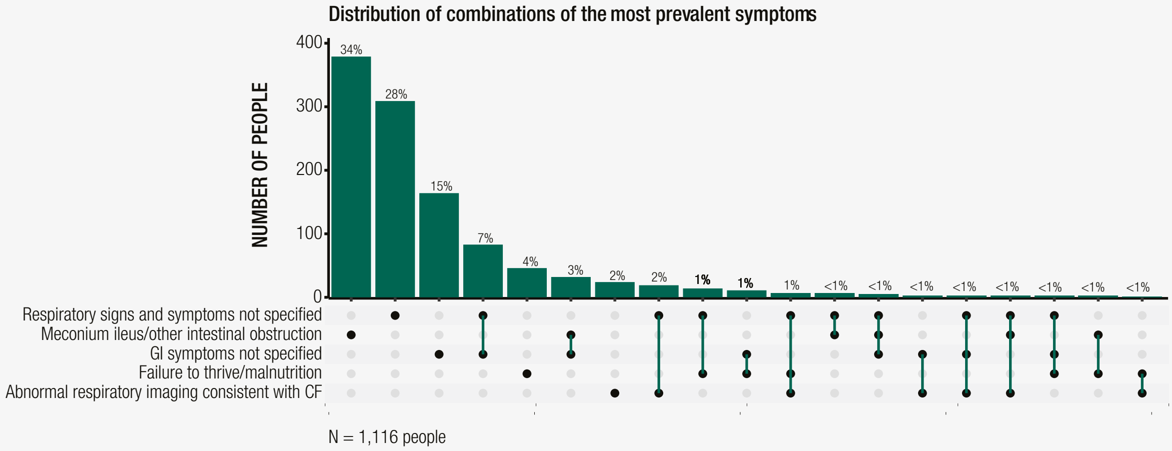


Factors Associated with the Diagnosis of CF

For the total cohort, a diagnosis of CF was confirmed or suggested by newborn screening (64.7%), clinical signs/symptoms (39.1%), family history (9.5%), and prenatal screening (2.5%) (Figure 1.6 and Table 1.3). Of those with clinical symptoms, the most common presentations were meconium ileus/intestinal obstruction (34.0%), respiratory signs and symptoms (28.0%), and gastrointestinal symptoms (15.0%). With multiple responses available, often there is an overlap in clinical symptoms and newborn screening or family history in the registry.

FIGURE 1.6: ACFDR 2023: FACTORS ASSOCIATED WITH DIAGNOSIS OF CF (WHOLE COHORT)





Over time, the proportion of new diagnoses made by newborn screening, prenatal screening, and family history has increased, while diagnoses via clinical symptoms have decreased (Table 1.3).

TABLE 1.3: ACFDR 1998 – 2023: FACTORS ASSOCIATED WITH DIAGNOSIS OF CF (2023 VS WHOLE COHORT)

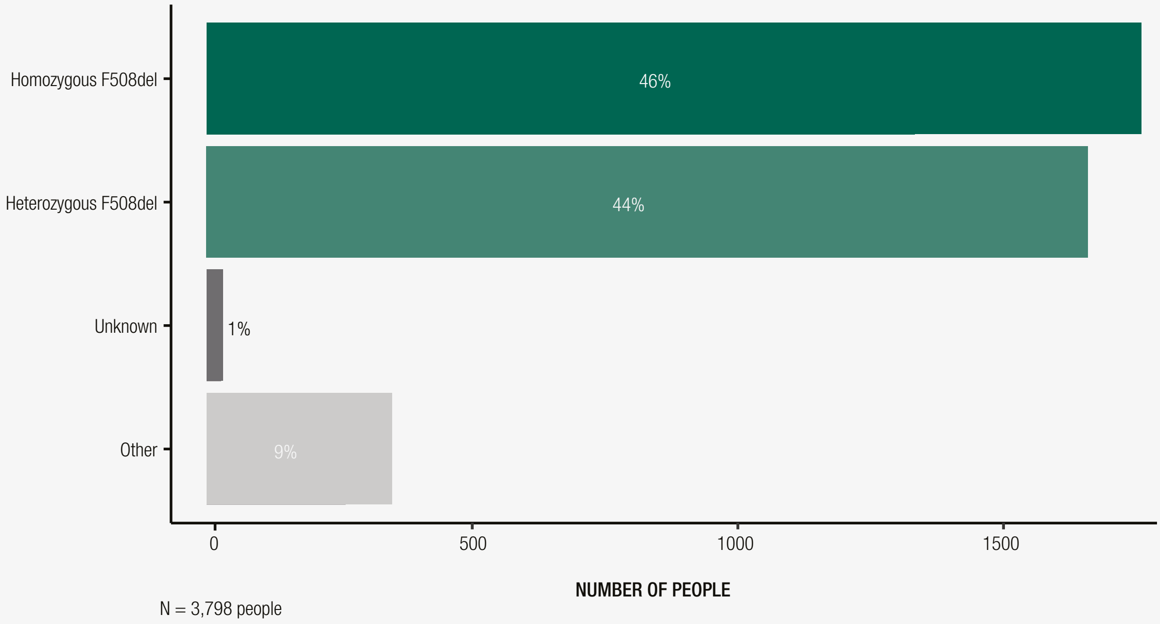
Diagnosis by	Total cohort (%)	2023 new diagnoses N = 68 (%)
Newborn screening	2,218/3,426 (64.7%)	48/68 (70.6%)
Clinical signs/symptoms	1,341/3,426 (39.1%)	19/68 (27.9%)
Family history	325/3,426 (9.5%)	9/68 (13.2%)
Prenatal screening	87/3,426 (2.5%)	5/68 (7.4%)
Not known	132/3,426 (3.9%)	0/68 (0.0%)

Genotype Information

Information regarding the specific genotype of individuals diagnosed with CF is critical, due to current treatments that are available for specific alleles or allele combinations. The CFTR gene has two alleles, and variations may exist in both alleles that are related to the development of CF symptoms (phenotype). Of the 3,798 people in the registry in 2023, 99.2% had at least one allele known and 96.3% had both alleles known. Only 31 (0.8%) people in the registry had two unknown alleles, with three-quarters of these being adults.

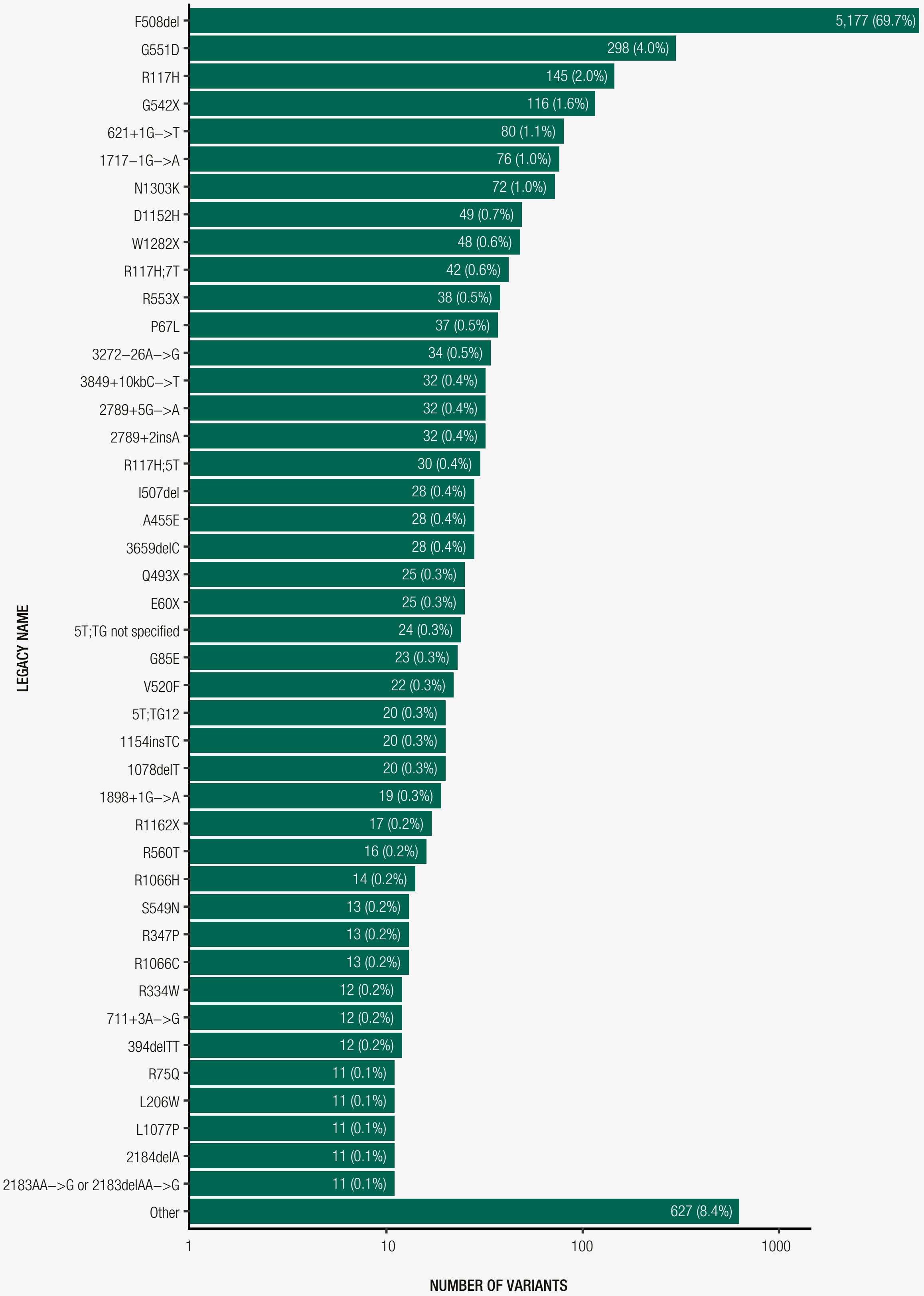
The most common variant is F508del. PwCF can either be homozygous to F508del (have two F508del alleles) or heterozygous (have one F508del allele). In 2023, the proportion of Australian pwCF who were homozygous for the F508del variant was 46.0%, and the proportion who are heterozygous was 44.0%, thus 90% of pwCF in Australia have F508del variants. A further 9.0% of pwCF do not have F508del alleles (Figure 1.7) with less than one percent being unknown (Figure 1.7).

FIGURE 1.7: ACFDR 2023: MOST COMMON CFTR VARIANT COMBINATIONS



The most common variant alleles other than F508del in 2023 were G551D (4.0%), R117H (2.0%) and G542X (1.6%) respectively, with 8.4% being unknown (Figure 1.8).

FIGURE 1.8: ACFDR 2023: MOST COMMON INDIVIDUAL ALLELE CFTR VARIANTS IN THE ACFDR



N = 7,424 mutations

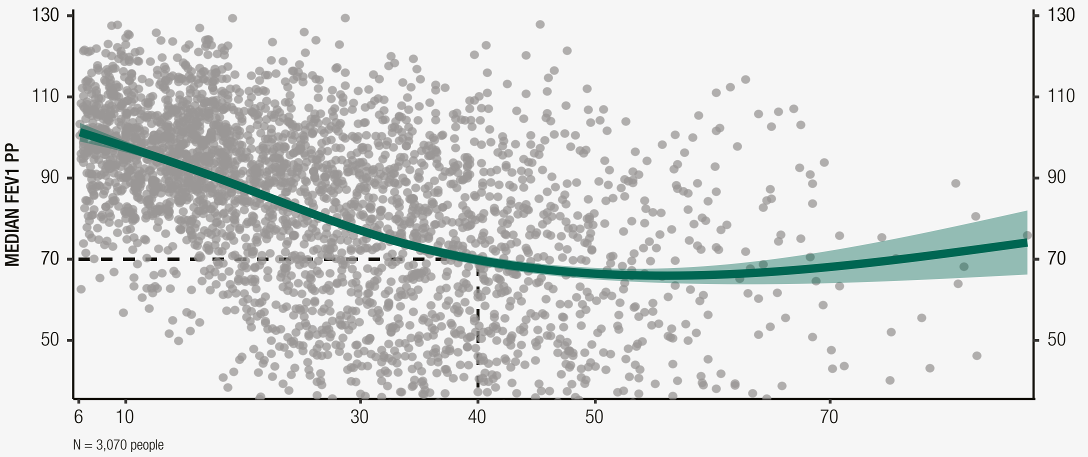
1.4 LUNG FUNCTION

For monitoring lung function in pwCF, the average of the highest Percentage Predicted Forced Expiratory Volume (litres) in 1 second (FEV1 pp) is recorded in each quarter of the year. Predicted values are based on the Global Lung Initiative (GLI) formulae. Lung function measures are aligned with methods used in the United States Cystic Fibrosis Foundation Patient Registry.

Over 80% of active pwCF in the ACFDR have lung function information (3,070 people) for 2023 (compared to 2,922 people in 2022). Four hundred and forty-nine (11.8%) pwCF in the registry are children younger than 6 years of age who do not routinely have lung function information recorded, and a further 7.3% of registry participants did not have lung function information recorded in 2023.

For 2023, the median lung function for pwCF, measured as FEV1 pp, is within the normal range for young children and adolescents (0 – 17) (Figure 1.9). At 40 years of age, the median FEV1 pp is 70.0.

FIGURE 1.9: ACFDR 2023: MEDIAN FEV1 PP BY AGE



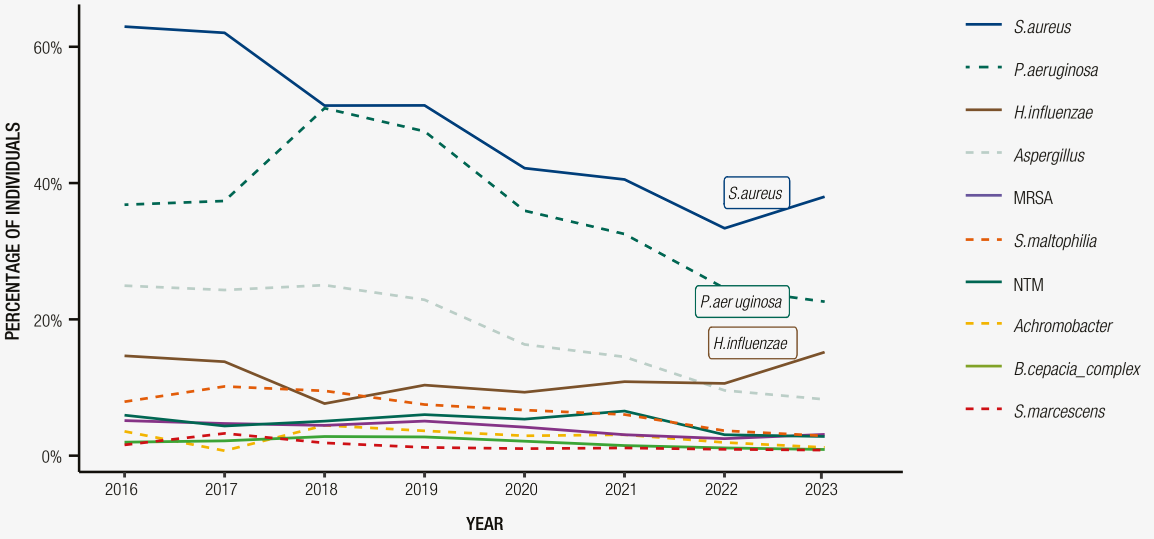
The solid trend line was estimated using a natural cubic spline with 3 degrees of freedom
Shaded area represent the 95% confidence intervals

1.5 MICROBIOLOGY

Figure 1.10 shows the prevalence of respiratory organisms commonly pathogenic to pwCF. There has been a notable reduction over a number of years in many high prevalence organisms, including *S.aureus, P.aeruginosa and* Aspergillus *spp*.

As of December 2023, the overall prevalence in the registry of S.aureus was 38.1%, *P.aeruginosa* was 22.7%, *and Aspergillus* spp was 8.3%. *H.influenzae* was more stable at 15.2%, and Non-Tuberculous Mycobacterium had a prevalence of 2.8%.

FIGURE 1.10: ACFDR 2016 – 2023: PREVALENCE OF RESPIRATORY MICROORGANISMS



1.6 CFTR MODULATORS

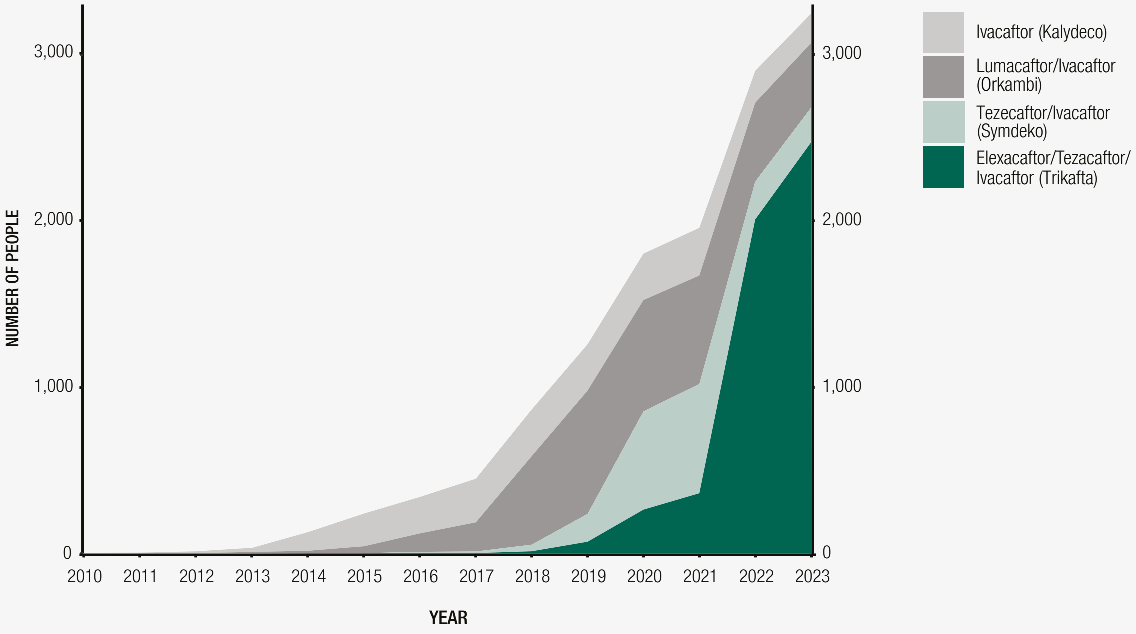
Disease-modifying therapies have the potential to dramatically reduce symptoms and increase survival for an increasing number of pwCF. Different therapies target different genetic variants, and not all pwCF may be eligible to receive CFTR modulators. Additionally, CFTR modulators are high-cost medicines and are generally available initially in Australia via special access schemes before being approved for listing on the Pharmaceutical Benefits Scheme (PBS).

Figure 1.11 illustrates the total number of participants in the 2023 active cohort who, at any point from 2010 to 2023, were prescribed at least one CFTR modulator, including ivacaftor (Kalydeco®), lumacaftor/ivacaftor (Orkambi®), tezacaftor/ivacaftor with ivacaftor (Symdeko®), and elexacaftor/tezacaftor/ivacaftor (Trikafta®). This may include individuals who switched CFTR modulator during this period.

A total of 3,680 pwCF (97%) in the registry had known eligibility status for CFTR modulators based on their genotype. Of these, 3,257, or 88.5% of all pwCF in the registry have been prescribed at least one modulator during 2010 to 2023.

The number of modulator initiations (commencements) in 2023 increased by 363; up from 2,895 in 2022 to 3,257 in 2023. This is primarily due to continued additional initiations for Trikafta, which increased by 466 prescriptions, while initiation of other modulators decreased during this 12-month period. Further information about CFTR modulators are provided in the paediatric and adult sections of this report.

FIGURE 1.11: ACFDR 2010 – 2023: CFTR MODULATOR USE IN THE 2023 COHORT



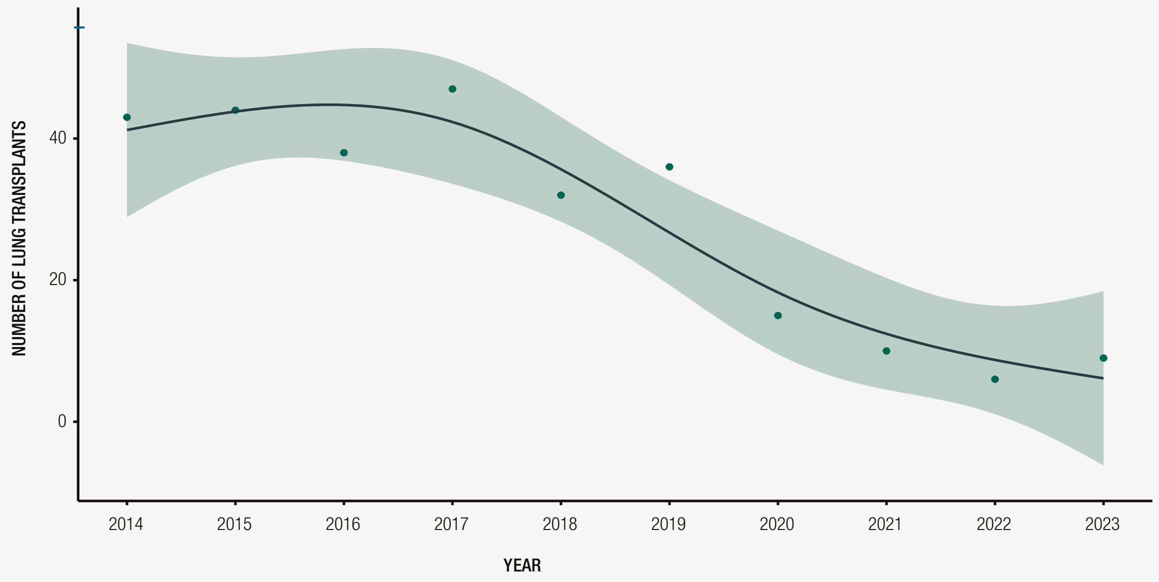
1.7 TRANSPLANTATION AND SURVIVAL

Transplantation

The most common transplantation procedure for people with CF is a bilateral (double) lung transplant. As CF is a systemic disease, other organs may also be severely affected by either the underlying disease or its related complications and require transplantation, including the kidney, liver or pancreas. Occasionally multi-organ transplants are required.

In 2023, there were a total of 12 transplants for pwCF; 9 of which were bilateral lung transplants of which 3 were performed in people younger than 30 years of age. The 3 non-lung transplants were comprised of liver and kidney transplants. There were 54 people who were evaluated for a transplant in 2023; 4 (7.4%) were waitlisted, and 4 (7.4%) were deferred from the waiting list. The number of annual bilateral lung transplants undertaken over the last decade is shown in Figure 1.12. There has been a substantial decline in bilateral lung transplants over the last few years among pwCF in Australia, consistent with international trends.

FIGURE 1.12: ACFDR 2014 – 2023: BILATERAL LUNG TRANSPLANTS



Solid trend line w as estimated using a natural cubic spline with three degrees of freedom
Shaded area illustrates the 95% confidence interval

Status of People with CF in the ACFDR

The (follow-up) status of people in the ACFDR is updated annually by CF centres. Many pwCF who have undergone organ transplantation may not have been followed up by the ACFDR, and their deaths may not be captured in the registry. Periodically data linkage is undertaken with the national death register to validate death data. This is undertaken via probabilistic matching due to the unidentified nature of registry data.

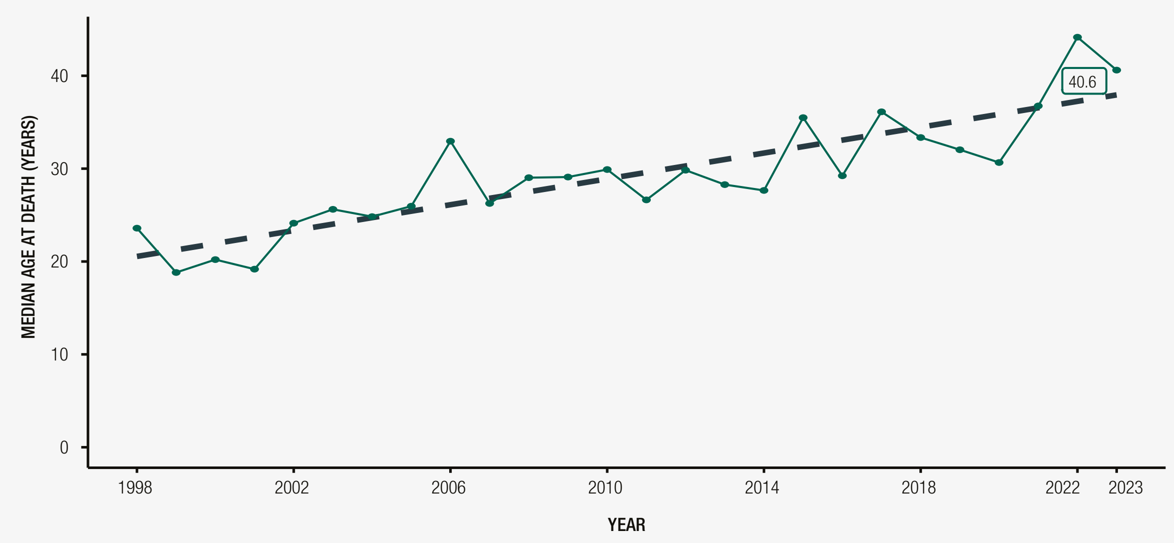
In 2023 the ACFDR recorded the deaths of 18 pwCF, eight of which (44%) were pwCF who had received a lung transplant. Five deaths (28%) occurred in pwCF less than 29 years; and 13 deaths occurred in pwCF of 30 years of age or higher.

In 2023, the causes of the 18 deaths among individuals with CF included post-transplant complications (4), pulmonary manifestations (8) (including some who had undergone transplants), liver failure, other CF-related causes (including some post-transplant cases), and non-CF-related causes.

Median Age of Death

The median age of death in 2023 was 40.6 years of age for pwCF, including those who had a lung transplant (Figure 1.13), and 48.3 years of age for pwCF excluding those who had a lung transplant. The median age of death continues to increase. Median age may vary from year to year given the relatively small number of deaths per annum. The median age of death differs from estimated survival, which estimates the lifespan of a person with CF born in a specific year.

FIGURE 1.13: ACFDR 1998 – 2023: MEDIAN AGE OF DEATH



Straight dashed line represents the overall trend estimated by a linear regression model

Survival

The median estimated survival for pwCF is determined on the basis of the individuals who are alive in the ACFDR in a given year. Internationally, CF registries have documented steady increases in median survival over recent years, attributed to advancements in treatments. This positive trend is expected to persist, with further improvements anticipated as more individuals with cystic fibrosis are managed with CFTR modulators.

Table 1.4a is inclusive of pwCF who have undergone a lung transplant, while Table 1.4b excludes pwCF who have undergone a lung transplant. Table 1.4a (also represented in Figure 1.14) shows, that the estimated 5-year survival has increased over a 10-year period from 47.0 years for pwCF born in 2008 – 12, to 60.6 years for pwCF born in 2018 – 22. The ACFDR is reporting survival data one year in arrears to allow for late notification of recent deaths to be captured by the registry.

TABLE 1.4A: ACFDR 2008 – 2022: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA (LUNG TRANSPLANTS INCLUDED)

Period	Median age and 95% CI (years)	Number of deaths/number at risk
2008 – 12	47 (43.5 – 51)	166/3,301
2009 – 13	45.9 (42.3 – 47.7)	187/3,380
2010 – 14	47.4 (45.3 – 53.6)	174/3,413
2011 – 15	47.4 (45.5 – 53.6)	174/3,495
2012 – 16	47.5 (45.4 – 54.3)	181/3,556
2013 – 17	49.7 (45.9 – 55.6)	179/3,587
2014 – 18	51.2 (48.3 – 56.9)	175/3,720
2015 – 19	51.2 (48 – 56.3)	180/3,789
2016 – 20	54.7 (50.6 – 59.8)	171/3,821
2017 – 21	56.9 (53 – 60.4)	154/3,861
2018 – 22	60.6 (58.2 – 76.8)	120/3,898

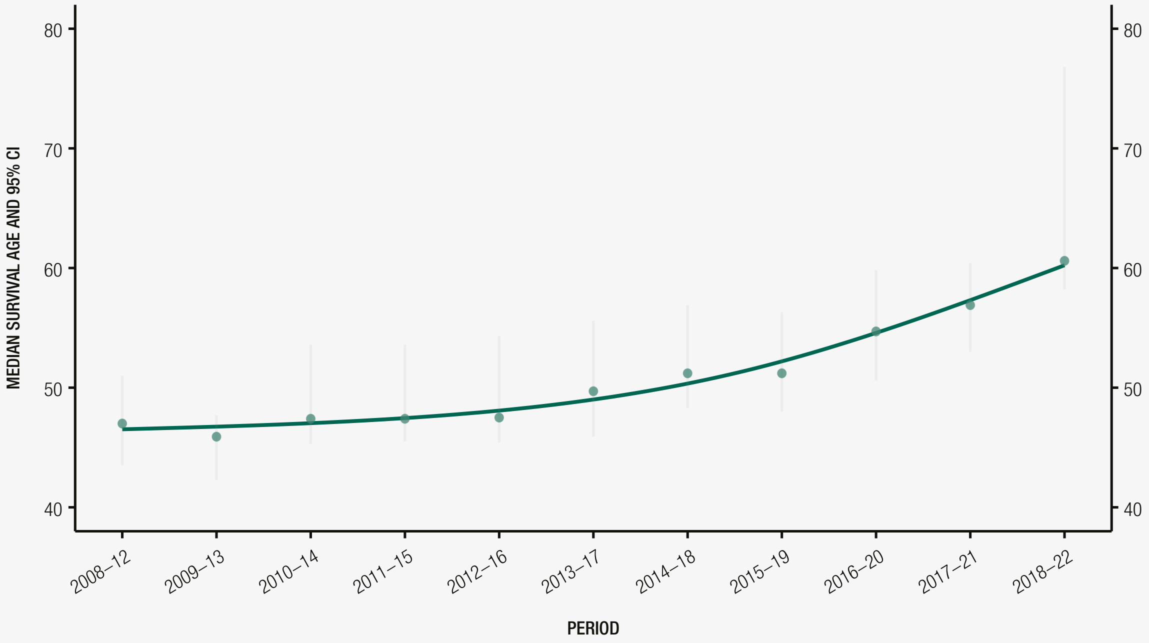
For pwCF, excluding those with lung transplants, survival is even higher (Table 1.4B). However, the N/A value for the upper 95% confidence limit indicates that the upper bound of the confidence interval for the median survival time could not be estimated. This is likely due to a combination of a high number of censored observations (patients who were still alive at the end of the study period) and a limited number of events (deaths). Continued follow-up will help improve the accuracy of our estimates.

