MONASH University

AUSTRALIAN CYSTIC FIBROSIS DATA REGISTRY

ANNUAL REPORT 2021

This publication was produced with the support of Cystic Fibrosis Australia.

Data Period

The data contained in this report was extracted from the ACFDR on April 27th 2022, and pertains to data that relates to patient events from January 1st to December 31st 2021. As the registry do es not capture data in real time, there can be a lag between occurrence of an event and 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
FEV	Forced Expiratory Volume
FEV1 % predicted	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

This report was produced with the support of Cystic Fibrosis Australia.

Susannah Ahern, Farhad Salimi, Marisa Caruso, Rasa Ruseckaite, Peter Wark, Andre Schultz and Jo Armstrong on behalf of the ACFDR. The ACFDR Registry Annual Report, 2021. Monash University, Department of Epidemiology and Preventive Medicine, August 2022, Report No 23.

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FOREWORD

FROM THE CYSTIC FIBROSIS AUSTRALIA CEO

The Australian Cystic Fibrosis Data Registry (ACFDR) is a critical project for Cystic Fibrosis Australia because it ensures the improvement of clinical outcomes, effectively directs research, enables clinical trials, and highlights areas for advocacy. Indeed, having robust data enables more informed information and better outcomes. The data registry is a critical tool to help better serve Australians living with cystic fibrosis.

It is because of the incredible CF community and their trust and willingness to allow their health data to be included that makes the ACFDR what it is today. Further, the CF centres around the country have done a great job in supporting the ACFDR as each and every day they are at the forefront of supporting people living with CF.

I would like to extend my sincere thanks to the Steering Committee for their oversight of the Data Registry and Monash University who administer and manage this essential work on behalf of Cystic Fibrosis Australia. We are committed to ensuring the ongoing development and effectiveness of the data registry as the needs in our community evolve and my sincere thanks to everyone involved in making this possible.

It is evident that, with our combined efforts, we can, together, help get the necessary insights needed to inform optimum health outcomes for the thousands of people living with cystic fibrosis in Australia. The complexity of CF means that the need for meaningful data has never been more important. Indeed, the ACFDR is invaluable in driving clinical improvement to bring a better quality of life and increased life expectancy. My hope is that treatment breakthroughs, innovation and other patient outcomes will continue to make life better for people living with cystic fibrosis.

Jo Armstrong
Chief Executive Officer
Cystic Fibrosis Australia

FROM THE REGISTRY CLINICAL LEAD

It is a great honour to write the forward to the ACFDR 2021 report in my first year as the clinical lead. I should begin firstly by thanking all of those who have made this report possible. Firstly the CF community, through CFA, thank you for continuing to support the registry financially and for all those people and their families living with CF who share their information. This is your registry, it belongs to the CF community and above all tells your story and once again this is a story of struggle but increasing success.

Thank you to the clinical teams that generously ensure the data is entered on time and with such great accuracy, the integrity and value of the registry only possible through these efforts. Through these efforts data completion in this report is 99.4%. I would also like to thank the Monash registry team under the leadership of Prof Susannah Ahern as data custodians for managing the registry so ably and professionally and for producing such a valuable publication.

I am mindful though that we are in the position today with the ACFDR only through the efforts of those who have gone before us. I need to acknowledge the important role that Prof Scott Bell has played in the ACFDR from its inception in 1998 to his stepping down as clinical lead in 2021. This is a remarkable achievement and one for which we all remain in your debt. I would also like to acknowledge the support of Nettie Burke as previous CEO, CFA in supporting the ACFDR throughout her tenure and establishing the registry under the supervision of the team at Monash.

The 2021 ACFDR report continues to break new ground and allows us an insight into the rapidly evolving situation that exists for people and their families living with CF. The report tells us there are more people in Australia with CF, they have better lung function and it continues to improve, there are fewer people infected with organisms such as Pseudomonas, since 2015 there has been a seven fold increase in people able to access CFTR modulators. Finally we continue to see improvements in survival and fewer people needing transplants.

We need to continue to look to the future, ensure the ACFDR continues to inform us about the changing needs and challenges for people with CF. We will continue the conversation with the CF community and clinicians as to how we can improve the ACFDR and its relevance in the care of people with CF. Plans are underway to allow it to play a critical role in the new process of centre peer review and quality improvement.

I hope you enjoy this report as much as I have.

Professor Peter Wark
Clinical Lead, Australian Cystic Fibrosis Data Registry

Senior staff specialist in Respiratory and Sleep Medicine at John Hunter Hospital, Newcastle and a conjoint Professor with the University of Newcastle

FROM THE REGISTRY DEPUTY CLINICAL LEAD

The ACFDR reflects a tremendous and excellent effort by the Australian CF community. People with CF and their families provide information to the Registry. CF care teams diligently collect and enter data. CF Centre Directors oversee processes at a local level and support the process on a national level. CFA funds the management of the Registry and provides data custodianship. The Clinical Outcomes Data Reporting and Research Program at Monash University manages the Registry whilst the ACFDR Steering Committee provides strategic direction and oversight.

Thank you to the clinical teams that generously ensure the value of a registry is directly related to the completeness and accuracy of data entry. Therefore, it is a pleasure to see that the 2021 ACFDR report is the most comprehensive report, with the highest level of data completeness (over 99%), since inception of the ACFDR over 20 years ago. The quality of data entered, and mechanisms for quality control have also improved. These improvements greatly enhance the value of the Registry for the CF community as it continues to advocate for people affected by CF, for CF centres as they compare their performance and effectiveness of clinical care against KPIs and against other CF centres, and for researchers who use the registry to analyse national data.

The above progress can be attributed to the efforts of all the stakeholders mentioned above. Special mention should be given to 6 years of strong leadership by the recent ACFDR clinical lead, Professor Scott Bell, skilful management by Prof Susannah Ahern and her team at Monash University, and strong support from the amazing Nettie Burke who recently stepped down from the role as CEO of CFA. It should also be recognised that funding from industry, channelled through Monash University, has allowed CF centres to employ staff to perform high quality data entry against strict timelines.

Do enjoy reading the 2021 report! An additional section on COVID-19 vaccination has been added since 2020. The Report shows many interesting trends e.g., that telehealth visits remained highly utilised since the rapid increase seen at the start of the pandemic. Importantly, survival for people with CF continues to improve!

The ACFDR is now at a stage where it excels at its core business. Various opportunities now exist to further enhance its functionality and usefulness to the CF community.

Associate Professor André Schultz
Deputy Clinical Lead, Australian Cystic Fibrosis Data Registry

Respiratory Physician Department of Respiratory Medicine, Child and Adolescent Health Service, Western Australia

INTRODUCTION

Clinical registries that monitor and review outcomes for people with cystic fibrosis (CF) have been in existence for many decades. Traditionally, clinical registries served primarily epidemiological purposes, however increasingly their benefits in driving quality improvement through comparative reporting; determining longer-term outcomes; and creating an evidence base for service planning and policy, are being recognised[1].

The Australian Cystic Fibrosis Data Registry (ACFDR) began operations in 1998 and hence has collected data on Australian people with CF for over 23 years. The 2021 ACFDR Annual Report includes information relating to over 3,600 people with CF, estimated to comprise over 95% of Australia's CF population. Collecting data from twenty-three paediatric, adult and mixed CF centres across Australia. The ACFDR dataset enables reporting in a manner generally consistent with other CF registries, such as those in Europe, Canada, the United Kingdom and the United States.

Australians newly diagnosed with CF are invited to participate in the registry through their treating CF centre. Participation is mainly via an opt-in consent method, noting that participation in the ACFDR is required for people with CF to receive PBS-subsidised CFTR modulator treatment. Information regarding the use of CFTR modulators among Australians with CF was introduced in the registry in 2019, and the ACFDR will have an important ongoing role in monitoring and reporting CFTR modulator use in the increasing proportion of people with CF that are eligible for these treatments, as more CFTR modulators become available.

The ACFDR is funded by Cystic Fibrosis Australia (CFA) and managed by Monash University, under a shared data custodianship arrangement. The registry is actively supported by a multidisciplinary Steering Committee with consumer representation, that leads the strategic direction of the ACFDR, reviews requests for access to ACFDR data, develops and reviews ACFDR policies and procedures, and reviews the quality of outputs from the Registry. The ACFDR Steering Committee provides outstanding leadership and advice across all these areas, and the success of the ACFDR is in large part due to its commitment and expertise.

The 2021 Annual Report is the third report to be developed with data collected via the ACFDR Data Quality Assurance Program, funded by Vertex Pharmaceuticals, that provides CF centres with payment for complete data. This has supported sites to provide very high levels of data completeness. The quality of this Annual Report's data, with core data elements at around 99% completeness, are a significant enhancement to the overall dataset. This allows the ACFDR to be increasingly confident that the data reported accurately reflects the epidemiological features and clinical outcomes of the Australian CF population. The data items covered by the QA program will continue to expand over time, providing important information about longer term outcomes and impacts of care on many aspects of life and wellbeing for people with CF.

SUMMARY OF 2015, 2017, 2019, 2020 AND 2021 REGISTRY DATA

THIS SECTION PROVIDES AN OVERVIEW OF THE CF POPULATION, HEALTH OUTCOMES, AND CARE IN AUSTRALIA FOR 2015, 2017, 2019, 2020[1] AND 2021.

	2015	2017	2019	2020	2021
PEOPLE WITH CYSTIC FIBROSIS					
Total people with CF in the ACFDR	3,379	3,151[2]	3,446	3,538	3,616
Age (median)	18.8 yrs	19.6 yrs	19.6 yrs	20.2 years	20.6 years
Age (mean)	20.9 yrs	21.7 yrs	22.0 yrs	22.6 years	23.0 years
Adults (≥ 18 yrs) number, (%);	1,756 / 52.0%	1,692 / 53.7%	1,854 / 53.8%	1,965 / 55.5%	2,019 / 55.8%
Adults: Males %	53.2%	53.7%	53.1%	52.8%	52.8%
CF DIAGNOSIS & GENOTYPING					
Newly diagnosed people with CF (pp)	98	72	66	74	92
% Diagnosis < 1 yr	73.5%	76.6%	85.0%	82.4%	82.6%
% Diagnosis ≥ 18 years	3.1%	4.2%	4.5%	10.8%	12.0%
Genotyped – one allele (two alleles)	91.7%	94.1%	96.0% (88.0%)	98.4% (92.2%)	98.4% (94.8%)
% F508del Homozygous	50.2%	49.8%	47.0%	47.0%	47.0%
% F508del Heterozygous	42.0%	36.6%	42.0%	43.0%	43.0%
CLINICAL MEASURES (LUNG FUNCTION & NUTRITION)*					
Median FEV1 % predicted children 6-17 years	90.0%	91.0%	91.0%	91.0%	93.0%
Median FEV1 % predicted adults ≥ 18 years	70.0%	68.0%	71.0%	70.0%	73.0%
Median weight for length percentile < 2 yrs	47th	50th	46th	51st	51st
Median BMI percentile children	54th	52nd	55th	57th	58th
Median BMI - adults kg/m^2	22.6	22.8	23.0	22.9	23.0
RESPIRATORY MICROBIOLOGY					
P. *aeruginosa (%)*	50.1%	55.9%	47.8%	41.6%	38.9%
S. *aureus (%)*	33.9%	50.9%	51.5%	47.1%	47.3%
Aspergillus *spp* (%)	18.2%	22.2%	22.9%	18.8%	17.5%
Non tuberculous mycobacterium (%)	2.8%	4.2%	5.9%	6.4%	8.1%
COMPLICATIONS					
% with Diabetes 12 - 17 years	N/A	N/A	N/A	17.3%	14.2%
% with Diabetes 18 - 29 years	N/A	N/A	N/A	21.5%	23.8%
% with Diabetes 30+ years	N/A	N/A	N/A	30.0%	29.9%
CFTR MANAGEMENT					
% taking modulator	7.3%	14.9%	37.7%	52.6%	55.2%
% with Physiotherapy review	N/A	N/A	N/A	N/A	85.7%
% with Dietician review	N/A	N/A	N/A	N/A	80.6%
% with Mental Health review ≥ 12 years	N/A	N/A	N/A	N/A	74.7%
TRANSPLANTS AND SURVIVAL					
Bilateral lung transplants	30	41	33	15	9
Deaths (Total CF deaths)	17	27	26	18	19
Median age of death	31.6 years	35.6 years	32.0 years	30.7 years	36.8 years
Survival median (cohort, 5 year)	47.4 years (2010-2014)	47.7years (2012-2016)	54.0 years (2014-2018)	53.0 years (2015-2019)	56.9 years (2016-2020)

* Please note the Lung Function and Nutritional calculations were updated in 2021 and subsequently the historical summary data has been amended to reflect this.

1. In 2018 the data registry changed platforms during that year and did not report data.
2. Total number of patients for 2017 is lower due to the exclusion of two sites for low completeness. These include one site from VIC and one NSW location.

Out of 3,616 people with CF, 2,019 (55.8%) were adults.

1. PEOPLE WITH CYSTIC FIBROSIS

1.1 OVERVIEW

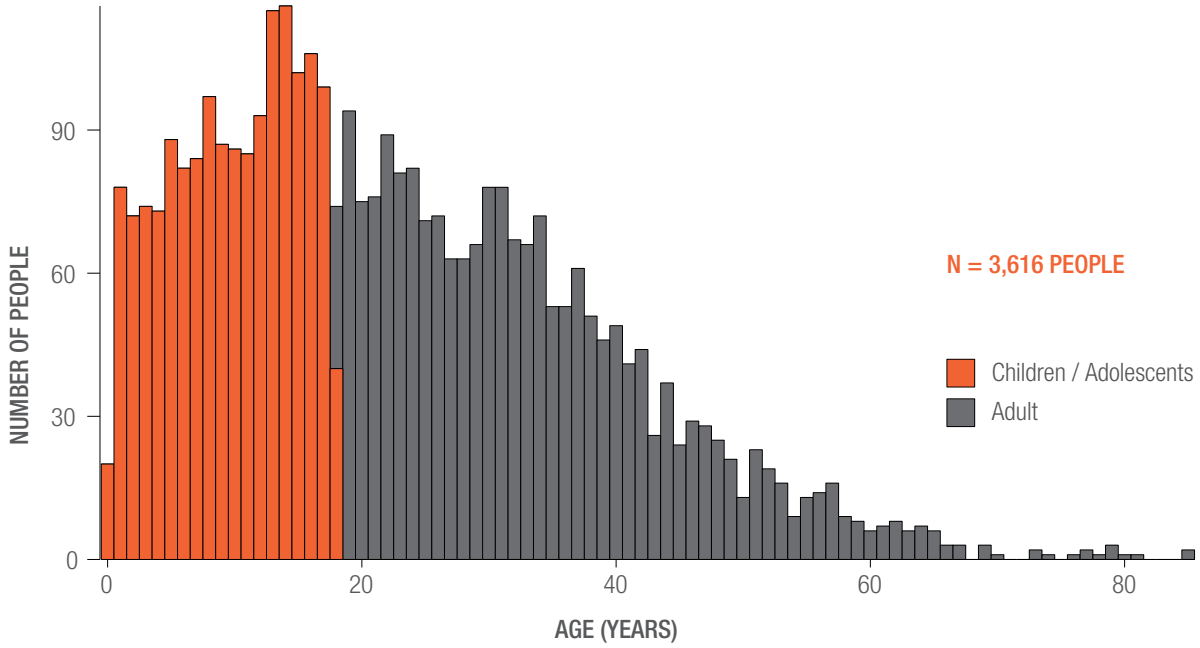
Cystic fibrosis (CF) is a recessive genetic condition which causes damage to the respiratory and digestive systems. This occurs as a result of a variant in the Cystic Fibrosis Transmembrane Conductance Regulator *(CFTR)* gene. Variants in the *CFTR* gene (which controls the movement of water and salt within the body), can disrupt the functioning of the CFTR protein found in the cells of the lungs and other parts of the body causing a build-up of thick mucus, which can lead to lung infections, destruction of the pancreas, and complications in other organs. This report highlights the epidemiological and clinical characteristics of people with CF that are captured in the ACFDR.

As the ACFDR is a registry that collects data from people with CF from the time of their diagnosis, a majority of the data reported is aggregate data i.e. data reported for all patients in the registry. Where data are reported only for a subset of people, such as those newly diagnosed in 2021, or those of a particular age or gender, this will be noted in the text and figures.

1.2 COHORT AGE AND GENDER CHARACTERISTICS

The Australian Cystic Fibrosis Data Registry (ACFDR) held records of 3,616 people with CF as of 31st December 2021. Figure 1.1 shows the age distribution of the total ACFDR cohort at the end of 2021.

FIGURE 1.1: ACFDR 2021: PEOPLE WITH CF IN AUSTRALIA BY AGE



The median age of the registry population was 20.6 years on 31st December 2021, higher than at the end of previous years, having been 20.2 years in 2020. Out of 3,616 people with CF, 1,597 (44.2%) were children (0-17) and 2,019 (55.8%) were adults (18+ years). 14.0% of people were 40 years and over.

TABLE 1.1 – ACFDR 2021: PEOPLE WITH CF BY AGE AND GENDER

AGE	FEMALE	MALE	TOTAL
< 2	45.3% (62)	54.7% (75)	137
2-5	50.0% (154)	50.0% (154)	308
6-11	44.1% (235)	55.9% (298)	533
12-17	52.0% (322)	48.0% (297)	619
18-29	48.4% (438)	51.6% (467)	905
30-39	44.6% (271)	55.4% (337)	608
≥ 40	44.7% (226)	55.3% (280)	506
Total	47.2% (1,708)	52.8% (1,908)	3,616

The median age for males at 21.1 years (20.6 years in 2020) remained higher than that for females at 20.2 years in 2021 (19.6 years in 2020). As of 31st December 2021, the proportion of males in the ACFDR was 52.8% and females were 47.2% of the ACFDR population (Table 1.1).

The age and gender distribution of people with CF as of the end of 2021 is shown in Figure 1.2.

FIGURE 1.2: ACFDR 2021: PEOPLE WITH CF BY AGE AND GENDER

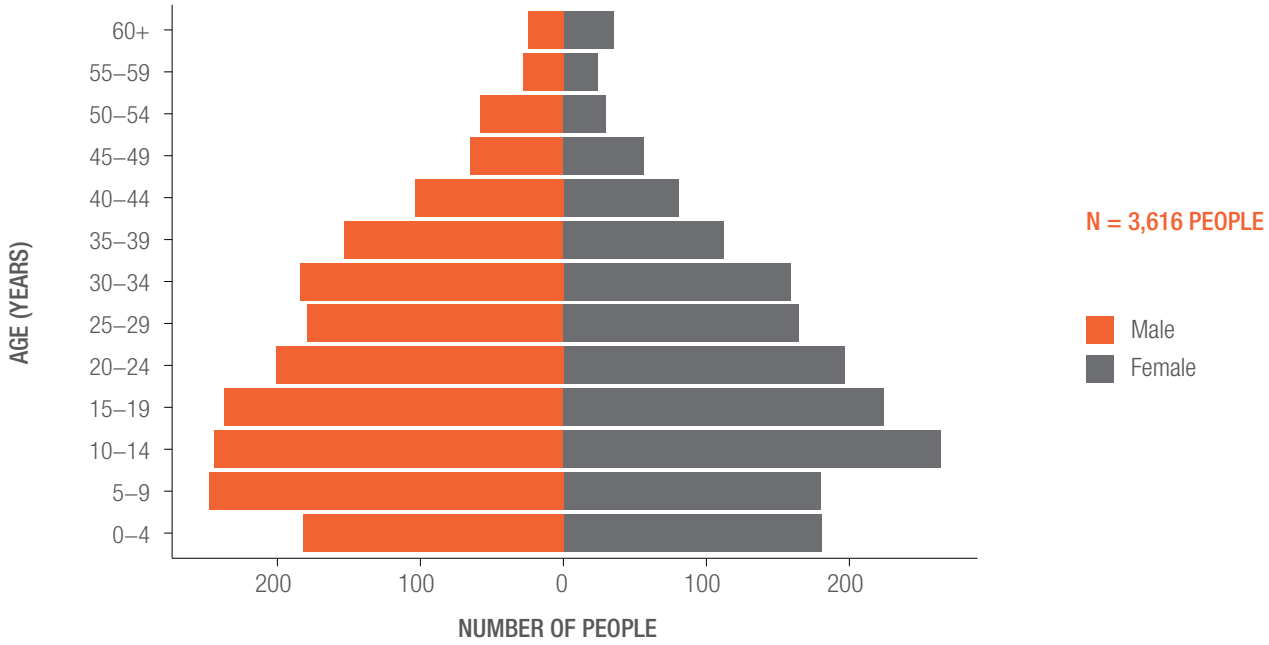
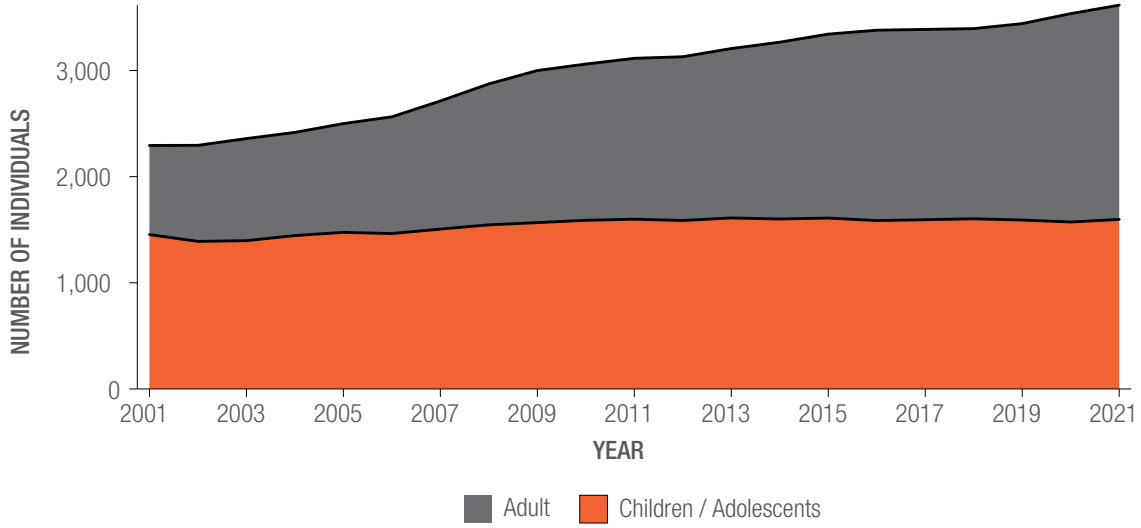


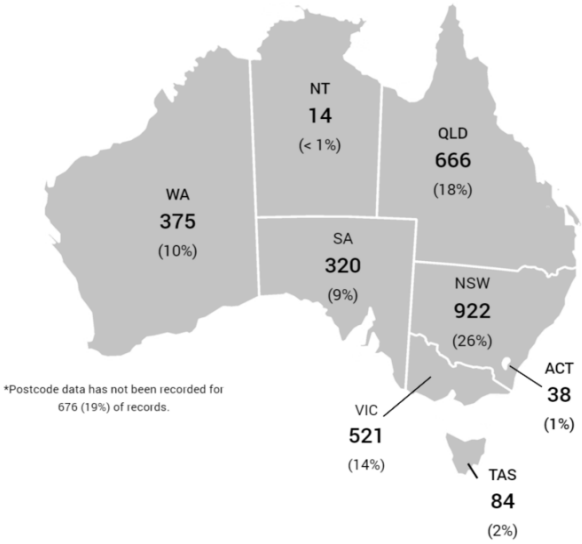
Figure 1.3 shows the number of people in the CF registry for the last 22 years, including the proportion who are adult for each year.

