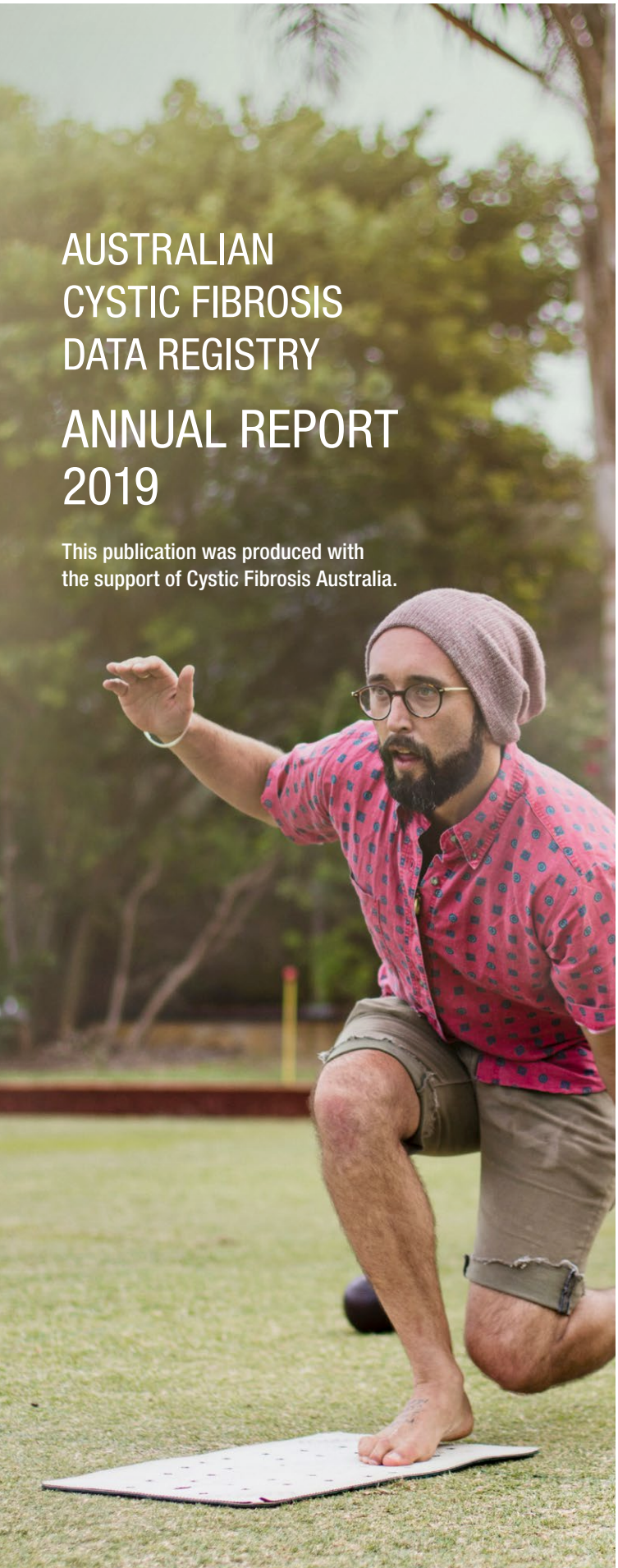
MONASH University

AUSTRALIAN CYSTIC FIBROSIS DATA REGISTRY

ANNUAL REPORT 2019

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 October 22 2020, and pertains to data that relates to patient events from January 1st to December 31st 2019. 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	Bronchi 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
FEV1PP	Forced Expiratory Volume (Litres) in 1 Second Predicted Percentage
GLI	Global Lung Initiative
IV	Intravenous
PBS	Pharmaceutical Benefits Scheme

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

Susannah Ahern, Rasa Ruseckaite, Farhad Salimi, Marisa Caruso, Scott Bell, Nettie Burke on behalf of the Australian Cystic Fibrosis Data Registry. The Australian Cystic Fibrosis Data Registry Annual Report, 2019. Monash University, Department of Epidemiology and Preventive Medicine, January 2021, Report No 21.

Any enquiries or comments regarding this publication, including requests regarding use or reproduction, should be directed to:

Australian Cystic Fibrosis Data Registry
Monash University
Level 3, 553 St Kilda Road,
Melbourne VIC 3004
Phone: +61 3 9903 1656
Email: med-acfdregistry@monash.edu

CYSTIC FIBROSIS Australia

MONASH University

The Thoracic Society of Australia & New Zealand
LEADERS IN LUNG HEALTH

CONTENTS

DATA EXTRACT PERIOD
ABBREVIATIONS
FOREWORD 2
INTRODUCTION 4
SUMMARY OF THE REGISTRY DATA 5

1. PEOPLE WITH CYSTIC FIBROSIS 7
1.1 Overview 7
1.2 Cohort Age and Gender Characteristics 7
1.3 Social Outcomes of People with CF 10

2. CF DIAGNOSIS AND GENOTYPING 13
2.1 New Diagnoses 13
2.2 Genotype 15

3. CLINICAL MEASURES 19
3.1 Lung Function 19
3.2 Nutrition: Weight, Height and Body Mass Index 24

4. CF MANAGEMENT 33
4.1 Clinical Encounters 33
4.2 CFTR Modulators 36
4.3 Microbiology 39

5. CF COMPLICATIONS AND THERAPIES 43
5.1 CF Lung Disease and Pulmonary Complications 43
5.2 Pulmonary Therapies 43
5.3 CF Endocrine Disease 45
5.4 CF Gastrointestinal Disease 46
5.5 Nutritional Supplements 47

6. TRANSPLANTATION AND SURVIVAL 49
6.1 Transplantation 49
6.2 Status of People with CF in the ACFDR 50
6.3 Median Age of Death 51
6.4 Survival 52

7. REGISTRY QUALITY ASSURANCE 53

8. ACADEMIC OUTPUTS 54

9. DATA ACCESS REQUESTS 55

10. APPENDICES 56
List of Figures 56
List of Tables 57
ACFDR Steering Committee Membership 2019 58
List of Participating Sites 59
ACFDR Coordinating Centre, Monash University 60
Access to Registry Data 60
Sponsors 60

FOREWORD

FROM THE CYSTIC FIBROSIS AUSTRALIA CEO

The Australian Cystic Fibrosis Data Registry (ACFDR) is the window to the cystic fibrosis (CF) soul here in Australia. The insights and health outcomes recorded have and will continue to change health outcomes for the better for Australians with CF.

The ACFDR is a valuable clinical improvement tool that informs health care for our cystic fibrosis community. It's also a research repository, that can support local and international studies and clinical trials to extend CF lives and ultimately find a cure for CF.

For a clinical data registry to be a valuable tool, health consumers must be willing to share their medical information and CF care centres must be committed to inputting quality data. We also need a talented and experienced team like Monash University's Registries Unit to manage all aspects of the registry and finally, we need a Steering Committee with insight, experience and a commitment to innovative data systems.

I would like to thank the CF community for their data, the CF Centres for their diligence, Monash University's Registries Unit for creating and managing such a valuable asset and the Steering Committee for their extensive oversight.

Over the past five years the ACFDR has gone through enormous change and has been rebuilt from the ground up. The ACFDR is now able to harmonise with international registries around the world and be 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 clinical care tools.

I am steadfast in my belief, that we have the team to make these a reality and that our registry will continue to improve care and support vital research initiatives.

Nettie Burke
Chief Executive Officer
Cystic Fibrosis Australia

CYSTIC FIBROSIS Australia

"I am steadfast in my belief, that we have the team to make these a reality and that our registry will continue to improve care and support vital research initiatives."

FROM THE REGISTRY CLINICAL LEAD

It is with great privilege that the Steering Committee and The Monash Registry team launch the 2019 Annual Report of the Australian Cystic Fibrosis Data Registry (ACFDR). There have been many opportunities but also challenges during the past year which everyone has felt, but despite the obvious distraction of the COVID-19 pandemic the Registry has continued to build in its reach, engagement and utility.

During the past year we've seen a number of new aspects of the Registry including:

i) Workflow adjustment due to the pandemic and the rapid changes in models of care dictated by that, and enhanced virtual care;
ii) Added pressure from the pandemic on data entry, also the agility of the Registry supported the ability to be able to collect data about virtual clinics and also home clinical measurements; and
iii) All during a period where the Monash team who largely worked from home during 2020.

In this period, there has been an increase in requests for access to Registry data from a wide range of groups nationally and internationally including clinicians, academics and industry. There were 9 data access requests in 2019, with data ranging from lung function, microbiology, genetic mutations, pregnancy outcomes and clinic information. The Registry has seen the implementation of an important funding support framework which has demonstrably increased data completeness. Consequently, this will allow a data quality assessment to be incorporated into the 2020 Registry report which will start early in 2021.

I'd like to acknowledge Cystic Fibrosis Australia, the Monash University ACFDR team and all members of the ACFDR Steering Committee. All members of the Steering Committee have contributed to feedback on the data and its presentation, providing support to the Monash team throughout 2020. The result is a more streamlined report with improved presentation data of data. It's a timely opportunity also to welcome a new community member, Pia Sappl who provides adult input into the direction of the Registry.

Additionally, I would like to acknowledge all of the hospital clinical staff including physicians, nurses and all members of the multi-disciplinary allied health team and data managers who continue to support the Registry above and beyond. A huge thank you also to all of the participating people with CF and their families who allow their data to contribute to the Registry. There is no doubt that engagement in the Registry has, and will continue to, support access to CFTR modulator (and other potentially novel therapies). In the future these data provide important outcome information about clinical response to CFTR modulators for government, industry, clinical teams and for people with CF and their families.

"In the future these data provide important outcome information about clinical response to CFTR modulators for government, industry, clinical teams and for people with CF and their families."

Professor Scott Bell, MBBS, MD, FRACP
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 20 years, since it began operations in 1998. It currently collects data from twenty-four paediatric, adult and combined paediatric and adult CF centres across Australia. It includes information relating to approximately 3500 people with CF, estimated to comprise over 95% of Australia's CF population. The ACFDR dataset covers a broad range of pulmonary and non-pulmonary elements as well as demographic and social information, reflecting on the multisystem nature of the disease and its management. The ACFDR dataset enables reporting in a manner generally consistent with other CF registries, such as those in New Zealand, Europe, Canada, the United Kingdom and the United States.

"The quality of this Annual Report's data, with core data elements at around 95% completeness, are a significant enhancement to the overall dataset."

Australians newly diagnosed with CF are invited to participate in the registry through their treating CF centre. Participation through the majority of centres is 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 is included for the first time in this 2019 Annual Report, 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. This report also for the first time, reports survival of Australians with CF, importantly showing that the longer term outcomes of Australians with CF are similar to those from comparable countries.

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 2019 Annual Report is the first 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 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.

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 THE REGISTRY DATA

OVERVIEW OF AUSTRALIAN CF POPULATION AND HEALTH OUTCOMES 2015, 2017 AND 2019

	2015	2017	2019
PEOPLE WITH CYSTIC FIBROSIS			
Total people with CF in the ACFDR	3,379	3,151	3,446
Age (median)	18.8 yrs	19.6 yrs	19.6 yrs
Age (mean)	20.9 yrs	21.7 yrs	22.0 yrs
Adults (≥ 18 yrs) number, (%);	1,756/52.0%	1,692/53.7%	1,854/53.8%
Adults: Males %	53.2%	53.7%	53.1%
CF DIAGNOSIS & GENOTYPING			
Newly diagnosed people with CF (pp)	98	72	66
% Diagnosis < 1 yr	73.5%	76.6%	85.0%
% Diagnosis > 18 years	3.1%	4.2%	4.5%
Genotyped – one allele (two alleles)	91.7%	94.1%	96.0% (88.0%)
% F508del Homozygous	50.2%	49.8%	47.0%
% F508del Heterozygous	42.0%	36.6%	42.0%
CLINICAL MEASURES (LUNG FUNCTION & NUTRITION)			
Median FEV1PP children 6-17 years	95.0%	95.0%	95.0%
Median FEV1PP adults 18 years and older	71.0%	71.0%	74.0%
Median weight for length percentile < 2 yrs	67th	75th	68th
Median BMI percentile children	64th	62nd	68th
Median BMI - adults kg/m2	22.9	23.2	23.5
RESPIRATORY MICROBIOLOGY			
P. aeruginosa (%)	50.1%	55.9%	47.8%
S. aureus (%)	33.9%	50.9%	51.5%
Aspergillus *spp* (%)	18.2%	22.2%	22.9%
Non tuberculous mycobacterium (%)	2.8%	4.2%	5.9%
TRANSPLANTS AND SURVIVAL			
Bilateral lung transplants	30	41	33
Deaths (Total CF deaths) (N)	17	27	26
Median age of death	31.6 years	35.6 years	32.0 years
Survival median (cohort, 5 year)	47.0 years	49.8 years	53.0 years

Out of 3,446 people with CF, 1,854 (53.8%) were adults (18+ years). 12.1% were 40+ years.

1. PEOPLE WITH CYSTIC FIBROSIS

1.1 OVERVIEW

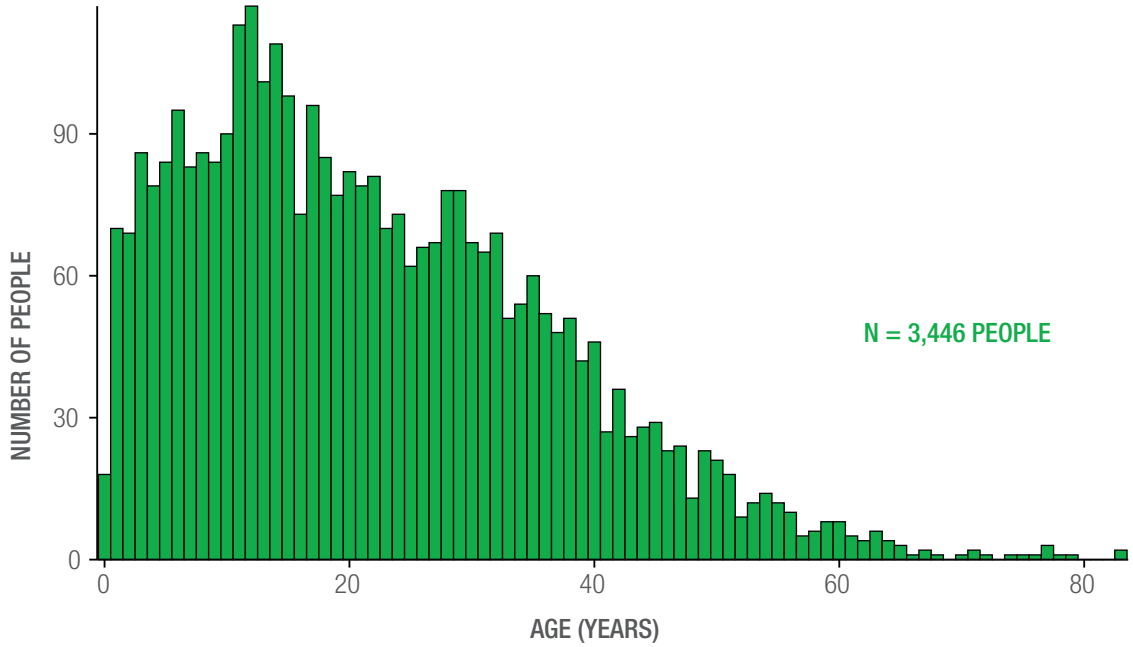
Cystic fibrosis (CF) is an autosomal recessive condition caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) genes. It presents primarily in infancy or early childhood, increasingly via genetic screening and prenatal diagnosis. CF causes chronic lung disease, however improvements in care and treatment over the last decades have consistently led to improvements in survival and wellbeing. This report highlights the epidemiological and clinical characteristics of the people with CF, that are captured in the ACFDR.

As the ACFDR is a registry that collects data from persons with CF from the time of their diagnosis to the time they leave the registry, 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 2019, or those of a particular age or gender, this will be noted in the text and figures.

1.2 COHORT AGE AND GENDER CHARACTERISTICS

As of 31st December 2019, the ACFDR held records of 3,446 people with CF collected from 23 CF centres in Australia. Figure 1.1 shows the age distribution of the total ACFDR cohort at the end of the 2019 calendar year.

FIGURE 1.1: ACFDR 2019: PEOPLE WITH CF IN AUSTRALIA BY AGE



The **mean age of the registry population was 22.0 years at 31st December 2019, an increase from a mean age of 21.7 years reported in 2017. The median age of the registry population was 19.6 years at 31st December 2019, remaining steady with a median age of 19.6 years in 2017.**

Out **of 3,446** people with CF, **1,592 were children (0-17 years, 46.2%)** and **1,854 were adults (18+ years, 53.8%). 12.1% of people were 40 years** and over (Table 1.1).

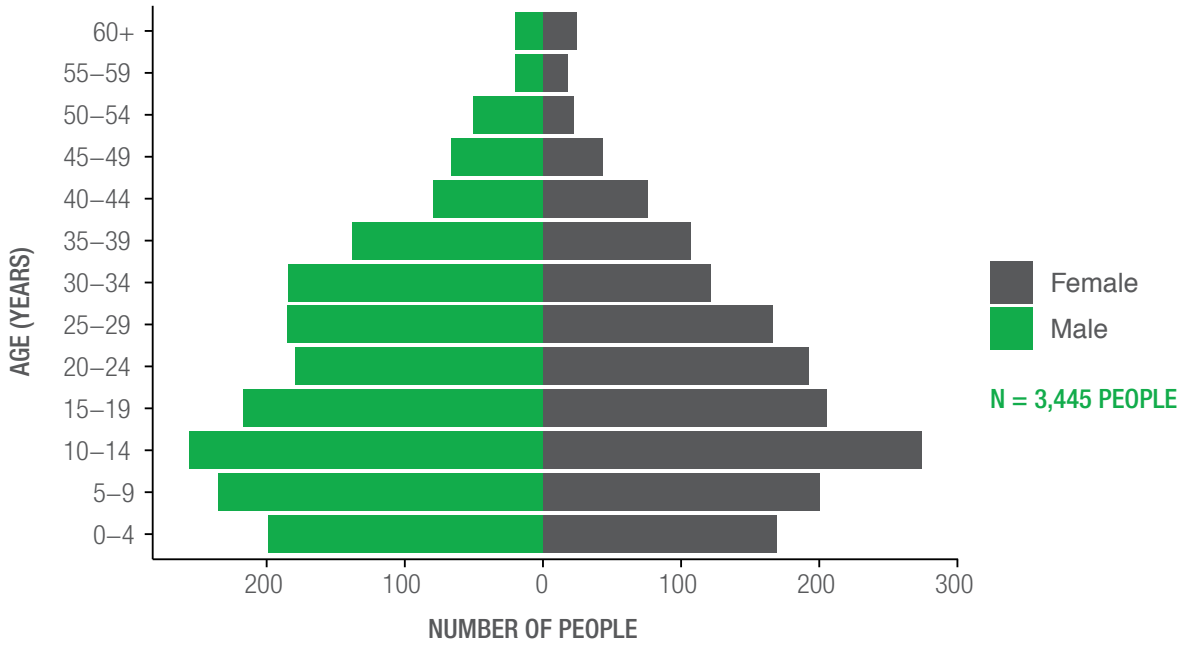
TABLE 1.1 – ACFDR 2019: PEOPLE WITH CF BY AGE AND GENDER

AGE	FEMALE	MALE	TOTAL
≤ 1	58.8% (30)	41.2% (21)	100.0% (51)
2-5	44.2% (141)	55.8% (178)	100.0% (319)
6-11	47.8% (252)	52.2% (275)	100.0% (527)
12-17	51.8% (312)	48.2% (290)	100.0% (602)
18-29	48.1% (435)	51.9% (470)	100.0% (905)
≥ 30	42.9% (447)	57.1% (594)	100.0% (1041)
Total	46.9% (1617)	53.1% (1828)	100.0% (3445)*

*N = 3,445 persons; one person did not have gender recorded

The age and gender distribution of people with CF as at the end of 2019 is shown in Figure 1.2

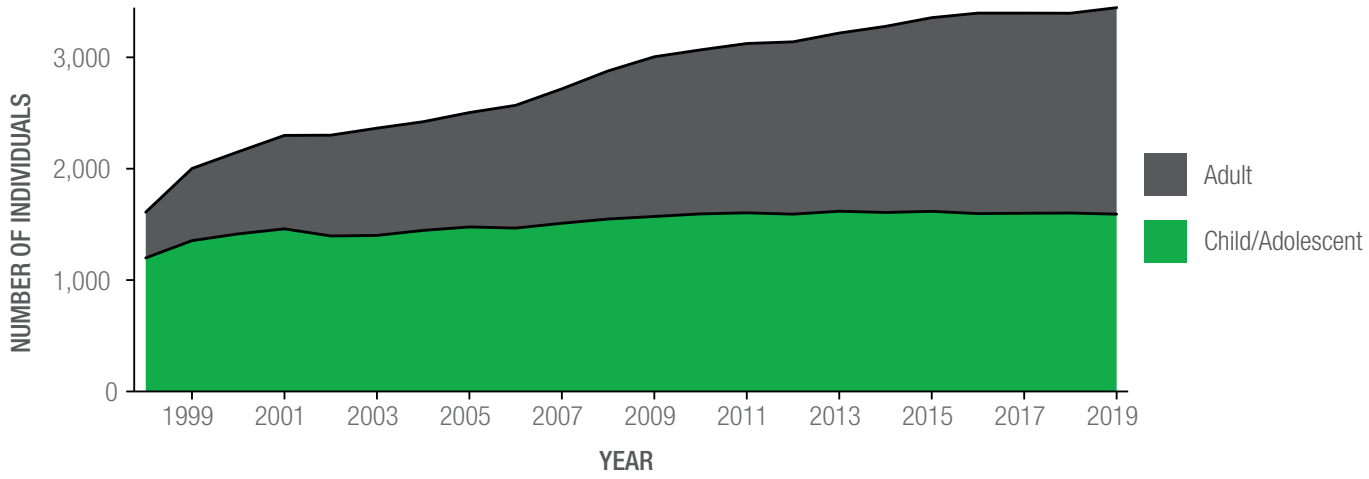
FIGURE 1.2: ACFDR 2019: PEOPLE WITH CF BY AGE AND GENDER



The median age for males (20.1 years) remained higher than that for females (19.0 years) in 2019. As at 31st December 2019, the proportion of males in the ACFDR was 53.1 % (53.7% in 2017) and females was 46.9% (46.3% in 2017).