TABLE 1.4B: ACFDR 2008 – 2022: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA (LUNG TRANSPLANT EXCLUDED)

Period	Median age and 95% CI (years)	Number of deaths/number at risk
2008 – 12	47.5 (45.9 – 57.4)	106/2,834
2009 – 13	47.4 (45.9 – 54.3)	114/2,921
2010 – 14	51 (47 – 58)	107/3,007
2011 – 15	52.6 (47.5 – 58)	99/3,071
2012 – 16	54.3 (48 – 70.7)	106/3,166
2013 – 17	56.9 (54 – 70.7)	104/3,216
2014 – 18	59.8 (56.3 – 70.7)	99/3,359
2015 – 19	63.3 (56.9 – 70.7)	97/3,447
2016 – 20	63.3 (59.2 – 73.8)	95/3,529
2017 – 21	63.8 (59.8 – NA)	84/3,601
2018 – 22	73.8 (63.8 – NA)	62/3,672

Survival is also shown graphically below for all pwCF in the registry (Figure 1.14).

FIGURE 1.14: ACFDR 2008 – 2022: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA (LUNG TRANSPLANTS INCLUDED)



Each dot and line represent the estimated median survival age and 95% CI, respectively
The smooth line was estimated by fitting a natural cubic spline with 3 degrees of freedom

2.

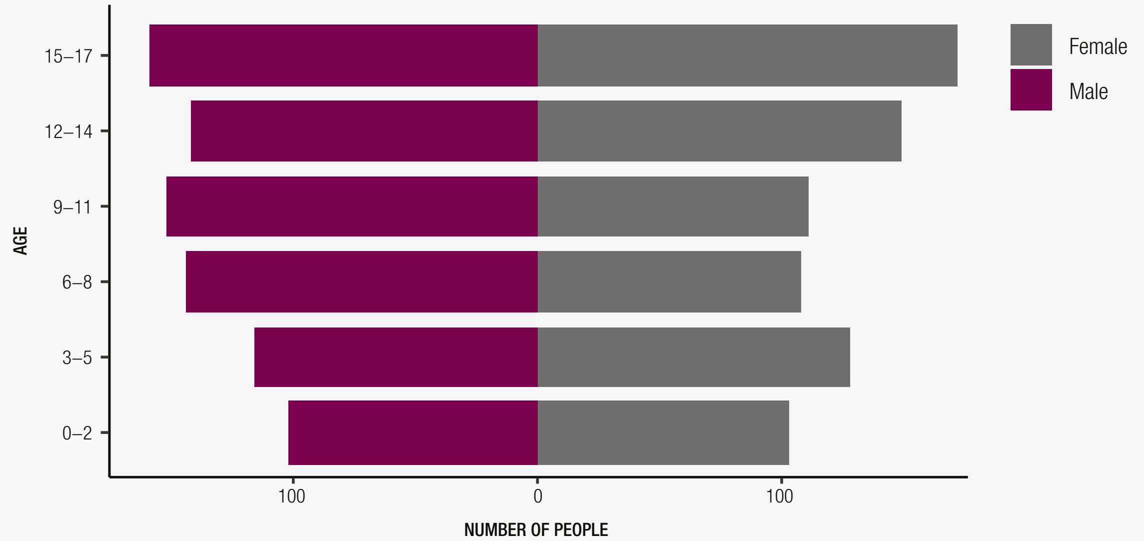
PAEDIATRIC DATA

2. PAEDIATRIC DATA

2.1 DEMOGRAPHIC INFORMATION

As of 31 December 2023, the ACFDR held data regarding 1,586 children and adolescents (0 – 17 years old) with CF, comprising 771 females and 815 males (Figure 2.1).

FIGURE 2.1: ACFDR PAEDIATRICS 2023: BY AGE AND SEX



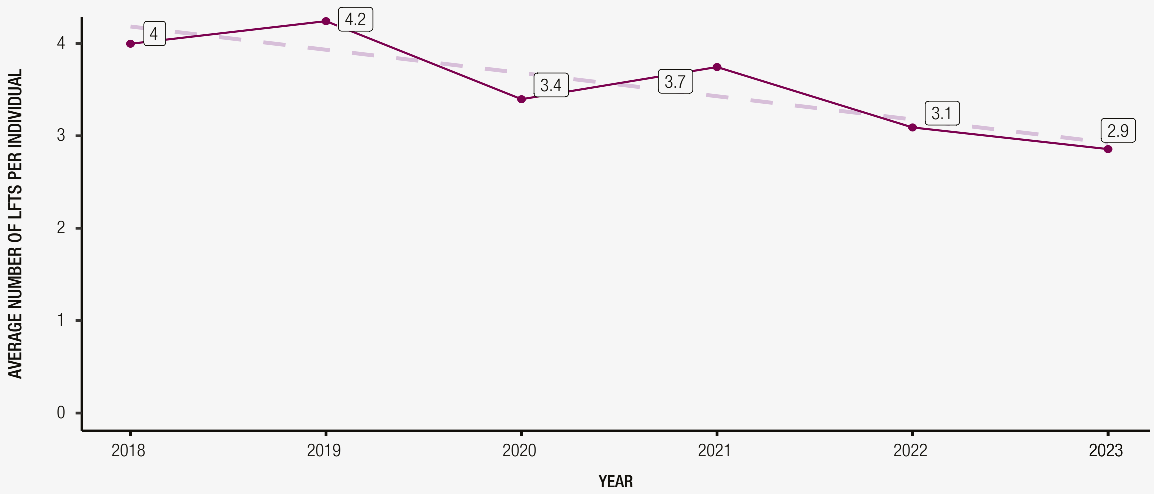
N = 1,586 people

2.2 CLINICAL MEASURES

Lung Function

Figure 2.2 illustrates the average number of spirometry tests per child recorded annually in the registry from 2018 to 2023. In 2018, children and adolescents averaged 4 tests each, however this has declined to 2.9 tests per child in 2023.

FIGURE 2.2: ACFDR PAEDIATRICS 2018 – 2023: AVERAGE NUMBER OF LUNG FUNCTION TESTS ENTERED PER INDIVIDUAL



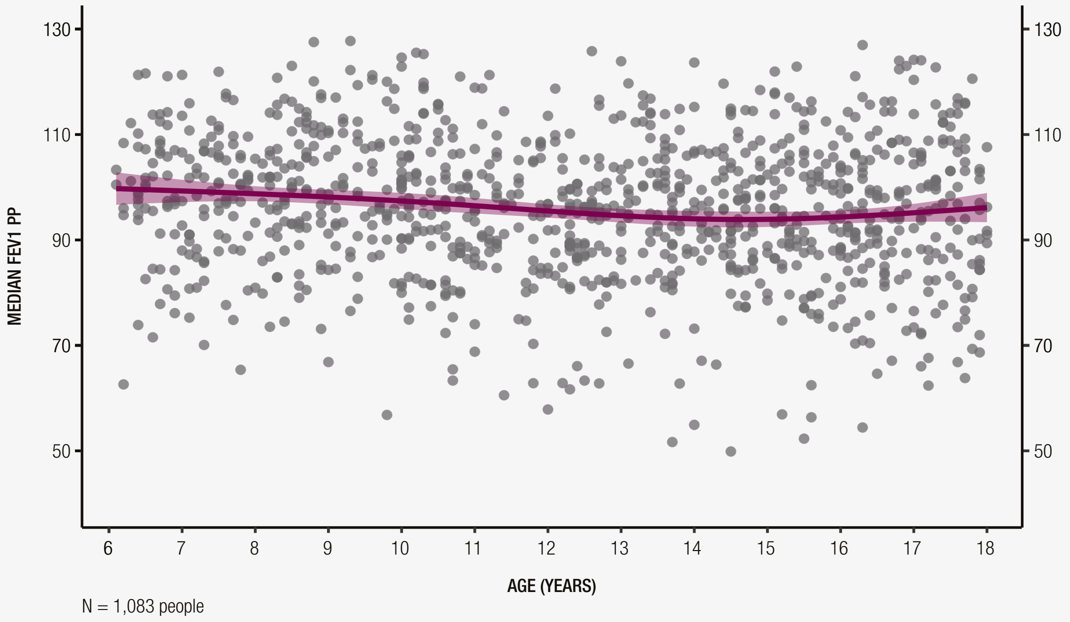
Straight dashed line represents the overall trend estimated by a linear regression model

Median Lung Function

For the monitoring of lung function in pwCF, the average of the highest FEV1 pp is recorded in each quarter of the year. Predicted values are based on the Global Lung Initiative (GLI) formulae. Lung function measures are aligned with methods used in the United States Cystic Fibrosis Foundation's Patient Registry, whereby annual measures of lung function, weight, and height are reported as an average of the maximum value from each quarter where measurements have been recorded.

The 2023 median lung function is shown in the scatterplot below for 1,083 children and adolescents. Over 11.8% of participants in the registry are children younger than 6 years of age who do not routinely have lung function information recorded, and a further 19.2% of paediatric registry participants did not have lung function information recorded in 2023 (Figure 2.3).

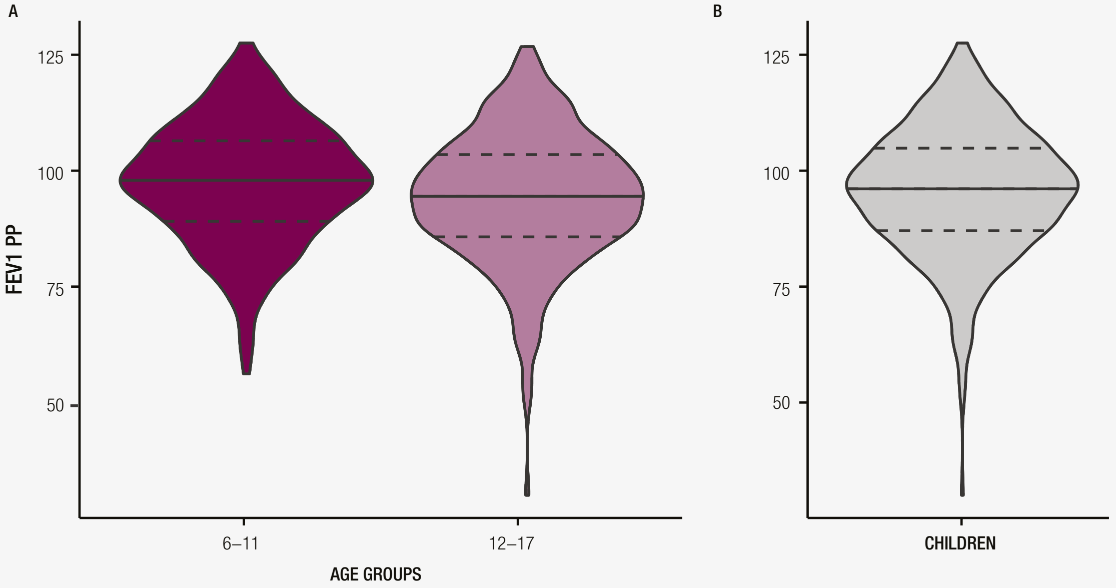
FIGURE 2.3: ACFDR PAEDIATRICS 2023: FEV1 PP BY AGE



The solid trend line was estimated using a natural cubic spline with 3 degrees of freedom
Shaded area represent the 95% confidence intervals

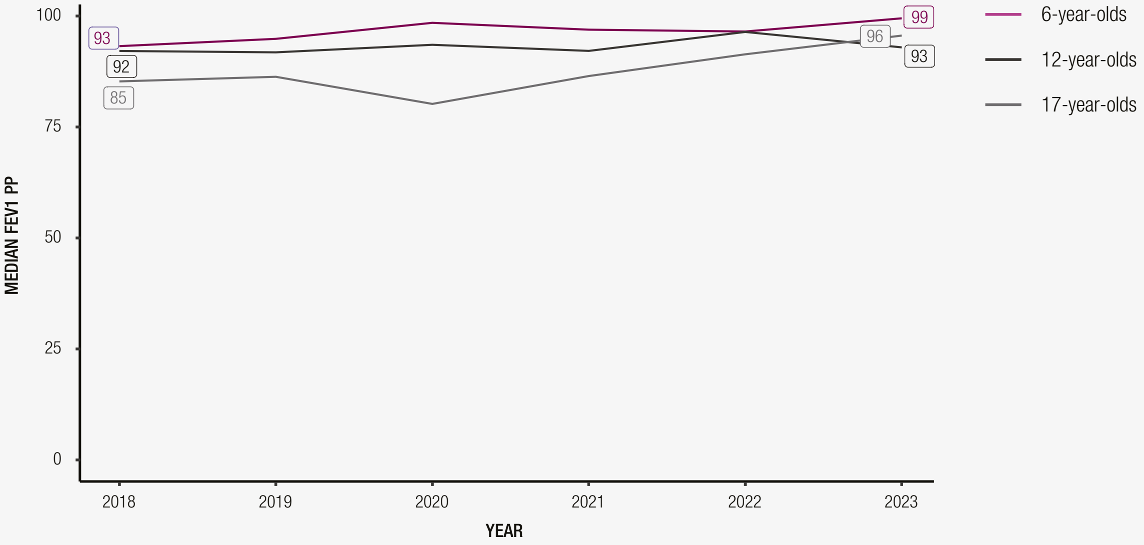
In 2023, the median FEV1 pp for 6 – 11-year-olds was 98.2 pp and for 12 – 17-year-olds was 95.3 pp. The median FEV1 pp for children and adolescents 6 – 17 years in 2023 was 96.6 pp (Figure 2.4).

FIGURE 2.4: ACFDR PAEDIATRICS 2023: MEDIAN FEV1 PP BY AGE GROUP



The median FEV1 pp for children and adolescents has increased over time. For 6-year-olds, it has increased from 93.0 pp in 2018 to 99.0 percent predicted in 2023; for 12-year-olds it has increased from 92.0 pp to 93.0 pp; and for 17-year-olds, it has increased from 85.0 pp to 96.0 pp in 2023 (Figure 2.5).

FIGURE 2.5: ACFDR PAEDIATRICS 2018 – 2023: MEDIAN FEV1 PP OVER TIME

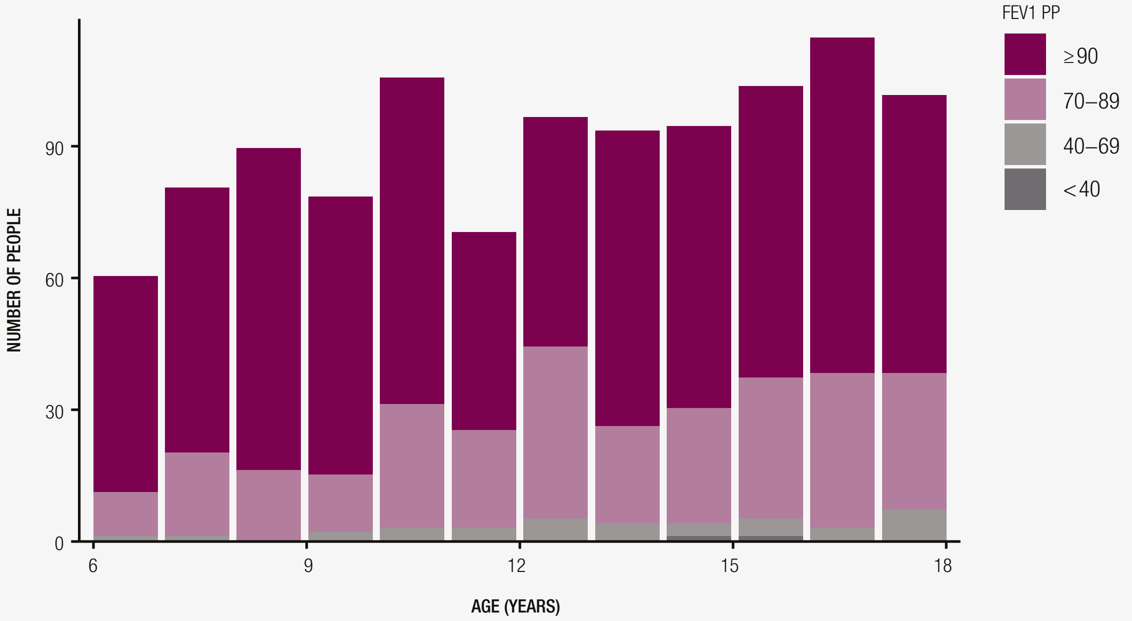


Labelled percentages illustrate median predFEV1 in 2003 and 2023
Dashed line represents all age group

Variation in Paediatric Lung Function

Paediatric lung function varies among different age groups. For 2023, in the 6 – 11 age range, over seventy-five percent of children (75.5%) had an FEV1 pp of 90 or higher, and 22.4% had an FEV1 pp of 70 – 89. Two thirds of children 12 – 17 years (64.6%) had an FEV1 pp >90, while 30.8% had an FEV1 pp of 70 – 89. A small proportion (2.1% of 6 – 11-year-olds, and 4.3% of 12 – 17-year-olds) had an FEV1 pp of 40 – 69pp (Figure 2.6).

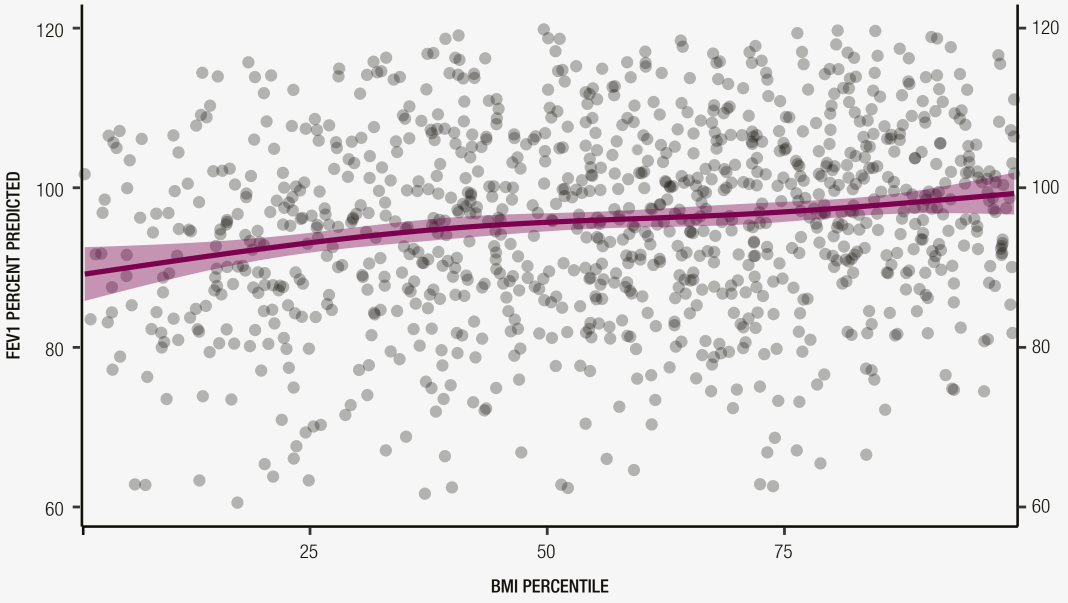
FIGURE 2.6: ACFDR PAEDIATRICS 2023: LUNG FUNCTION BY AGE



Lung Function and Body Mass Index

The relationship between FEV1 pp and Body Mass Index (BMI) for 2023 is shown in Figure 2.7. In general, as BMI increases, so does FEV1 pp.

FIGURE 2.7: ACFDR PAEDIATRICS 2023: FEV1 PP VS BMI PERCENTILE



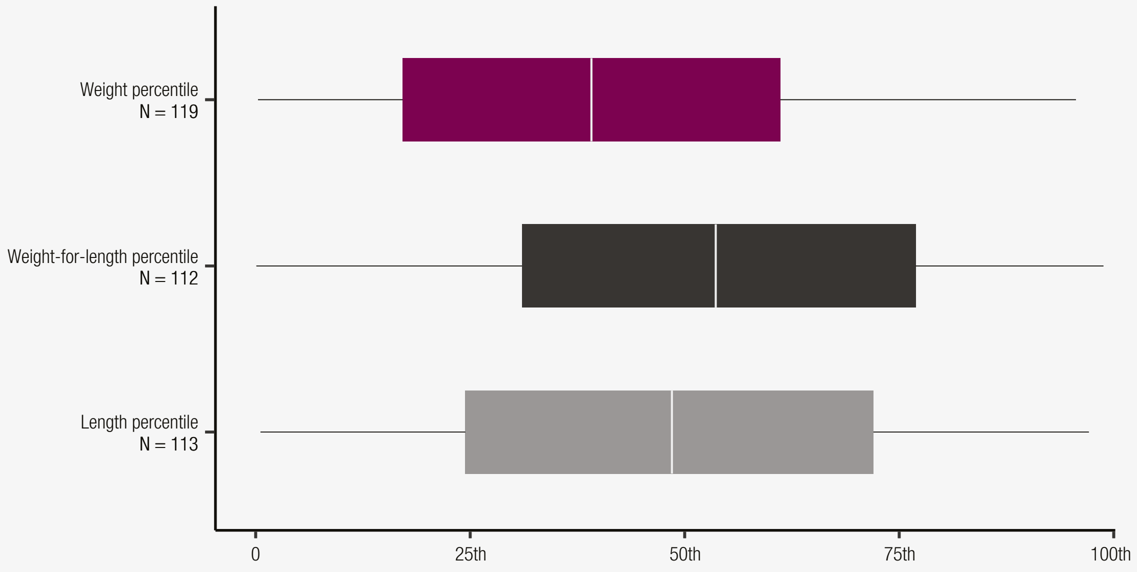
N = 1,083 people aged 6–17 years

Solid line was estimated using a natural cubic spline with 3 degrees of freedom
Shaded area represents 95% confidence interval

Nutrition

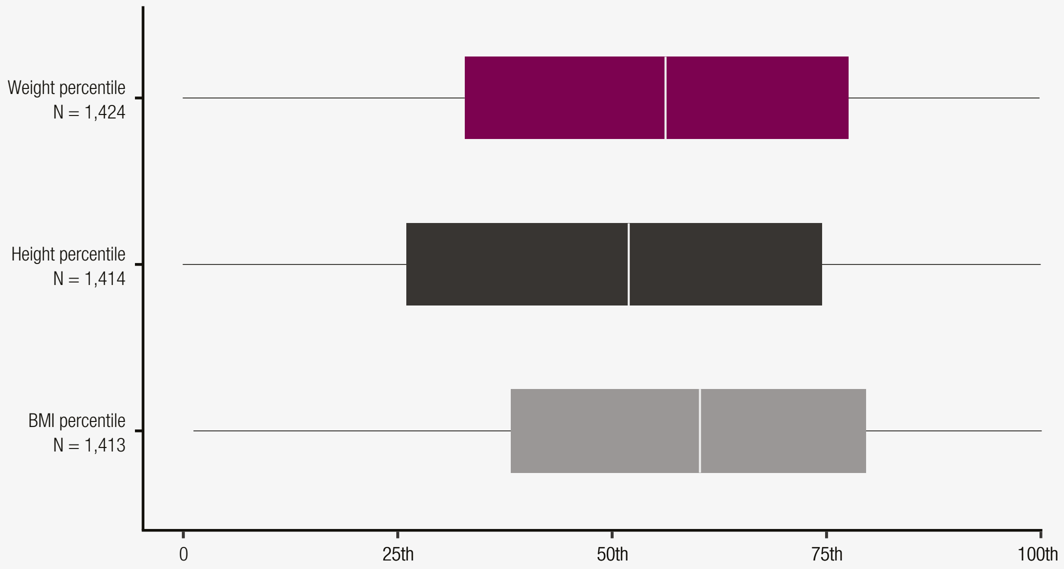
For 2023, infants (<24 months of age) had a median weight of 39th percentile; the median length was the 49th percentile; and the median weight-for-length was the 54th percentile (Figure 2.8).

FIGURE 2.8: ACFDR PAEDIATRICS 2023: WEIGHT, LENGTH, AND WEIGHT-FOR-LENGTH PERCENTILES LESS THAN 24 MONTHS



In 2023, for children and adolescents aged 2 – 17 years, the median weight was 52nd percentile, median height was 56th percentile, and median BMI was 60th percentile. These figures represent the best weight, height, and BMI per individual averaged over a 12-month period (Figure 2.9).

FIGURE 2.9: ACFDR PAEDIATRICS 2023: WEIGHT, HEIGHT, AND BMI PERCENTILES AGE 2 – 17 YEARS



Children 2–17 years
Height and BMI percentiles were calculated using WHO growth chart
Weight percentiles were calculated using CDC growth chart

Nutritional status for the majority of male and female children and adolescents with CF was in the optimal and acceptable BMI percentile ranges for 2023 (Table 2.1).

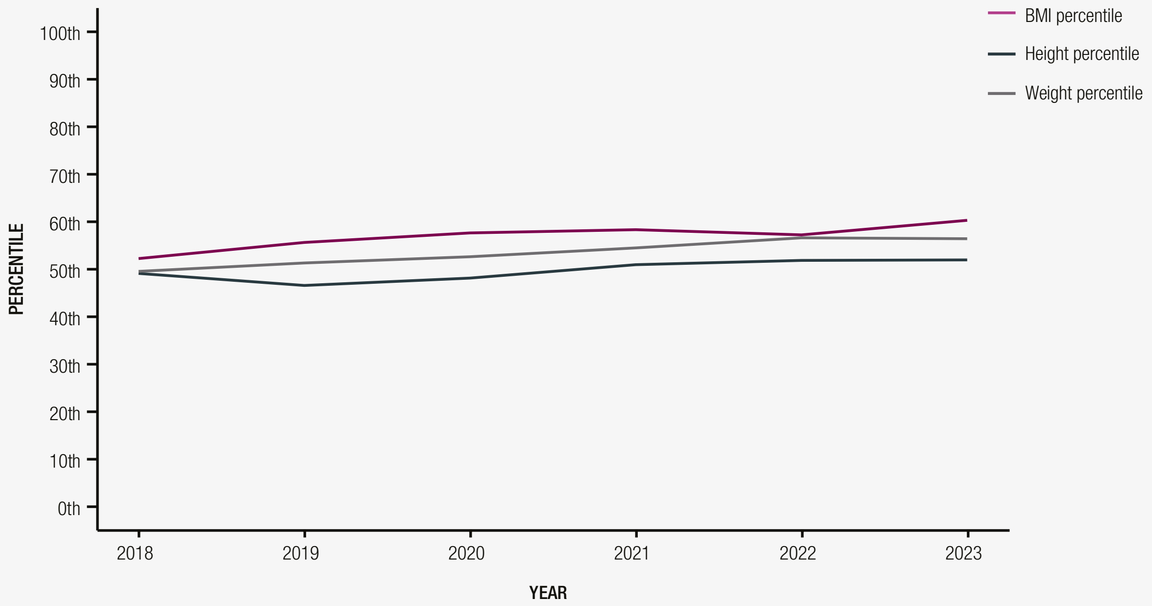
TABLE 2.1: ACFDR PAEDIATRICS 2023: <2 – 17 YEARS NUTRITIONAL STATUS

Nutritional status*	<2 years	2 – 5 years	6 – 11 years	12 – 17 years	Total (N = 1,519)
Optimal/acceptable	88.7% (94)	65.0% (191)	71.9% (365)	69.7% (426)	70.8% (1,076)
Overweight/obese	0.0% (0)	24.5% (72)	15.6% (79)	13.7% (84)	15.5 % (235)
Suboptimal/undernourished	11.3% (12)	10.5% (31)	12.6% (64)	16.5% (101)	13.7% (208)

*High BMI (obese range): BMI >95th percentile using CDC growth chart (children and adolescents 2 – 18 years)
High BMI (overweight range): BMI 85th-95th percentile using CDC growth chart (children and adolescents 2 – 18 years)
Optimal: weight-for-lengths >50th percentile (infants 0 – 1 years); BMI 50th-85th percentile using CDC growth chart (children and adolescents 2 – 18 years)
Acceptable: weight-for-lengths 25th-50th percentile (infants 0 – 1 years); BMI 25th-50th percentile (children and adolescents 2 – 18 years)
Suboptimal: weight-for-lengths 10th-25th percentile (infants 0 – 1 years); BMI 10th-25th percentile (children and adolescents 2 – 18 years)
Undernourished: persistent weight for length <10th percentile (infants 0 – 1 years); BMI <10th percentile (children and adolescents 2 – 18 years)

Over the last 6 years the median height for children and adolescents aged 2 – 17 has increased by 3 percentile points (from the 49th percentile to the 52nd percentile); weight has increased by 7 percentile points (from the 49th percentile to the 56th percentile). As a result, the average BMI also increased by 8 percentile points during this time, from the 52nd to the 60th percentile (Figure 2.10).

FIGURE 2.10: ACFDR PAEDIATRICS 2018 – 2023: 2 – 17 YEARS MEDIAN NUTRITIONAL PERCENTILES

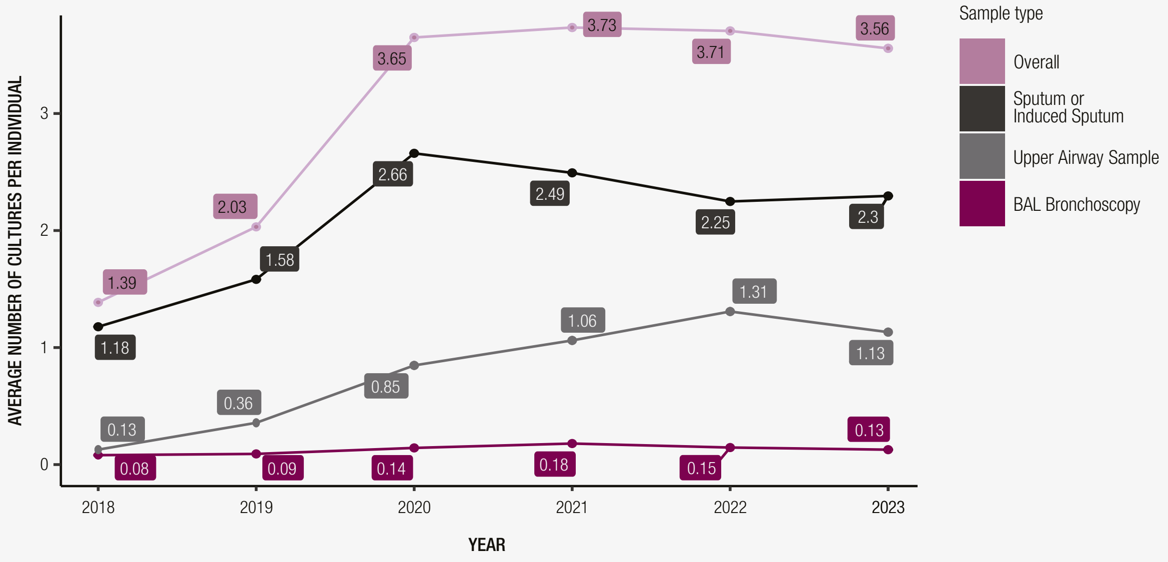


Microbiology

The average number of respiratory samples collected by the registry per child each year over a 6-year period is shown in Figure 2.11. The number of respiratory samples increased from 1.39 per person in 2018 to an average of 3.73 per child in 2021, then decreased slightly to 3.56 samples in 2023.

