MONASH University

AUSTRALIAN CYSTIC FIBROSIS DATA REGISTRY

ANNUAL REPORT 2020

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

Addendum: Version 1.1

Revisions that were made to this version (1.1) of the 2020 ACFDR Annual Report include;

Table 4.1, Table 4.2 and Figure 4.3.

This corrected version (1.1) supersedes all versions of the 2020 ACFDR Annual Report.

Data Period

The data contained in this report was extracted from the ACFDR on April 20th 2021, and pertains to data that relates to patient events from January 1st to December 31st 2020. As the registry does 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, Scott Bell, Nettie Burke on behalf of the ACFDR. The ACFDR Registry Annual Report, 2020. Monash University, Department of Epidemiology and Preventive Medicine, July 2021, Report No 22

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CYSTIC FIBROSIS Australia

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The Thoracic Society of Australia & New Zealand
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FOREWORD

FROM THE CYSTIC FIBROSIS AUSTRALIA CEO

The work we do would be impossible without the help and trust of our CF Community. The CF community steps up time and time again for the CF cause. One notable display of trust in our efforts is their willingness to allow their health data to be included in the Australian Cystic Fibrosis Data Registry (ACFDR), a crucial project that improves clinical outcomes, directs research, streamlines advocacy and supports clinical trials.

The CF Centres also deserve our praise and thanks for their cooperation with the ACFDR. They are in many ways the front line of our fight for Lives Unaffected by CF.

Finally, we want to thank the Steering Committee for their extensive oversight of the Data Registry, and of course Monash University's Registries Unit who created and managed this valuable asset.

The ACFDR records insights and health outcomes capable of changing the face of CF in this country. The future of Health is information, and the unrivalled complexity of CF as a condition means that good data is indispensable to progress.

The ACFDR is a valuable clinical improvement tool and also a research repository that can support local and international studies and clinical trials to extend CF lives, reduce the burden of CF and ultimately find a cure for CF.

Over the past six years the ACFDR has gone through enormous change, being rebuilt from the ground up. The ACFDR is now able to harmonise with international registries around the world as an even more effective clinical improvement and research tool.

Cystic Fibrosis Australia is committed to the ACFDR and together with Monash and the Steering Committee we have plans for the future that include consumer centric strategies and enhanced connectivity with clinical care tools.

With our partners and community members on board, we have the team we need to grow and support this ambitious and vital registry. A smarter, brighter future for CF care.

Nettie Burke
Chief Executive Officer
Cystic Fibrosis Australia

CYSTIC FIBROSIS Australia

"The ACFDR records insights and health outcomes capable of changing the face of CF in this country."

FROM THE REGISTRY CLINICAL LEAD

This year the 2020 Annual Report of the ACFDR is launched earlier and in a more comprehensive manner than any of the earlier reports in the prior twenty-one years. As you will see the numbers of Australians with CF entered into the Registry has continued to rise and the completeness of data across the dataset is greater than before. This demonstrates wonderful collaboration between the Monash Registry Team, Cystic Fibrosis Australia and all of the CF centres, nationally.

Congratulations to everyone! In particular I'd like to call out the data entry teams across each of the CF centres who work day in and day out entering the data on the patients attending the centres. This is no small feat and the support provided for the Registry data entry has culminated in the best report to date. I hope you will agree there are a number of highlights in this year's Registry's report, including the reporting of growing numbers of Australians with CF on CFTR modulators including ivacaftor (Kalydeco), lumacaftor-ivacaftor (Orkambi), tezacaftor-ivacaftor (Symdeko) and elexacaftor-tezacaftor-ivacaftor (Trikafta).

As a result of the COVID-19 pandemic, virtual clinics and consultations have increased rapidly for the CF community. These are highlighted on page 27 in the Registry Report. More detail is provided on key clinical outcomes including survival and transplantation. Median survival for Australians with CF continues to increase and importantly in 2020 there was a significant reduction in the numbers of Australian's with CF undergoing transplantation. Whilst the COVID-19 pandemic may have had some impact on numbers it is highly likely that this is an early but significant signal of the impact of CFTR modulators on the health and wellbeing of Australians with CF. May this continue in the future. It has been noted by our transplant colleagues that there are much smaller numbers of people with CF being referred for consideration and assessment for lung transplantation, and lower numbers of people with CF actively listed for lung transplantation.

A key development of the utility of the Registry has been the increasing numbers of researchers requesting access to the Registry. In the past twelve months there have been fifteen such projects and we look forward to seeing the outcomes of the utilization of the Registry data over the coming years.

I'd like to thank the Monash Registry Team and the members of the ACFDR Steering Committee, specifically to thank a number of retiring committee members including Professor Claire Wainwright, Professor Peter Middleton, Lucy Keatley, Dr Susannah King and Morgan Gollan. Cystic Fibrosis Australia (CFA), the Monash Registry Team and the ACFDR Steering Committee are currently evaluating many excellent expressions of interest as there is a significant changing of the guard.

I wanted to specifically thank CFA's Chief Executive, Nettie Burke, for her tireless energy and work to support the CF community over the past six years at the helm. Her impact, her lobbying and her client-centric focus has been outstanding and she will be sorely missed by the CF community. Though, I'm sure Government ministers and the PBAC will take some time to not instantly recognise her number appearing on their mobile phones when she calls to highlight the importance of CFTR modulators and critical need for government to fund them!

Finally, it's been an honour and a great learning experience to participate on the Steering Committee since its commencement in 1998 and for the past five years as the Clinical Lead of the Registry and the Chair of the Steering Committee. I will be handing over the baton at the end of 2021. I look forward to continuing to watch the growth of the Registry over the coming years.

Professor Scott Bell, MBBS, MD, FRACP, FThorSoc
Clinical Lead, Australian Cystic Fibrosis Data Registry
Chief Executive Officer, Translational Research Institute, Brisbane
Senior Physician, Department of Thoracic Medicine,
The Prince Charles Hospital, Brisbane

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) has been collecting data on Australian people with CF for over 21 years. The 2020 ACFDR Annual Report includes information relating to over 3500 people with CF, estimated to comprise over 95% of Australia's CF population. 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 usually 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 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 2020 Annual Report is the second 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 95% 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 Data QA program expanded in 2020 to include complications and treatment information, and will continue to expand in 2021 providing further information about life and wellbeing for people with CF.

"The 2020 ACFDR Annual Report includes information relating to over 3,500 people with CF, estimated to comprise over 95% of Australia's CF population."

1. Ahern S, Dean J, Liman J, Ruseckaite R, Burke N, Gollan M, Keatley L, King S, Kotsimbos T, Middleton PG, Schultz A, Wainwright C, Wark P, Bell S. Redesign of the Australian Cystic Fibrosis Data Registry: a multidisciplinary collaboration. Paediatr Respir Rev. 2020 Mar 26:S1526-0542(20)30028-2. doi: 10.1016/j.prrv.2020.03.001

SUMMARY OF 2015, 2017, 2019 AND 2020 REGISTRY DATA

THIS SECTION PROVIDES AN OVERVIEW OF THE CF POPULATION, HEALTH OUTCOMES, AND CARE IN AUSTRALIA FOR 2015, 2017, 2019 & 2020[2]	2015	2017	2019	2020
PEOPLE WITH CYSTIC FIBROSIS				
Total people with CF in the ACFDR	3,379	3,151[3]	3,446	3,538
Age (median)	18.8 yrs	19.6 yrs	19.6 yrs	20.2 years
Age (mean)	20.9 yrs	21.7 yrs	22.0 yrs	22.6 years
Adults (≥ 18 yrs) number, (%);	1,756 / 52.0%	1,692 / 53.7%	1,854 / 53.8%	1,965 / 55.5%
Adults: Males %	53.2%	53.7%	53.1%	52.8%
CF DIAGNOSIS & GENOTYPING				
Newly diagnosed people with CF (pp)	98	72	66	74
% Diagnosis < 1 yr	73.5%	76.6%	85.0%	82.4%
% Diagnosis ≥ 18 years	3.1%	4.2%	4.5%	10.8%
Genotyped – one allele (two alleles)	91.7%	94.1%	96.0% (88.0%)	98.4% (92.2%)
% F508del Homozygous	50.2%	49.8%	47.0%	47.0%
% F508del Heterozygous	42.0%	36.6%	42.0%	43.0%
CLINICAL MEASURES (LUNG FUNCTION & NUTRITION)				
Median FEV1 % predicted children 6-17 years	95.0%	95.0%	95.0%	96.0%
Median FEV1 % predicted adults 18 years and older	71.0%	71.0%	74.0%	74.0%
Median weight for length percentile < 2 yrs	67th	75th	68th	76th
Median BMI percentile children	64th	62nd	68th	69th
Median BMI - adults kg/m^2	22.9	23.2	23.5	23.3
RESPIRATORY MICROBIOLOGY				
P. aeruginosa (%)	50.1%	55.9%	47.8%	41.6%
S. aureus (%)	33.9%	50.9%	51.5%	47.1%
Aspergillus *spp* (%)	18.2%	22.2%	22.9%	18.8%
Non tuberculous mycobacterium (%)	2.8%	4.2%	5.9%	6.4%
COMPLICATIONS				
% with Diabetes ≥ 12 years	N/A	N/A	N/A	23.7%
CFTR MODULATORS				
% taking CFTR modulator at end 2020	N/A	N/A	N/A	51.7%
TRANSPLANTS AND SURVIVAL				
Bilateral lung transplants	30	41	33	15
Deaths (Total CF deaths) (N)	17	27	26	18
Median age of death	31.6 years	35.6 years	32.0 years	30.7 years
Survival median (cohort, 5 year)	47.0 years	49.8 years	53.0 years	54.3 years

2. In 2018 the data registry changed platforms during that year and did not report data.

3. Total number of patients for 2017 is lower due to the exclusion of two sites for low completeness.

Out of 3,538 people with CF, 1,965 (55.5%) were adults (18+ years), 12.8% of people were 40 years and over.

1. PEOPLE WITH CYSTIC FIBROSIS

1.1 OVERVIEW

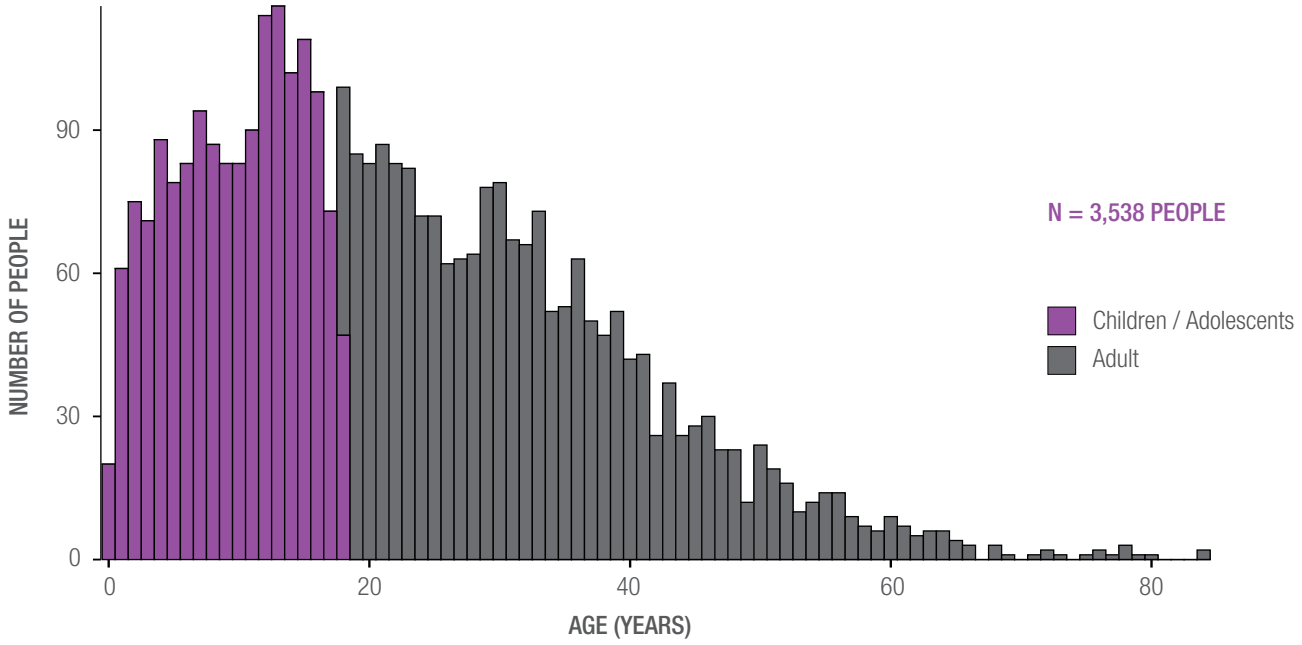
Cystic fibrosis (CF) is a recessive genetic condition which causes damage to the respiratory and digestive systems. This occurs as a result of a variant in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. Variants in the CFTR gene (which controls the movement of water and salt within 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 is reported only for a subset of persons, such as those newly diagnosed in 2020, or those of a particular age or gender, this will be noted in the text and figures.

1.2 COHORT AGE AND GENDER CHARACTERISTICS

Collected from 23 CF centres in Australia, the Australian Cystic Fibrosis Data Registry (ACFDR) held records of 3,538 people with CF as of 31st December 2020. Figure 1.1 shows the age distribution of the total ACFDR cohort at the end of 2020.

FIGURE 1.1: ACFDR 2020: PEOPLE WITH CF IN AUSTRALIA BY AGE



The median age of the registry population was 20.2 years on 31st December 2020, higher than at the end of previous years, having been 19.6 years in 2019. Out of 3,538 people with CF, 1,573 were children (0-17) and 1,965 (55.5%) were adults (18+ years), 12.8% of people were 40 years and over.

TABLE 1.1 – ACFDR 2020: PEOPLE WITH CF BY AGE AND GENDER

AGE	FEMALE	MALE	TOTAL
< 2	55.9% (66)	44.1% (52)	118
2-5	44.9% (145)	55.1% (178)	323
6-11	47.1% (248)	52.9% (279)	527
12-17	51.6% (312)	48.4% (293)	605
18-29	48.0% (441)	52.0% (478)	919
30-39	43.8% (259)	56.2% (333)	592
≥ 40	43.8% (199)	56.2% (255)	454
Total	47.2% (1,670)	52.8% (1,868)	3,538

The median age for males at 20.6 years (20.1 years in 2019) remained higher than that for females at 19.6 years in 2020 (19.0 years in 2019). As of 31st December 2020, 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 2020 is shown in Figure 1.2

FIGURE 1.2: ACFDR 2020: PEOPLE WITH CF BY AGE AND GENDER

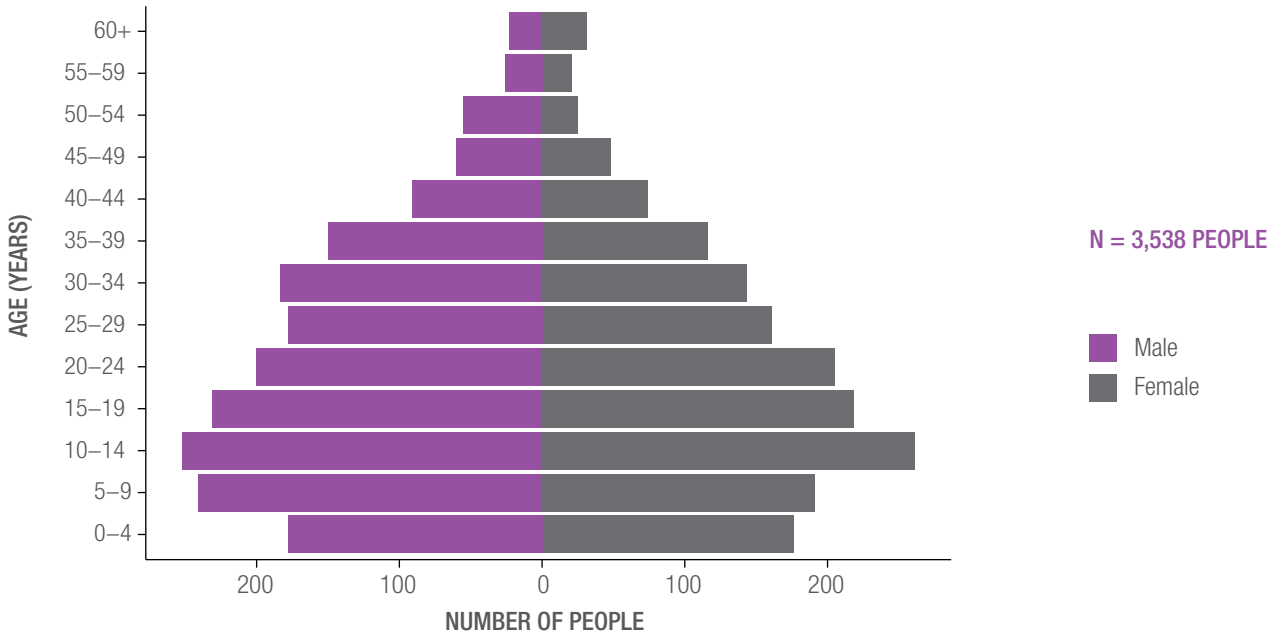
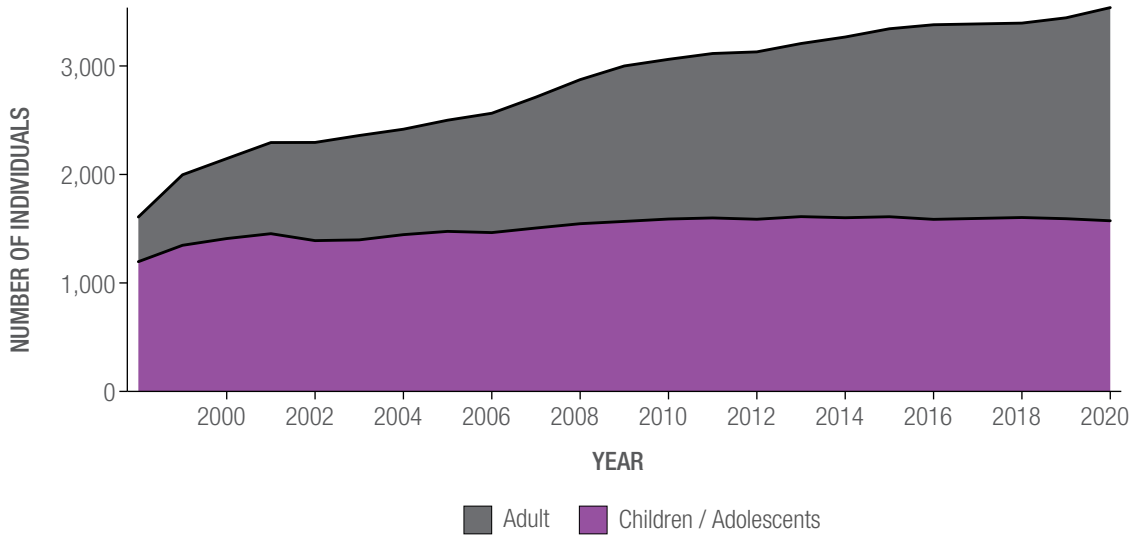


Figure 1.3 shows the number of people in the CF registry for the last 21 years, including the proportion who are adult for each year. As of 31st December, 2020, the proportion who were adult were 55.5% compared to 53.8% in 2019.

FIGURE 1.3: ACFDR 1998-2020: PAEDIATRIC VS ADULTS PROFILE OVER TIME



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

Those who receive their CF care at centres in each of Australia's jurisdictions are shown in Figure 1.4.

FIGURE 1.4: ACFDR 2020: DISTRIBUTION BY STATE / TERRITORY

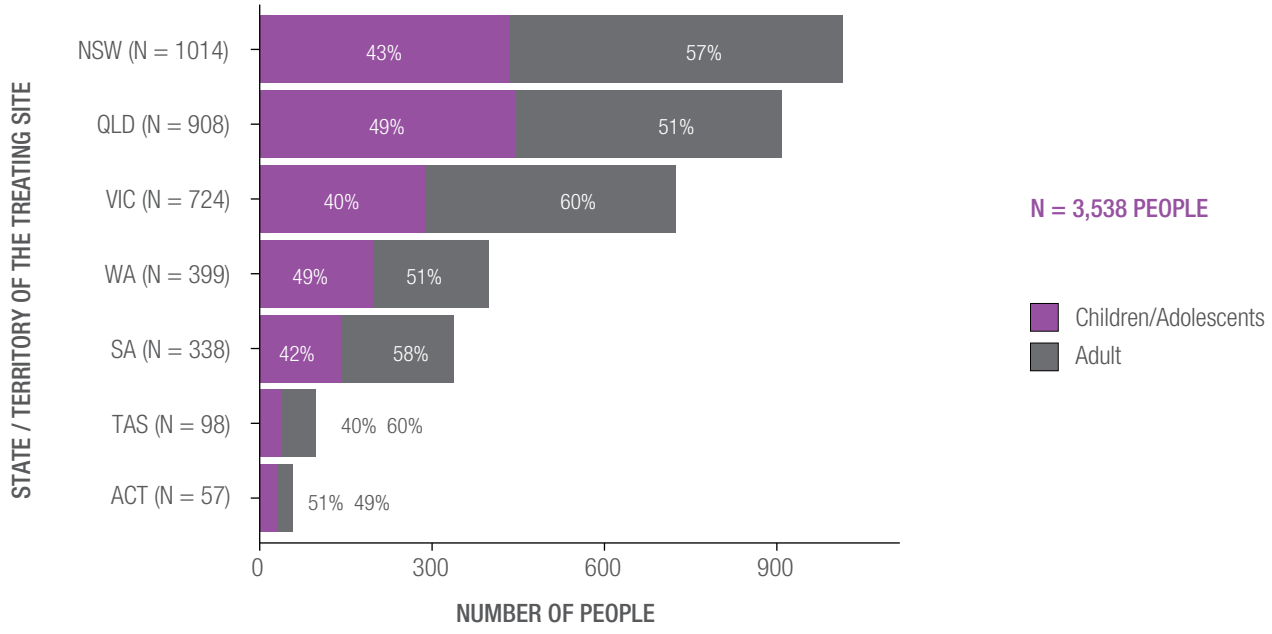


Figure 1.4 shows the distribution of people with CF across Australian jurisdictions, including paediatric vs adult distribution. Jurisdiction is based on the postcode of the CF centre location, rather than the postcode of the individual. From 2021, individual postcode information will be a mandatory data item, which will be cross-referenced against CF centre postcode to improve the accuracy of this information.