Figure 1.3 shows the number of people in the CF registry for the last 20 years, including the proportion who are adult for each year. It is noted that there was systematic under-reporting by adult centres in the very early years of the ACFDR. The number of people in the registry has grown over time, and of these, the proportion who are adult has increased. As of 31st December, 2019, the proportion who were adult were 53.8 %.

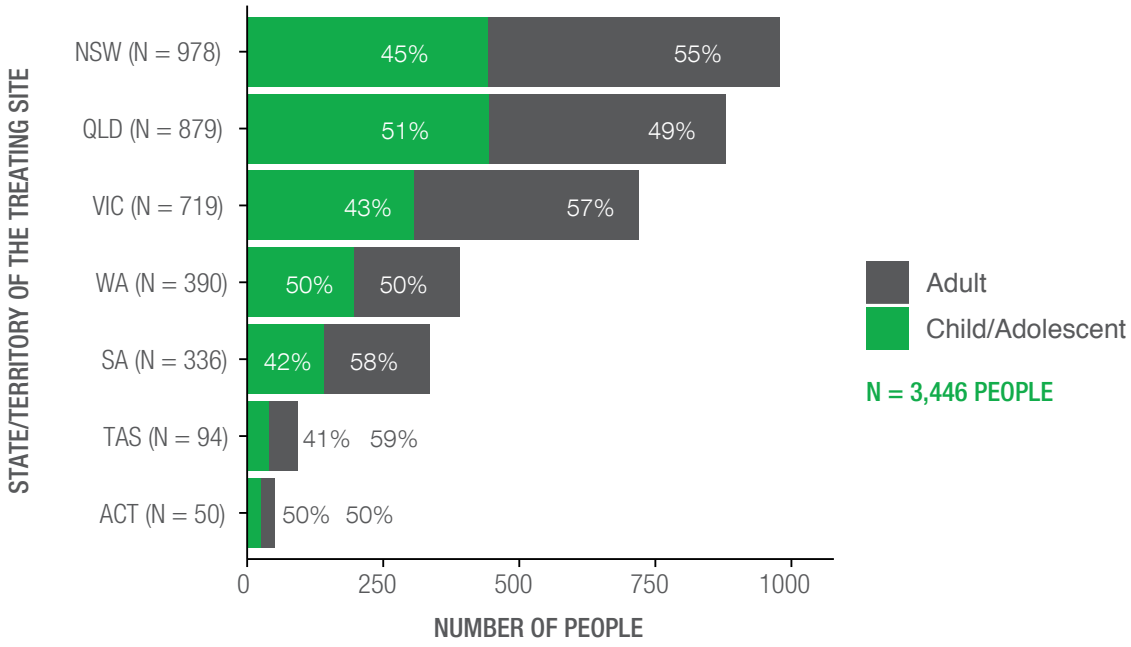
FIGURE 1.3: ACFDR 1998-2019: PEOPLE WITH CF – PAEDIACTRIC VS ADULTS PROFILE OVER TIME



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

The proportion of the people with CF, who receive their CF care at centres in each of Australia's jurisdictions are shown below (Figure 1.4).

FIGURE 1.4: ACFDR 2019: PEOPLE WITH CF – DISTRIBUTION BY STATE/TERRITORY



CF centres in New South Wales manage the greatest number of people with CF of any jurisdiction, followed by Queensland and Victoria. The proportion of people with CF who are adult varies across jurisdictions, from the lowest at 49% in Queensland to the highest at 59% in Tasmania.

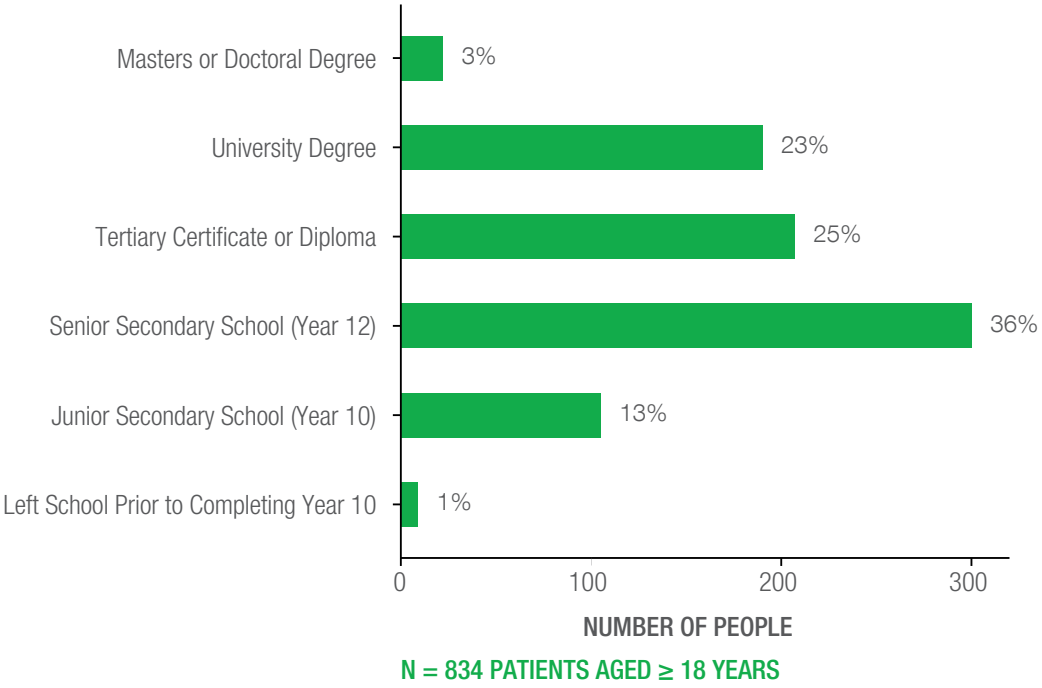
1.3 SOCIAL OUTCOMES OF PEOPLE WITH CF

As symptom management improves and survival increases, persons with CF are involved in greater numbers in education, employment and having a family. More than 40% of adults with CF in the ACFDR have information recorded about their social outcomes.

EDUCATIONAL OUTCOMES

Of the 834 adults with CF with information regarding education in the ACFDR, the proportion who completed a tertiary certificate, diploma, undergraduate or postgraduate degree is 51%, with those completing a University education being 26% (Figure 1.5). Those currently working towards degrees are not captured in this data.

FIGURE 1.5: ACFDR 2019: HIGHEST EDUCATIONAL ATTAINMENT OF PEOPLE WITH CF

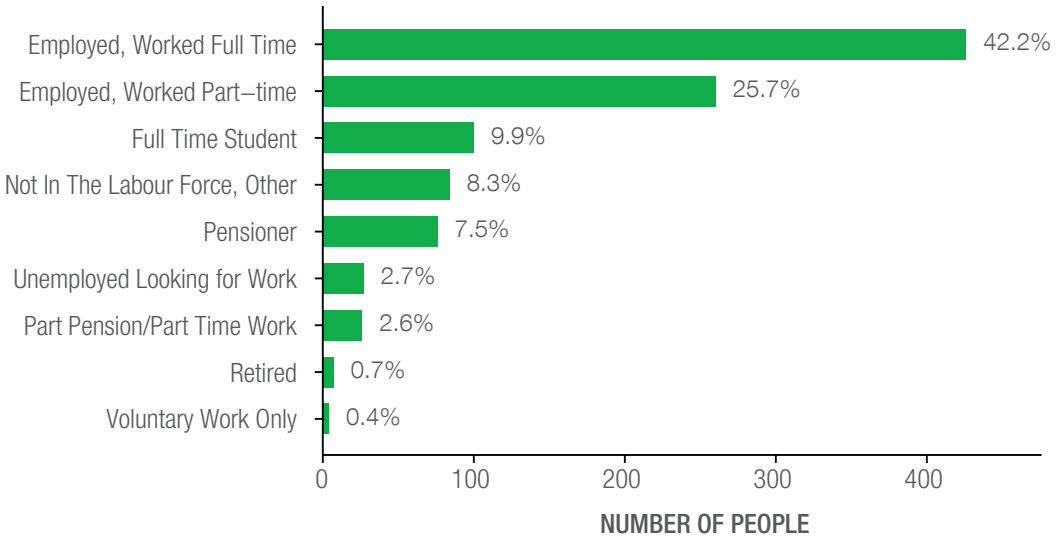


N = 834 PATIENTS AGED ≥ 18 YEARS

EMPLOYMENT STATUS

Of the 1,011 adults with CF with information regarding employment in the ACFDR, 42.1% were in full time employment, a further 25.7% were in part-time employment, and a further 10.0% were in full time study (Figure 1.6). Approximately 10% received a part or full pension, and a further 11% were not in the labour force or were looking for work.

FIGURE 1.6: ACFDR 2019: EMPLOYMENT STATUS OF PEOPLE WITH CF

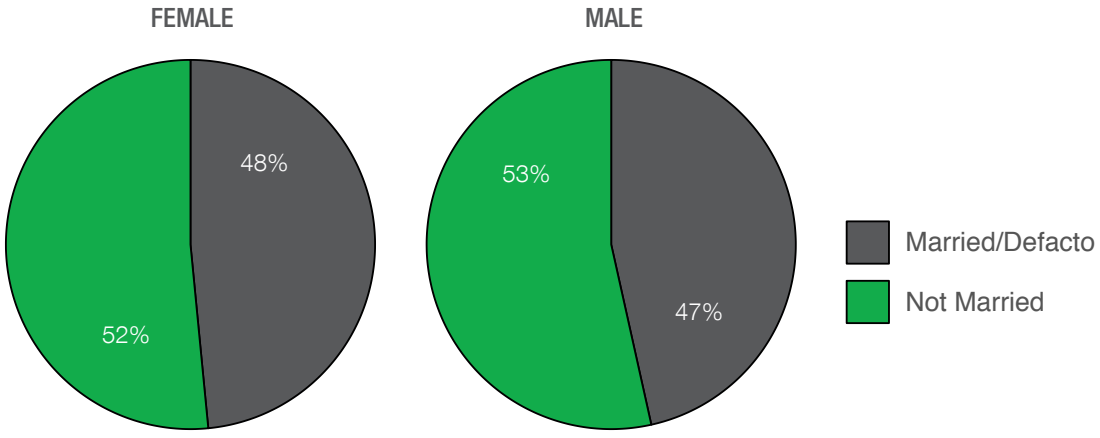


N = 1,011 PATIENTS AGED ≥ 18 YEARS WITH DATA RECORDED

RELATIONSHIP STATUS

Of the 1,079 adults with information regarding marital status in the ACFDR, 48% of women and 47% of men with CF were married or in a defacto relationship (Figure 1.7).

FIGURE 1.7: ACFDR 2019: MARITAL STATUS OF PEOPLE WITH CF



N = 1,079 PATIENTS AGED ≥ 18 YEARS

There were 66 diagnoses of CF, notified to the registry for 2019.

2. CF DIAGNOSIS AND GENOTYPING

2.1 NEW DIAGNOSES

There were sixty-six diagnoses of CF, notified to the registry for 2019. Of these, 56 (85%) people were diagnosed at less than one year of age, 7 people diagnosed between 1-10 years, and 3 people were diagnosed over the age of 18 years (Table 2.1).

TABLE 2.1 - ACFDR 2019: AGE AT DIAGNOSES FOR NEWLY DIAGNOSED PERSONS WITH CF

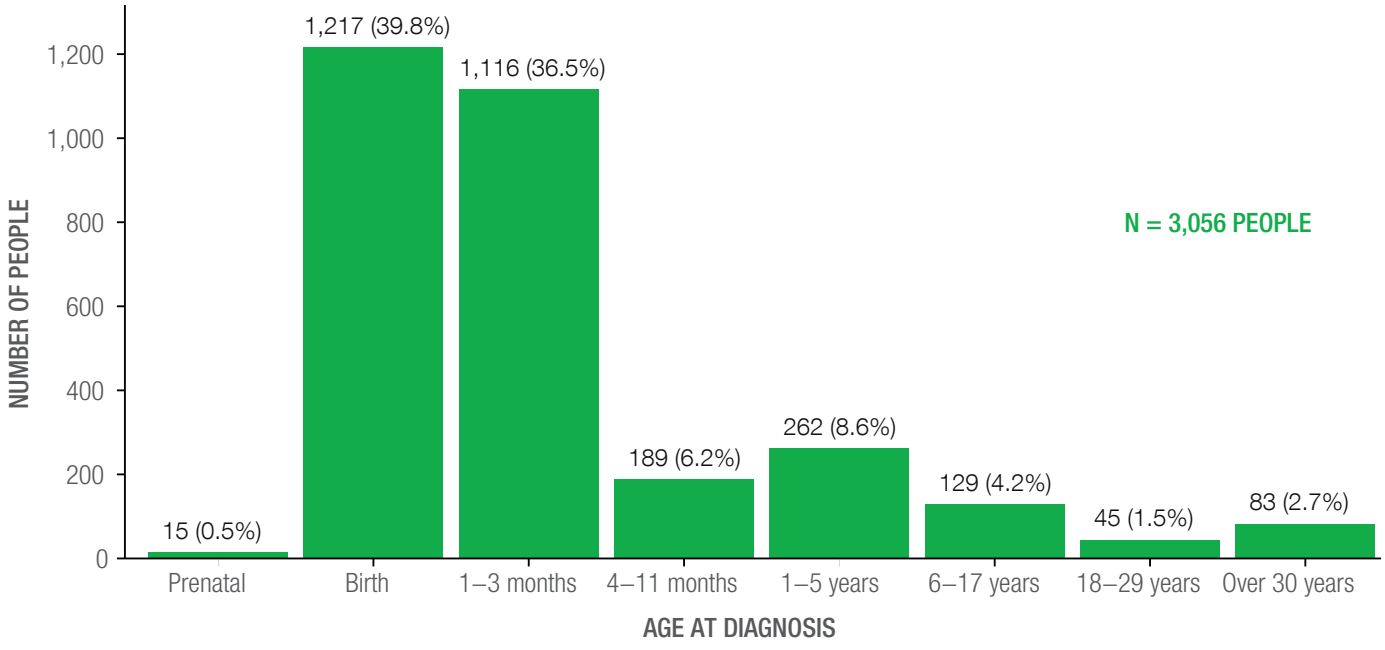
AGE	NUMBER	%
< 1 year	56	85.0%
1-10 years	7	10.5%
11-17 years	0	0.0%
18+ years	3	4.5%
Total	66	100.0%

For 2019, the diagnosis was suggested by newborn screening in nearly two thirds (64.7%), clinical signs/symptoms in 17%, family history in 10.6% and prenatal screening in 7.1%.

For new diagnoses in 2019 the most common clinical symptoms/signs were failure to thrive/malnutrition (36%), meconium ileus/intestinal obstruction (29%) and/or other presentations of respiratory signs/symptoms, persistent respiratory infection, sinus disease or infertility.

The age of diagnosis for people with CF from the whole ACFDR cohort is shown in Figure 2.1.

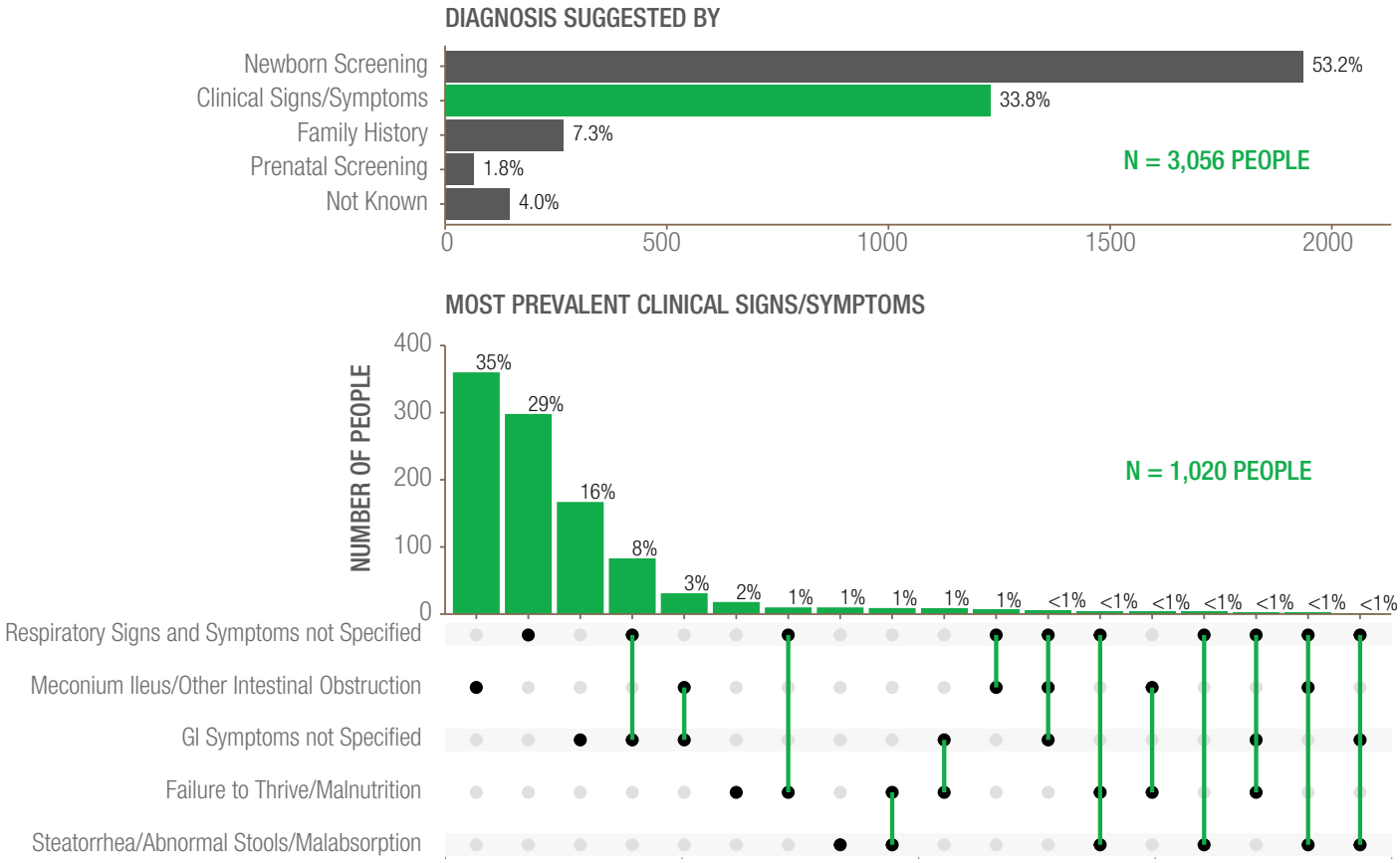
FIGURE 2.1: ACFDR 1998-2019: PEOPLE WITH CF – AGE AT DIAGNOSIS FOR WHOLE COHORT



88.7% of people (3,056 persons) with CF in the ACFDR have their age of diagnosis recorded. Approximately 83% of the ACFDR cohort was diagnosed at less than 1 year of age. Diagnosis for the total ACFDR cohort was determined via newborn screening for 53.2%, presentation of clinical symptoms or signs for 33.8%, investigation from a family history of CF (7.3%), with 1.8 % being diagnosed by prenatal screening (see Figure 2.2).

The most prevalent combinations of clinical symptoms and signs for the total cohort at the time of diagnosis were meconium ileus/intestinal obstruction (35%); respiratory symptoms or signs (29%); other gastrointestinal symptoms (16%); or a combination of the above. Less common presentations included failure to thrive and malabsorption. The method of diagnosis, and presenting clinical symptoms/signs for the whole ACFDR cohort is presented in Figure 2.2 below.

FIGURE 2.2: ACFDR 1998-2019: METHOD OF DIAGNOSIS AND PRESENTING SYMPTOMS/SIGNS



This highlights that over the last 20 years that diagnoses determined via newborn screening, family history and prenatal screening have increased, whereas diagnoses suggested by clinical symptoms have decreased (Table 2.2).

TABLE 2.2 - ACFDR 1998-2019: COMPARISON OF DIAGNOSTIC CHARACTERISTICS FOR TOTAL COHORT VS 2019 NEW DIAGNOSES

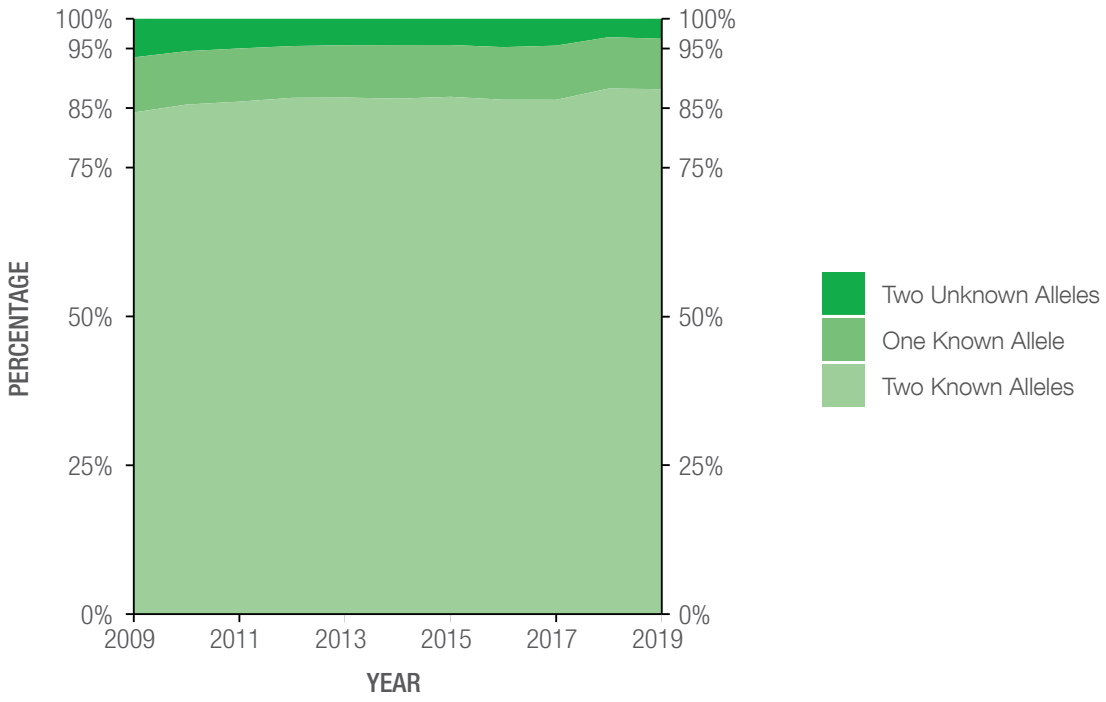
DIAGNOSTIC SUGGESTED BY	TOTAL CF COHORT (%)	2019 NEW DIAGNOSES (%)
Newborn screening	53.2	64.7
Clinical symptoms/signs	34.0	17.6
Family history	7.3	10.6
Prenatal screening	1.8	7.1
Not known	4.5	0.0

2.2 GENOTYPE

The gene that causes CF was discovered in 1989. As CF is an autosomal recessive condition, for a person to have CF, they require a mutation in both copies of the CFTR gene. Since 1989, scientists have found more than 1,700 different mutations in the CFTR gene that can cause CF. The most common mutation is delta F508, accounting for approximately 70% of mutations in Caucasian populations.