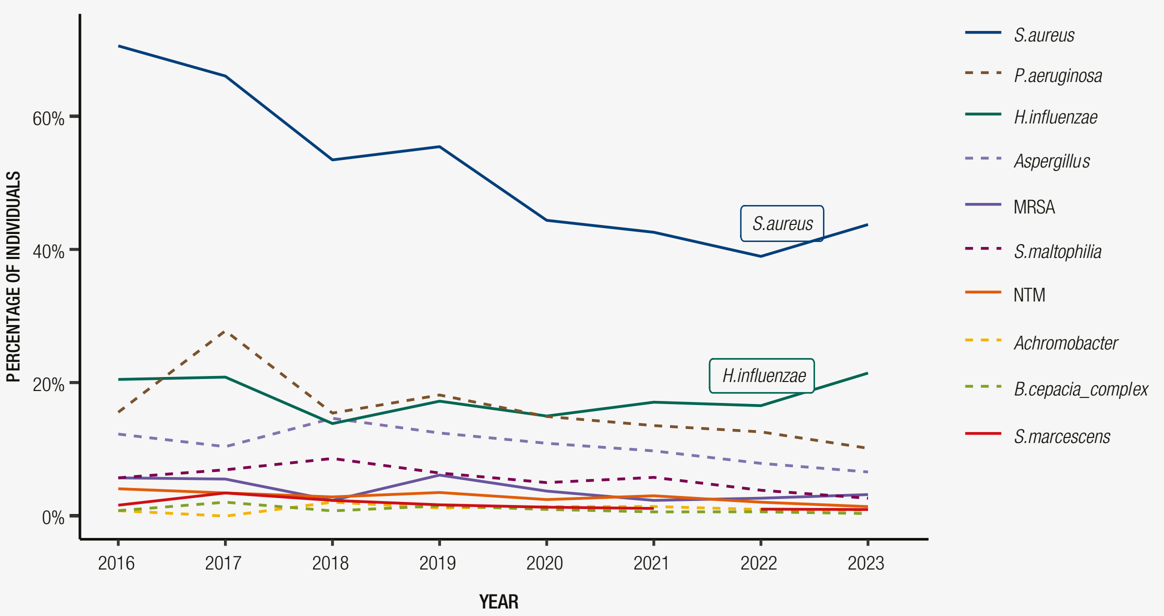
When considering the specific sample types, sputum/induced sputum samples accounted for a significant portion, from 1.18 samples per child in 2018 to 2.3 samples in 2023. BAL Bronchoscopy samples increased slightly from 0.08 per child in 2018 to 0.13 in 2023. Notably, Upper Airway samples (throat swabs, cough swabs, nasopharyngeal swabs and sinus wash), increased, more substantially during this period, from 0.13 in 2018 to 1.13 in 2023.

FIGURE 2.11: ACFDR PAEDIATRICS 2018 – 2023: MEAN NUMBER OF RESPIRATORY SAMPLES PER INDIVIDUAL



The prevalence of some of the most common paediatric microorganisms has changed over the last 6 years. The prevalence of *S.aureus* was 70.5% for children with CF in 2016 and has decreased to 43.7% in 2023; the prevalence of *Aspergillus* spp was 12.3% in 2016 and has decreased to 6.6% in 2023. The prevalence of *P.aeruginosa* has decreased from a peak of 27.8% in 2017 to 10.2% by 2023. The prevalence of less common paediatric microorganisms has remained similar over this period (Figure 2.12).

FIGURE 2.12: ACFDR PAEDIATRICS 2016 – 2023: PREVALENCE OF RESPIRATORY MICROBIOLOGY



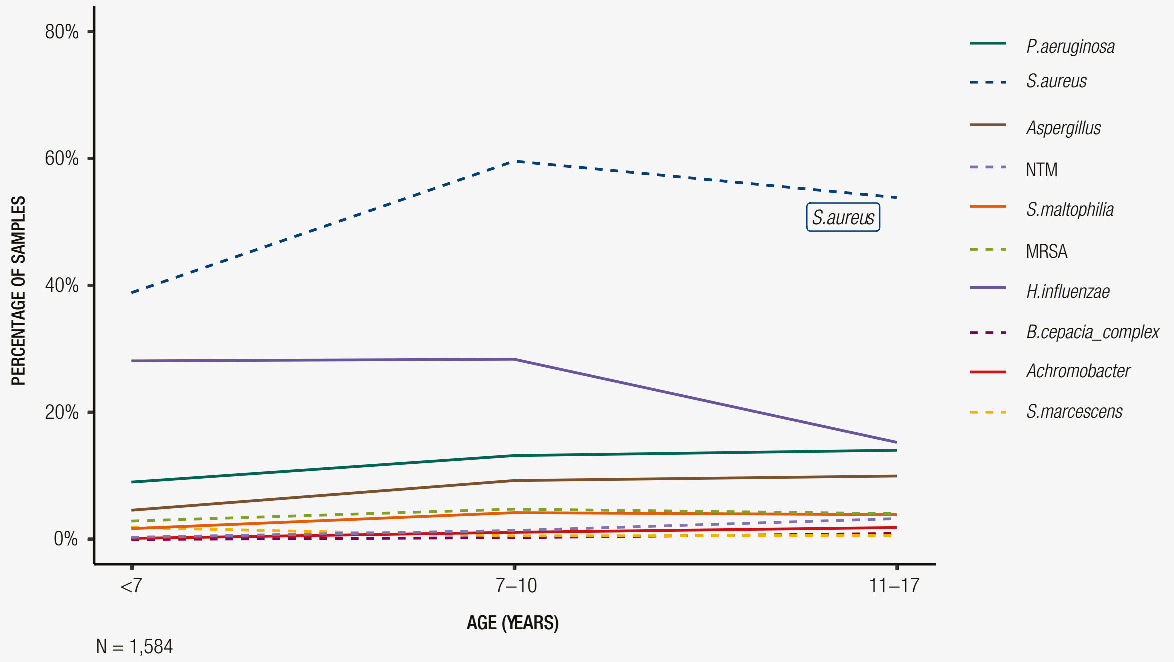
Of the 1,584 microbiology culture samples collected in 2023, the most common pathogen across all age groups was *S.aureus*, with the prevalence increasing with age (Table 2.2). The next most common pathogen among children and adolescents up to 11 years of age was *H.influenzae,* with *P.aeruginosa* being the next most common pathogen for adolescents aged 12 – 17 years. The prevalence of *P.aeruginosa* increases with age, being 9.0% for children <7 years, 13.0% for children and adolescents 7 – 11 years, and 14.0% for adolescents aged 12 – 17 years. *Aspergillus* spp also increases with increasing age, with a prevalence of 5.0% in children <7 years and 10.0% in adolescents 12 – 17 years. This is also shown graphically in Figure 2.13.

For children younger than seven years, 125 lower airway samples were collected by bronchoalveolar lavage (BAL) in 2023. The most common organisms identified in this age group in 2023 included *S.aureus* (19.0%), *H.influenzae* (18.0%), *Aspergillus* spp (10.0%), *P.aeruginosa* (8.0%), and *S.marcescens* (4.0%) (Table 2.2).

TABLE 2.2: ACFDR PAEDIATRICS 2023: PREVALENCE OF RESPIRATORY MICROORGANISMS BY AGE

	BAL samples	All samples		
	<7 years	<7 years	7 – 11 years	12 – 17 years
Number of samples in the age range	528	528	364	690
Number of samples taken in 2023	125	587	356	641
Number of patients	125	494	333	624
S.aureus	24/125 (19%)	228/587 (39%)	212/356 (60%)	345/641 (54%)
H.influenzae	22/125 (18%)	165/587 (28%)	101/356 (28%)	98/641 (15%)
P.aeruginosa	10/125 (8%)	53/587 (9%)	47/356 (13%)	90/641 (14%)
Aspergillus spp	13/125 (10%)	27/587 (5%)	33/356 (9%)	64/641 (10%)
B.cepacia_complex	0/125 (0%)	0/587 (0%)	1/356 (0%)	6/641 (1%)
MRSA	0/125 (0%)	17/587 (3%)	17/356 (5%)	26/641 (4%)
Achromobacter spp	0/125 (0%)	1/587 (0%)	4/356 (1%)	12/641 (2%)
S.maltophilia	1/125 (1%)	10/587 (2%)	15/356 (4%)	25/641 (4%)
S.marcescens	2/25 (2%)	11/587 (2%)	2/356 (1%)	4/641 (1%)
Nontuberculous mycobacteria	1/125 (1%)	2/587 (0%)	5/356 (1%)	21/641 (3%)

FIGURE 2.13: ACFDR PAEDIATRICS 2023: PREVALENCE OF RESPIRATORY MICROORGANISMS BY AGE



In 2023, nontuberculous mycobacteria (NTM) including *M.abscessus* were rarely reported in children less than seven years. The prevalence of NTM among 7 – 11-year-olds in 2023 was 1.5% and in 12 – 17-year-olds was 3.2%. The prevalence of *M.abscessus* among 7 – 11-year-olds In 2023 was 0.8% and among 12 – 17-year-olds was 1.6%. From 2021, the prevalence of NTM and *M.abscessus* has decreased each year (Table 2.3).

TABLE 2.3: ACFDR PAEDIATRICS 2016 – 2023: NON-TUBERCULOUS MYCOBACTERIUM (NTM) INFECTION

Age	Organism	2017	2019	2021	2022	2023
<7	NTM	0/7(0.0%)	1/101(1.0%)	1/339(0.3%)	0/413(0.0%)	2/494(0.4%)
<7	*M.abscessus*	0/7(0.0%)	0/101(0.0%)	1/339(0.3%)	0/413(0.0%)	0/494(0.0%)
7 – 11	NTM	0/58(0.0%)	2/198(1.0%)	11/383(2.9%)	6/394(1.5%)	6/398(1.5%)
7 – 11	*M.abscessus*	0/58(0.0%)	1/198(0.5%)	3/383(0.8%)	1/394(0.3%)	3/398(0.8%)
12 – 17	NTM	5/75(6.7%)	20/283(7.1%)	41/556(7.4%)	36/567(6.3%)	18/559(3.2%)
12 – 17	*M.abscessus*	2/75(2.7%)	12/283(4.2%)	19/556(3.4%)	22/567(3.9%)	9/559(1.6%)

2.3 CF MANAGEMENT

Clinic Visits

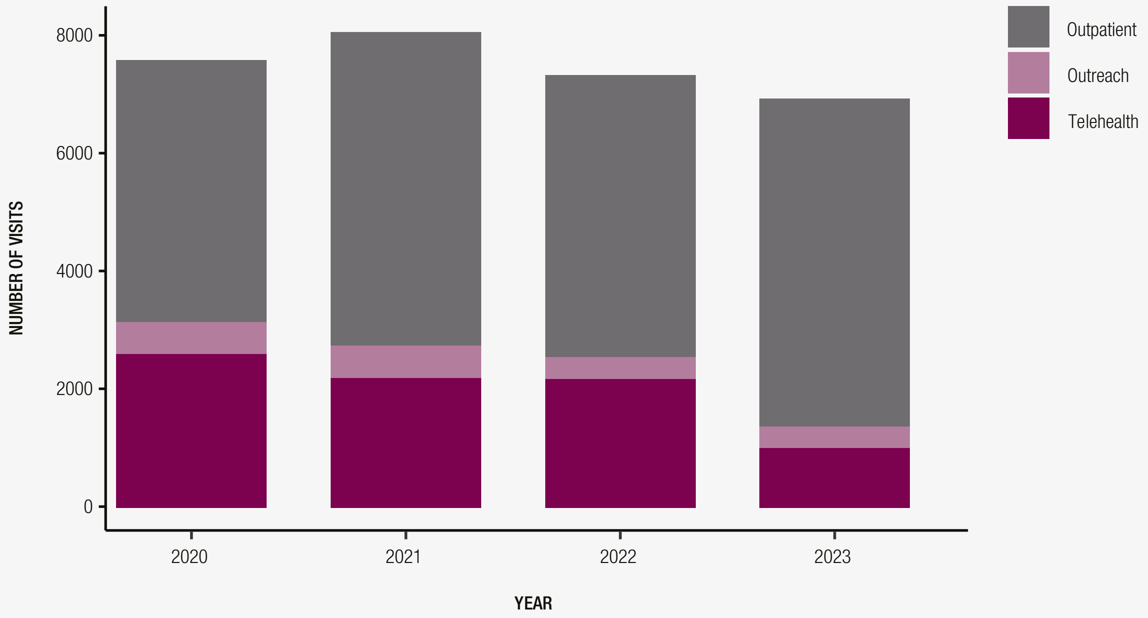
Table 2.4 and Figure 2.14 show the total number of clinical visits for the paediatric population in the registry per year over the last 4 years. The total number of clinical visits peaked in 2021 (8,120 encounters), with visits declining since then to a total of 7,085 in 2023.

The nature of clinical visits has also changed during this time. During the COVID-19 pandemic, the proportion of telehealth visits (audio and/or visual visits conducted at home or in a healthcare setting) for children and adolescents were 34.0% in 2020, decreasing to 14.6% in 2023. The proportion of outreach visits also decreased from 7.0% in 2020 to 5.3% in 2023 (Table 2.4 and Figure 2.14).

TABLE 2.4: ACFDR PAEDIATRICS 2020 – 2023: TOTAL NUMBER OF VISITS RECORDED PER YEAR

Visit type	2020	2021	2022	2023
Outpatient	4,467 (58.0%)	5,337 (66.0%)	4,805 (65.0%)	5,562 (80.1%)
Outreach	540 (7.0%)	549 (7.0%)	370 (5.0%)	368 (5.3%)
Telehealth	2,631 (34.0%)	2,203 (27.0%)	2,191 (30.0%)	1,013 (14.6%)
Total	7,655 (100%)	8,120 (100%)	7,439 (100%)	7,085 (100%)

FIGURE 2.14: ACFDR PAEDIATRICS 2020 – 2023: TOTAL NUMBER OF VISITS RECORDED BY YEAR



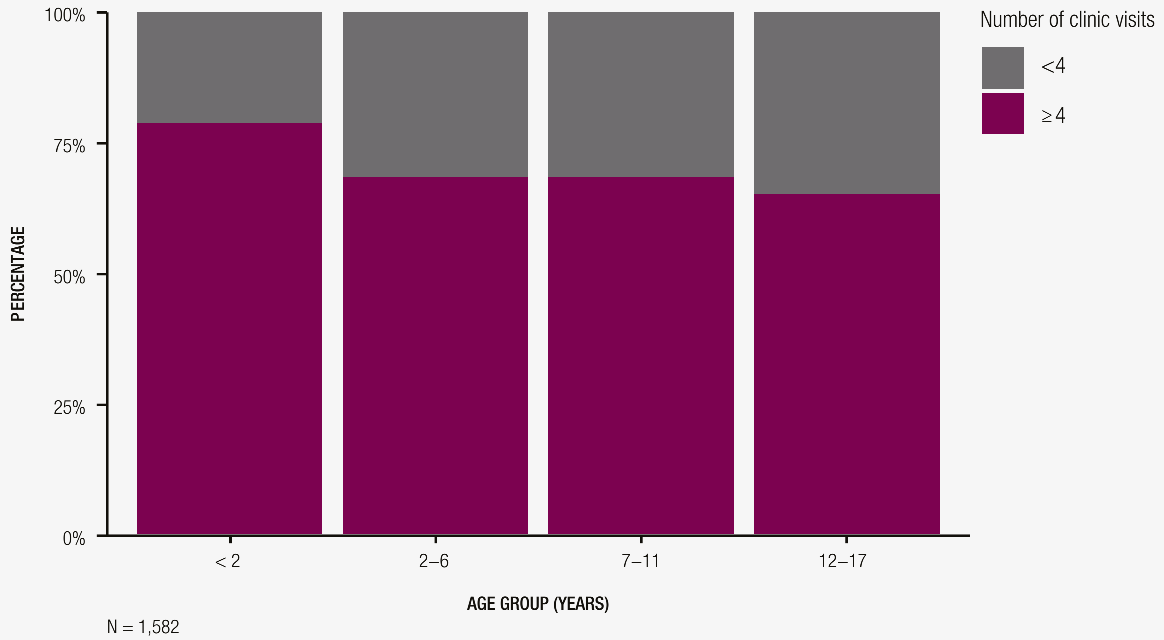
CF Standards of Care

The Australian CF Standards of Care for pwCF recommend four clinic visits (or equivalent) per year. In 2023 the number of children with CF who had at least 4 clinic visits was 1,074 (68.0%) overall, compared to 1,123 (80.0%) in 2021 (Table 2.5). Clinical encounters were highest among children <2 years old at 79.0%, followed by 2 – 6 and 7 – 11 years' old at 68.0%. Adolescents were slightly less likely to have at least 4 clinic visits per year at 65.0% (Figure 2.15).

TABLE 2.5: ACFDR PAEDIATRICS 2021 – 2023: AGE GROUPS WITH 4 OR MORE CLINICAL VISITS

	Number with 4+ clinic visits		
Age	2021	2022	2023 (N = 1,582)
<2	104 (76.9)	101 (70.0%)	100 (79.0%)
2 – 6	276 (79.0%)	263 (66.0%)	274 (68.0%)
7 – 11	398 (69.0%)	277 (62.0%)	298 (68.0%)
12 – 17	435 (70.0%)	415 (66.0%)	402 (65.0%)
Total	1,213 (80.0%)	1,053 (65.2%)	1,074 (68.0%)

FIGURE 2.15: ACFDR PAEDIATRICS 2023: PROPORTION OF PARTICIPANTS HAVING 4 OR MORE CLINICAL VISITS

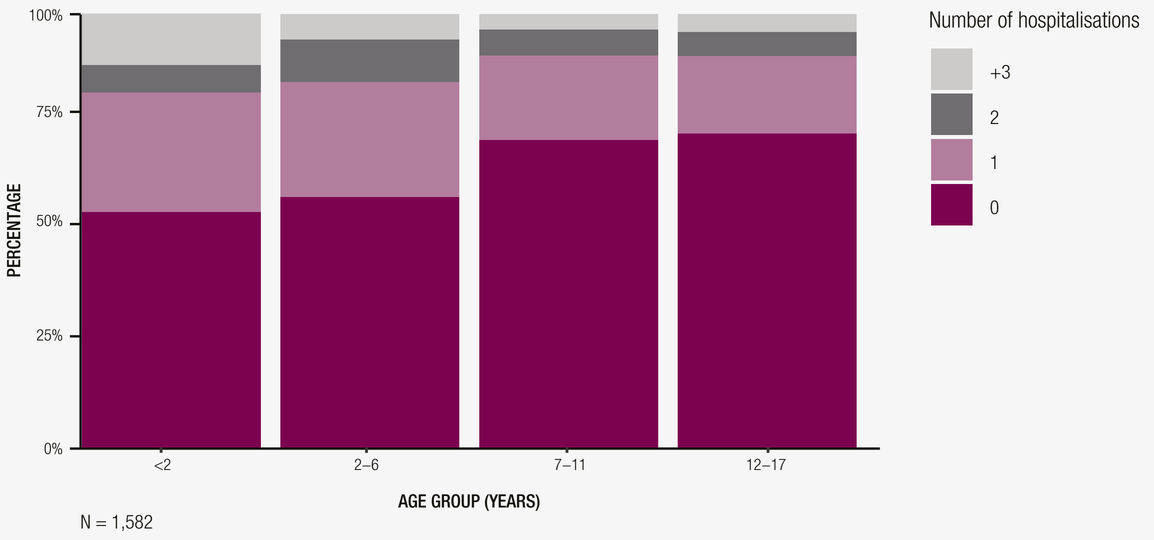


Hospitalisations

There was a total of 856 hospitalisations for children and adolescents in 2023. A majority (54.3%) of children younger than 2 years of age did not have any hospitalisations in 2023, while 27.6% had 1 hospitalisation, 6.3% had 2 hospitalisations, and 11.8% had 3 or more hospitalisations (Figure 2.16). In the 2 – 6-year age range in 2023, 57.9% had no hospitalisations, with 26.4% having 1, 9.7% having 2, and 6.0% having 3 or more hospitalisations.

Lower proportions of hospitalisations were noted for older children and adolescents. For the 7 – 11 age group, over 70% (70.9%) had no hospitalisations, while 19.5% had 1, 6.0% had 2, and 3.7% had at least 3 hospitalisations. Similarly, among adolescents aged 12 – 17, 72.5% had no hospitalisations, while 17.8% had 1, 5.5% had 2, and 4.2% had at least 3 hospitalisations (Figure 2.16). This may be related to the earlier uptake of CFTR modulators in the older paediatric age groups compared to the younger age groups.

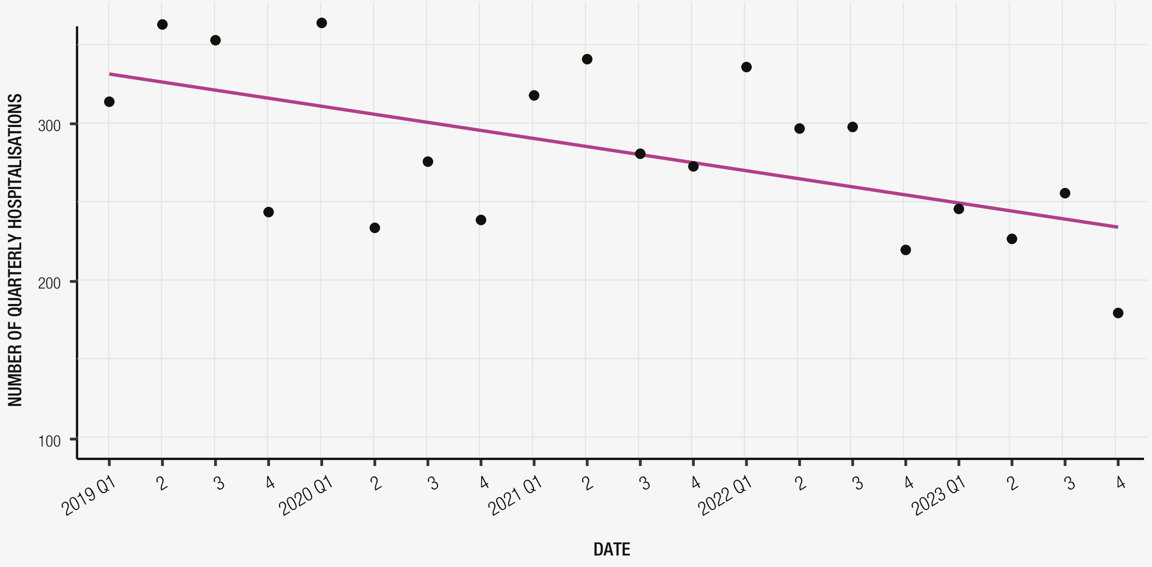
FIGURE 2.16: ACFDR PAEDIATRICS 2019 – 2023: HOSPITALISATIONS BY AGE GROUP



Paediatric Hospitalisations over time

Paediatric hospitalisations have reduced since 2019, showing a decrease from 322 admissions in Quarter 1 of 2019 to 180 admissions in Quarter 4 of 2023, a reduction of 44% over the last 5 years.

FIGURE 2.17: ACFDR PAEDIATRICS 2019 – 2023: HOSPITALISATIONS PER QUARTER



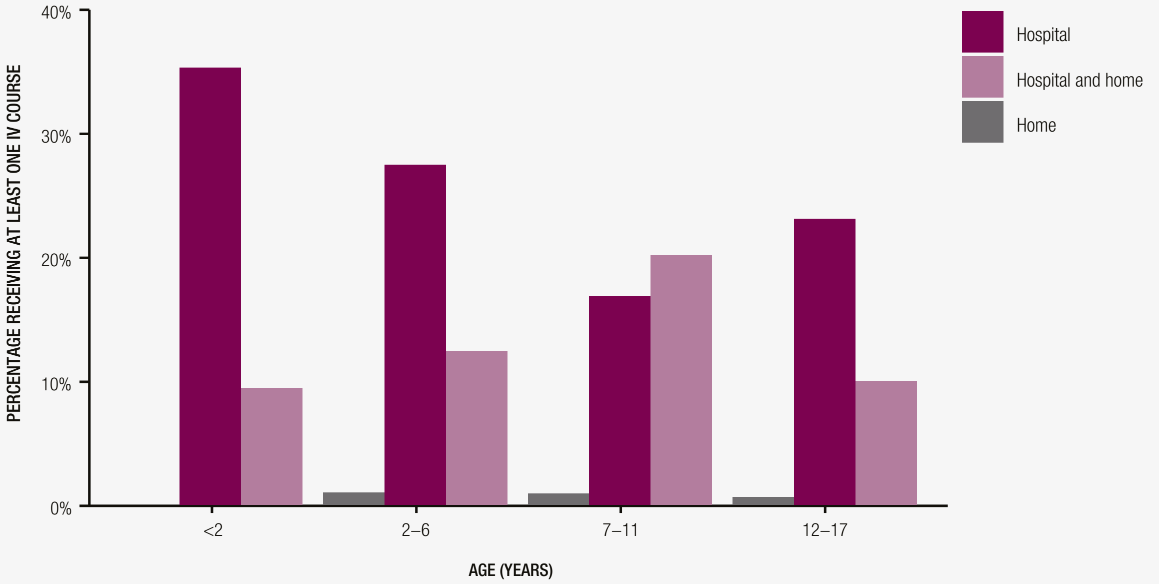
IV Antibiotic therapy

The most common reason for hospitalisations for pwCF is to be treated with IV antibiotics for respiratory exacerbation.

In 2023, the vast majority of IV therapy treatments for children occurred in hospital, with 17.3% of children <2 years, 13.5% of children 2 – 6 years, 8.3% of 7 – 11-year-olds, and 11.3% of 12 – 17-year-olds reporting receiving hospital IV therapy (Fig 2.18).

The use of combined hospital and home IV antibiotics was greatest among 7 – 11-year-olds, at 10.1%, followed by 6.2% of 2 – 6-year-olds, 5% of 12 – 17-year-olds and 4.7% of children less than 2 years of age. In 2023, very few children or adolescents received solely home-based IV therapy, with no children less than 2 years of age and only 0.3 – 0.5% of 2 – 17-year-olds reporting this.

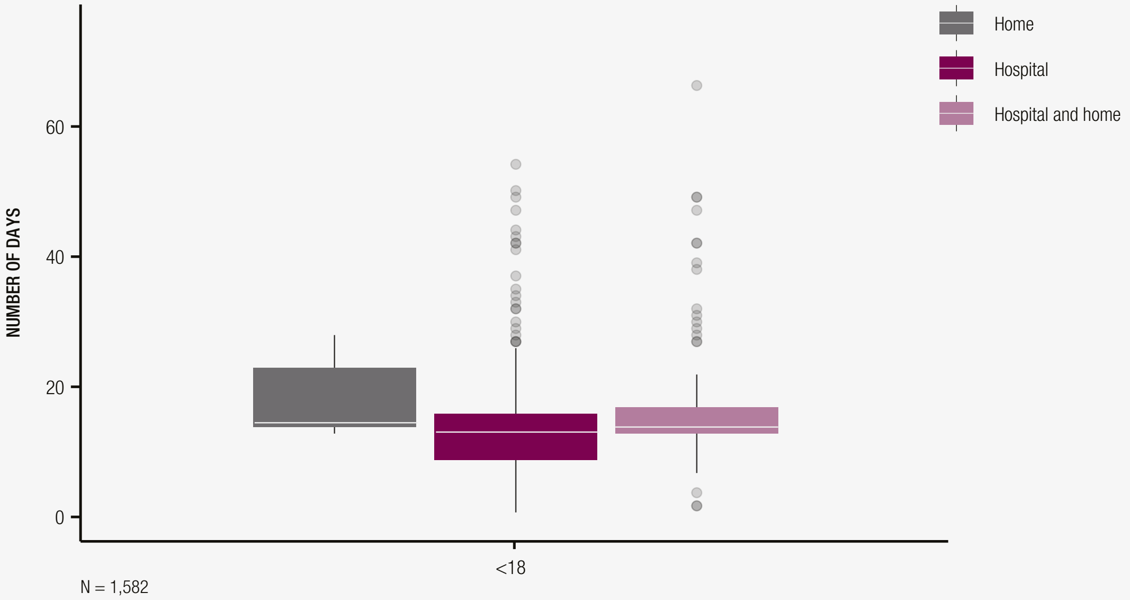
FIGURE 2.18: ACFDR PAEDIATRICS 2023: PARTICIPANTS RECEIVING AT LEAST ONE COURSE OF IV ANTIBIOTIC THERAPY



N = 1,582

The median duration of IV antibiotic therapy in hospital was 13 days, with 14 days for therapy at home or in combination with hospital time (Figure 2.19).

FIGURE 2.19: ACFDR PAEDIATRICS 2023: MEDIAN DAYS IV ANTIBIOTIC THERAPY



N = 1,582

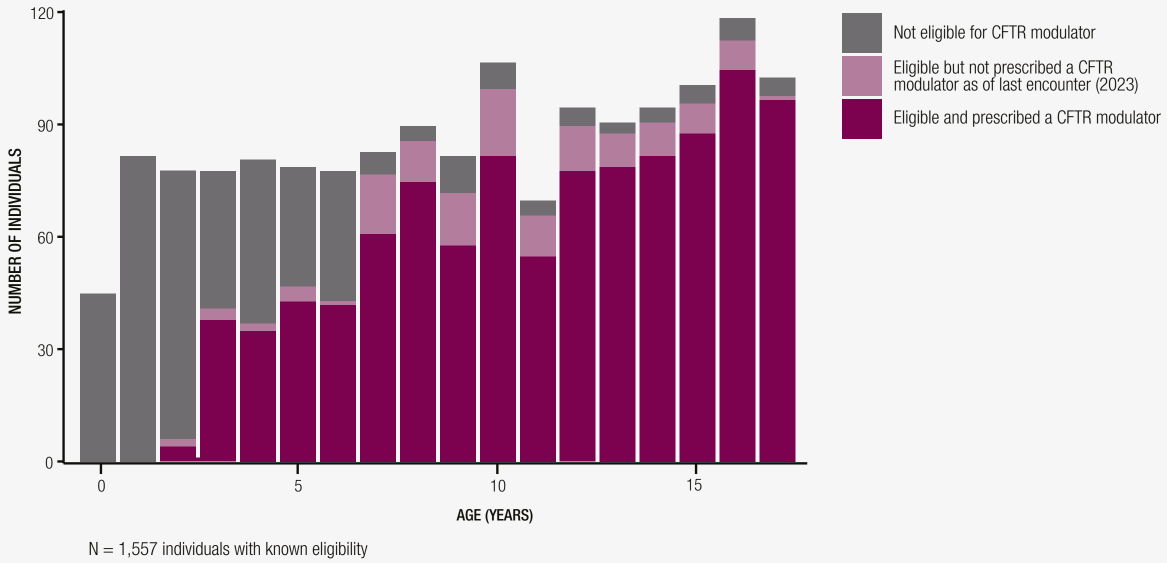
CFTR Modulators

Data were calculated from pwCF who were on a modulator as of 31 December 2023. Data presented here reflect only those pwCF (excluding transplant recipients) who had CFTR modulator data entered into the registry, which generally includes those prescribed modulators available via the PBS.