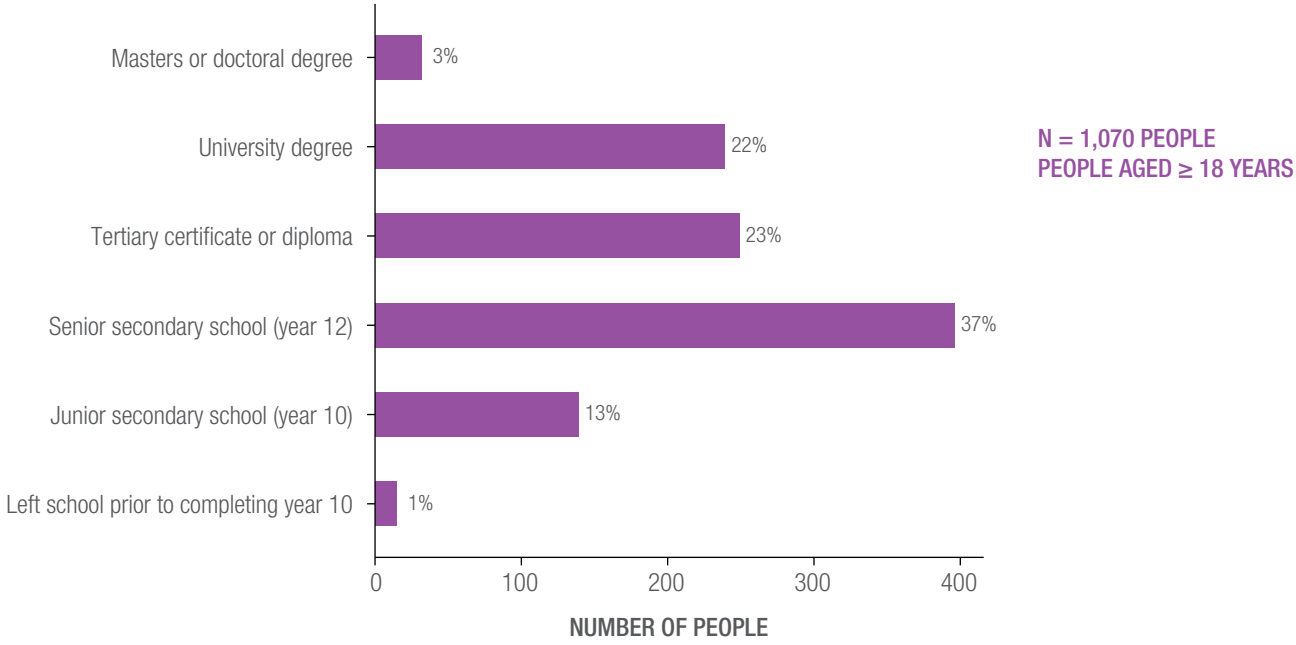
1.3 SOCIAL OUTCOMES OF PEOPLE WITH CF

Over half (51.0%) of adults with CF in the ACFDR have information recorded about their social outcomes. As symptom management improves and survival increases, persons with CF are involved in greater numbers in education, employment and having a family.

EDUCATIONAL OUTCOMES

Of the 1,070 adults with CF with information regarding education in the ACFDR, the proportion who completed a tertiary certificate, diploma, undergraduate or postgraduate degree is 48.0%, with those completing University education being 25.0% (Figure 1.5).

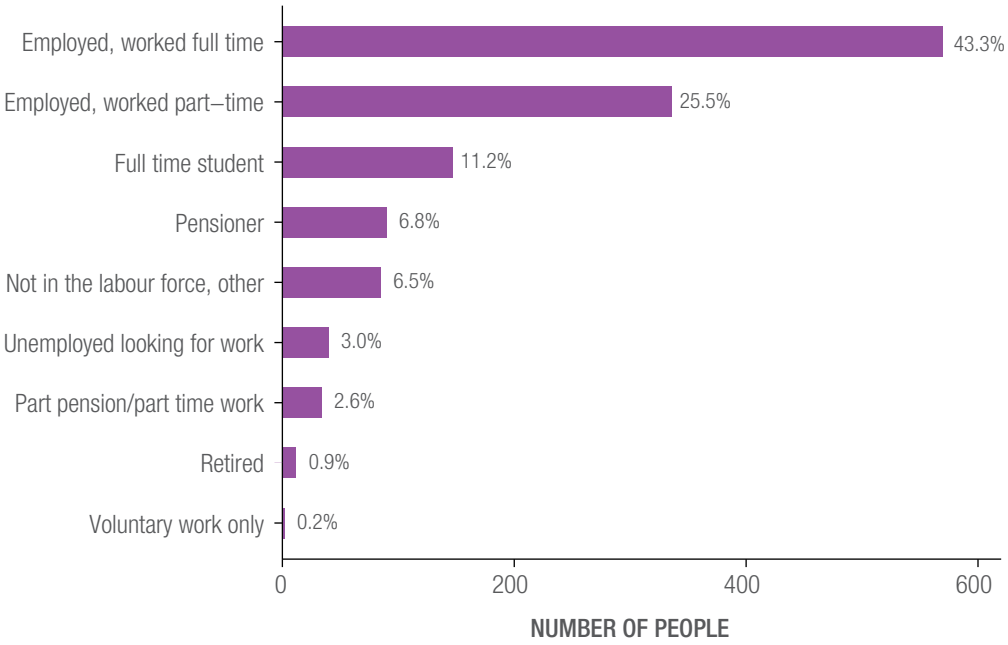
FIGURE 1.5: ACFDR 2020: HIGHEST EDUCATIONAL ATTAINMENT



EMPLOYMENT STATUS

In the ACFDR 1,316 adults with CF have information regarding employment status. Forty three point three percent were in full-time employment, 25.5% were in part-time employment, and a further 11.2% were in full-time study. Nine percent of people with CF received a part or full pension, and a further 9.5% were not in the labour force or were looking for work (Figure 1.6).

FIGURE 1.6: ACFDR 2020: EMPLOYMENT STATUS

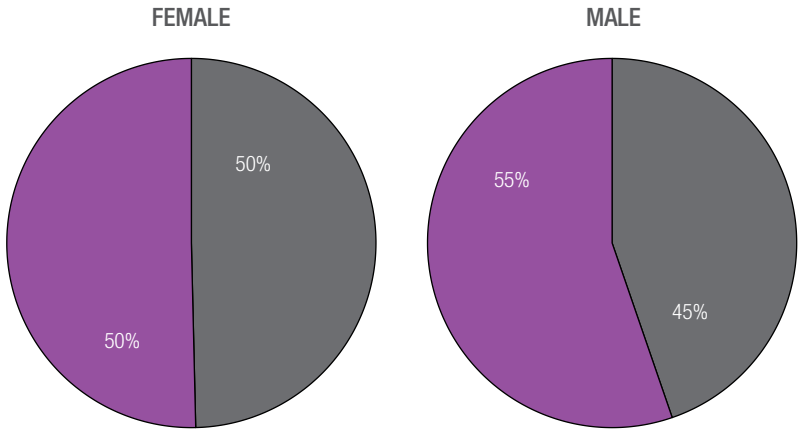


N = 1,316 PEOPLE
PEOPLE AGED ≥ 18 YEARS
WITH DATA RECORDED

RELATIONSHIP STATUS

Half (50.0%) of women and 45.0% of men with CF were married or in a de facto relationship, of the 1,434 adults with information regarding marital status in the ACFDR (Figure 1.7).

FIGURE 1.7: ACFDR 2020: MARITAL STATUS



N = 1,434 PEOPLE AGED
≥ 18 YEARS

Not married
Married / Defacto

There were 74 diagnoses of CF, notified to the registry for 2020.

2. CF DIAGNOSIS AND GENOTYPING

2.1 NEW DIAGNOSES

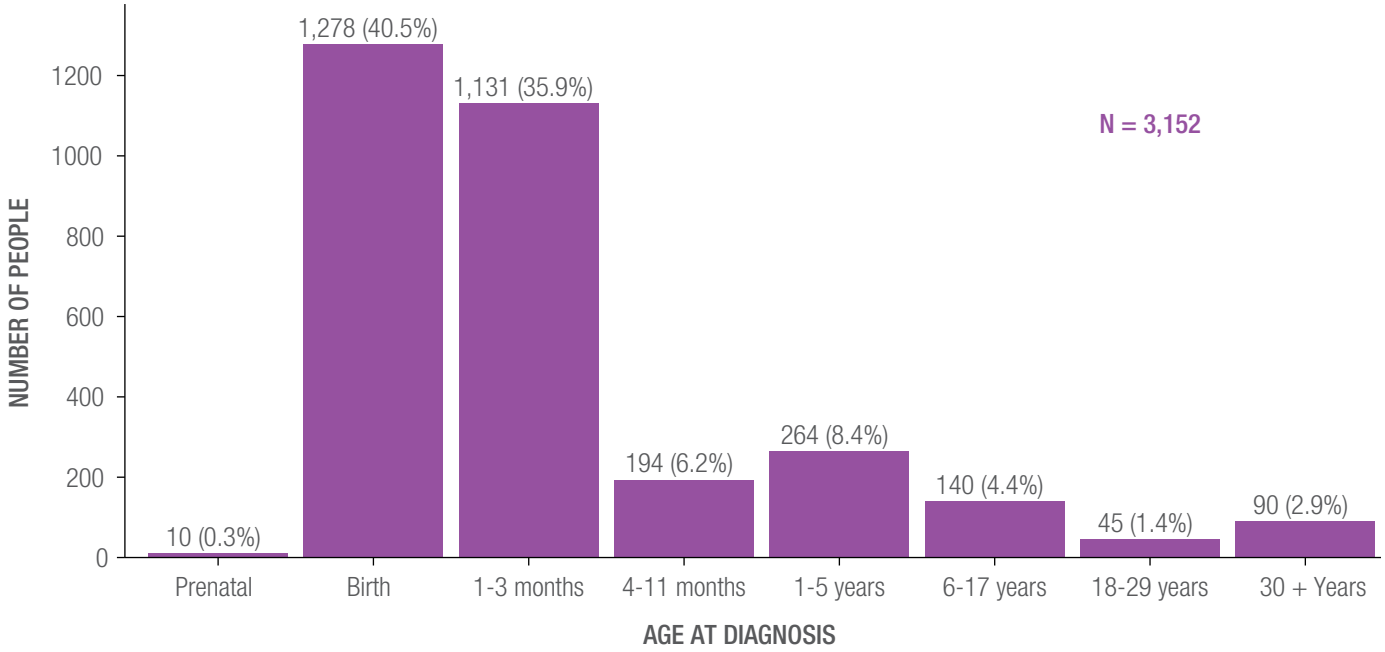
There were 74 new diagnoses of CF notified to the registry in 2020. Of these, 61 people (82.4%) were diagnosed at less than one year of age, 5 people were diagnosed between 1-17 years and 8 people were diagnosed over the age of 18 years. There were no new cases where the diagnosis date was unknown (Table 2.1).

TABLE 2.1 - ACFDR 2020: AGE AT DIAGNOSES FOR NEWLY DIAGNOSED PERSONS

AGE	NUMBER	%
< 1 year	61	82.4%
1-17 years	5	6.8%
18+ years	8	10.8%
Total	74	100.0%

The majority (89.1%) of persons with CF in the ACFDR have their age of diagnosis recorded; 82.9% of the ACFDR cohort was diagnosed at less than 1 year of age. The age of diagnosis for people with CF from the whole ACFDR cohort is shown in Figure 2.1.

FIGURE 2.1: ACFDR 1998-2020: AGE AT DIAGNOSIS FOR WHOLE COHORT



Diagnosis for the majority of people in the ACFDR was via newborn screening (53.2%), with 33.6% having clinical symptoms or signs at the time of diagnosis (Figure 2.2). Few (7.6%) had a family history of CF and 2.0% had a diagnosis confirmed by prenatal screening.

The most common clinical symptoms/signs were meconium ileus/intestinal obstruction (35%), respiratory signs/symptoms (29%) and other gastrointestinal symptoms (16%) (Figure 2.2).

FIGURE 2.2: ACFDR 1998-2020: METHOD OF DIAGNOSIS AND PRESENTING SYMPTOMS/SIGNS

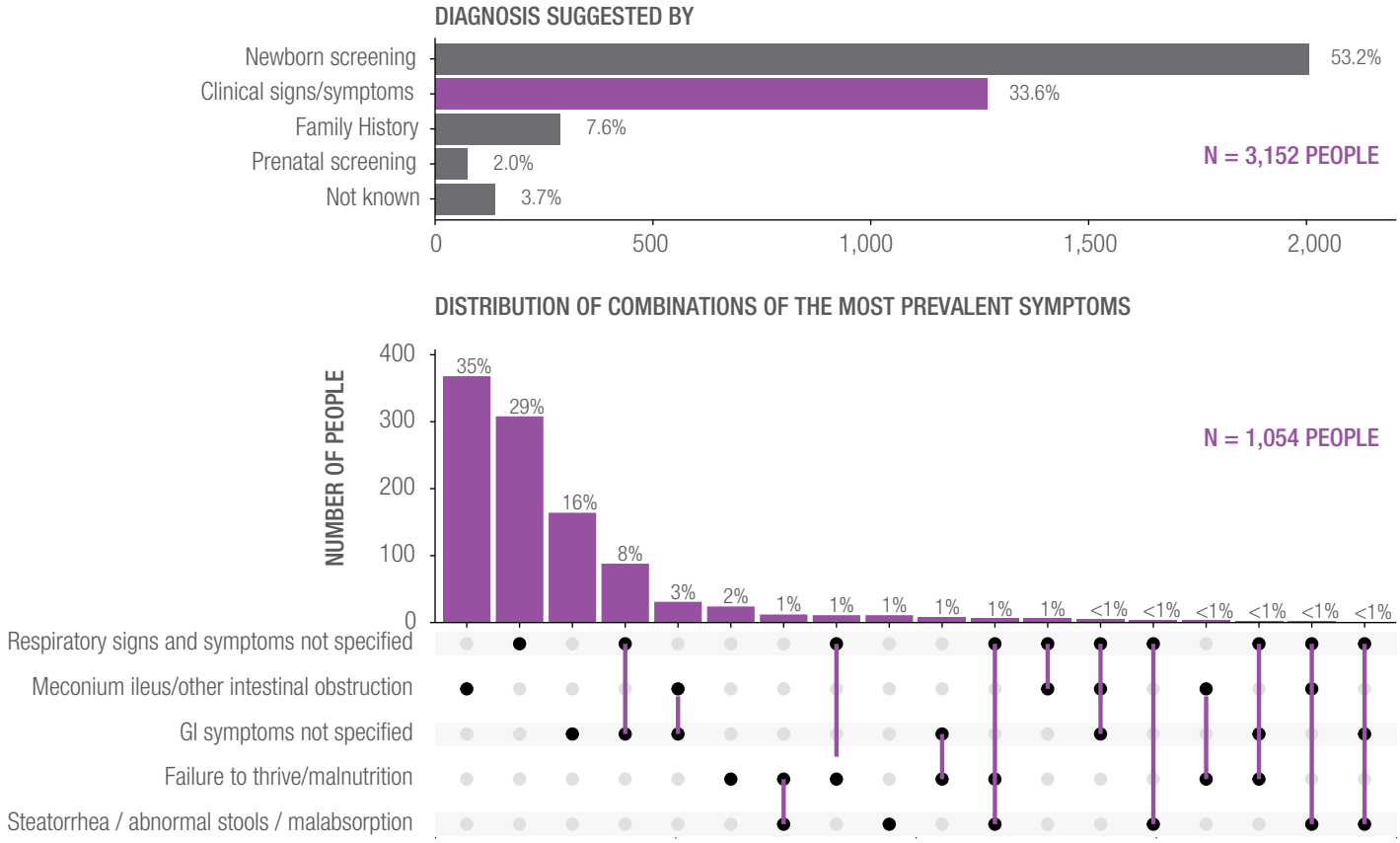


Table 2.2 highlights that diagnosis by family history and prenatal screening have increased over the last 20 years.

TABLE 2.2 - ACFDR 1998-2020: COMPARISON OF DIAGNOSTIC CHARACTERISTICS

DIAGNOSIS BY	TOTAL CF COHORT (%)	2020 NEW DIAGNOSES (%)
Newborn screening	2,006 / 3,152 (53.2%)	57 / 74 (52.8%)
Clinical symptoms/signs	1,268 / 3,152 (33.6%)	34 / 74 (31.5%)
Family history	287 / 3,152 (7.6%)	11 / 74 (10.2%)
Prenatal screening	74 / 3,152 (2.0%)	6 / 74 (5.6%)
Not known	138 / 3,152 (3.7%)	0 / 74 (0.0%)

2.2 GENOTYPE

Everyone inherits two copies of the CFTR gene. However, some of the inherited copies are variants. Since discovery of this gene in 1989, there have been over 1,700 variants identified. These variants can either be homozygous, the same, or heterozygous, different mutations. The most common mutation is F508 del.

The proportion of people with CF with two known alleles (gene variant) has increased from 84.0% to 92.0% from 2009-2020. Those with at least one known allele have increased from 94.0% to 98.0%, and the proportion with both alleles unknown has reduced from 6.0% to 2.0% 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 and Table 2.3. While 94.2% of infants less than one year of age have two known alleles, this decreases to 86.4% for people over 40 years, and 74.1% for people over the age of 60 years.

FIGURE 2.3: ACFDR 2020: PERCENTAGE OF ACFDR COHORT WITH GENOTYPE COMPLETE

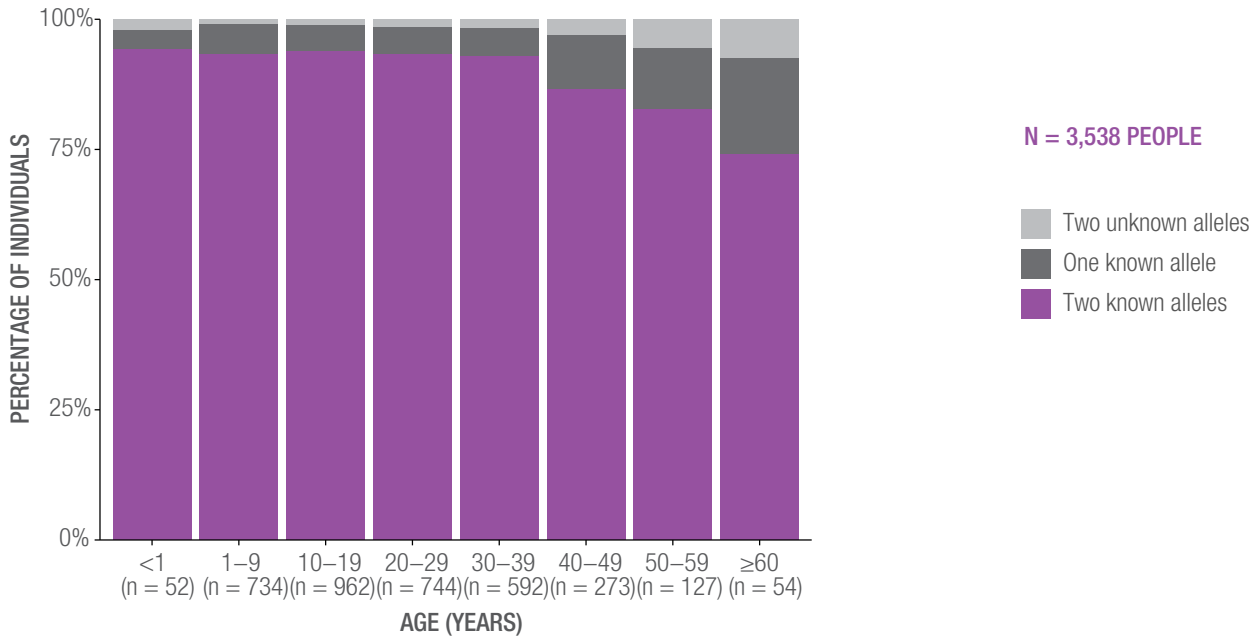


TABLE 2.3 - ACFDR 2020: PERCENTAGE OF PERSONS WITH KNOWN VARIANTS BY AGE GROUP

AGE IN YEARS	N	ONE KNOWN ALLELE	TWO KNOWN ALLELES	TWO UNKNOWN ALLELES
[0-1]	52	2 (3.8%)	49 (94.2%)	1 (1.9%)
[1-10]	734	42 (5.7%)	685 (93.3%)	7 (1.0%)
[10-20]	962	49 (5.1%)	903 (93.9%)	10 (1.0%)
[20-30]	744	39 (5.2%)	694 (93.3%)	11 (1.5%)
[30-40]	592	32 (5.4%)	550 (92.9%)	10 (1.7%)
[40-50]	273	29 (10.6%)	236 (86.4%)	8 (2.9%)
[50-60]	127	15 (11.8%)	105 (82.7%)	7 (5.5%)
[60+]	54	10 (18.5%)	40 (74.1%)	4 (7.4%)

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 1,520 people who are heterozygous for F508del (i.e. have one F508del variant) the most common combination (alleles) are F508del/G551D (14.0%), F508del/R117H (6.4%), and F508del/G542X (5.0%), with F508del gating variants (excluding G551D) make up 1.1% (Figure 2.4 B).