FIGURE 1.3: ACFDR 1998-2021: PAEDIATRIC VS ADULTS PROFILE OVER TIME



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

FIGURE 1.4: ACFDR 2021: DISTRIBUTION BY POSTCODE



The majority (81.31%) of people with CF have their postcode data recorded in the registry.
The distribution of people with CF based on the available postcode data is displayed in Figure 1.4

Those who receive their CF care at centres in each of Australia's jurisdictions are shown in Figure 1.5.

FIGURE 1.5: ACFDR 2021: DISTRIBUTION BY STATE/ TERRITORY

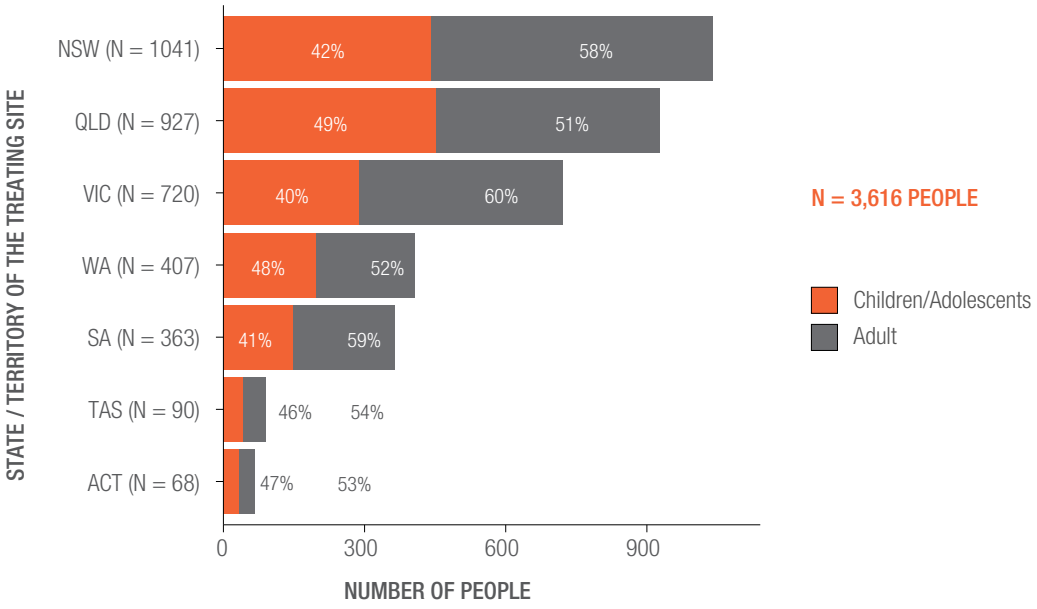


Figure 1.5 shows the distribution of people with CF across Australian jurisdictions, including paediatric vs adult distribution. Jurisdiction is based on the CF centre location, rather than the postcode of the individual from 2021.

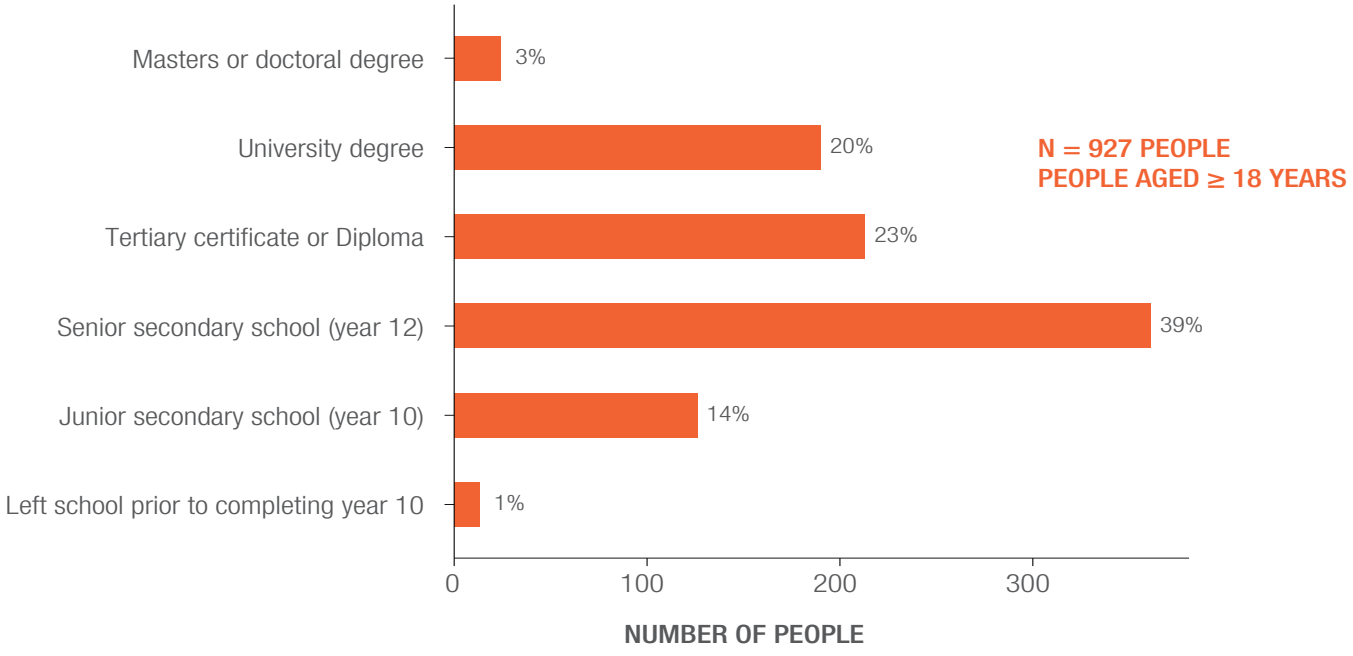
1.3 SOCIAL OUTCOMES OF PEOPLE WITH CF

Over half (54.0%) of adults with CF in the ACFDR have information recorded about their social outcomes. As symptom management improves and survival increases, people with CF are involved in greater numbers in education, employment and having a family.

EDUCATIONAL OUTCOMES

Of the 927 adults with CF with information regarding education in the ACFDR, the proportion who completed a tertiary certificate, diploma, undergraduate or postgraduate degree is 46.0%, with those completing University education being 20.0% (Figure 1.6).

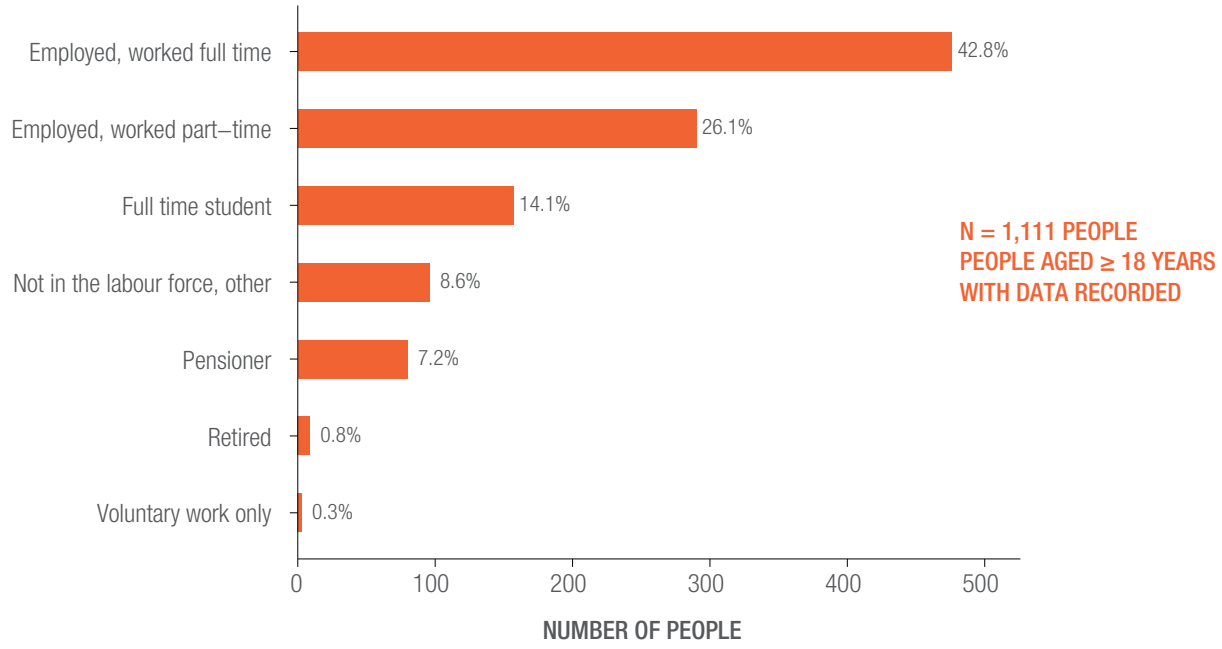
FIGURE 1.6: ACFDR 2021: HIGHEST EDUCATIONAL ATTAINMENT



EMPLOYMENT STATUS

In the ACFDR 1,111 adults with CF have information regarding employment status. Forty two point eight percent were in full-time employment, 26.1% were in part-time employment, and a further 14.1% were in full-time study. Eight point six percent of people with CF were not in the labour force or were looking for work, and a further 7.2% received a pension (Figure 1.7).

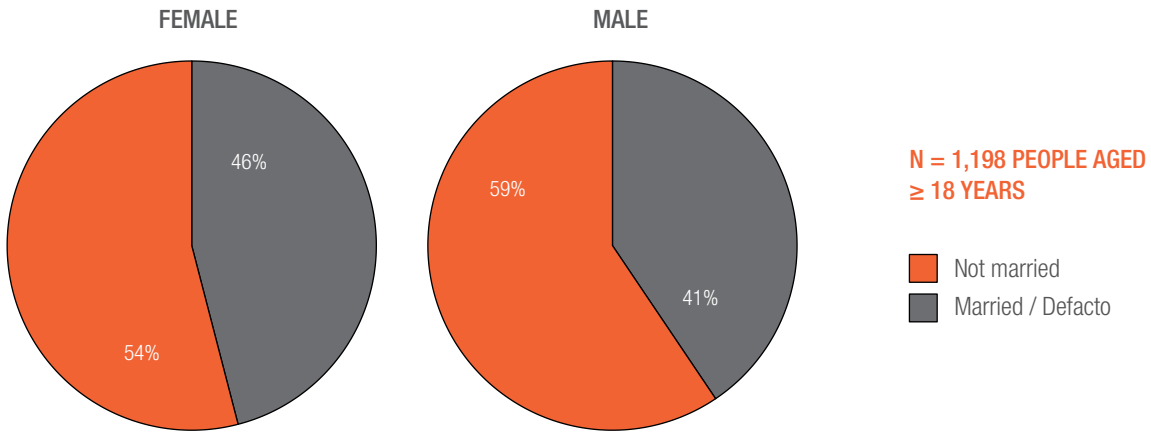
FIGURE 1.7: ACFDR 2021: EMPLOYMENT STATUS



RELATIONSHIP STATUS

Under half (46.0%) of women and 41.0% of men with CF were married or in a de facto relationship, of the 1,198 adults with information regarding marital status in the ACFDR (Figure 1.8).

FIGURE 1.8: ACFDR 2021: MARITAL STATUS



PREGNANCY STATUS

As of 31st December 2021 there were 21 women with CF who had delivered children in 2021, and 13 women who were pregnant at the end of 2021.

92 new diagnoses of CF notified to the registry in 2021. Of these, 76 (82.6%) people were diagnosed at less than one year of age.

2. CF DIAGNOSIS AND GENOTYPING

2.1 NEW DIAGNOSES

There were 92 new diagnoses of CF notified to the registry in 2021 compared to 74 in 2020. Of these, 76 (82.6%) people were diagnosed at less than one year of age, 1 person was diagnosed between 1-5 years, 4 were diagnosed between 6-17 years, and 11 people were diagnosed over the age of 18 years. There were no new cases where the diagnosis date was unknown (Table 2.1).

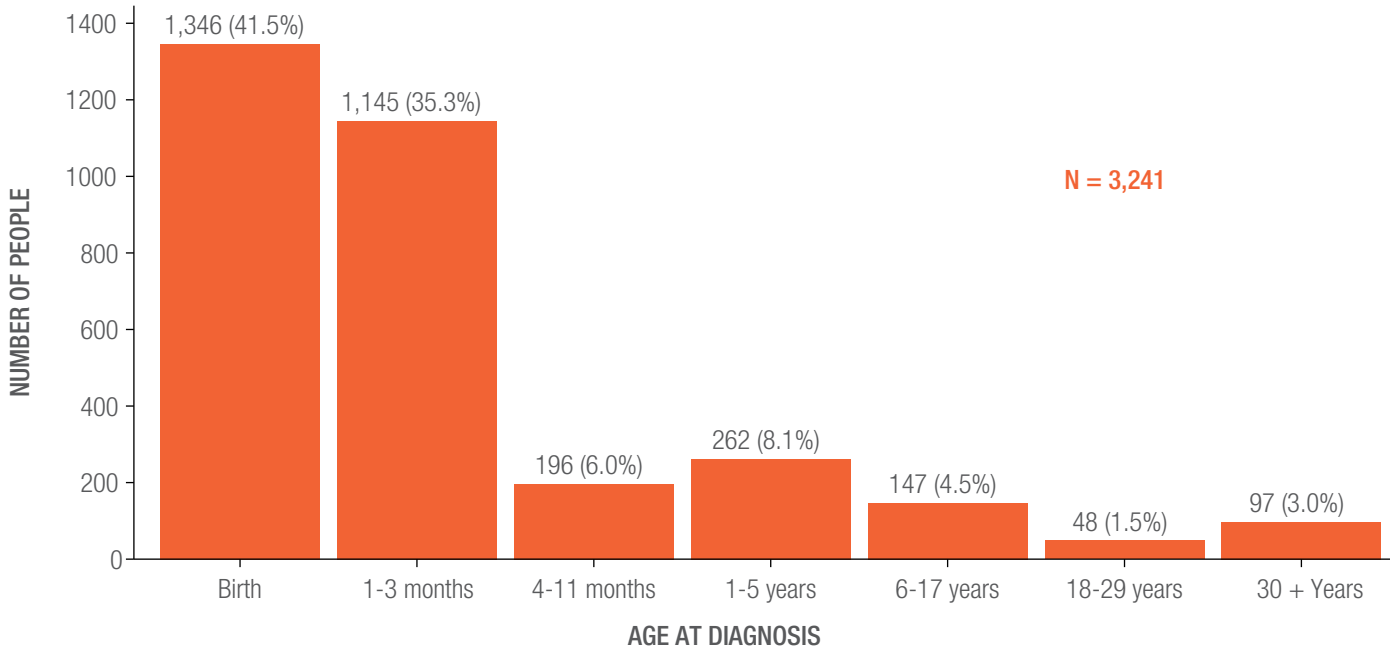
TABLE 2.1 - ACFDR 2021: AGE AT DIAGNOSIS FOR NEWLY DIAGNOSED

AGE	NUMBER	%
<1-5	77	83.7%
6-17	4	4.3%
18-29	3	3.3%
30+	8	8.7%
Total	92	100.0%

The majority (89.6%) of people with CF in the ACFDR have their age of diagnosis recorded; with 82.6% of the ACFDR cohort diagnosed at less than 6 year of age, 4.3% diagnosed between 6-17 years of age and 12.0% were diagnosed over 18 years old. The age of diagnosis for people with CF from the whole ACFDR cohort is shown in Figure 2.1.

Diagnosis is confirmed through a variety of laboratory tests, please refer to Figure 2.2 for a breakdown of the diagnosis method.

FIGURE 2.1: ACFDR 1998-2021: AGE AT DIAGNOSIS FOR THE WHOLE COHORT



Diagnosis for the majority of people in the ACFDR was via newborn screening (64.2%), with 40.0% having clinical symptoms or signs at the time of diagnosis (Figure 2.2). Few (9.3%) had a family history of CF and 2.4% had a diagnosis confirmed by prenatal screening.

The most common clinical symptoms/signs were meconium ileus/intestinal obstruction (35%), respiratory signs/symptoms (27%) and other gastrointestinal symptoms (15%) (Figure 2.2).

FIGURE 2.2: ACFDR 1998-2021: METHOD OF DIAGNOSIS AND PRESENTING SYMPTOMS/ SIGNS

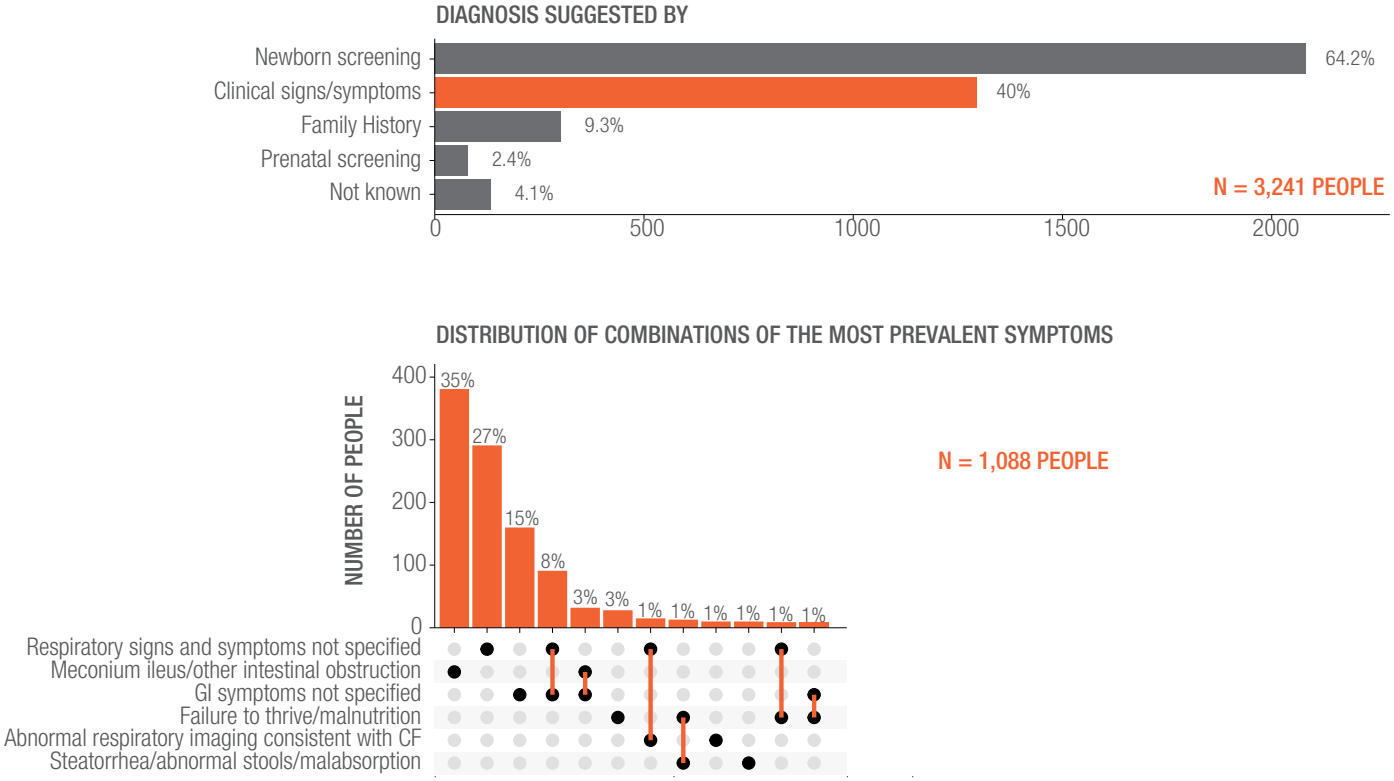


Table 2.2 highlights that diagnoses by newborn screening, family history and prenatal screening has increased over the last 21 years.

TABLE 2.2: ACFDR 1998-2021: COMPARISON OF DIAGNOSTIC CHARACTERISTICS FOR TOTAL COHORT VS 2021 NEW DIAGNOSIS

DIAGNOSIS BY	TOTAL CF COHORT (%)	2021 NEW DIAGNOSES (%)
Newborn screening	2,082/3,241 (64.2%)	65/92 (7.7%)
Clinical symptoms/signs	1295/3,241 (40.0%)	29/92 (31.5%)
Family history	301/3,241 (9.3%)	13/92 (14.1%)
Not known	133/3,241 (4.1%)	0/92 (0.0%)
Prenatal screening	79/3,241 (2.4%)	6/92 (6.5%)

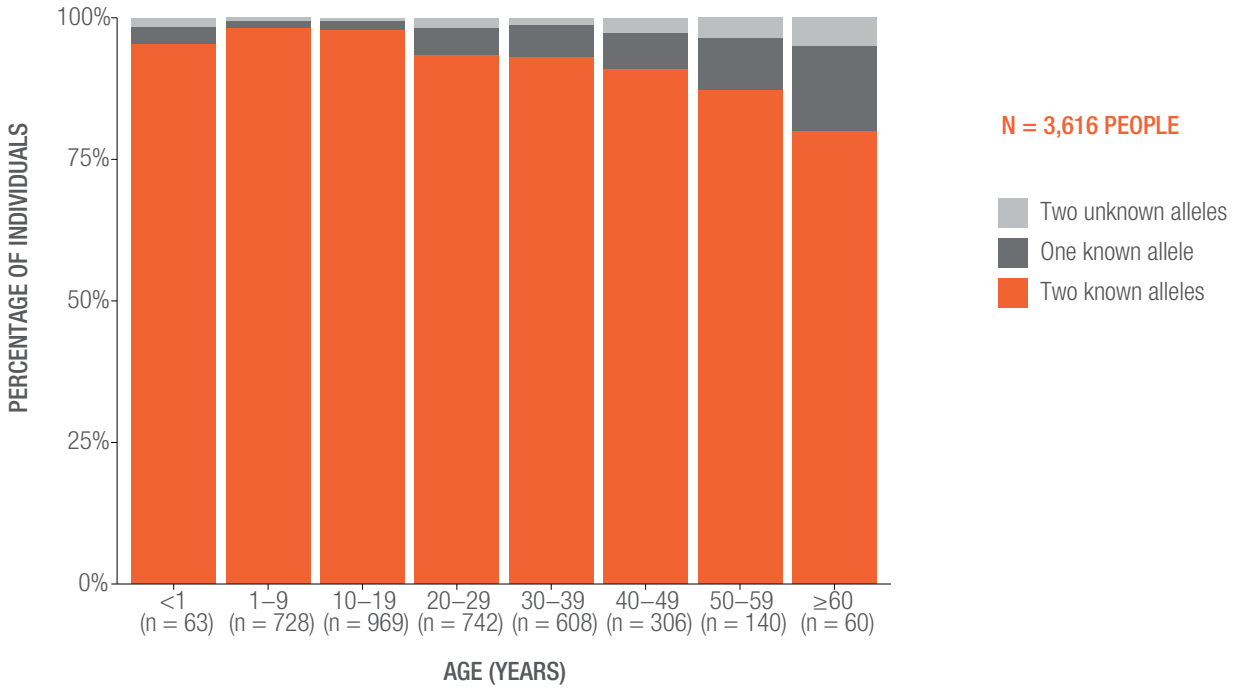
2.2 GENOTYPE

Everyone inherits two copies of the CFTR gene. Since discovery of this gene in 1989, there have been over 1,700 variants of the gene identified. The most common variant is F508del. People with CF can be either homozygous (have two copies) or heterozygous (have one copy) for the F508del variant.