Of the 1,582 children and adolescents in the registry, eligibility status for a CFTR modulator was known/recorded for 98.4% (1,557 people) in 2023.

Of these, 406 children and adolescents (26.1%) were not eligible for a modulator; 65.6% (1,022 children and adolescents) were eligible and prescribed a modulator; and 8.3% (129 children and adolescents) were eligible and not prescribed a modulator in 2023. Eligibility varies according to age, with 100% of children <12 months ineligible, and nearly all 12-year-olds eligible for a CFTR modulator. Eligibility was determined based on age at the start of the year to identify those eligible during that year, whereas the age groups in the data are defined by age at the end of the year (Figure 2.20).

FIGURE 2.20: ACFDR PAEDIATRICS 2023: CFTR ELIGIBILITY AND PRESCRIBING BY AGE

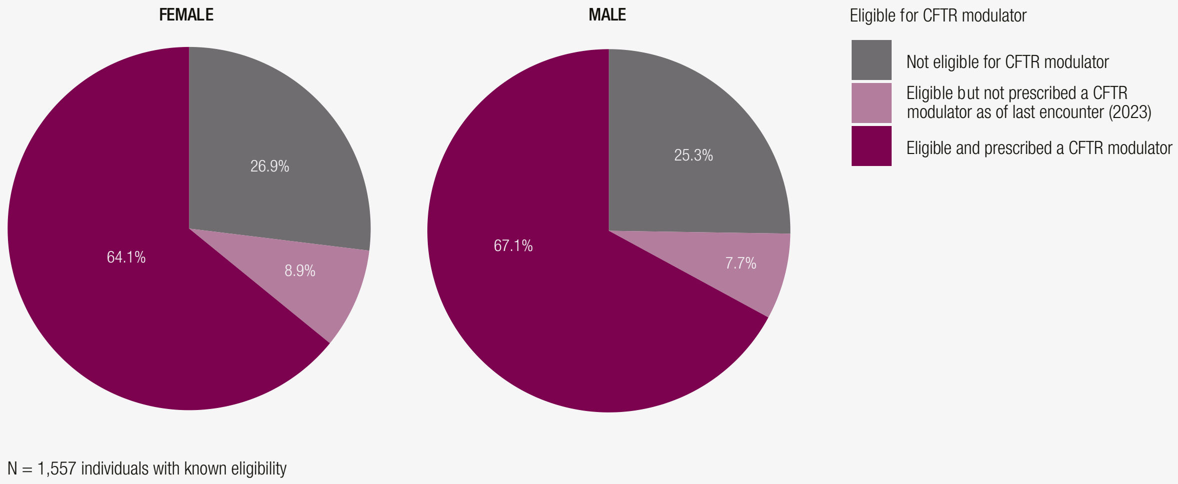


The figures below show the eligibility and prescribing information for male and female children and adolescents with CF. The denominator is 1,557 children and adolescents with CF where eligibility for a modulator is recorded in the registry based on genotype.

Figure 2.21 shows that 26.9% of girls and 25.3% of boys were not eligible for a CFTR modulator. This is a significant decrease compared to 2022, when 39% of females and 41% of males were not eligible.

Of the paediatric population, 64.1% of females and 67.1% of males were eligible and prescribed a modulator, whereas 8.9% of females and 7.7% of males were eligible but not prescribed a modulator.

FIGURE 2.21: ACFDR PAEDIATRICS 2023: ELIGIBILITY AND PRESCRIBING OF CFTR MODULATORS BY GENDER



Ivacaftor (KALYDECO®)

Ivacaftor is available on the Pharmaceutical Benefits Scheme (PBS) for people who have CF, who are aged one year and older, and who have one of the following gating (class III) gene changes in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R. In the tables below the numerator is those on the drug and the denominator is the eligible population (based on genotype).

As of 31 December 2023, 70% of eligible 1 – 5-year-olds and 40% of children aged 6 years or older were prescribed Ivacaftor (Table 2.6). Reasons for discontinuation of Ivacaftor are shown in Table 2.7.

TABLE 2.6: ACFDR PAEDIATRICS 2023: IVACAFTOR USE BY AGE

Age (years)	On Ivacaftor anytime	On Ivacaftor as of 31 Dec 2023	Previously on Ivacaftor and discontinued as of 31 Dec 2023
1 – 5	22/30 (73%)	21/30 (70.0%)	1/30 (3.3%)
≥6	69/80 (86%)	32/80 (40.0%)	37/80 (46.2%)

TABLE 2.7: ACFDR PAEDIATRICS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM IVACAFTOR

N (%)	Reasons for discontinuation/switch in modulator
22 (56.4%)	Other intolerance/adverse events and reasons
15 (38.5%)	Switch to other CFTR modulator
1 (2.6%)	Liver impairment/intolerance

Lumacaftor/Ivacaftor (ORKAMBI®)

Lumacaftor/Ivacaftor is a combination therapy available on the PBS for pwCF, who are aged two years and older, and who have two copies of the F508del gene change in the CFTR gene.

As of 31 December 2023, 87.8% of eligible 2 – 5-year-olds and 36.3% of children aged 6 years or older were prescribed Lumacaftor/Ivacaftor (Table 2.8). Reasons for discontinuation of Ivacaftor are shown in Table 2.9.

TABLE 2.8: ACFDR PAEDIATRICS 2023: LUMACAFTOR/IVACAFTOR USE BY AGE

Age (years)	On Lumacaftor/Ivacaftor anytime	On Lumacaftor/Ivacaftor as of 31 Dec 2023	Previously on Lumacaftor/ Ivacaftor and discontinued as of 31 Dec 2023
2 – 5	133/139 (96%)	122/139 (87.8%)	11/139 (7.9%)
≥6	375/531 (71%)	193/531 (36.3%)	182/531 (34.3%)

TABLE 2.9: ACFDR PAEDIATRICS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM LUMACAFTOR/IVACAFTOR

N (%)	Reasons for discontinuation/switch in modulator
124 (64.2%)	Switch to other CFTR modulator
37 (19.2%)	Other intolerance/adverse events and reasons
19 (9.8%)	Liver impairment/intolerance
9 (4.7%)	Pulmonary side effect/intolerance
4 (2.1%)	Concomitant drug interaction

Tezacaftor/Ivacaftor and Ivacaftor (SYMDEKO®)

Tezacaftor/ivacaftor is also a combination therapy available on the PBS for pwCF, who are aged 12 years and older, and who have one copy of the following changes in the CFTR gene: E56K, R117C, F508del, S977F, F1074L, 3849+10kbC→T, P67L, E193K, D579G, F1052V, D1152H, R74W, L206W, 711+3A→G, K1060T, D1270N, D110E, R352Q, E831X, A1067T, 2789+5G→A, D110H, A455E, S945L, R1070W, 3272 – 26A→G.

As of 31 December 2023, 6.6% of eligible 12 – 17-year-olds were prescribed Lumacaftor/Ivacaftor (Table 2.10). Reasons for discontinuation of Tezacaftor/Ivacaftor are shown in Table 2.11.

TABLE 2.10: ACFDR PAEDIATRICS 2023: TEZACAFTOR/IVACAFTOR USE BY AGE

Age (years)	On Tezacaftor/Ivacaftor anytime	On Tezacaftor/Ivacaftor as of 31 Dec 2023	Previously on Tezacaftor/ Ivacaftor and discontinued as of 31 Dec 2023
12 – 17	87/258 (34%)	17/258 (6.6%)	70/258 (27.1%)

TABLE 2.11: ACFDR PAEDIATRICS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM TEZACAFTOR/IVACAFTOR

N (%)	Reasons for discontinuation/switch in modulator
62 (88.6%)	Switch to other CFTR modulator
7 (10.0%)	Liver impairment/intolerance and reasons
1 (1.4%)	Concomitant drug interaction

Elexacaftor/Tezacaftor/Ivacaftor (TRIKAFTA®)

Elexacaftor/tezacaftor/ivacaftor (ETI) is a triple combination therapy available on the PBS in April 2022 for pwCF aged 6+ years and older, with at least one copy of the F508del gene change in the CFTR gene.

As of 31 December 2023, 77.1% of eligible 6 – 11-year-olds and 87.2% of eligible 12 – 17-year-olds were prescribed Trikafta (Table 2.12). Reasons for discontinuation/change of dose of Ivacaftor are shown in Table 2.13.

TABLE 2.12: ACFDR PAEDIATRICS 2023: ELEXACAFTOR/TEZACAFTOR/IVACAFTOR USE BY AGE

Age (years)	On ETI anytime	On ETI as of 31 Dec 2023	Previously on ETI and discontinued as of 31 Dec 2023
6 – 11	355/450 (79%)	347/450 (77.1%)	8/450 (1.8%)
12 – 17	508/576 (88%)	502/576 (87.2%)	6/576 (1.0%)

TABLE 2.13: ACFDR PAEDIATRICS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM ELEXACAFTOR/TEZACAFTOR/IVACAFTOR

N (%)	Reasons for discontinuation/change
61 (64.1%)	Other intolerance/adverse events and reasons
28 (29.5%)	Liver impairment/intolerance
4 (4.2%)	Switch to other CFTR modulator
1 (1.1%)	Concomitant drug interaction
1 (1.1%)	Pulmonary side effect/intolerance

2.4 COMPLICATIONS AND THERAPIES

CF Pulmonary Disease

In 2023 there were nine children/adolescents who were admitted to hospital with haemoptysis, of which one required embolisation. No children required hospitalisation for pneumothorax in 2023.

CF Pulmonary Therapies — Maintenance Antibiotics

The use of maintenance antibiotic therapy for children and adolescents in 2023 is depicted in Figure 2.22 and Table 2.14. Inhaled antibiotics are more frequently used by older children, with percentages increasing from 11.6% in children under 6 to 16.8% in adolescents aged 12 – 17. Use of regular oral antibiotics decreases with increasing age, from 38.1% in the under 6 group to 23.5% in the 12 – 17 age range, while macrolide use is similar, 12.5% for those under 6 years and 13.6% for those 12 – 17 years.

FIGURE 2.22: ACFDR PAEDIATRICS 2023: MAINTENANCE ANTIBIOTIC THERAPY BY AGE GROUP

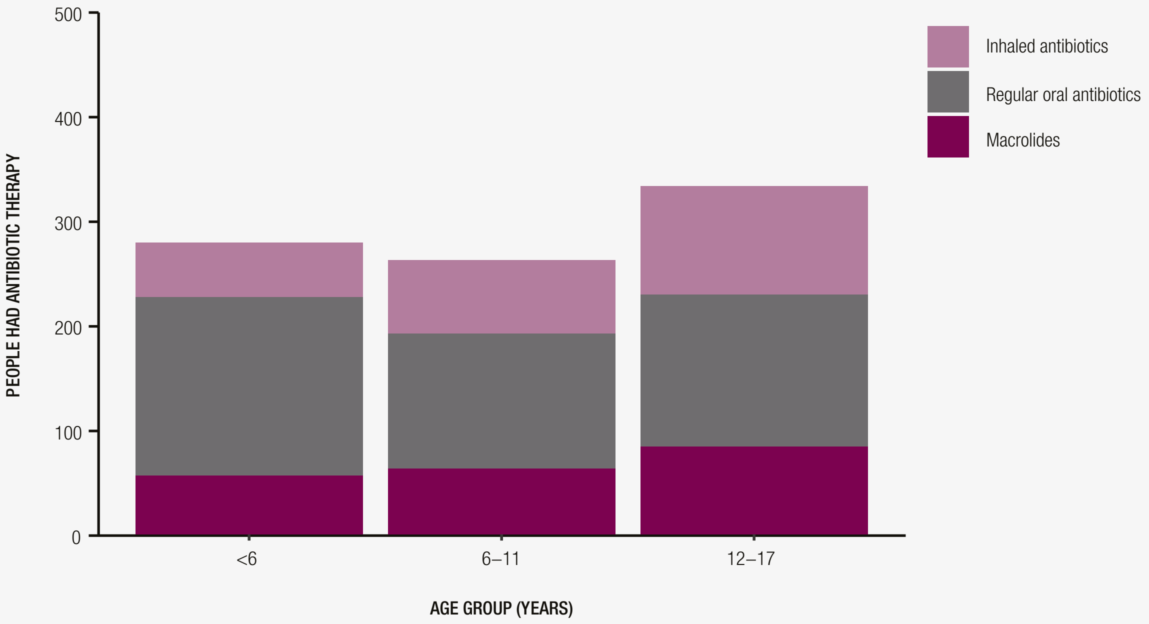


TABLE 2.14: ACFDR PAEDIATRICS 2023: MAINTENANCE ANTIBIOTIC THERAPY BY AGE GROUP

	<6 (N = 449)	6 – 11 (N = 515)	12 – 17 (N = 618)
Inhaled antibiotics	52 (11.6%)	70 (13.6%)	104 (16.8%)
Regular oral antibiotics	171 (38.1%)	129 (25.0%)	145 (23.5%)
Macrolides	56 (12.5%)	63 (12.2%)	84 (13.6%)

CF Lung Therapies — Non-Antibiotic Management

The most used adjuvant lung therapies among children and adolescents are dornase alpha, hypertonic saline and bronchodilators, with use generally increasing with age (Table 2.15). Inhaled corticosteroid use also increases with age, as does inhaled mannitol use. Oral corticosteroids are less commonly used, by approximately 1 – 4% of children and adolescents across the age groups.

TABLE 2.15: ACFDR PAEDIATRICS 2023: NON-ANTIBIOTIC LUNG THERAPIES BY AGE GROUP

	<6 (N = 449)	6 – 11 (N = 515)	12 – 17 (N = 618)
Dornase alpha	146 (32.5%)	368 (71.5%)	450 (72.8%)
Hypertonic saline	126 (28.1%)	238 (46.2%)	262 (42.2%)
Bronchodilators	78 (17.4%)	216 (41.9%)	269 (43.5%)
Inhaled mannitol	0 (0.0%)	7 (1.4%)	61 (9.9%)
Inhaled corticosteroids	31 (6.9%)	79 (15.3%)	133 (21.5%)
Oral corticosteroids	5 (1.1%)	21 (4.1%)	22 (3.6%)
Long term oxygen therapy	0 (0.0%)	0 (0.0%)	2 (0.3%)
Non-invasive ventilation	1 (0.2%)	0 (0.0%)	2 (0.3%)

CF Diabetes

CF-related diabetes is a common complication in adults with CF, but one that may manifest in older children.

The incidence of impaired glucose tolerance reported in 2023 was very low for young children, with 2.1% of children less than 12 reporting impaired glucose tolerance, and 2.0% reporting diabetes. For adolescents 12 – 17 years, the prevalence of these increased to 13.8% and 11.8% respectively. Approximately 90% of children with diabetes were treated with insulin. Most insulin use by children and adolescents was long term (chronic) use (Table 2.16).

TABLE 2.16: ACFDR PAEDIATRICS 2023: DIABETIC STATUS BY AGE GROUP

Diabetic status	<12 (N = 964)	12 – 17 (N = 618)
Normal, (no diabetes or impaired glucose tolerance)	840 (87.1%)	411 (66.5%)
Impaired glucose tolerance	20 (2.1%)	85 (13.8%)
Diabetes	19 (2.0%)	73 (11.8%)
Not known	85 (8.8%)	49 (7.9%)
Diabetes treatment type	<12 (N = 19)	12 – 17 (N = 73)
Insulin	17 (89.5%)	66 (90.4%)
Hypoglycaemics	0 (0.0%)	1 (1.4%)
Insulin and hypoglycaemics	2 (10.5%)	0 (0.0%)
Diet/lifestyle management only	0 (0.0%)	2 (2.7%)
No treatment for diabetes	0 (0.0%)	4 (5.5%)
Insulin use	<12 (N = 19)	12 – 17 (N = 65)
Intermittent insulin use	0 (0.0%)	3 (4.6%)
Chronic insulin use	17 (89.5%)	52 (80.0%)
Insulin use, duration unknown	2 (10.5%)	10 (15.4%)

CF Gastrointestinal Disease

Gastrointestinal complications of CF are not common in children and adolescents. In 2023, the most common gastrointestinal complication among children was gastroesophageal reflux, at 8.2% of <12-year-olds, and 10.2% of 12 – 17-year-olds. Less than 5% of children recorded hepatic complications in 2023 (Table 2.17).

TABLE 2.17: ACFDR PAEDIATRICS 2023: STOMACH AND LIVER DISEASE

	<12	12 – 17
Gastroesophageal reflux	78/964 (8.2%)	63/618 (10.2%)
Liver disease, non-cirrhosis (includes viral hepatitis, fatty liver)	24/921 (2.6%)	28/575 (4.9%)
Liver disease, cirrhosis (image confirmed)	8/905 (0.9%)	13/560 (2.3%)
Liver disease, cirrhosis with portal hypertension	8/905 (0.9%)	14/561 (2.5%)

In 2023, pancreatitis was very uncommon among children, with ≤1% of children/teenagers reporting acute or recurrent pancreatitis (Table 2.18). However, 74.6% of children <12 years, and 79.6% of adolescents 12 – 17 years reported pancreatic insufficiency.

TABLE 2.18: ACFDR PAEDIATRICS 2023: PANCREATITIS BY AGE

Pancreatitis	<12 (N = 945)	12 – 17 (N = 604)
Acute (first pancreatitis event this current year)	5 (0.5%)	2 (0.3%)
No history of pancreatitis	938 (99.3%)	601 (99.5%)
Recurrent pancreatitis (history of more than one event of pancreatitis)	2 (0.2%)	1 (0.2%)
Pancreatic status		
Insufficient	719 (74.6%)	492 (79.6%)

Osteopenia and Bone Density

Bone mineral density scans are not routinely performed on children younger than 10 years unless clinically indicated. For adolescents older than 10 years who had their bone density status reported to the ACFDR in 2023, 25.0% had osteopenia, 3.0% had osteoporosis, and 3.7% reported a fracture (Table 2.19).

TABLE 2.19: ACFDR PAEDIATRICS 2023: BONE DENSITY FOR ADOLESCENTS

Bone mineral density	10 – 17 (N = 100)
Normal	72 (72.0%)
Osteopenia	25 (25.0%)
Osteoporosis	3 (3.0%)
Fracture	29 (3.7%)

Nutritional Supplementation

Table 2.20 reveals the usage of pancreatic enzymes and nutritional supplements across age groups in 2023. For those under 12, 73.8% used pancreatic enzymes, 76.3% took fat-soluble vitamin supplements, and 61.7% used salt replacement therapy. Among 12 to 17-year-olds, 77.0% used pancreatic enzymes, 75.1% took vitamin supplements, and 61.3% used salt replacement therapy.

TABLE 2.20: ACFDR PAEDIATRICS 2023: NUTRITIONAL SUPPLEMENTS BY AGE

	<12 (N = 964)	12 – 17 (N = 618)
Pancreatic enzymes	711 (73.8%)	476 (77.0%)
Vitamin supplements (Fat soluble vitamins A, D, E and K)	736 (76.3%)	464 (75.1%)
Salt replacement therapy	595 (61.7%)	379 (61.3%)

The use of nutritional support among children and adolescents in 2023 was low (Table 2.21). Eight percent of children aged less than 12 years and six percent of children aged 12 or greater required oral supplements. Otherwise, nutritional support was uncommon.

TABLE 2.21: ACFDR PAEDIATRICS 2023: NUTRITIONAL SUPPORT BY AGE

	<12 (N = 964)	12 – 17 (N = 618)
Oral	81 (8.4%)	30 (6.1%)
Gastrostomy tube	35 (3.6%)	47 (7.5%)
Nasogastric tube	12 (1.2%)	3 (0.5%)
Jejunostomy tube	1 (0.1%)	0 (0.0%)
Parenteral nutrition	4 (0.4%)	2 (0.3%)

Multidisciplinary Care

Multidisciplinary care is a cornerstone of effective, contemporary CF management. In 2023, a majority of children and adolescents participated in an annual physiotherapy appointments and dietician review (Table 2.22). Approximately half of the children with CF had a social work review annually, approximately one quarter had a mental health screen or review (for children 12 years or older) or a gastroenterology review. Proportions who had reviews are generally similar for younger children and adolescents except for endocrine reviews, which were performed for nearly 20% of adolescents but only 3% of younger children.

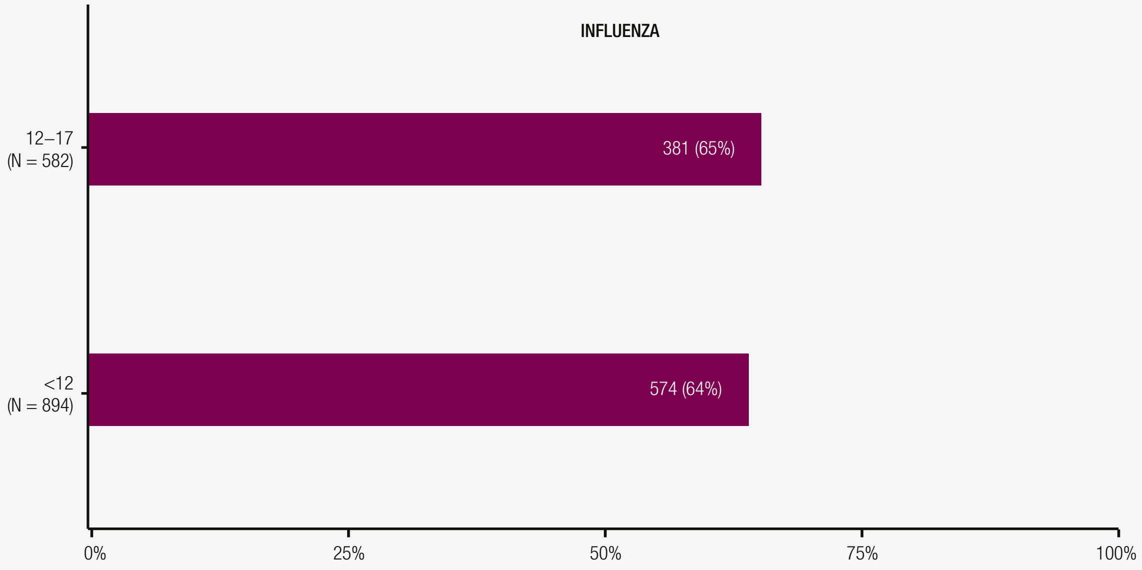
TABLE 2.22: ACFDR PAEDIATRICS 2023: ANNUAL MULTIDISCIPLINARY CARE APPOINTMENTS BY AGE GROUP

Preventive care	<12 (N = 964)	12 – 17 (N = 618)
Physiotherapy review	909/960 (94.7%)	590/617 (95.6%)
Dietitian review	823/964 (85.4%)	522/618 (84.5%)
Social work review	540/964 (56.0%)	323/618 (52.3%)
Mental health review	NA	167/951 (27.6%)
Gastroenterologist review	235/964 (24.4%)	160/618 (25.9%)
Endocrine review	32/964 (3.3%)	120/618 (19.4%)

Preventive Care: Vaccinations

Influenza immunisation is recommended for individuals with CF aged six months and older on an annual basis. Sixty-five percent of children aged 12 – 17 years, and 64.0% of children aged less than 12 years were recorded as being immunised against influenza in 2023 (Figure 2.23). This is the same proportion as that recorded by the registry in 2022.

FIGURE 2.23: ACFDR PAEDIATRICS 2023: VACCINATIONS BY AGE GROUP



3.

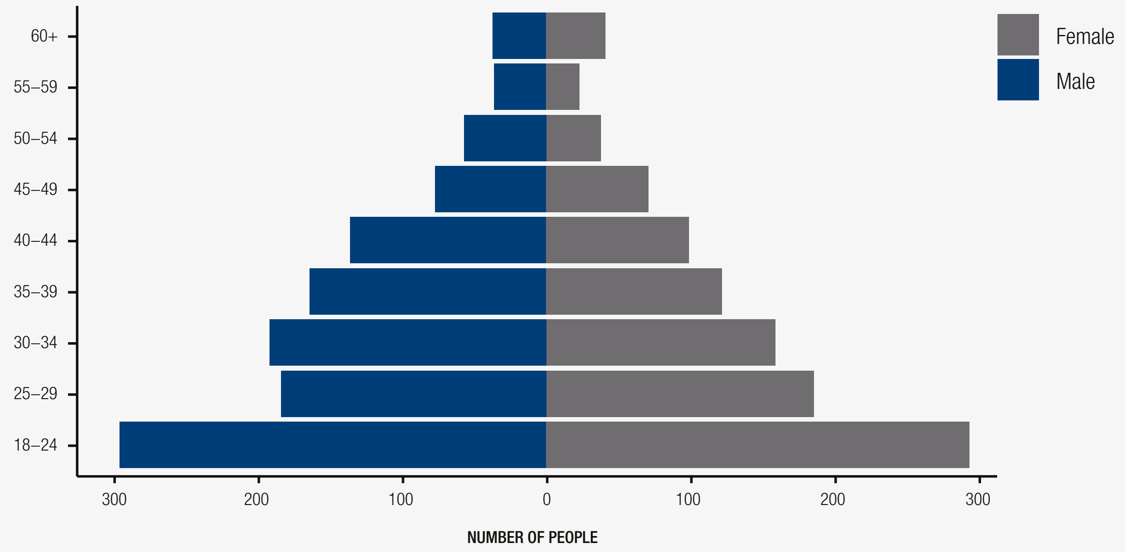
ADULT DATA

3. ADULT DATA

3.1 ADULTS WITH CYSTIC FIBROSIS

As of 31 December 2023, the ACFDR held data regarding 2,212 adults with CF, of which 1,033 were female and 1,179 were male. This chapter discusses management and clinical outcomes of adult patients in the registry (Figure 3.1).

FIGURE 3.1: ACFDR ADULTS 2023: AGE AND SEX



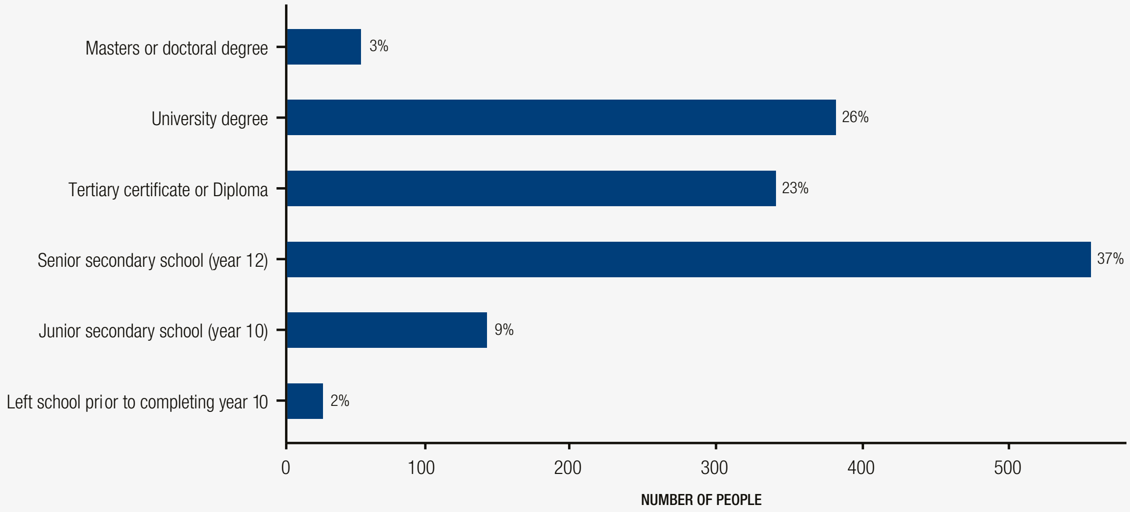
N = 2,212 people

Socioeconomic Characteristics

Educational Attainment

Of the 1,465 (66.0%) adults with CF for whom education information was available in the ACFDR in 2023, 26.0% had completed a university degree (an increase from 21.0% in 2022) and 23.0% had completed a tertiary certificate or diploma (an increase from 21.0% in 2022). Thirty-seven percent of adults nominated senior secondary school as their highest educational attainment, a decrease from 40.0% in 2022 (Figure 3.2).

FIGURE 3.2: ACFDR ADULTS 2023: HIGHEST EDUCATIONAL ATTAINMENT



N = 1,465 people aged ≥18 years

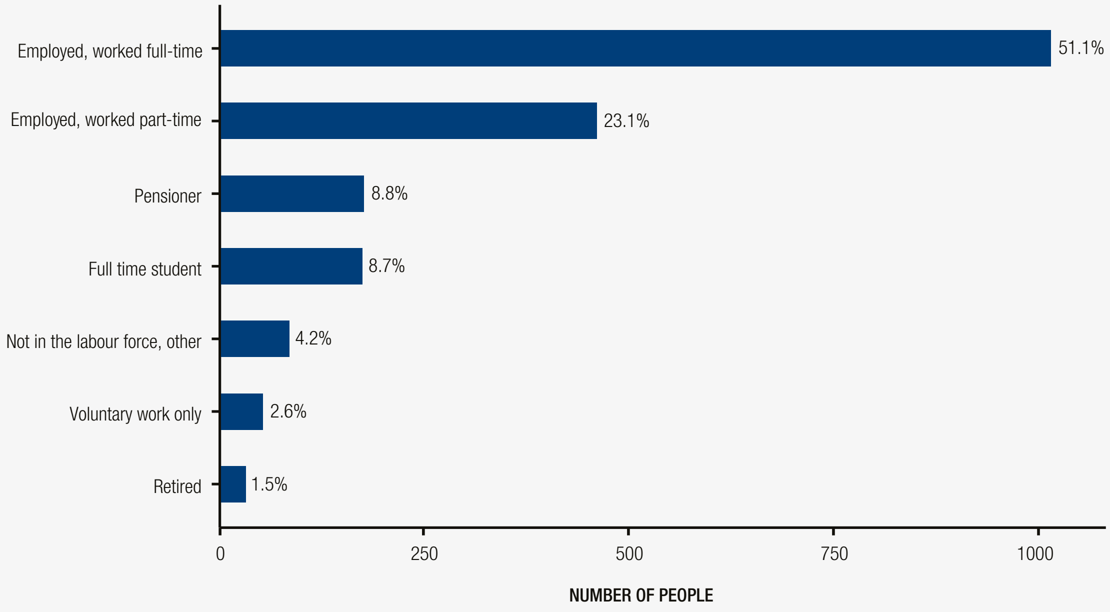
Table 3.1 compares the level of educational attainment of pwCF to the broader Australian Population (Australian Bureau Statistics (ABS) data as of May 2023). Senior secondary school was the most common educational attainment level for pwCF, followed by a bachelor degree; compared to the general population where a tertiary certificate or diploma was the most common educational attainment followed by a Bachelor degree. However, as noted above, educational attainment for pwCF has been increasing in recent years.