The proportion of persons with CF in the ACFDR with known mutations has increased over the last decade (2009 – 2019). The proportion of people with CF with two known alleles (gene mutation) has increased from 84% to 88% over this time, those with at least one known allele has increased from 94% to 96%, and the proportion with both alleles unknown has reduced from 6% to 3% over the same period (Figure 2.3).

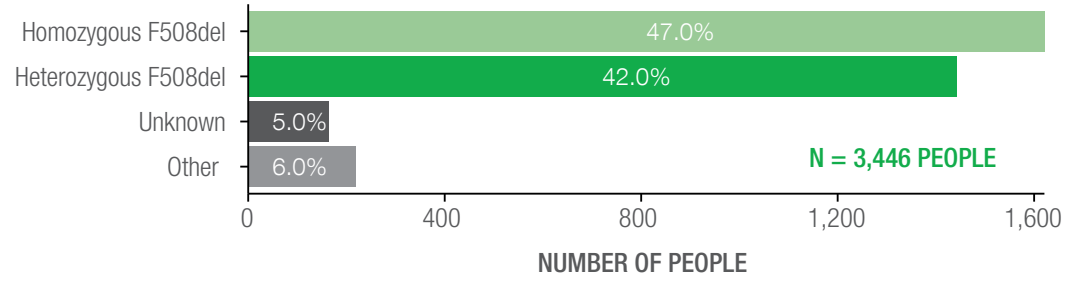
FIGURE 2.3: ACFDR 2009-2019: PERCENTAGE OF ACFDR COHORT WITH GENOTYPE COMPLETE



Approximately 89% of people with CF in the ACFDR with their genotype recorded are either homozygous (47%) or heterozygous (42%) for the F508del mutation. i.e. 89% have at least one F508del mutation (Figure 2.4). An assumption was made in this analysis that the vast majority of the 11% 'not known/unknown' alleles were not F508del.

Of those who are heterozygous for F508del (i.e. have one F508del mutation), the most common second mutations (alleles) are G551D (14.3%), R117H (6.8%), and G542X (4.9%). However, approximately 44% of other mutation combinations of heterozygous F508del mutations comprise individually less than 1% of the total of group (Figures 2.4 and 2.5).

FIGURE 2.4: ACFDR 1998-2019: MOST COMMON CFTR MUTATION COMBINATIONS IN PEOPLE WITH CF



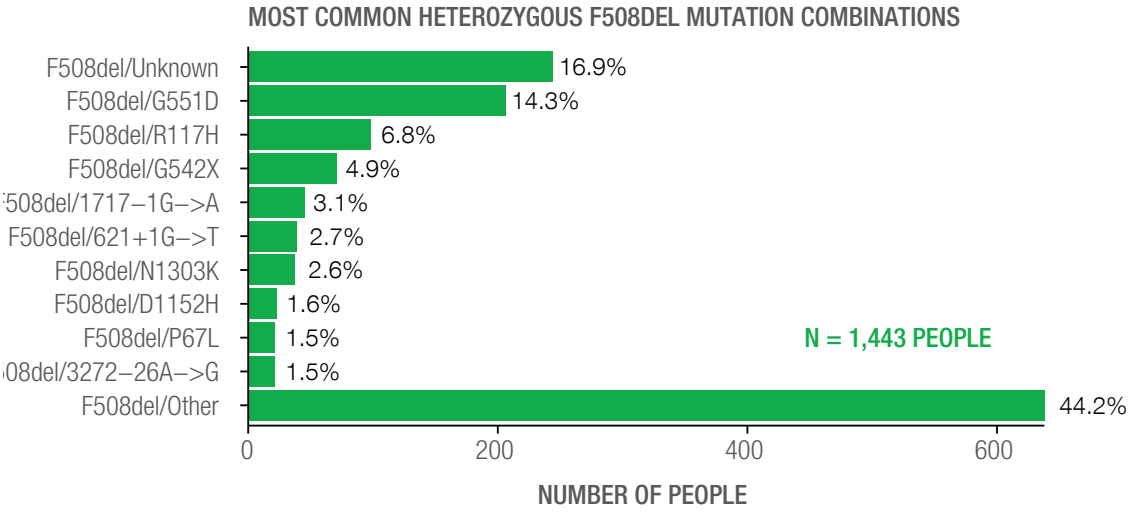
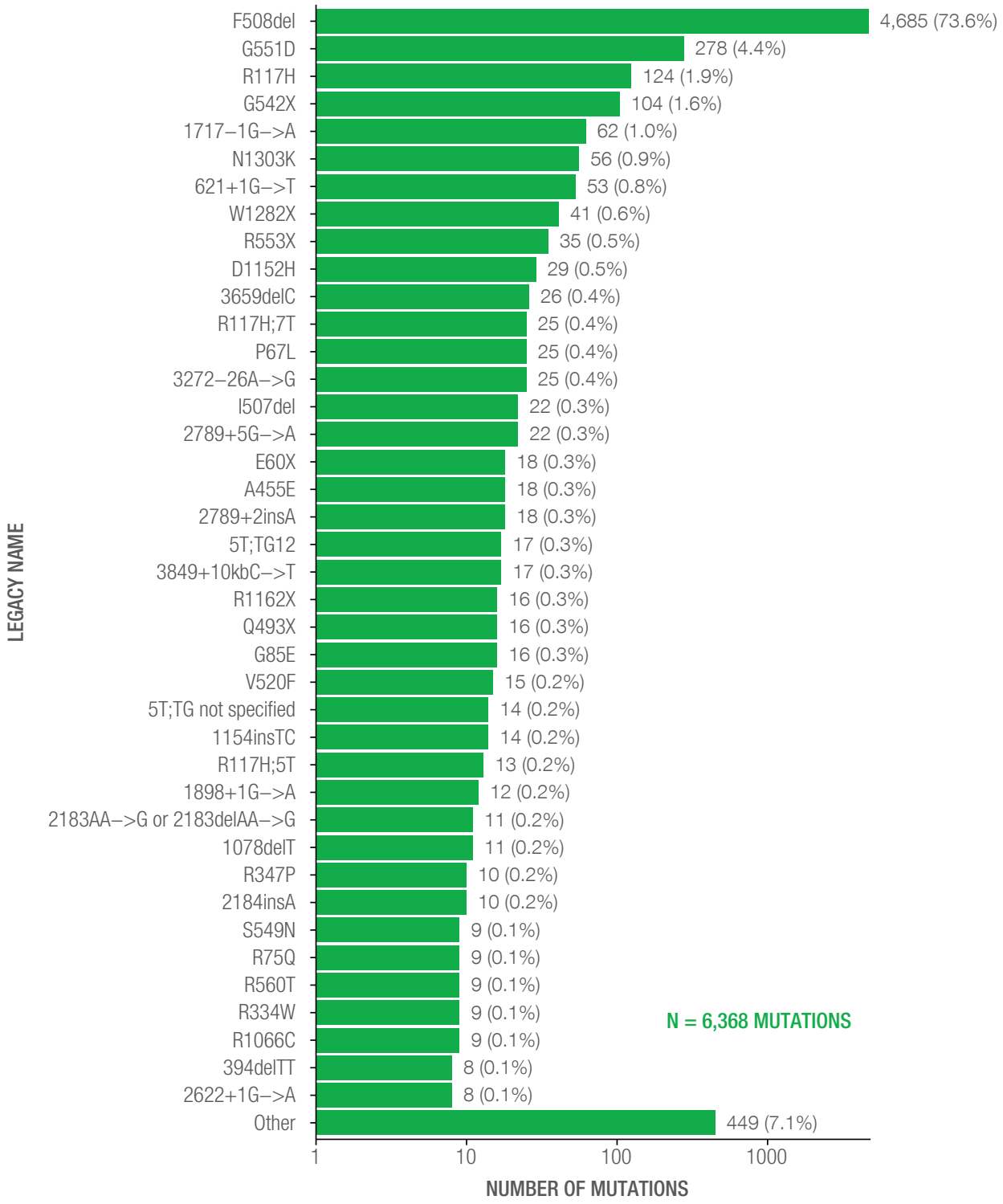


Figure 2.5 below shows that of the 6,368 individual allele mutations captured in the ACFDR, that the most common are F508del (73.4%), followed by G551D (4.4%), R117H (1.9%), G542X (1.6%), and 1717_1G → A (1.0%). The remaining mutations comprise less than 1% each.

FIGURE 2.5: ACFDR 2019 MOST COMMON INDIVIDUAL ALLELE CFTR MUTATION IN THE ACFDR



Median lung function, measured as FEV1pp, is within the normal range for young children.

3. CLINICAL MEASURES

3.1 LUNG FUNCTION

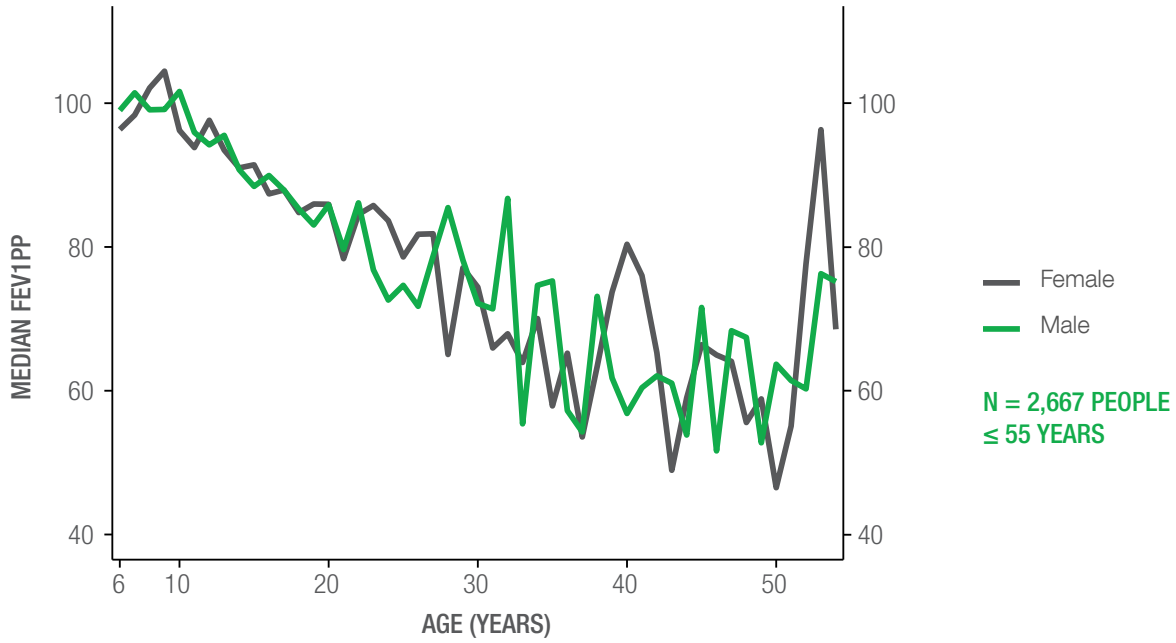
CHILDREN AND ADULTS

Lung function measures compiled for this report are aligned with methods used in the United States' Cystic Fibrosis Foundation's Patient Registry, that is the lung function measure included for each person is the average of the highest FEV1 percent predicted (FEV1PP) value recorded in each quarter of the year. Predicted values are based on Global Lung Initiative (GLI) formulae.

Approximately 80% of people up to the age of 55 years with CF in the ACFDR have lung function information (2,667 people) for 2019 in the registry. Ten percent of participants in the registry are children less than 6 years who do not routinely have lung function information recorded, and a further 10% of registry participants did not have lung function information recorded in 2019.

Median lung function for people with CF, measured as FEV1PP, is within the normal range for young children (Figure 3.1). At approximately 30 years of age, median FEV1 is lower than 70 percent of predicted, the level at which moderate lung function impairment is experienced.

FIGURE 3.1: ACFDR COHORT: BEST MEDIAN FEV1PP BY AGE



Lung function for people with CF varies by age and sex. Only a small proportion of children with CF (being less than 5% of 6-11 year olds, and between 9.9 – 11.8% of 12-17 year olds) have a FEV1PP at < 70%. In the 18-29 year age group, 32.6% of females and 34.1% of males have FEV1PP at < 70%; and for the 30+ age group, the proportion is 53.7% for females and 54.9% for males (Figure 3.2 and Table 3.1).

FIGURE 3.2: ACFDR COHORT: LUNG FUNCTION BY AGE AND SEX

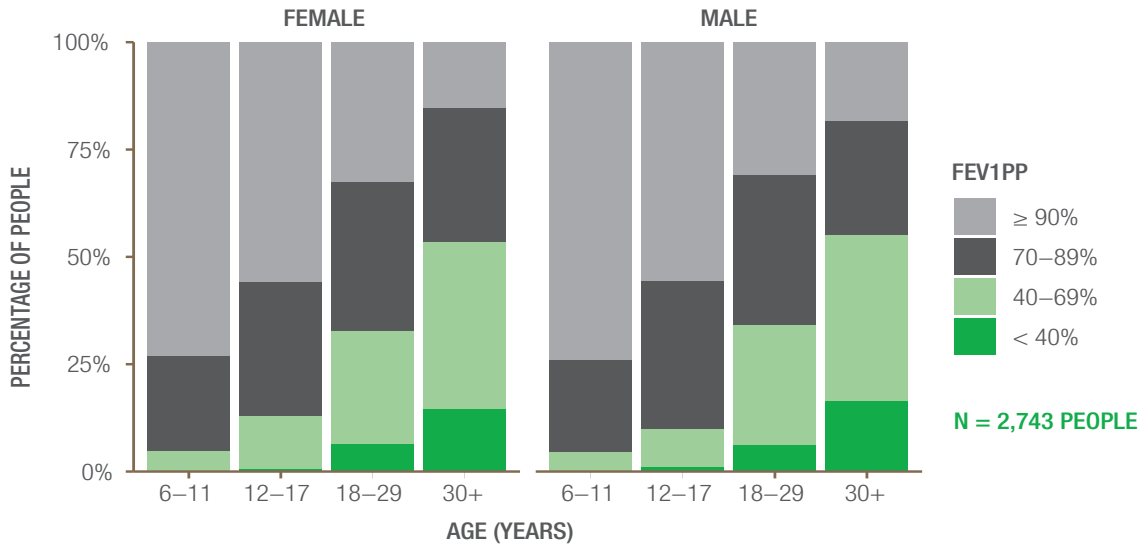


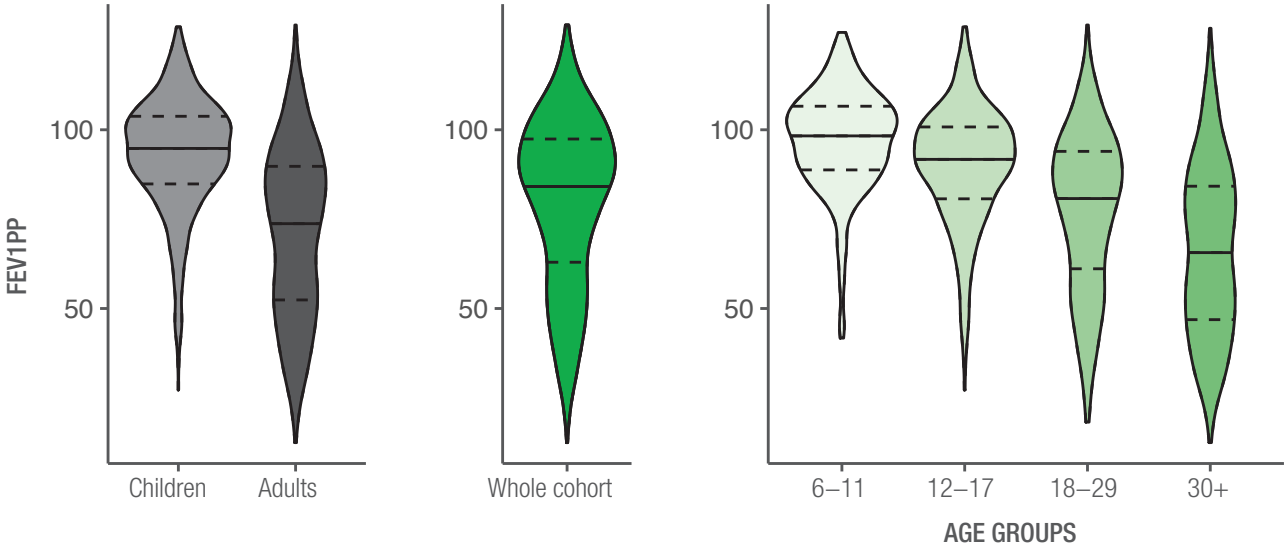
TABLE 3.1 - ACFDR COHORT: FEV1PP < 70% BY AGE AND SEX

FEMALE	AGE GROUP	n (%)
	6-11yrs	12 (4.8%)
	12-17yrs	32 (11.8%)
	18-29yrs	134 (32.6%)
	30+yrs	201 (53.7%)
MALE	**AGE GROUP**	**n (%)**
	6-11yrs	11 (4.5%)
	12-17yrs	28 (9.9%)
	18-29yrs	143 (34.1%)
	30+yrs	279 (54.9%)

MEDIAN FEV1PP

FIGURE 3.3: ACFDR COHORT: MEDIAN FEV1PP BY AGE AND FOR TOTAL COHORT

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



N = 2,743

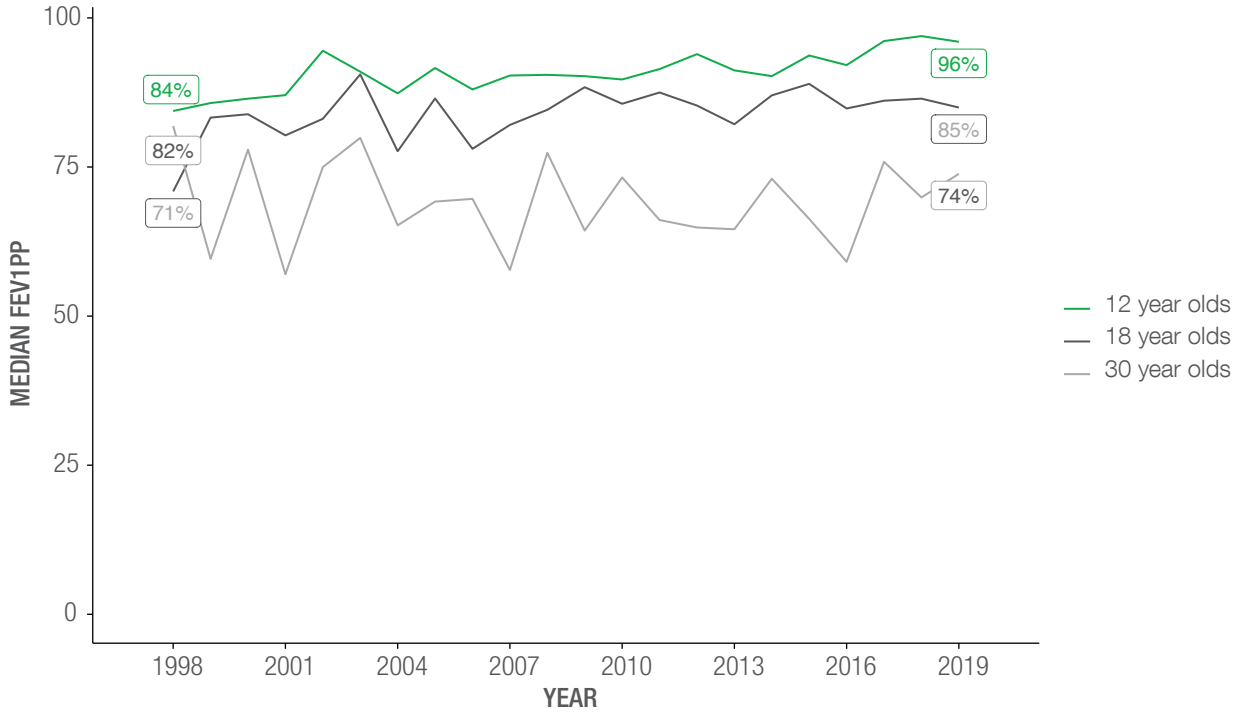
The median FEV1P for children (6-17 years) was 95%.

The median FEV1P for adults (18+ years) was 74%.

The median FEV1P for the whole cohort in 2019 was 85%.

The median FEV1PP for persons with CF decreases with increasing age. For the different age groupings, in the 6-11 year cohort, the median FEV1P is 99%, and for children 12-17 years, the median FEV1P is 92%. The median FEV1PP reduces to 82% for the 18-29 year age group, 69% for the 30-40 year age group, and 63% at 40 years and older.