The proportion of people with CF with two known alleles (gene variant) has increased from 92.0% to 94.8% from 2020-2021. Those with at least one known allele have increased from 98.0% to 98.4%, and the proportion with both alleles unknown has reduced from 2.0% to 1.3% over the same period (see Summary Table page 5).

The percentage of people with CF with known variants by age group is shown in Figure 2.3. While 95.2% of infants less than one year of age have two known alleles, this decreases to 90.8% for people over 40 years, and 80.0% for people over the age of 60 years.

FIGURE 2.3: ACFDR 2021: PERCENTAGE OF ACFDR WITH GENOTYPE COMPLETE



Ninety percent of people with CF in the ACFDR are either homozygous (47.0%) or heterozygous (43.0%) for the F508del variant i.e. 90.0% have at least one F508del variant (Figure 2.4 A). An assumption was made in this analysis that the vast majority of the 10.0% 'unknown/other' alleles were not F508del.

Of the 1,569 people who are heterozygous for F508del (i.e. have one F508del variant), the most common second variant and combinations (alleles), are F508del/G551D (13.8%), F508del/R117H (6.4%), and F508del/G542X (5.0%) (Figure 2.4 B).

FIGURE 2.4: ACFDR 2021: MOST COMMON CFTR VARIANT COMBINATIONS

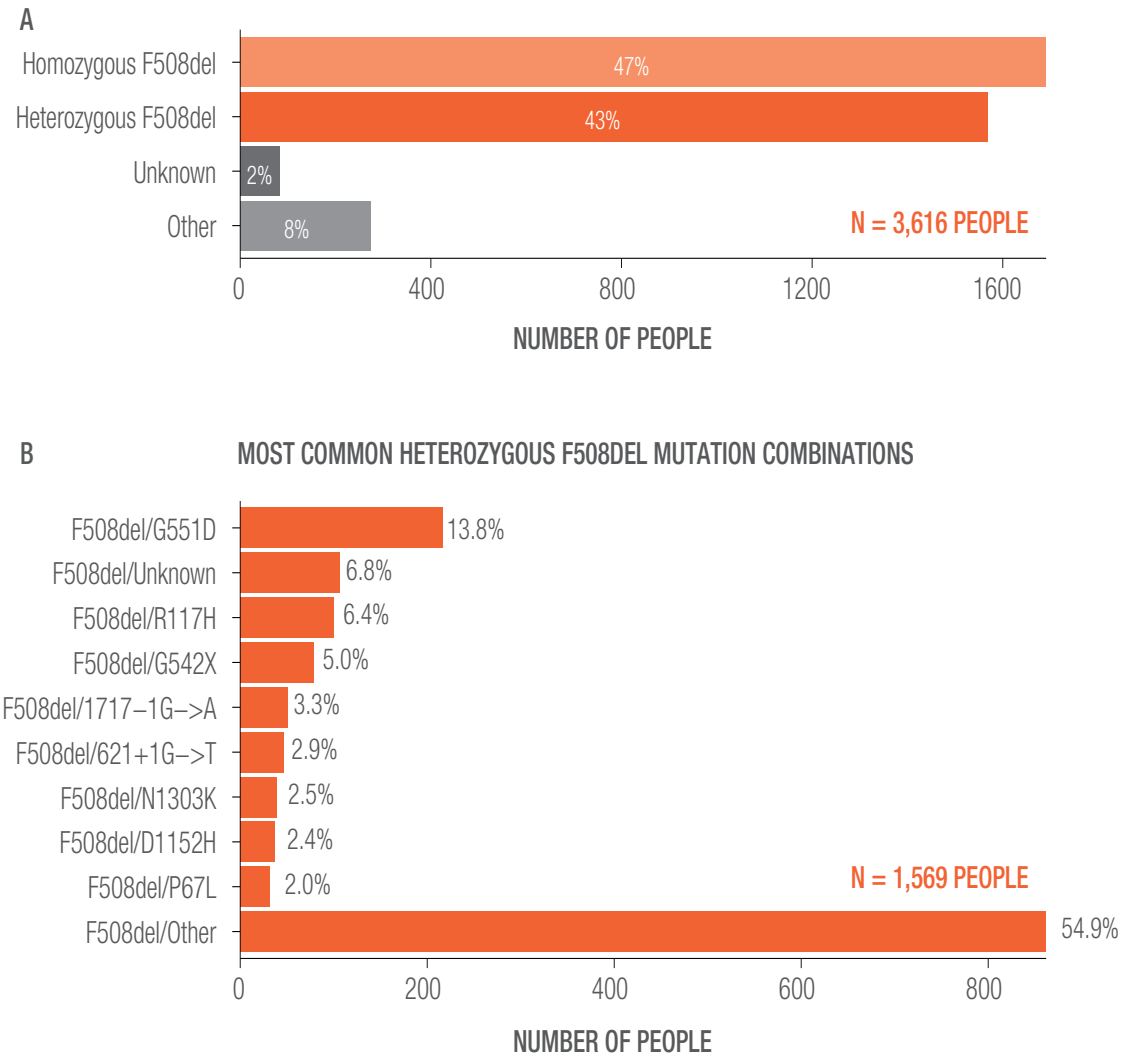
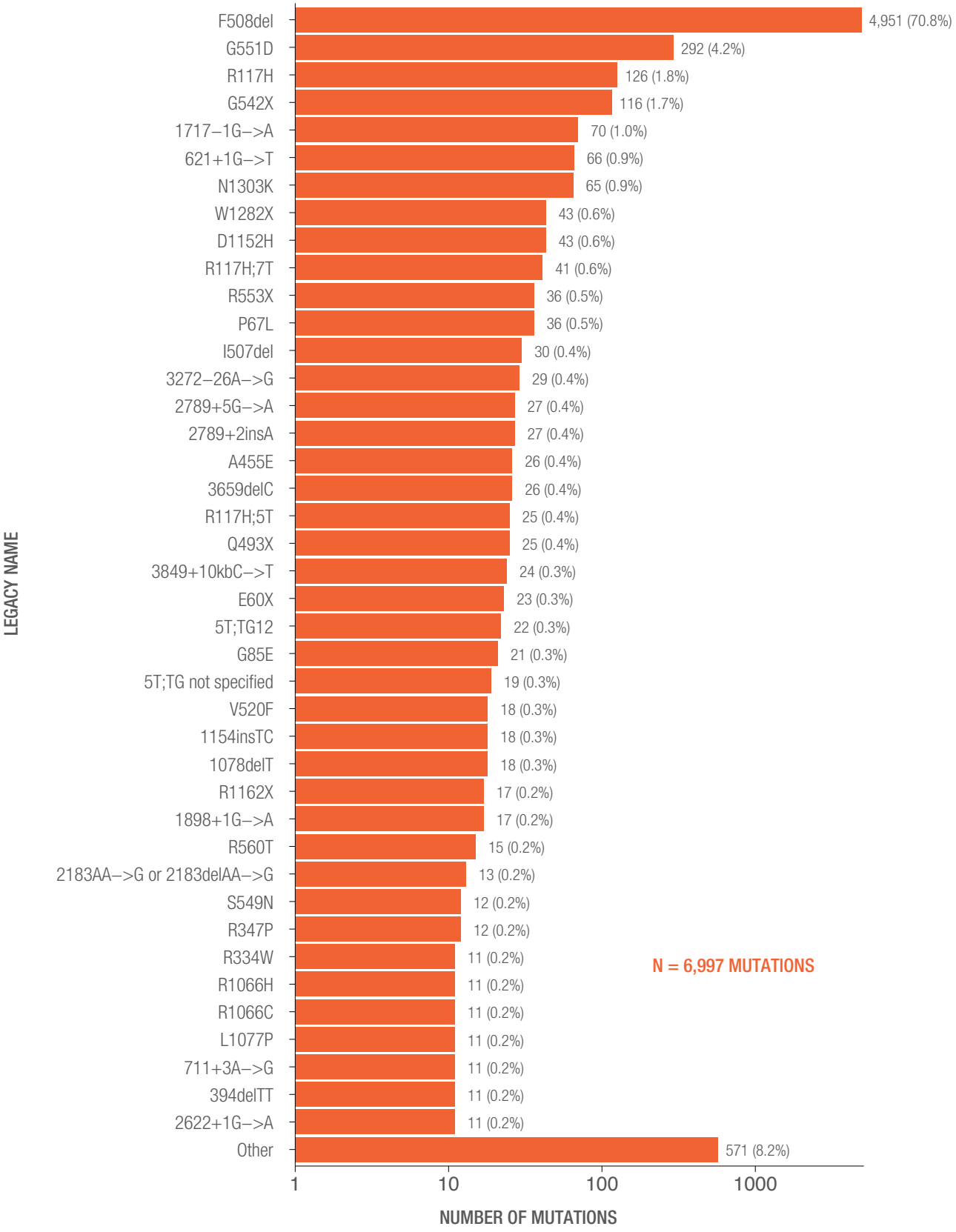


Figure 2.5 below shows that of the 6,997 individual allele variants captured in the ACFDR, that the most common are F508del (70.8%), followed by G551D (4.2%), R117H (1.8%), G542X (1.7%), and 1717_1G_>A (1.0%). The remaining variants comprise less than 1.0% each. The 40 or so most common individual allele variants and their proportion are shown below.

FIGURE 2.5: ACFDR 2021 MOST COMMON INDIVIDUAL ALLELE CFTR VARIANTS IN THE ACFDR



The median FEV1 % predicted for the whole cohort in 2021 was 82.0%.

3. CLINICAL MEASURES

3.1 LUNG FUNCTION

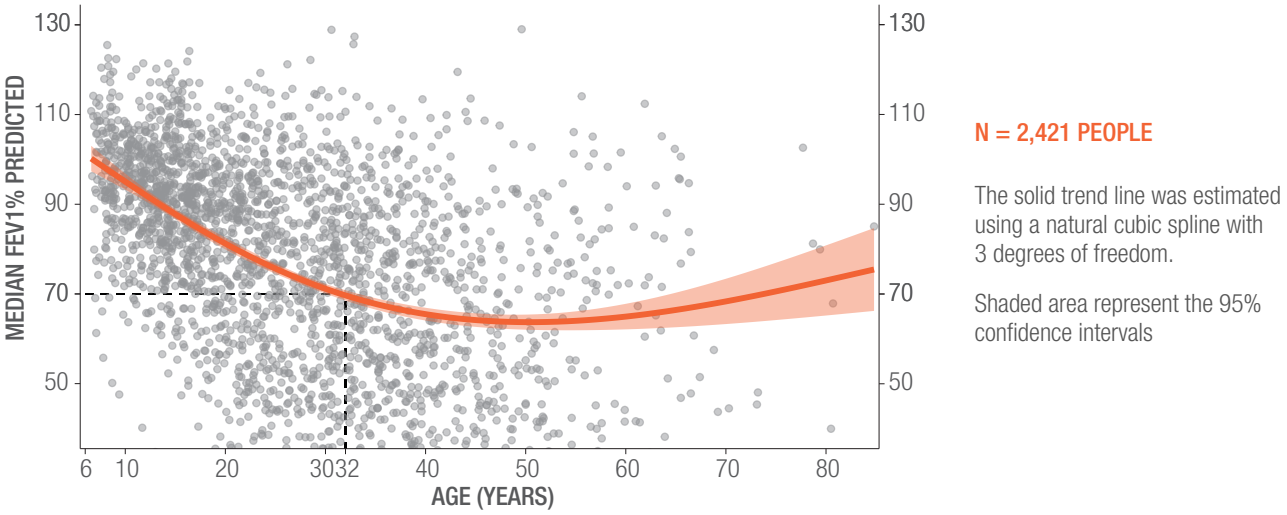
CHILDREN AND ADULTS

For the monitoring of lung function in people with CF, the average of the highest FEV1 % predicted 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.

Approximately two thirds of people with CF in the ACFDR have lung function information (2,421 people) for 2021 (compared to 2,707 people in 2020). Over 12% of participants in the registry are children less than 6 years of age who do not routinely have lung function information recorded, and a further 20.7% of registry participants did not have lung function information recorded in 2021, lower than for previous years.

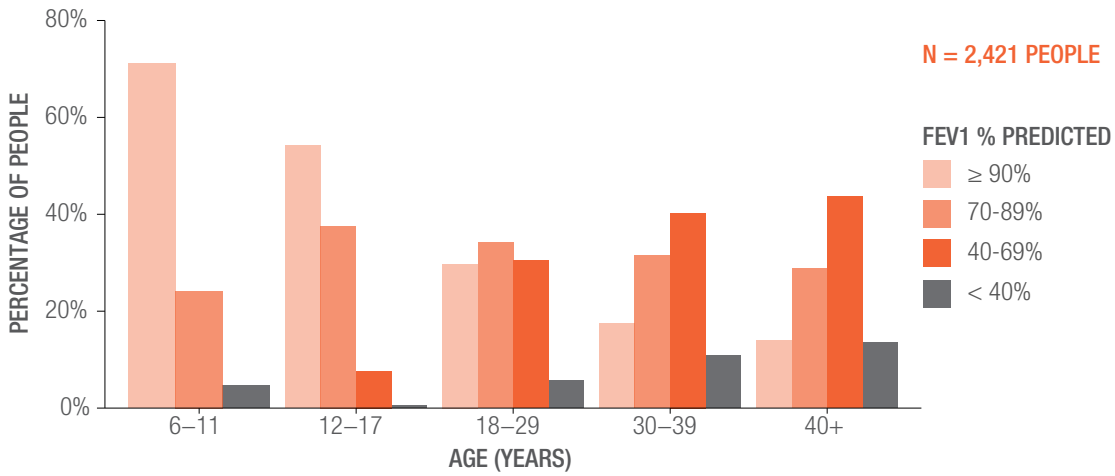
Average lung function for people with CF, measured as FEV1 % predicted is within the normal range for young children (Figure 3.1). At approximately 32 years of age, median FEV1 % predicted is lower than 70% of predicted, a level that denotes moderate lung function impairment.

FIGURE 3.1: ACFDR 2021: MEDIAN FEV1 % PREDICTED BY AGE



Lung function for people with CF varies by age and sex. A small proportion of children with CF, 4.3 – 5.0% of 6-11 year olds, and between 4.3 – 11.6% of 12-17 year olds have a FEV1 % predicted at < 70.0%. In the 18-29 year age group, 33.8 – 38.4% have FEV1 % predicted at < 70.0%. These values increase with increasing range, for the 30-39 age group, the proportion is 46.5 – 56.8% and for the 40+ those with FEV1 % predicted < 70% are 54.9 - 59.0% (Figure 3.2).

FIGURE 3.2: ACFDR 2021: LUNG FUNCTION BY AGE



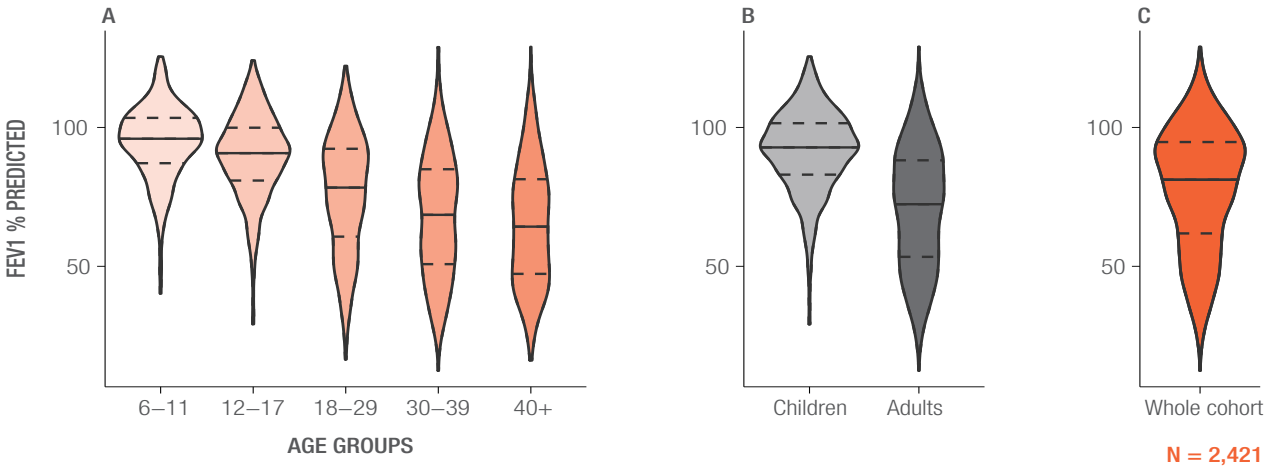
MEDIAN FEV1 % PREDICTED

Figure 3.3 A shows the median FEV1 % predicted for people with CF decreases with age. In the 6-11 year cohort, the median FEV1 % predicted is 96.0% and for children 12-17 years, 91.2%. The median FEV1 % predicted reduces to 78.5% for the 18-29 age group, 69.0% for the 30-40 year old, and 64.2% for those 40 years and older.

The median FEV1 % predicted for children aged 6-17 years is 93.0% and the median FEV1 % predicted for adults aged 18+ years is 73.0% (Figure 3.3 B).

The median FEV1 % predicted for the whole cohort in 2021 was 82.0% (Figure 3.3 C).

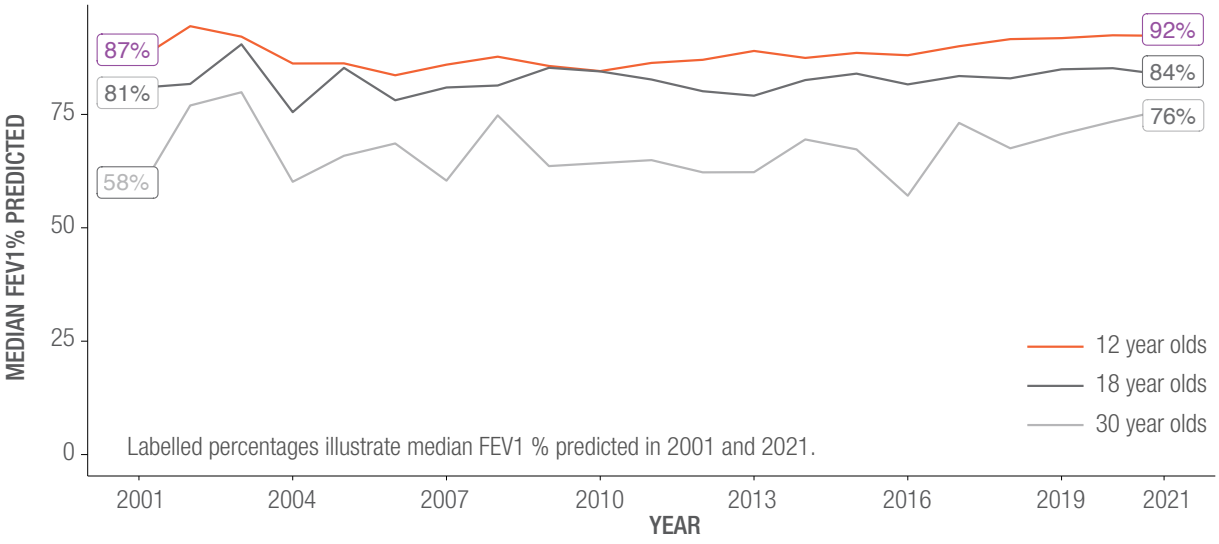
FIGURE 3.3: ACFDR 1998-2021: MEDIAN FEV1 % PREDICTED BY AGE FOR TOTAL COHORT



Horizontal dashed lines represent 25th and 75th percentiles
Horizontal solid line represents 50th percentile (median)

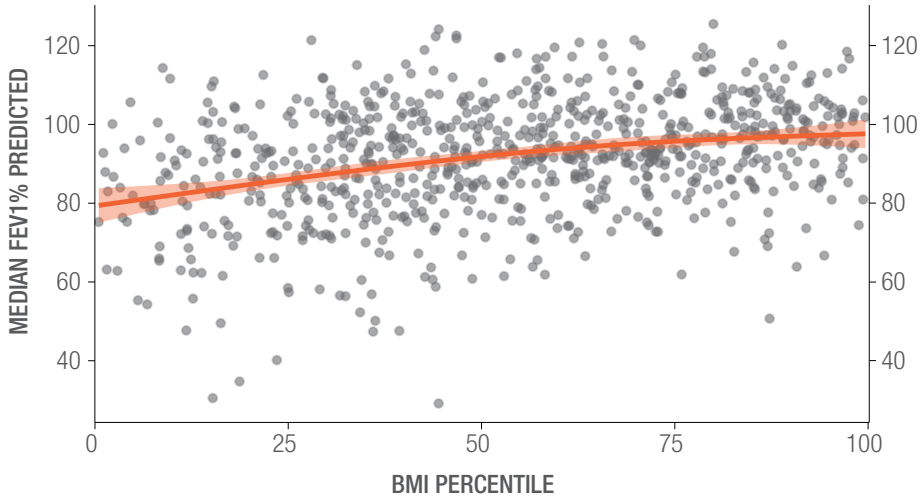
The median FEV1 % predicted has increased over time, particularly for the older age cohorts. For 12 year olds, it has increased from 87.0% in 2001 to 92.0% in 2021, an increase of 5 (4.4%). For 18 year olds the FEV1 % predicted has increase from 81.0% in 2001 to 84.0% in 2021. For 30 year olds, the graph is more variable due to smaller numbers, nevertheless an increased trend appears, especially in the last few years (Figure 3.4).