TABLE 3.1: ACFDR ADULTS 2023: HIGHEST EDUCATIONAL ATTAINMENT

Highest educational attainment	ACFDR (N = 1,465)	ABS data (%), May 2023 for 15 – 74-year olds
Masters or doctoral degree	50 (3.0%)	8.1%
University/Bachelor degree	374 (26.0%)	20.3%
Tertiary certificate or Diploma	333 (23.0%)	30.4%
Senior secondary school (year 12)	458 (37.0%)	18.1%
Junior secondary school (year 10)	136 (9.0%)	9.8%
Left school prior to completing year 10	24 (2.0%)	6.0%

Within the ACFDR dataset, information on employment status was available for 1,980 adults (89.5%) with CF. Among them, 51.0% were engaged in full-time employment (compared with 44% in 2022), 23.0% were in part-time employment (compared to 25.0% in 2022), and 9.0% were enrolled in full-time study (compared to 13.0% in 2022) (Figure 3.3).

FIGURE 3.3: ACFDR ADULTS 2023: EMPLOYMENT STATUS

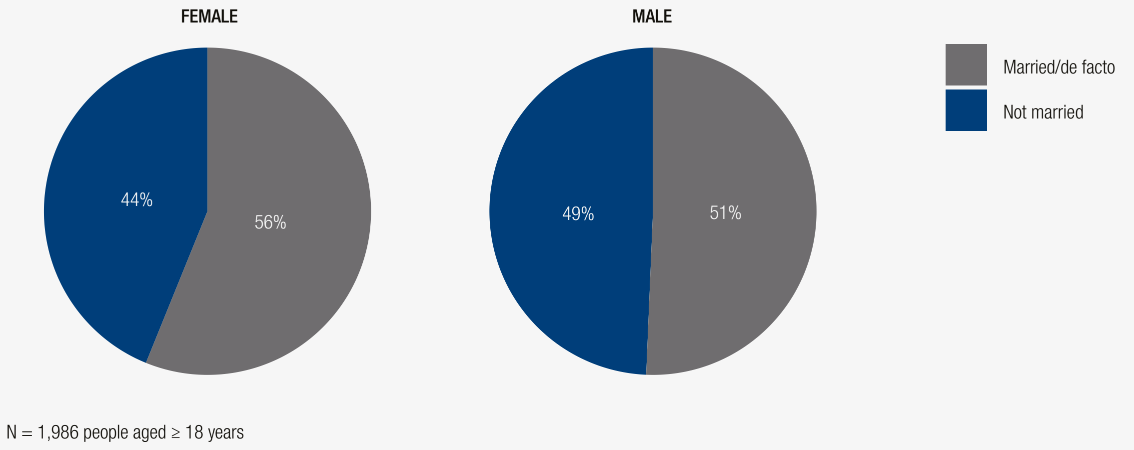


N = 1,980 people aged ≥18 years with data recorded

Marital Status

Information regarding marital status was available for 1,986 adults in the registry (90.0%). Of these, 56.0% of women and 51.0% of men were either married or in a de facto relationship (Figure 3.4), a significant increase from the previous year.

FIGURE 3.4: : ACFDR ADULTS 2023: MARITAL STATUS

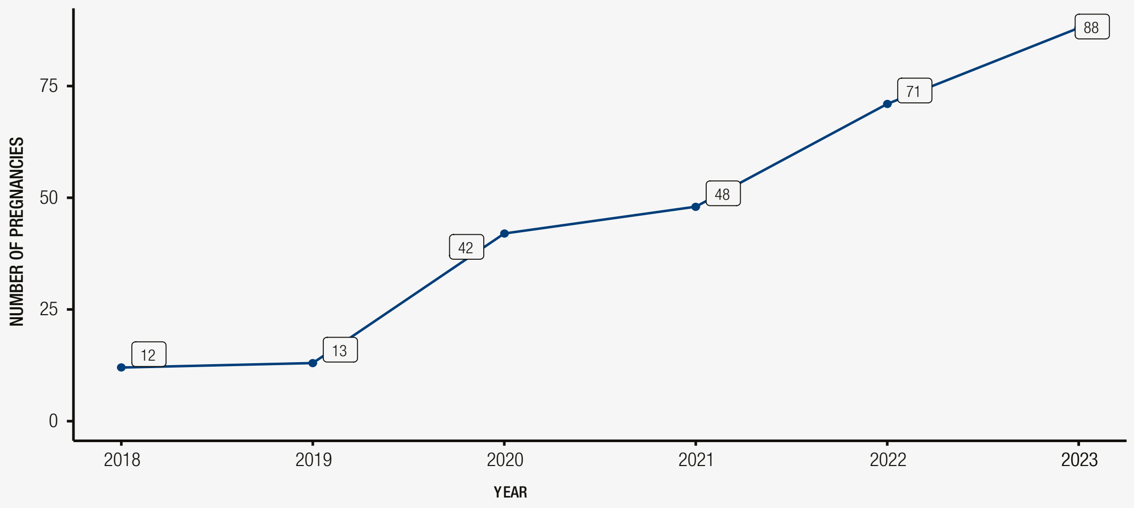


Pregnancies for People with CF

From this point in the clinical data, adults with lung transplants (N = 144) have been excluded from the analysis.

In 2023, new pregnancies continued to increase, with 88 new pregnancies, an additional 17 from the 71 recorded in 2022 (Figure 3.5). There were 37 (51.7%) live births and 31 (43.1%) people still pregnant as of 31 December 2023 (Table 3.2).

FIGURE 3.5: ACFDR ADULTS 2023: PREGNANCY



Based on the annual general update and sign off data

TABLE 3.2: ACFDR ADULTS 2023: PREGNANCY STATUS

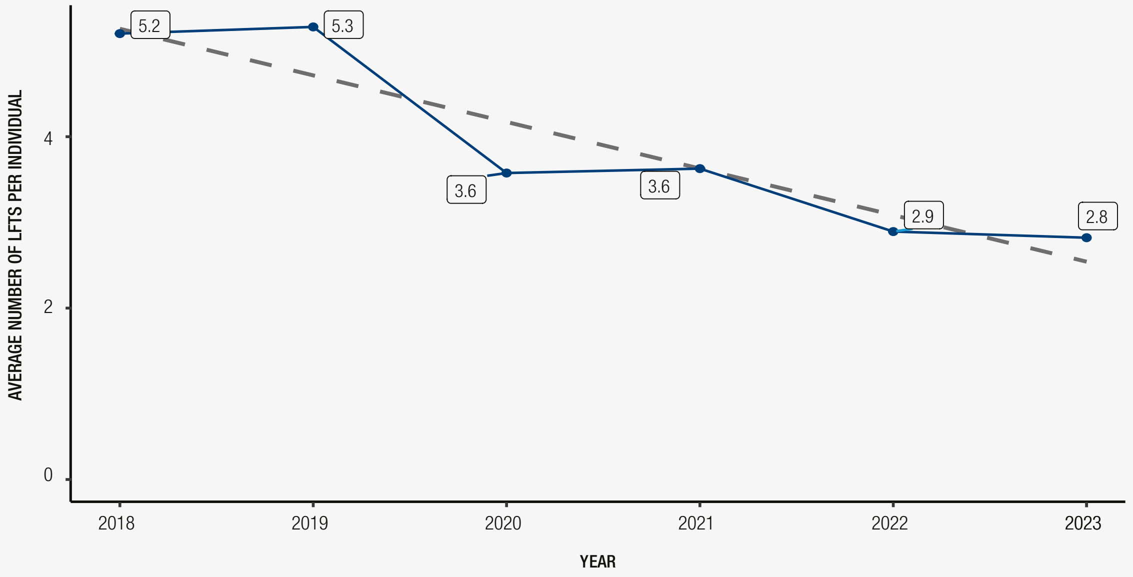
Status	≥18 (N = 88)
Currently pregnant	31 (43.1%)
Live birth	37 (51.7%)
Other (Miscarriage, stillbirth or termination/unknown outcome)	<5 (5.5%)

3.2 CLINICAL MEASURES

Lung Function

Figure 3.6 depicts the annual average number of lung function (spirometry) tests per adult recorded in the registry from 2018 to 2023. In 2018, adults averaged 5.2 tests each, however data from 2023 indicates there was an average of 2.8 tests per adult.

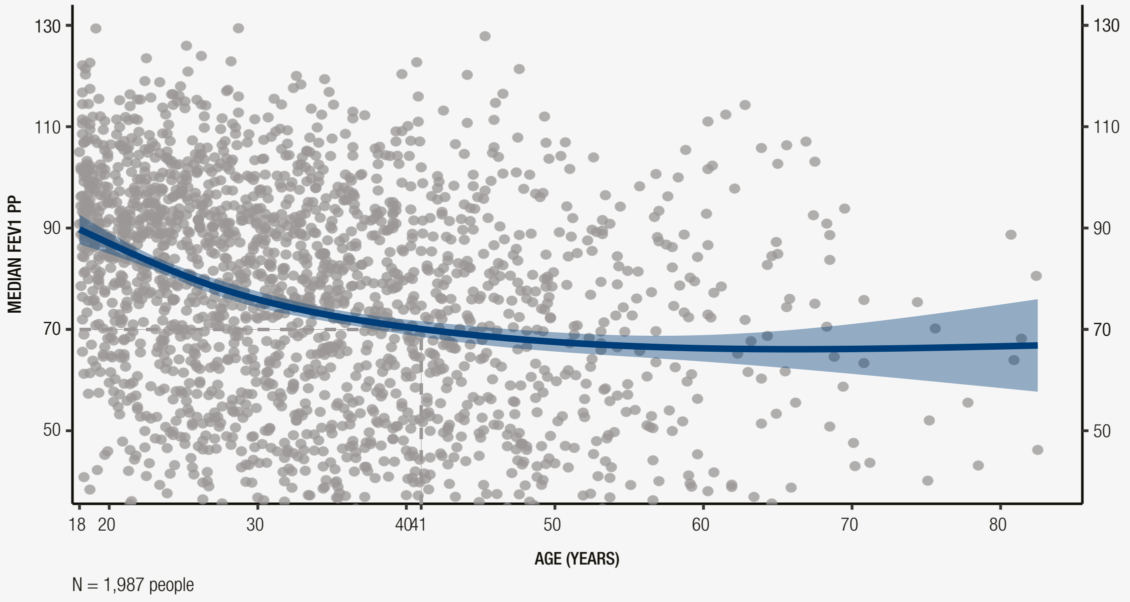
FIGURE 3.6: ACFDR ADULTS 2018 – 2023: AVERAGE NUMBER LUNG FUNCTION TESTS ENTERED PER INDIVIDUAL



Straight dashed line represents the overall trend estimated by a linear regression model

There were 1,987 (90%) adults in 2023 in the registry who had their lung function measures recorded. The adult lung function results reveal a progressive decline in median FEV1 pp with increasing age (Figure 3.7). The median age at which an FEV1 pp of 70.0 is recorded was 40 years in 2023, an increase from 36 years in 2022.

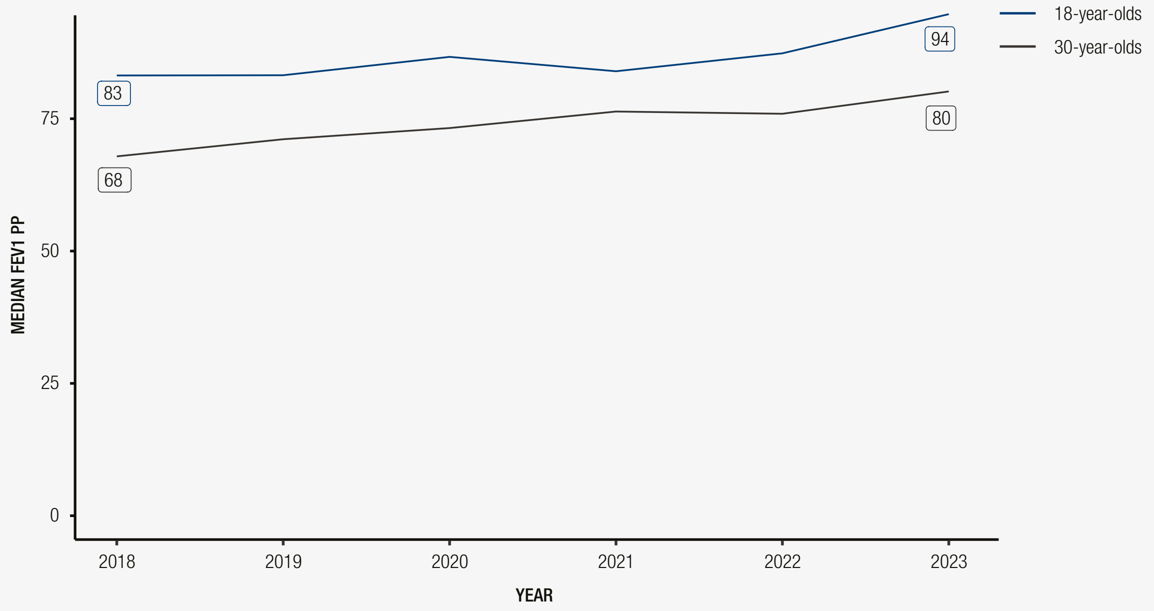
FIGURE 3.7: ACFDR ADULTS 2023: FEV1 PP BY AGE



The solid trend line was estimated using a natural cubic spline with 3 degrees of freedom
Shaded area represent the 95% confidence intervals

The median FEV1 pp has increased over time. For 18-year-olds, it has increased from 83pp in 2018 to 94pp in 2023, an 11% increase. For pwCF of age 30 years, the median FEV1 pp in 2023 was 80, an increase of 12% from 68 in 2022 (Figure 3.8).

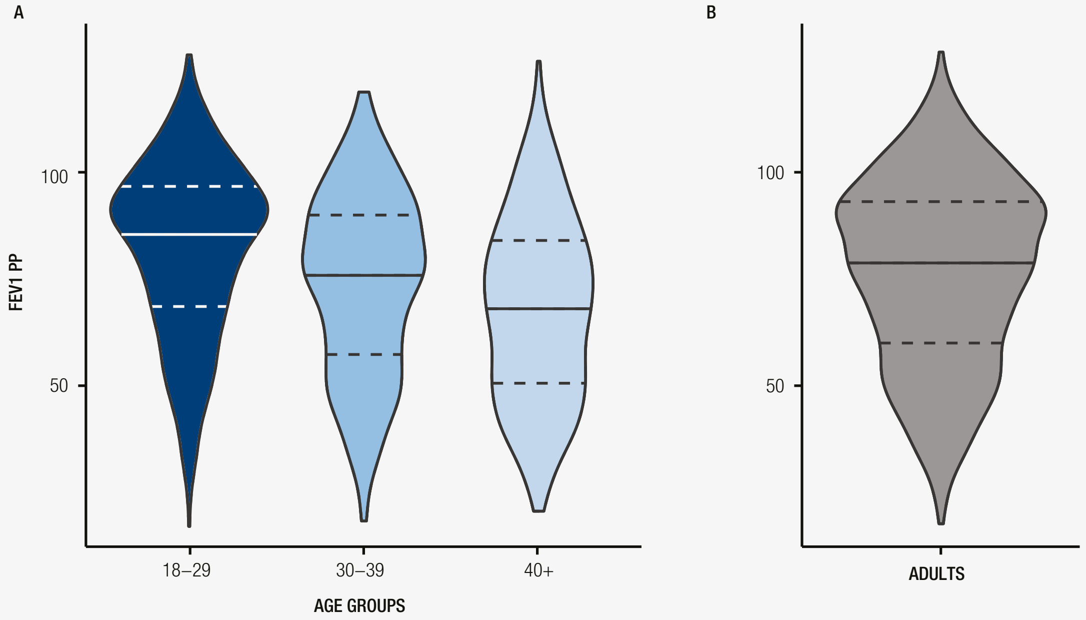
FIGURE 3.8: ACFDR ADULTS 2018 – 2023: MEDIAN FEV1 PP OVER TIME



Labelled percentages illustrate median predFEV1 in 2003 and 2023
Dashed line represents all age groups

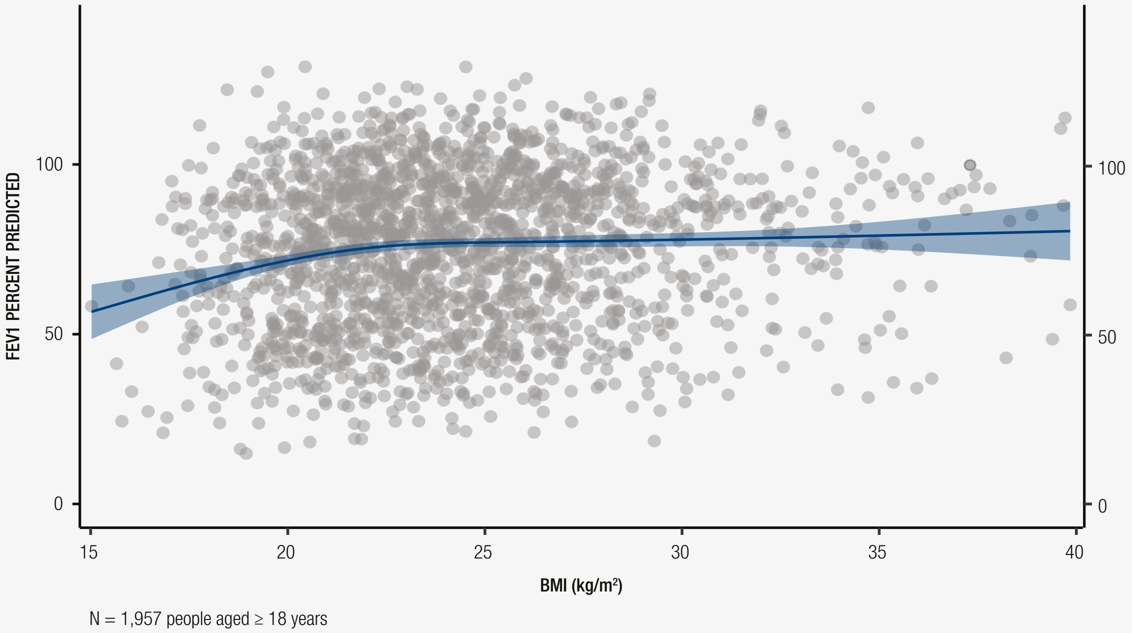
In 2023, the median FEV1 pp for adults overall was 78.6 (Figure 3.9 B), with the median FEV1 pp for 18 – 29 -year-olds being 86.7; for 30 – 39-year olds being 76.3, and for 40+-year-olds being 67.8 (Figure 3.9).

FIGURE 3.9: ACFDR ADULTS 2023: MEDIAN FEV1 PP



For pwCF ages 18 – 40 years, FEV1 pp increased with increasing BMI, although, at BMIs into the high 20's, this appears to variably affect FEV1 pp. PwCF over 40 years are not included due to fewer numbers which makes the data difficult to interpret due to increased variability (Figure 3.10).

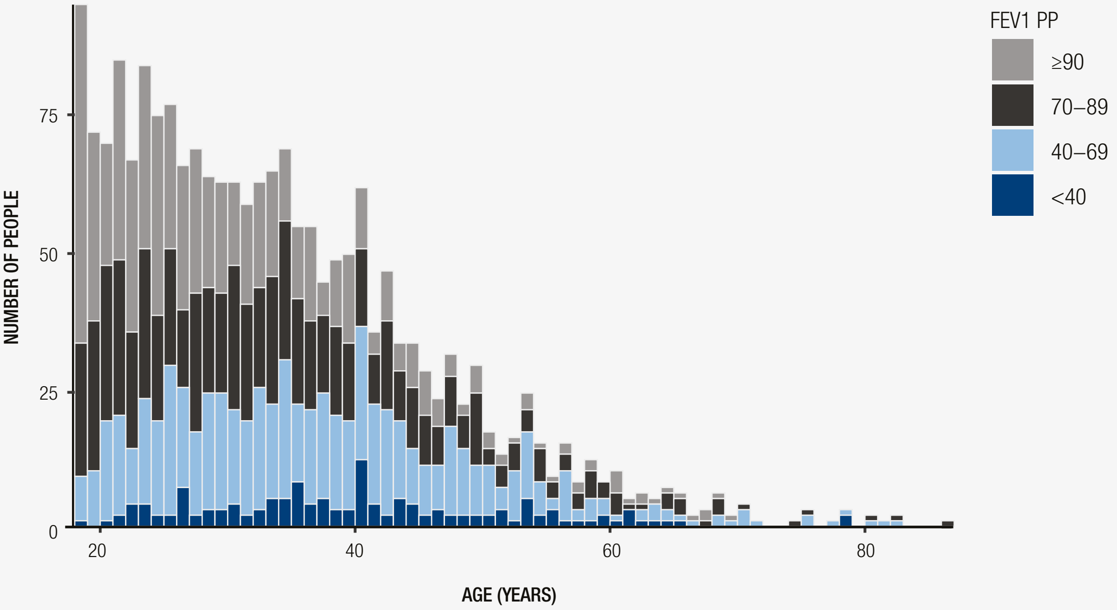
FIGURE 3.10: ACFDR ADULTS 2023: FEV1 PP VS BMI PERCENTILE



Solid line was calculated using a natural cubic spline with 3 degrees of freedom
Shaded area represents 95% confidence interval

There is variation in lung function from the median in individuals with CF (Figure 3.11). For 18 – 29-year-olds, 42% have an FEV1 pp of ≥90%, 31% have an FEV1 pp of 70 – 89%, 23% have an FEV1 pp of 40 – 69pp, and 3.5% have FEV1 pp of <40pp. For those aged 30 – 39 years, the most common FEV1 pp range is 70 – 89 pp (at 34%), followed by 40 – 69 pp (at 32%), ≥90% (at 26%), and 7.5% at <40 pp. For adults 40 years and older, the most common FEV pp range is 40 – 69 pp (at 41%), followed by 70 – 89 pp (at 30%), ≥90% pp at 17%, and <40 pp at 13% of the cohort.

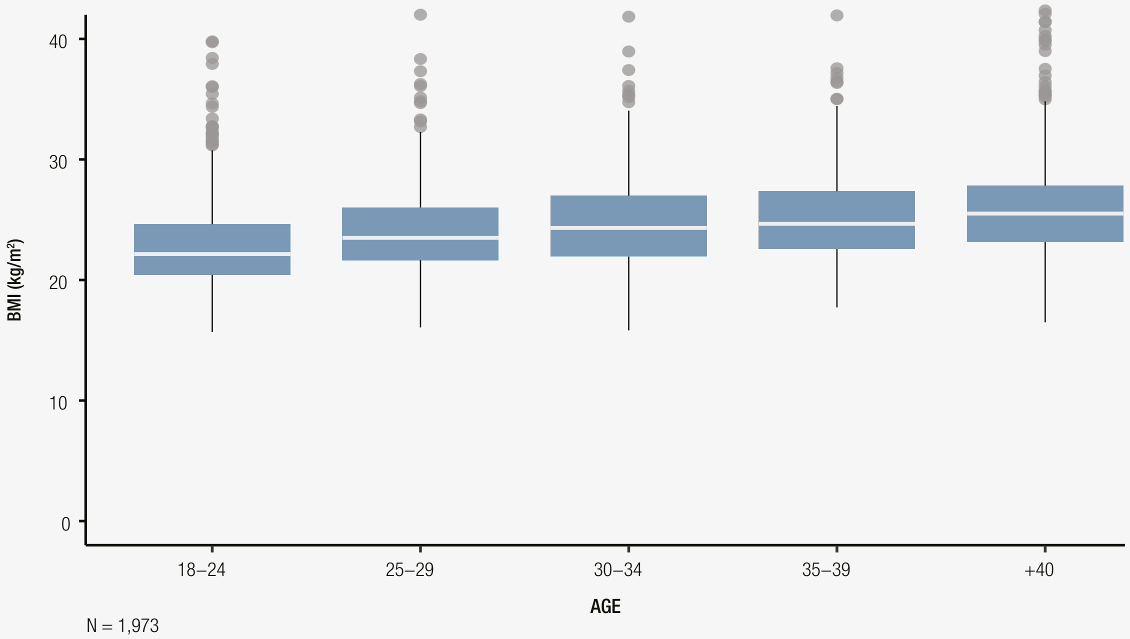
FIGURE 3.11: ACFDR ADULTS 2023: LUNG FUNCTION VARIABILITY



Nutrition (Body Mass Index)

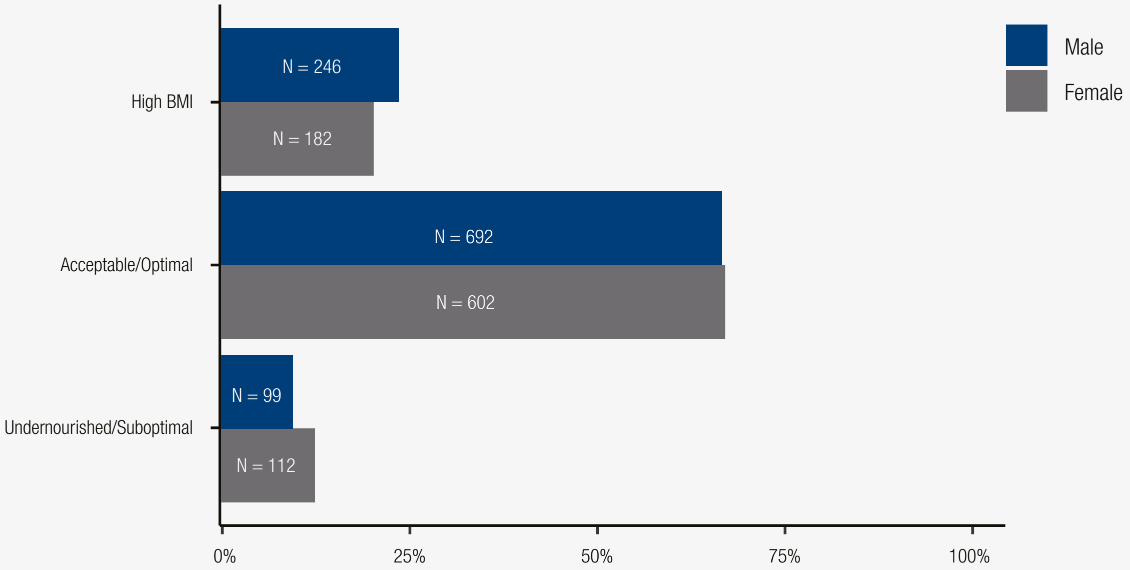
Body Mass Index (BMI) data for adults with CF increases with increasing age. For 2023, in the 18 – 24 age group, the median BMI was 22.1, for the 25 – 29 age group it was 23.4, for 30 – 34 age group it was 24.3 and for 35 – 39 age group it was 24.6. The highest median BMI was observed in the 40 and above age category, with a value of 25.4 (Figure 3.12).

FIGURE 3.12: ACFDR ADULTS 2023: BMI BY AGE



Approximately two-thirds of adults with CF have a BMI in the optimal/acceptable range recorded in 2023 (66.7% of males and 67.2% of females). Approximately 23.7% of males and 20.3% of females have a high BMI, while 12.5% of females and 9.5% of males have a suboptimal BMI (Figure 3.13).

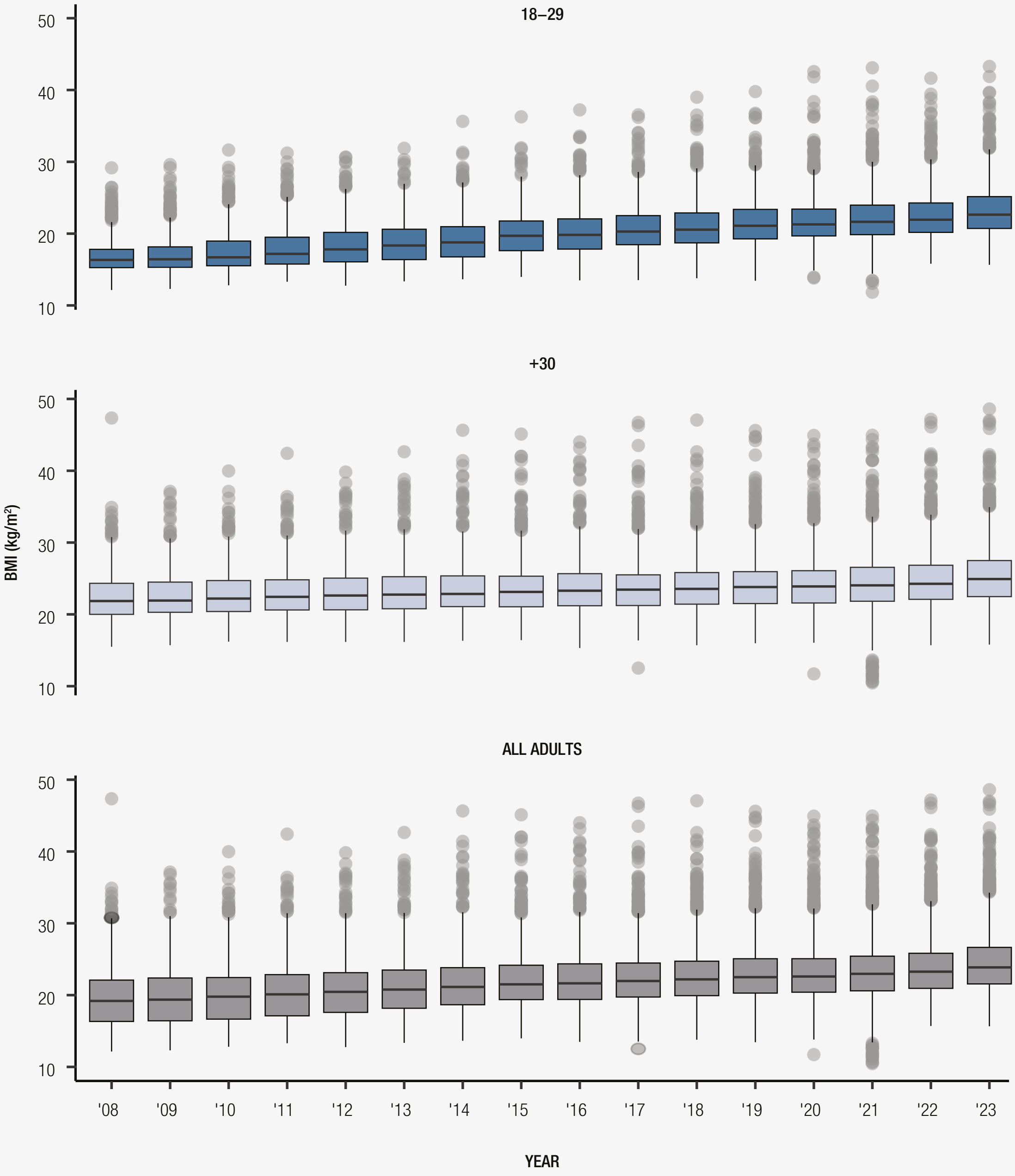
FIGURE 3.13: ACFDR ADULTS 2023: BMI BY SEX



High BMI: BMI >27 kg/m²
Optimal: Female BMI 22–27 kg/m², Male BMI 23–27 kg/m²
Acceptable: Female BMI 20–22 kg/m², Male BMI 20–23 kg/m²
Suboptimal: BMI <20 kg/m²
Undernourished: BMI <18.5 kg/m²

The BMI data for the adult CF population, revealed a consistent upward trajectory over the years. In the 18 – 29 age group, the median BMI has risen steadily from 16.3 in 2008 to 22.6 in 2023. A similar pattern was observed in the 30-year age group, where the median BMI increased from 21.9 in 2008 to 24.9 in 2023. When considering all adults with CF, the overall median BMI has showed a continuous increase from 19.2 in 2008 to 23.9 in 2023 (Figure 3.14).