However, approximately 50.0% of other allele variants associated with heterozygous F508del combinations are comprised of individual variants that each make up less than 1.0% of the total (Figure 2.4 B).

FIGURE 2.4: ACFDR 2020: MOST COMMON CFTR VARIANT COMBINATIONS

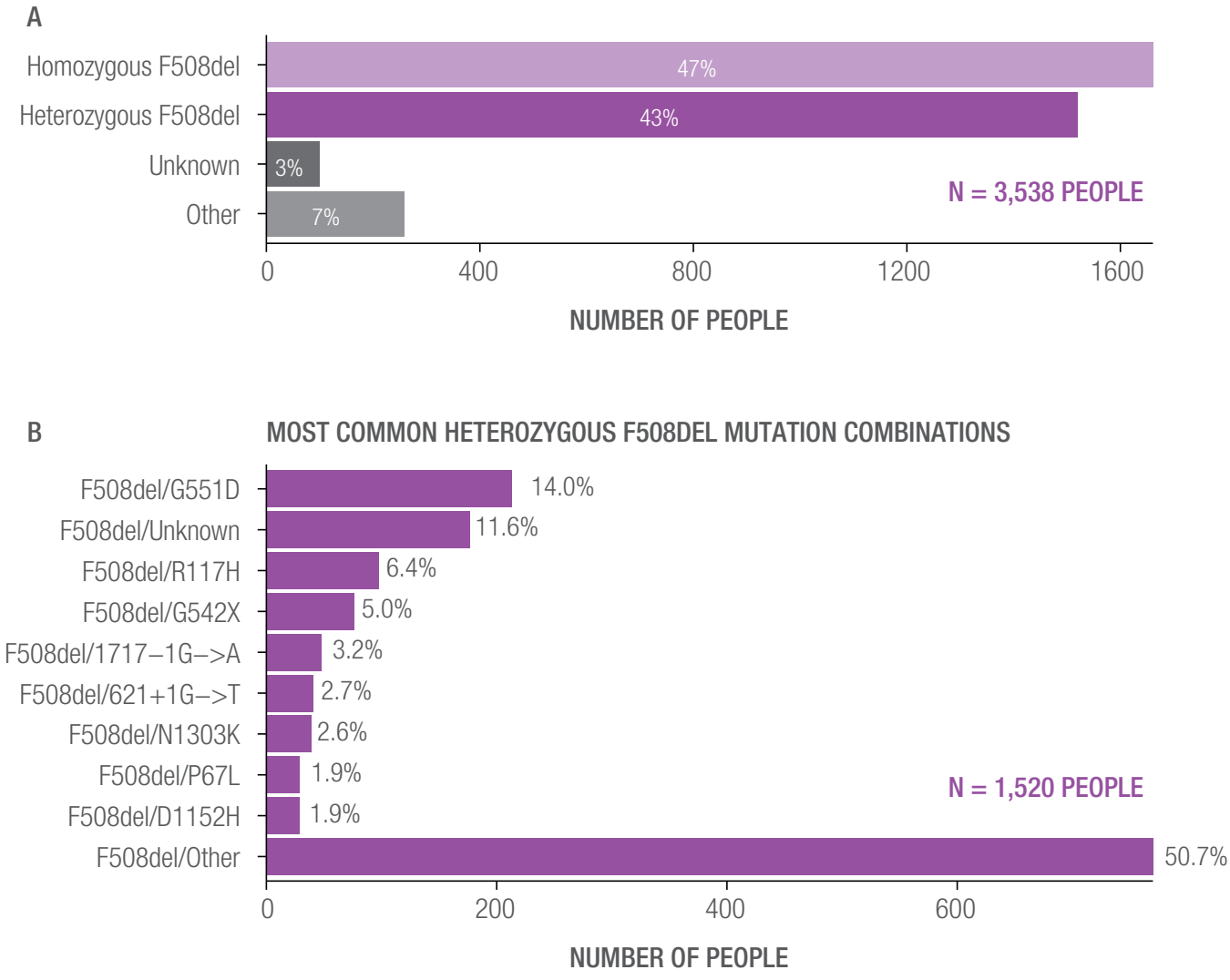
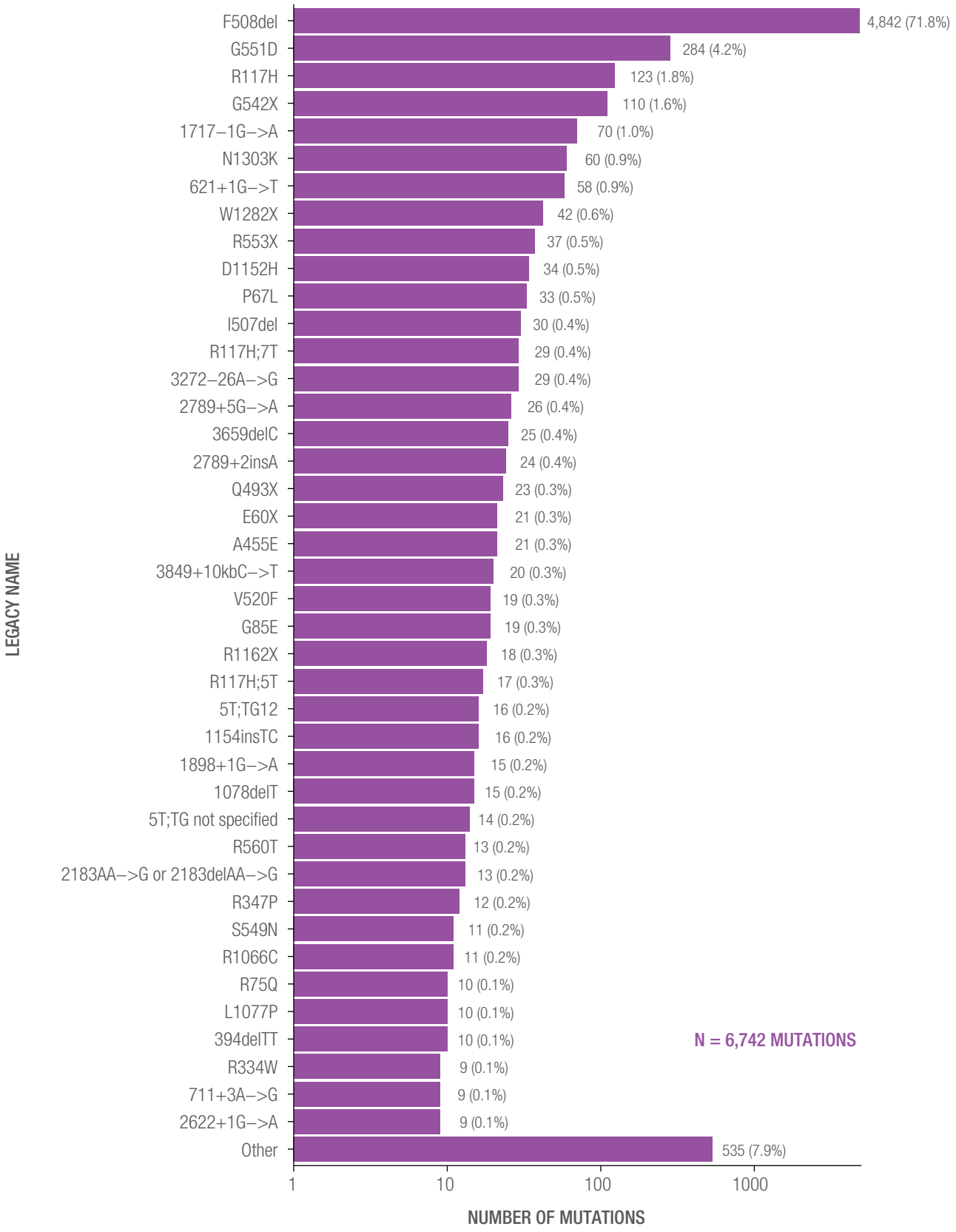


Figure 2.5 below shows that of the 6,742 individual allele variants captured in the ACFDR, that the most common are F508del (71.8%), followed by G551D (4.2%), R117H (1.8%), G542X (1.6%), and 1717_1G_>A (1.0%). The remaining variants comprise less than 1.0% each. The 40 or so most common individual allele variants and their proportion are shown below.

FIGURE 2.5: ACFDR 2020 MOST COMMON INDIVIDUAL ALLELE CFTR VARIANT IN THE ACFDR



The median FEV1 % predicted for the whole cohort in 2020 was 84.0%.

3. CLINICAL MEASURES

3.1 LUNG FUNCTION

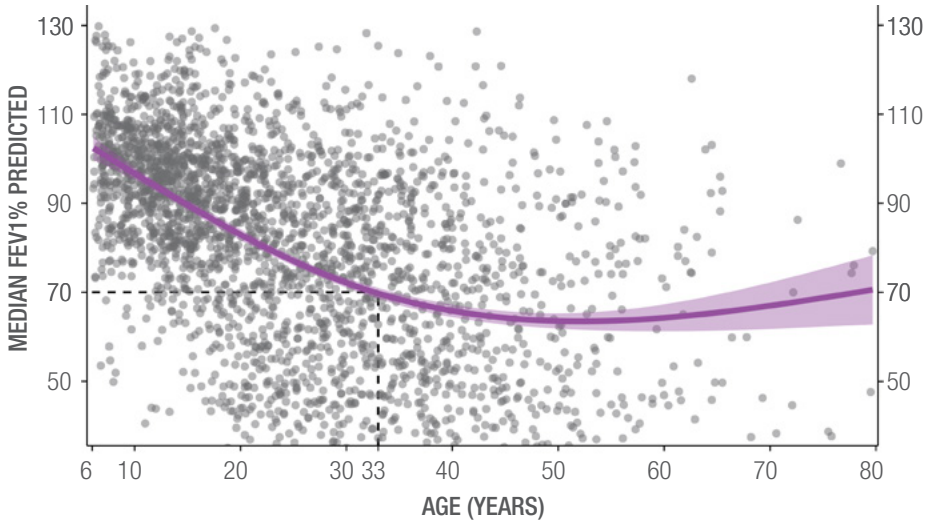
CHILDREN AND ADULTS

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.

Approximately 76.5% of people with CF in the ACFDR have lung function information (2,707 people) for 2020 (compared to 2,667 people in 2019). Over twelve percent 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 11.0% of registry participants did not have lung function information recorded in 2020, slightly lower than for previous years.

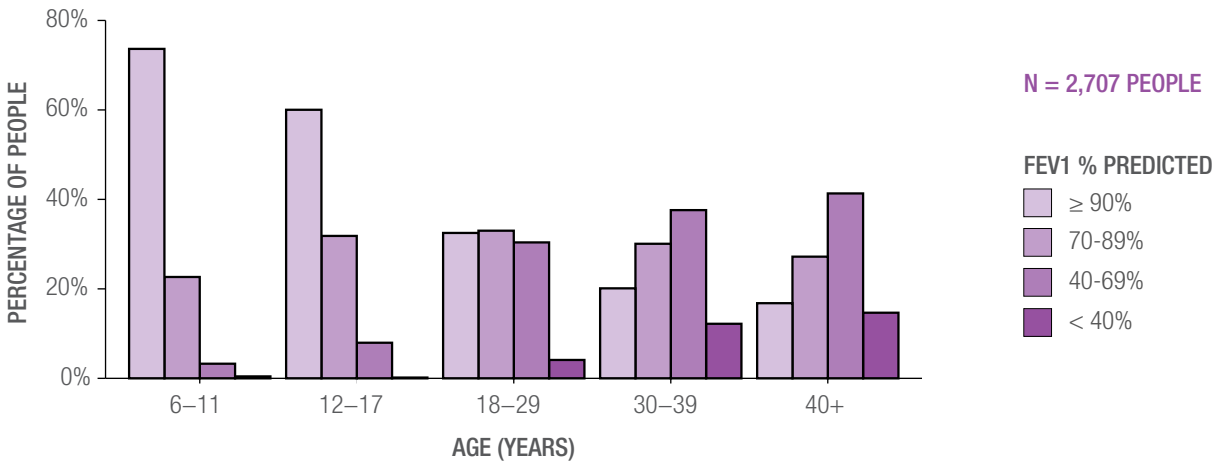
Average lung function for people with CF, measured as FEV1 % predicted is within the normal range for young children (Figure 3.1). At approximately 33 years of age, median FEV1 % predicted is lower than 70% of predicted, the level at which moderate lung function impairment is experienced.

FIGURE 3.1: ACFDR 2020: MEDIAN FEV1 % PREDICTED BY AGE



Lung function for people with CF varies by age and sex. A small proportion of children with CF, 3.7% of 6-11 year olds, and 8.2% of 12-17 year olds have a FEV1 % predicted at < 70.0%. In the 18-29 year age group, 34.5% have FEV1 % predicted at < 70.0%. These values increase with increasing range, for the 30-39 age group, the proportion is 49.8% and for the 40+ those with FEV1 % predicted < 70% are 56.0%% (Figure 3.2).

FIGURE 3.2: ACFDR 2020: LUNG FUNCTION BY AGE



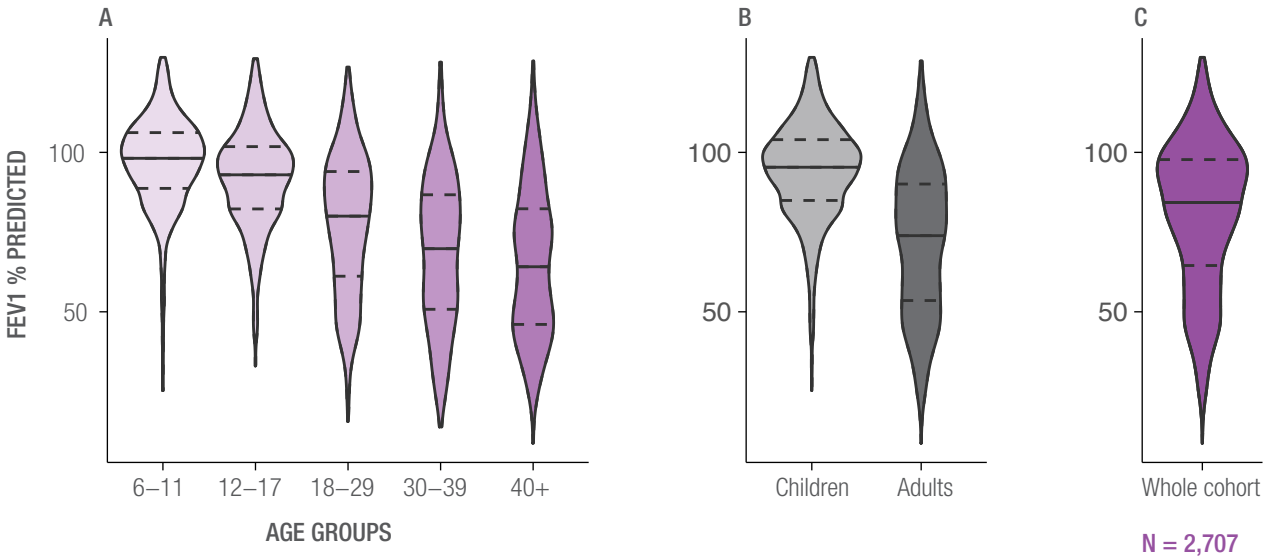
MEDIAN FEV1 % PREDICTED

Figure 3.3A shows the median FEV1 % predicted for persons with CF decreases with age. In the 6-11 year cohort, the median FEV1 % predicted is 99.0% and for children 12-17 years, 93.0%. The median FEV1 % predicted reduces to 80.0% for the 18-29 age group, 70.0% for the 30-40 year old, and 65.0% for those 40 years and older.

The median FEV1 % predicted for children aged 6-17 years is 96.0% and the median FEV1 % predicted for adults aged 18+ years is 74.0% (Figure 3.3B).

The median FEV1 % predicted for the whole cohort in 2020 was 84.0% (Figure 3.3C).

FIGURE 3.3: ACFDR 2020: MEDIAN FEV1 % PREDICTED BY AGE FOR TOTAL COHORT

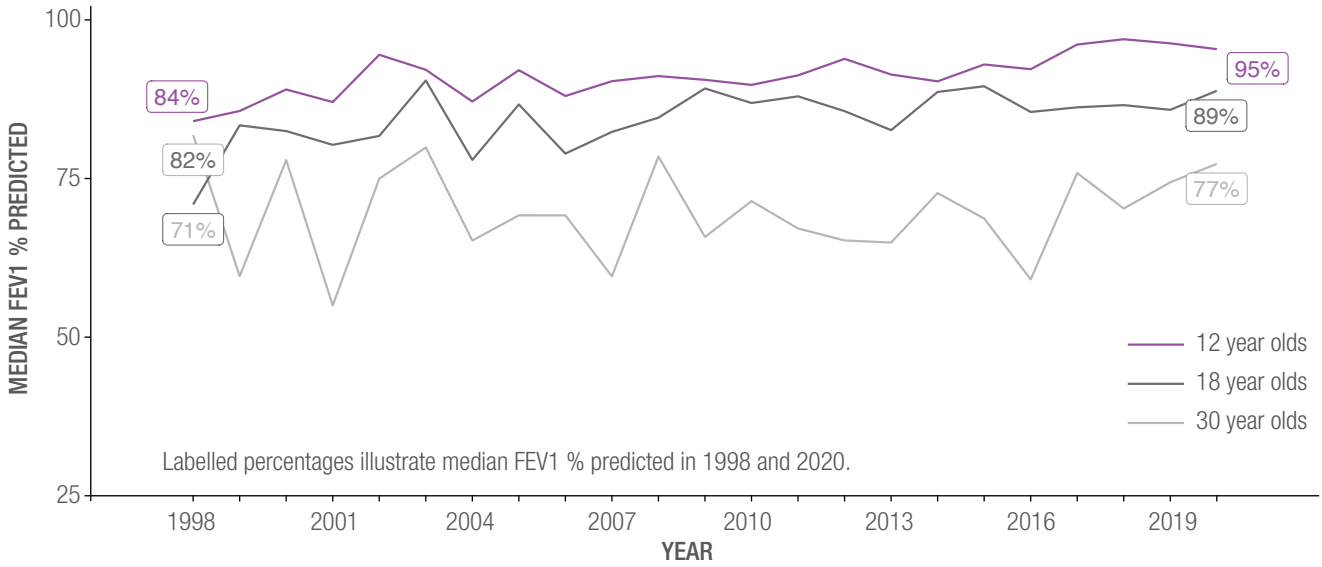


Horizontal dashed line represent 25th and 75th percentiles.

Horizontal solid line represents 50th percentile (median)

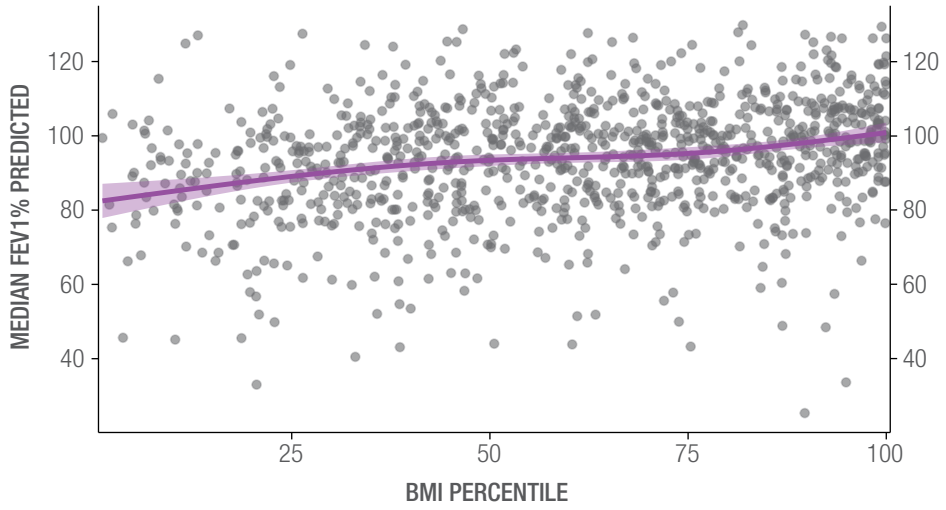
The median FEV1 % predicted has increased over time, particularly for the younger age cohorts. For 12 year olds, it has increased from 84.0% in 1998 to 95.0% in 2020, an increase of 11.0%. For 18 year olds the FEV1 % predicted has increased from 71.0% in 1998 to 89.0% in 2020. FEV1 % predicted for 30 year old cohorts have varied over time around the high 70s%, however it is noted that this age group has had improved survival despite less improvement in lung function (Figure 3.4).