FIGURE 3.4: ACFDR 1918-2021: MEDIAN FEV1 % PREDICTED OVER TIME



There is a relationship between FEV1 % predicted and Body Mass Index (BMI), whereas BMI percentile increases towards 100%, FEV1 % predicted increases (Figure 3.5).

FIGURE 3.5: ACFDR 2021: FEV1 % PREDICTED VS BMI PERCENTILE FOR 6-17 YEARS



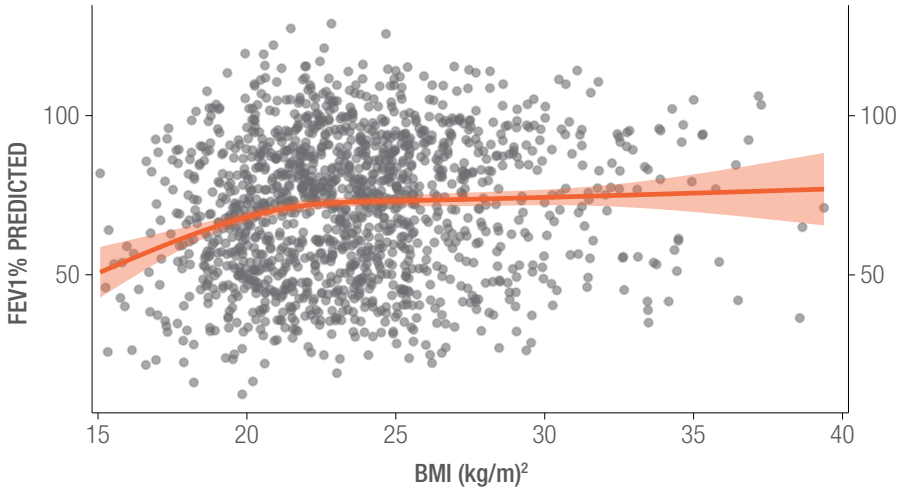
N = 807 PEOPLE AGED 6–17 YEARS

Solid line was estimated using a natural cubic spline with 3 degrees of freedom

Shaded area represent the 95% confidence intervals

For people with CF ages 18-40 years, FEV1 % predicted increases, although, at BMIs into the high 20s, this appears to variably affect FEV1 % predicted. People with CF over 40 years are not included due to fewer numbers, making the data difficult to interpret due to increased variability (Figure 3.6).

FIGURE 3.6: ACFDR 2021: MEDIAN FEV1 % PREDICTED VS BMI AGES ≥ 18 YEARS



N = 1,475 PEOPLE AGED ≥ 18 YEARS

Solid line was estimated using a natural cubic spline with 3 degrees of freedom

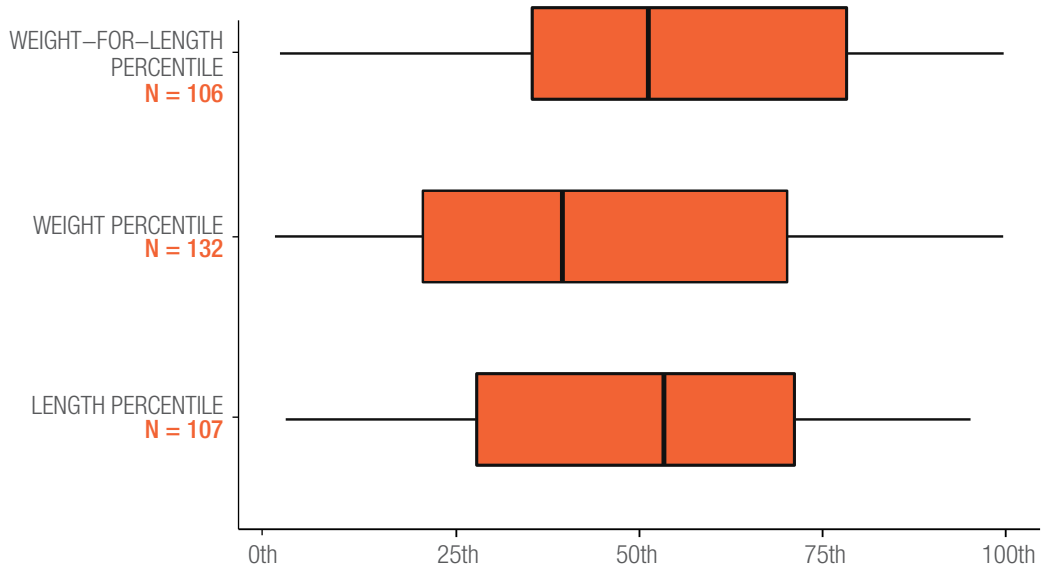
Shaded area represent the 95% confidence intervals

3.2 NUTRITION: WEIGHT, HEIGHT AND BODY MASS INDEX

< 24 MONTHS

As of 2021, nutritional outcomes for very young children (< 24 months) in the ACFDR show that the median length percentile was 53rd, the median weight percentile was 39th, and the median weight for length percentile was 51st (Figure 3.7).

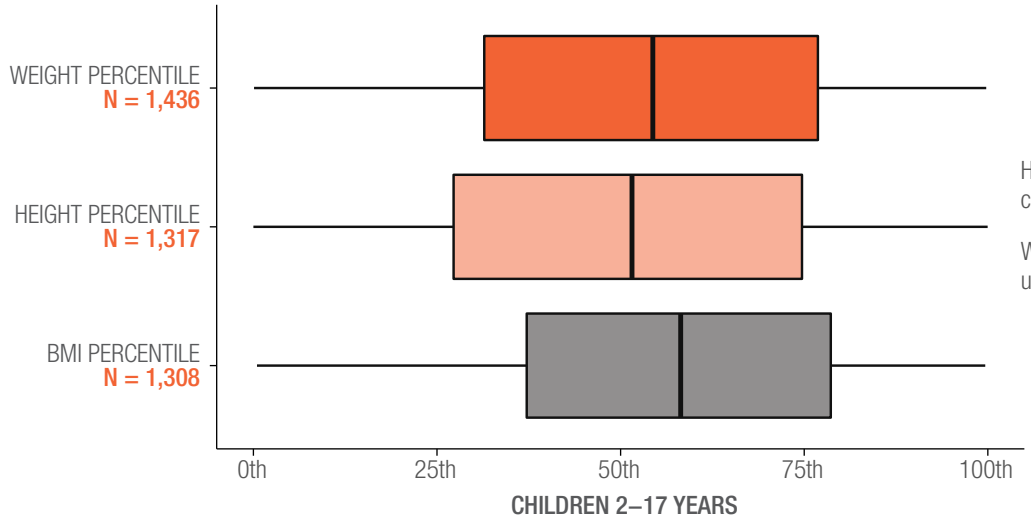
FIGURE 3.7: ACFDR 2021: WEIGHT FOR LENGTH, WEIGHT & LENGTH PERCENTILES FOR INFANTS < 24 MONTHS



CHILDREN 2-17 YEARS

For children aged 2-17 years, the median weight was 52nd percentile, median height was 54th percentile, and the median BMI was 58th percentile. These figures represent best weight, best height, and best BMI, averaged over a 12 month period (Figure 3.8)

FIGURE 3.8: ACFDR 2021: BMI, WEIGHT AND HEIGHT PERCENTILES AGES 2-17 YEARS



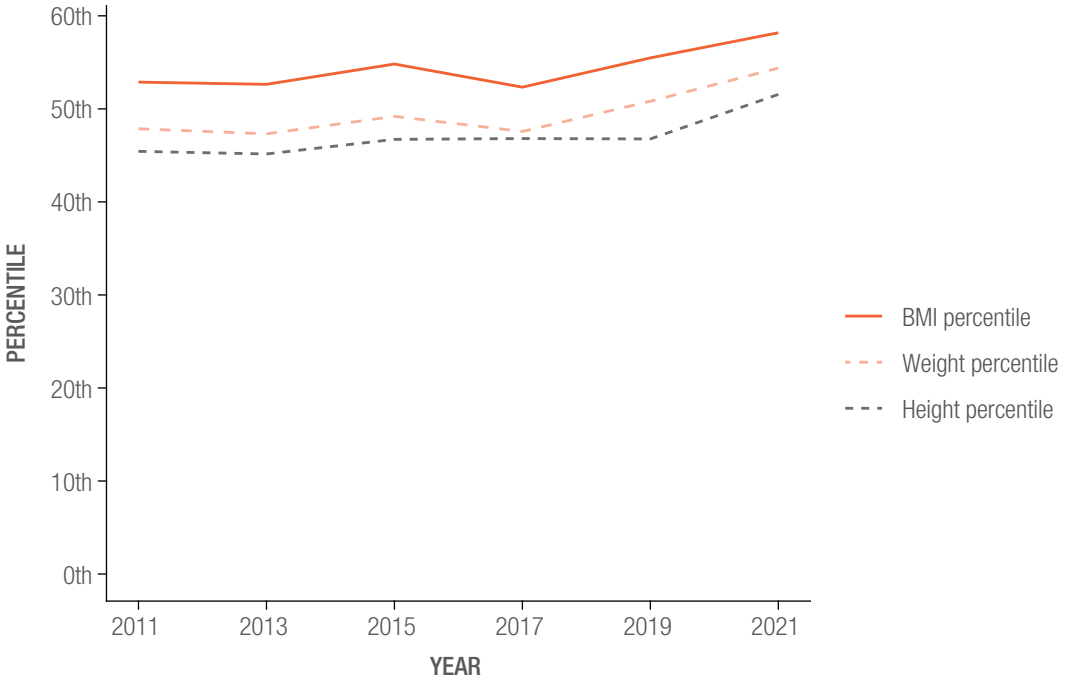
Height and BMI percentiles were calculated using WHO growth chart

Weight percentiles were calculated using CDC growth chart

Over the last 10 years, the height and weight of children 2-17 years with CF has increased.

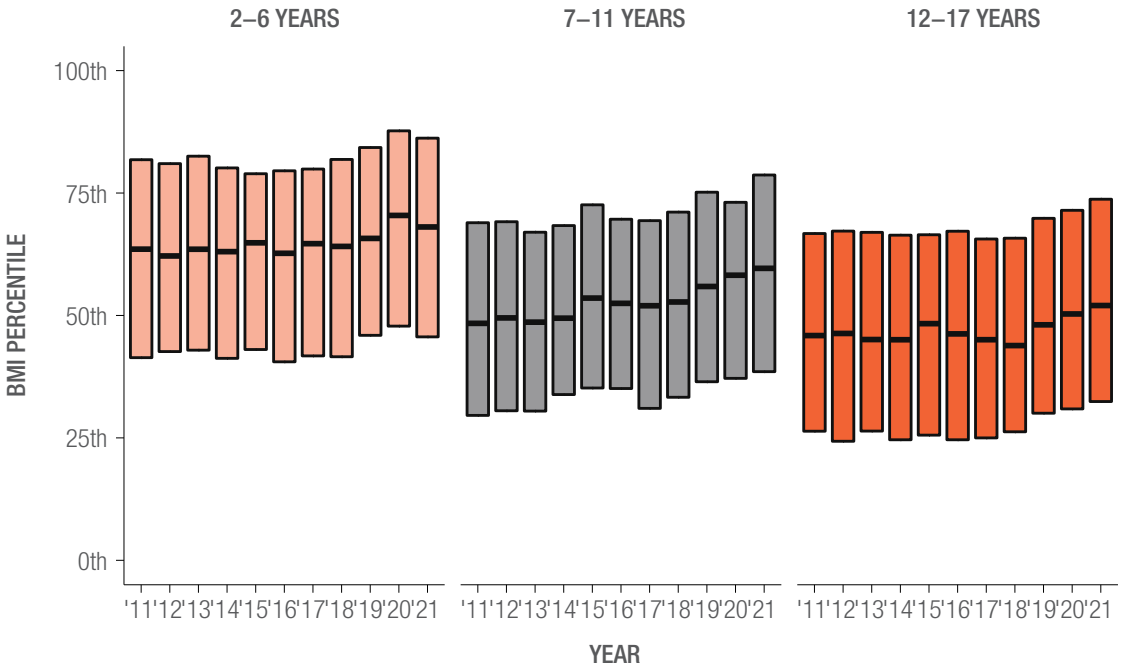
Children in this age group have increased in height by 6 percentile points (from 45th percentile to 52nd percentile), with a concomitant increase in weight of 6 percentile points (from 48th percentile to 54th percentile). As a result, average BMI has also increased 51st to 58th over time.

FIGURE 3.9: ACFDR 2010-2021: MEDIAN NUTRITIONAL STATUS PERCENTILES IN CHILDREN 2-17



The BMI percentile for children > 2 years over time has shown modest increase across the different age cohorts as demonstrated in Figure 3.10.

FIGURE 3.10: ACFDR 2011-2021: MEDIAN CHILD-ADOLESCENT BMI



CHILDREN AND ADOLESCENTS

Nutritional status for both male and female children with CF as of 2021 shows that the majority are in the optimal and acceptable BMI percentile ranges (Table 3.1).

TABLE 3.1 – ACFDR 2021: NUTRITIONAL STATUS FOR CHILDREN < 2 – 18 YEARS

NUTRITIONAL STATUS*	< 2	2-5	6-11	12-17	TOTAL
Normal/Acceptable	88.0% (88)	68.4% (162)	69.8% (340)	71.2% (416)	71.4% (1,006)
Overweight/Obese	0.0% (0)	27.0% (64)	18.5% (90)	12.3% (72)	16.1% (226)
Suboptimal/Undernourished	12.0% (12)	4.6% (11)	11.7% (57)	16.4% (96)	12.5% (176)

*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).

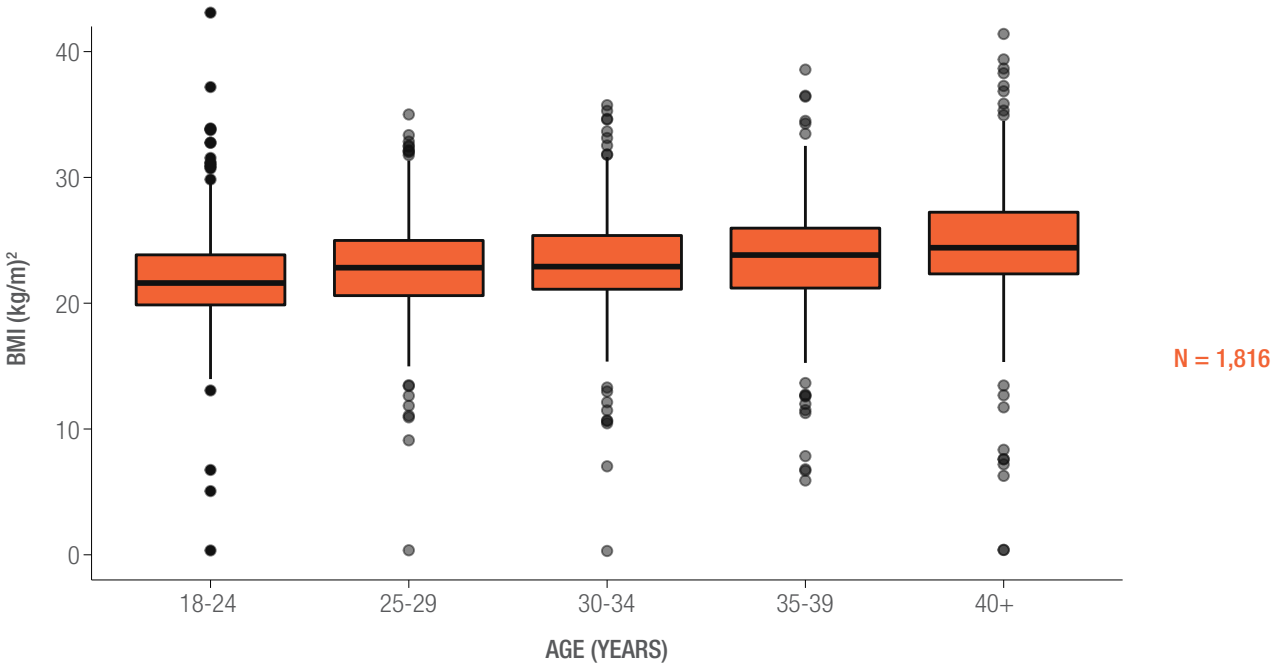
Suboptimal: Weight-for-length 10th-25th percentile (infants 0-1 years); BMI 10th-25th percentile (children and adolescents 2-18 years).

Undernourished: Persistent weight for length < 10th percentile (infants 0-1 years); BMI < 10th percentile (children and adolescents 2-18 years)^

ADULT NUTRITION

The median BMI for adults with CF increases with age. Adults from ages 18-24 years have a median BMI of 21.6; ages 25-29 have a median BMI of 22.8 years; ages 30-34 have a median BMI of 22.9; ages 35-39 have a median BMI of 23.8 and adults 40 years and older have a BMI of 24.8 (Figure 3.11).

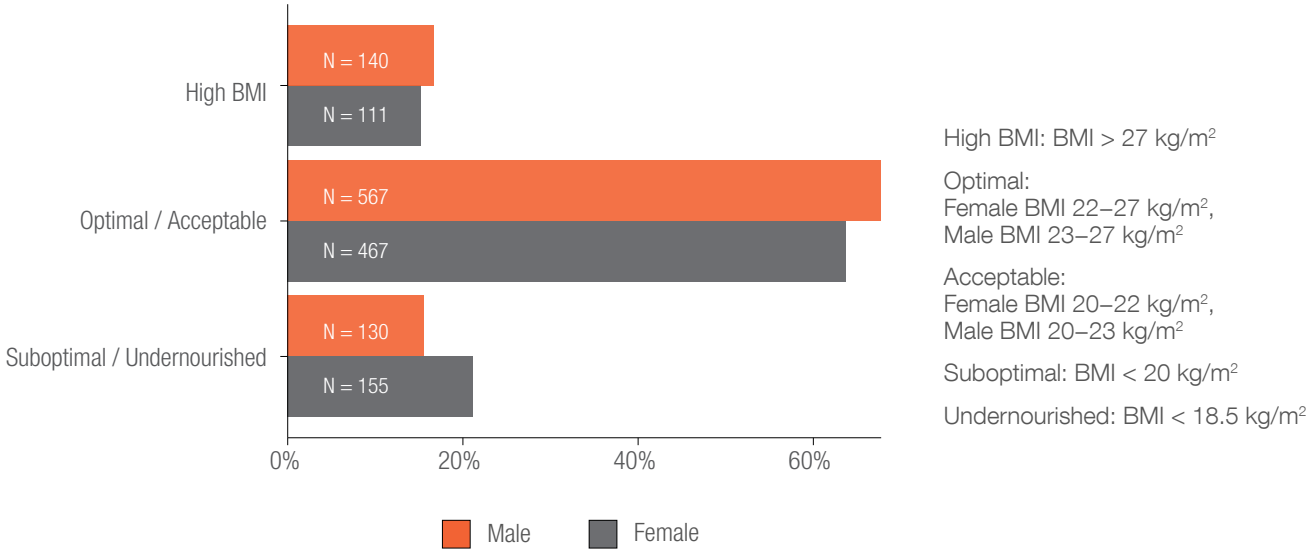
FIGURE 3.11: ACFDR 2021: BMI ADULTS 40+ YEARS



^ Saxby N, Painter C, Kench A, King S, Crowder T, Van der Haak N and the Australian and New Zealand Cystic Fibrosis Nutrition Guideline Authorship Group (2017). Nutrition Guidelines for Cystic Fibrosis in Australia and New Zealand, ed. Scott C. Bell, Thoracic Society of Australia and New Zealand, Sydney.

Adult males and females with CF are predominantly in the optimal and acceptable range for BMI. Outside of this BMI range, females are more likely to have suboptimal BMI or be undernourished, whereas males are more likely to have a higher than optimal BMI (Figure 3.12).

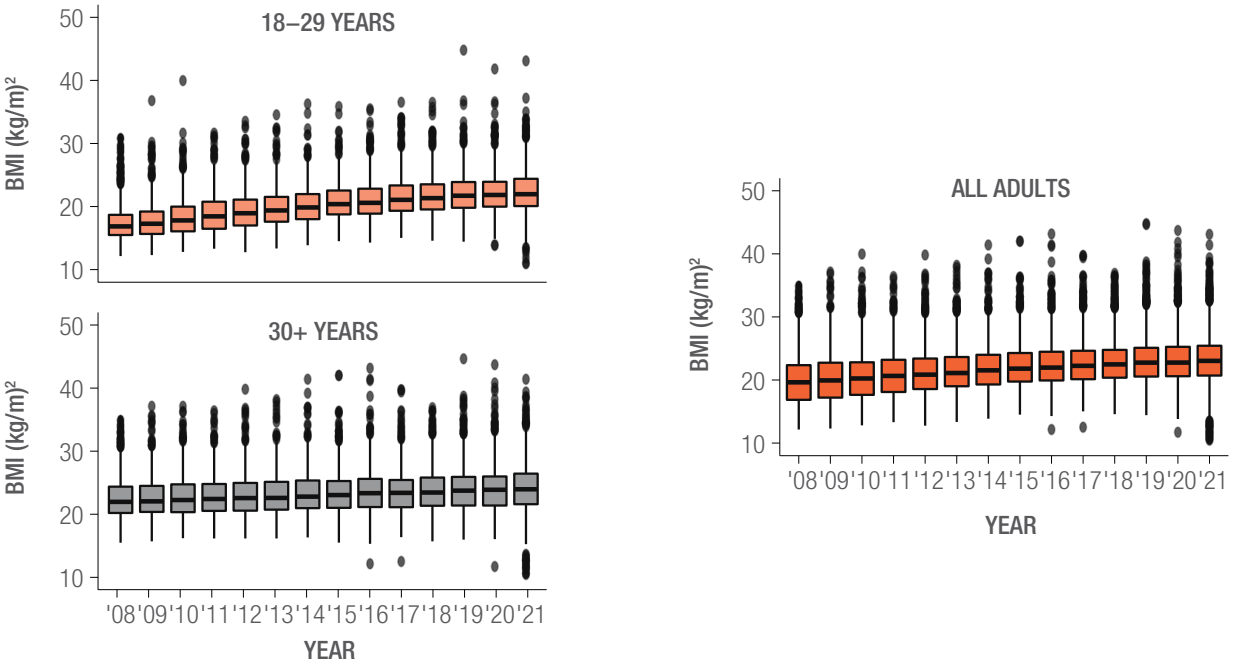
FIGURE 3.12: ACFDR 2021: BMI BY GENDER FOR ADULTS 18+ YEARS



TRENDS OVER TIME

Over the last decade, the median adult BMI has been increasing. For adults 18-29 years, the median BMI (kg/m2) has increased from 16.8 to 21.9; for adults over 30 years, the median BMI has increased from 21.9 to 23.9. For all adults during 2008-2021 the median BMI has increased from 19.6 to 22.9 (Figure 3.13).