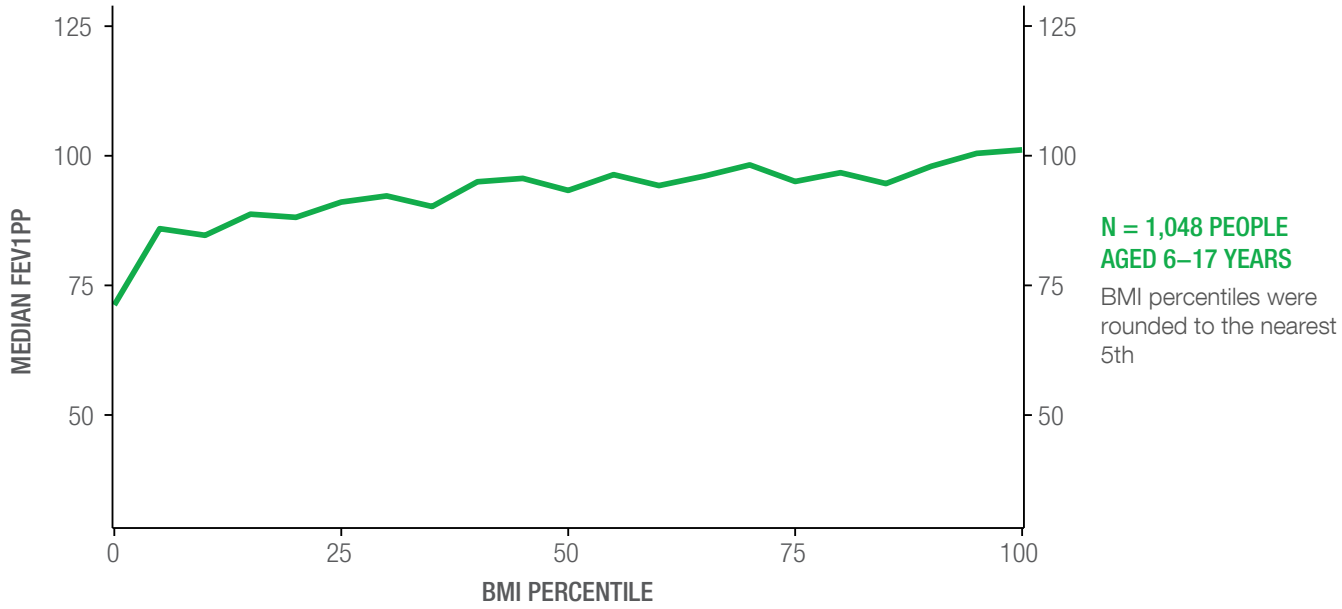
FIGURE 3.4: ACFDR COHORT: MEDIAN FEV1PP OVER TIME



Labelled percentages illustrate median FEV1PP in 1998 and 2019

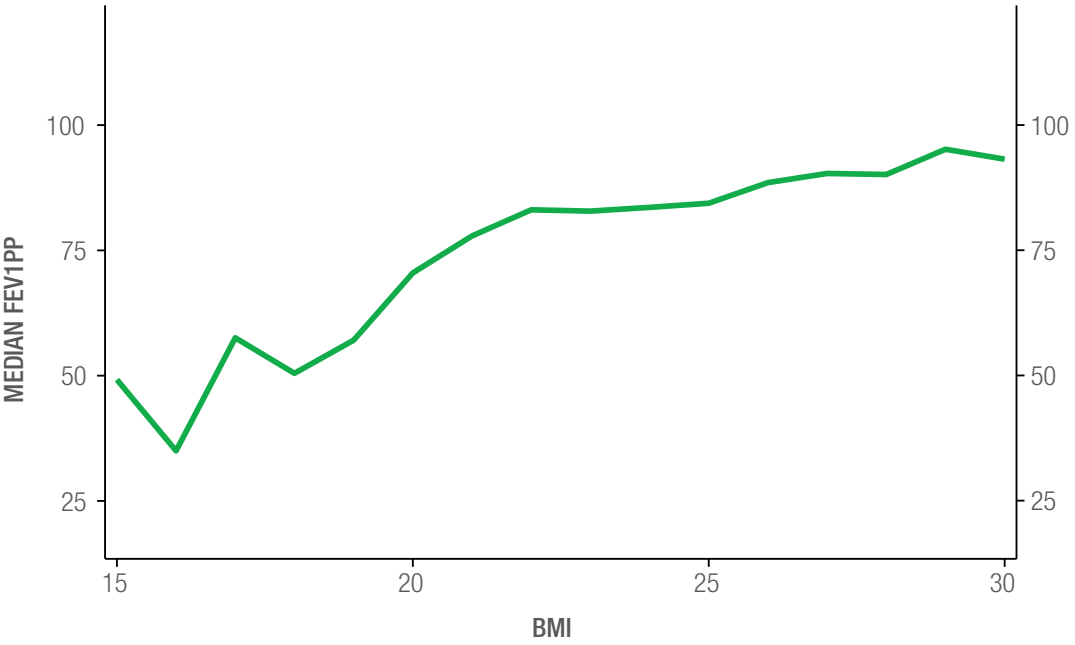
The median FEV1PP has increased over time particularly for the younger age cohorts. For 12 year olds, it has increased from 84% in 1998 to 96% in 2019, an increase of 12%. Increases in FEV1PP for 18 year and 30 year old cohorts has been more modest over time, and is likely confounded to some extent by low quality data in the first few years of the registry.

FIGURE 3.5: ACFDR 2019: FEV1PP VS BMI PERCENTILE FOR PERSONS WITH CF AGES 6-17 YEARS



There is a relationship between FEV1PP and Body Mass Index (BMI), whereas BMI percentile increases, FEV1PP increases (Figure 3.5).

FIGURE 3.6: ACFDR 2019: MEDIAN FEV1PP VS BMI FOR PERSONS WITH CF AGES 18-30 YEARS



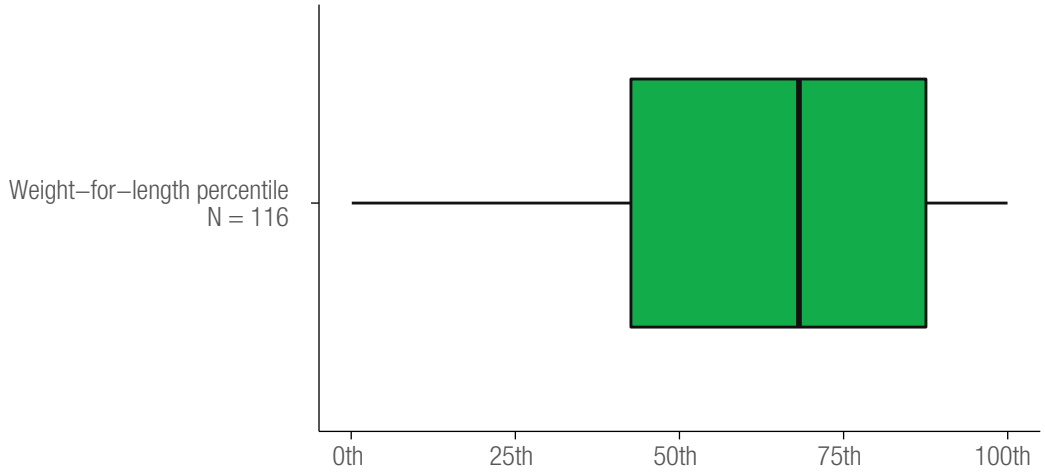
Similarly, for people with CF ages 18-30 years, FEV1PP increases, although at BMIs in the high 20s, this appears to negatively affect FEV1PP. Persons with CF over 30 years are not included due to small numbers, making the data difficult to interpret due to increased variability.

3.2 NUTRITION: WEIGHT, HEIGHT AND BODY MASS INDEX

INFANTS < 24 MONTHS

As of 2019, nutritional outcomes for 116 very young children (< 2 years) in the ACFDR show that the median weight for length percentile was 68th.

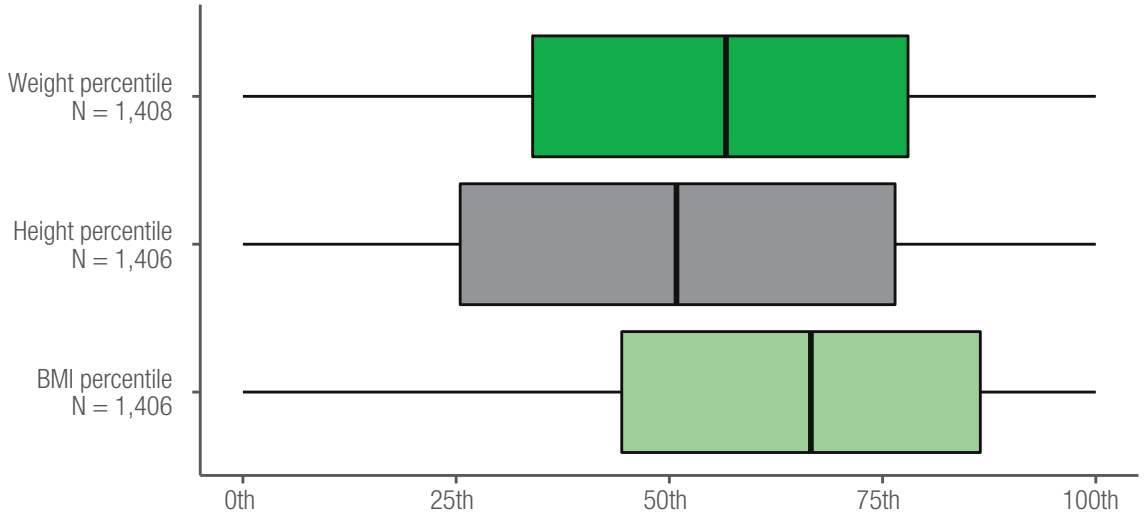
FIGURE 3.7: ACFDR 2019: NUTRITIONAL OUTCOMES FOR INFANTS < 24 MONTHS



CHILDREN 2-17 YEARS

As of 2019, for children aged 2-17 years, the median weight was 57th percentile, the median height was 51st percentile, and the median BMI was 68th percentile.

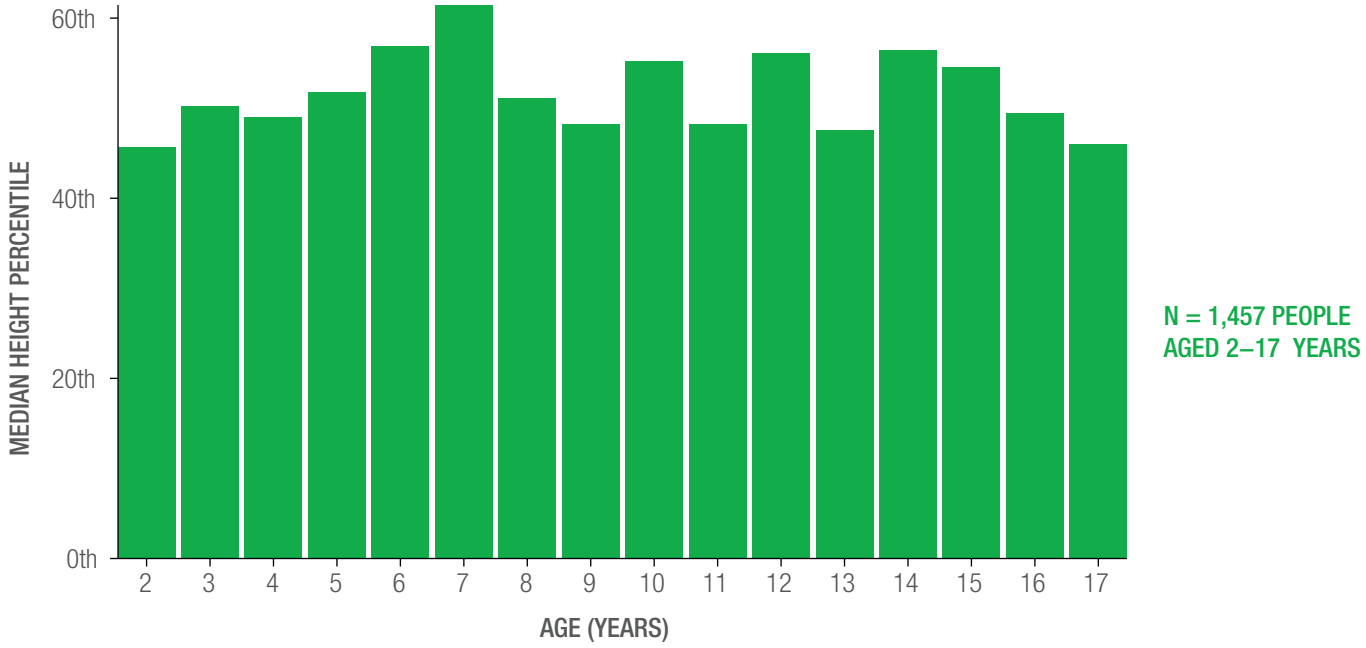
FIGURE 3.8: ACFDR 2019: BMI, WEIGHT AND HEIGHT PERCENTILES AGES 2-17 YEARS



CHILDREN 2–17 YEARS
Height and BMI percentiles were calculated using WHO growth chart.
Weight percentiles were calculated using CDC growth chart

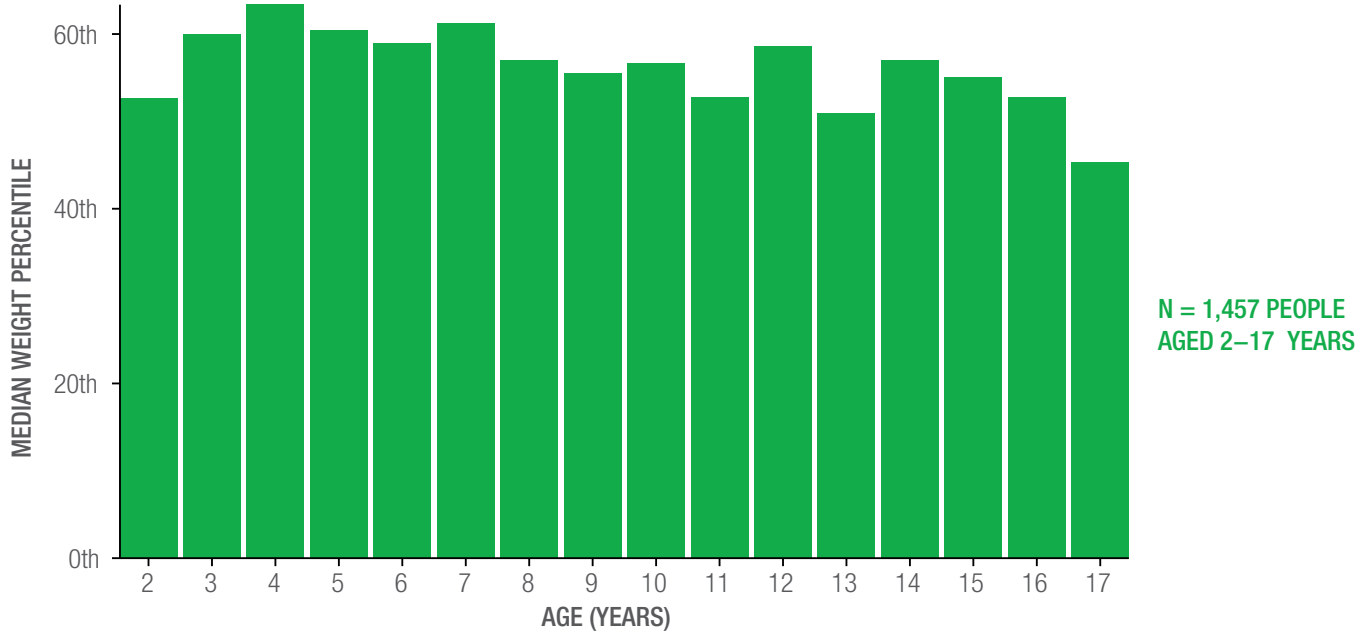
Individual age height percentiles for ages 2-17 years show consistent height around the median (as per Figure 3.9) across this age group.

FIGURE 3.9: ACFDR 2019: HEIGHT PERCENTILES CHILDREN AGES 2-17 YEARS



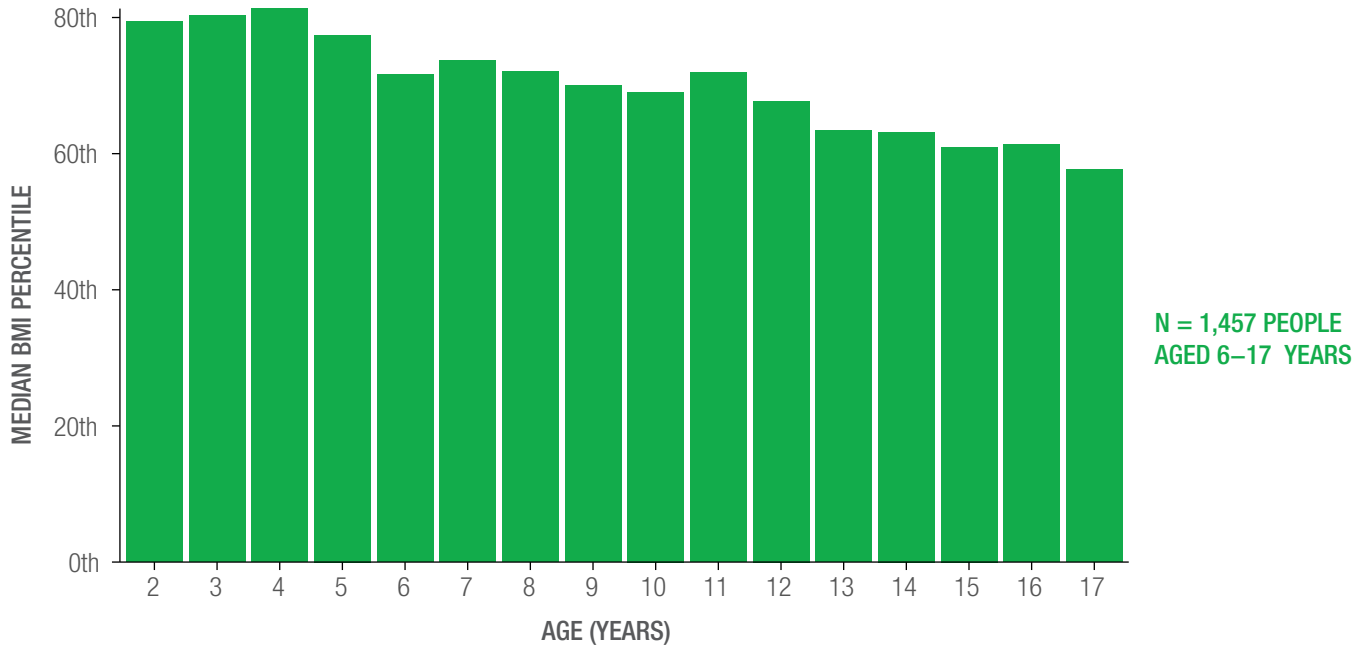
Individual age weight percentiles for ages 2-17 years show a reduction in weight percentile during this period, from 53rd at age 2 years, to 45th at age 17 years.

FIGURE 3.10: ACFDR 2019: WEIGHT PERCENTILES CHILDREN AGES 2-17 YEARS



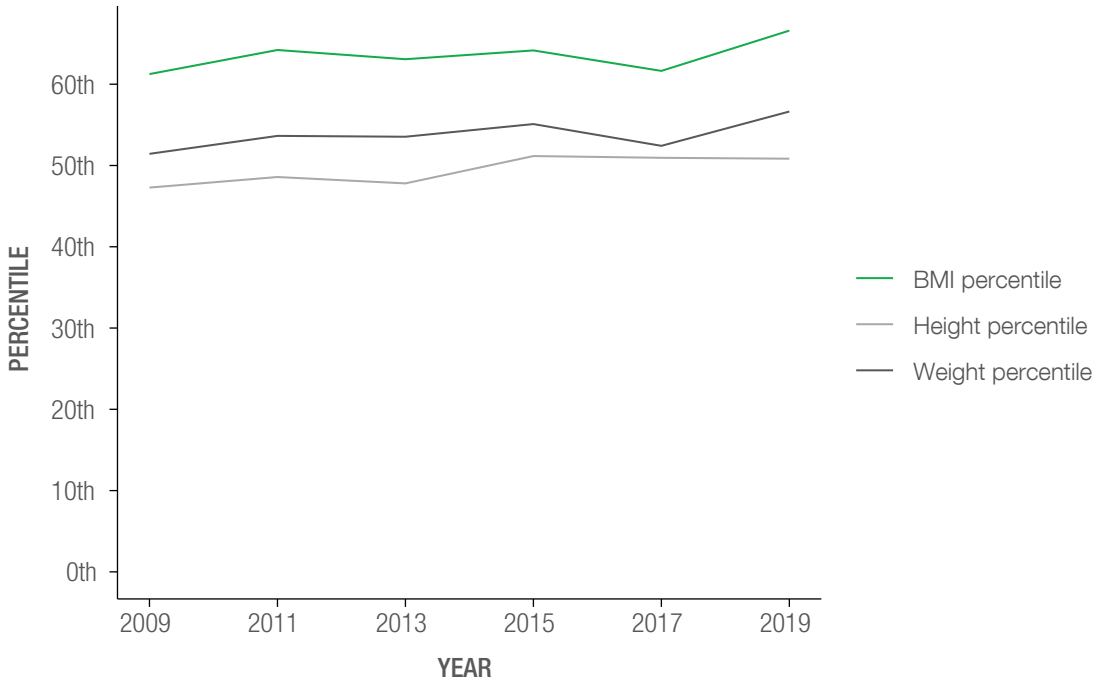
Individual age BMI percentiles for ages 2-17 years show a reduction in BMI percentile during this period, from 82nd at age 2, to 58th at age 17. This data reflects consistent linear growth but a drop off in weight in adolescence, potentially due to a combination of energy demands, reduction in adherence to diet/treatments or increasing disease severity.