FIGURE 3.4: ACFDR 1998-2020: MEDIAN FEV1 % PREDICTED OVER TIME



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

FIGURE 3.5: ACFDR 2020: FEV1 % PREDICTED VS BMI PERCENTILE FOR 6-17 YEARS



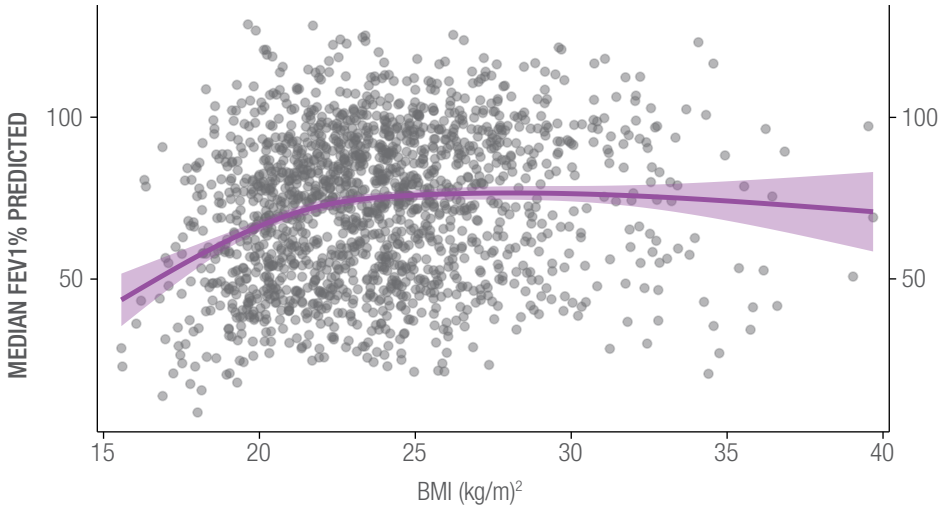
N = 1,036 PEOPLE AGED 6–17 YEARS

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 18-30 years, FEV1 % predicted increases, although, at BMIs into the high 20s, this appears to variably affect FEV1 % predicted. Persons 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 2020: MEDIAN FEV1 % PREDICTED VS BMI AGES ≥ 18 YEARS



N = 1,644 PEOPLE AGED ≥ 18 YEARS

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

Shaded area represent the 95% confidence intervals

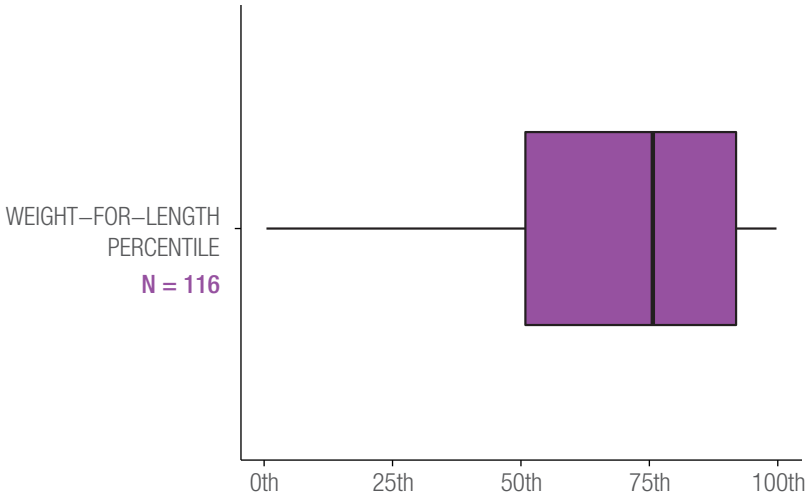
3.2 NUTRITION: WEIGHT, HEIGHT AND BODY MASS INDEX

INFANTS < 24 MONTHS

As of 2020, the nutritional outcomes for 116 children < 2 year old in the ACFDR show that the median weight for length percentile was 76th compared to 68th percentile in 2019 (Figure 3.7).

As of 2020, nutritional outcomes for 116 very young children (< 24 months) in the ACFDR show that the median length percentile was 68th, the median weight percentile was 55th, and the median weight for length percentile was 76th. Due to the relatively low numbers of infants < 24 months, the overall weight-for-length percentile has been noted to fluctuate each year.

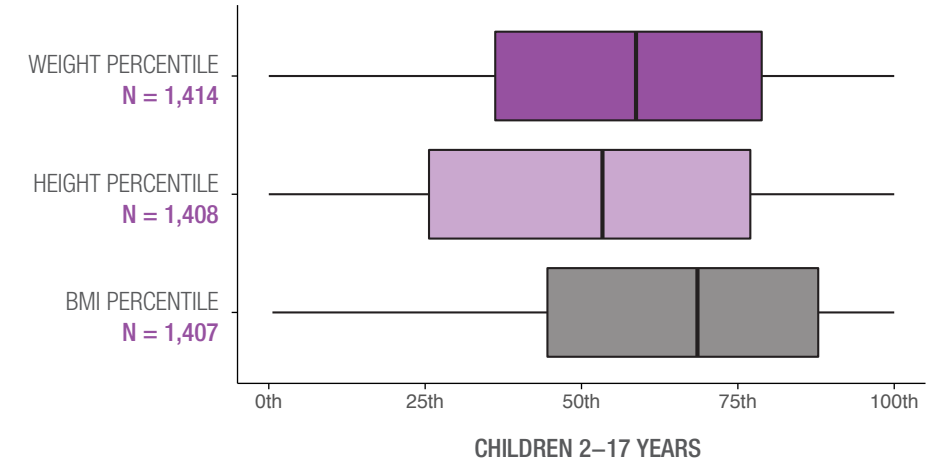
FIGURE 3.7: ACFDR 2020: NUTRITIONAL OUTCOMES FOR INFANTS < 24 MONTHS



CHILDREN 2-17 YEARS

For children aged 2-17 years, the median weight was 59th percentile (57th in 2019), median height was 53rd percentile (51st in 2019), and the median BMI was 69th percentile (68th in 2019). These figures represent best weight, best height, and best BMI, but do not relate to the same measurement collected on the same day (Figure 3.8).

FIGURE 3.8: ACFDR 2020: BMI, WEIGHT AND HEIGHT PERCENTILES AGES 2-17 YEARS



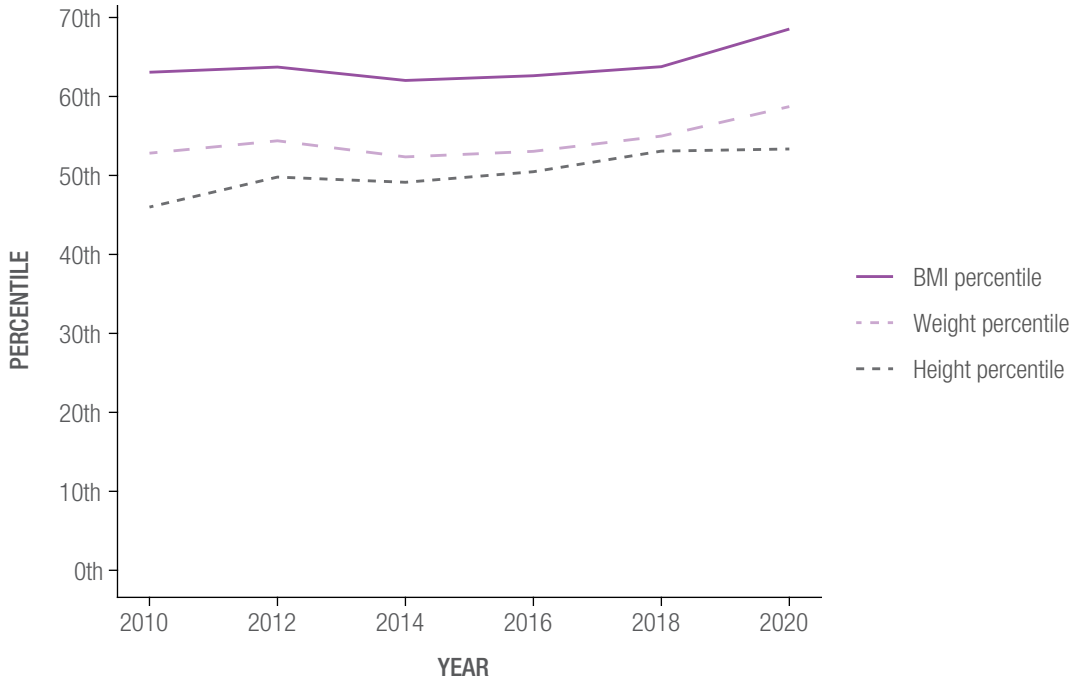
Height and BMI percentiles were calculated using WHO growth chart

Weight percentiles were calculated using CDC growth chart

Over the last 10 years, the median height and weight of children 2-17 years with CF have increased. It is noted that the number in this cohort is much greater than for children < 24 months, increasing the reliability of these findings.

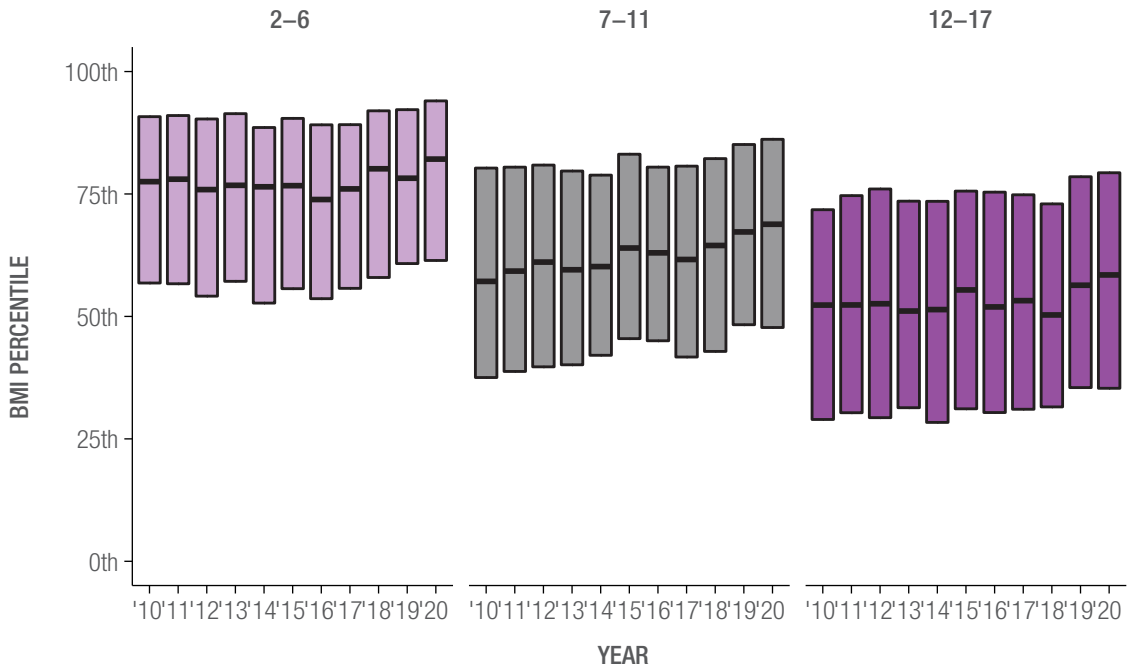
Children in this age group have increased in height by 7 percentile points (from 46th percentile to 53rd percentile), with a concomitant increase in weight of 6 percentile points (from 53rd percentile to 59th percentile). As a result, the average BMI has remained relatively stable at 62nd-69th over time (Figure 3.9).

FIGURE 3.9: ACFDR 2010-20120: MEDIAN NUTRITIONAL STATUS PERCENTILES 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 2010-2020: MEDIAN CHILD-ADOLESCENT BMI



Nutritional status for both male and female children with CF as of 2020 shows that the majority are in the optimal and acceptable BMI percentile ranges (Table 3.2).

TABLE 3.2 – ACFDR 2020: NUTRITIONAL STATUS FOR CHILDREN < 2 – 18 YEARS

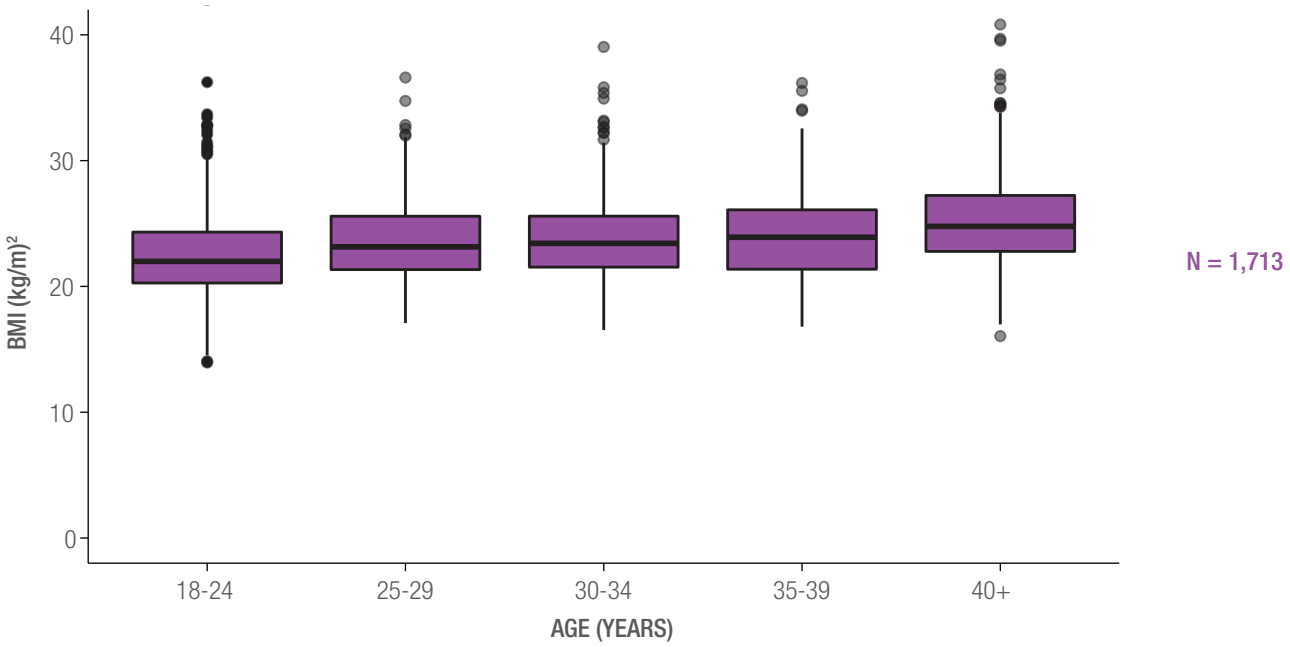
NUTRITIONAL STATUS*	< 2	2-5	6-11	12-17	TOTAL
High BMI percentile (obese / overweight range)	N/A (0)	48.2% (150)	28.2% (144)	20.1% (118)	27.1% (412)
Normal (optimal / acceptable)	93.8% (106)	47.9% (149)	64.7% (330)	65.8% (387)	47.7% (352)
Low (suboptimal / undernourished)	6.2% (7)	3.9% (12)	7.1% (36)	14.1% (83)	9.0% (138)

*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 increasing age. Adults from ages 18-24 years have a median BMI of 22.0; ages 25-29 have a median BMI of 23.1 years; ages 30-34 have a median BMI of 23.4; ages 35-39 have a median BMI of 23.9 and adults 40 years and older have a BMI of 24.8 (Figure 3.11).

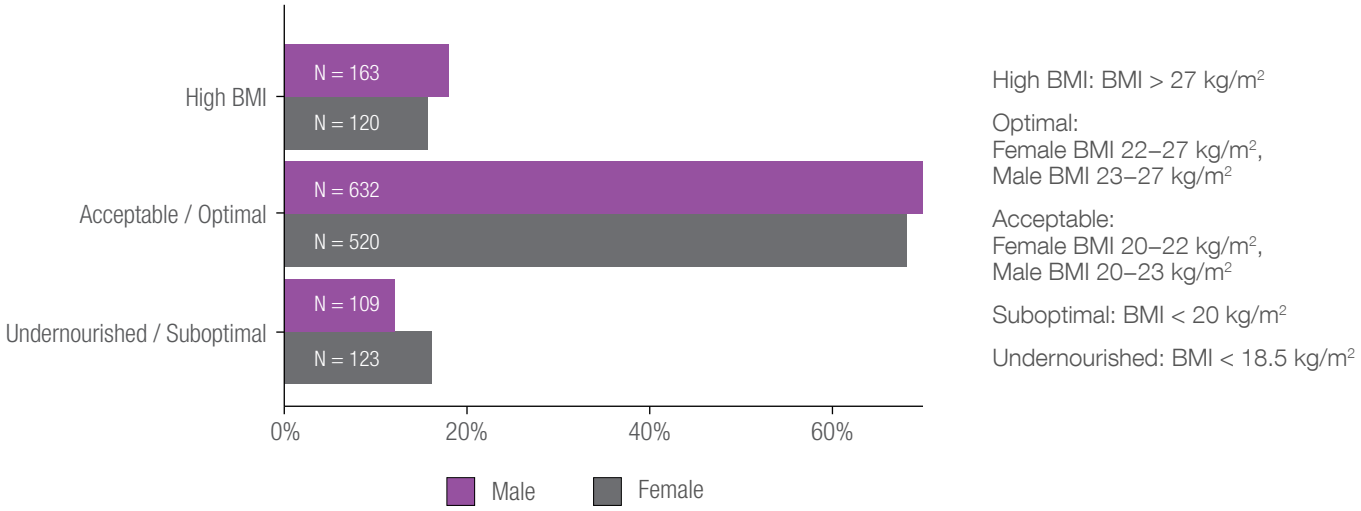
FIGURE 3.11: ACFDR 2020: BMI ADULTS 18+ YEARS



* Circles in the box plots represent outliers.

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).