FIGURE 3.14: ACFDR ADULTS 2008 – 2023: MEDIAN BMI

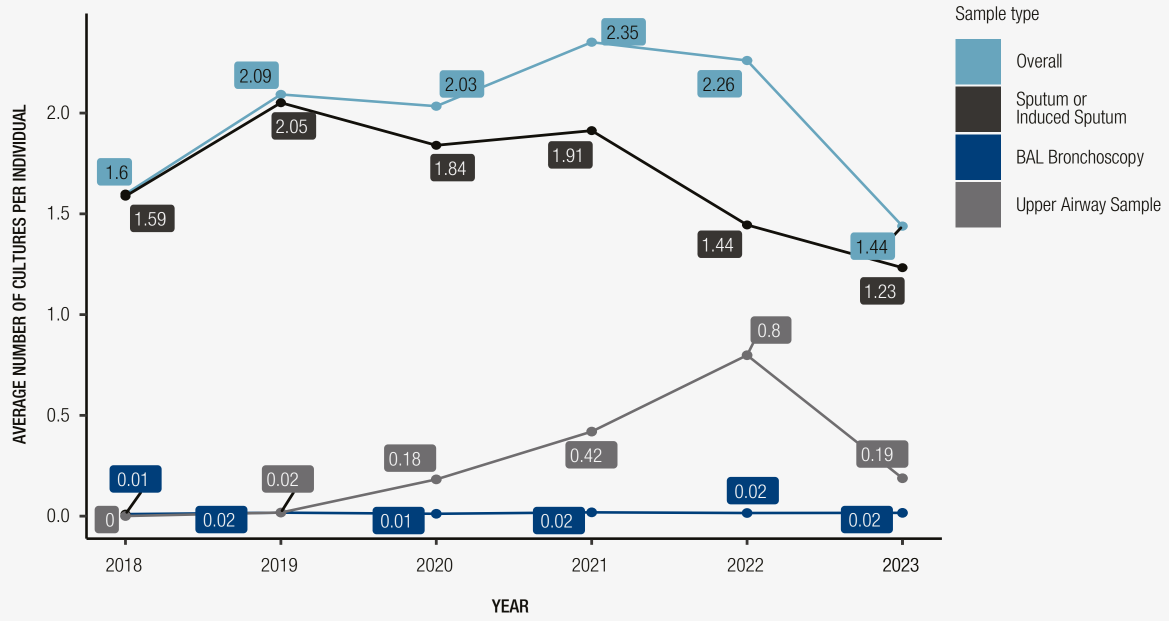


Microbiology

Microbiology Samples

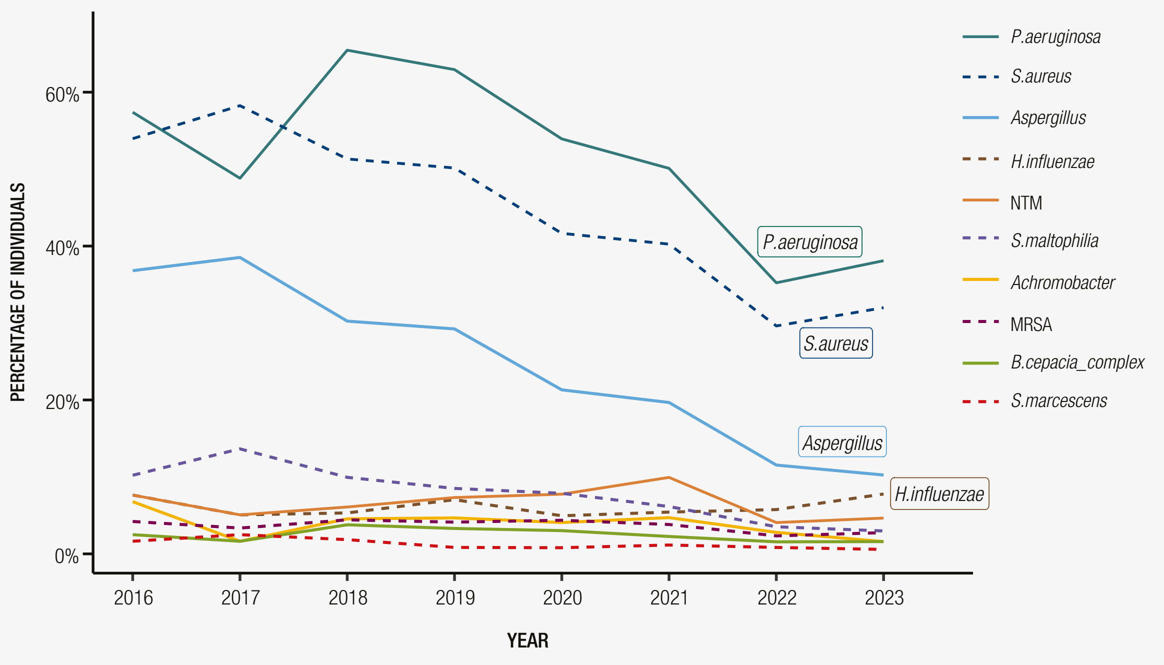
The average number of respiratory samples collected per adult from 2018 to 2023 is depicted in Figure 3.15. From 2018 to 2023 there was an increase in the overall number of respiratory samples per adult (peaking at 2.35 in 2021), however this has declined significantly in 2023 to an average of 1.44 samples. The most common respiratory samples collected for adults are sputum/induced sputum, which has followed this trend. Upper airway samples also increased from 2018 to 2022, however declined in 2023.

FIGURE 3.15: ACFDR ADULTS 2018 – 2023: AVERAGE NUMBER OF RESPIRATORY SAMPLES PER INDIVIDUAL



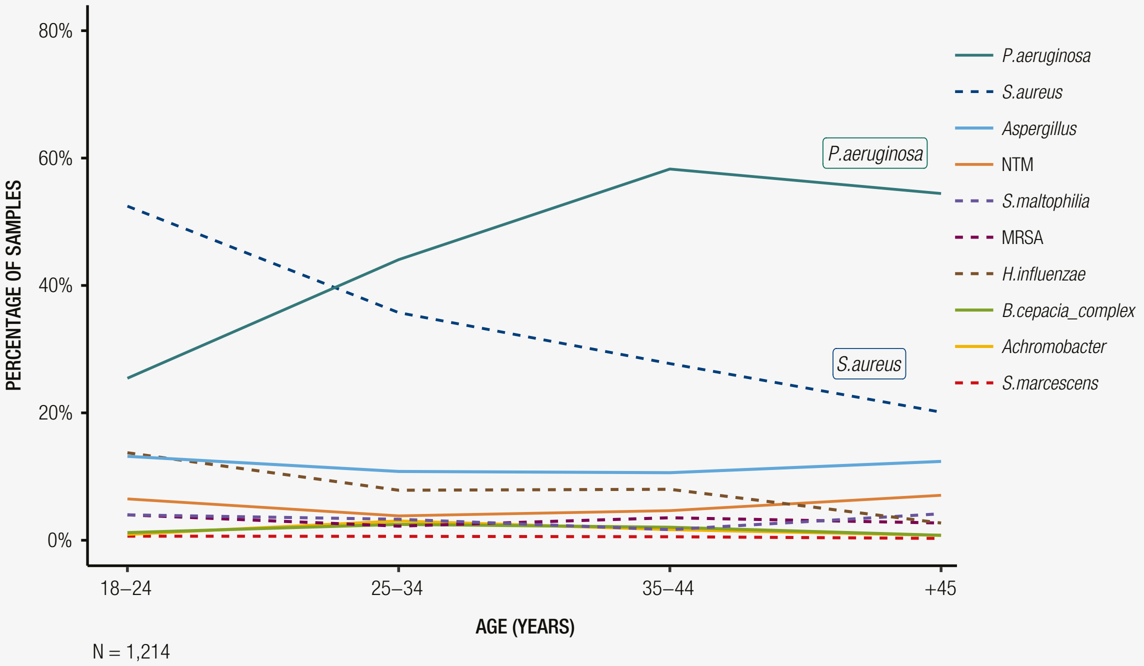
The prevalence of specific organisms commonly affecting pwCF has generally declined over the last eight years (Figure 3.16). The prevalence of *P.aeruginosa* has decreased from a high of 65.3% in 2018 to 38.0% by 2023. *S.aureus* has decreased from a peak of 58.1% in 2017 to 32.0% in 2023. The prevalence of *Aspergillus* spp has declined from a peak of 38.5% in 2017 to 10.3% in 2023. The prevalence of less common microorganisms remained fairly similar over this period with the exception of *H.influenzae* which remained steady from 2016 (7.7%) to 2023 (7.8%).

FIGURE 3.16: ACFDR ADULTS 2016 – 2023: PREVALENCE OF RESPIRATORY MICROBIOLOGY



Microbiology results for adults from 1,214 samples collected in 2023 show the prevalence of specific microorganisms for different age groups of pwCF. The largest variations with age are for *P.aeruginosa,* which has a prevalence of 25% among 18 – 24-year olds, increasing to a prevalence of 58% for 35 – 44-year-olds. Conversely, the prevalence of *S.aureus* decreased from 52% for 18 – 24-year-olds to 20% for pwCF at 45 years of age (Figure 3.17 and Table 3.3). The prevalence of remaining organisms is fairly consistent across the age groups, with the exception of *H.influenzae*, which decreases from 14% for 18 – 24-year-olds to 3% for pwCF at 45 years of age.

FIGURE 3.17: ACFDR ADULTS 2023: PREVALENCE OF RESPIRATORY MICROORGANISMS BY AGE



N = 1,214

TABLE 3.3: ACFDR ADULTS 2023: PREVALENCE OF RESPIRATORY MICROORGANISMS BY AGE

	All samples			
	18 – 24	25 – 34	35 – 44	45
Number of samples in the age range	586	695	474	343
Number of samples taken in 2023	361	375	270	208
Number of patients	357	372	265	206
P.aeruginosa	92/361 (25%)	165/375 (44%)	157/270 (58%)	113/208 (54%)
H.influenzae	50/361 (14%)	30/375 (8%)	22/270 (8%)	6/208 (3%)
B.cepacia_complex	5/361 (1%)	10/375 (3%)	6/270 (2%)	2/208 (1%)
S.aureus	189/361 (52%)	134/375 (36%)	75/270 (28%)	42/208 (20%)
MRSA	15/361 (4%)	9/375 (2%)	10/270 (4%)	6/208 (3%)
Achromobacter spp	4/361 (1%)	12/375 (3%)	5/270 (2%)	2/208 (1%)
S.maltophilia	15/361 (4%)	13/375 (3%)	5/270 (2%)	9/208 (4%)
S.marcescens	3/361 (1%)	3/375 (1%)	2/270 (1%)	1/208 (0%)
Aspergillus spp	48/361 (13%)	41/375 (11%)	29/270 (11%)	26/208 (12%)
NTM	24/361 (7%)	15/375 (4%)	13/270 (5%)	15/208 (7%)

Non Tuburculous Mycobacterium Prevalence

Non-Tuburculous Mycobacterium (NTM), particularly *M.abscessus* infection, has been associated with poorer outcomes for pwCF. NTM infection rates, including by *M.abscessus* for pwCF increased from 2017, peaking in 2021. Since then, infection rates have returned to levels similar to those in earlier years (Table 3.4).

TABLE 3.4: ACFDR ADULTS 2017 – 2023: NON-TUBERCULOUS MYCOBACTERIUM (NTM) INFECTION

Age	Organism	2017	2018	2019	2020	2021	2022	2023
18 – 30	NTM	4/79 (5.1%)	26/363 (7.2%)	50/491 (10.2%)	86/716 (12.0%)	103/733 (14.1%)	57/749 (7.6%)	32/549 (5.8%)
	M.abscessus	2/79 (2.5%)	12/363 (3.3%)	23/491 (4.7%)	40/716 (5.6%)	31/733 (4.2%)	25/749 (3.3%)	15/549 (2.7%)
+30	NTM	2/36 (5.6%)	22/410 (5.4%)	30/568 (5.3%)	48/760 (6.3%)	77/764 (10.1%)	33/834 (4.0%)	33/651 (5.1%)
	M.abscessus	2/36 (5.6%)	8/410 (2.0%)	8/568 (1.4%)	14/760 (1.8%)	13/764 (1.7%)	8/834 (1.0%)	8/651 (1.2%)

3.3 CF MANAGEMENT

Clinical Visits

Traditionally, pwCF have had regular clinical visits with multidisciplinary teams. Standards of care for pwCF have recommended four clinical visits per year. The number of clinical visits for pwCF increased from 2020 during the COVID-19 pandemic, with the introduction of telehealth visits replacing or complementing traditional face to face clinical visits.

For the last four years, the number of clinical visits for adults with CF has been between 9,000 and 10,000 per year, reducing to 8,901 in 2023. Between 2020 to 2023, approximately 50% of visits used telehealth. This has declined to 40% for 2023. The proportion of outreach visits remained constant around 1% during this period (Figure 3.18 and Table 3.5).

FIGURE 3.18: : ACFDR ADULTS 2020 – 2023: TOTAL NUMBER OF VISITS RECORDED PER YEAR

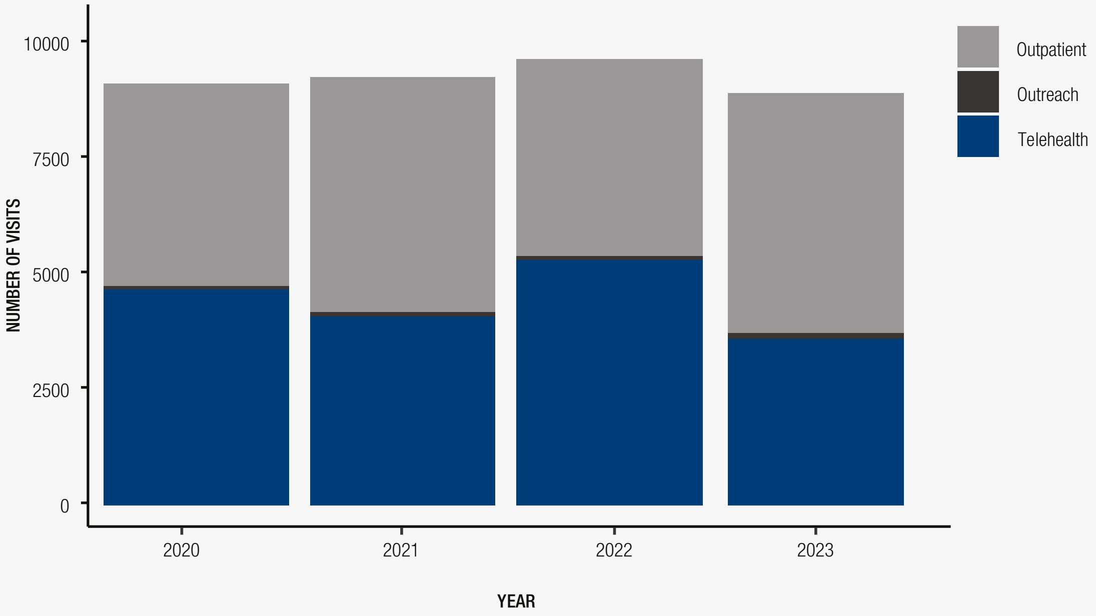


TABLE 3.5: ACFDR ADULTS 2020 – 2023: TOTAL NUMBER OF CLINICAL VISITS

Visit type	2020	2021	2022	2023
Outpatient	4,676 (48.0%)	5,404 (55.0%)	4,620 (45.0%)	5,162 (58.2%)
Outreach	66 (1.0%)	90 (1.0%)	86 (1.0%)	131 (1.5%)
Telehealth	4,907 (51.0%)	4,328 (44.0%)	5,574 (54.0%)	3,571 (40.3%)
Total	9,713 (100.0%)	9,981 (100.0%)	10,340 (100.0%)	8,901 (100.0%)

Standards of Care

The Australian CF Standards of Care for pwCF recommend four clinical visits per year. In 2023 the number of adults with CF who had at least 4 clinic visits was 1,183 (56.0%) overall. This was similar among pwCF of 18 – 24 years (57.0%) and those who were 30+ years old (56.0%) (Figure 3.19). This proportion declined over time for both age groups (Table 3.6).

FIGURE 3.19: ACFDR ADULTS 2023: 4 OR MORE CLINICAL VISITS

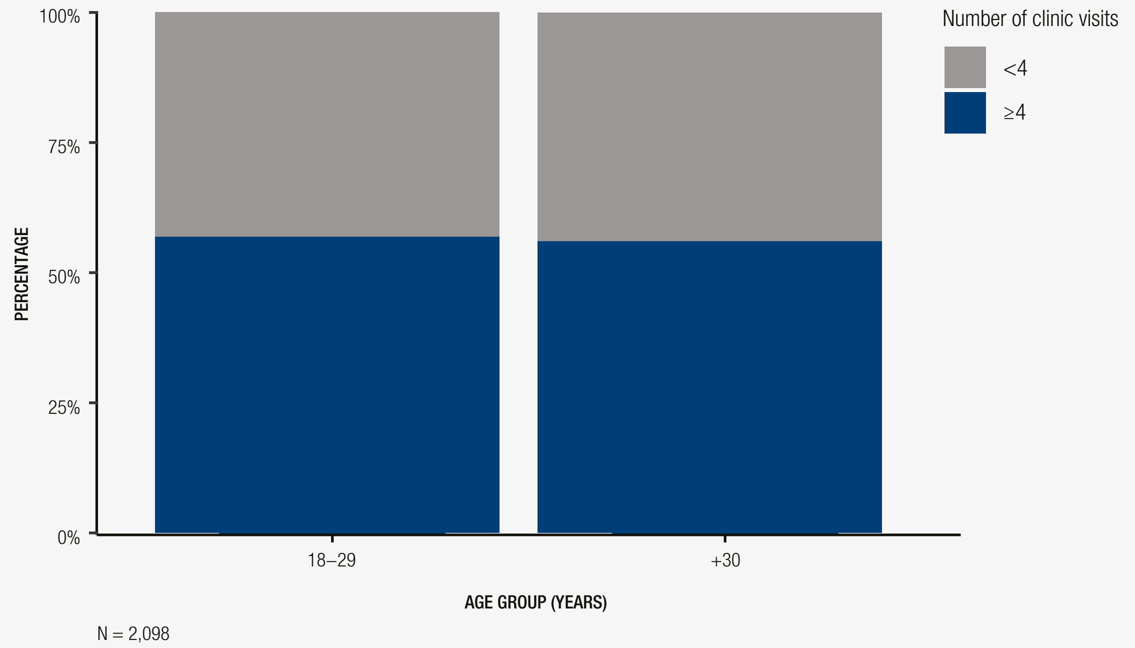


TABLE 3.6: ACFDR ADULTS 2021 – 2023: PROPORTION WITH 4 OR MORE CLINICAL VISITS BY AGE

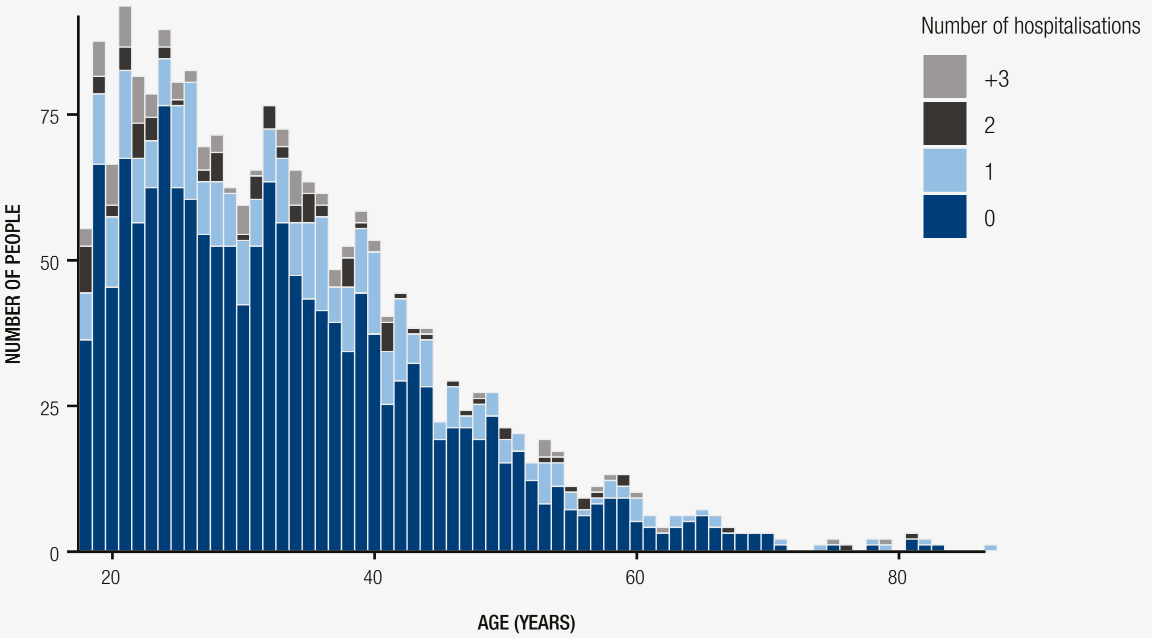
	Number/% with 4+ visits		
Age	2021	2022	2023
18 – 29	607 (67.0%)	568 (61.0%)	537 (57.0%)
30+	669 (63.0%)	735 (62.0%)	646 (56.0%)
Total	1,217 (60.3%)	1,303 (64.5%)	1,183 (56.0%)

Hospitalisations

In 2023, data regarding adult hospitalisations was reported for all adults, excluding those with transplants (114), totalling 2,098 adults.

Approximately three quarters of adults (75.0% of 18 – 29-year-olds and 73.3% of adults aged 30 years or older) did not have any hospitalisations in 2023. Of 18 – 29-year-olds, 15.2% had 1 hospitalisation, 4.0% had 2 hospitalisations, and 5.6% had 3 or more hospitalisations. For adults with CF aged 30 years or more, 19.0% had 1, 4.3% had 2, and 3.4% had 3 or more hospitalisations during 2023 (Figure 3.20 and Table 3.7).

FIGURE 3.20: ACFDR ADULTS 2023: HOSPITALISATIONS BY AGE



N = 2,098

TABLE 3.7: ACFDR ADULTS 2023: HOSPITALISATIONS BY AGE

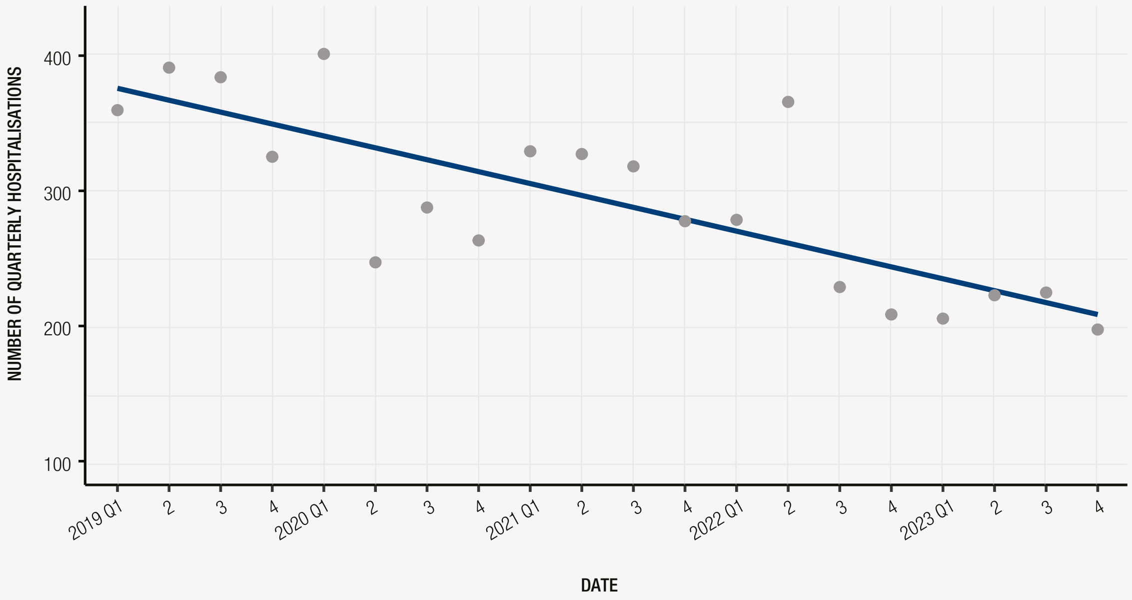
Age	Hospitalisations	N (%)
18 – 29	0	710 (75.1%)
	1	144 (15.2%)
	2	38 (4.0%)
	3+	53 (5.6%)

Age	Hospitalisations	N (%)
30+	0	845 (73.3%)
	1	219 (19%)
	2	50 (4.3%)
	3+	39 (3.4%)

Adult Hospitalisations

Adult hospitalisations per quarter continued to decrease steadily from 2019 to 2023, from a peak of 390 admissions for Quarter 2, 2019 to a low of 199 admissions for Quarter 4 of 2023. This represents a reduction of 51.0% in adult hospitalisations during this four-year period (Figure 3.21).

FIGURE 3.21: ACFDR ADULTS 2019 – 2023: HOSPITALISATIONS PER QUARTER



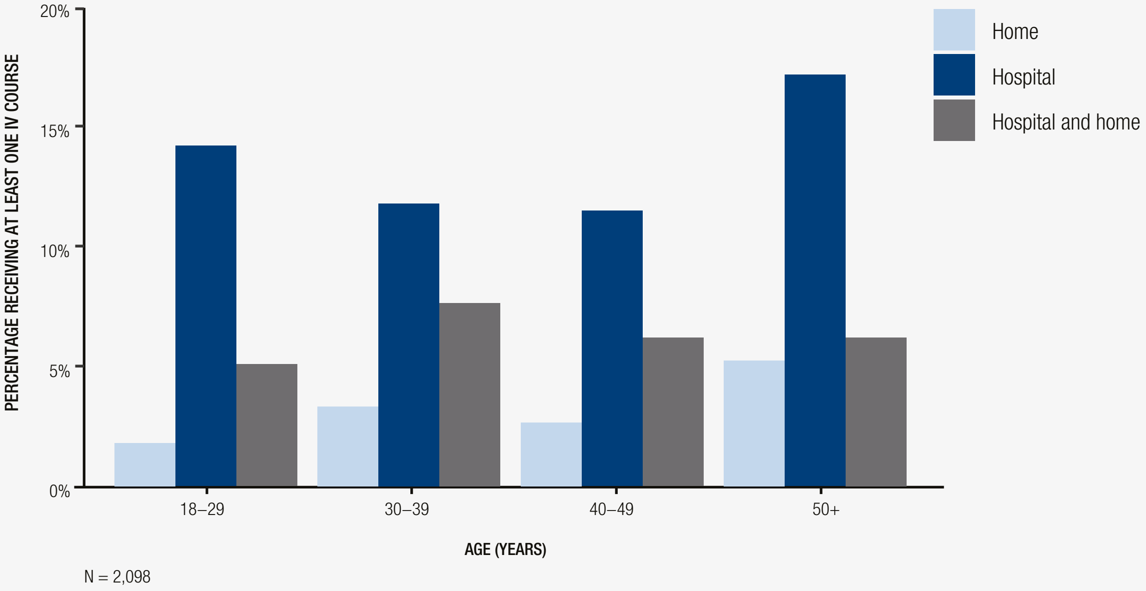
IV Antibiotic Therapy

In 2023, there were 465 adults who received at least one course of IV antibiotic therapy; this represents 22% of all adults with CF (excluding adults who had a lung transplant).

The most common setting for treatment with IV antibiotic therapy was hospital only, with 280 adults being admitted to hospital only for IV antibiotics, followed by 128 adults receiving treatment in hospital then at home, and 57 adults receiving IV treatment at home only (Figure 3.22).

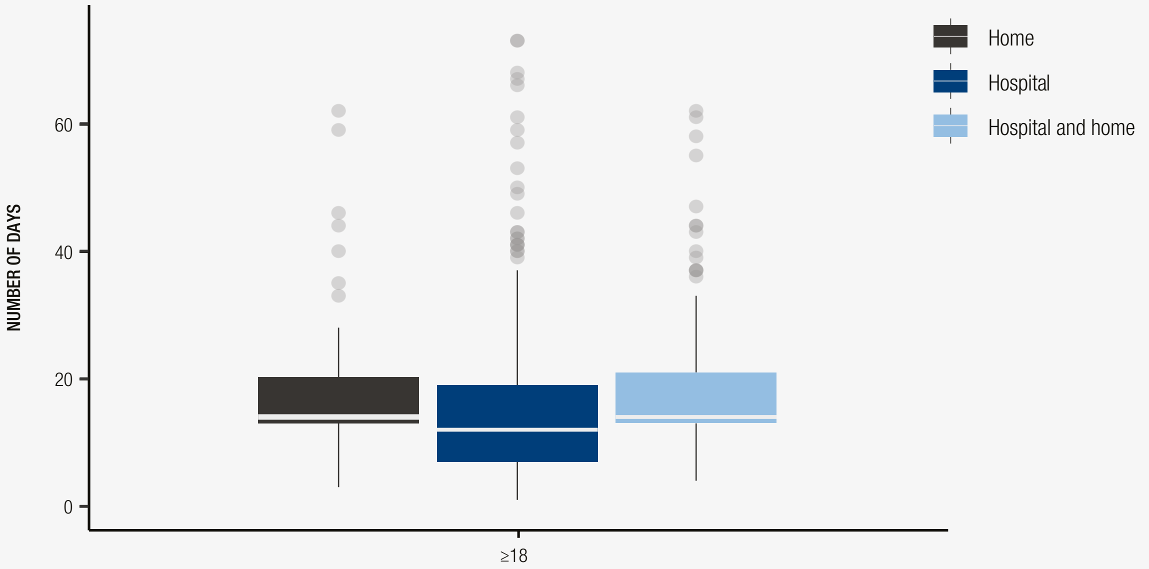
The age groups most likely to receive IV antibiotics were those aged 50+ years (28.5% of the cohort), followed by those aged 30 – 39 years (22.7% of the cohort), those 18 – 29 years (21.1%) and those aged 40 – 49 years (14% of the cohort).

FIGURE 3.22: ACFDR ADULTS 2023: IV ANTIBIOTIC THERAPY BY AGE



In 2023, the median duration of IV antibiotic therapy in hospital only was 12 days, with a median of 14 days of therapy for adults receiving hospital at home or combined hospital and home (Figure 3.23).