FIGURE 3.13: ACFDR 2008-2021: MEDIAN ADULT BMI



^ Saxby N, Painter C, Kench A, King S, Crowder T, Van der Haak N and the Australian and New Zealand Cystic Fibrosis Nutrition Guideline Authorship Group (2017). Nutrition Guidelines for Cystic Fibrosis in Australia and New Zealand, ed. Scott C. Bell, Thoracic Society of Australia and New Zealand, Sydney.

In 2021, 60.0% of all clinical encountres were face to face and 36.0% of visits were via telehealth.

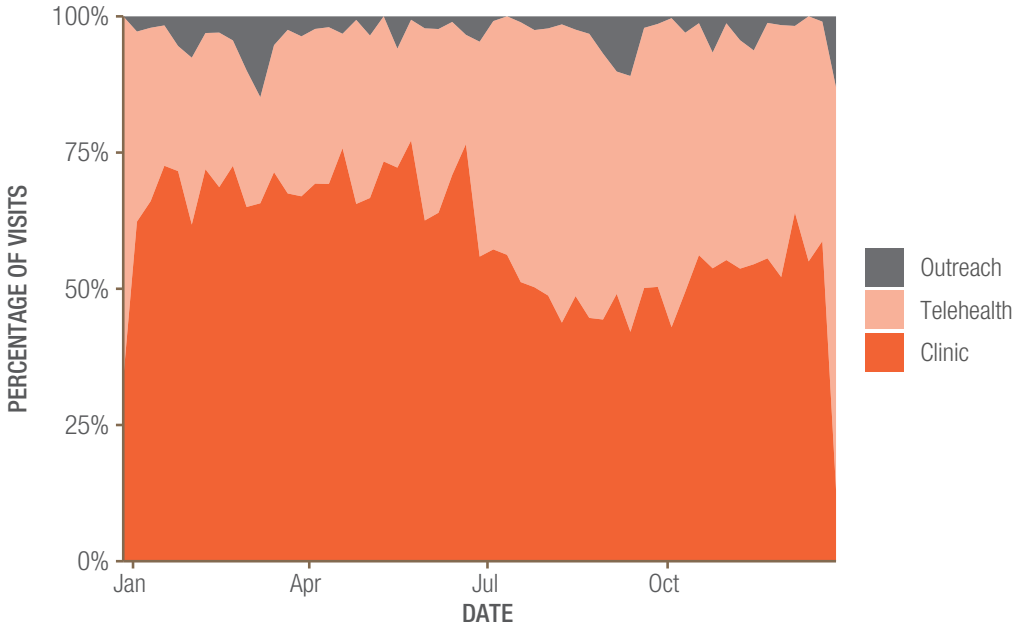
4. CF MANAGEMENT (ENCOUNTERS, CFTR MODULATORS AND MICROBIOLOGY)

4.1 CLINICAL ENCOUNTERS

The *Cystic Fibrosis Standards of Care Australia*[4] (2008) provides for key standards of ambulatory care for people with CF. This includes that treatment should be coordinated by a multi-disciplinary team in specialised CF centres, and that all people with CF should be seen at least four times per year (including at least twice by the CF specialist team).

Traditionally, most clinical encounters have been via face to face visits at CF clinics, with a small proportion of people with CF, usually those in rural/regional areas, being reviewed at outreach services or via telehealth. Since the onset of the COVID-19 pandemic, lockdowns have been part of the Australian response to managing the health crisis. These were introduced at various times to reduce transmission of the virus. From late 2020, the health response shifted towards shorter and more targeted lockdowns by State and Territory Governments to manage outbreaks within their respective jurisdictions. The care clinical centres have been providing has been influenced by lockdown rules and different pressures on the health system, as they varied by state and over time. Throughout 2021, Figure 4.1 shows proportion of telehealth compared to face to face encounters.

FIGURE 4.1 – ACFDR 2021: TYPES OF CLINICAL ENCOUNTERS



In 2021, 60.0% of all clinical encounters were face to face, 36.0% of encounters were via telehealth, compared to 3.6% of outreach visits. The overall number of clinical encounters entered into the registry in 2021 was 18,012 (Table 4.1).

TABLE 4.1 - ACFDR 2020-2021: OVERALL VISIT TYPE

VISIT TYPE	2020	2021
Clinic	9,101 (53%)	10,825 (60%)
Telehealth	7,465 (43%)	6,546 (36%)
Outreach	606 (4%)	641 (4%)
Total	17,172 (100%)	18,012 (100%)

4. Bell S C, Robinson P J; Fitzgerald D A. Cystic Fibrosis Standards of Care, Australia 2008. Cystic Fibrosis Australia North Ryde Sydney NSW 2113

There were 16,350 clinical measures (lung function) recorded in 2021, of these 20.5% were undertaken in the patients home. 98.4% of those measure recorded in the patient's home were collected using their own equipment. Infants up to 6 years were the most likely to have clinician/technician support at home although overall only 39 measures reported this (Table 4.2 and 4.3).

TABLE 4.2 ACFDR 2021: WHERE CLINICAL MEASURES ARE RECORDED

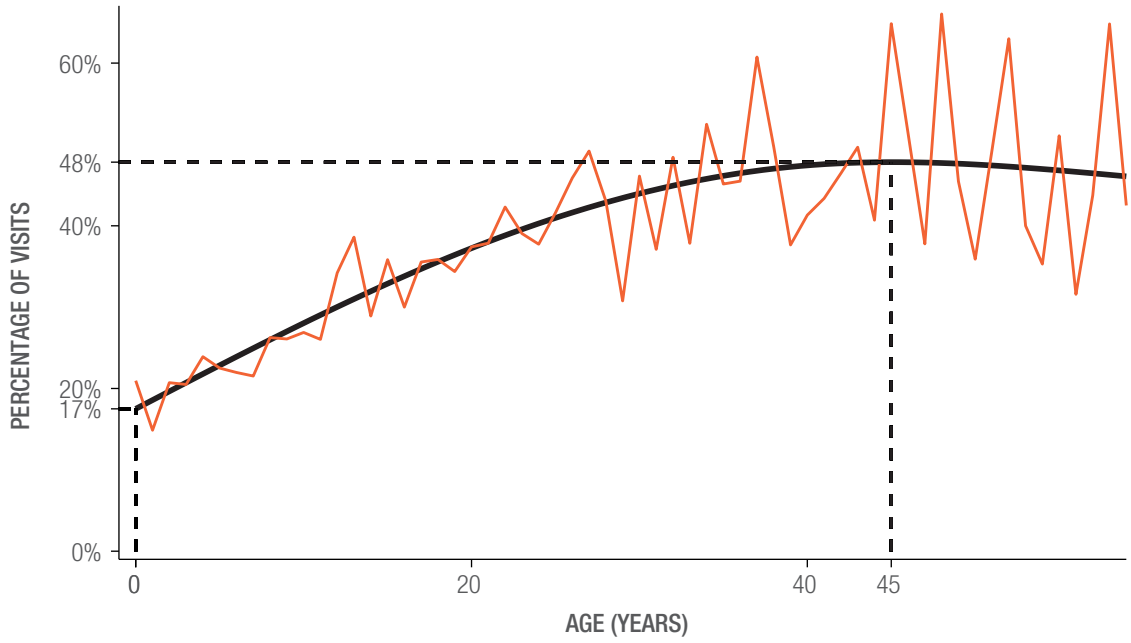
WHERE WERE THE CLINICAL MEASURES RECORDED	N (%)
In patient's home	3,352 (20.50%)
In clinic/hospital	12,998 (79.50%)
Total	**16,350 (100%)**

TABLE 4. 3 ACFDR 2021: WHO RECORDED THE CLINICAL MEASURES AT HOME

WHO RECORDED THE CLINICAL MEASUREMENT	N (%)
The patient with their own equipment	3,298 (98.40%)
Clinician/Technician with their own equipment	39 (1.20%)
Unknown	15 (0.40%)
Total	**3,352 (100%)**

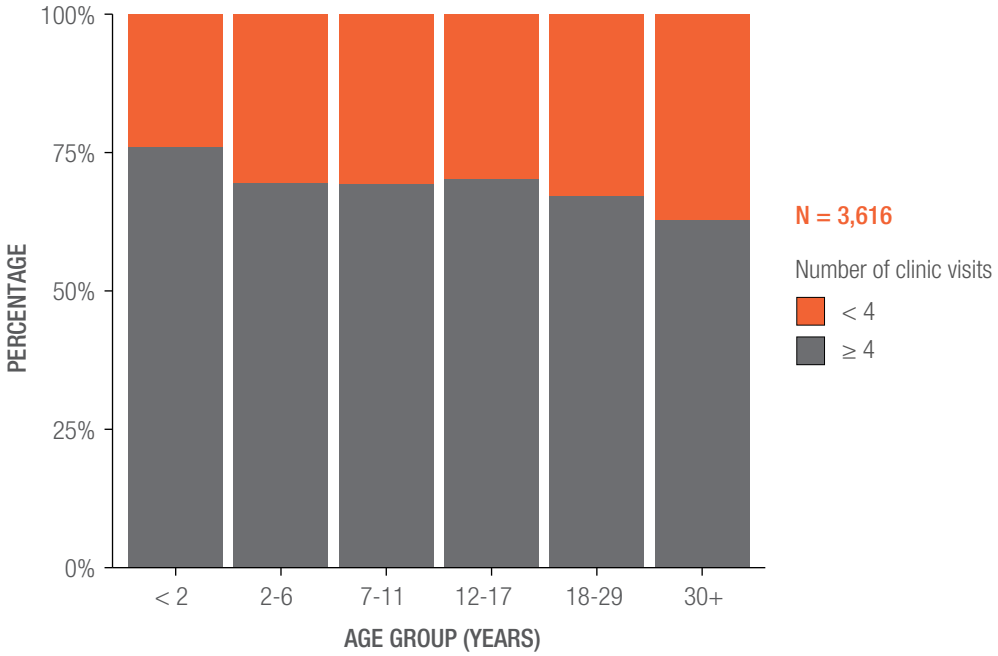
Figure 4.2 shows variation in age of those who utilised telehealth. Infants less than 1 year of age had the lowest percentage of telehealth consultations (at 17.0% compared to 23.4% in 2020). Older children and adults were more likely to utilise telehealth, with a peak of 48.0% of people with CF aged 45 years using telehealth in 2021 compared to 51.9% (aged 37 years) in 2020.

FIGURE 4.2 – ACFDR 2021: PERCENTAGE OF TELEHEALTH BY AGE



In 2021, clinical encounters from 3,616 people with CF were recorded. The number of all people with CF who had at least 4 clinic visits in 2021 was 2,427 (67.0%) overall, compared to 2,106 (62.0%) in 2020. This was highest among those < 2 years old at 76.0%, followed by 2-6 and 12-17 years old's at 70.0%, and the proportion who had at least 4 clinic visits was lowest among people 30+ years old at 63.0% (Figure 4.3 and Table 4.4).

FIGURE 4.3: ACFDR 2021: PROPORTION OF PEOPLE (BY AGE) HAVING 4 OR MORE CLINICAL ENCOUNTERS



The Australian CF Standards of Care recommend a minimum of 4 clinic (or equivalent) encounters per year. The total number with 4+ clinical encounters recorded in 2021 was 2,429 compared to 2,106 in 2020 (Table 4.4).

TABLE 4.4 - ACFDR 2021: AGE GROUPS WITH 4+ CLINICAL ENCOUNTERS

	NUMBER WITH 4+ ENCOUNTERS	
AGE	2020	2021
< 2	75 (64.0%)	104 (76.0%)
2-6	224 (56.0%)	276 (70.0%)
7-11	210 (46.9%)	308 (69.0%)
12-17	338 (56.0%)	435 (70.0%)
18-29	591 (64.0%)	607 (67.0%)
30+	668 (64.0%)	669 (63.0%)
Total	2,106 (60.0%)	2,429 (67.0%)

Of those people who had 4+ clinical encounters recorded in 2021, 1,593 (65.6%) recorded a mixed model of care, 709 (29.2%) people had all their visits as face to face only. We don't know if it was patient preference or service preference, and a small number, 127 (5.2%) had telehealth encounters for all their appointments (Table 4.5).

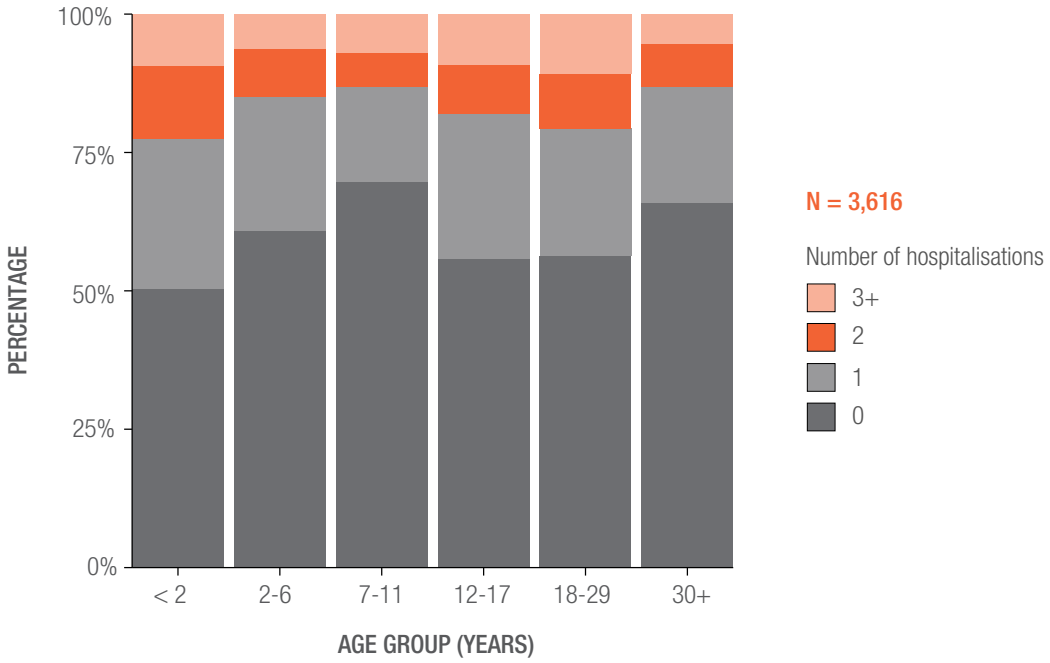
TABLE 4.5 - ACFDR 2021: 4+ CLINICAL ENCOUNTER TYPE

CLINICAL ENCOUNTER TYPE	N (%)
Mixed	1,593 (65.6%)
Face to face only	709 (29.2%)
Telehealth only	127 (5.2%)
Total	**2,429 (100%)**

HOSPITALISATIONS

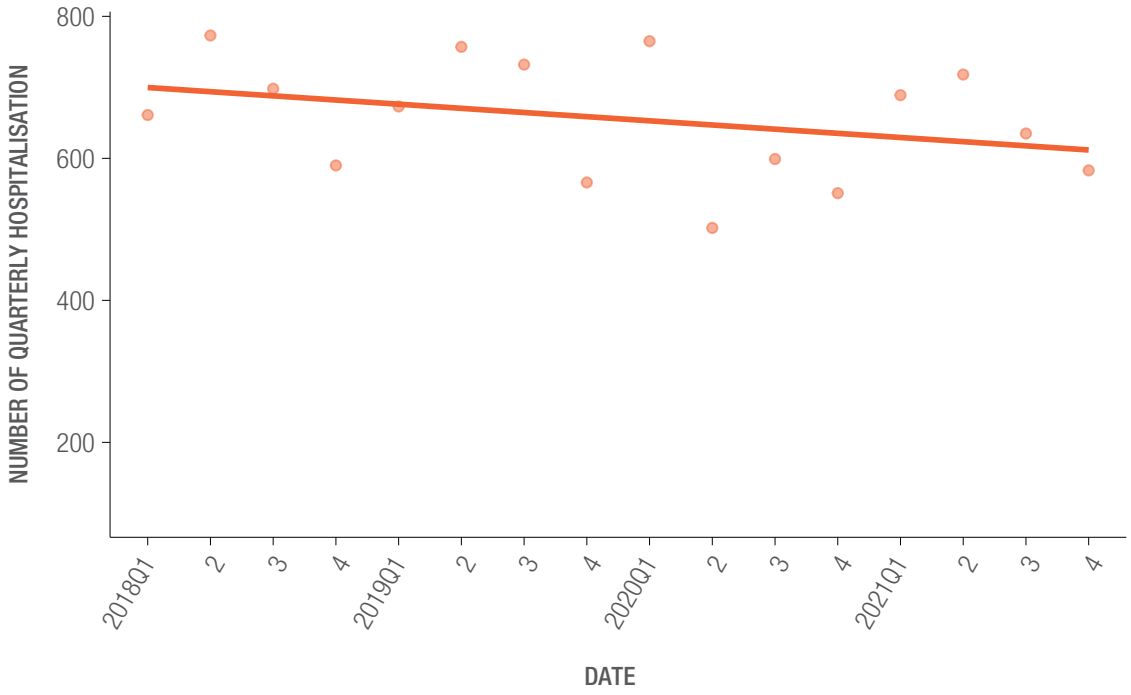
All people with CF had information regarding hospitalisations recorded in the ACFDR in 2021. The majority (approximately 61.0% overall) of people with CF did not have any hospitalisations, with the highest proportion having no hospitalisations being children 7-11 years (69.0%, Figure 4.4), and the lowest proportion having no hospitalisations being infants < 2 years at 50.4%.

FIGURE 4.4: ACFDR 2021: NUMBER OF HOSPITALISATIONS



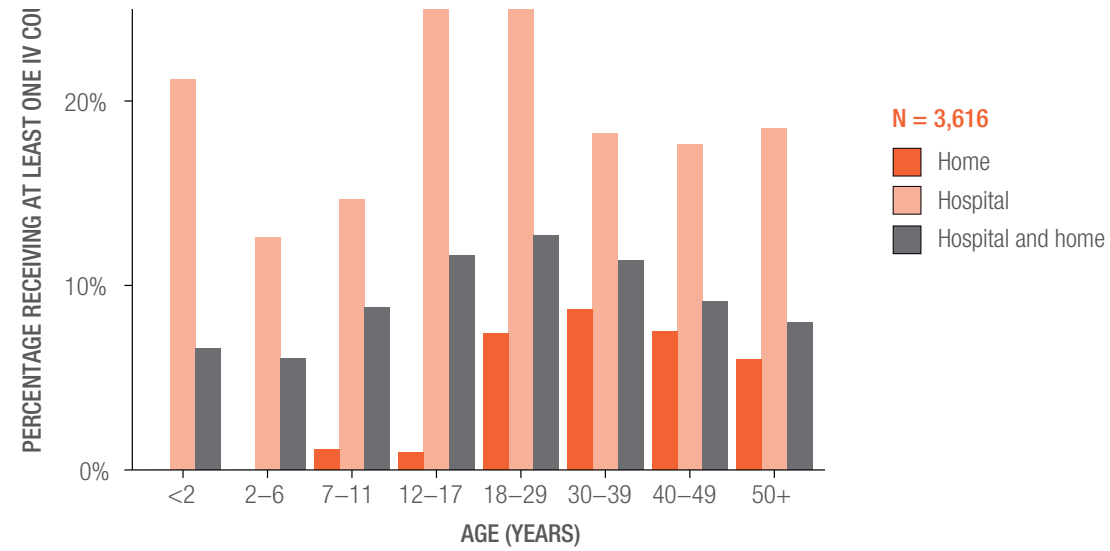
There is an overall downward trend in the number of hospitalisations from 2018 through to 2021. There were 673 recorded in quarter 1 2019, and 583 in quater 4 of 2021. Seasonal variation in hospitalisations is displayed in Figure 4.5 below, with higher hospital attendances in winter than summer months.

FIGURE 4.5 : ACFDR 2018–2021: NUMBER OF HOSPITALISATIONS PER QUARTER



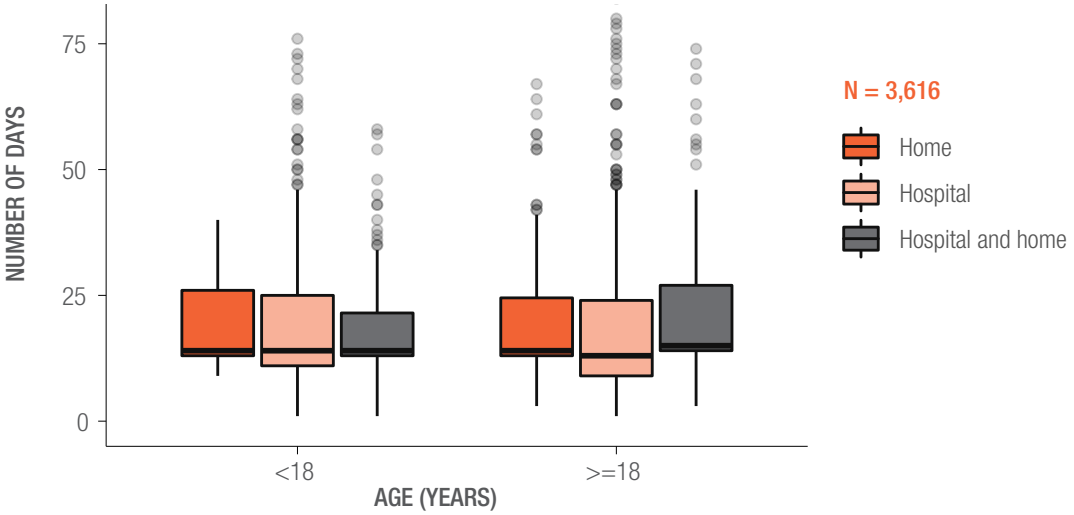
IV ANTIBIOTIC THERAPY

FIGURE 4.6: ACFDR 2021: PROPORTION OF PEOPLE (BY AGE GROUP) RECEIVING AT LEAST ONE COURSE OF IV ANTIBIOTIC THERAPY



The most common reason for hospitalisations for people with CF is to have IV antibiotics for a respiratory infection. In 2021, the proportion of those requiring IV antibiotic therapy in hospital was 21% for people less than 2 years of age, to 28.0% at 18-29 years of age, 27% for 12-17 year olds and 18.0% at over 50 years of age. The proportion having home IV therapy is only 7.0% for people 18-29 years of age, peaking at 9.0% for adults of ages 30-49 years. The number of hospital and home days (whereby people with CF are initially treated in hospital with IV Ab and then transition to home to continue IV treatment) peaks at 13% for people 18-29 years of age, followed by 12% for 12-17 years (Figure 4.6). The median number of days that people with CF spent receiving IV antibiotic therapy is shown in Figure 4.7.