FIGURE 3.11: ACFDR 2019: BMI PERCENTILES CHILDREN AGES 2-17 YEARS



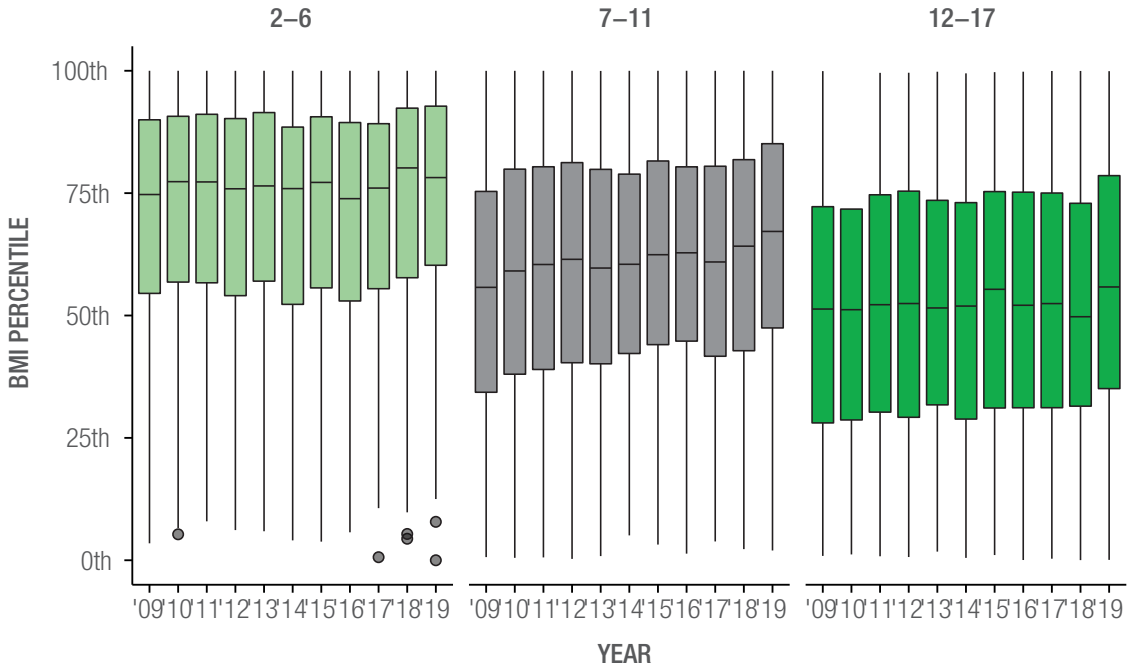
Over the last 10 years, the height and weight of children 2-17 years with CF has increased. Children in this age group have increased in height by 4 percentile points (from 47th percentile to 51st percentile), with a concomitant increase in weight of 5 percentile points (from 51st percentile to 57th percentile). As a result, average BMI has increased from 61st-68th over time.

FIGURE 3.12: ACFDR 2009-2019: MEDIAN NUTRITIONAL STATUS PERCENTILES CHILDREN 2-17



BMI percentile for children over time has shown modest increases over time, being most pronounced in the 7-11-year age group.

FIGURE 3.13: ACFDR 2009-2019: MEDIAN CHILD-ADOLESCENT BMI



CHILD AND ADOLESCENTS

Nutritional status for female children with CF as of 2019 shows that the majority (57% - 68%) are in the optimal and acceptable BMI percentile ranges (Table 3.2).

TABLE 3.2 – ACFDR 2019: NUTRITIONAL STATUS FOR CHILDREN < 2 – 17 YEARS: FEMALES

FEMALE					
Nutritional Status*	**< 2**	**2-5**	**6-11**	**12-17**	**Total**
High BMI percentile (obese range)	N/A	20.9% (28)	7.1% (19)	7.6% (21)	9.2% (68)
High BMI percentile (overweight range)	N/A	20.1% (27)	12.8% (34)	13.1% (36)	13.1% (97)
Optimal	73.0% (46)	40.3% (54)	48.9% (130)	44.4% (122)	47.7% (352)
Acceptable	17.5% (11)	17.2% (23)	19.2% (51)	24.7% (68)	20.7% (153)
Suboptimal	9.5% (6)	1.5% (2)	9.4% (25)	7.6% (21)	7.3% (54)
Undernourished	0.0% (0)	0.0% (0)	2.6% (7)	2.5% (7)	1.9% (14)

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

TABLE 3.3- ACFDR 2019: NUTRITIONAL STATUS FOR CHILDREN < 2 – 17 YEARS: MALES

MALE					
Nutritional Status*	**< 2**	**2-5**	**6-11**	**12-17**	**Total**
High BMI percentile (obese range)	N/A	25.3% (44)	9.0% (24)	7.6% (22)	11.6% (90)
High BMI percentile (overweight range)	N/A	26.4% (46)	17.9% (48)	9.3% (27)	15.6% (121)
Optimal	70.2% (33)	37.9% (66)	51.1% (137)	30.8% (89)	41.8% (325)
Acceptable	25.5% (12)	7.5% (13)	18.3% (49)	32.2% (93)	21.5% (167)
Suboptimal	4.3% (2)	2.3% (4)	2.6% (7)	13.1% (38)	6.6% (51)
Undernourished	0.0% (0)	0.6% (1)	1.1% (3)	6.9% (20)	3.1% (24)

Nutritional status for male children with CF as of 2019 shows that the majority (46% - 96%) are in the optimal and acceptable BMI percentile ranges (Table 3.3).

PANCREATIC SUFFICIENCY AND NUTRITIONAL OUTCOMES AGE 2-17 YEARS

Of the total 1,382 2-17-year olds, 18% are pancreatic sufficient, and 82% are pancreatic insufficient. Of those children and adolescents that were pancreatic sufficient, 17% were in the acceptable and 33% were in the optimal weight range (total 50%). A further 20% were in the overweight and 21% were in the obese weight range.

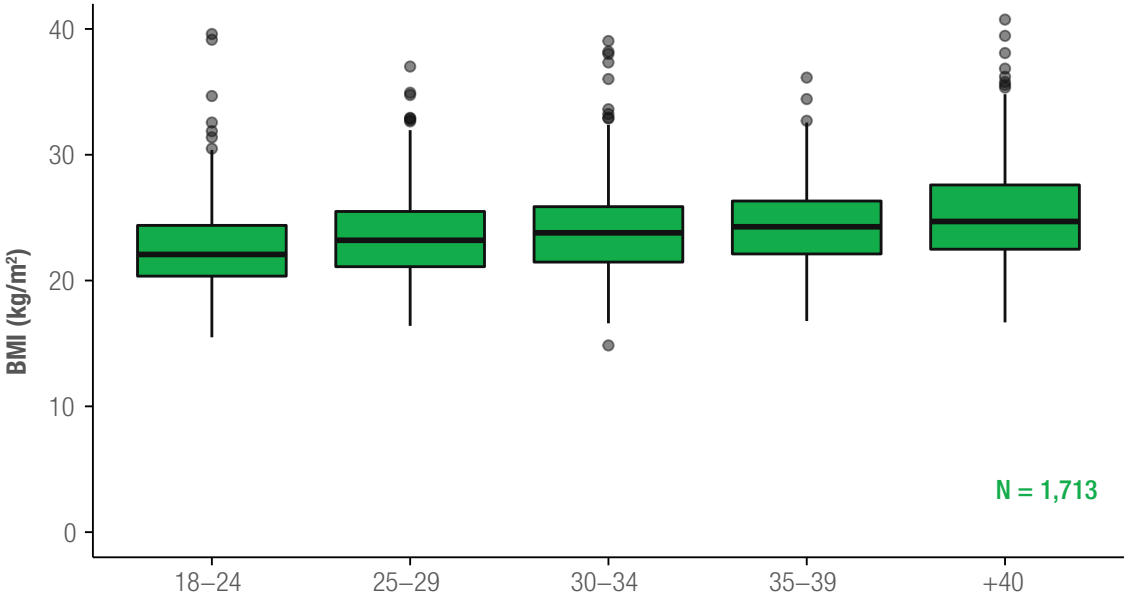
TABLE 3.4 – ACFDR 2019: PANCREATIC SUFFICIENCY AND NUTRITIONAL OUTCOMES AGES 2-17 YEARS

	UNDERNOURISHED	SUBOPTIMAL	ACCEPTABLE	OPTIMAL	OVERWEIGHT	OBESE	
Sufficient	2%	7%	17%	33%	20%	21%	100%
Insufficient	3%	7%	22%	43%	14%	11%	100%

*** Circles in the box plots represent outliers.**

ADULT NUTRITION

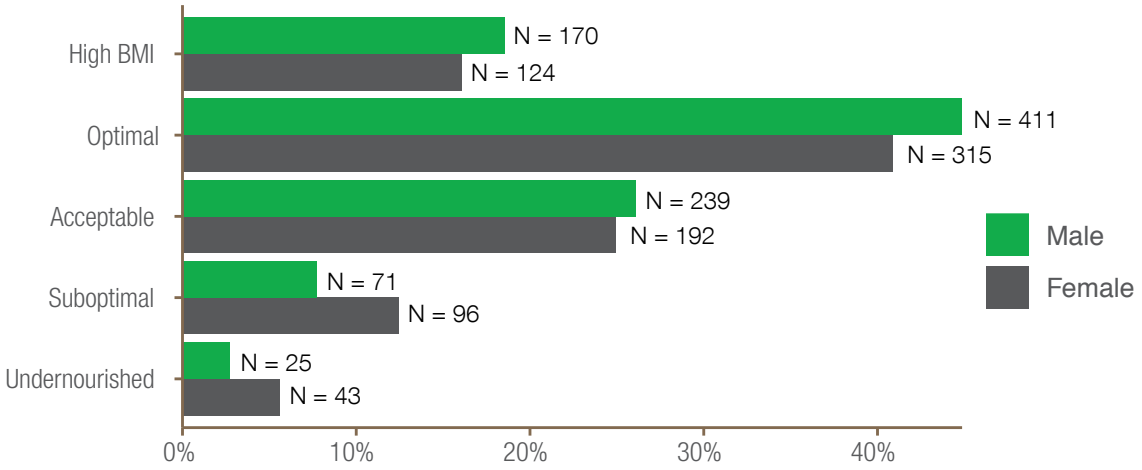
FIGURE 3.14: ACFDR 2019: BMI: ADULTS 18+ YEARS



* Circles in the box plots represent outliers.

The median BMI for adults with CF increases with increasing age. Adults from ages 18-24 years have a median BMI of 22.1 years; ages 25-29 have a median BMI of 23.2 years; ages 30-34 have a median BMI of 23.8; ages 30-34 have a median BMI of 24.3 and adults 40 years and older have a BMI of 24.7 (Figure 3.14).

FIGURE 3.15: ACFDR 2019: BMI BY GENDER FOR ADULTS 18+ YEARS



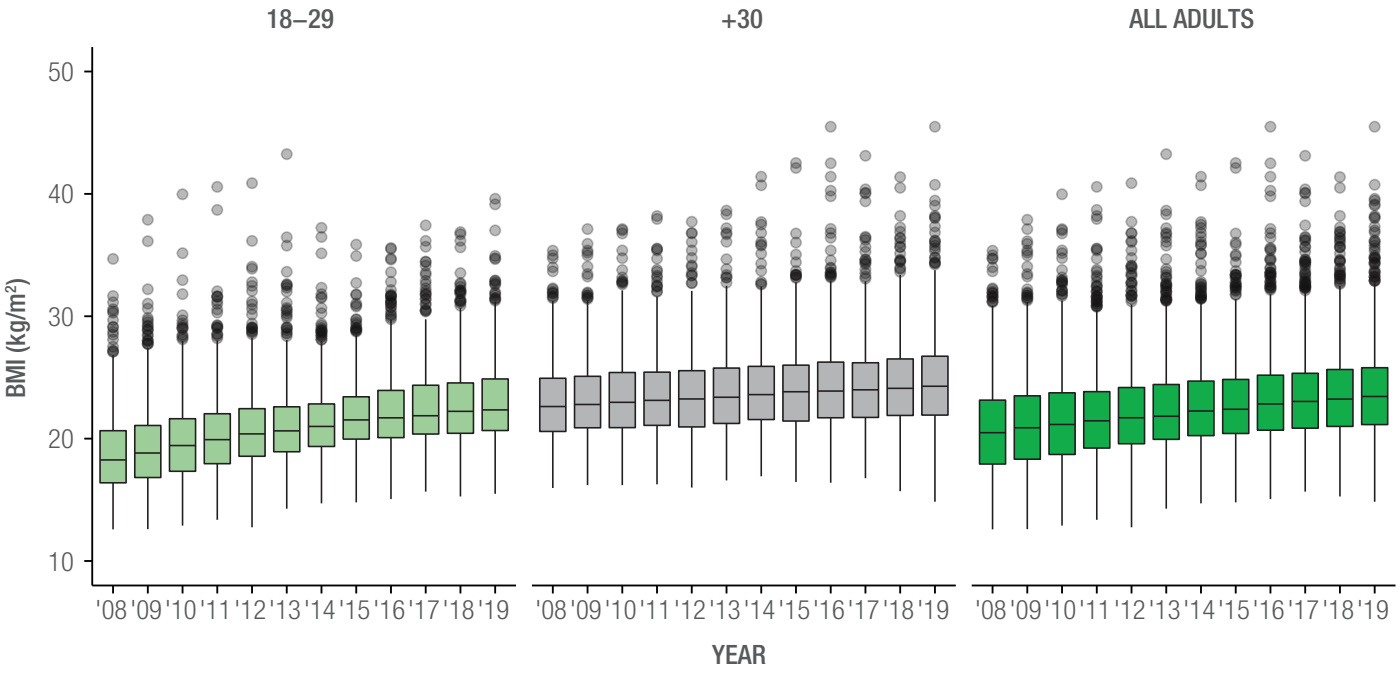
High BMI: BMI > 27 kg/m^2
Optimal: Female BMI 22–27 kg/m^2, Male BMI 23–27 kg/m^2
Acceptable: Female BMI 20–22 kg/m^2, Male BMI 20–23 kg/m^2
Suboptimal: BMI < 20 kg/m^2
Undernourished: BMI < 18.5

Adult males and females with CF are predominantly in the optimal and acceptable range for BMI, with the average BMI for males 24 and 23 for females. 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.

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 18.3 to 22.4; for adults over 30 years the median BMI has increased from 22.6 to 24.3. For all adults during 2001-2019 the median BMI has increased from 20.5 to 23.5.

FIGURE 3.16: ACFDR 2008-2019 MEDIAN ADULT BMI



79.4% of those with CF aged 12-17 years had at least 4 clinic visits in 2019.

4. CF MANAGEMENT

4.1 CLINICAL ENCOUNTERS

People with CF have regular clinical assessments, usually by a multidisciplinary team, to optimise their management. The total number of clinical encounters in 2019 was 33,358, of which 80% were outpatient visits at CF centres.

The Cystic Fibrosis Standards of Care Australia[2] (2008) provides for key standards of outpatient (clinic) care for people with CF. This includes that treatment should be co-ordinated by a multidisciplinary 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).

Ninety-four percent of people with CF had information regarding their clinical encounters recorded for 2019. The proportion of all people with CF who had at least 4 clinic visits in 2019 was approximately 71%, with the proportion being highest among 12-17 year olds at 79.4%, and lower among those 30 years and older at 65.4%. Information has been provided by 94% of people participating in the registry.

FIGURE 4.1: ACFDR 2019: PROPORTION OF PEOPLE WITH CF (BY AGE) HAVING 4 OR MORE OUTPATIENT (CLINIC) VISITS IN 2019

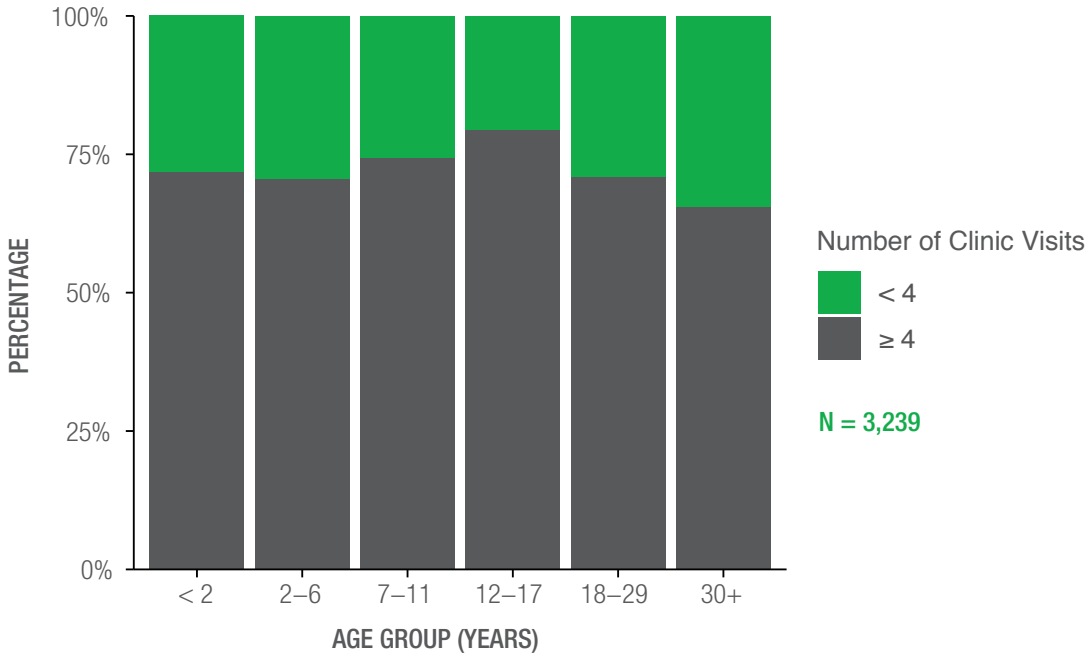


TABLE 4.1 – ACFDR 2019: NUMBER OF CLINICAL ENCOUNTERS IN 2019

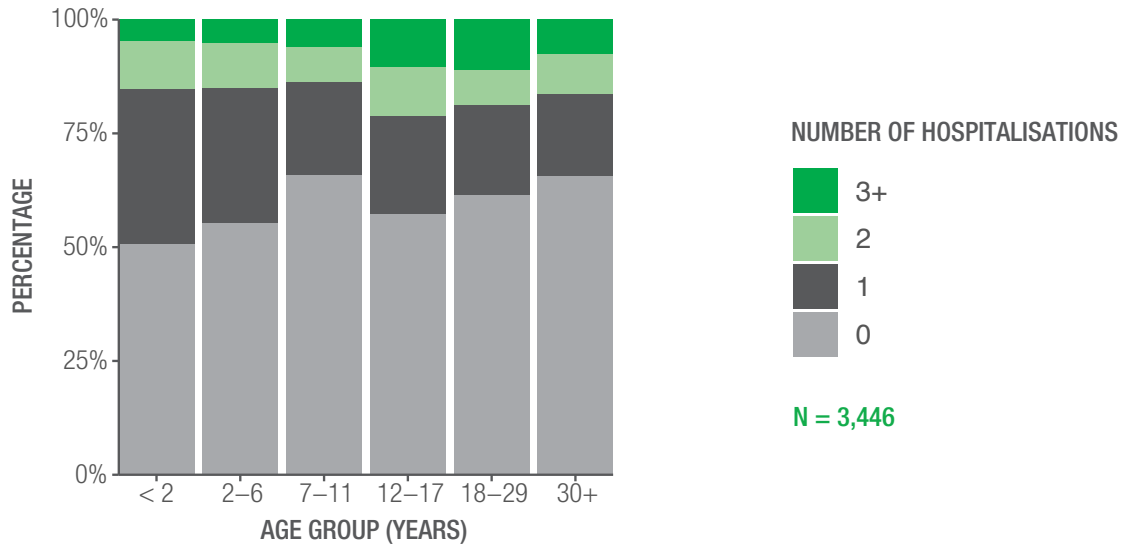
AGE	NUMBER WITH 4+ VISITS	%
< 2	84	71.8%
2-6	289	70.5%
7-11	323	74.3%
12-17	448	79.4%
18-29	587	70.8%
30+	578	65.4%
Total (mean)	2,309	71.0%

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

HOSPITALISATIONS

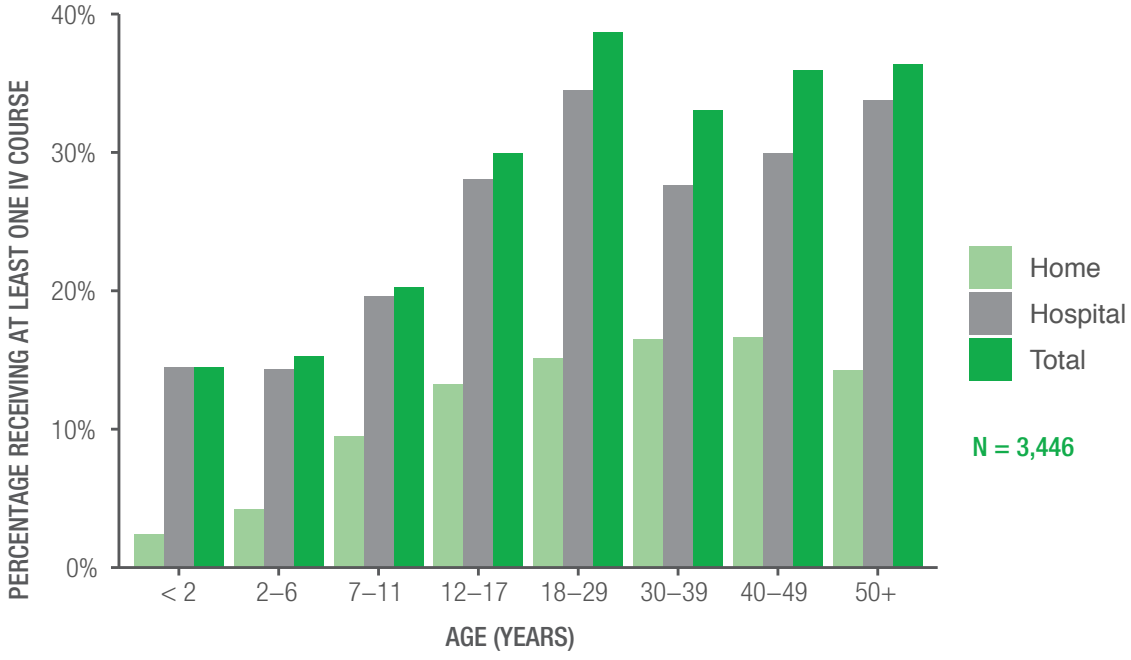
All people with CF had information regarding hospitalisations recorded in the ACFDR in 2019. In 2019, the majority (approximately 61%) of people with CF did not have any hospitalisations in 2019 (Figure 4.2). This proportion increased with increasing age, being 50.8% for children less than two years, and 65.7% for people with CF over 30 years of age. The proportion having one hospitalisation decreased with increasing age, while the proportion having three or more hospitalisations increased with increasing age, from 4.8% for children less than 2 years to 7.6% for people 30 years and over. This suggests that the majority of adults with CF are not requiring regular hospitalisation (perhaps this reflects survival bias due to less severe CF mutations in this group). However, from the teenage years into adulthood there is a small but significant cohort (approximately 10-11%) that require regular (3+ per year) hospitalisations.