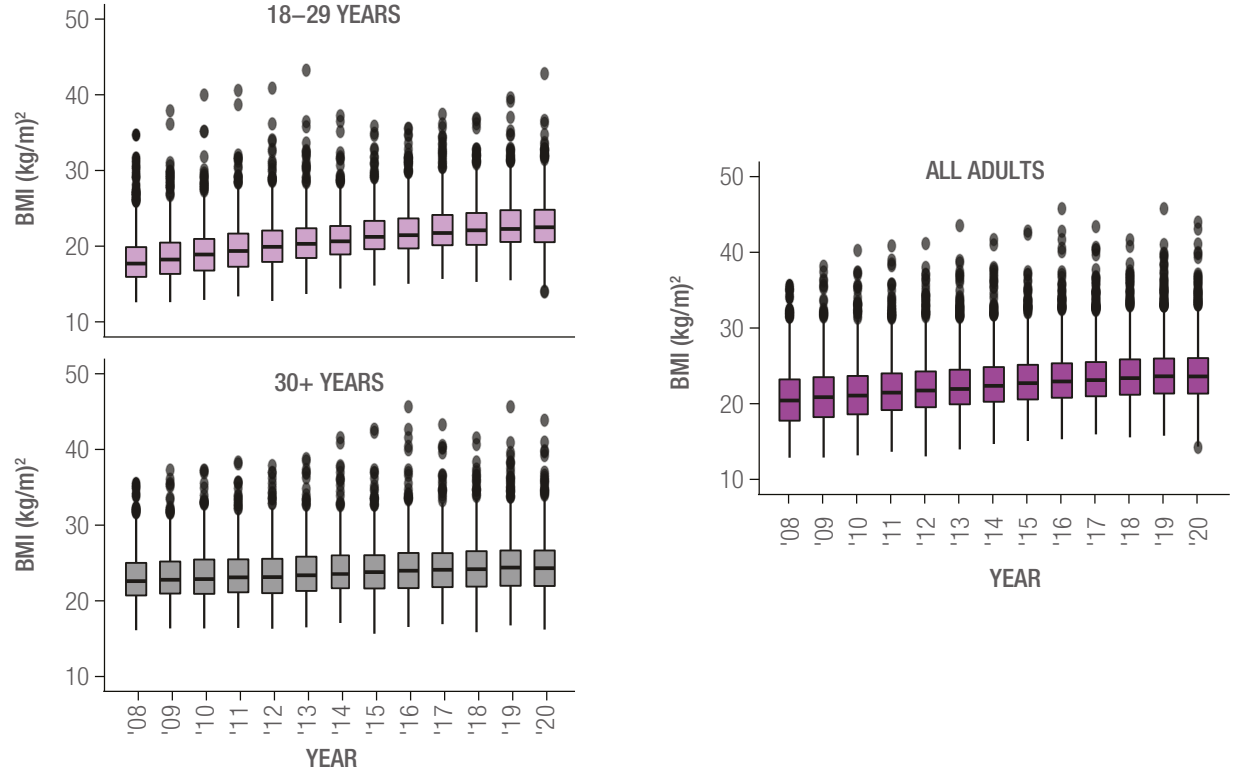
FIGURE 3.12: ACFDR 2020: BMI BY GENDER FOR ADULTS 18+ YEARS



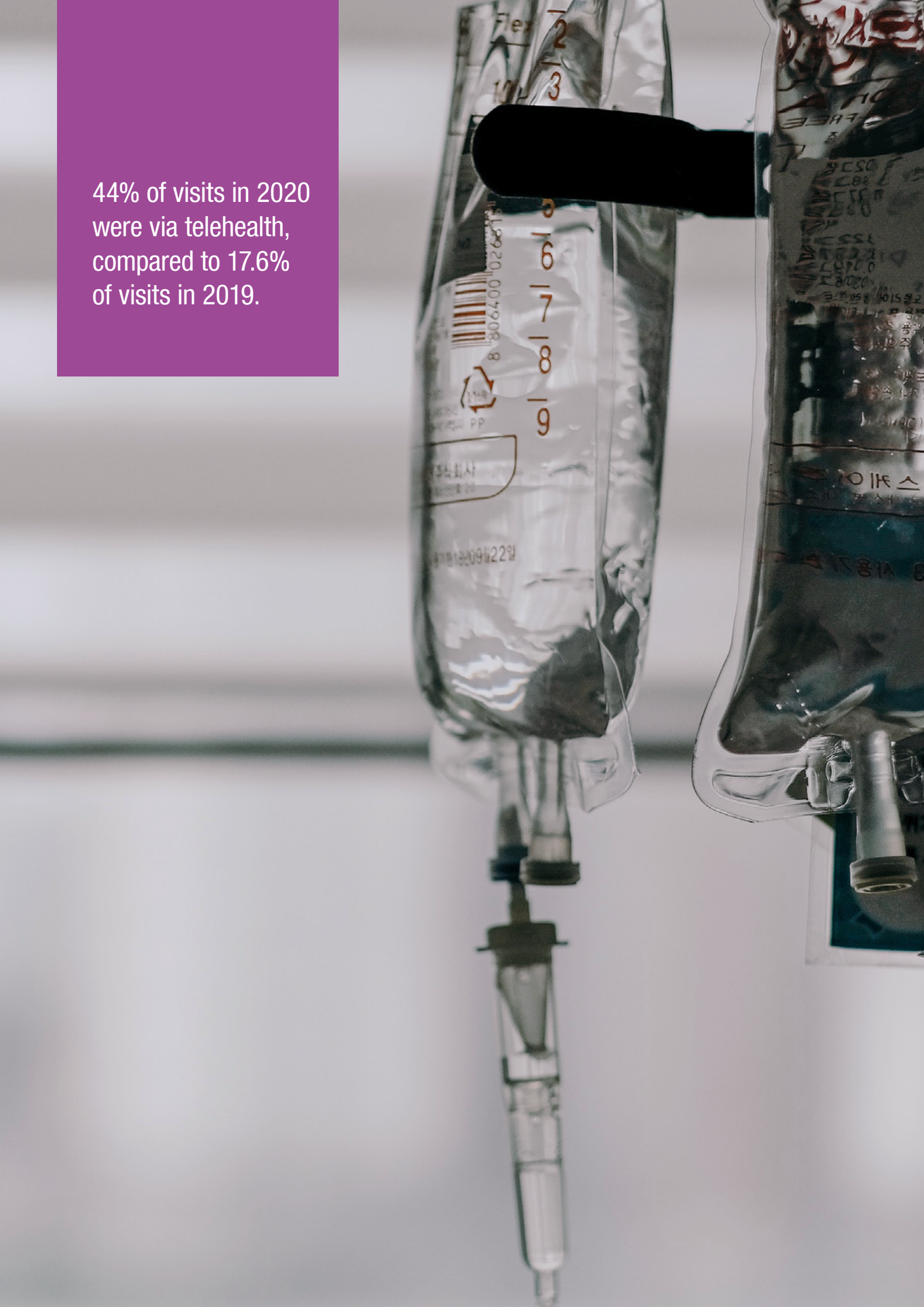
TRENDS OVER TIME

Over the last decade, the median adult BMI has been increasing. For adults 18-29 years, the median BMI (kg/m)^2 has increased from 17.7 to 22.5; for adults over 30 years, the median BMI has increased from 22.4 to 24.2 For all adults during 2008-2020 the median BMI has increased from 20.1 to 23.3 (Figure 3.13).

FIGURE 3.13: ACFDR 2008-2020: MEDIAN ADULT BMI



44% of visits in 2020 were via telehealth, compared to 17.6% of visits in 2019.



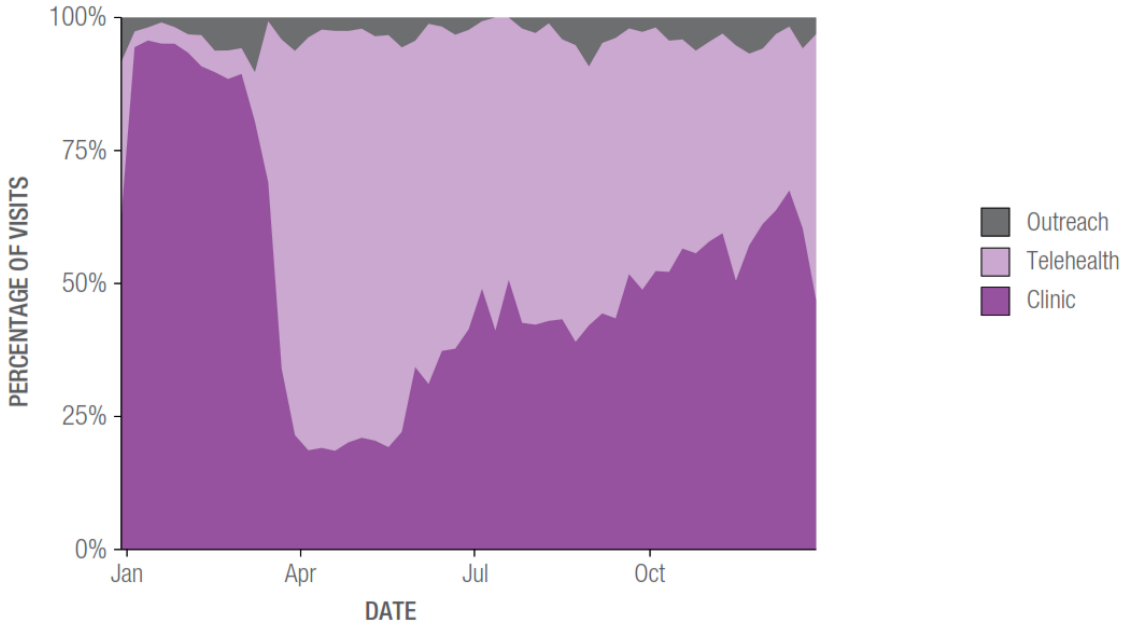
4. CF MANAGEMENT (ENCOUNTERS, CFTR MODULATORS AND MICROBIOLOGY)

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. However in March-April 2020, the COVID-19 pandemic led to a sudden shift across Australia away from face to face visits towards some form of remote clinical encounter (telehealth). The proportion of face to face visits gradually increased again from mid-2020, however never reached the levels previously seen at the beginning of the year. These changes in the way care was delivered in 2020 due to the global pandemic is shown in Figure 4.1.

FIGURE 4.1: ACFDR 2020: TYPES OF CLINICAL ENCOUNTERS



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

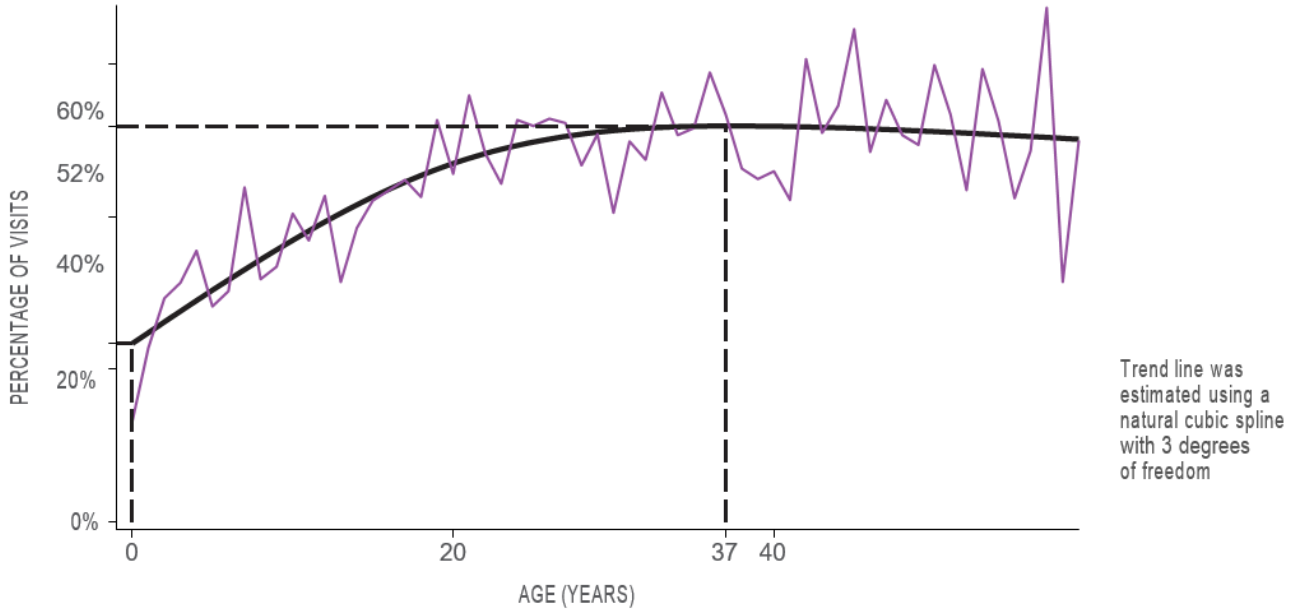
In 2020, 52.3% of all clinic visits were face to face, 44.1% of visits in 2020 were via telehealth, compared to 3.6% of outreach visits. The overall number of clinical encounters entered into the registry in 2020 was 16,743 (Table 4.1).

TABLE 4.1 – ACFDR 2020: OVERALL VISIT TYPE

VISIT TYPE	2020
Outreach	604 (3.6%)
Telehealth	7,389 (44.1%)
Clinic	8,750 (52.3%)
Total	16,743 (100.0%)

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 (23.4% of this age group). Older children and adults were more likely to utilise telehealth, with a peak of 51.9% of people with CF aged 37 years using telehealth in 2020.

FIGURE 4.2 – ACFDR 2020: PERCENTAGE OF TELEHEALTH BY AGE



In 2020, clinical visits from 3,389 people with CF were recorded. The proportion of all people with CF who had at least 4 clinic visits in 2020 was approximately 2,106 (62.0%) overall. This was highest among those 30+ and the 18-29 year old at 64.0%, and <2 years old at 64.0%. The proportion who had at least 4 clinic visits was lowest among people 7-11 years old at 49.1% (Figure 4.3 and Table 4.2).

The Australian CF Standards of Care recommend a minimum of 4 clinic (or equivalent) visits per year. The total number of clinical visits recorded in 2020 was 2,106 (Table 4.2).

FIGURE 4.3: ACFDR 2020: PROPORTION OF PEOPLE (BY AGE) HAVING 4 OR MORE CLINIC VISITS

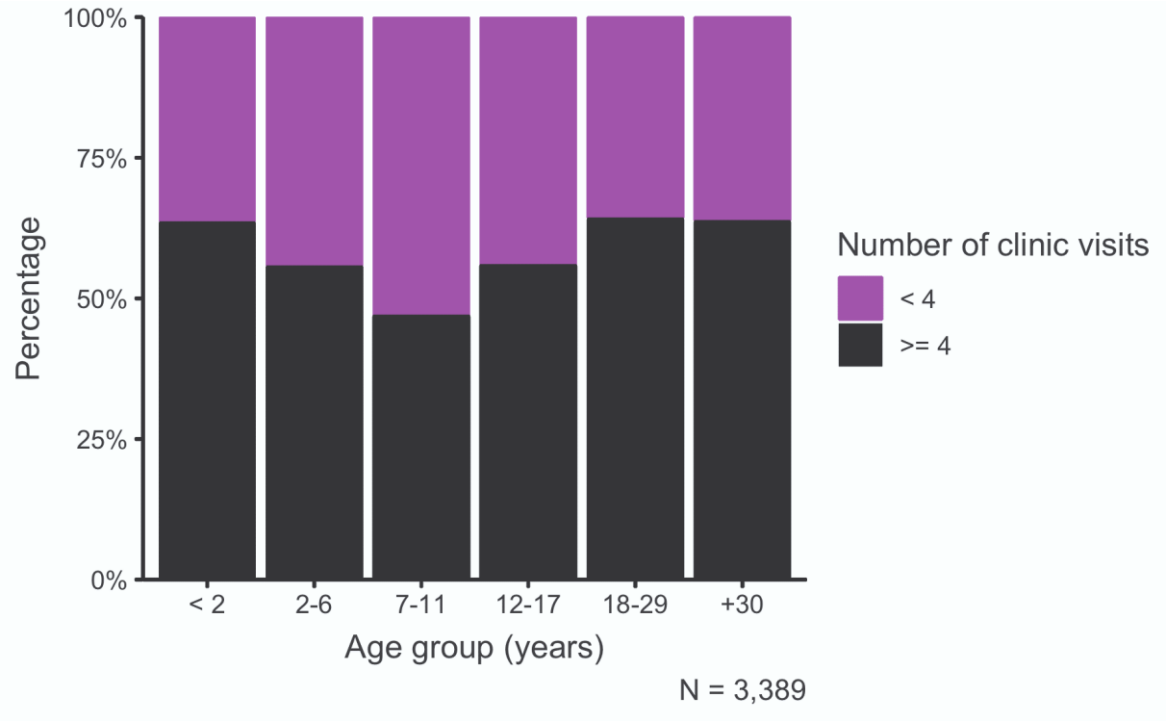


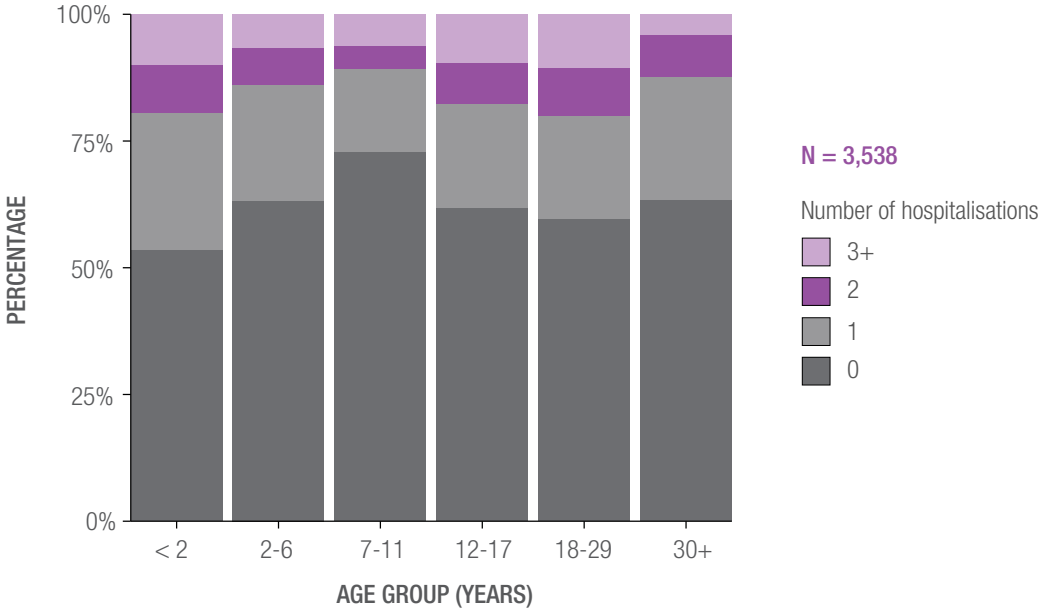
TABLE 4.2 – ACFDR 2020: AGE GROUPS WITH 4+ CLINICAL VISITS

	NUMBER WITH 4+ VISITS
AGE	2020
< 2	75 (64.0%)
2-6	224 (56.0%)
7-11	210 (46.9%)
12-17	338 (56.0%)
18-29	591 (64.0%)
30+	668 (64.0%)
Total	2,106 (60.0%)

HOSPITALISATIONS

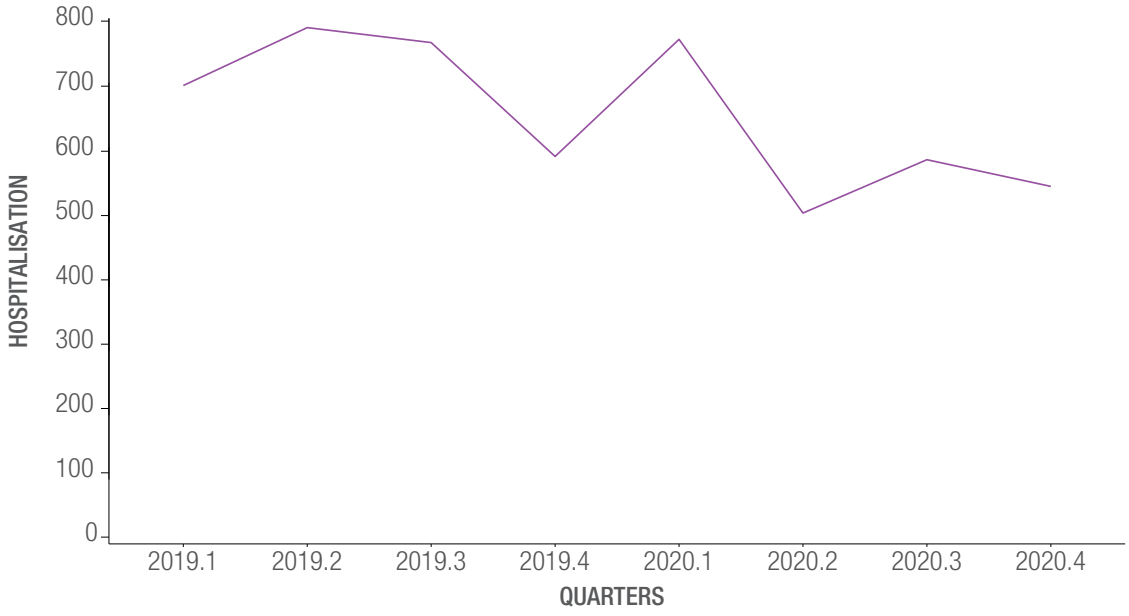
All people with CF had information regarding hospitalisations recorded in the ACFDR in 2020. The majority (approximately 63.0% overall) of people with CF did not have any hospitalisations , with the highest proportion having no hospitalisations being children 7-11 years (72.8%, Figure 4.4), and the lowest proportion having no hospitalisations being infants < 2 years at 53.4%.

FIGURE 4.4: ACFDR 2020: NUMBER OF HOSPITALISATIONS



COVID-19 also had an impact on the overall number of hospitalisations, similar to the number of clinical encounters, for 2020 compared with previous years. In 2019, hospital admissions peaked during quarter 2 and 3 (March – September), however in 2020 the number of hospital admissions fell dramatically from Q1 and remained much lower throughout the year (Figure 4.5). The total number of hospitalisations for 2020 was 2,410, which is approximately 85% of the total number of hospitalisations (2,850) in 2019. This suggests that the COVID-19 pandemic had a more significant effect in reduction in clinic/telehealth visit numbers than on the number of hospitalisations.