FIGURE 4.7: ACFDR 2021: MEDIAN HOME AND HOSPITAL IV ANTIBIOTIC DAYS (CHILDREN VS ADULTS)



The median number of days that people with CF spent receiving IV antibiotic therapy in hospital was 14 days for children (< 18 years) and 13 days for adults (≥ 18 years). The median number of days receiving home IV therapy was 14 days for both adults and children. The number of hospital and home days was 14 days for children and 15 days for adults in 2021.

4.2 CFTR MODULATORS

Disease-modifying therapies have the potential to dramatically reduce symptoms and increase survival for an increasing number of people with CF. Different therapies target different genetic variants, and not all people with CF 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).

Data were calculated from people with CF who were on a modulator as of December 31st 2021. In the tables below the numerator is those on the drug and the denominator is the eligible population (based on genotype).

Data presented here reflect only those people with CF who had CFTR modulator data entered into the registry, which is generally those on modulators available via the Pharmaceutical Benefits Scheme (PBS).

IVACAFTOR (KALYDECO®)

Ivacaftor was first approved for use in Australia on the PBS from December 2014 for people with CF who had the G551D gating variant, at 9.5% of the CF population in Australia. Ivacaftor was initially PBS listed for people with CF aged 6+ years with a G551D variant, however is currently PBS listed for patients aged 12 months and over with a gating variant. Note that while R117H was approved by TGA it is not PBS listed for ivacaftor and is not included in the eligible population.

TABLE 4.6 – ACFDR 2021: IVACAFTOR USE AS OF DECEMBER 2021

AGE (YEARS)	ON KALYDECO ANYTIME	ON KALYDECO AS OF 31 DEC 2021	PREVIOUSLY ON KALYDECO AND DISCONTINUED AS OF 31 DEC 2021
1-5	19 / 24 (79.0%)	19 / 24 (79.0%)	0 / 24 (0.0%)
≥ 6	293 / 308 (95.0%)	270 / 308 (87.7%)	23 / 308 (7.5%)

The proportion of people with CF with gating variants eligible for ivacaftor who were taking ivacaftor as of December 31, 2021 was 79.0% for children less than and including 5 years, and 87.7% for those six years and older (Table 4.6). 23 people had previously used and discontinued Ivacaftor as of December 31, 2020. Reasons for discontinuation/change included intolerance/adverse event (1), liver impairment/intolerance (1), pregnancy (1), switching to another CFTR modulator (10) and other reason (10) (Table 4.7).

TABLE 4.7 – ACFDR 2021: REASONS FOR DISCONTINUATION/CHANGE OF IVACAFTOR AS OF DECEMBER 2021

NUMBER (%)	REASON FOR DISCONTINUATION/CHANGE
10 (43.5%)	Other reason[5]
10 (43.5%)	Switch to other CFTR modulator
1 (4.3%)	Pregnancy
1 (4.3%)	Liver impairment/intolerance
1 (4.3%)	Other intolerance/adverse event

5. Other reasons include; Moved to a clinical trial (n=3) , transplant (n=2), weight gain (n=1), unknown reason (n=4)

LUMACAFTOR/IVACAFTOR (ORKAMBI®)

Lumacaftor/ivacaftor was approved for use in Australia on the PBS in October 2018, for people with CF with two copies of the F508del variant, which comprises 47.0% of people in the ACFDR. Initially available for those aged 6 years and over, as of October 2019, it also became available for children from the age of 2 years.

TABLE 4.8 – ACFDR 2021: LUMACAFTOR/IVACAFTOR USE AS OF DECEMBER 2021

AGE (YEARS)	ON ORKAMBI ANYTIME	ON ORKAMBI AS OF 31 DEC 2021	PREVIOUSLY ON ORKAMBI AND DISCONTINUED AS OF 31 DEC 2021
2-5	108/ 125 (86.0%)	94 / 125 (75.2%)	14 / 125 (11.2%)
≥ 6	1,053 / 1,491 (71.0%)	628 / 1,491 (42.1%)	425 / 1,491 (28.5%)

The proportion of people with CF who were homozygous for F508del aged 6 years and over who were taking lumacaftor/ivacaftor as of December 31st 2021 was 42.1%, and 75.2% of the eligible population 2-5 years of age were also taking lumacaftor/ivacaftor (Table 4.8). There have been 439 people who have discontinued/changed this medication (Table 4.9). The most common reasons were a switch to another CFTR modulator (234), pulmonary intolerance/side effect (65), other (60), other intolerance/adverse event (52), liver impairment/intolerance (21), concomitant drug interaction (5) and pregnancy (2).

TABLE 4.9 – ACFDR 2021: REASONS FOR DISCONTINUATION/CHANGE OF LUMACAFTOR/IVACAFTOR AS OF DECEMBER 2021

NUMBER (%)	REASON FOR DISCONTINUATION/CHANGE
234 (53.3%)	Switch to other CFTR modulator
65 (14.8%)	Pulmonary side effect/intolerance
60 (13.7%)	Other reason[6]
52 (11.8%)	Other intolerance/adverse event
21 (4.8%)	Liver impairment/intolerance
5 (1.1%)	Concomitant drug interaction
2 (0.5%)	Pregnancy

6. Other reasons include; Moved to a clinical trial (n=17), felt no benefit (n=7), family/personal choice (n=4), transplant (n=4), unwell (n=4), mental health reasons (n=4), feeding issues (n=4), , insufficient supply (n=3), fertility planning (n=2), cost (n=1), unknown reason (n=10).

TEZACAFTOR/IVACAFTOR AND IVACAFTOR (SYMDEKO®)

Tezacaftor/ivacaftor and ivacaftor was approved for use in Australia on the PBS in December 2019 for people aged 12 and above with CF. Tezacaftor/ivacaftor and ivacaftor is PBS listed for patients with one of these following variants whether they have F508del or not - P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G, 3849+10kbC→T, E56K, R74W, D110E, D110H, E193K, E831X, F1052V, K1060T, A1067T, F1074L, and D1270N. Is it worth noting there is some crossover in eligible patients between tezacaftor/ivacaftor and ivacaftor, and lumacaftor/ivacaftor given both are PBS listed for F508del homozygous patients.

TABLE 4.10 – ACFDR 2021: TEZACAFTOR/IVACAFTOR USE AS OF DECEMBER 2021

AGE (YEARS)	ON SYMDEKO ANYTIME	ON SYMDEKO AS OF 31 DEC 2021	PREVIOUSLY ON SYMDEKO AND DISCONTINUED AS OF 31 DEC 2021
12-17	132 / 279 (47.0%)	117 / 279 (41.9%)	15 / 279 (5.4%)
≥ 18	626 / 1,058 (59%)	512 / 1,058 (48.4%)	114 / 1,058 (10.8%)

As of December 2021, 41.9% of the eligible population of 12-17 year olds were taking tezacaftor/ivacaftor, and 48.4% of eligible adults were taking it (Table 4.10). 129 people had discontinued/changed the medication during 2021. Reasons included that they had switched to another CFTR modulator (61), other reasons (29), other intolerance/adverse event (20), pulmonary intolerance/side effect (10), liver impairment/intolerance (6), pregnancy (2), or concomitant drug interaction (1) (Table 4.11).

TABLE 4.11 – ACFDR 2021: REASONS FOR DISCONTINUATION/CHANGE OF TEZACAFTOR/IVACAFTOR AS OF DECEMBER 2021

NUMBER (%)	REASON FOR DISCONTINUATION/CHANGE
61 (47.3%)	Switch to other CFTR modulator
29 (22.5%)	Other reason[7]
20 (15.5%)	Other intolerance/adverse event
10 (7.8%)	Pulmonary side effect/intolerance
6 (4.7%)	Liver impairment/intolerance
2 (1.6%)	Pregnancy
1 (0.8%)	Concomitant drug interaction

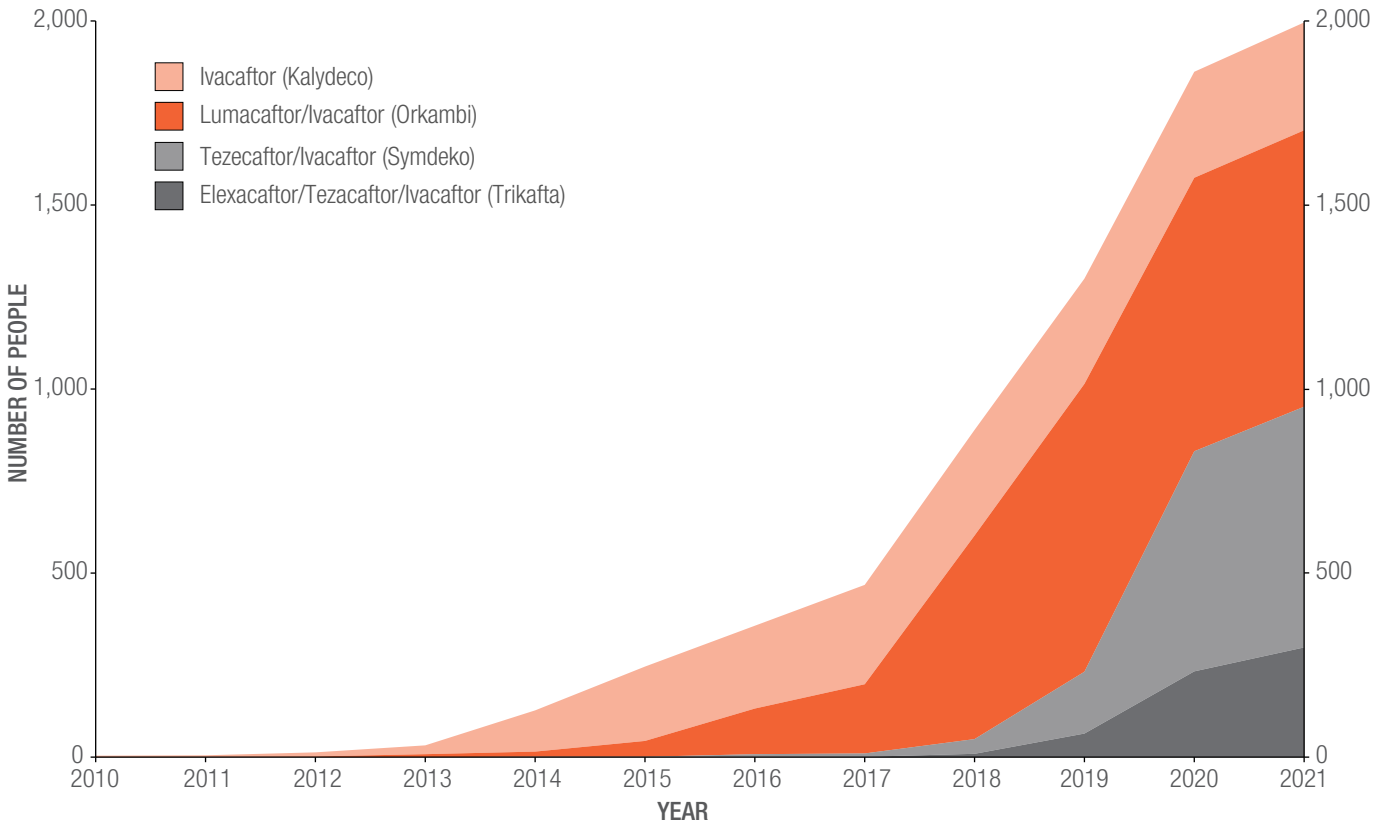
7. Other reasons include; Commence drug trial (n=6), fertility planning (n=4), nil adherence (5), mental health reasons (n=3), no improvement to warrant expense (n=2), weight gain (n=2), antibiotic treatment (n=1), transplant (n=1), social issues (n=1) travel (n=1), unknown reason (n=3)

ELEXACAFTOR/TEZACAFTOR/IVACAFTOR (TRIKAFTA®)

Elexacaftor/tezacaftor/ivacaftor is a CFTR modulator for people with CF who have at least one copy of the F508del variant and another variant that is CF causing. Elexacaftor/tezacaftor/ivacaftor was TGA registered 24 March 2021 and PBS listed 1 April 2022 for use in Australia. As of 31 December 2021, 295 (12%) people with cystic fibrosis over the age of 12 in Australia are recorded as having received elexacaftor/tezacaftor/ivacaftor.

Figure 4.8 shows the increasing numbers of people with CF in Australia who are taking CFTR modulators, and how these have varied over time. Ivacaftor was the first CFTR modulator to be available, for the eligible population that had gating genotype variants, and its use has remained relatively steady over time. This has been followed by uptake of lumacaftor/ivacaftor, then tezacaftor/ivacaftor, and then elexacaftor/tezacaftor/ivacaftor. As of December 2021, 1,996 people with CF (55.2 % of the total population on the ACFDR) are taking a CFTR modulator. This is compared to 1,862 (52.6%) people who were taking a modulator at the end of 2020.

FIGURE 4.8: ACFDR 2010-2021: PEOPLE ON CFTR MODULATORS AS OF DECEMBER 31ST 2021



4.3 MICROBIOLOGY

From the 3,616 people with CF in 2021, 3,097 microbiology culture samples were taken. The most common respiratory microorganism up until early adulthood is S. *aureus,* and after this the most common is P. *aeruginosa* which peaked at 71.0% in 2021 for adults aged 35-45+ years. The third most common organism in 2021 was Aspergillus *spp.* which was present in more than 10% of people with CF from 7 years, peaking at 30% for those aged 18-24 years (Figure 4.9, Table 4.12).

FIGURE 4.9: ACFDR 2021: RESPIRATORY MICROBIOLOGY BY AGE

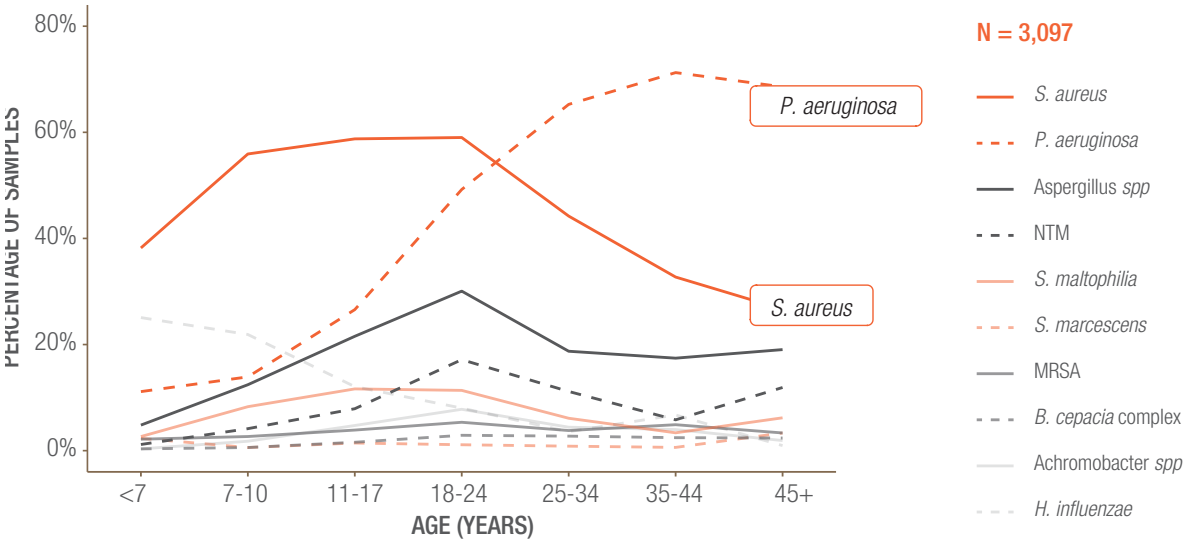


TABLE 4.12– ACFDR 2021: BAL SAMPLES RESPIRATORY MICROORGANISMS BY AGE

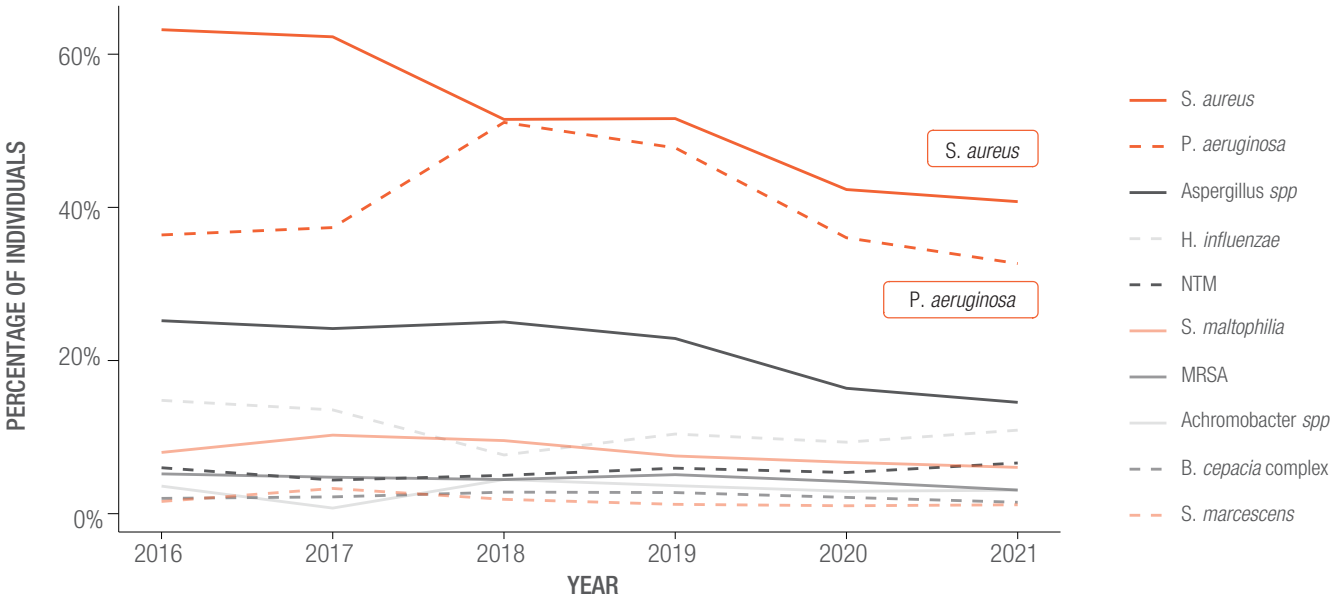
	ALL SAMPLES						
	< 7	7 - 10	11 - 17	18 - 24	25 - 34	35 - 44	45 +
Number in age range	534	353	710	561	687	450	321
Number of samples taken in 2021	602	338	696	449	475	327	210
Number of patients	501	310	642	443	464	318	209
P. *aeruginosa*	67 / 602 (11%)	47 / 338 (14%)	185 / 696 (27%)	221 / 449 (49%)	310 / 475 (65%)	233 / 327 (71%)	144 / 210 (69%)
H. *influenzae*	151 / 602 (25%)	74 / 338 (22%)	84 / 696 (12%)	36 / 449 (8%)	17 / 475 (4%)	22 / 327 (7%)	2 / 210 (1%)
B. *cepacia complex*	2 / 602 (0%)	2 / 338 (1%)	11 / 696 (2%)	13 / 449 (3%)	13 / 475 (3%)	8 / 327 (2%)	5 / 210 (2%)
S. *aureus*	230 / 602 (38%)	189 / 338 (56%)	409 / 696 (59%)	265 / 449 (59%)	210 / 475 (44%)	107 / 327 (33%)	56 / 210 (27%)
MRSA	13 / 602 (2%)	9 / 338 (3%)	27 / 696 (4%)	24 / 449 (5%)	18 / 475 (4%)	16 / 327 (5%)	7 / 210 (3%)
Achromobacter *spp*	2 / 602 (0%)	6 / 338 (2%)	33 / 696 (5%)	35 / 449 (8%)	21 / 475 (4%)	13 / 327 (4%)	4 / 210 (2%)
S. *maltophilia*	16 / 602 (3%)	28 / 338 (8%)	81 / 696 (12%)	51 / 449 (11%)	29 / 475 (6%)	11 / 327 (3%)	13 / 210 (6%)
S. *marcescens*	14 / 602 (2%)	2 / 338 (1%)	10 / 696 (1%)	5 / 449 (1%)	4 / 475 (1%)	2 / 327 (1%)	7 / 210 (3%)
Aspergillus *spp*	29 / 602 (5%)	42 / 338 (12%)	150 / 696 (22%)	135 / 449 (30%)	89 / 475 (19%)	57 / 327 (17%)	40 / 210 (19%)
NTM	7 / 602 (1%)	14 / 338 (4%)	55 / 696 (8%)	77 / 449 (17%)	53 / 475 (11%)	19 / 327 (6%)	25 / 210 (12%)

TABLE 4.13– ACFDR 2021: RESPIRATORY MICROORGANISMS BY AGE

BAL SAMPLES	
	< 7
No. of samples taken in 2021	150
No. of patients	150
H. *influenzae*	40 / 150 (27%)
S. *aureus*	39 / 150 (26%)
Aspergillus *spp*	15 / 150 (10%)
P. *aeruginosa*	15 / 150 (10%)
S. *marcescens*	6 / 150 (4%)
S. *maltophilia*	4 / 150 (3%)
NTM	3 / 150 (2%)
Achromobacter *spp*	1 / 150 (1%)
MRSA	2 / 150 (1%)
B. *cepacia* complex	0 / 150 (0%)

For children younger than seven years, lower airway samples may be collected by bronchoalveolar lavage (BAL). The most common organisms identified in this age group in 2021 included H. *influenzae* (27.0%), S. *aureus* (26.0%), Aspergillus *spp* (10.0%), P. *aeruginosa* (10.0%), and S. *marcescens* (4.0%) (Table 4.13, Figure 4.10).

FIGURE 4.10: ACFDR 2016-2021: PREVALENCE OF RESPIRATORY MICROORGANISMS



The prevalence of some of the most common organisms has changed over the last 6 years. The prevalence of S. *aureus* was 63.2% for people with CF in 2016 and has decreased to 40.7% in 2021, and the prevalence of Aspergillus *spp* was 25.2% in 2016 and has decreased to 14.5% in 2021. The prevalence of P. *aeruginosa* has decreased from a high of 51.1% in 2018 to 32.7% 2021. The prevalence of less common microorganisms has remained fairly similar over this period (Table 4.14).

Non-tuberculous mycobacterium (NTM) infection is negligible below 7 years of age, however infection rates are higher in older teenagers and younger adults. NTM infection is at 8.9% in 12-17 year olds, and 15.7% in 18–30 year olds. M. abscessus, an organism that may be associated with a poorer prognosis in CF, also had its highest rate of infection in 18-30 year olds, at 4.7% in 2021 (Table 4.14).