FIGURE 4.2: ACFDR 2019: NUMBER OF HOSPITALISATIONS IN 2019 FOR PEOPLE WITH CF



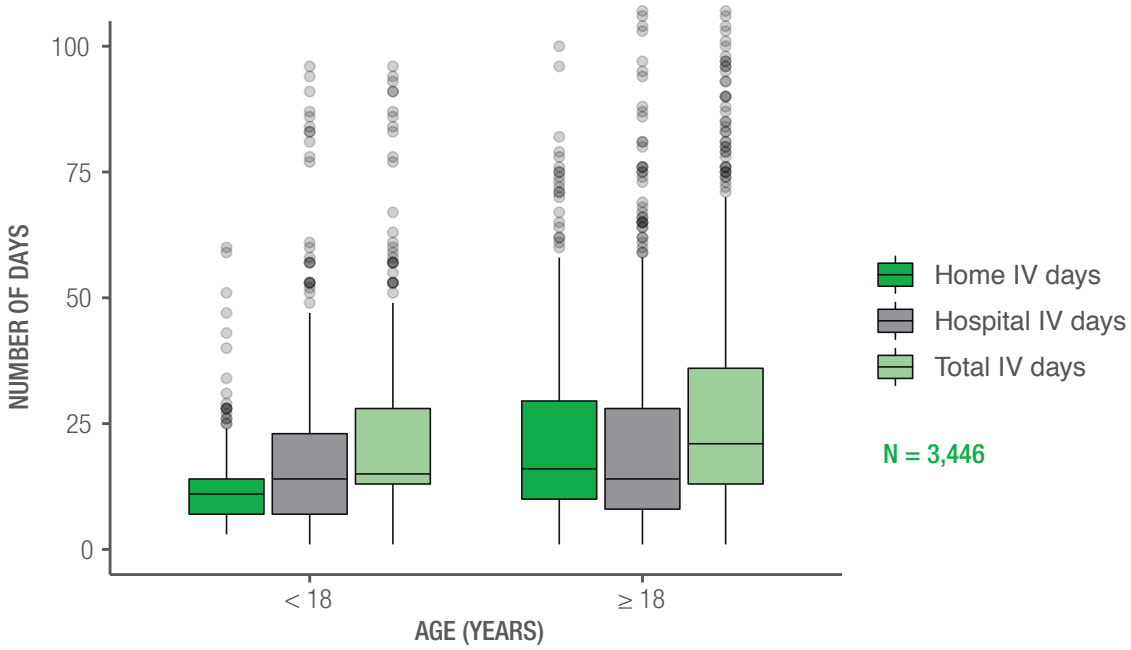
IV THERAPY

FIGURE 4.3: ACFDR 2019: PROPORTION OF PEOPLE WITH CF (BY AGE GROUP) RECEIVING AT LEAST ONE COURSE OF IV THERAPY IN 2019



In total, 22% of children and 36% of adults required IV therapy in 2019. The most common reason for hospitalisation for people with CF is to have intravenous (IV) antibiotics for a respiratory infection. The proportion of those requiring IV therapy in hospital increased from 15% for people less than 2 years of age, to 35% at 18-29 years of age and 34% at over 50 years of age. Similarly, the proportion having home IV therapy is only 2% for people less than two years of age, and is 17% for adults of ages 30 – 49 years. The overall total proportion of people with CF requiring home or hospital (total) IV therapy is 15% for very young children (< 2 years) to well over 30% for adults of all ages (peaking at 39% for young adults 18-29 years) (Figure 4.3).

FIGURE 4.4: ACFDR 2019: MEDIAN ACCUMULATED HOME AND HOSPITAL IV DAYS FOR PEOPLE WITH CF (CHILDREN VS ADULTS)



The median number of days that people with CF spent receiving IV therapy is shown in Figure 4.3.

The median number of accumulated days that people with CF spent receiving IV therapy in hospital was 14 days people for both children (< 18 years) and adults 18+ years). However, the median number of accumulated days receiving home IV therapy was higher for adults (16 days) compared with children (11 days). The median total accumulated (hospital and home) number of days people with CF who required IV therapy in 2019 was 15 days for children and 21 days for adults in 2019.

4.2 CFTR MODULATORS

A number of disease-modifying therapies for CF have been developed over the last few years, and have the potential to dramatically reduce symptoms and increase survival for an increasing number of people with CF. Different therapies target different genetic mutations, thus 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).

IVACAFTOR (KALYDECO®)

Ivacaftor was first approved for use in Australia on the PBS from July 2013 for people with CF who had the G551D gating mutation, estimated at approximately 6% of the CF population in Australia. It was initially approved for use in people with at least 1 copy of the G551D mutation in the CFTR gene of ages 6 years and older. It has since been expanded to include other gating mutations and most recently for people with the R117H mutation. The number of people potentially eligible for specific CFTR modulators in the tables below are shown in brackets; however the numbers are indicative only, as eligibility based on age and mutation varies during the reporting period.

TABLE 4.2 – ACFDR 2019: IVACAFTOR USE AS OF DECEMBER 2019

	TAKING IVACAFTOR AS OF 31ST DECEMBER 2019	TAKING IVACAFTOR AND DISCONTINUED AS OF 31ST DECEMBER 2019
12 months – 5 years (total 30)	18 / 30 (60.0%)	0 / 30 (0.0%)
6 + years (total 389)	243 / 389 (62.5%)	12 / 389 (3.1%)

The proportion of people with CF with gating mutations eligible for Ivacaftor who were taking Ivacaftor as of December 31, 2019 was 60% for children less than 5 years, and 62.5% for those six years and older (Table 4.2). Twelve people were previously using and discontinued Ivacaftor as of December 31, 2019. Reasons for discontinuation included intolerance/adverse event (1), pregnancy (1), switching to another CFTR modulator (3) and other, being moved to CFTR trial and transplant (7).

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 mutation, which comprises 47% 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 4.3 – ACFDR 2019: LUMACAFTOR/IVACAFTOR USE AS OF DECEMBER 2019

	TAKING LUMACAFTOR/IVACAFTOR AS OF 31ST DECEMBER 2019	PREVIOUSLY TAKING LUMACAFTOR/IVACAFTOR DISCONTINUED AS OF 31ST DECEMBER 2019
2 – 5 years (total 114)	14 / 114 (12.0 %)	0 / 114 (0.0 %)
6 + years (total 1,447)	757 / 1447 (52.0 %)	180 / 1,447 (12.0 %)

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 2019 was 52% (Table 4.3). Only 12% of the eligible population 2-5 years of age were taking it as of December 31st, however it had only been made available two months earlier. There have been 180 people who have discontinued this medication with reasons noted in Table 4.4. The most common reasons were pulmonary intolerance/side effect (29%), other intolerance/adverse event (25%), other (23%), switch to other CFTR modulator (14%) and liver impairment/intolerance (7%).

TABLE 4.4 – ACFDR 2019: REASONS FOR DISCONTINUATION OF LUMACAFTOR/IVACAFTOR AS OF DECEMBER 2019

N	REASON
52	Pulmonary side effect/intolerance
46	Other, intolerance/adverse event
41	Other reason (clinical trials, mental health, transplant, low adherence)
25	Switch to other CFTR modulator
13	Liver impairment/intolerance
2	Pregnancy
1	Concomitant drug interaction

TEZACAFTOR/IVACAFTOR (SYMDECO®)

Tezacaftor/Ivacaftor was approved for use in Australia on the PBS in March 2019 for people aged 12 and above with CF with two copies of the F508del mutation in the CFTR gene. It is also available for a people with one F508del mutation and one of a number of residual function mutations for which it is approved, including 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.

TABLE 4.5 – ACFDR 2019: TEZACAFTOR/IVACAFTOR USE AS OF DECEMBER 2019

	TAKING TEZACAFTOR/IVACAFTOR AS OF 31 DECEMBER 2019	PREVIOUSLY ON TEZACAFTOR/IVACAFTOR AND DISCONTINUED AS OF 31 DECEMBER 2019
12-17 years (total 254)	28 / 254 (11.0 %)	0 / 254 (0.0%)
18 + years (total 883)	111 / 883 (12.6 %)	7 / 883 (0.8 %)

As of December 2019 (less than 12 months after it was approved on the PBS), 11% of the eligible population of 12-17 year olds were taking Tezacaftor/Ivacaftor, and 12.6% of eligible adults were taking it (Table 4.5). Seven people had discontinued the medication during 2019; two due to intolerance/adverse event, 1 switched to another CFTR modulator, and 4 for other reasons (Transplants and social issues).

ELEXACAFTOR/TEZACAFTOR/IVACAFTOR (TRIKAFTA®)

Elexacaftor/tezacaftor/ivacaftor is a new CFTR modulator for people with CF who have at least one copy of the F508del mutation or another mutation that is approved. Currently, it 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 2019, 55 people with CF in Australia are recorded as having received elexacaftor/tezacaftor/ivacaftor.

4.3 MICROBIOLOGY

Of the 3,446 people with CF in 2019, 1,852 (53.7%) microbiology culture samples were taken in 2019. For children and young adults (< 24 years) the most common organism of samples collected in 2019 was S. *aureus* (peak at 66% for 11-17 year olds); and for adults > 25 years, the most common organism of samples collected in people with CF was P. *aeruginosa* (peak at 84% for 35-44 year olds) (Figure 4.5 and Table 4.6).

FIGURE 4.5: ACFDR 2019: RESPIRATORY MICROBIOLOGY BY AGE IN 2019

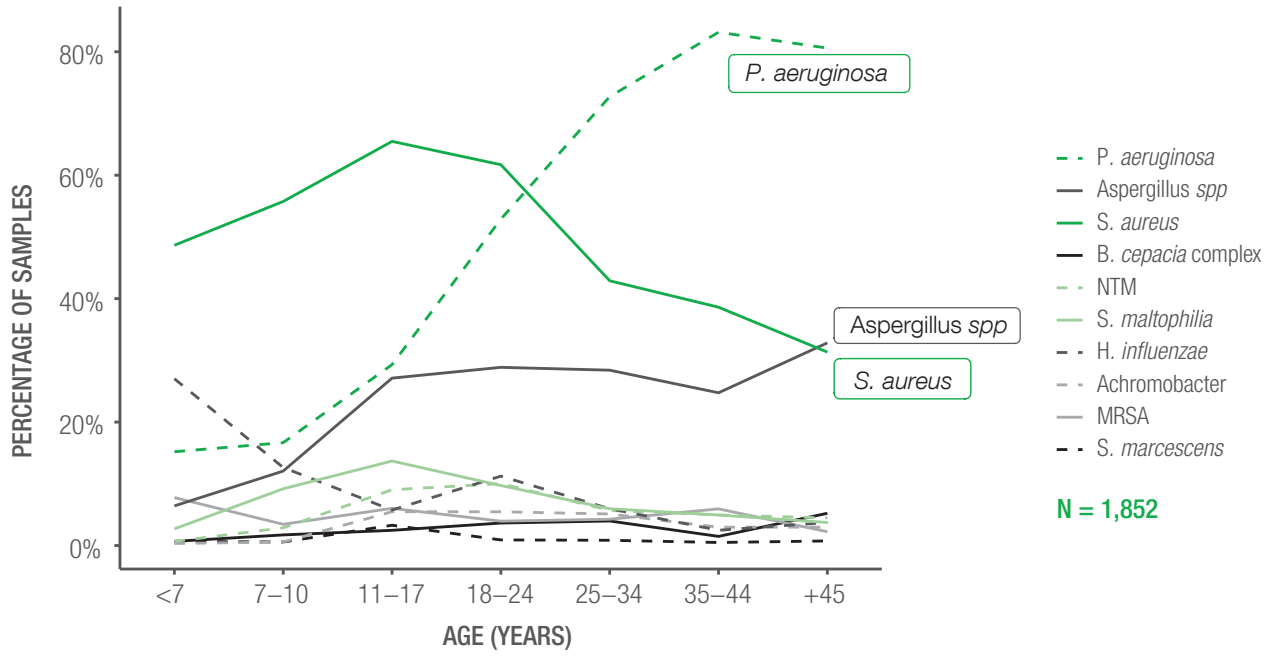


TABLE 4.6 – ACFDR 2019: RESPIRATORY MICROORGANISMS BY AGE IN 2019

BAL SAMPLES		ALL SAMPLES						
	< 7	< 7	7 - 10	11 - 17	18 - 24	25 - 34	35 - 44	45 +
No. in age range	550	550	348	694	535	656	400	263
No. of samples taken in 2019	88	303	164	361	330	346	202	136
P. *aeruginosa*	11 / 88 (12%)	45 / 303 (15%)	29 / 164 (18%)	105 / 361 (29%)	172 / 330 (52%)	254 / 346 (73%)	169 / 202 (84%)	108 / 136 (79%)
H. *influenzae*	17 / 88 (19%)	82 / 303 (27%)	21 / 164 (13%)	21 / 361 (6%)	37 / 330 (11%)	21 / 346 (6%)	5 / 202 (2%)	5 / 136 (4%)
B. *cepacia* complex	0 / 88 (0%)	2 / 303 (1%)	3 / 164 (2%)	9 / 361 (2%)	12 / 330 (4%)	14 / 346 (4%)	3 / 202 (1%)	7 / 136 (5%)
S. *aureus*	18 / 88 (20%)	144 / 303 (48%)	98 / 164 (60%)	238 / 361 (66%)	202 / 330 (61%)	149 / 346 (43%)	79 / 202 (39%)	42 / 136 (31%)
MRSA	2 / 88 (2%)	21 / 303 (7%)	6 / 164 (4%)	20 / 361 (6%)	13 / 330 (4%)	15 / 346 (4%)	11 / 202 (5%)	3 / 136 (2%)
Achromobacter	1 / 88 (1%)	1 / 303 (0%)	1 / 164 (1%)	22 / 361 (6%)	19 / 330 (6%)	18 / 346 (5%)	6 / 202 (3%)	4 / 136 (3%)
S. *maltophilia*	3 / 88 (3%)	9 / 303 (3%)	16 / 164 (10%)	54 / 361 (15%)	33 / 330 (10%)	21 / 346 (6%)	11 / 202 (5%)	5 / 136 (4%)
S. *marcescens*	0 / 88 (0%)	2 / 303 (1%)	1 / 164 (1%)	12 / 361 (3%)	3 / 330 (1%)	3 / 346 (1%)	1 / 202 (0%)	1 / 136 (1%)
Aspergillus *spp*	10 / 88 (11%)	22 / 303 (7%)	21 / 164 (13%)	104 / 361 (29%)	100 / 330 (30%)	102 / 346 (29%)	50 / 202 (25%)	44 / 136 (32%)
NTM	0 / 88 (0%)	2 / 303 (1%)	6 / 164 (4%)	35 / 361 (10%)	34 / 330 (10%)	20 / 346 (6%)	10 / 202 (5%)	7 / 136 (5%)

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

For children younger than seven years, lower airway samples may be taken by bronchoalveolar lavage (BAL). The most common organisms identified in this age group in 2019 included S. *aureus* (20%), H. *influenzae* (19%), P. *aeruginosa* (12%), Aspergillus *spp* (11%).

FIGURE 4.6: ACFDR 2019: RESPIRATORY MICROORGANISMS AGE LESS THAN 7 YEARS

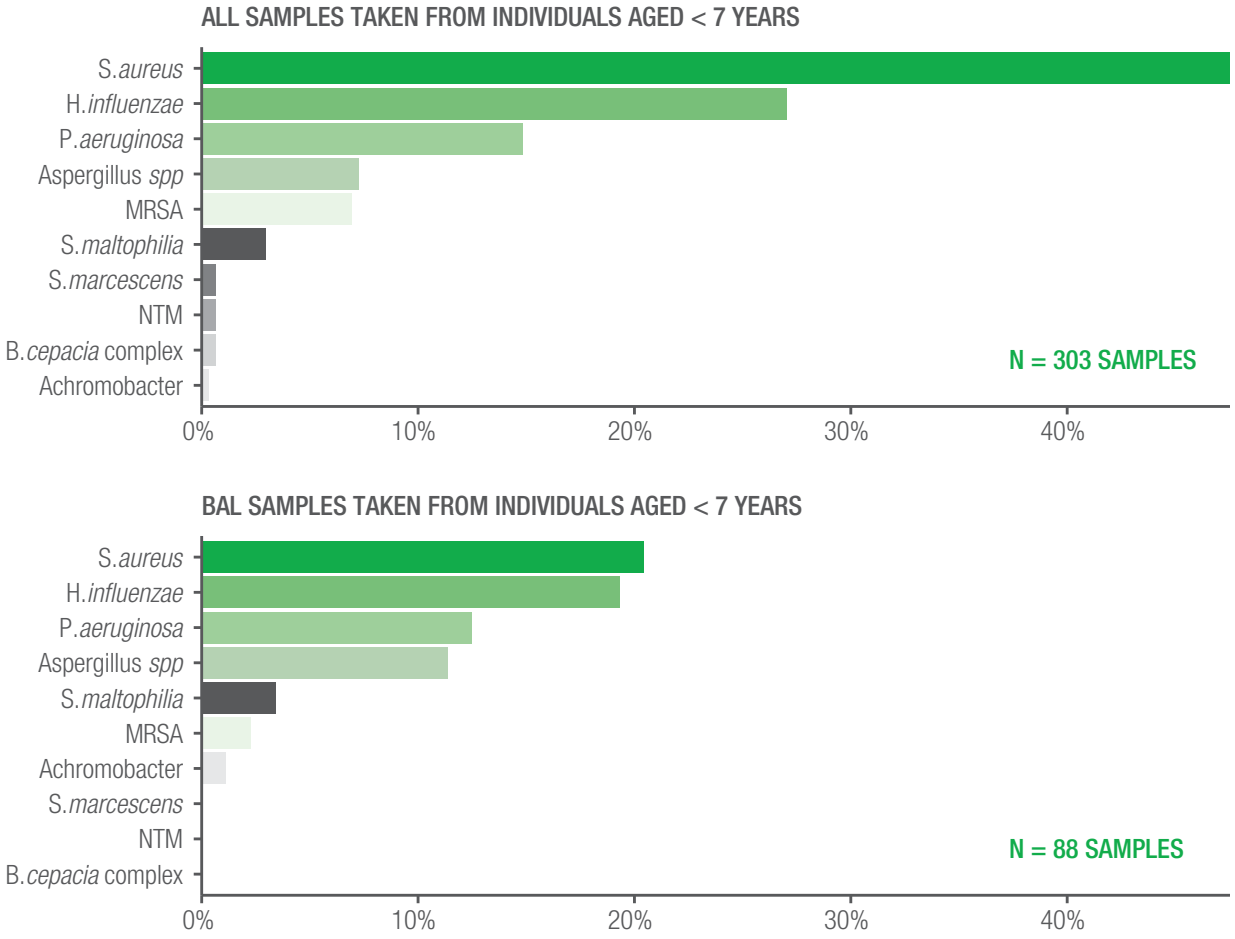
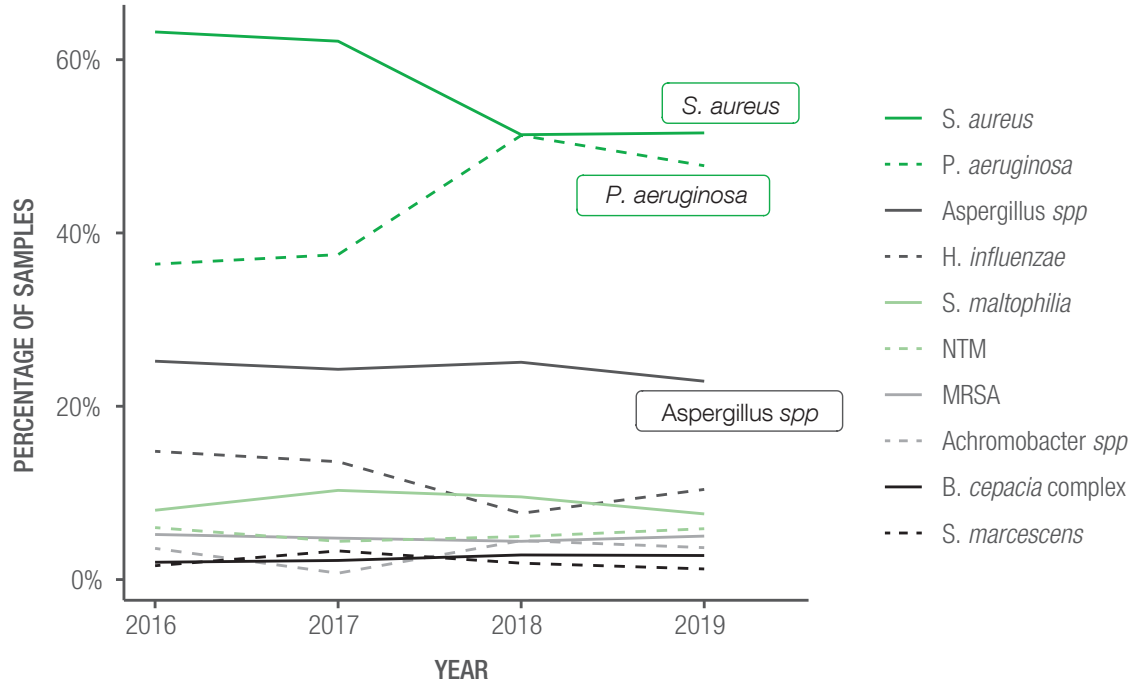


FIGURE 4.7: ACFDR 2016-2019: PREVALENCE OF RESPIRATORY MICROORGANISMS



The prevalence of some of the most common organisms has changed over the last 4 years. The prevalence of S. *aureus* was 63% for the samples taken from people with CF in 2016 and has decreased to 52% in 2019, while the prevalence of P. *aeruginosa* has increased from 36% in 2016 to 48% in 2019.