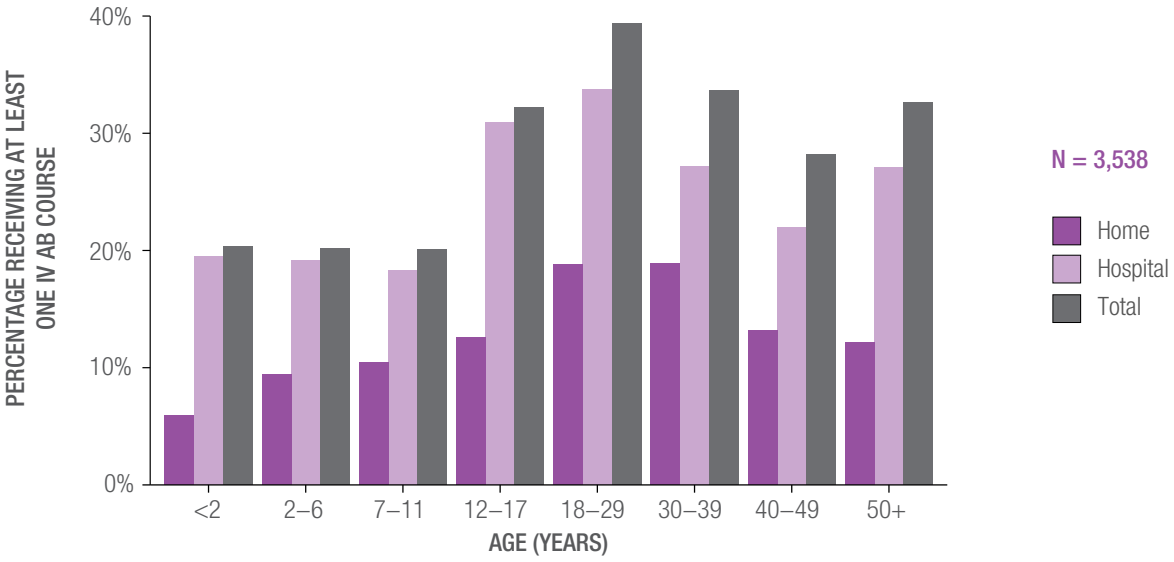
FIGURE 4.5 : ACFDR 2019–2020: NUMBER OF HOSPITALISATIONS PER QUARTER



IV ANTIBIOTIC THERAPY

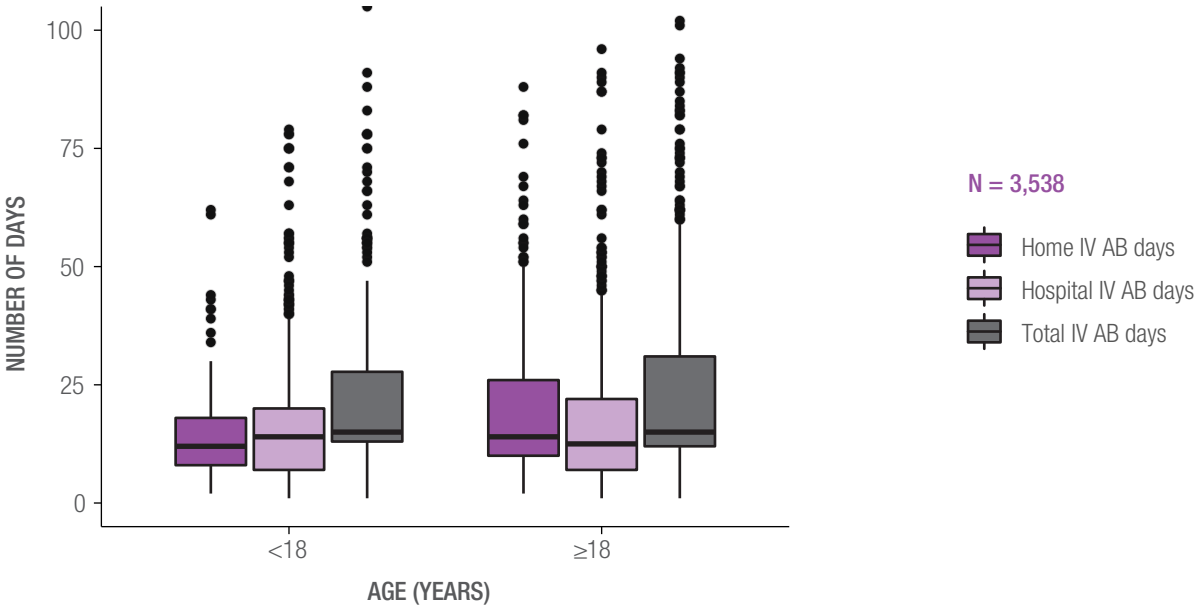
The most common reason for hospitalisations for people with CF is to have IV antibiotics for a respiratory infection. In 2020, a total of 23.0% of children and 34.0% of adults required intravenous (IV) antibiotic therapy. The proportion of those requiring IV antibiotic therapy in hospital increased from 19% for people less than 2 years of age, to 34.0% at 18-29 years of age, and 27.0% at over 50 years of age. Similarly, the proportion having home IV therapy is only 6% for people less than two years of age, peaking at 19% for adults of ages 30 – 49 years. The overall proportion of people with CF requiring home or hospital (total) IV antibiotic therapy is 20% for very young children (< 2 years) to well over 30.0% for adults of all ages (peaking at 34.0% for young adults 18-29 years) (Figure 4.6).

FIGURE 4.6: ACFDR 2020: PROPORTION OF PEOPLE (BY AGE GROUP) RECEIVING AT LEAST ONE COURSE OF IV ANTIBIOTIC THERAPY



The median number of accumulated days that people with CF spent receiving IV antibiotic therapy in hospital was 14 days for both children (< 18 years) and adults (18+ years). However, the median number of accumulated days receiving home IV therapy was higher for adults (14 days) compared with children (12 days). The median total accumulated (hospital and home) number of days people with CF who required IV antibiotic therapy in 2020 was 15 days for both children and adults in 2020, this was lower than in 2019 at 21 total days Figure 4.7.

FIGURE 4.7: ACFDR 2020: MEDIAN ACCUMULATED HOME AND HOSPITAL IV ANTIBIOTIC DAYS (CHILDREN VS ADULTS)



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 2020. 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 persons with CF who had CFTR modulator data entered into the registry, which is generally those on modulators available via the 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, estimated at approximately 8.0% 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 Ivacaftor was approved by the TGA for the variant R117H, it is not PBS listed for ivacaftor and is not included in the eligible population.

TABLE 4.3 – ACFDR 2020: IVACAFTOR USE AS OF DECEMBER 2020

AGE (YEARS)	ON KALYDECO ANYTIME	ON KALYDECO AS OF 31 DEC 2020	PREVIOUSLY ON KALYDECO AND DISCONTINUED AS OF 31 DEC 2020
1-5	19 / 22 (86.0%)	19 / 22 (86.0%)	0 / 22 (0.0%)
≥ 6	285 / 302 (94.0%)	261 / 302 (86.4%)	24 / 302 (7.9%)

The proportion of people with CF with gating variants eligible for ivacaftor who were taking ivacaftor as of December 31, 2020 was 86.0% for children less than and including 5 years, and 86.4% for those six years and older (Table 4.3). 24 people had previously used and discontinued Ivacaftor as of December 31, 2020. Reasons for discontinuation included intolerance/adverse event (1), liver impairment/intolerance (1), pregnancy (2), switching to another CFTR modulator (8) and other reason (12) (Table 4.4).

TABLE 4.4 – ACFDR 2020: REASONS FOR DISCONTINUATION OF IVACAFTOR AS OF DECEMBER 2020

NUMBER	REASON FOR CHANGE
12	Other reason[5]
8	Switch to other CFTR modulator
2	Pregnancy
1	Liver impairment/intolerance
1	Other intolerance/adverse event

5. Other reasons include; Moved to a clinical trial (n=4) , transplant (n=3), 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 on 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 4.5 – ACFDR 2020: LUMACAFTOR/IVACAFTOR USE AS OF DECEMBER 2020

AGE (YEARS)	ON ORKAMBI ANYTIME	ON ORKAMBI AS OF 31 DEC 2020	PREVIOUSLY ON ORKAMBI AND DISCONTINUED AS OF 31 DEC 2020
2-5	111 / 140 (79.0%)	102 / 140 (72.9%)	9 / 140 (6.4%)
≥ 6	1018 / 1,465 (69.0%)	629 / 1,465 (42.9%)	389 / 1,465 (26.6%)

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 2020 was 42.9%, and 72.9% of the eligible population 2-5 years of age were also taking lumacaftor/ivacaftor (Table 4.5). There have been 398 people who have discontinued this medication (Table 4.6). The most common reasons were a switch to another CFTR modulator (203), pulmonary intolerance/side effect (62), other (56), other intolerance/adverse event (50), liver impairment/intolerance (20), concomitant drug interaction (5) and pregnancy (2).

TABLE 4.6 – ACFDR 2020: REASONS FOR DISCONTINUATION OF LUMACAFTOR/IVACAFTOR AS OF DECEMBER 2020

NUMBER	REASON FOR CHANGE
203	Switch to other CFTR modulator
62	Pulmonary side effect/intolerance
56	Other reason[6]
50	Other intolerance/adverse event
20	Liver impairment/intolerance
5	Concomitant drug interaction
2	Pregnancy

6. Other reasons include; Moved to a clinical trial (n=16), family/personal choice (n=7), transplant (n=4) , insufficient supply (n=4), unwell (n=4), mental health reasons (n=3), feeding issues (n=3), fertility planning (n=2), felt no benefit (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. It is 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 4.7 – ACFDR 2020: TEZACAFTOR/IVACAFTOR USE AS OF DECEMBER 2020

AGE (YEARS)	ON SYMDEKO ANYTIME	ON SYMDEKO AS OF 31 DEC 2020	PREVIOUSLY ON SYMDEKO AND DISCONTINUED AS OF 31 DEC 2020
12-17	120 / 285 (42.0%)	112 / 285 (39.3%)	8 / 285 (2.8%)
≥ 18	532 / 1,014 (52.0%)	448 / 1,014 (44.2%)	84 / 1,014 (8.3%)

As of December 2020, 39.3% of the eligible population of 12-17 year olds were taking tezacaftor/ivacaftor, and 44.2% of eligible adults were taking it (Table 4.7). 92 people had discontinued the medication during 2020. Reasons included that they had switched to another CFTR modulator (45), other reasons (21), other intolerance/adverse event (14), pulmonary intolerance/side effect (6), liver impairment/intolerance (4), pregnancy (1), or concomitant drug interaction (1) (Table 4.8).

TABLE 4.8 – ACFDR 2020: REASONS FOR DISCONTINUATION OF TEZACAFTOR/IVACAFTOR AS OF DECEMBER 2020

NUMBER	REASON FOR CHANGE
45	Switch to other CFTR modulator
21	Other reason[7]
14	Other intolerance/adverse event
6	Pulmonary side effect/intolerance
4	Liver impairment/intolerance
1	Pregnancy
1	Concomitant drug interaction

7. Other reasons include; Fertility planning (n=4), transplant (n=3) , drug trial (n=3), no improvement to warrant expense (n=2), antibiotic treatment (n=1), mental illness (n=1), social issues (n=1) unwell (n=1), weight gain (n=1), unknown reason (n=4)

ELEXACAFTOR/TEZACAFTOR/IVACAFTOR (TRIKAFTA®)

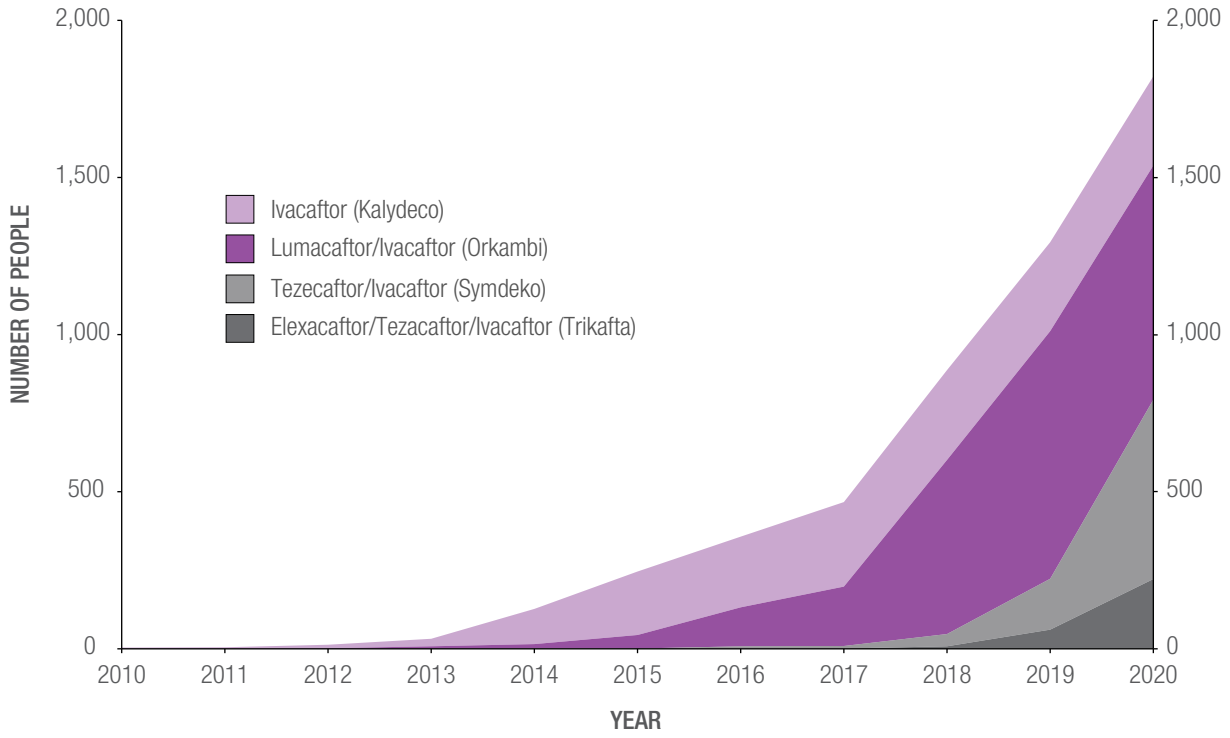
Elexacaftor/tezacaftor/ivacaftor is a CFTR modulator for people with CF who have at least one copy of the F508del variant or another variant that is approved. It currently does not have Therapeutic Goods Administration or PBS approval for use in Australia, although it is accessible via clinical trials and the special access scheme in certain circumstances for people over the age of 12 years. As of 31 December 2020, 224 people with CF in Australia are recorded as having received elexacaftor/tezacaftor/ivacaftor (Table 4.9).

TABLE 4.9 – ACFDR 2020: ELEXACAFTOR/TEZACAFTOR/IVACAFTOR USE AS OF DECEMBER 2020

AGE (YEARS)	ON TRIKAFTA AS OF 31 DEC 2020
≥12	224 / 2,203 (10.0%)

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/tezacafotr/ivacaftor. As of December 2020, 1,822 people with CF (or approximately 51.7% of the total population on the ACFDR) have been prescribed a CFTR modulator.

FIGURE 4.8: ACFDR 2010-2020: PEOPLE ON CFTR MODULATORS AS OF DECEMBER 31ST 2020



4.3 MICROBIOLOGY

From the 3,538 people with CF in 2020, 2,878 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 plateaued to 72-76% for adults aged 35-45+ years. The third most common organism in 2020 was Aspergillus *spp*. which was present in more than 10% of people with CF from 7 years, peaking at 31% for those aged 18-24 years (Figure 4.9 and Table 4.10).

FIGURE 4.9: ACFDR 2020: RESPIRATORY MICROBIOLOGY BY AGE

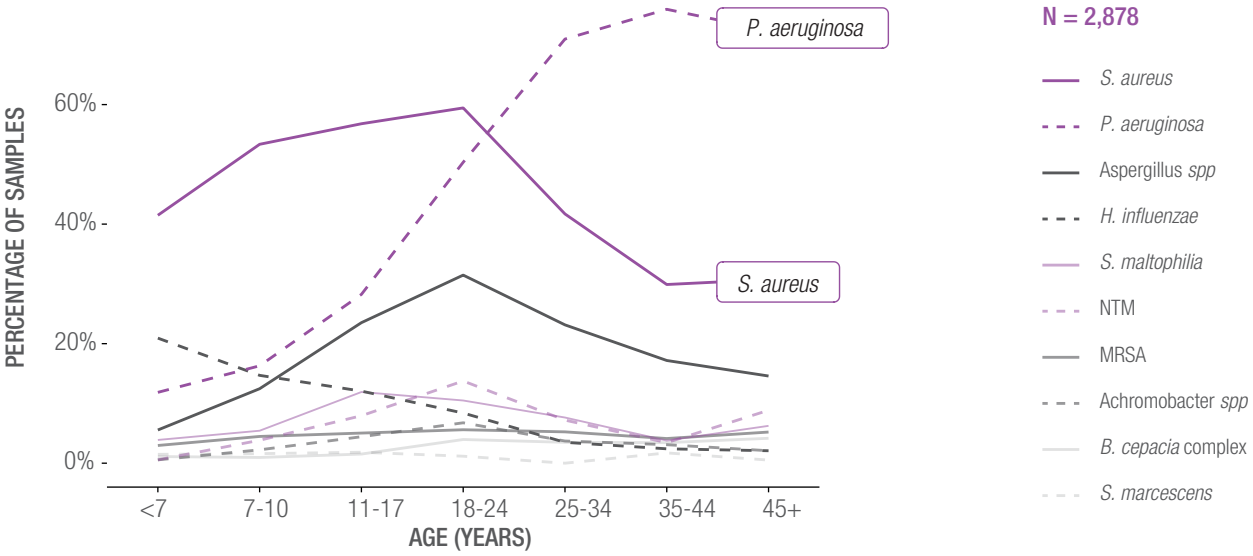


TABLE 4.10– ACFDR 2020: RESPIRATORY MICROORGANISMS BY AGE

BAL SAMPLES		ALL SAMPLES						
	< 7	< 7	7 - 10	11 - 17	18 - 24	25 - 34	35 - 44	45 +
No. in age range	520	520	354	699	580	665	431	289
No. of samples taken in 2020	121	540	313	655	429	458	291	192
P. aeruginosa	15 / 121 (12.0%)	64 / 540 (12.0%)	51 / 313 (16.0%)	185 / 655 (28.0%)	216 / 429 (50.0%)	325 / 458 (71.0%)	221 / 291 (76.0%)	139 / 192 (72.0%)
H. influenzae	24 / 121 (20.0%)	113 / 540 (21.0%)	46 / 313 (15.0%)	79 / 655 (12.0%)	36 / 429 (8.0%)	16 / 458 (3.0%)	7 / 291 (2.0%)	4 / 192 (2.0%)
***B. cepacia* complex**	0 / 121 (0.0%)	6 / 540 (1.0%)	3 / 313 (1.0%)	10 / 655 (2.0%)	17 / 429 (4.0%)	16 / 458 (3.0%)	10 / 291 (3.0%)	8 / 192 (4.0%)
S. aureus	27 / 121 (22.0%)	224 / 540 (41.0%)	167 / 313 (53.0%)	372 / 655 (57.0%)	255 / 429 (59.0%)	191 / 458 (42.0%)	87 / 291 (30.0%)	59 / 192 (31.0%)
MRSA	2 / 121 (2.0%)	16 / 540 (3.0%)	14 / 313 (4.0%)	33 / 655 (5.0%)	24 / 429 (6.0%)	24 / 458 (5.0%)	12 / 291 (4.0%)	10 / 192 (5.0%)
Achromobacter *spp*	1 / 121 (1.0%)	3 / 540 (1.0%)	7 / 313 (2.0%)	29 / 655 (4.0%)	29 / 429 (7.0%)	17 / 458 (4.0%)	9 / 291 (3.0%)	4 / 192 (2.0%)
S. maltophilia	5 / 121 (4.0%)	21 / 540 (4%.0)	17 / 313 (5.0%)	78 / 655 (12.0%)	45 / 429 (10.0%)	35 / 458 (8.0%)	11 / 291 (4.0%)	12 / 192 (6.0%)
S. marcescens	2 / 121 (2.0%)	8 / 540 (1.0%)	5 / 313 (2.0%)	12 / 655 (.02%)	5 / 429 (1.0%)	0 / 458 (0.0%)	5 / 291 (2.0%)	1 / 192 (1.0%)
Aspergillus *spp*	17 / 121 (14.0%)	30 / 540 (6.0%)	39 / 313 (12.0%)	154 / 655 (24.0%)	135 / 429 (31.0%)	106 / 458 (23.0%)	50 / 291 (17.0%)	28 / 192 (15.0%)
NTM	1 / 121 (1.0%)	3 / 540 (1.0%)	12 / 313 (4.0%)	52 / 655 (8.0%)	59 / 429 (14.0%)	33 / 458 (7.0%)	10 / 291 (3.0%)	17 / 192 (9.0%)

NOTE: The denominator is the number of samples in each age group.

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 2020 included *S. aureus* (22.0%), *H. influenzae* (20.0%), Aspergillus *spp* (14.0%), *P. aeruginosa* (12.0%), and MRSA (2.0%). (Table 4.10, Figure 4.10).