TABLE 4.14 – ACFDR 2016-2021: NON-TUBERCULOUS MYCOBACTERIUM (NTM) INFECTION BY AGE

AGE (YEARS)	ORGANISM	2016	2017	2018	2019	2020	2021
< 7	NTM	0/17 (0.0%)	0/30 (0.0%)	0/85 (0.0%)	2/175 (1.1%)	2/404(0.5%)	6/501 (1.2%)
	M. *abscessus*	0/17 (0.0%)	0/30 (0.0%)	0/85 (0.0%)	0/175 (0.0%)	0/404 (0.0%)	2/501 (0.4%)
7 - 11	NTM	1/48 2.1%)	0/55 (0.0%)	3/142 (2.1%)	4/210 (1.9%)	12/369 (3.3%)	14/389 (3.6%)
	M. *abscessus*	0/48 (0.0%)	0/55 (0.0%)	3/142 (2.1%)	3/210 (1.4%)	7/369 (1.9%)	4/389 (1.0%)
12 - 17	NTM	5/79 (6.3%)	7/82 (8.5%)	12/187 (6.4%)	26/285 (9.1%)	39/553 (7.1%)	50/563 (8.9%)
	M. *abscessus*	1/79 (1.3%)	2/82 (2.4%)	9/187 (4.8%)	15/285 (5.3%)	21/553 (3.8%)	22/563 (3.9%)
18 - 30	NTM	6/60 (10.0%)	3/65 (4.6%)	27/375 (7.2%)	46/498 (9.2%)	82/658 (12.5%)	108/687 (15.7%)
	M. *abscessus*	1/60 (1.7%)	3/65 (4.6%)	11/375 (2.9%)	21/498 (4.2%)	38/658 (5.8%)	32/687 (4.7%)
30 +	NTM	3/38 (7.9%)	2/31 (6.5%)	20/400 (5.0%)	29/546 (5.3%)	42/740 (5.7%)	65/747 (8.7%)
	M. *abscessus*	1/38 (2.6%)	2/31 (6.5%)	8/400 (2.0%)	9/546 (1.6%)	13/740 (1.8%)	12/747 (1.6%)

5. CF COMPLICATIONS AND THERAPIES

This chapter includes systemic complications and treatments related to the underlying pathophysiology of CF, including specific pulmonary complications and therapies; endocrine disturbance including cystic fibrosis-related diabetes (CFRD), insulin and non-insulin management, and osteopenia/osteoporosis; and gastrointestinal disease including gastroesophageal reflux. It also includes preventive care and participation in research.

5.1 CF LUNG DISEASE AND PULMONARY COMPLICATIONS

Major lung complications such as a significant haemoptysis (bleeding from the lungs) or pneumothorax, were uncommon in 2021, with incidence increasing with increasing age (Table 5.1).

TABLE 5.1 – ACFDR 2021: LUNG COMPLICATIONS

	< 12 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Haemoptysis	3/978 (0.3%)	29/619 (4.7%)	116/904 (12.8%)	95/1,114 (8.5%)	243/3,615 (6.7%)
Haemoptysis requiring embolization	0/978 (0.0%)	1/619 (0.2%)	7/904 (0.8%)	6/1,114 (0.5%)	14/3,615 (0.4%)
Pneumothorax	0/978 (0.0%)	1/619 (0.2%)	6/904 (0.7%)	3/1,114 (0.3%)	10/3,615 (0.3%)

5.2 PULMONARY THERAPIES

A mainstay of medical treatment for CF lung disease is preventive and therapeutic antibiotic therapy that may be oral or inhaled.

TABLE 5.2 - ACFDR 2021: CF PULMONARY DISEASE: MAINTENANCE ANTIBIOTIC THERAPY

	< 6 YEARS	6-11 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Inhaled antibiotics	58/445 (13.0%)	84/533 (15.8%)	179/619 (28.9%)	343/905 (37.9%)	482/1,114 (43.3%)	1146/3,616 (31.7%)
Regular oral antibiotics	207/445 (46.5%)	189/533 (35.5%)	204/619 (33.0%)	169/905 (18.7%)	229/1,114 (20.6%)	998/3,616 (27.6%)
Macrolides	23/445 (5.2%)	60/533 (11.3%)	118/619 (19.1%)	353/905 (39.0%)	633/1,114 (56.8%)	1187/3,616 (32.8%)

Approximately one third of people with CF received macrolide and/or inhaled antibiotic therapy in 2021, with adults having a higher usage than children. Regular oral antibiotics however were more likely to be used by children, with over one third using these, compared with approximately 18.7% of adults (Table 5.2).

TABLE 5.3 - ACFDR 2021: CF PULMONARY DISEASE: OTHER LUNG THERAPIES

	< 6 YEARS	6-11 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Dornase alpha	145/445 (32.6%)	396/533 (74.3%)	499/619 (80.6%)	572/905 (63.2%)	583/1,114 (52.3%)	2195/3,616 (60.7%)
Hypertonic saline	98/445 (22.0%)	249/533 (46.7%)	290/619 (46.8%)	492/905 (54.4%)	511/1,114 (45.9%)	1640/3,616 (45.4%)
Inhaled mannitol	2/445 (0.4%)	8/533 (1.5%)	95/619 (15.3%)	47/905 (5.2%)	36/1,114 (3.2%)	188/3,616 (5.2%)
Bronchodilators	74/445 (16.6%)	229/533 (43.0%)	344/619 (55.6%)	604/905 (66.7%)	744/1,114 (66.8%)	1995/3,616 (55.2%)
Inhaled corticosteroids	34/445 (7.6%)	105/533 (19.7%)	170/619 (27.5%)	401/905 (44.3%)	592/1,114 (53.1%)	1302/3,616 (36.0%)
Oral corticosteroids	8/445 (1.8%)	28/533 (5.3%)	46/619 (7.4%)	38/905 (4.2%)	111/1,114 (10.0%)	231/3,616 (6.4%)
Long term oxygen therapy	1/445 (0.2%)	2/533 (0.4%)	4/619 (0.6%)	9/904 (1.0%)	25/1,114 (2.2%)	41/3,615 (1.1%)
Non-invasive ventilation	2/445 (0.4%)	3/533 (0.6%)	9/619 (1.5%)	21/904 (2.3%)	32/1,114 (2.9%)	67/3,615 (1.9%)

Non-invasive ventilation is used in 5.2% of all adults, whereas long term oxygen therapy is used to support 1.0% in 18-29 year olds, and 2.2% in 30 year olds (Table 5.3).

In 2021, the most commonly used non-modulator therapies were dornase alpha (60.7%), bronchodilators (55.2%), hypertonic saline (45.4%), and inhaled corticosteroids (36.0%). Less commonly used were oral corticoid steroids (6.4%), and inhaled mannitol (5.2%). A number of these therapies are not available to younger children, e.g. inhaled mannitol is not available on the PBS for children < 6 years, and similarly most children of this age cannot use dry powder inhalers.

5.3 CF ENDOCRINE DISEASE

Almost than 1 in 5 people with information regarding diabetic status (661 people, 18.3%) had a diagnosis of CF related diabetes (CFRD) in 2021. The prevalence of diabetes increases with age, with 14.2% of 12-17-year olds having CFRD, increasing to 30.0% of people with CF over the age of 30 years (Table 5.4).

TABLE 5.4 - ACFDR 2021: DIABETIC STATUS BY AGE

	<12 (N = 978)	12-17 (N = 619)	18-29 (N = 904)	30+ (N = 1,114)	TOTAL (N = 3,615)
Normal, (no diabetes or impaired glucose tolerance)	697 (71.3%)	343 (55.4%)	484 (53.5%)	554 (49.7%)	2,078 (57.5%)
Impaired glucose tolerance	23 (2.4%)	84 (13.6%)	102 (11.3%)	129 (11.6%)	338 (9.3%)
Diabetes	22 (2.2%)	88 (14.2%)	217 (24.0%)	334 (30.0%)	661 (18.3%)
Not known	236 (24.1%)	104 (16.8%)	101 (11.2%)	97 (8.7%)	538 (14.9%)

Of the 661 people with CFRD, 660 people had data recorded in the registry of their treatment, 85.9% were managed primarily with insulin; 7.7% were managed by diet/lifestyle strategies alone, 4.5% were treated with oral hypoglycaemic agents with or without insulin and 1.8% no treatment was identified (Table 5.5).

TABLE 5.5 - ACFDR 2021: CF RELATED DIABETES (CFRD) TREATMENT BY AGE

DIABETES TREATMENT TYPE	< 12 (N = 22)	12-17 (N = 88)	18-29 (N = 217)	30+ (N = 334)	TOTAL (N = 661)
Missing	0	0	1	0	1
Insulin	21 (95.5%)	85 (96.6%)	187 (86.6%)	274 (82.0%)	567 (85.9%)
Oral hypoglycaemics	1 (4.5%)	0 (0.0%)	4 (1.9%)	15 (4.5%)	20 (3.0%)
Insulin and hypoglycaemics	0 (0.0%)	1 (1.1%)	5 (2.3%)	4 (1.2%)	10 (1.5%)
Diet/lifestyle management only	0 (0.0%)	0 (0.0%)	16 (7.4%)	35 (10.5%)	51 (7.7%)
No treatment for diabetes identified	0 (0.0%)	2 (2.3%)	4 (1.9%)	6 (1.8%)	12 (1.8%)

The vast majority (94.6%) of people with CFRD on insulin were prescribed continuous insulin (Table 5.6).

TABLE 5.6 - ACFDR 2021: INSULIN USE FOR PEOPLE WITH CFRD BY AGE

INSULIN USE	< 12 (N = 22)	12-17 (N = 81)	18-29 (N = 188)	30+ (N = 282)	TOTAL (N = 573)
Intermittent insulin use	0 (0.0%)	8 (9.9%)	5 (2.7%)	6 (2.1%)	19 (3.3%)
Continuous insulin use	19 (86.4%)	66 (81.5%)	182 (96.8%)	275 (97.5%)	542 (94.6%)
Insulin use, duration unknown	3 (13.6%)	7 (8.6%)	1 (0.5%)	1 (0.4%)	12 (2.1%)

TABLE 5.7 - ACFDR 2021: BONE DENSITY (OSTEOPENIA, OSTEOPOROSIS) BY AGE (AS MEASURED BY BONE DENSITOMETRY)

BONE MINERAL DENSITY	10-17 (N = 172)	18-29 (N = 275)	30+ (N = 380)	TOTAL (N = 827)
Normal	112 (65.1%)	175 (63.6%)	176 (46.3%)	463 (56.0%)
Osteopenia	57 (33.1%)	82 (29.8%)	151 (39.7%)	290 (35.1%)
Osteoporosis	3 (1.7%)	18 (6.5%)	53 (13.9%)	74 (8.9%)
Fracture	13 (1.6%)	9 (1.1%)	19 (1.8%)	41 (1.5%)

Bone mineral density scans are not generally undertaken on children less than 10 years of age. For those people with CF who had their bone density status reported to the ACFDR in 2021 (827 people), 35.1% had osteopenia, and 8.9% had osteoporosis, with 1.5% of those reporting a fracture in 2021 (Table 5.7).

5.4 CF GASTROINTESTINAL DISEASE

Pancreatic insufficiency associated with CF may lead to a range of gastrointestinal complications including gastro-oesophageal reflux, elevated liver enzymes, liver disease (cirrhotic and non-cirrhotic) and pancreatitis.

As per Table 5.8, 28.7% of people with CF with complications reported in the ACFDR had gastro-oesophageal reflux. Small proportions of patients had liver disease or pancreatitis. The proportion of people with CF who are pancreatic insufficient varies from 74.9% to 83.5% depending on age. (Tables 5.8 and 5.9).

TABLE 5.8 - ACFDR 2021: GASTROINTESTINAL COMPLICATIONS ASSOCIATED WITH LIVER DISEASE BY AGE

GI COMPLICATION	< 12	12-17	18-29	30+	TOTAL
Gastric oesophageal reflux	85/978 (8.7%)	80/618 (12.9%)	297/820 (36.2%)	528/1,030 (51.3%)	990/3,446 (28.7%)
Liver disease, non-cirrhosis (includes viral hepatitis, fatty liver)	78/946 (8.2%)	80/571 (14.0%)	70/841 (8.3%)	69/1,035 (6.7%)	297/3,393 (8.8%)
Liver disease, cirrhosis (image confirmed)	14/882 (1.6%)	31/522 (5.9%)	24/795 (3.0%)	41/1,007 (4.1%)	110/3,206 (3.4%)
Liver disease, cirrhosis with portal hypertension	6/874 (0.7%)	9/500 (1.8%)	35/806 (4.3%)	24/990 (2.4%)	74/3,170 (2.3%)

TABLE 5.9 - ACFDR 2021: PANCREATITIS BY AGE

	< 12 (N = 943)	12-17 (N = 553)	18-29 (N = 743)	30+ (N = 820)	TOTAL (N = 3,059)
PANCREATITIS					
Acute (first pancreatitis event this current year)	1 (0.1%)	5 (0.8%)	2 (0.2%)	1 (0.1%)	9 (0.3%)
No history of pancreatitis	950 (99.7%)	602 (98.4%)	809 (97.4%)	932 (94.6%)	3,293 (97.4%)
Pancreatitis, not specified	0 (0.0%)	1 (0.2%)	4 (0.5%)	9 (0.9%)	14 (0.4%)
Recurrent pancreatitis (history of more than one event of pancreatitis)	2 (0.2%)	4 (0.7%)	16 (1.9%)	43 (4.4%)	65 (1.9%)
PANCREATIC STATUS					
Insufficient	743 (76.0%)	509 (82.2%)	756 (83.5%)	834 (74.9%)	2,842 (78.6%)

5.5 NUTRITIONAL SUPPLEMENTS

For 2021, the reported use of pancreatic enzymes and nutritional supplements is shown in Table 5.10. A high proportion (79.5%) take pancreatic enzymes, 71.1% take fat soluble vitamin supplements and 49.1% take salt tablets. Supplement use is reported across all age groups.

TABLE 5.10 - ACFDR 2021: PEOPLE WHO RECEIVED NUTRITIONAL SUPPLEMENTS BY AGE

SUPPLEMENT USE	< 12 (N = 978)	12-17 (N = 619)	18-29 (N = 905)	30+ (N = 1114)	TOTAL (N = 3,616)
Pancreatic enzymes	738 (75.5%)	505 (81.6%)	756 (83.5%)	874 (78.5%)	2,873 (79.5%)
Vitamin supplements (fat soluble vitamins A, D, E and K)	703 (71.9%)	472 (76.3%)	645 (71.3%)	752 (67.5%)	2,572 (71.1%)
Salt replacement	669 (68.4%)	424 (68.5%)	359 (39.7%)	325 (29.2%)	1,777 (49.1%)

TABLE 5.11 - ACFDR 2021: NUTRITIONAL SUPPORT

	< 12 (N = 968)	12-17 (N = 568)	18-29 (N = 795)	30+ (N = 892)	TOTAL (N = 3,223)
Oral	97 (9.9%)	67 (10.8%)	76 (8.4%)	55 (4.9%)	295 (8.2%)
Gastrostomy tube	41 (4.2%)	51 (8.2%)	29 (3.2%)	8 (0.7%)	129 (3.6%)
Nasogastric tube	9 (0.9%)	2 (0.3%)	4 (0.4%)	5 (0.4%)	20 (0.6%)
Jejunostomy tube	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	1 (0.0%)
Parenteral nutrition	4 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	5 (0.1%)

The proportion of people with CF with information recorded in the ACFDR who required nutritional support was small. While 8.2% required oral supplemental nutrition, very few required enteral feeding, and of those the majority were via gastrostomy tube (3.6%) (Table 5.11).

5.6 PREVENTIVE CARE

The percentage of all people with CF receiving preventive care in 2021 is displayed in table 5.12. Eighty-five point seven percent of people received an annual physiotherapy review, 80.6% received an annual dietician review and for those aged 12 years and over, 74.7% received a mental health review.

TABLE 5.12 - ACFDR 2021: PREVENTIVE CARE

PREVENTIVE CARE	2021
Physiotherapy review	3,024 (85.7%)
Dietitian review	2,841 (80.6%)
Mental Health review	1,321 (74.7%)

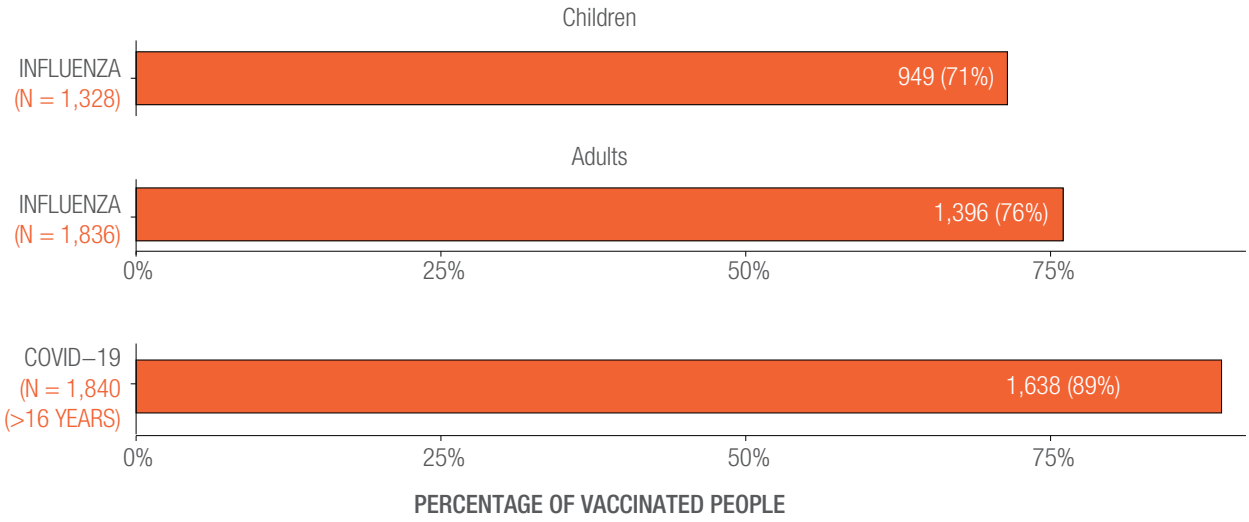
5.7 VACCINATION

Influenza immunization is recommended for individuals with CF age six months and older on an annual basis. Immunization coverage among adults was higher than children, with 76.0% of individuals 18 years or older immunized compared to 71.0% of those under 18 years of age.

In Australia COVID-19 vaccination had a staged rollout. People aged 16-59 years were eligible for vaccination from June 2021, 12-15 years old were eligible from August 2021, and 5-11 year oldâ•Žs became eligible from January 2022. The proportion of people with CF 16 years of age or older who were vaccinated with at least 1 dose for COVID-19 by 31st December was 89%.

In 2021, 23 people with CF were diagnosed with COVID-19, 19 of those being adults and 4 of those were children. Only 1 person who was diagnosed with COVID-19 required hospitalisation in 2021

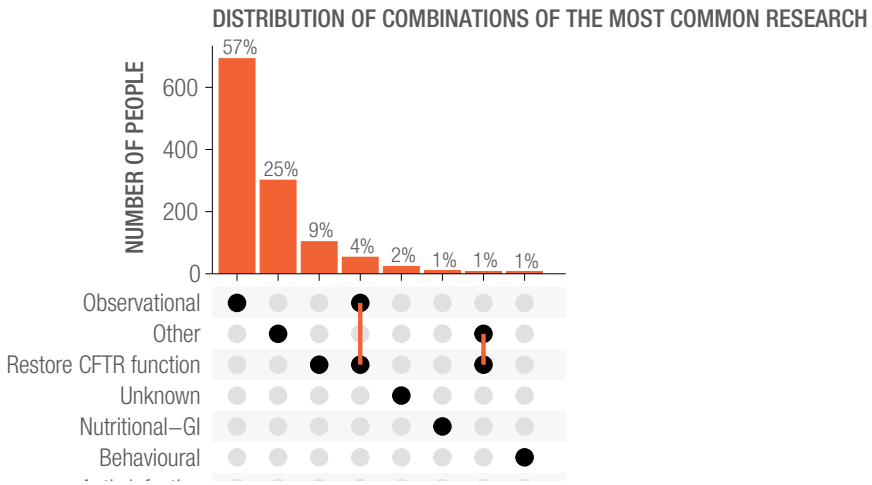
FIGURE 5.1: ACFDR 2021: VACCINATIONS



5.8 CLINICAL RESEARCH

In 2021, 2,297 people (65.2%) participated in clinical research. The majority participated in observational studies (57%) with 9% participating in CFTR modulator studies (Figure 5.2).

FIGURE 5.2: ACFDR 2021: CLINICAL RESEARCH PARTICIPATION



In 2021, there were 9 bilateral lung transplants for people with CF.

6. TRANSPLANTATION AND SURVIVAL

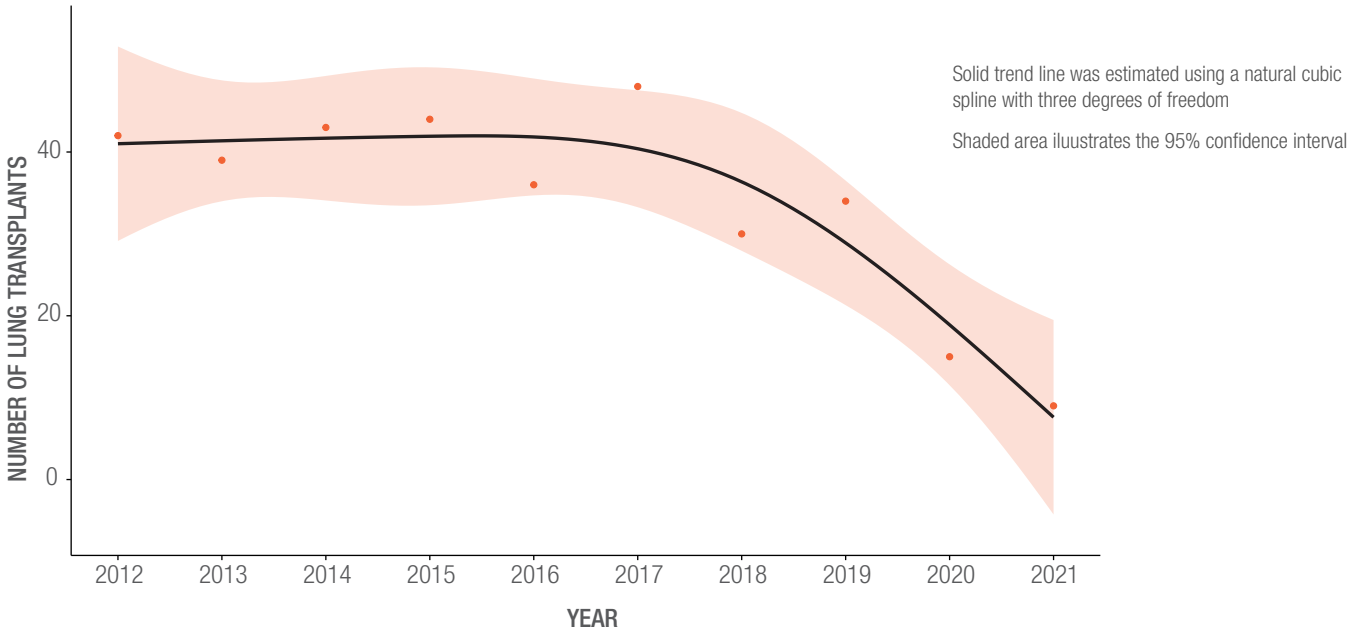
6.1 TRANSPLANTATION

In Australia approximately 33-40% of lung transplants are performed in adults with CF[8]. The most common transplantation procedure 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 transplantation of the kidney, liver or pancreas. Occasionally multi-organ transplants, especially liver and lung are required.