Others remained relatively steady throughout this period e.g. Aspergillus *spp* was prevalent in 25% in 2016 and remained at 23% in 2019; H. *influenzae* was 15% in 2016 and 10% in 2019; S. *maltophilia* remained at 8% in 2016 and 2019 and NTM remained at 6% for this period.

TABLE 4.7 – ACFDR 2019: NON-TUBERCULOUS MYCOBACTERIUM (NTM) INFECTION BY AGE

AGE (YEARS)	ORGANISM	2016	2017	2018	2019
< 7	NTM	0.0% (0 /37)	0.0% (0 /53)	0.0% (0 /148)	0.8% (2 /264)
	M. *abscessus*	0.0% (0 /37)	0.0% (0 /53)	0.0% (0 /148)	0.0% (0 /264)
7 - 11	*NTM*	3.8% (2 /53)	1.8% (1 /57)	5.7% (8 /141)	4.9% (10 /206)
	M. *abscessus*	0.0% (0 /53)	0.0% (0 /57)	5.0% (7 /141)	3.9% (8 /206)
12 - 17	*NTM*	8.2% (7 /85)	9.0% (8 /89)	6.8% (12 /177)	9.9% (28 /283)
	M. *abscessus*	2.4% (2 /85)	4.5% (4 /89)	4.0% (7 /177)	5.7% (16 /283)
18 - 30	*NTM*	8.3% (3 /36)	2.7% (1 /37)	6.8% (26 /385)	8.9% (45 /506)
	M. *abscessus*	0.0% (0 /36)	2.7% (1 /37)	2.3% (9 /385)	3.2% (16 /506)
30	*NTM*	8.6% (3 /35)	6.7% (2 /30)	4.5% (16 /354)	4.8% (23 /478)
	M. *abscessus*	2.9% (1 /35)	6.7% (2 /30)	2.3% (8 /354)	2.3% (11 /478)

Non-tuberculous mycobacterium (NTM) infection is negligible in the samples taken from the individuals below 7 years of age, however infection rates are higher in the samples taken from older teenagers and younger adults. NTM infection is at approximately 10% in samples taken from 12-17 year olds, and 9% in the samples taken from 18-30 year olds. M. *abscessus,* an organism that may be associated with a poor prognosis in CF, also has its highest rate of infection in the samples taken from 12-17 year olds, at 5.7%.

Approximately 1/3 of people with CF received macrolide or inhaled antibiotic therapy.

5. CF COMPLICATIONS AND THERAPIES

This chapter includes systemic complications and treatments related to the underlying pathophysiology of CF, including specific pulmonary complications and antibiotic and other 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 nutritional supplements and supports. While ACFDR data completeness for complications and treatments for people with CF has increased since 2017 from approximately 30% to 50%, it remains likely that the information in this Chapter has been under-reported. The following information relates to the whole ACFDR cohort for which information has been provided in 2019.

5.1 CF LUNG DISEASE AND PULMONARY COMPLICATIONS

TABLE 5.1 – ACFDR 2019: LUNG COMPLICATIONS BY AGE GROUPINGS

	< 12 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Haemoptysis	1/380 (0.3%)	11/228 (4.8%)	54/487 (11.1%)	57/540 (10.6%)	123/1,635 (7.5%)
Haemoptysis requiring embolization	0/380 (0.0%)	2/228 (0.9%)	4/487 (0.8%)	6/540 (1.1%)	12/1,635 (0.7%)
Pneumothorax	1/379 (0.3%)	0/228 (0.0%)	4/487 (0.8%)	3/540 (0.6%)	8/1,634 (0.5%)

*An individual may have more than one complication

Major lung complications such as a significant haemoptysis (bleeding from the lungs) or pneumothorax, were uncommon in 2019, with incidence increasing with increasing age.

5.2 PULMONARY THERAPIES

A mainstay of medical treatment for CF lung disease is preventive and therapeutic antibiotic therapy that may be as oral or inhaled. Use of intravenous antibiotics for acute infections is discussed in the previous chapter.

TABLE 5.2 - ACFDR 2019: CF PULMONARY DISEASE: ANTIBIOTIC THERAPIES

	< 6 YEARS	6-11 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Inhaled antibiotics	24/179 (13.4%)	43/203 (21.2%)	82/228 (36.0%)	176/520 (33.8%)	236/582 (40.5%)	561/1,712 (32.8%)
Regular oral antibiotics	66/179 (36.9%)	67/203 (33.0%)	82/228 (36.0%)	82/520 (15.8%)	88/582 (15.1%)	385/1,712 (22.5%)
Macrolides	5/179 (2.8%)	31/203 (15.3%)	42/228 (18.4%)	228/520 (43.8%)	311/582 (53.4%)	617/1,712 (36.0%)

Approximately one third of people with CF received macrolide or inhaled antibiotic therapy in 2019, 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 15% of adults.

TABLE 5.3 - ACFDR 2019: CF PULMONARY DISEASE: OTHER LUNG THERAPIES

	< 6 YEARS	6-11 YEARS	12-17 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Long oxygen therapy	0/177 (0.0%)	1/203 (0.5%)	2/228 (0.9%)	10/487 (2.1%)	24/541 (4.4%)	37/1,636 (2.3%)
Non-invasive ventilation	1/177 (0.6%)	1/203 (0.5%)	2/228 (0.9%)	24/487 (4.9%)	32/541 (5.9%)	60/1,636 (3.7%)

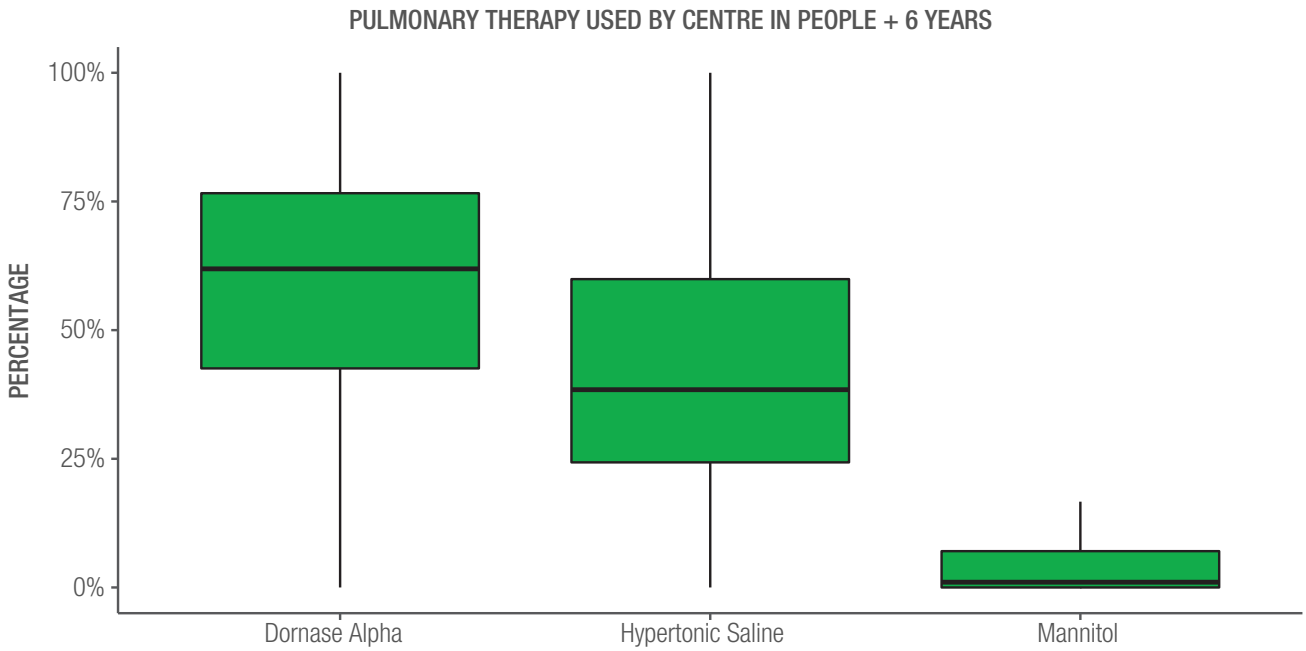
Non-invasive ventilation is used to support acute exacerbation in 5-6% of adults, whereas long term oxygen therapy is used to support 2.1% in 18-29 year olds, and 4.4% in 30 year olds (Table 5.3).

TABLE 5.4 - ACFDR 2019: CF PULMONARY DISEASE: LUNG THERAPY MEDICATIONS

	< 6 YEARS	6-11 YEARS	12-17 YEARS	18-29 YEARS	30 YEARS	TOTAL
Bronchodilators	25/179 (14.0%)	81/203 (39.9%)	114/228 (50.0%)	301/520 (57.9%)	320/582 (55.0%)	841/1,712 (49.1%)
Inhaled corticosteroids	7/179 (3.9%)	46/203 (22.7%)	73/228 (32.0%)	215/520 (41.3%)	248/582 (42.6%)	589/1,712 (34.4%)
Oral corticosteroids	4/179 (2.2%)	18/203 (8.9%)	20/228 (8.8%)	37/520 (7.1%)	77/582 (13.2%)	156/1,712 (9.1%)
Mannitol	0/179 (0.0%)	9/203 (4.4%)	20/228 (8.8%)	28/520 (5.4%)	20/582 (3.4%)	77/1,712 (4.5%)
Dornase alpha	49/179 (27.4%)	152/203 (74.9%)	188/228 (82.5%)	306/520 (58.8%)	314/582 (54.0%)	1009/1,712 (58.9%)
Hypertonic saline	56/179 (31.3%)	105/203 (51.7%)	134/228 (58.8%)	238/520 (45.8%)	242/582 (41.6%)	775/1,712 (45.3%)

Many people with CF are prescribed non-antibiotic lung therapies include muco-active therapies such as mannitol, hypertonic saline and dornase alpha, as well as bronchodilators and corticosteroids. In 2019, the most commonly used of these were dornase alpha (58.9%), bronchodilators (49.1%), hypertonic saline (45.3%), and inhaled corticosteroids (34.4%). Less commonly used were oral corticoid steroids (9.1%), mannitol (4.5%), non-invasive ventilation (3.7%) and long-term oxygen therapy (2.3%). 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 children of this age cannot use dry powder inhalers.

FIGURE 5.1: ACFDR 2019: USE OF PULMONARY THERAPIES BY CENTRE IN PEOPLE WITH CF AGES 6 YEARS AND OVER



The ends of the box are the upper and lower quartiles (25th and 75th percentiles)
The median is marked by a vertical line inside the box
The whiskers are the two lines outside the box that extend to the highest and lowest observations

The median use proportion of therapies by centre can be derived by calculating the use at each of the 24 CF centres, and then deriving the median of these centre proportions.

The median use of dornase alpha by CF centres was 61% of the CF population, for hypertonic saline was 38.4% and for mannitol was 1%, although the large variation in use at the centre level is shown in the box plots. These figures compared with those in Table 5.4 suggest that while dornase alpha was consistently used across most CF centres, that use of Hypertonic saline and Mannitol is more concentrated in fewer CF centres.

5.3 CF ENDOCRINE DISEASE

TABLE 5.5 - ACFDR 2019: DIABETIC STATUS FOR PEOPLE WITH CF BY AGE

	< 12 (N = 379)	12-17 (N = 228)	18-29 (N = 487)	30+ (N = 542)	TOTAL (N = 1,636)
Impaired glucose tolerance	8 (2.1%)	37 (16.2%)	89 (18.3%)	97 (17.9%)	231 (14.1%)
CF related diabetes	13 (3.4%)	51 (22.4%)	117 (24.0%)	165 (30.4%)	346 (21.1%)

More than 1 in 5 people with information regarding diabetic status (346 people, 21.1%) had a diagnosis of CF-related diabetes in 2019. The prevalence of diabetes increases with age, with 22.4% of 12-17-year old's having CFRD, increasing to 30.4% of people with CF over the age of 30 years.

TABLE 5.6 - ACFDR 2019: CF RELATED DIABETES (CFRD) TREATMENT BY AGE

	< 12 (N = 13)	12-17 (N = 51)	18-29 (N = 117)	30+ (N = 165)	TOTAL (N = 346)
Insulin	13 (100.0%)	49 (96.1%)	103 (88.0%)	136 (82.4%)	301 (87.0%)
Hypoglycaemics	0 (0.0%)	0 (0.0%)	1 (0.9%)	10 (6.1%)	11 (3.2%)
Insulin and hypoglycaemics	0 (0.0%)	0 (0.0%)	3 (2.6%)	4 (2.4%)	7 (2.0%)
Diet/lifestyle management only	0 (0.0%)	0 (0.0%)	8 (6.8%)	14 (8.5%)	22 (6.4%)
No treatment for diabetes	0 (0.0%)	2 (3.9%)	2 (1.7%)	1 (0.6%)	5 (1.4%)

Of the 346 people with CFRD recorded in the registry, 87% were managed primarily with insulin; 6.3% were managed by diet/lifestyle strategies, and 5.2% were treated with hypoglycaemics with or without insulin.

TABLE 5.7 - ACFDR 2019: INSULIN USE FOR PEOPLE WITH CFRD BY AGE

	< 12 (N = 13)	12-17 (N = 49)	18-29 (N = 106)	30+ (N = 140)	TOTAL (N = 308)
Intermittent insulin use	1 (7.7%)	3 (6.1%)	2 (1.9%)	3 (2.1%)	9 (2.9%)
Chronic insulin use	12 (92.3%)	46 (93.9%)	98 (92.5%)	128 (91.4%)	284 (92.2%)
Insulin use, duration unknown	0 (0.0%)	0 (0.0%)	6 (5.7%)	9 (6.4%)	15 (4.9%)

The vast majority (92%) of people with CFRD on insulin required chronic (ongoing) insulin.

TABLE 5.8 - ACFDR 2019: RELATED REDUCED BONE DENSITY (OSTEOPENIA, OSTEOPOROSIS) BY AGE

	10-17	18-29	30+	TOTAL
Osteopenia	43/105 (41.0%)	100/365 (27.4%)	166/463 (35.9%)	309/933 (33.1%)
Osteoporosis	5/105 (4.8%)	19/365 (5.2%)	49/463 (10.6%)	73/933 (7.8%)
Fracture	14/288 (4.9%)	6/463 (1.3%)	10/500 (2.0%)	30/1,251 (2.4%)

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 (933 people), 33% had osteopenia, and approximately 8% had osteoporosis, with 2.4% reporting a fracture in 2019.

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.

TABLE 5.9 - ACFDR 2019: GASTROINTESTINAL COMPLICATIONS ASSOCIATED WITH PANCREATIC INSUFFICIENCY BY AGE

	< 12	12-17	18-29	30+	TOTAL
Gastric oesophageal reflux	30/379 (7.9%)	47/228 (20.6%)	153/487 (31.4%)	227/541 (42.0%)	457/1,635 (28.0%)
Abnormal liver function (elevated enzymes)	41/380 (10.8%)	40/228 (17.5%)	94/487 (19.3%)	146/540 (27.0%)	321/1,635 (19.6%)
Liver disease, non-cirrhosis (includes viral hepatitis, fatty liver)	6/343 (1.7%)	3/190 (1.6%)	21/398 (5.3%)	27/408 (6.6%)	57/1,339 (4.3%)
Liver disease, cirrhosis (image confirmed)	4/340 (1.2%)	2/189 (1.1%)	13/397 (3.3%)	15/403 (3.7%)	34/1,329 (2.6%)
Liver disease, cirrhosis with portal hypertension	0/339 (0.0%)	7/192 (3.6%)	13/402 (3.2%)	12/402 (3.0%)	32/1,335 (2.4%)
Acute (first pancreatitis event this current year)	0/351 (0.0%)	1/209 (0.5%)	2/472 (0.4%)	0/513 (0.0%)	3/1,545 (0.2%)
Pancreatitis, not specified	1/351 (0.3%)	0/209 (0.0%)	1/472 (0.2%)	7/513 (1.4%)	9/1,545 (0.6%)
Recurrent pancreatitis	1/351 (0.3%)	4/209 (1.9%)	12/472 (2.5%)	26/513 (5.1%)	43/1,545 (2.8%)

Approximately 28% of persons with CF with complications reported in the ACFDR had gastro-oesophageal reflux and 19.6% had abnormal liver function. Small proportions of patients had liver disease or pancreatitis. All complications increased with increasing age.

5.5 NUTRITIONAL SUPPLEMENTS

For 2019, the reported use of pancreatic enzymes and nutritional supplements is below:

TABLE 5.10 - ACFDR 2019: PEOPLE WITH CF WHO RECEIVED NUTRITIONAL SUPPLEMENTS BY AGE

	< 12 (N = 382)	12 - 17 (N = 228)	18 - 29 (N = 520)	30 + (N = 582)	TOTAL (N = 1,712)
Pancreatic enzymes	268 (70.2%)	191 (83.8%)	400 (76.9%)	418 (71.8%)	1,277 (74.6%)
Vitamin supplements	268 (70.2%)	178 (78.1%)	371 (71.3%)	395 (67.9%)	1,212 (70.8%)
Salt tablets	158 (41.4%)	118 (51.8%)	192 (36.9%)	151 (25.9%)	619 (36.2%)

As can be seen from Table 5.9, the proportion of people with CF from each age group who take pancreatic enzymes is closely correlated with the proportion who are pancreatic insufficient (from those who reported this information). A high proportion (approximately 70%) of people with CF also take vitamin supplements, with approximately one third of people taking salt tablets. These supplements are reported across all age groups.

TABLE 5.11 - ACFDR 2019: NUTRITIONAL SUPPORT

	<12 (N = 382)	12-17 (N = 228)	18-29 (N = 520)	30+ (N = 582)	TOTAL (N=1,712)
Gastrostomy tube	24 (6.3%)	26 (11.4%)	15 (2.9%)	3 (0.5%)	68 (4.0%)
Nasogastric tube	9 (2.4%)	9 (3.9%)	2 (0.4%)	4 (0.7%)	24 (1.4%)
Oral supplements	34 (8.9%)	35 (15.4%)	58 (11.2%)	44 (7.6%)	171 (10.0%)
Jejunostomy tube	1 (0.3%)	0 (0.0%)	1 (0.2%)	1 (0.2%)	3 (0.2%)
Total parenteral nutrition	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	1 (0.1%)

Use of supplemental enteral nutrition is required to treat poor weight gain or weight loss not improved with oral supplements and dietary intake, particularly in children. The proportion of people with CF with information recorded in the ACFDR who required nutritional support was small. While 10% required oral supplemental nutrition, very few required enteral feeding, and of those the majority were via gastrostomy tube.

In 2019, there were 33 bilateral lung transplants for people with CF.

6. TRANSPLANTATION AND SURVIVAL

6.1 TRANSPLANTATION

For a majority of people with CF, progressive respiratory deterioration is the primary cause of death, and lung transplantation may improve life expectancy and quality of life. In Australia approximately 33-40% of lung transplants are performed in adults with CF[3]. 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.

TABLE 6.1 – ACFDR 2019: BILATERAL LUNG TRANSPLANTS IN PEOPLE WITH CF

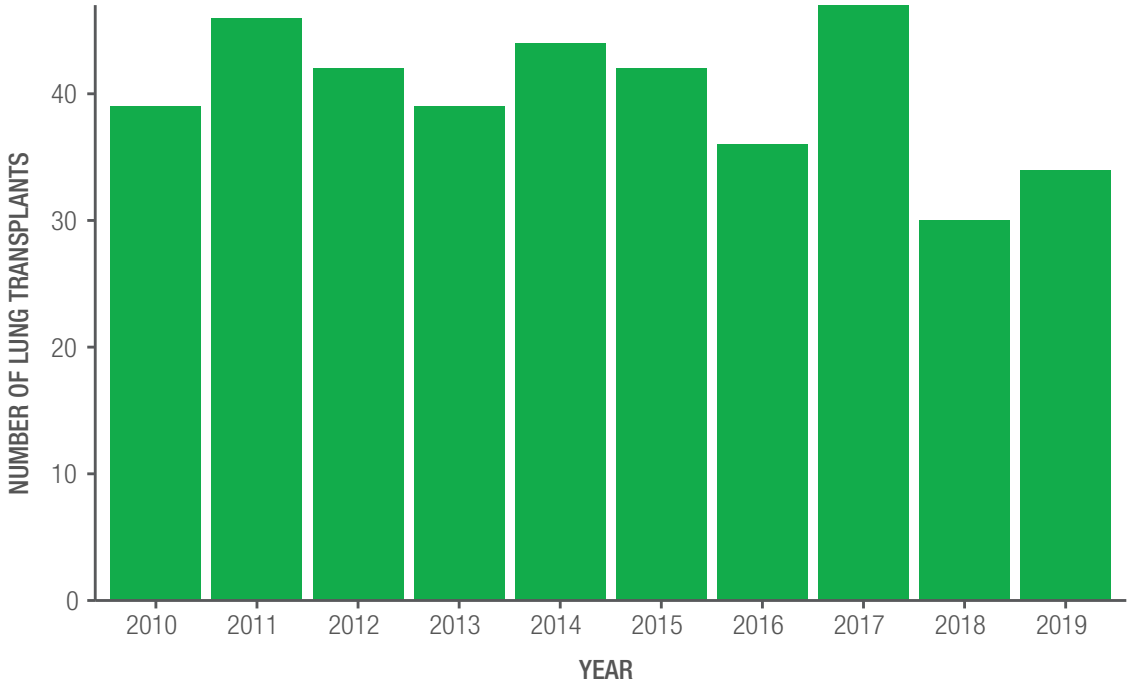
BILATERAL LUNG TRANSPLANTS	< 18 YEARS	18-29 YEARS	30+ YEARS	TOTAL
Male	1	4	9	14 (42%)
Female	1	7	11	19 (58%)
Total	2	11	20	33 (100%)

In 2019, there were 33 bilateral lung transplants for people with CF. Forty-two percent of these were for males and fifty-eight percent were for females. Over 60% of bilateral lung transplants were undertaken on people with CF of ages 30 years and older; with one third of transplants occurring for people of ages 18-29 years. Two bilateral lung transplants were undertaken in children < 18 years.