FIGURE 4.10: ACFDR 2020: RESPIRATORY MICROBIOLOGY BY AGE < 7 YEARS

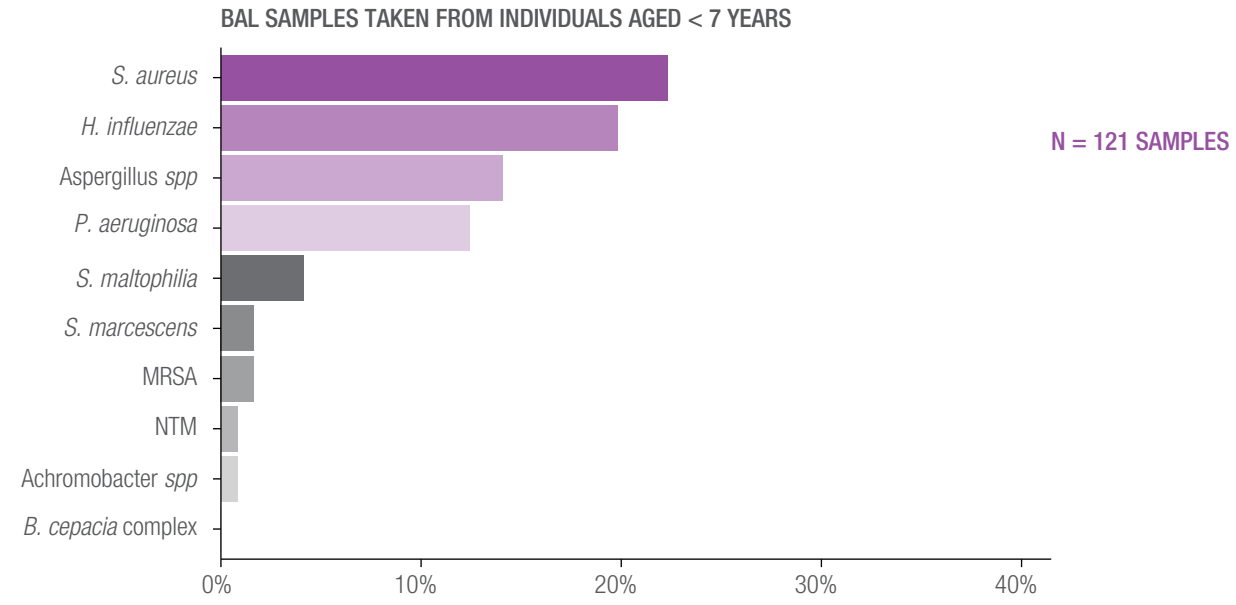
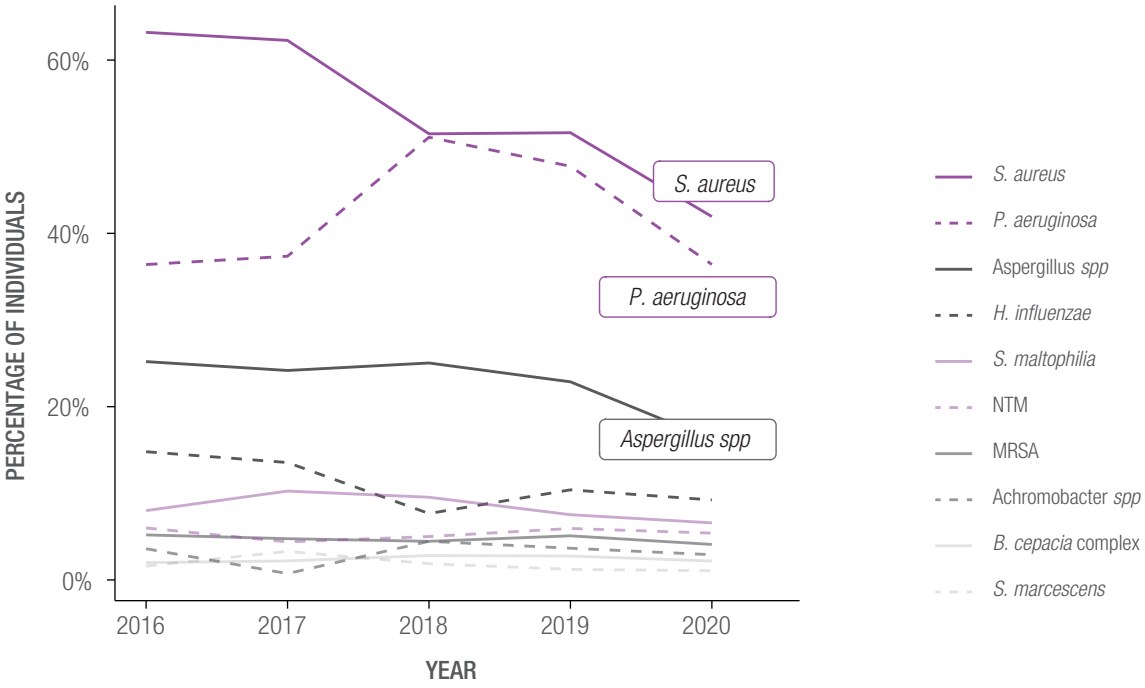


FIGURE 4.11: ACFDR 2016-2020: PREVALENCE OF RESPIRATORY MICROORGANISMS



The prevalence of some of the most common organisms has changed over the last 5 years (Figure 4.11). The prevalence of *S. aureus* was 63.0% for people with CF in 2016 and has decreased to 50.0% in 2020, and the prevalence of Aspergillus *spp* was 25% in 2016 and has decreased to 16.0% in 2020. The prevalence of *P. aeruginosa* has decreased from a high of 51.1% in 2018 to 36.0% 2020. The prevalence of less common microorganisms has remained fairly similar over this period (Table 4.11).

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 8.4% in 12-17 year olds, and 11.9% 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 5.2% in 2020 (Table 4.11). There has been a gradual increase in *M. abscessus* infections in all age groups over the last 5 years.

TABLE 4.11 – ACFDR 2020: NON-TUBERCULOUS MYCOBACTERIUM (NTM) INFECTION BY

AGE (YEARS)	ORGANISM	2016	2017	2018	2019	2020
< 7	NTM	0 / 25 (0.0%)	0 / 42 (0.0%)	0 / 120 (0.0%)	2 / 220 (0.9%)	3 / 465(0.6%)
	M. abscessus	0 / 25 (0.0%)	0 / 42 (0.0%)	0 / 120 (0.0%)	0 / 220 (0.0%)	0 / 465 (0.0%)
7 - 11	*NTM*	1 / 50 (2.0%)	0 / 54 (0.0%)	3 / 126 (2.4%)	5 / 196 (2.6%)	14 / 372 (3.8%)
	M. abscessus	0 / 50 (0.0%)	0 / 54 (0.0%)	3 / 126 (2.4%)	4 / 196 (2.0%)	9 / 372 (2.4%)
12 - 17	*NTM*	6 / 81 (7.4%)	7 / 83 (8.4%)	15 / 195 (7.7%)	30 / 292 (10.3%)	45 / 534 (8.4%)
	M. abscessus	1 / 81 (1.2%)	2 / 83 (2.4%)	9 / 195 (4.6%)	17 / 292 (5.8%)	26 / 534 (4.9%)
18 - 30	*NTM*	5 / 48(10.4%)	3 / 51 (5.9%)	26 / 380 (6.8%)	47 / 502 (9.4%)	77 / 648 (11.9%)
	M. abscessus	1 / 48 (2.1%)	3 / 51 (5.9%)	10 / 380 (2.6%)	19 / 502 (3.8%)	34 / 648 (5.2%)
30 +	*NTM*	3 / 37 (8.1%)	2 / 31 (6.5%)	18 / 377 (4.8%)	27 / 522 (5.2%)	39 / 701 (5.6%)
	M. abscessus	1 / 37 (2.7%)	2 / 31 (6.5%)	8 / 377 (2.1%)	11 / 522 (2.1%)	13 / 701 (1.9%)

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, liver disease and related supplements and supports.

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 2020, with incidence increasing with increasing age (Table 5.1).

TABLE 5.1 – ACFDR 2020: LUNG COMPLICATIONS

	< 12 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Haemoptysis	4 / 968 (0.4%)	17 / 566 (3.0%)	76 / 791 (9.6%)	80 / 886 (9.0%)	177 / 3,211 (5.5%)
Haemoptysis requiring embolization	0 / 968 (0.0%)	3 / 566 (0.5%)	9 / 791 (1.1%)	2 / 886 (0.2%)	14 / 3,211 (0.4%)
Pneumothorax	0 / 968 (0.0%)	2 / 567 (0.4%)	6 / 791 (0.8%)	7 / 886 (0.8%)	15 / 3,212 (0.5%)
Either of the above complications	4 / 968 (0.4%)	19 / 566 (3.4%)	80 / 791 (10.1%)	85 / 886 (9.6%)	188 / 3,211 (5.9%)

*An individual may have more than one complication

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 2020: CF PULMONARY DISEASE: ANTIBIOTIC THERAPIES

	< 6 YEARS	6-11 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Inhaled antibiotics	54 / 441 (12.2%)	95 / 527 (18.0%)	169 / 568 (29.8%)	295 / 795 (37.1%)	361 / 892 (40.5%)	974 / 3,223 (30.2%)
Regular oral antibiotics	190 / 441 (43.1%)	175 / 527 (33.2%)	177 / 568 (31.2%)	117 / 795 (14.7%)	124 / 892 (13.9%)	783 / 3,223 (24.3%)
Macrolides	14 / 441 (3.2%)	62 / 527 (11.8%)	104 / 568 (18.3%)	326 / 795 (41.0%)	521 / 892 (58.4%)	1,027 / 3,223 (31.9%)

Approximately one third of people with CF received macrolide and/or inhaled antibiotic therapy in 2020, 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 14.0% of adults (Table 5.2).

TABLE 5.3 - ACFDR 2020:CF PULMONARY DISEASE: OTHER LUNG THERAPIES

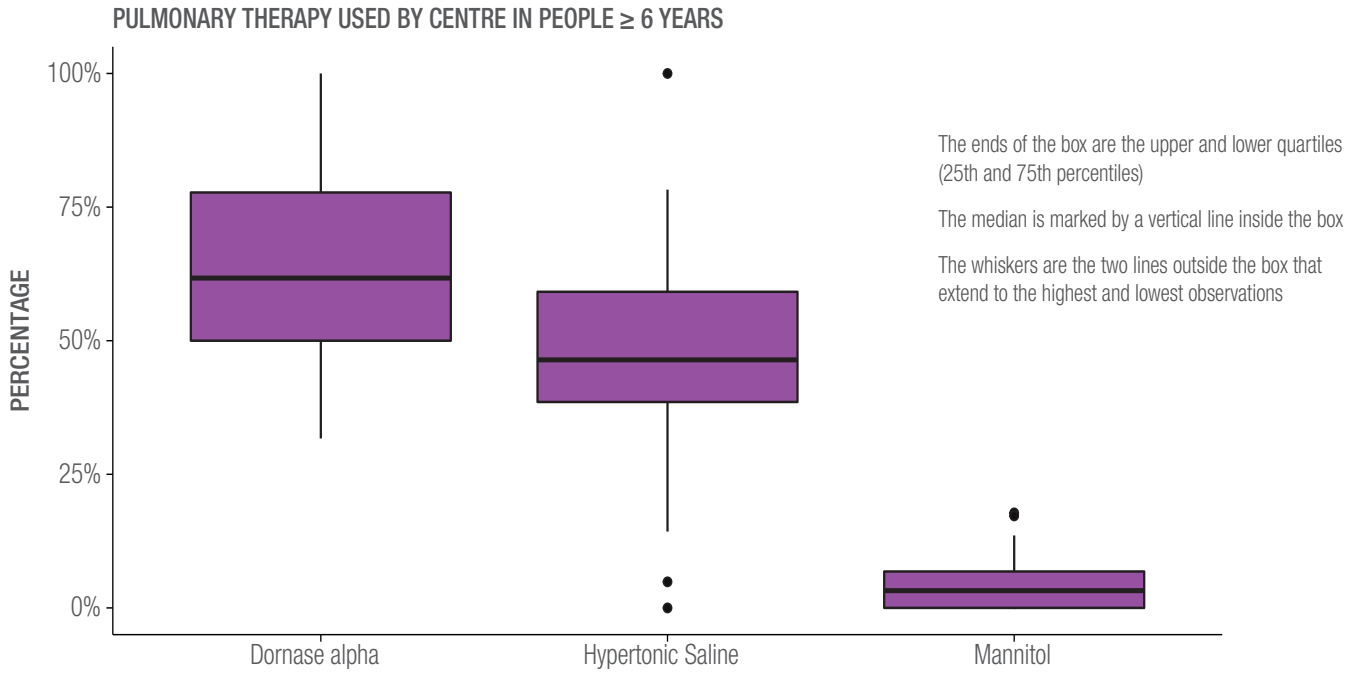
	< 6 YEARS	6-11 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Long oxygen therapy	0 / 441 (0.0%)	3 / 527 (0.6%)	4 / 568 (0.7%)	12 / 791 (1.5%)	20 / 886 (2.3%)	39 / 3,213 (1.2%)
Non-invasive ventilation	4 / 441 (0.9%)	4 / 527 (0.8%)	6 / 567 (1.1%)	15 / 790 (1.9%)	23 / 886 (2.6%)	52 / 3,211 (1.6%)
Oral corticosteroids	5 / 441 (1.1%)	18 / 527 (3.4%)	41 / 568 (7.2%)	37 / 795 (4.7%)	103 / 892 (11.5%)	204 / 3,223 (6.3%)
Inhaled corticosteroids	27 / 441 (6.1%)	96 / 527 (18.2%)	169 / 568 (29.8%)	364 / 795 (45.8%)	445 / 892 (49.9%)	1,101 / 3,223 (34.2%)
Mannitol	1 / 441 (0.2%)	18 / 527 (3.4%)	89 / 568 (15.7%)	64 / 795 (8.1%)	27 / 892 (3.0%)	199 / 3,223 (6.2%)
Dornase alpha	137 /441 (31.1%)	387 / 527 (73.4%)	439 / 568 (77.3%)	477 / 795 (60.0%)	440 / 892 (49.3%)	1,880 / 3,223 (58.3%)
Hypertonic saline	91 / 441 (20.6%)	24 / 527 (46.7%)	278 / 568 (48.9%)	428 / 795 (53.8%)	380 / 892 (42.6%)	1,423 / 3,223 (44.2%)
Bronchodilators	67 / 441 (15.2%)	230 / 527 (43.6%)	308 / 568 (54.2%)	525 / 795 (66.0%)	544 / 892 (61.0%)	1,674 / 3,223 (51.9%)

Non-invasive ventilation is used to support acute pulmonary exacerbations in 2.3% of all adults, whereas long term oxygen therapy is used to support 1.5% in 18-29 year olds, and 2.3% in 30 year olds (Table 5.3)

Many people with CF are prescribed non-antibiotic lung therapies including muco-active therapies such as mannitol, hypertonic saline and dornase alpha, bronchodilators and corticosteroids (Table 5.3). In 2020, the most commonly used of these were dornase alpha (58.3%), bronchodilators (51.9%), hypertonic saline (44.2%), and inhaled corticosteroids (34.2%). Less commonly used were oral corticosteroids (6.3%), and mannitol (6.2%). 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.

There is variation in the use of muco-active therapies at the centre level. Figure 5.1 shows the median use of Dornase alpha (61.7%), Hypertonic Saline (46.4%) and Mannitol (3.2%) by each CF centre in 2020.

FIGURE 5.1: ACFDR 2020: USE OF PULMONARY THERAPIES BY CENTRE AGES 6 YEARS AND OVER



5.3 CF ENDOCRINE DISEASE

Almost 1 in 5 people with information regarding diabetic status (552 people, 17.2%) had a diagnosis of CF related diabetes (CFDR) in 2020. The prevalence of diabetes increases with age, with 17.3% of 12-17-year old's having CFRD, increasing to 30.0% of people with CF over the age of 30 years (Table 5.4).

TABLE 5.4 - ACFDR 2020: DIABETIC STATUS BY AGE

	< 12 (N = 968)	12-17 (N = 568)	18-29 (N = 790)	30+ (N = 886)	TOTAL (N = 3,212)
Normal, (no diabetes or impaired glucose tolerance)	528 (54.5%)	272 (47.9%)	411 (52.0%)	409 (46.2%)	1620 (50.4%)
Impaired glucose tolerance	23 (2.4%)	85 (15.0%)	113 (14.3%)	118 (13.3%)	339 (10.6%)
Diabetes	18 (1.9%)	98 (17.3%)	170 (21.5%)	266 (30.0%)	552 (17.2%)
Not known	399 (41.2%)	113 (19.9%)	96 (12.2%)	93 (10.5%)	701 (21.8%)

Of the 552 people with CFRD, 500 persons had data recorded in the registry of their treatment, 84% were managed primarily with insulin; 11.6% were managed by diet/lifestyle strategies/no treatment, and 4.4% were treated with hypoglycaemics with or without insulin (Table 5.5).

TABLE 5.5 - ACFDR 2020: CF RELATED DIABETES (CFRD) TREATMENT BY AGE

	< 12 (N = 18)	12-17 (N = 98)	18-29 (N = 148)	30+ (N = 236)	TOTAL (N = 500)
Insulin	16 (88.9%)	89 (90.8%)	125 (84.5%)	190 (80.5%)	420 (84.0%)
Hypoglycaemics	0 (0.0%)	0 (0.0%)	3 (2.0%)	10 (4.2%)	13 (2.6%)
Insulin and hypoglycaemics	0 (0.0%)	1 (1.0%)	3 (2.0%)	5 (2.1%)	9 (1.8%)
Diet / lifestyle management / no treatment	2 (11.1%)	8 (8.2%)	17 (11.5%)	31(13.1%)	58 (11.6%)

The vast majority (94.4%) of people with CFRD on insulin required continuous insulin (Table 5.6).

TABLE 5.6 - ACFDR 2020: INSULIN USE FOR PEOPLE WITH CFRD BY AGE

INSULIN USE	< 12 (N = 16)	12-17 (N = 90)	18-29 (N = 128)	30+ (N = 195)	TOTAL (N = 429)
Intermittent insulin use	0 (0.0%)	5 (5.6%)	9 (7.0%)	1 (0.5%)	15 (3.5%)
Continuous insulin use	16 (100.0%)	78 (86.7%)	117 (91.4%)	194 (99.5%)	405 (94.4%)
Insulin use, duration unknown	0 (0.0%)	0 (0.0%)	6 (5.7%)	9 (6.4%)	15 (4.9%)

TABLE 5.7 - ACFDR 2020: RELATED REDUCED BONE DENSITY (OSTEOPENIA, OSTEOPOROSIS) BY AGE

BONE MINERAL DENSITY	10-17 (N = 216)	18-29 (N = 557)	30+ (N = 675)	TOTAL (N = 1,448)
Normal	140 (64.8%)	373 (67.0%)	345 (51.1%)	858 (59.3%)
Osteopenia	70 (32.4%)	158 (28.4%)	249 (36.9%)	477 (32.9%)
Osteoporosis	6 (2.8%)	26 (4.7%)	81 (12.0%)	113 (7.8%)

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 2020 (1,448 people), 32.9% had osteopenia, and 7.8% had osteoporosis, with 2.0% reporting a fracture in 2020 (Tables 5.7 and 5.8).

TABLE 5.8 - ACFDR 2020: RELATED REDUCED BONE DENSITY (FRACTURES) BY AGE

FRACTURE	10-17 (N = 743)	18-29 (N = 755)	30+ (N = 842)	TOTAL (N = 2,340)
Yes	23 (3.1%)	11 (1.5%)	13 (1.5%)	47 (2.0%)
No	720 (96.9%)	744 (98.5%)	829 (98.5%)	2,293 (98.0%)

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 5.9 24.7% of people with CF with complications reported in the ACFDR had gastro-oesophageal reflux, and 17.7% had abnormal liver function. Small proportions of patients had liver disease or pancreatitis. The proportion of people with CF who are pancreatic insufficient varies from 74% to 83% depending on age (Tables 5.9 and 5.10).

TABLE 5.9 - ACFDR 2020: GASTROINTESTINAL COMPLICATIONS ASSOCIATED WITH LIVER DISEASE BY AGE

GI COMPLICATION	< 12	12-17	18-29	30+	TOTAL
Gastric oesophageal reflux	77 / 968 (8.0%)	86 / 568 (15.1%)	247 / 792 (31.2%)	385 / 886 (43.5%)	795 / 3,214 (24.7%)
Abnormal liver function (elevated enzymes)	166 / 968 (17.1%)	111 / 568 (19.5%)	130 / 790 (16.5%)	160 / 886 (18.1%)	567 / 3,212 (17.7%)
Liver disease, non-cirrhosis (includes viral hepatitis, fatty liver)	14 / 808 (1.7%)	23 / 464 (5.0%)	41 / 671 (6.1%)	32 / 742 (4.3%)	110 / 2,685 (4.1%)
Liver disease, cirrhosis (image confirmed)	11 / 806 (1.4%)	17 / 460 (3.7%)	19 / 667 (2.8%)	23 / 736 (3.1%)	70 / 2,669 (2.6%)
Liver disease, cirrhosis with portal hypertension	6 / 804 (0.7%)	10 / 458 (2.2%)	20 / 665 (3.0%)	17 / 735 (2.3%)	53 / 2,662 (2.0%)

TABLE 5.10 - ACFDR 2020: 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)	2 (0.2%)	0 (0.0%)	5 (0.7%)	1 (0.1%)	8 (0.3%)
Pancreatitis, not specified	1 (0.1%)	2 (0.4%)	6 (0.8%)	22 (2.7%)	31 (1.0%)
Recurrent pancreatitis (history of more than one event of pancreatitis)	1 (0.1%)	5 (0.9%)	16 (2.2%)	39 (4.8%)	61 (2.0%)
No history of pancreatitis	939 (99.6%)	546 (98.7%)	716 (96.4%)	758 (92.4%)	2,959 (96.7%)
PANCREATIC STATUS					
Insufficient	746 (77.1%)	472 (83.1%)	660 (83.0%)	660 (74.0%)	2,538 (78.7%)

5.5 NUTRITIONAL SUPPLEMENTS

For 2020, the reported use of pancreatic enzymes and nutritional supplements is shown in Table 5.11. A high proportion (approximately 75.0%) of people with CF take fat soluble vitamin supplements, with approximately half the people with CF taking salt tablets. Supplement use are reported across all age groups.