In 2021, there were a total of 12 transplants for people with CF, 9 were bilateral lung transplants of which 5 were performed in those below 30 years of age. The 3 non lung transplants were made up of liver and pancreas transplants.

There were 68 people who were evaluated for a transplant in 2021, 7 (10.3%) were on a wait list, and 9 (13.2%) were deferred from the waiting list in 2021. The number of annual bilateral lung transplants undertaken over the last decade is shown in Figure 6.1. There has been a decline in bilateral lung transplants over the last few years among people with CF in Australia. It is not clear why this decline has occurred. This may be due to the use of CFTR modulator therapy and we cannot rule out the effect of COVID-19 having led to fewer transplants occurring and fewer pulmonary exacerbations.

FIGURE 6.1: ACFDR 2012-2021: BILATERAL LUNG TRANSPLANTS



8. The Australia and New Zealand Cardiothoracic Organ Transplant Registry: 19th Annual Report, 1984-2014. Keogh A and Pettersson R, eds. ANZCOTR, Darlinghurst, 2014.

6.2 STATUS OF PEOPLE WITH CF IN THE ACFDR

The status of people in the ACFDR is updated annually by CF centres. Many people with CF who have a lung transplant are not followed up by the ACFDR, and their deaths may thus not be captured in the registry data. Periodically data linkage is undertaken with the national death register to validate death data. This is undertaken via probabilistic matching due to the de-identified nature of the data.

In 2021 the ACFDR recorded the deaths of 19 people with CF. Thirteen (68.0%) of these deaths occurred in people aged 30 years and over, six deaths (31.5%) occurred in young adults (18-29 years), while no deaths occurred in persons less than 18 years. Eleven (57.8%) of those deaths were people with CF who had received a transplant.

Of the 19 deaths in 2021, 3 had an unknown cause, 2 were unrelated to CF, 5 were related to CF including from pulmonary manifestations of CF (most common), 6 were post-transplant complications, intestinal manifestations, or (3) other causes related to CF or unspecified.

6.3 MEDIAN AGE OF DEATH

The median age of the deaths in 2021 was 36.8 years of age (Figure 6.2). The median age of death has been increasing since 1998. Median age may vary from year to year given the relatively small number of deaths per annum. The median age of death is different from estimated survival, which aims to estimate the survival of a person with CF who is born within a particular year(s).

FIGURE 6.2: ACFDR 1998-2021: MEDIAN AGE OF DEATH FOR PEOPLE WITH CF IN AUSTRALIA

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

6.4 SURVIVAL

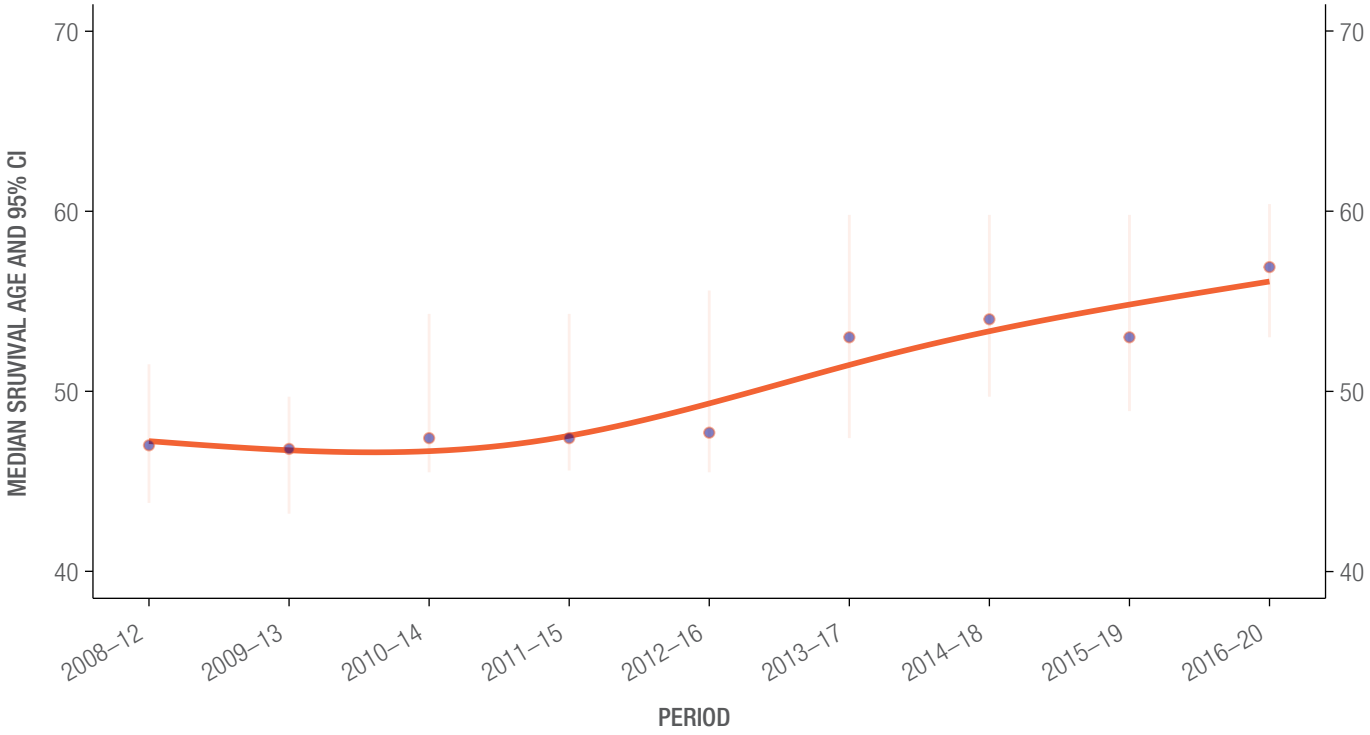
Median estimated survival for people with CF is determined based on the people who are alive in the ACFDR in a given year or years. Internationally, CF registries have documented steady increases in median survival over recent years due to better treatments, and this is expected to continue to increase as more people with CF are managed with CFTR modulators.

TABLE 6.2 – ACFDR 2010-2020: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA (5-YEAR COHORTS AND 10 YEAR SURVIVAL)

PERIOD	YEAR	MEDIAN AGE AND 95% CONFIDENCE INTERVAL (YEARS)	N DEATHS / N AT RISK
2010-14	**2014**	47.4 (45.5 - 54.3)	172 / 3,406
2011-15	**2015**	47.4 (45.6 - 54.3)	171 / 3,486
2012-16	**2016**	47.7 (45.5 - 55.6)	177 / 3,546
2013-17	**2017**	53.0 (47.4 - 59.8)	170 / 3,573
2014-18	**2018**	54.0 (49.7 - 59.8)	166 / 3,705
2015-19	**2019**	53.0 (48.9 - 59.8)	171 / 3,774
2016-20	**2020**	56.9 (53 - 60.4)	162 / 3,802

Table 6.4 (represented in Figure 6.3), shows that the estimated 5-year survival has increased over a 5-year period from 47.4 years for people with CF born in 2010-14, to 56.9 years for people with CF born in 2016-20. The ACFDR is reporting survival data one year in arrears to allow for late notification of recent deaths to be captured by the registry.

FIGURE 6.3: ACFDR 2008-2020: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA (5-YEAR COHORTS)



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

7. REGISTRY QUALITY ASSURANCE

Registry quality assurance comprises review of data completeness and data quality. Quality assurance processes regarding data completion are undertaken by the ACFDR Data Manager and Registry Coordinator when data is entered via the web–based system, via system validation checks, and follow up of incomplete data with the participating centres.

DATA COMPLETENESS

Similar to international registry comparisons, completeness of ACFDR data varies significantly depending on the data type, but also varies by centre. Table 7.1 summarises the main categories of the ACFDR data, and the percentage of data completeness for each.

2019-2021. TABLE 7.1 – ACFDR 2019-2021: DATA AVAILABILITY

	2019			2020			2021		
DATA ITEM	TOTAL	NUMBER	PERCENT	TOTAL[9]	NUMBER	PERCENT	TOTAL	NUMBER	PERCENT
Demographics Form	3,568	3,565	100.0%	3,648	3,648	100.0%	3,719	3,719	100%
Diagnosis Form	3,568	3,525	99.0%	3,648	3,619	99.0%	3,719	3,697	99%
Clinical measures Q1	3,568	3,472	97.0%	3,648	3,492	96.0%	3,719	3,700	99%
Clinical measures Q2	3,568	3,451	97.0%	3,648	3,477	95.0%	3,719	3,701	100%
Clinical measures Q3	3,568	3,430	96.0%	3,648	3,480	95.0%	3,719	3,698	99%
Clinical measures Q4	3,568	3,425	96.0%	3,648	3,576	98.0%	3,719	3,698	99%
Hospitalisations/home IV Q1	3,568	3,447	97.0%	3,648	3,447	96.0%	3,719	3,698	99%
Hospitalisations/home IV Q2	3,568	3,420	96.0%	3,648	3,476	92.0%	3,719	3,700	99%
Hospitalisations/home IV Q3	3,568	3,408	96.0%	3,648	3,474	95.0%	3,719	3,697	99%
Hospitalisations/home IV Q4	3,568	3,394	95.0%	3,648	3,568	98.0%	3,719	3,695	99%
CFTR modulators	3,568	3,385	95.0%	3,648	3,496	96.0%	3,719	3,698	99%
Transplants	3,568	3,362	94.0%	3,648	3,364	92.0%	3,719	3,700	99%
Complications & Treatment	N/A	N/A	N/A	3,648	3287	90.0%	3,719	3,697	99%
Overall data entry % completed			95.8%			95.5%[10]			99.4%

While the above table lists the completeness percentage, the ACFDR has begun auditing the CF sites, beginning with 3 audits at the Victorian CF centres completed in 2021 and more to follow in 2022.

9. This table encompasses all records, including those that are shared and transferred between CF centres.
10. A delay in data entry from 2 sites at the time of 2020 report data extract, resulted in a NSW and VIC site not having all their data represented in the ACFDR 2020 Annual Report

8. 2021 ACADEMIC OUTPUTS

PUBLICATIONS

Acceptability of patient reported outcome measures (PROMs) in a cystic fibrosis data registry
Ratnayake, I., Ahern, S. & Ruseckaite, R., 19 Jul 2021, In: BMJ Open Respiratory Research. 8, 1, 8 p., e000927.

COVID-19 vaccine prioritisation for people with cystic fibrosis
Carr, S. B., Cosgriff, R., Harutyunyan, S., Middleton, P. G., Ruseckaite, R., Ahern, S., Daneau, G., Filho, L. V. R. F. D. S., Stephenson, A. L., Cheng, S. Y., Melo, J., Corvol, H., Burgel, P. R., Nährlich, L., McKone, E., Colombo, C., Salvatore, M., Padoan, R., Abdrakhmanov, O., Gulmans, V. & 18 others, , Jul 2021, In: Journal of Cystic Fibrosis. 20, 4, p. 715-716 2 p.

Perceptions of telehealth among patients with cystic fibrosis and their caregivers during COVID-19 pandemic in Australia
Ruseckaite, R., Herdiman, J. & Ahern, S., 15 Oct 2021, In: Journal of Cystic Fibrosis. 20, Supplement 2, p. S159 1 p.

Redesign of the Australian Cystic Fibrosis Data Registry: A multidisciplinary collaboration
Ahern, S., Dean, J., Liman, J., Ruseckaite, R., Burke, N., Gollan, M., Keatley, L., King, S., Kotsimbos, T., Middleton, P. G., Schultz, A., Wainwright, C., Wark, P. & Bell, S., Mar 2021, In: Paediatric Respiratory Reviews. 37, p. 37-43 7 p.

CONFERENCE PRESENTATIONS

Perceptions of telehealth among patients with cystic fibrosis and their caregivers during COVID-19 pandemic in Australia
Ruseckaite, R., Herdiman, J. & Ahern, S., NACFC – 2021. Poster presentation

'International comparison of survival in cystic fibrosis between Canada, France, and Australia' Coriati, A, Ma, X, Sykes, J, Stanojevic, S, Ruseckaite, R, Lemonnier, L, Tate, J, Byrnes, CA, Bell, S, Burgel, P, & Stephenson, A 2021, NACFC – 2021. Poster presentation

'The Australian Cystic Fibrosis Data Registry (ACFDR) Maximising Registry Data Value Requires Optimising Data Quality' Caruso M , Ruseckaite R, Liman J, Salimi F, Ahern A., ACFC – 2021 poster presentation

'Lung function over the life course of paediatric and adult patients with cystic fibrosis from a large multi-centre registry.' Salimi F. et al, ACFC – 2021 poster presentation

9. DATA ACCESS REQUESTS

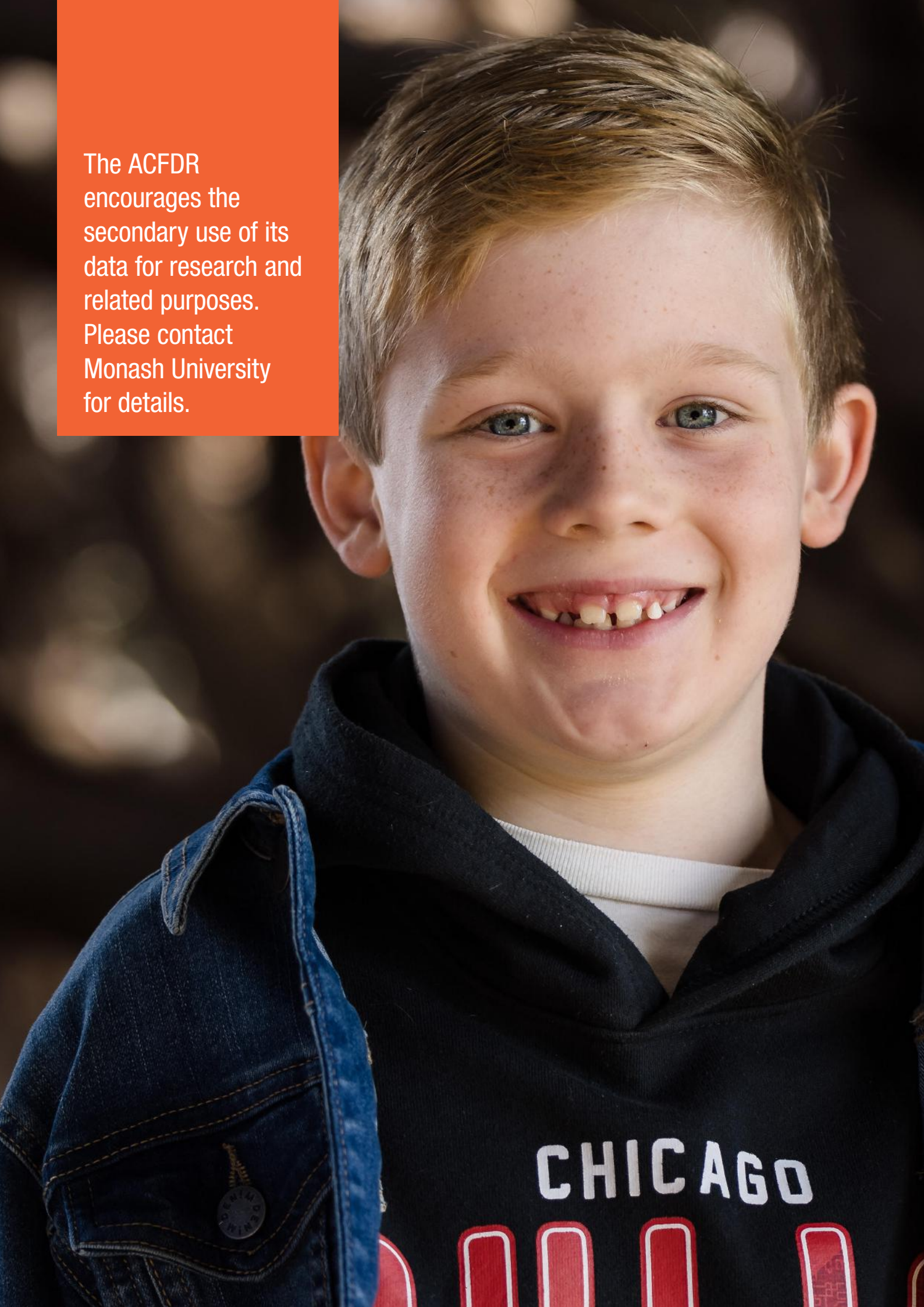
The ACFDR encourages the secondary use of its data for research and related purposes. Eighteen data access requests were received and approved for the ACFDR in 2021.

DATE (2021)	NAME	ORGANISATION	REQUEST TYPE	REQUEST
30/01	Anne Stephenson	Organisation Unity Health Toronto, St. Michael's Hospital	Research	International Comparisons in Health Outcomes and Survival in Cystic Fibrosis between France, Canada, Australia and New Zealand
26/02	Petrina Fraccaro/ Daniel Henderson	Gold Coast University Hospital	Non-research	Data requested regarding admissions, home Iv's, hospitalisations, clinical measures
8/03	Michael Doumit	Macquarie University	Research	Clinical outcomes in people with CF before and after implementation of telehealth in response to COVID19
22/03	Sharon Hunt	The Children's Hospital Westmead	Non-research	2020-Site 204 Nutrition and Lung function
28/04	Scott Bell/ Christine Duplancic	QIMR Berghofer Medical Research Institute	Research	The emerging problem of nontuberculous mycobacteria infection in people with cystic fibrosis
28/04	Sarath Ranganathan	Royal Children's Hospital	Research	Access to RCH Respiratory Microbiology Results for use in AREST CF: Detection of early lung disease in Cystic Fibrosis
14/05	Maxine Orre	Vertex Pharmaceuticals	Non-research	Understanding the Burden of Illness in People with Cystic Fibrosis
20/05	Maxine Orre	Vertex Pharmaceuticals	Non-research	Rate of decline in FEV1 in patients treated with lumacaftor/ivacaftor [or Tezacaftor/Ivacaftor]
4/06	Andrew Tai	Women's and Children's Hospital	Research	The impact of CF outcomes based on post codes and social economic status
14/06	Flynn Adaway/ Rasa Ruseckaite	Monash University	Research	Patient Reported Outcome Measures in Children and Adolescents with Cystic Fibrosis
25/06	Maxine Orre	Vertex Pharmaceuticals	Non-research	Vertex CFTRm use and discontinuation tables – as planned for inclusion in 2020 ACFDR report
20/07	Michael Doumit	Macquarie University	Research	Clinical outcomes in people with CF before and after implementation of telehealth in response to COVID19
20/07	Anysha Walia, Ed Giles	Department of Paediatric Gastroenterology, Monash Children's Hospital	Research	Comparing nutritional and clinical outcomes in paediatric cystic fibrosis patients with and without percutaneous endoscopic gastrostomy tubes
5/08	Maxine Orre	Vertex Pharmaceuticals	Non-research	CF patient population – CFTR mutation by state
3/09	Maxine Orre	Vertex Pharmaceuticals	Non-research	Rate of decline in FEV1 in patients treated with lumacaftor/ivacaftor [or Tezacaftor/Ivacaftor]
28/09	Maxine Orre	Vertex Pharmaceuticals	Non-research	Rate of decline in FEV1 in patients treated with lumacaftor/ivacaftor [or Tezacaftor/Ivacaftor]
25/10	Scott Bell/ Christine Duplancic	QIMR Berghofer Medical Research Institute	Research	The emerging problem of nontuberculous mycobacteria infection in people with cystic fibrosis
23/11	Maxine Orre	Vertex Pharmaceuticals	Non-research	CF patient population – CFTR mutation by state

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 costs for data extraction and/or analysis.

The ACFDR encourages the secondary use of its data for research and related purposes. Please contact Monash University for details.



APPENDICES

List of Figures

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Registry Steering Committee Membership 2021

Steering Committee Members	Role/Specialisation	Institution/Association
Professor Susannah Ahern	Coordinating Investigator / Academic Lead	Monash University, VIC
Professor Scott Bell	Clinical Lead ACFDR / CF Adult Physician	The Prince Charles Hospital, QLD
Ms Nettie Burke	CEO	Cystic Fibrosis Australia
Professor Claire Wainwright	CF Physician – Paediatrics	Queensland Children's Hospital, QLD
Dr Andre Schultz	CF Physician – Paediatrics	Perth Children's Hospital, WA
Professor Peter Wark	CF Physician – Adults	John Hunter Hospital, NSW
Professor Peter Middleton	CF Physician – Adults	Westmead Hospital, NSW
A/Professor Tom Kotsimbos	CF Physician – Adults	Alfred Health, VIC
Siobhain Mulrennan	CF Physician – Adults	Sir Charles Gairdner Hospital, WA
Tonia Douglas	CF Physician – Paediatrics	Queensland Children's Hospital, QLD
Dr Rasa Ruseckaite	Data Manager – ACFDR	Monash University, VIC
Dr Susannah King	Dietician	Alfred Health, VIC
Dr Nathan Ward	Physiotherapist	Royal Adelaide Hospital, SA
Sue Morey	Nurse Practitioner	Sir Charles Gairdner Hospital, WA
Ms Lucy Keatley	CF Clinical Nurse Consultant	Westmead Hospital, NSW
Pia Sappl	Consumer Representative	NSW
Chloe Arthur	Consumer Representative	QLD
Honor Rose	Consumer Representative	VIC

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

Site	
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

MONASH University

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: Professor Susannah Ahern

Registry Data Manager: Dr Rasa Ruseckaite

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**

The ACFDR would like to take this opportunity to thank the CF community members for the use of their photos they have kindly supplied for this Annual Report.

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