In 2019, two young adults (18-29 years) had another organ transplanted, one with a kidney, and one with a liver. One older adult (30+ years) had a multi-organ transplant (heart, bilateral lung and liver).

The number of annual bilateral lung transplants undertaken over the last decade is shown in Figure 6.1 below.

FIGURE 6.1: ACFDR 2010-2019: BILATERAL LUNG TRANSPLANTS IN PEOPLE WITH CF



3. 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 (alive/deceased) is updated annually by CF centres. Periodically data linkage is undertaken with national death to validate death data. This is undertaken via probabilistic matching due to the de-identified nature of the data.

In 2019 the ACFDR recorded the deaths of 26 people with CF. Fifteen (58%) of these deaths occurred in people aged 30 years and over, ten deaths (39%) occurred in young adults (18-29 years), and one death occurred in a person less than 18 years. The causes of 2019 deaths were primarily related to post-transplant complications of the underlying pulmonary manifestations of CF, as represented in Table 6.2, below.

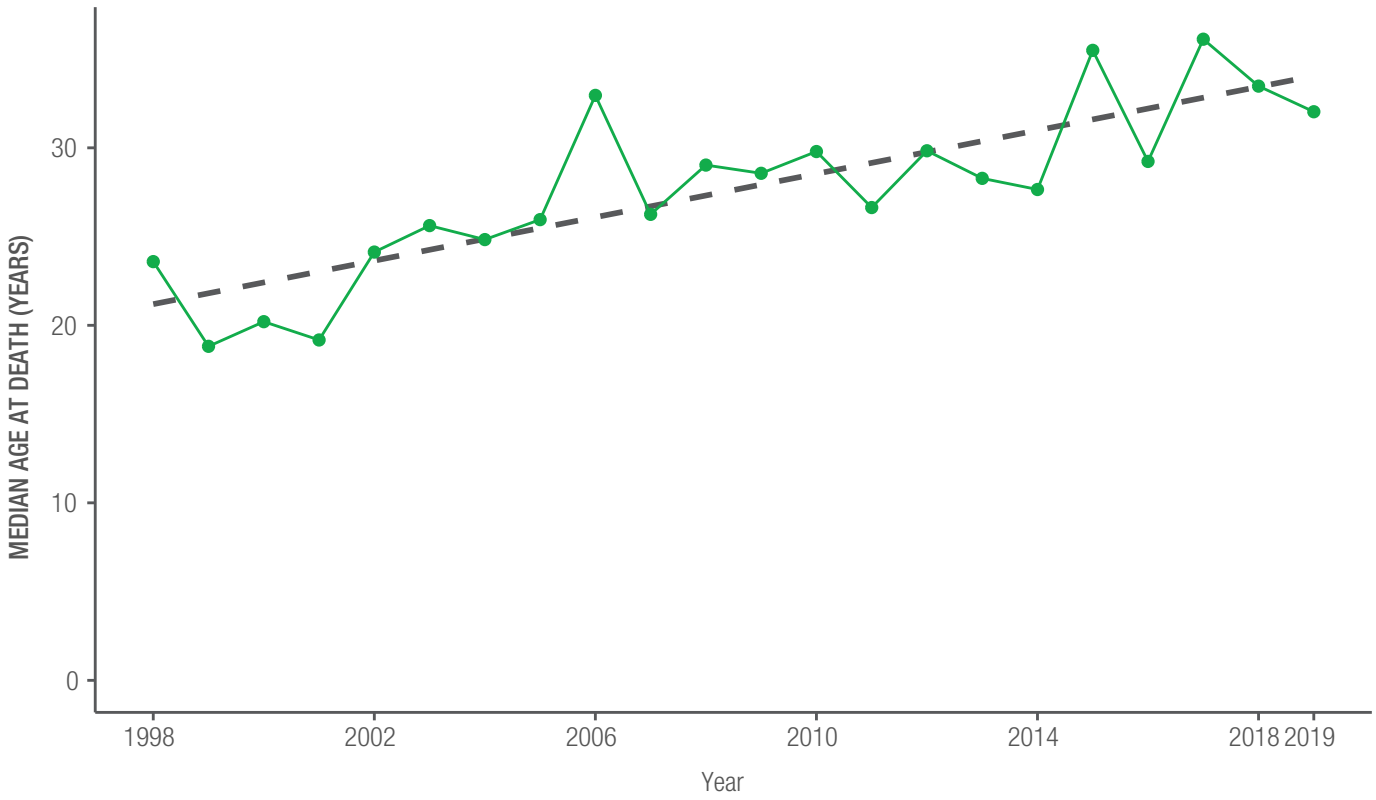
TABLE 6.2 – ACFDR 2019: CAUSES OF DEATH FOR PEOPLE WITH CF

CAUSE OF DEATH	< 29 YEARS	30+ YEARS	TOTAL
CF related post-transplant complications	5	4	9 (34.6%)
CF with pulmonary manifestations	2	6	8 (30.8%)
CF-related other/unspecified	1	1	2 (7.6%)
Death unrelated to CF	1	1	2 (7.6%)
CF with intestinal manifestations	0	1	1 (3.8%)
Unknown/missing	2	2	4 (15.4%)
Total	11	15	26

6.3 MEDIAN AGE OF DEATH

The median age of the deaths in 2019 was 32 years of age. The median age of death for the period 2010-2019 was 31, while the median age of death for the ACFDR from 1998 was 27.3, highlighting the increasing age of the population with CF in Australia (Figure 6.2). 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 1998-2019: 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.

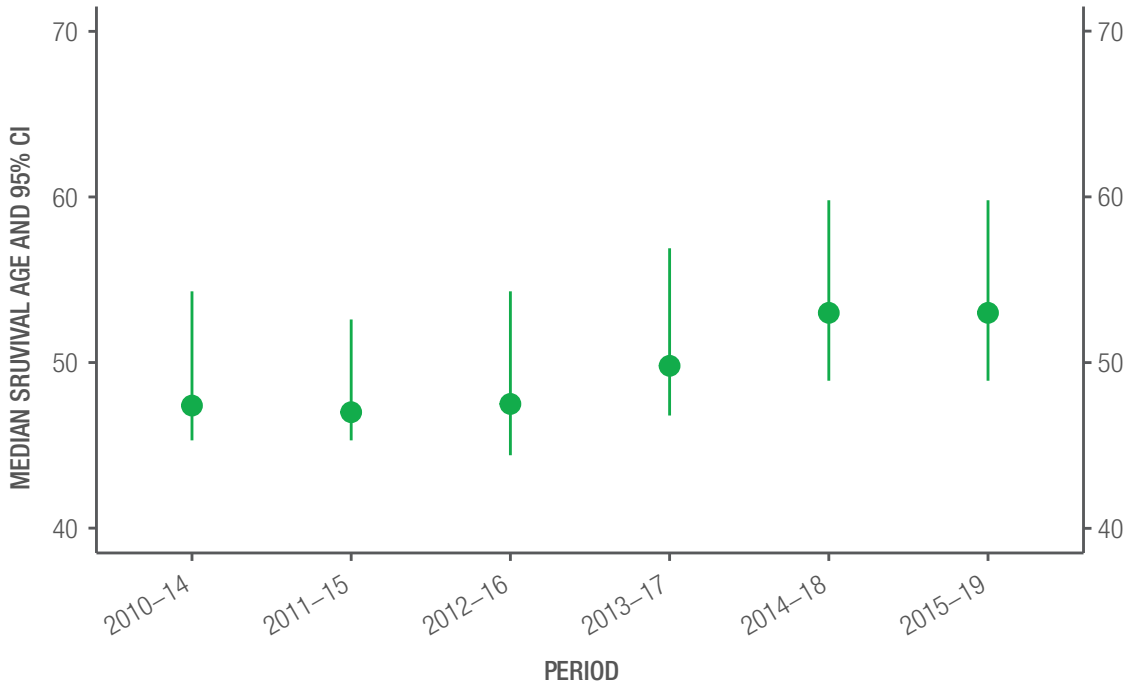
Median survival can be expressed in 5-year cohorts (Table 6.3, Figure 6.1), or for the total ACFDR cohort (Table 6.3).

TABLE 6.3 – ACFDR 2010-2019: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA (5-YEAR COHORTS AND 10 YEAR SURVIVAL)

PERIOD	MEDIAN AGE (95% CI)	N AT RISK	N DEATHS
2010-14	47.4 (45.3-54.3)	3,401	172
2011-15	47.0 (45.3-52.6)	3,431	171
2012-16	47.5 (44.4-54.3)	3,503	177
2013-17	49.8 (46.8-56.9)	3,526	170
2014-18	53.0 (48.9-59.8)	3,676	166
2015-19	53.0 (48.9-59.8)	3,724	169
2010-19	51.2 (48.9-56.3)	4,130	341

Table 6.3 (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 years for people with CF born in 2015-2019. The median survival for people with CF born in the last 10 years is 51.2 years.

FIGURE 6.3: ACFDR 2010-2019: MEDIAN SURVIVAL OF PEOPLE WITH CF IN AUSTRALIA (5-YEAR COHORTS)



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 core ACFDR data for 2019, and the percent of data available for 2019.

TABLE 7.1 – ACFDR 2019: DATA AVAILABILITY

DATA ITEM	2019		
	TOTAL *	NUMBER	PERCENT
Demographics *Aboriginal & Torres Strait Islander Status *Country of Birth	3,568	3,565	100%
Diagnosis *Date of CF diagnosis *Clinical signs/symptoms *Diagnosis sweat test *Pancreatic status *Genetic mutation dDetails	3,568	3,525	99%
Clinical measures Q1	3,568	3,472	97%
Clinical measures Q2	3,568	3,451	97%
Clinical measures Q3	3,568	3,430	96%
Clinical measures Q4	3,568	3,425	96%
Hospitalisations/home IV Q1	3,568	3,447	97%
Hospitalisations/home IV Q2	3,568	3,420	96%
Hospitalisations/home IV Q3	3,568	3,408	96%
Hospitalisations/home IV Q4	3,568	3,394	95%
CFTR modulators	3,568	3,385	95%
Transplants	3,568	3,362	94%
Annual sign off *Annual general update *Transplant details *Social details	3,568	3,353	94%
Overall data entry % completed for 2019 records			95.80%

This table includes all records of people with CF including those that are shared and transferred between CF centres.

8. ACADEMIC OUTPUTS

PRESENTATIONS

1. Ruseckaite R. PROMs in the Australian Cystic Fibrosis Data Registry. 13th Australasian Cystic Fibrosis Conference 2019, Perth, 2019 (Invited talk)
2. Ratnayake I. Measuring Quality of Life in Cystic Fibrosis. 13th Australasian Cystic Fibrosis Conference 2019, Perth, 2019 (Invited talk)
3. Ahern S. Utilising the ACFDR for Real World Outcomes 13th Australasian Cystic Fibrosis Conference 2019, Perth, 2019 (Invited talk)
4. Ruseckaite R., Ahern S., Earnest A., King S., Schultz A., Middleton P, Bell S. Survival of Patients with Cystic Fibrosis: A Longitudinal Study Using Australian Patient Registry Data. 42nd European Cystic Fibrosis Conference, Liverpool, 2019
5. Ahern S., Ruseckaite R., Dean J., Emerging registry uses requires adaptable systems: reinventing the Australian Cystic Fibrosis Data Registry (ACFDR). 42nd European Cystic Fibrosis Conference, Liverpool, 2019
6. Ruseckaite R., Ahern S., Salimi F., Earnest A., Bell S. on behalf of the Australian Cystic Fibrosis Data Registry Steering Committee. Survival and Mortality in Cystic Fibrosis: Observations from a Data Linkage Study of the Australian Patient Registry and National Death Index. NHMRC Symposium on Research Translation, Melbourne, 2019
7. Ruseckaite R., Ahern S. Ratnayake I. Measuring What Matters: Health-Related Quality of Life in Patients with Cystic Fibrosis. 33rd North American Cystic Fibrosis Conference, Nashville, 2019
8. Ruseckaite R., Ahern S. Ratnayake I. Patient-Reported Outcome Measures in Cystic Fibrosis. 26th Annual Conference of International Society for Quality of Life Research, San Diego, 2019

9. DATA ACCESS REQUESTS

The ACFDR encourages the secondary use of its data for research and related purposes.

Nine data access requests were received and approved for the ACFDR in 2019.

DATE	NAME	ORGANISATION	REQUEST TYPE	REQUEST	OUTPUTS
31/01/2019	Jan Howie	CF Western Australia	Non-research	Prevalence of major organisms in lungs	
14/02/2019	Maxine Orre	Vertex Pharmaceuticals	Non-research	ACFDR data availability and completeness	
25/02/2019	Donald Anderson	John Hunter Children's Hospital	Research	Audit-change in clinic management	
20/03/2019	Peter Wark	John Hunter Adults Hospital	Research	JHH Adults audit of clinical practice	
15/04/2019	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	Oral Presentation at the Australasian Cystic Fibrosis Conference (2019). Title: "Longitudinal study of the Real life clinical Outcomes in Australian Patients with Cystic fibrosis." AWARD: Best oral presentation in Quality improvement SIG.
20/05/2019	James Trauer/ Milinda Abayawardana	Monash University, Epidemiological Modelling Unit	Non-research	A feasibility study –ACFDR Data Visualisation utilising Microsoft Power BI (MS-PBI)	
4/06/2019	Arul Earnest	Monash University	Research	Lung function over the life course of people with Cystic Fibrosis	Earnest A., Salimi F., Wainwright C., Bell SB., Ruseckaite R., Ranger T., Kotsimbos T., Ahern S. Lung function over the life course of paediatric and adult patients with cystic fibrosis: a large multi-centre longitudinal registry-based study. Sci Rep. 2020 Oct 15;10(1):17421. doi: 10.1038/s41598-020-74502-1.
8/10/2019	Kate Gonski	Sydney Children's Westmead	Research	Implications of CO2 retention in children with Cystic Fibrosis (CF)- a 15-year follow-up	
10/12/2019	Peter Middleton	Westmead Hospital	Research	Audit of Pregnancy outcomes in women with CF in Australia	

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

Figure 1.1	ACFDR 2019: People with CF in Australia by Age
Figure 1.2	ACFDR 2019: People with CF by Age and Gender
Figure 1.3	ACFDR 1998-2019: People with CF – Paediactric VS Adults Profile Over Time
Figure 1.4	ACFDR 2019: People with CF– Distribution by State/Territory
Figure 1.5	ACFDR 2019: Highest Educational Attainment of People with CF
Figure 1.6	ACFDR 2019: Employment Status of People with CF
Figure 1.7	ACFDR 2019: Marital Status of People with CF
Figure 2.1	ACFDR 1998-2019: People With CF– Age at Diagnosis for Whole Cohort
Figure 2.2	ACFDR 1998-2019: Method Of Diagnosis and Presenting Symptoms/Signs
Figure 2.3	ACFDR 2009-2019: Percentage of ACFDR Cohort with Genotype Complete
Figure 2.4	ACFDR 1998-2019: Most Common CFTR Mutation Combinations in People with CF
Figure 2.5	ACFDR 2019: Most Common Individual Allele CFTR Mutation in the ACFDR
Figure 3.1	ACFDR COHORT: Best Median FEV1PP by Age
Figure 3.2	ACFDR COHORT: Lung Function by Age and Sex
Figure 3.3	ACFDR COHORT: Median FEV1PP by Age and for Total Cohort
Figure 3.4	ACFDR COHORT: Median FEV1PP Over Time
Figure 3.5	ACFDR 2019: FEV1PP VS BMI Percentile for Persons with CF Ages 6-17 Years
Figure 3.6	ACFDR 2019: Median FEV1PP VS BMI For Persons With CF Ages 18-30 Years
Figure 3.7	ACFDR 2019: Nutritional Outcomes for Infants < 24 Months
Figure 3.8	ACFDR 2019: BMI, Weight and Height Percentiles Ages 2-17 Years
Figure 3.9	ACFDR 2019: Height Percentiles Children Ages 2-17 Years
Figure 3.10	ACFDR 2019: Weight Percentiles Children Ages 2-17 Years
Figure 3.11	ACFDR 2019: BMI Percentiles Children Ages 2-17 Years
Figure 3.12	ACFDR 2009-2019: Median Nutritional Status Percentiles Children 2-17
Figure 3.13	ACFDR 2009-2019: Median Child-Adolescent BMI
Figure 3.14	ACFDR 2019: BMI Adults 18+ Years
Figure 3.15	ACFDR 2019: Nutritional Outcomes By Gender For Adults 18+ Years
Figure 3.16	ACFDR 2008-2019 Median Adult BMI
Figure 4.1	ACFDR 2019: Proportion of People with CF (By Age) Having 4 or More Outpatient (Clinic) Visits in 2019
Figure 4.2	ACFDR 2019: Number of Hospitalisations in 2019 for People with CF
Figure 4.3	ACFDR 2019: Proportion of People with CF (By Age Group) Receiving at Least One Course of IV Therapy in 2019
Figure 4.4	ACFDR 2019: Median Accumulated Home and Hospital IV Days for People with CF (Children Vs Adults)
Figure 4.5	ACFDR 2019: Respiratory Microbiology by Age in 2019
Figure 4.6	ACFDR 2019: Respiratory Microorganisms Age Less than 7 Years
Figure 4.7	ACFDR 2016-2019: Prevalence of Respiratory Microorganisms
Figure 5.1	ACFDR 2019: Use of Pulmonary Therapies by Centre in People with CF Ages 6 Years and Over
Figure 6.1	ACFDR 2010-2019: Bilateral Lung Transplants in People with CF
Figure 6.2	ACFD 1998- 2019: Median Age of Death for People with CF in Australia
Figure 6.3	ACFDR 2010-2019: Median Survival of People with CF in Australia (5-Year Cohorts)

List of Tables

Table 1.1	ACFDR 2019: People with CF By Age and Gender
Table 2.1	ACFDR 2019: Age at Diagnosis for Newly Diagnosed Persons with CF
Table 2.2	ACFDR 1998-2019: Comparison of Diagnostic Characteristics for Total Cohort VS 2019 New Diagnoses
Table 3.1	ACFDR 1998-2019: FEV1PP < 70% by Age and Sex
Table 3.2	ACFDR 2019: Nutritional Status for Children < 2 – 17 Years: Females
Table 3.3	ACFDR 2019: Nutritional Status for Children < 2 – 17 Years: Males
Table 3.4	ACFDR 2019: Pancreatic Sufficiency and Nutritional Outcomes Ages 2-17 Years
Table 4.1	ACFDR 2019: Number of Clinical Encounters in 2019
Table 4.2	ACFDR 2019: IVACAFTOR Use as of December 2019
Table 4.3	ACFDR 2019: LUMACAFTOR/IVACAFTOR Use as of December 2019
Table 4.4	ACFDR 2019: Reasons For Discontinuation of LUMACAFTOR/IVACAFTOR as of December 2019
Table 4.5	ACFDR 2019: TEZACAFTOR/IVACAFTOR Use as of December 2019
Table 4.6	ACFDR 2019: Respiratory Microorganisms By Age In 2019
Table 4.7	ACFDR 2019: Non-Tuberculous Mycobacterium (NTM) Infection by Age
Table 5.1	ACFDR 2019: Lung Complications by Age Groupings
Table 5.2	ACFDR 2019: CF Pulmonary Disease: Antibiotic Therapies
Table 5.3	ACFDR 2019: CF Pulmonary Disease: Other Lung Therapies
Table 5.4	ACFDR 2019: CF Pulmonary Disease: Lung Therapy Medications
Table 5.5	ACFDR 2019: Diabetic Status for People with CF by Age
Table 5.6	ACFDR 2019: CF Related Diabetes (CFRD) Treatment by Age
Table 5.7	ACFDR 2019: Insulin Use For People With Cfrd by Age
Table 5.8	ACFDR 2019: Related Reduced Bone Density (Osteopenia, Osteoporosis) by Age by Age
Table 5.9	ACFDR 2019: Gastrointestinal Complications Associated with Pancreatic Insufficiency by Age
Table 5.10	ACFDR 2019: People with CF Who Received Nutritional Supplements by Age
Table 5.11	ACFDR 2019: Nutritional Support
Table 6.1	ACFDR 2019: Bilateral Lung Transplants in People with CF
Table 6.2	ACFDR 2019: Causes of Death for People with CF
Table 6.3	ACFDR 2010-2019: Median Survival of People with CF in Australia (5-Year Cohorts and 10 Year Survival)
Table 7.1	ACFDR 2019: Data Availability

ACFDR Steering Committee Membership (2019)

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 Morgan Gollan	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 and Children's Hospital (WCH)	Paediatric
Perth Children's Hospital (PCH)	Paediatric
Sir Charles Gairdner Hospital (SCG)	Adult
Royal Hobart Children's 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

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 (0)3 9903 1656

Access to Registry data

Requests for information from the Australian Cystic Fibrosis Data Registry are welcome.

Application should be made to the ACFDR Coordinating Centre, Monash University.

Email: **med–acfdregistry@monash.edu**

Sponsors

MONASH University

DESIGNED AND PRODUCED BY MPS MONASH: 373538 MARCH 2021. CRICOS PROVIDER: MONASH UNIVERSITY 00008C.