TABLE 5.11 - ACFDR 2020: PEOPLE WHO RECEIVED NUTRITIONAL SUPPLEMENTS BY AGE

SUPPLEMENT USE	< 12 (N = 968)	12-17 (N = 568)	18-29 (N = 795)	30+ (N = 892)	TOTAL (N = 3,223)
Pancreatic enzymes	728 (75.2%)	470 (82.7%)	644 (81.0%)	666 (74.7%)	2,508 (77.8%)
Vitamin supplements (fat soluble vitamins A, D, E and K)	761 (78.6%)	454 (79.9%)	584 (73.5%)	604 (67.7%)	2,403 (74.6%)
Salt tablets	602 (62.2%)	360 (63.4%)	365 (45.9%)	281 (31.5%)	1,608 (49.9%)

TABLE 5.12 - ACFDR 2020: NUTRITIONAL SUPPORT

	< 12 (N = 968)	12-17 (N = 568)	18-29 (N = 795)	30+ (N = 892)	TOTAL (N = 3,223)
Oral	82 (8.5%)	52 (9.2%)	92 (11.6%)	63 (7.1%)	289 (9.0%)
Gastrostomy tube	51 (5.3%)	59 (10.4%)	37 (4.7%)	9 (1.0%)	156 (4.8%)
Nasogastric tube	15 (1.5%)	5 (0.9%)	3 (0.4%)	6 (0.7%)	29 (0.9%)
Jejunostomy tube	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)	2 (0.1%)
Parenteral nutrition	4 (0.4%)	2 (0.4%)	0 (0.0%)	0 (0.0%)	6 (0.2%)

The proportion of people with CF with information recorded in the ACFDR who required nutritional support was small. While 9.0% required oral supplemental nutrition, very few required enteral feeding, and of those the majority were via gastrostomy tube (Table 5.12).

In 2020, there were 15 bilateral lung transplants for people with CF.

6. TRANSPLANTATION AND SURVIVAL

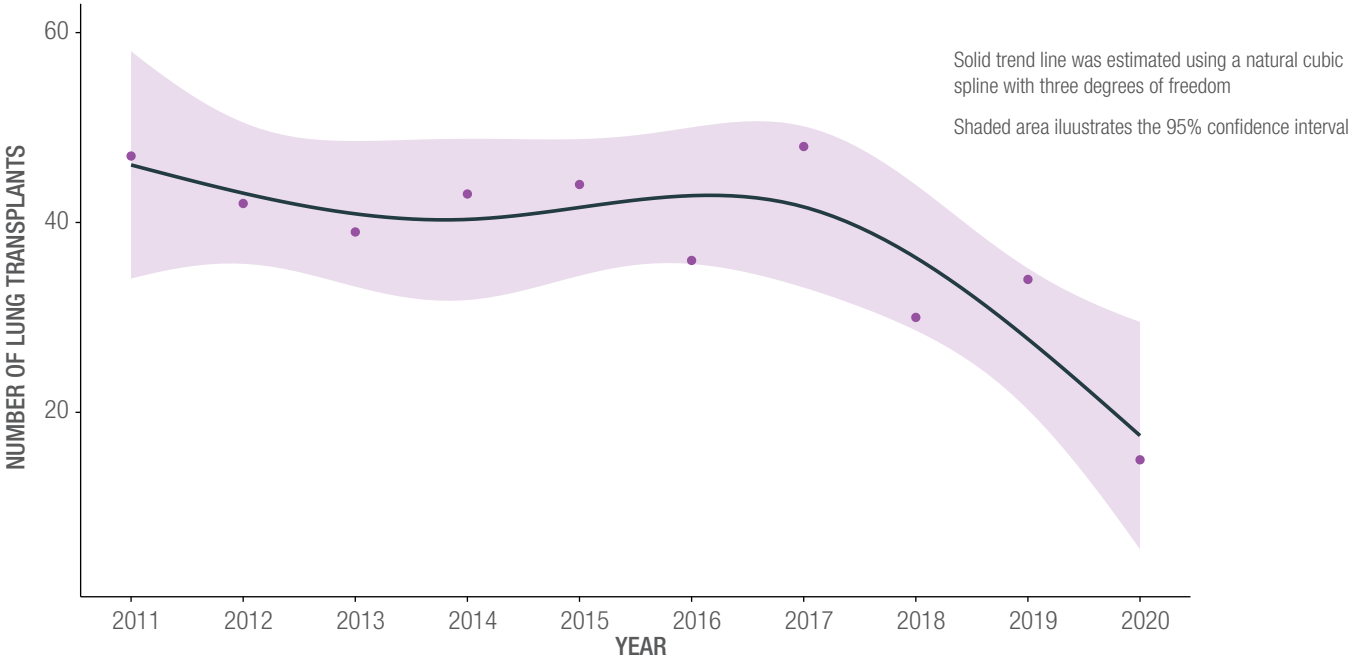
6.1 TRANSPLANTATION

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 (such as diabetes) and require transplantation, including the kidney or liver. Occasionally multi-organ transplants are required.

In 2020, there were 15 bilateral lung transplants for people with CF. Forty-seven percent of these were for males and fifty-three percent were for females. 60.0% of bilateral lung transplants were undertaken on people with CF of ages 30 years and older; with under one third of transplants occurring for people of ages 18-29 years.

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 potentially due to increasing use of CFTR modulators, and it is possible that COVID-19 may have also impacted this in 2020.

FIGURE 6.1: ACFDR 2010-2020: 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 persons 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.

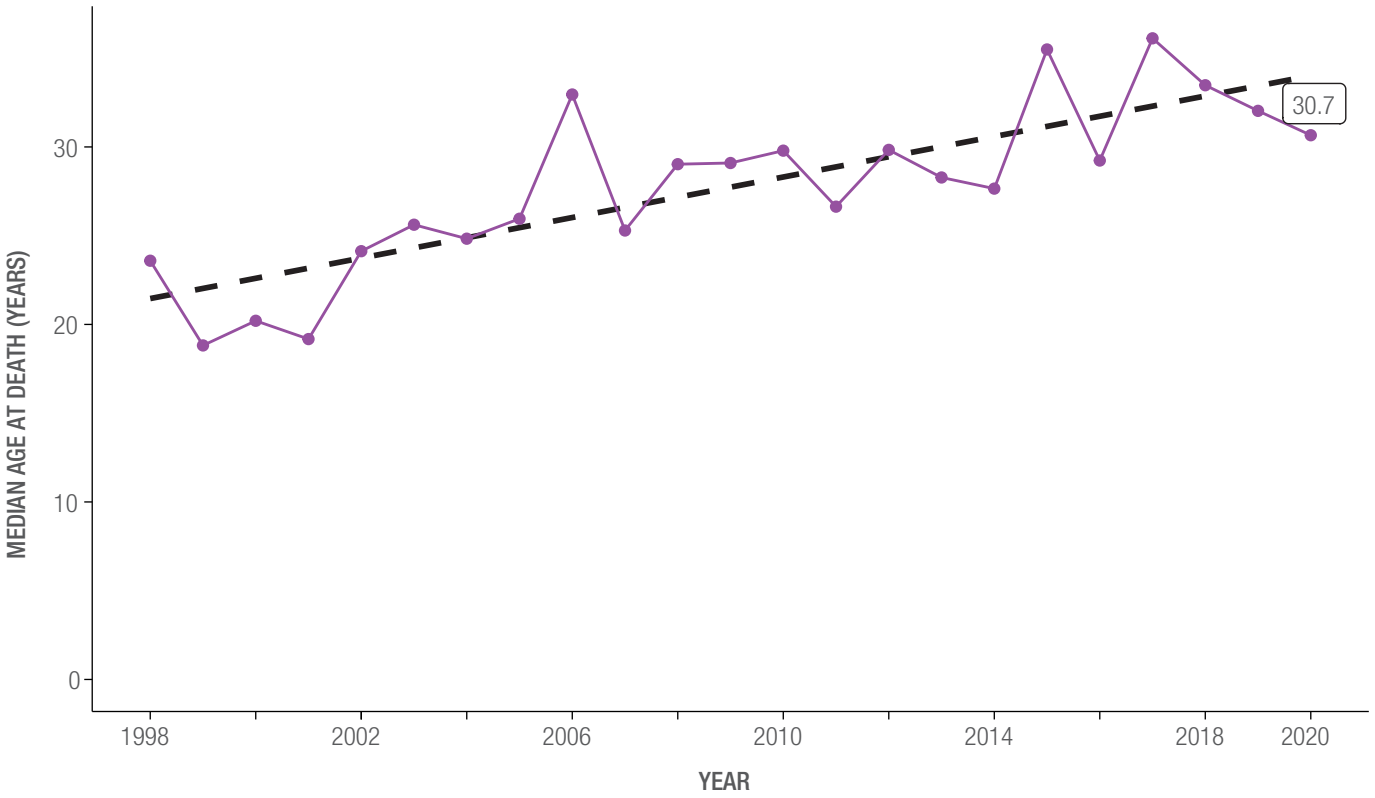
In 2020 the ACFDR recorded the deaths of 18 people with CF. Nine (50.0%) of these deaths occurred in people aged 30 years and over, seven deaths (38.0%) occurred in young adults (18-29 years), and two deaths occurred in a person less than 18 years. Six (33.3%) of those deaths were people with CF who had received a transplant.

Of the 18 deaths in 2020, 4 had an unknown cause; 4 were unrelated to CF; and 10 were related to CF including from pulmonary manifestations of CF (most common), post-transplant complications, intestinal manifestations, or other causes related to CF.

6.3 MEDIAN AGE OF DEATH

The median age of death in 2020 was 30.7 years. This is an increase from a median age of death of around 20 years of age approximately 20 years ago. Median age of death 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 1998-2020: 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

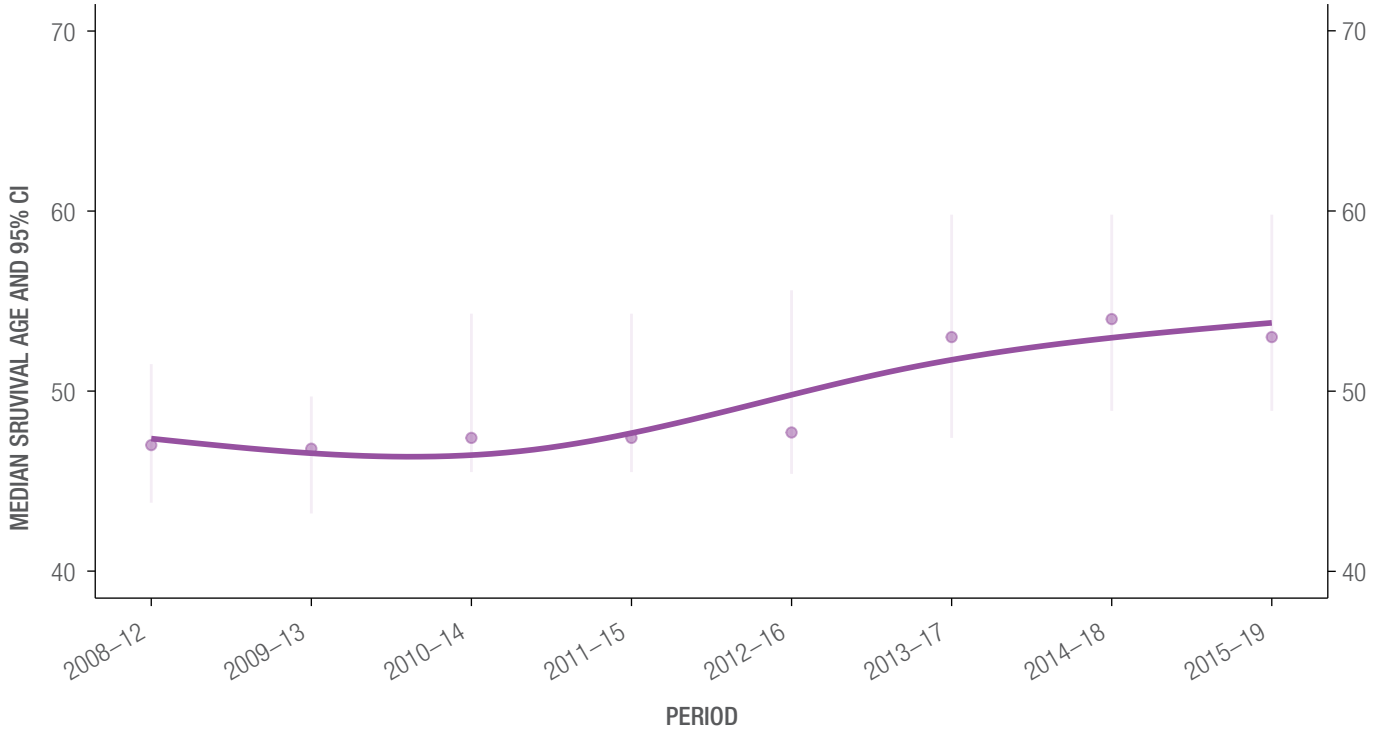
Median estimated survival is determined based on the people who are alive in the ACFDR in a given year or years. Internationally, CF registries have documented steady increases in median survival over recent years due to better treatments, and this is expected to continue to increase as more people with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

TABLE 6.1 – ACFDR 2010-2019: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA

PERIOD	YEAR	MEDIAN AGE AND 95% CONFIDENCE INTERVAL (YEARS)	N AT RISK	N DEATHS
2010-14	**2014**	47.4 (45.5 to 54.3)	3,403	172
2011-15	**2015**	47.4 (45.5 to 54.3)	3,480	171
2012-16	**2016**	47.7 (45.4 to 55.6)	3,543	177
2013-17	**2017**	53.0 (47.4 to 59.8)	3,569	170
2014-18	**2018**	54.0 (48.9 to 59.8)	3,707	166
2015-19	**2019**	53.0 (48.9 to 59.8)	3,772	171

Table 6.1 (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 53.0 years for people with CF born in 2015-19. 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 slightly depending on the data type, but also varies by centre.

Table 7.1 summarises main categories of the ACFDR data, and the percent of data available for 2019 and 2020.

TABLE 7.1 – ACFDR 2019-2020: DATA AVAILABILITY

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

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. 2020 ACADEMIC OUTPUTS

PUBLICATIONS

Cosgriff R, Ahern S, Bell SC, Brownlee K, Burgel PR, Byrnes C, Corvol H, Cheng SY, Elbert A, Faro A, Goss CH, Gulmans V, Marshall BC, McKone E, Middleton PG, Ruseckaite R, Stephenson AL, Carr SB; Global Registry Harmonization Group. *A multinational report to characterise SARS-CoV-2 infection in people with cystic fibrosis.* J Cyst Fibros. 2020 May;19(3):355-358. doi: 10.1016/j.jcf.2020.04.012. Epub 2020 Apr 25.

Earnest A, Salimi F, Wainwright CE, Bell SC, Ruseckaite R, Ranger T, Kotsimbos T, Ahern S. *Lung function over the life course of paediatric and adult patients with cystic fibrosis from a large multi-centre registry.* Sci Rep. 2020 Oct 15;10(1):17421. doi: 10.1038/s41598-020-74502-1.

McClenaghan E, Cosgriff R, Brownlee K, Ahern S, Burgel PR, Byrnes CA, Colombo C, Corvol H, Cheng SY, Daneau G, Elbert A, Faro A, Goss CH, Gulmans V, Gutierrez H, de Monestrol I, Jung A, Justus LN, Kashirskaya N, Marshall BC, McKone E, Middleton PG, Mondejar-Lopez P, Pastor-Vivero MD, Padoan R, Rizvi S, Ruseckaite R, Salvatore M, Stephenson AL, Filho LVRDS, Melo J, Zampoli M, Carr SB; Global Registry Harmonization Group. *The global impact of SARS-CoV-2 in 181 people with cystic fibrosis.* J Cyst Fibros. 2020 Nov;19(6):868-871. doi: 10.1016/j.jcf.2020.10.003. Epub 2020 Nov 4.

Ratnayake I, Ahern S, Ruseckaite R. *A systematic review of patient-reported outcome measures (PROMs) in cystic fibrosis.* BMJ Open. 2020;10(10):e033867.

Ratnayake I, Ahern S, Ruseckaite R. *Patient-Reported Outcome Measures in Cystic Fibrosis: Protocol for a Systematic Review.* JMIR Res Protoc. 2020 May 6;9(5):e15467. doi: 10.2196/15467.

CONFERENCE PRESENTATIONS

Ruseckaite R. Ratnayake I, Ahern S. *Evaluation of Patient Reported Outcome Measures in Patients with Cystic Fibrosis* (virtual poster presentation). 21-23 Oct, 2020, The North American Cystic Fibrosis Conference

Ruseckaite R. Ratnayake I, Ahern S. *Patient Reported Outcome Measures in Modern Cystic Fibrosis Population* (virtual poster presentation).19-23 Oct, 2020, The 27th Annual International Society Quality of Life Conference

9. DATA ACCESS REQUESTS

The ACFDR encourages the secondary use of its data for research and related purposes. Fifteen data access requests were received and approved for the ACFDR in 2020.

DATE	NAME	ORGANISATION	REQUEST TYPE	REQUEST
7/01/2020	Maxine Orr	Vertex Pharmaceuticals	Non-research	Long-term evaluation of effectiveness and safety outcomes among Australian patients who initiate Orkambi therapy between the ages of 6 and 11 for TGA
14/01/2020	Katherine Frayman	Royal Children's Hospital	Research	Long term outcomes following early infection and inflammation in a birth cohort with CF
30/01/2020	Scott Bell/ Christine Duplancic	QIMR Berghofer Medical Research Institute	Research	Nontuberculous mycobacteria infection in people with CF
1/02/2020	Anne Stephenson	Organisation Unity Health Toronto, St. Michael's Hospital	Research	Health Outcomes and Survival in CF between France, Canada, Australia and New Zealand
30/03/2020	Dolar Vergil	Australian Institute of Health and Welfare	Non-research	Prevalence of CF in Australia, by age, sex, severity and state/territory
13/05/2020	Efrat Gordon	Eloxx Phramaceuticals	Non-research	Prevalence of CF in Australia of Class 1 and Class 2 mutations
23/06/2020	Karen Raraigh	Johns Hopkins University	Research	The Clinical and Functional Translation of CFTR (CFTR2)
7/07/2020	Marianne Yvernel	Mylan	Non-research	Analysis of the most recent data on the CF patient population
8/07/2020	Claire Wainwright	Queensland Children's Hospital	Non-research	Audit of clinical outcomes for Children's health QLD CF service
9/07/2020	Sheila Sivam/ Amelia Lim	Royal Prince Alfred Hospital	Research	Adult diagnosis of CF in Australia
7/08/2020	Maxine Orr	Vertex Pharmaceuticals	Non-research	Rate of decline in FEV1 in patients treated with lumacaftor/ivacaftor
7/08/2020	Maxine Orr	Vertex Pharmaceuticals	Non-research	Epidemiology and disease characterization of cystic fibrosis by genotype
28/08/2020	John Huetsch	ArrowHead Pharmaceuticals	Non-research	Request to identify CF patients of Australian CF centers who may qualify for future clinical trials of ArrowHead drugs
7/09/2020	Peter Wark / Anna Tai	John Hunter Hospital	Research	Comparing outcomes for patients with CF gating mutations, comparing Australia and New Zealand; similar genetics, differences in access to Ivacaftor
25/09/2020	Claire Wainwright	Queensland Children's Hospital	Research	ACFBAL Follow-up Studies: FAB & GAIN

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.

10. APPENDICES

List of Figures

List of Tables

ACFDR Steering Committee Membership (2020)

Steering Committee Members	Role/Specialisation	Institution/Association
Professor Susannah Ahern	Coordinating Investigator / Academic Lead	Monash University, VIC
Professor Scott Bell	Clinical Lead ACFDR / CF Physician	The Prince Charles Hospital, QLD
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
Ms Nettie Burke	CEO	Cystic Fibrosis Australia
Dr Rasa Ruseckaite	Data Manager – ACFDR	Monash University, VIC
Dr Susannah King	Dietitian	Alfred Health, VIC
Ms Lucy Keatley	CF Clinical Nurse Consultant	Westmead Hospital, NSW
Ms Pia Sappl	Consumer Representative	NSW

List of Participating Sites

Site	
Sydney Children's Hospital (SCH)	Paediatric
The Children's Hospital, Westmead (CHW)	Paediatric
Royal Prince Alfred Hospital (RPA)	Adult
Westmead Hospital (WMH)	Adult
Gosford Hospital (GOS)	Paediatric and Adult
John Hunter Children's Hospital (JHC)	Paediatric
John Hunter Hospital (JHH)	Adult
Royal Children's Hospital (RCH)	Paediatric
The Alfred Hospital (ALF)	Adult
Monash Medical Centre (MMC)	Paediatric and Adult
The Prince Charles Hospital (TPCH)	Adult
Mater Hospital (MAH)	Adult

Site	
Gold Coast University Hospital (GCH)	Adult
Queensland Children's Hospital (QCH)	Paediatric
Royal Adelaide Hospital (RAH)	Adult
Women's and Children's Hospital (WCH)	Paediatric
Perth Children's Hospital (PCH)	Paediatric
Sir Charles Gairdner Hospital (SCG)	Adult
Royal Hobart Hospital (RHH)	Paediatric & Adult
Launceston General Hospital (LGH)	Paediatric
North West Regional Hospital (BUR)	Paediatric
The Canberra Hospital (CHA)	Adult
Centenary Hospital for Women & Children (CHW)	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**

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