FIGURE 3.23: ACFDR ADULTS 2023: MEDIAN DAYS IV ANTIBIOTICS

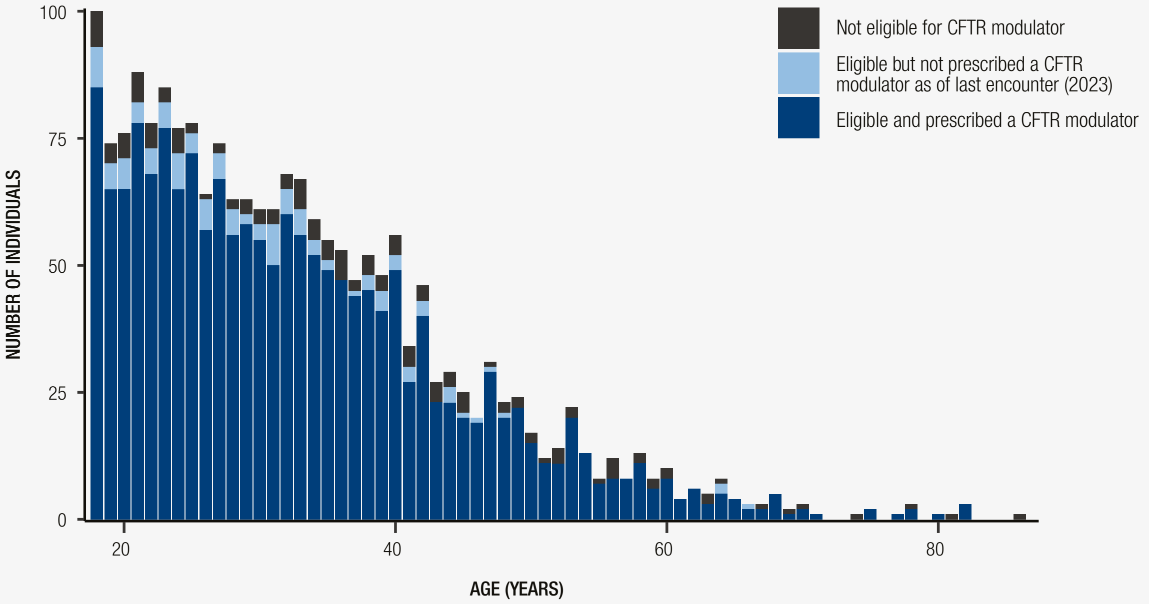


N = 2,098

CFTR Modulators

Disease-modifying therapies reduce pulmonary exacerbations, improve quality of life, and improve nutritional parameters for an increasing number of pwCF. Different therapies target different genetic variants, and not all pwCF may be eligible to receive CFTR modulators. Data were calculated from pwCF who were on a modulator as of 31 December 2023. This is generally those pwCF on modulators available via the PBS. In 2023, 2,000 adults had their eligibility for a CFTR modulator (based on genotype) known (95.3% of adults). Figure 3.24 shows that the vast majority of these adults with known eligibility were prescribed a modulator at the end of 2023.

FIGURE 3.24: ACFDR ADULTS 2023: CFTR MODULATOR ELIGIBILITY AND PRESCRIBING BY AGE

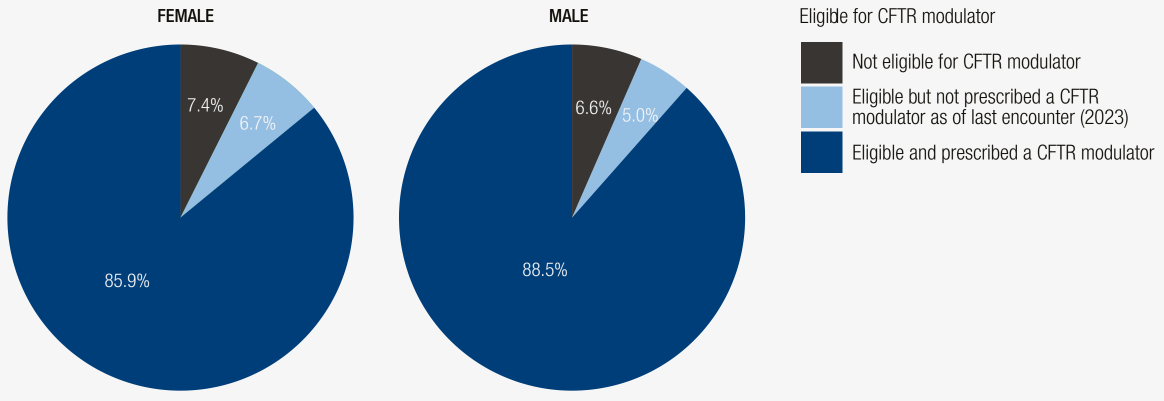


N = 2,000 individuals with known eligibility

Of the 2,000 adults in the registry in 2023 who had known eligibility for a modulator, 7% of both females and males were not eligible for a CFTR modulator. Eighty-six percent of females and 88% of males were eligible and prescribed a modulator, with 7% of females and 5% of males being eligible and not prescribed a modulator (Figure 3.25).

This is an increase in modulator update from 2022, when 80% of females and 83% of males respectively were prescribed modulators, and 13% and 9% respectively were eligible but not prescribed. The proportion of adults not eligible for a modulator remained constant at 7%.

FIGURE 3.25: ACFDR ADULTS 2023: COMBINED ELIGIBILITY AND PRESCRIPTION OF CFTR MODULATORS



N = 2,000 individuals with known eligibility

Specific CFTR Modulator Use

In the tables below the numerator is those on the drug and the denominator is the eligible population (based on genotype).

Ivacaftor (KALYDECO®)

Ivacaftor is available on the PBS for pwCF, who are aged one year and older, and who have one of the following gating (class III) gene changes in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R.

As at 31 December 2023, 37.9% of the eligible population for Ivacaftor were prescribed the modulator, with 83.0% having been prescribed the modulator previously and 45.3% having discontinued it. The majority discontinued Ivacaftor to switch to another modulator (87.6%) (Tables 3.8 and 3.9).

TABLE 3.8: ACFDR ADULTS 2023: IVACAFTOR USE

Age (years)	On Ivacaftor anytime	On Ivacaftor as of 31 Dec 2023	Previously on Ivacaftor and discontinued as of 31 Dec 2023
≥18	193/232 (83.0%)	88/232 (37.9%)	105/232 (45.3%)

TABLE 3.9: ACFDR ADULTS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM IVACAFTOR

N (%)	Reasons for discontinuation/switch in modulator
92 (87.6%)	Switch to other CFTR modulator
11 (10.4%)	Liver impairment/intolerance and reasons
1 (1.0%)	Concomitant drug interaction
1 (1.0%)	Pregnancy

Lumacaftor/Ivacaftor (ORKAMBI®)

Lumacaftor/Ivacaftor is a combination therapy available on the PBS for pwCF, are aged two years and older, and have two copies of the F508del gene change in the CFTR gene.

As at 31 December 2023, 13.0% of the eligible population for Lumacaftor/Ivacaftor were prescribed the modulator, with 68.0% having been prescribed the modulator previously and 55.0% having discontinued it. The majority discontinued Lumacaftor/Ivacaftor to switch to another modulator (74.6%) (Tables 3.10 and 3.11).

TABLE 3.10: ACFDR ADULTS 2023: LUMACAFTOR/IVACAFTOR USE

Age (years)	On Lumacaftor/Ivacaftor anytime	On Lumacaftor/Ivacaftor as of 31 Dec 2023	Previously on Lumacaftor/Ivacaftor and discontinued as of 31 Dec 2023
≥18	661/968 (68.0%)	126/968 (13.0%)	535/968 (55.0%)

TABLE 3.11: ACFDR ADULTS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM LUMACAFTOR/IVACAFTOR

N (%)	Reasons for discontinuation/switch in modulator
399 (74.6%)	Switch to other CFTR modulator
74 (13.8%)	Other intolerance/adverse event and reason
55 (10.3%)	Pulmonary side effect/intolerance
4 (0.7%)	Liver impairment/intolerance
2 (0.4%)	Pregnancy
1 (0.2%)	Concomitant drug interaction

Tezacaftor/Ivacaftor (SYMDEKO®)

Tezacaftor/Ivacaftor is also a combination therapy available on the PBS for pwCF, are aged 12 years and older, and who have one copy of the following changes in the CFTR gene: E56K, R117C, F508del, S977F, F1074L, 3849+10kbC→T, P67L, E193K, D579G, F1052V, D1152H, R74W, L206W, 711+3A→G, K1060T, D1270N, D110E, R352Q, E831X, A1067T, 2789+5G→A, D110H, A455E, S945L, R1070W, 3272 – 26A→G.

As at 31 December 2023, 15% of the eligible population for Tezacaftor/Ivacaftor were prescribed the modulator, with 65% having been prescribed the modulator previously and 50% having discontinued it. The majority discontinued Tezacaftor/Ivacaftor to switch to another modulator (85.1%) (Tables 3.12 and 3.13).

TABLE 3.12: ACFDR ADULTS 2023: TEZACAFTOR/IVACAFTOR USE

Age (years)	On Tezacaftor/Ivacaftor and Ivacaftor anytime	On Tezacaftor/Ivacaftor and Ivacaftor as of 31 Dec 2023	Previously on Tezacaftor/Ivacaftor and Ivacaftor and discontinued as of 31 Dec 2023
≥18	707/1,094 (65.0%)	164/1,094 (15.0%)	543/1,094 (50.0%)

TABLE 3.13: ACFDR ADULTS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM TEZACAFTOR/IVACAFTOR

N (%)	Reasons for discontinuation/switch in modulator
462 (85.1%)	Switch to other CFTR modulator
64 (11.9%)	Other intolerance/adverse event and reason
9 (1.7%)	Pulmonary side effect/intolerance
4 (0.7%)	Liver impairment/intolerance
3 (0.6%)	Pregnancy

Elexacaftor/Tezacaftor/Ivacaftor (TRIKAFTA®)

Elexacaftor/Tezacaftor/Ivacaftor (TRIKAFTOR/ETI) is a triple combination therapy available on the PBS on the 1 April 2022 for pwCF aged 12 years and older, with at least one copy of the F508del gene change in the CFTR gene.

As at 31 December 2023, 89.3% of the eligible population for Elaxacaftor/Tezacaftor/Ivacaftor were prescribed the modulator, with 90.0% having been prescribed the modulator previously and 0.9% having discontinued it. In total, 175 adults with CF discontinued Elexacaftor/Tezacaftor/Ivacaftor, with the most common reasons being an adverse event/intolerance (40.6%), liver impairment/intolerance (21.7%), other reason (30.3%) or pregnancy (5.1%) (Tables 3.14 and 3.15).

TABLE 3.14: ACFDR ADULTS 2023: ELEXACAFTOR/TEZACAFTOR/IVACAFTOR USE

Age (years)	On ETI anytime	On ETI as of 31 Dec 2023	Previously on ETI and discontinued as of 31 Dec 2023
≥18	1,698/1,882 (90.0%)	1,681/1,882 (89.3%)	17/1,882 (0.9%)

Table 3.15 shows the reasons for discontinuation and changes in dosage of Trikafta.

TABLE 3.15: ACFDR ADULTS 2023: REASONS FOR DISCONTINUATION/SWITCH FROM ELEXACAFTOR/TEZACAFTOR/IVACAFTOR

N (%)	Reasons for discontinuation/change
157 (63.6%)	Other intolerance/adverse event and reason
50 (20.2%)	Liver impairment/intolerance
11 (4.5%)	Pregnancy
3 (1.2%)	Concomitant drug interaction
26 (10.5%)	Switch to other CFTR modulator

3.4 COMPLICATIONS AND THERAPIES

CF Pulmonary Disease

In 2023, the rate of haemoptysis requiring hospital admission was 5.5% for adults 18 – 29 years (compared to 8.9% in 2022), and 7.2% for those aged 30+ (compared to 8.9% in 2022). Embolisation was required for 0.4% of haemoptysis presentations for 18 – 29-year-olds and 0.1% for 30+ year-olds. Pneumothoraces occurred in 0.3% of 18 – 29-year-olds and 30+ year-olds.

CF Pulmonary Therapies — Maintenance Antibiotics

A mainstay of medical treatment for CF lung disease is preventive and therapeutic antibiotic therapy that may be administered orally or inhaled. Among individuals aged 18 – 29, 22.6% were prescribed inhaled antibiotics, 16.8% were on regular oral antibiotics, and 25.8% were using macrolides (Figure 3.26 and Table 3.16). In the 30+ age group, 31.3% were on inhaled antibiotics, 16.9% were on regular oral antibiotics, and 45.1% were using macrolides (Figure 3.26 and Table 3.16).

FIGURE 3.26: ACFDR ADULTS 2023: MAINTENANCE ANTIBIOTIC THERAPY BY AGE

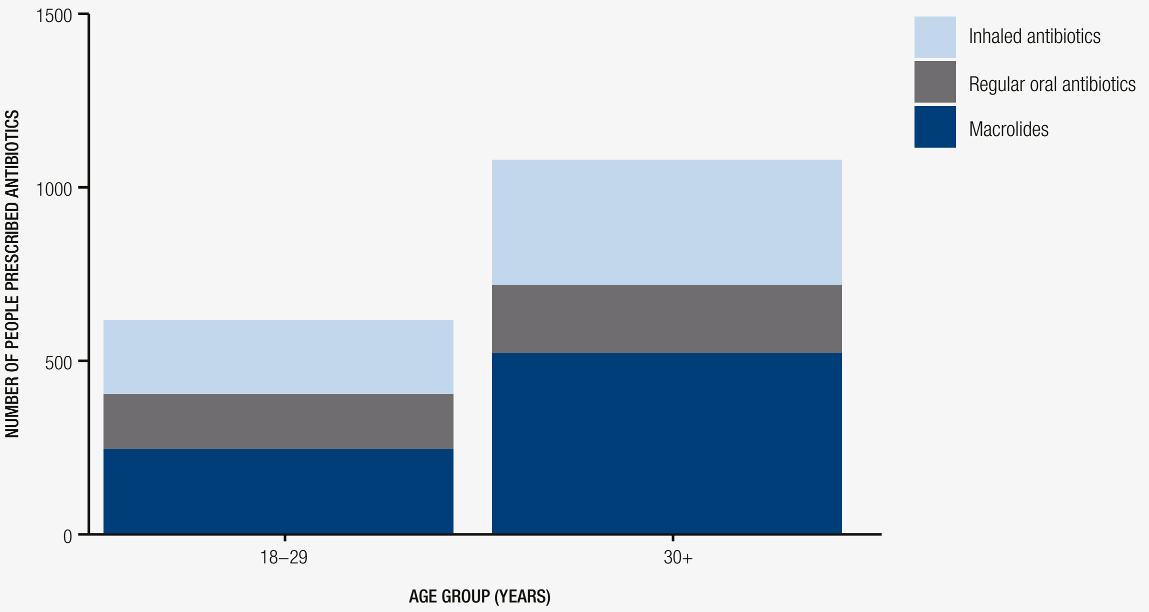


TABLE 3.16: ACFDR ADULTS 2023: MAINTENANCE ANTIBIOTIC THERAPY BY AGE

Antibiotic therapy type	18 – 29 (N = 942)	30+ (N = 1,151)
Inhaled antibiotics	213 (22.6%)	360 (31.3%)
Regular oral antibiotics	158 (16.8%)	195 (16.9%)
Macrolides	243 (25.8%)	519 (45.1%)

CF Lung Therapies — Non-Antibiotic Management

In 2023, among adults 18 – 29 years, a majority used bronchodilators (53.6%) and dornase alpha (51.1%), approximately one third used inhaled corticosteroids (34.8%), and 41.8% used hypertonic saline (Table 3.17). Less commonly used drugs were inhaled mannitol (5.3%), oral corticosteroids (2.3%), non-invasive ventilation (1.8%) and long-term oxygen therapy (0.4%) (Table 3.17).

In 2023, among adults aged 30 years or older there was a slightly higher use of bronchodilators (56.7%), inhaled corticosteroids (48.6%), and oral corticosteroids (3.6%). A large minority also used dornase alpha (42.2%) and hypertonic saline (38.6%), whereas the use of inhaled mannitol was uncommon compared to younger adults (2.7%). Nearly 3% of adults over 30 years of age required non-invasive ventilation, with 1.9% on long term oxygen therapy.

Compared to 2022, fewer 18 – 29-year-olds in 2023 used a majority of these adjuvant therapies. There was a slight increase in the use of inhaled mannitol and oral corticosteroids, with long-term oxygen therapy use remaining stable. Similarly, for older adults 30+, there was reduced use of all of these therapies with the exception of slightly increased use of oral corticosteroids and long term oxygen use.

TABLE 3.17: ACFDR ADULTS 2023: NON-ANTIBIOTIC MANAGEMENT BY AGE

Non-antibiotic management type	18 – 29 (N = 942)	30+ (N = 1,190)
Bronchodilators	505/942 (53.6%)	653/1,151 (56.7%)
Inhaled corticosteroids	328/942 (34.8%)	559/1,151 (48.6%)
Dornase alpha	481/942 (51.1%)	486/1,151 (42.2%)
Hypertonic saline	394/942 (41.8%)	444/1,151(38.6%)
Inhaled mannitol	50/942 (5.3%)	31/1,151 (2.7%)
Oral corticosteroids	22/942 (2.3%)	42/1,151 (3.6%)
Non-invasive ventilation	15/826 (1.8%)	27/979 (2.8%)
Long term oxygen therapy	3/823 (0.4%)	19/979 (1.9%)

CF Related Diabetes

In 2023, fifty-five percent of 18 – 29-year olds and 54% of 30+year-olds did not have impaired glucose tolerance. The proportion of those with diabetes was 24.5% for 18 – 29-year olds and 26.9% for those aged 30 years or more (Table 3.18).

TABLE 3.18: ACFDR ADULTS 2023: DIABETIC STATUS BY AGE

Diabetic status	18 – 29 (N = 942)	30+ (N = 1,151)
Normal, (no diabetes or impaired glucose tolerance)	520 (55.2%)	624 (54.2%)
Impaired glucose tolerance	109 (11.6%)	137 (11.9%)
Diabetes	231 (24.5%)	310 (26.9%)
Not known	82 (8.7%)	80 (7.0%)

Of those with diabetes, the vast majority are treated with insulin: 83.5% of 18 – 29-year-olds and 72.6% of those 30 years or older. Approximately 10% of 18 – 29-year-olds and 17% of those 30+ years of age use diet/lifestyle management only, and 6% of those 30+ use oral hypoglycemics only (Table 3.19).

TABLE 3.19: ACFDR ADULTS 2023: DIABETIC TREATMENT BY AGE

Diabetes treatment type	18 – 29 (N = 231)	30+ (N = 310)
Insulin	193 (83.5%)	225 (72.6%)
Oral hypoglycemics	<5	19 (6.1%)
Insulin and oral hypoglycemics	<5	7 (2.3%)
Diet/lifestyle management only	22 (9.5%)	51 (16.5%)
No treatment for diabetes	10 (4.3%)	8 (2.6%)

Of those that use insulin, the vast majority (96.0% of 18 – 29-year-olds and 96.6% of 30+ year-olds) require chronic insulin administration. Just over 2.9% of 18 – 29-year-olds and 2.1% of 30+ year-olds use insulin intermittently (Table 3.20).

TABLE 3.20: ACFDR ADULTS 2023: INSULIN USE BY AGE

Insulin use	18 – 29 (N = 174)	30+ (N = 236)
Intermittent insulin use	5 (2.9%)	5 (2.1%)
Chronic insulin use	167 (96.0%)	228 (96.6%)
Insulin use, duration unknown	<5	<5

CF Gastrointestinal Disease

Stomach and Liver

Gastrointestinal complications for people with CF include those related to the stomach, pancreas and liver. In 2023, among adults aged 18 – 29, 24.4% experienced gastroesophageal reflux, increasing to 40.1% for those aged 30 years and older.

The most common liver disease for pwCF is acute (non-cirrhotic) liver disease which affected 6.1% of 18 – 29 -year-olds and 6.7% of 30+ year-olds in 2023. Chronic liver disease affected 5% of 18 – 29-year-olds and 5.3% of 30+ year-olds in 2023 (Table 3.21).

TABLE 3.21: ACFDR ADULTS 2023: GASTROINTESTINAL COMPLICATIONS BY AGE

	18 – 29	30+
Gastroesophageal reflux	230/942 (24.4%)	462/1,151 (40.1%)
Liver disease, non-cirrhosis (includes viral hepatitis, fatty liver)	54/886 (6.1%)	73/1,085 (6.7%)
Liver disease, cirrhosis (image confirmed)	16/848 (1.9%)	37/1,049 (3.5%)
Liver disease, cirrhosis with portal hypertension	27/859 (3.1%)	19/1,031 (1.8%)

Pancreatic Disease

The majority of adult participants in the registry were pancreatic insufficient. In 2023, 83.5% of pwCF aged 18 – 29, and 73.0% of those aged 30 years or older, were pancreatic insufficient. The vast majority of pwCF do not have a history of acute or chronic pancreatitis (Table 3.22).

TABLE 3.22: ACFDR ADULTS 2023: PANCREATIC DISEASE BY AGE

Pancreatic status	18 – 29 (N = 942)	30+ (N = 1,151)
Insufficient	787 (83.5%)	840 (73.0%)

Pancreatitis	18 – 29 (N = 788)	30+ (N = 910)
Acute (first pancreatitis event this current year); pancreatitis not otherwise specified	<5	<5
Recurrent pancreatitis (history of more than one event of pancreatitis)	17 (2.2%)	34 (3.7%)
No history of pancreatitis	767 (97.3%)	873 (95.9%)

Bone Density Status and Osteopenia

CF can cause reduced bone mineral density (osteopenia) or osteoporosis, which may increase the risk of bone fractures.

In 2023, of those that recorded results from bone mineral density scans, 58.7% of 18 – 29-year-olds and 41.4% of 30+ year-olds reported bone mineral density within the normal range. Osteopenia was reported by 33.0% of 18 – 29-year-olds and 44.1% of 30+ year-olds, and osteoporosis was reported by 8.4% and 14.5% respectively. Twenty fractures were reported, with 6 (0.8%) among 18 – 29-year-olds and 14 (1.6%) among 30+ year-olds (Table 3.23).

TABLE 3.23: ACFDR ADULTS 2023: BONE DENSITY STATUS

Bone mineral density	18 – 29 (N = 179)	30+ (N = 256)
Normal	105 (58.7%)	106 (41.4%)
Osteopenia	59 (33.0%)	113 (44.1%)
Osteoporosis	15 (8.4%)	37 (14.5%)
Bone mineral density	**(N = 752)**	**(N = 903)**
Fracture	6 (0.8%)	14 (1.6%)

Cancer

Of the ACFDR's adult cohort, nine diagnoses of cancer were reported, of which three were colorectal cancers.

Nutritional Supplementation

Pancreatic enzymes have been a mainstay of treatment for pancreatic insufficiency for pwCF. In 2023, 80.1% of those aged 18 – 29 and 75.8% of those aged 30 years or older used pancreatic enzymes. A majority (67% and 63% respectively) also used Vitamin supplements, with 32% and 19% respectively using salt replacement therapy.

A small proportion of adults required nutritional support in 2023, 5% or less of the population. The exception was the use of a nasogastric tube by 8.4% of 18 – 29-year-olds during this period (Table 3.24).

TABLE 3.24: ACFDR ADULTS 2023: NUTRITIONAL SUPPLEMENTS BY AGE

Nutritional supplementation	18 – 29 (N = 942)	30+ (N = 1,151)
Pancreatic enzymes	755 (80.1%)	873 (75.8%)
Vitamin supplements (Fat soluble vitamins A, D, E and K)	635 (67.4%)	720 (62.6%)
Salt replacement therapy	304 (32.3%)	217 (18.9%)

Nutritional support	(N = 942)	(N = 1,151)
Oral	33 (3.5%)	5 (0.4%)
Gastrostomy tube	<5	<5
Nasogastric tube	79 (8.4%)	59 (5.1%)
Jejunostomy tube	<5	<5
Parenteral nutrition	<5	<5

Multidisciplinary Care

Multidisciplinary care is a mainstay of CF treatment, and for the last few years the ACFDR has been recording the proportion of pwCF who have annual reviews by allied health and medical specialists.

Table 3.25 shows that the majority of people with CF participate in annual physiotherapy and dietitian reviews. Just under half participate in annual social work reviews; approximately thirty percent participate in endocrine reviews, and approximately one quarter participate in mental health or gastroenterologist reviews. In general, younger adults tend to receive slightly more multidisciplinary care than older adults with CF.

TABLE 3.25: ACFDR ADULTS 2023: MULTIDISCIPLINARY CARE REVIEWS BY AGE

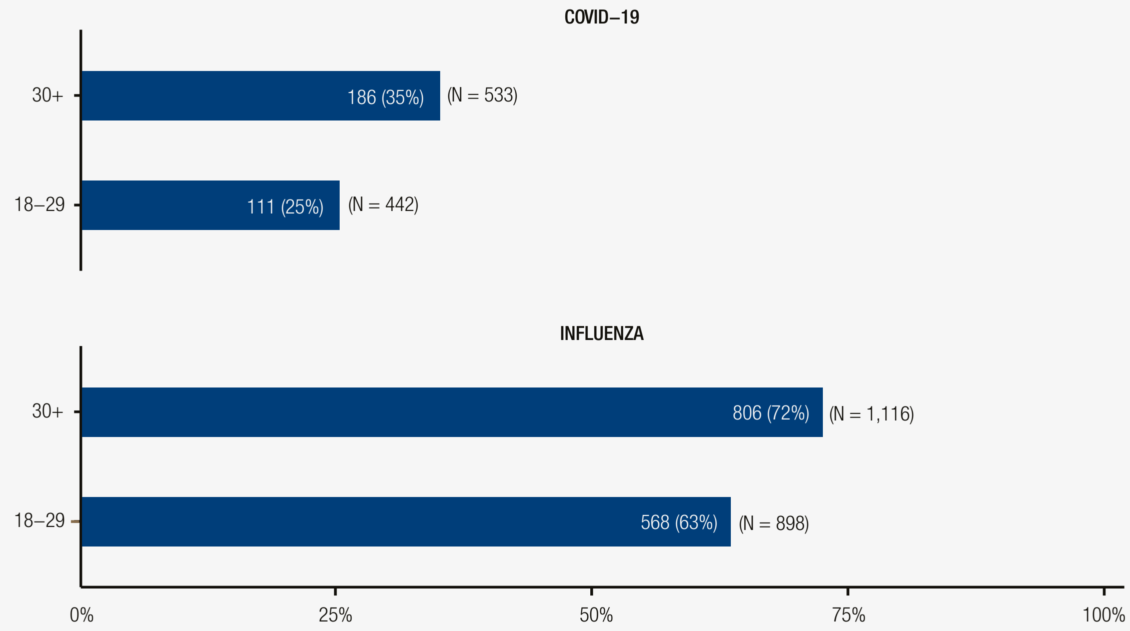
Preventive care	18 – 29 (N = 933)	30+ (N = 1,191)
Physiotherapy review	759/960 (80.7%)	889/961 (77.3%)
Dietitian review	681/942 (72.3%)	818/1,151(71.1%)
Social work review	454/932 (48.7%)	459/1,137 (40.4%)
Endocrine review	244/932 (26.2%)	370/1,138 (32.5%)
Mental health review	218/931 (23.4%)	248/1,147 (21.6%)
Gastroenterologist review	173/816 (21.2%)	247/972 (25.4%)

Vaccination

Ninety-one percent of adults recorded influenza vaccination data in 2023. Of these, 72% of adults aged 30 years or older, and 63% of adults aged 18 – 29 years reported receiving an influenza vaccination.

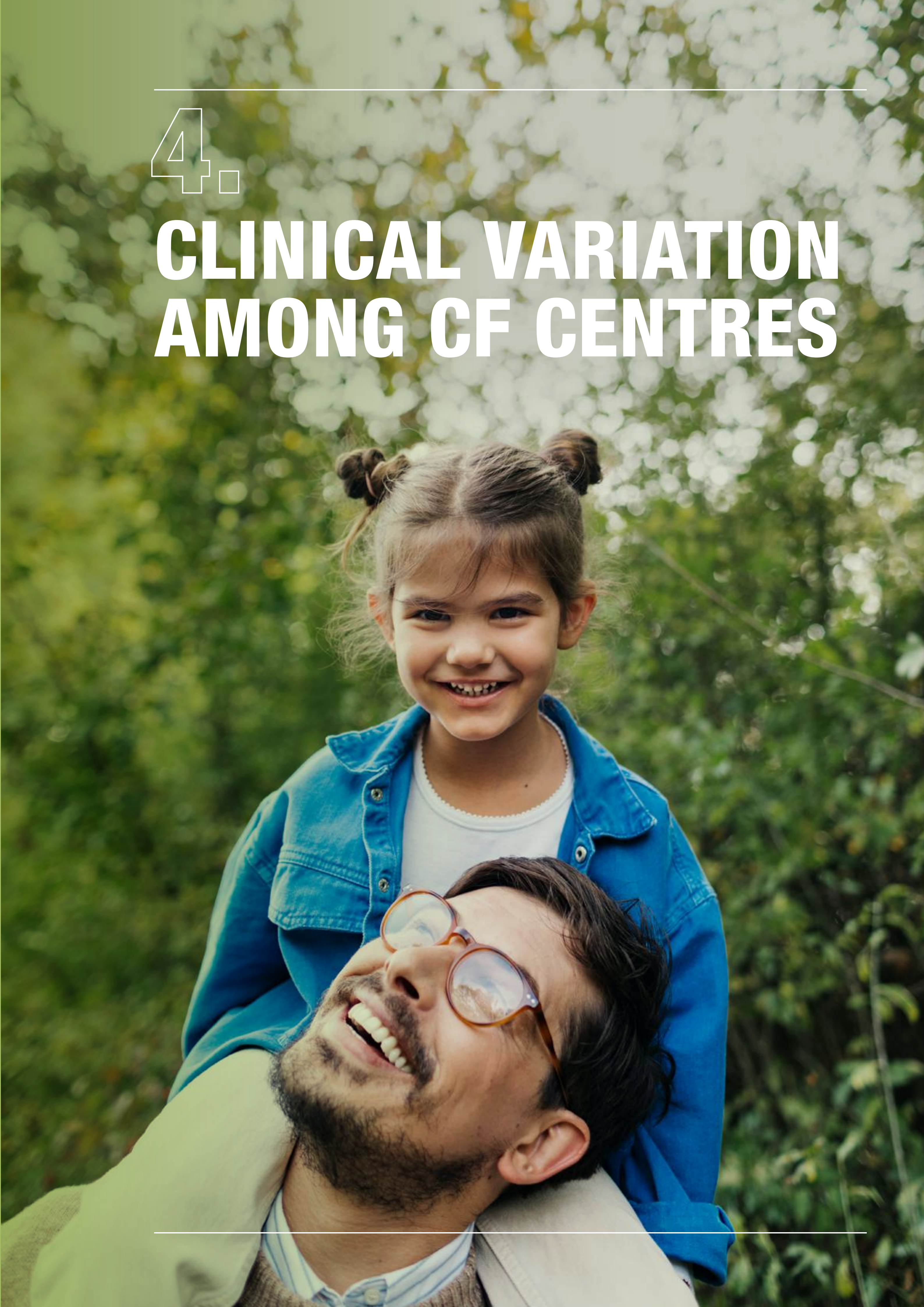
Forty-five percent of adults reported their COVID-19 vaccination status. Thirty-five percent of adults aged 30 years or older had information recorded regarding vaccination for COVID-19 vaccination in 2023, while 25% of adults aged 18 – 29 reported receiving COVID-19 vaccination during 2023 (Figure 3.27).

FIGURE 3.27: ACFDR ADULTS 2023: VACCINATIONS BY AGE



4.

CLINICAL VARIATION AMONG CF CENTRES



4. CLINICAL VARIATION AMONG CF CENTRES

4.1 RISK-ADJUSTED CLINICAL INDICATORS (FUNNEL PLOTS)

Risk-adjusted funnel plots that identify clinical variation between CF centres are a new addition to the AFCDR annual report. Risk-adjusted funnel plots were generated to enable identification of variation in clinical outcomes and CFTR modulator uptake across participating sites.

When interpreting funnel plots:

- The horizontal axis (x-axis) shows the number of patients seen at each site being examined.
- The vertical axis (y-axis) shows the mean of each quality indicator by site.
- The overall mean across all sites is shown by the horizontal dashed line.
- The two contour lines above and below this dashed line represents the 95% and 99.8% control limits.

Any site crossing the 99.8% control limit may be deemed a statistical outlier and further evaluation may be necessary to identify the cause of this variation in outcome from the rest.

FEV 1pp plots are risk adjusted for age, sex and height, when calculating FEV1 pp for pwCF homozygous for F508del.

FEV1 pp is used for all CF centres; BMI for adult CF centres; and BMI percentiles for paediatric CF centres.

Age groups are based on patient age at 31 December 2023. Measures are aligned with methods used in the United States Cystic Fibrosis Foundation's Patient Registry, whereby annual measures of lung function, weight and height are reported as an average of the maximum value from each quarter.

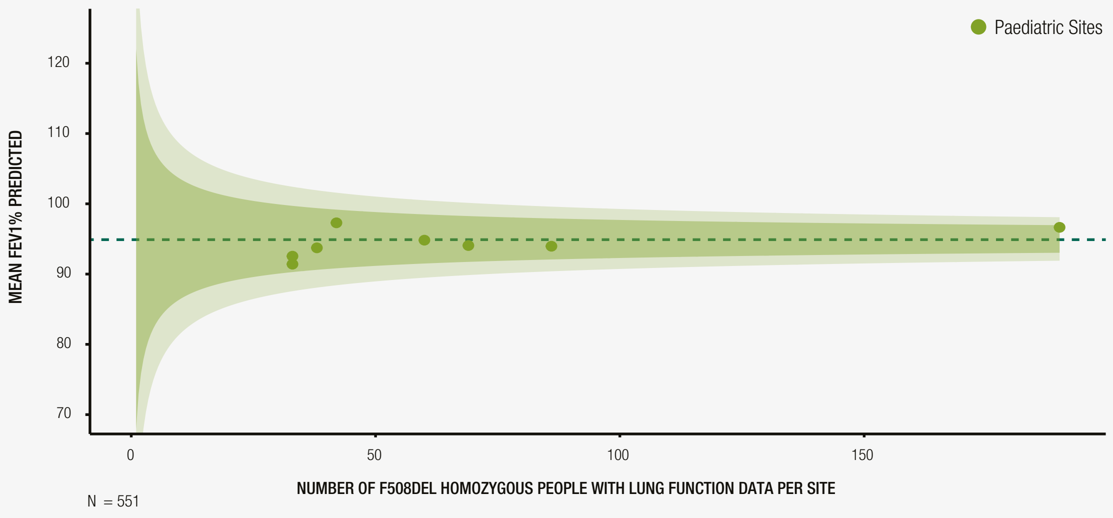
For pwCF who had measurements taken at more than one centre, annual values contributing to the charts and tables for each of these centres were compiled from all clinical measurements reported by any centre.

Height and BMI percentiles were calculated using the WHO growth chart, and Weight percentiles were calculated using the CDC growth chart. The included population at each centre comprises patients whose status in the registry overall is current at the end of the reference year and who had clinical measurements taken at the centre and reported to the registry during that year. Figures and tables in the report are shown for those with the data available.

Paediatrics: Variation in Respiratory Function

Figure 4.1 funnel plot shows the mean FEV1 pp for different paediatric sites (N = 8). Each circle represents a site, with the x-axis showing the number of F508del homozygous individuals at that site, and the y-axis showing the mean FEV1 pp. The horizontal dashed line at 95% represents the overall average FEV1 pp across all sites. The shaded areas indicate the 95% and 99.8% control limits, which reflect the expected variation due to chance. The data of two paediatric sites are not shown due to small numbers. The remaining sites display a range of mean FEV1 pp values from 91.4% to 97.3%, with patient numbers varying between 33 and 190 per site.

FIGURE 4.1: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: MEAN FEV1 PP AT PAEDIATRIC SITES

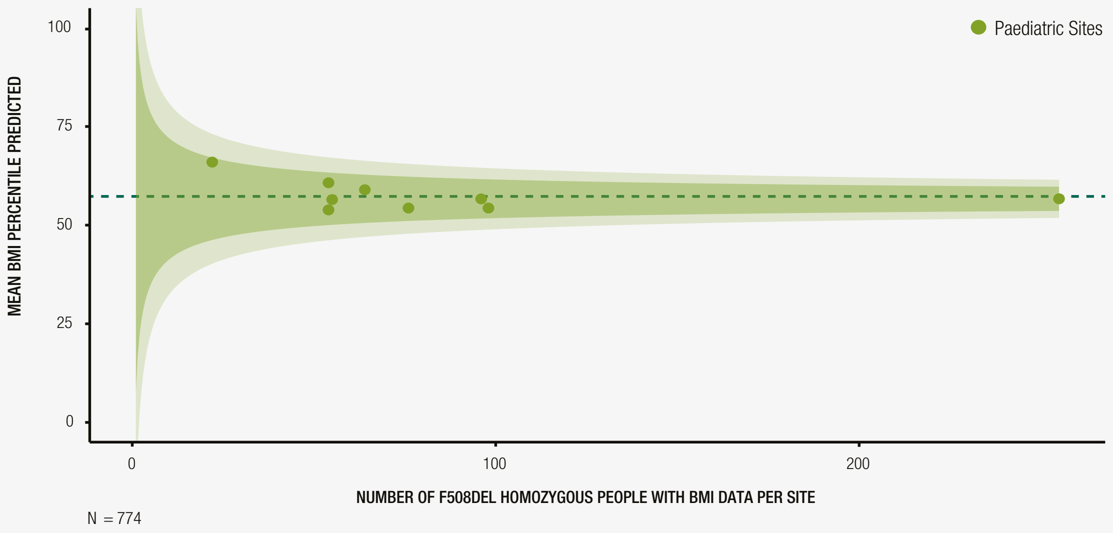


Shaded areas represent 95 and 99.8% control limits
Mean FEV1% predicted in all paediatric sites = 95%
Mean was calculated across all the measurements
Age, sex and height were standardised for when calculating FEV1 % predicted
Sites with fewer than 20 cases are not shown

Paediatrics: Variation in BMI

Figure 4.2 illustrates the average BMI percentiles across different paediatric sites (N = 9). The horizontal dashed line at 57% indicates the overall average BMI percentile across all paediatric sites. One site's data is not displayed due to small number of pwCF at that site. Among the remaining sites, the mean BMI percentiles were within narrow control limits (95%), ranging from approximately 53.9% to 66.0%. The number of people for these sites varied from 22 to 255.

FIGURE 4.2: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: MEAN BMI% AT PAEDIATRIC SITES



Shaded areas represent 95 and 99.8% control limits
Mean BMI percentile in all paediatric sites = 57%
Mean was calculated across all the measurements
Age, sex and height were standardised for when calculating BMI % predicted
Sites with fewer than 20 cases are not shown

Adults: Variation in Lung Function

Figure 4.3 illustrates ACFDR clinical variation at adult sites, focusing on mean FEV1 pp (N = 12). The plot shows the relationship between the number of F508del homozygous people with lung function data per site, with the overall mean FEV1 pp across all adult sites at 75%. Most sites fall within the expected variation. One site is removed from analysis due to low numbers.

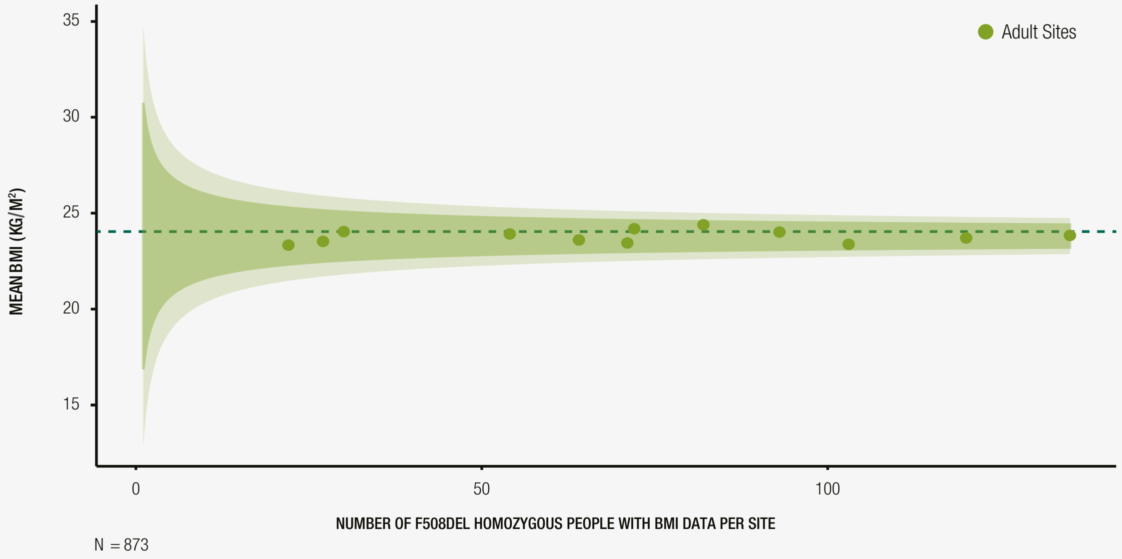
FIGURE 4.3: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: MEAN FEV1 PP AT ADULT SITES

Shaded areas represent 95 and 99.8% control limits
Mean FEV1% predicted in all adult sites = 75%
Mean was calculated across all the measurements
Age,sex and height were standardised for when calculating FEV1 % predicted
Sites with fewer than 20 cases are not shown

Adults: Variation in BMI

Figure 4.4 presents clinical variation of mean BMI% at adult sites for F508del homozygous individuals, Illustrating the relationship between the number of people with BMI data per site and the mean BMI (N = 12). The overall mean BMI across all adult sites is 24 kg/m². Most sites fall within the expected variation limits, with one site omitted from the analysis due to low numbers (Figure 4.4).

FIGURE 4.4: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: MEAN BMI% AT ADULT SITES

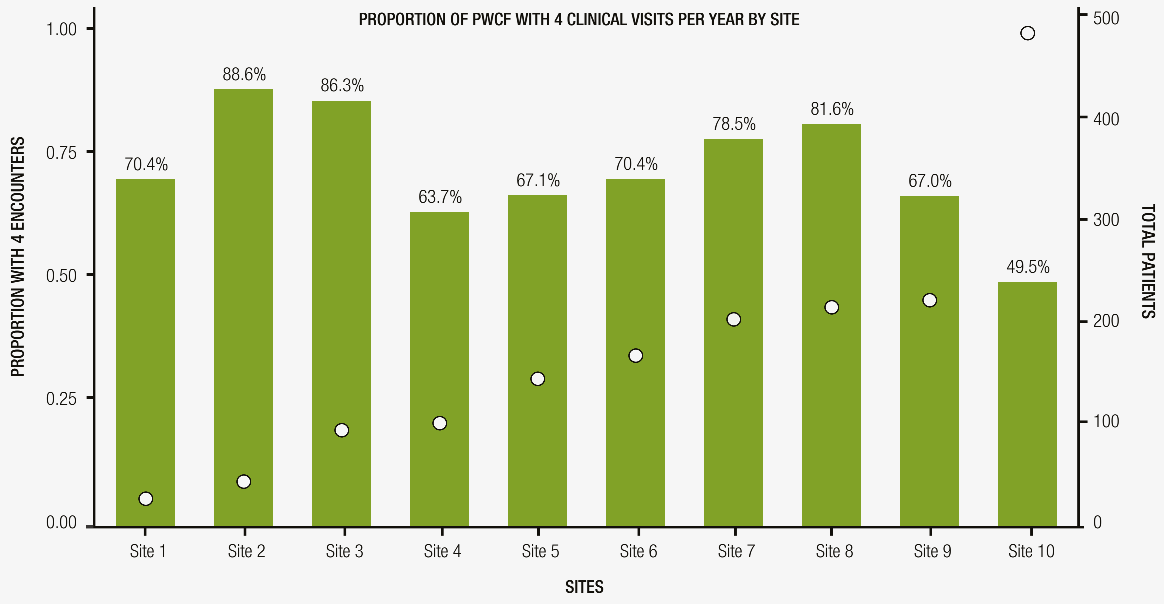


Shaded areas represent 95 and 99.8% control limits
2 Mean BMI in all adult sites = 24 kg/m
Age,sex and height were standardised for when calculating BMI predicted
Sites with fewer than 20 cases are not shown

Paediatrics: Proportion of Individuals with four visits per year

The proportion of pwCF with 4 clinical visits per year, across 10 different paediatric sites is shown in Figure 4.5. The proportions vary considerably between sites, ranging from a low of 49.5% at Site 10 to highs of 88.6% and 86.3% at Sites 2 and 3 respectively. Most sites have between 60 – 80% pwCF receiving four clinical visits per year. The white dots indicate the total number of pwCF at each site, with the scale shown at the right.

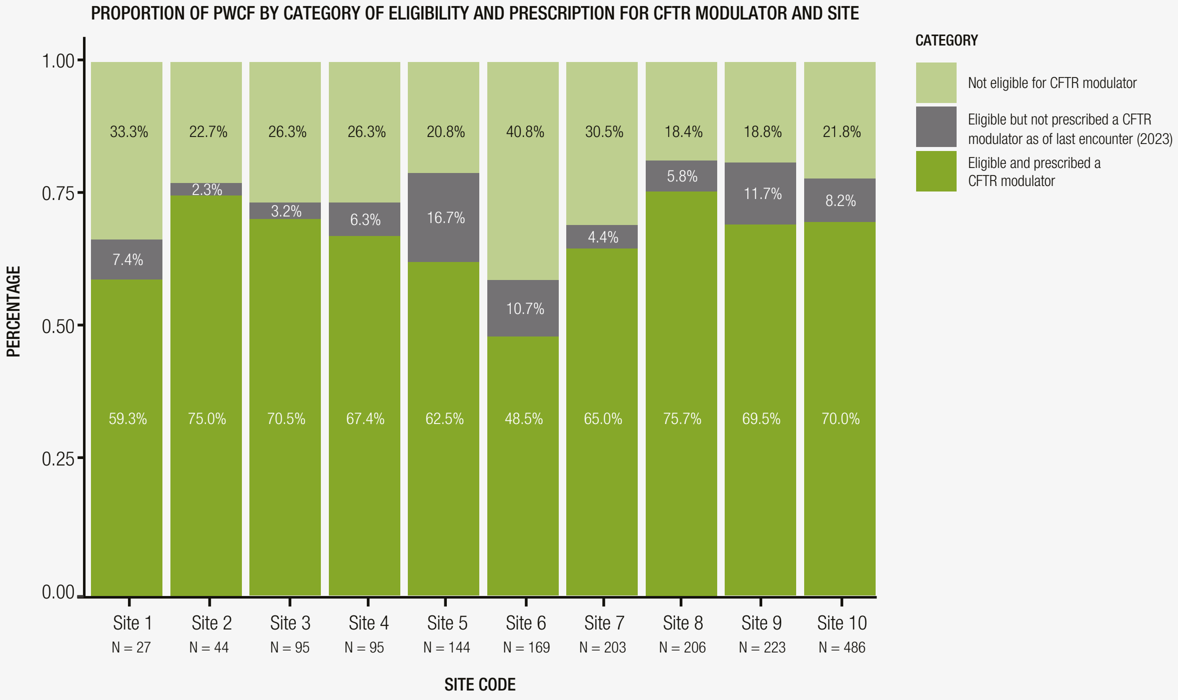
FIGURE 4.5: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: PAEDIATRIC SITES WITH 4 ANNUAL CLINICAL VISITS



Paediatrics: Proportion of eligible Individuals prescribed a Modulator

The proportion of paediatric pwCF eligible for and prescribed CFTR modulators varies across 10 sites (Figure 4.6). The proportion of pwCF eligible and prescribed a CFTR modulator ranges from 48.5% (Site 6) to 75.7% (Site 8), with most sites falling between 60 – 75%. The proportion of pwCF who are not eligible for CFTR modulators ranges from 18.4% (Site 8) to 40.8% (Site 6). A smaller proportion of pwCF at each site are eligible but not prescribed a modulator, varying from 2.3% (Site 2) to 16.7% (Site 5).

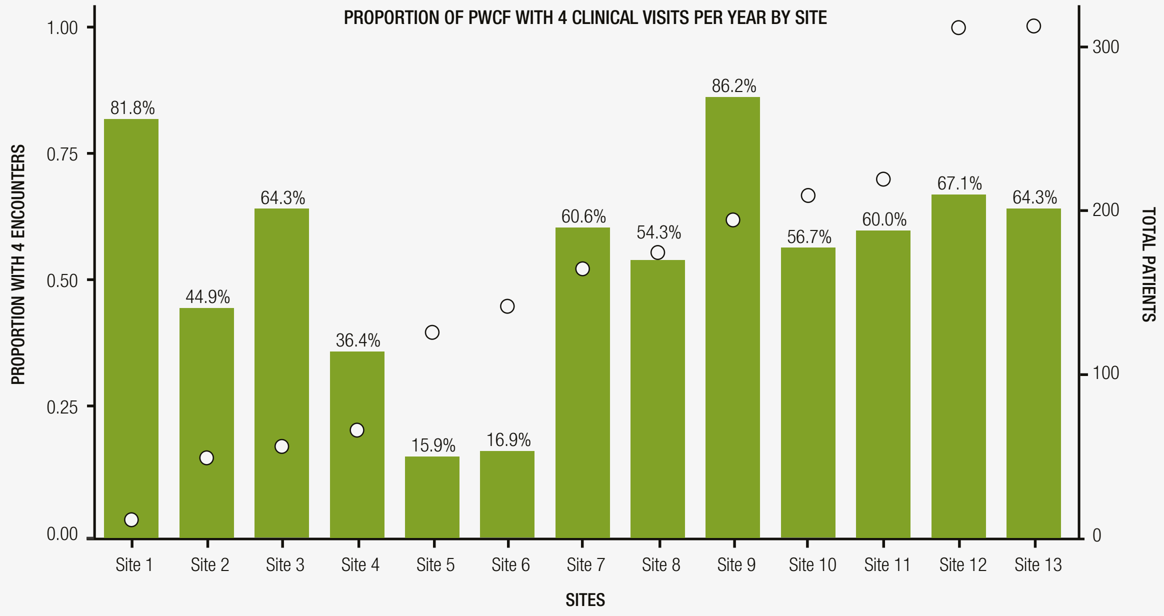
FIGURE 4.6: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: PROPORTION AT PEADIATRIC SITES THAT ARE ELIGIBLE AND PRESCRIBED A CFTR MODULATOR



Adults: Proportion of Individuals with four visits per year

Figure 4.7 shows the proportion of pwCF with 4 annual clinical visits across 13 adult sites. The proportions range from a low of 15.9% at Site 5 to a high of 86.2% at Site 9. The majority of sites fall between 40% and 70%. Sites 12 and 13 have the highest total number of pwCF, while Site 1 has the lowest number. The white dots indicate the total number of patients at each site, with the scale shown on the right.

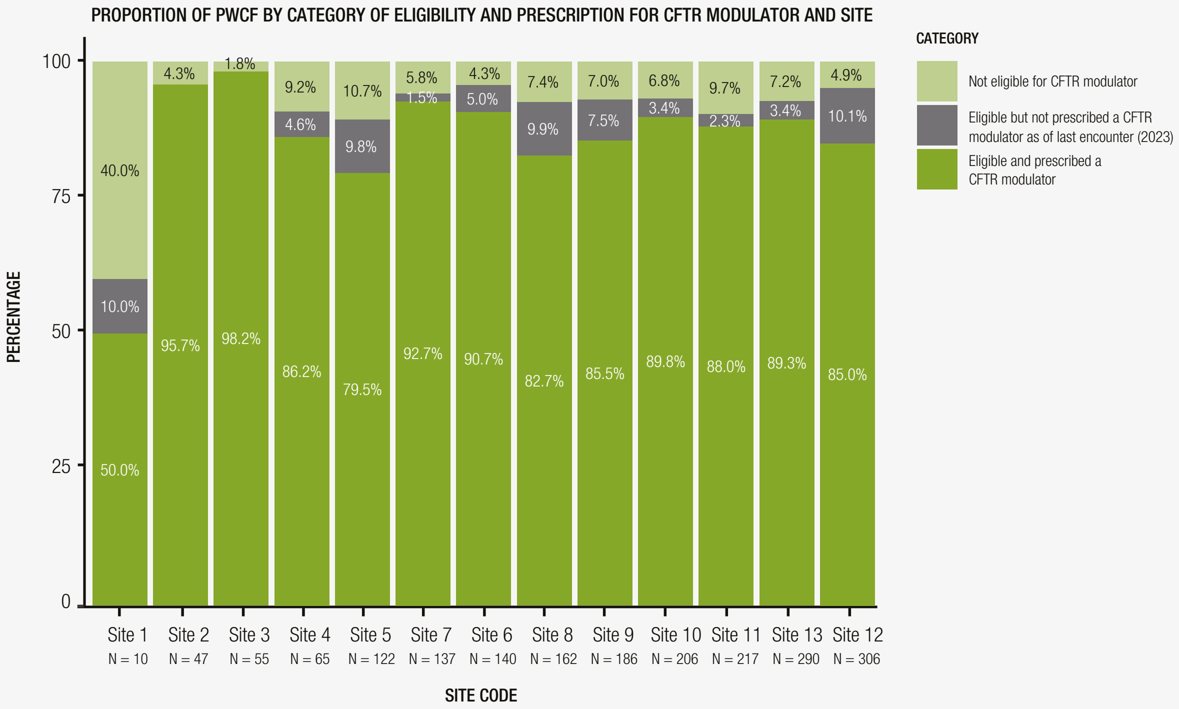
FIGURE 4.7: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: ADULT SITES WITH 4 ANNUAL CLINICAL VISITS



Adults: Proportion of eligible Individuals Prescribed a Modulator

The proportion of pwCF by category of eligibility and prescription for CFTR modulators across adult sites is shown in Figure 4.8. The majority of pwCF at all sites are eligible and prescribed a CFTR modulator, with percentages ranging from 79.5% (Site 5) to 98.2% (Site 3). A smaller proportion of pwCF are eligible but not prescribed a CFTR modulator, varying from 1.8% (Site 3) to 10.1% (Site 12).

FIGURE 4.8: ACFDR CLINICAL VARIATION AMONG CF CENTRES 2023: PROPORTION AT ADULT SITES THAT ARE ELIGIBLE AND PRESCRIBED A CFTR MODULATOR



5. 2023 ACADEMIC OUTPUTS

Publications

Shanthikumar S, Ruseckaite R, Corda J, Mulrennan S, Ranganathan S, Douglas *T. Telehealth use in Australian cystic fibrosis centers: Clinician experiences.* Pediatr Pulmonol. 2023 Oct;58(10):2906 – 2915. doi: 10.1002/ppul.26612. Epub 2023 Jul 21. PMID: 37477510.

Shum BOV, Sng LMF, Ruseckaite R, Henner I, Twine N, Bauer DC, Wilgen U, Pretorius C, Barahona P, Ungerer JPJ, Bennett G. *The inequity of targeted cystic fibrosis reproductive carrier screening tests in Australia.* Prenat Diagn. 2023 Jan;43(1):109 – 116. doi: 10.1002/pd.6285. Epub 2022 Dec 15. PMID: 36484552.

Doumit M, Chuang S, Middleton P, Selvadurai H, Sivam S, Ruseckaite R, Ahern S, Mallitt KA, Pacey V, Gray K, Jaffe A. *Clinical outcomes of adults and children with cystic fibrosis during the COVID-19 pandemic.* J Cyst Fibros. 2023 May;22(3):581 – 586. doi: 10.1016/j.jcf.2022.09.006. Epub 2022 Sep 16. PMID: 36163166; PMCID: PMC9477965.

Conference Presentations

NACFC 2023, Phoenix, AZ, 2023. Ruseckaite et al. *Data quality audit of the Australian Cystic Fibrosis Data Registry: A pilot study.* Poster presentation.

NACFC 2023, Phoenix, AZ, 2023: Ruseckaite et al. *Associations between clinical variables and health-related quality of life in children and adolescents with cystic fibrosis: A scoping review.* Poster presentation.

NACFC 2023, Phoenix, AZ, 2023. Semenchuk et al on behalf CF Registry Global Collaboration. *The impact of COVID-19 on lung function and nutritional status in cystic fibrosis. A global observational study.* Poster presentation.

TSANZ 2023, Christchurch NZ, 2023. Ahern et al. *Enhancing CF registry data quality: A collaborative endeavour.* Poster presentation.

6. DATA ACCESS REQUESTS

The ACFDR encourages the secondary use of its data for research and related purposes. Seven data access requests were received and approved for the ACFDR in 2023.

Date	Name	Organisation	Request type	Request
3-Jan	Maxine Orre	Vertex Pharmaceuticals	Non-research	Orkambi 6 – 11 Post-Marketing commitment study extension (6 – 11 PMC)
2-Feb	Peter Middleton	Westmead Hospital, Sydney	Research	Assessment of pregnancy numbers and outcomes in CF in Australia
3-Mar	Zoe Xiang Li	BGI Health (AU) Company Pty Ltd	Non-research	Top 200 CFTR variants in the Australian population
14-Apr	John Massie	Royal Children Hospital, Melbourne	Research	Diagnosis of CF by newborn screening in Australia
9-Jun	Maxine Orre	Vertex Pharmaceuticals	Non-research	CF patient population by age and mutation; clinical parameters for subgroups
28-Aug	Arul Earnest	Monash University	Research	Bayesian spatio-temporal modelling of specific types of infection, poor lung function (FEV1%), and optimal BMI% among cystic fibrosis patients in Victoria and areal level determinants
15-Dec	Maxine Orre	Vertex Pharmaceuticals	Non-research	CF patient population by age and mutation; clinical parameters for subgroups in 2 – 5-year-olds

How can I request data from the ACFDR?

Data access requests are subject to approval by the registry's Steering Committee and relevant ethics committees, and Monash University's conditions of use. Interested researchers/individuals are advised to contact Monash University for details and to arrange consideration of their research proposal. In accordance with the ACFDR data access policy, a fee may be charged to recover the costs of data extraction and/or analysis.

APPENDICES

LIST OF FIGURES

LIST OF TABLES

REGISTRY STEERING COMMITTEE MEMBERSHIP 2023

Steering Committee Members	Role/Specialisation	Institution/Association
Professor Susannah Ahern	Coordinating Investigator/Academic Lead	Monash University, VIC
Professor Peter Wark	Clinical Lead ACFDR/CF Adult Physician	The Alfred Hospital, VIC
Dr Andre Schultz	Deputy Lead/CF Paediatric Physician	Perth Children's Hospital, WA
Dr Rasa Ruseckaite	Deputy Monash Academic Lead ACFDR	Monash University, VIC
Ms Jo Armstrong	CEO Cystic Fibrosis Australia	Cystic Fibrosis Australia
A/Professor Tom Kotsimbos	CF Adult Physician	Alfred Health, VIC
Dr Siobhain Mulrennan	CF Adult Physician	Sir Charles Gairdner Hospital, WA
Dr Tonia Douglas	CF Paediatric Physician	Queensland Children's Hospital, QLD
Dr Katherine Frayman	CF Paediatric Physician	Royal Children's Hospital, VIC
Dr Nathan Ward	Physiotherapist	Royal Adelaide Hospital, SA
Sue Morey OAM	Nurse Practitioner	Sir Charles Gairdner Hospital, WA
Pia Sappl	Consumer Representative	NSW
Chloe Arthur	Consumer Representative	QLD
Honor Rose	Consumer Representative	VIC
Caz Boyd	Consumer Representative	WA

LIST OF PARTICIPATING SITES

Site	
Centenary Hospital for Women & Children (CHW)	Paediatric
Gold Coast University Hospital (GCH)	Adult
Gosford Hospital (GOS)	Paediatric and Adult
John Hunter Children's Hospital (JHC)	Paediatric
John Hunter Hospital (JHH)	Adult
Launceston General Hospital (LGH)	Paediatric
Mater Hospital (MAH)	Adult
Monash Medical Centre (MMC)	Paediatric and Adult
North West Regional Hospital (BUR)	Paediatric
Perth Children's Hospital (PCH)	Paediatric
Queensland Children's Hospital (QCH)	Paediatric
Royal Adelaide Hospital (RAH)	Adult
Royal Children's Hospital (RCH)	Paediatric
Royal Hobart Hospital (RHH)	Paediatric & Adult
Royal Prince Alfred Hospital (RPA)	Adult
Sir Charles Gairdner Hospital (SCG)	Adult
Sydney Children's Hospital (SCH)	Paediatric
The Alfred Hospital (ALF)	Adult
The Canberra Hospital (CHA)	Adult
The Children's Hospital, Westmead (CHW)	Paediatric
The Prince Charles Hospital (PCH)	Adult
Westmead Hospital (WMH)	Adult
Women's and Children's Hospital (WCH)	Paediatric

ACFDR COORDINATING CENTRE, MONASH UNIVERSITY

The ACFDR coordinating team encourages contact regarding all registry related activities and operations, including access to data through the email account below

Email: med–acfdregistry@monash.edu
Registry Academic Lead: Prof Susannah Ahern
Deputy Monash Academic Lead: Dr Rasa Ruseckaite
Principal Data Science Lead: Dr Ahmad Reza Pourghaderi
Registry Coordinator: Marisa Caruso
Phone: +61 3 9903 1656

ACCESS TO REGISTRY DATA

Requests for information from the ACFDR are welcome
Application should be made to the ACFDR Coordinating Centre, Monash University.
Email: med–acfdregistry@monash.edu

ELECTRONIC DATA CAPTURE

Study data was collected and managed using REDCap electronic data capture tool hosted and managed by Helix (Monash University).[1, 2]

REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

1. PA Harris, R Taylor, R Thielke, J Payne, N Gonzalez, JG. Conde, Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support, J Biomed Inform. 2009 Apr;42(2):377 – 81.
2. PA Harris, R Taylor, BL Minor, V Elliott, M Fernandez, L O'Neal, L McLeod, G Delacqua, F Delacqua, J Kirby, SN Duda, REDCap Consortium, The REDCap consortium: Building an international community of software partners, J Biomed Inform. 2019 May 9 [doi: 10.1016/j.jbi.2019.103208]

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Produced by Pidgeon Ward
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