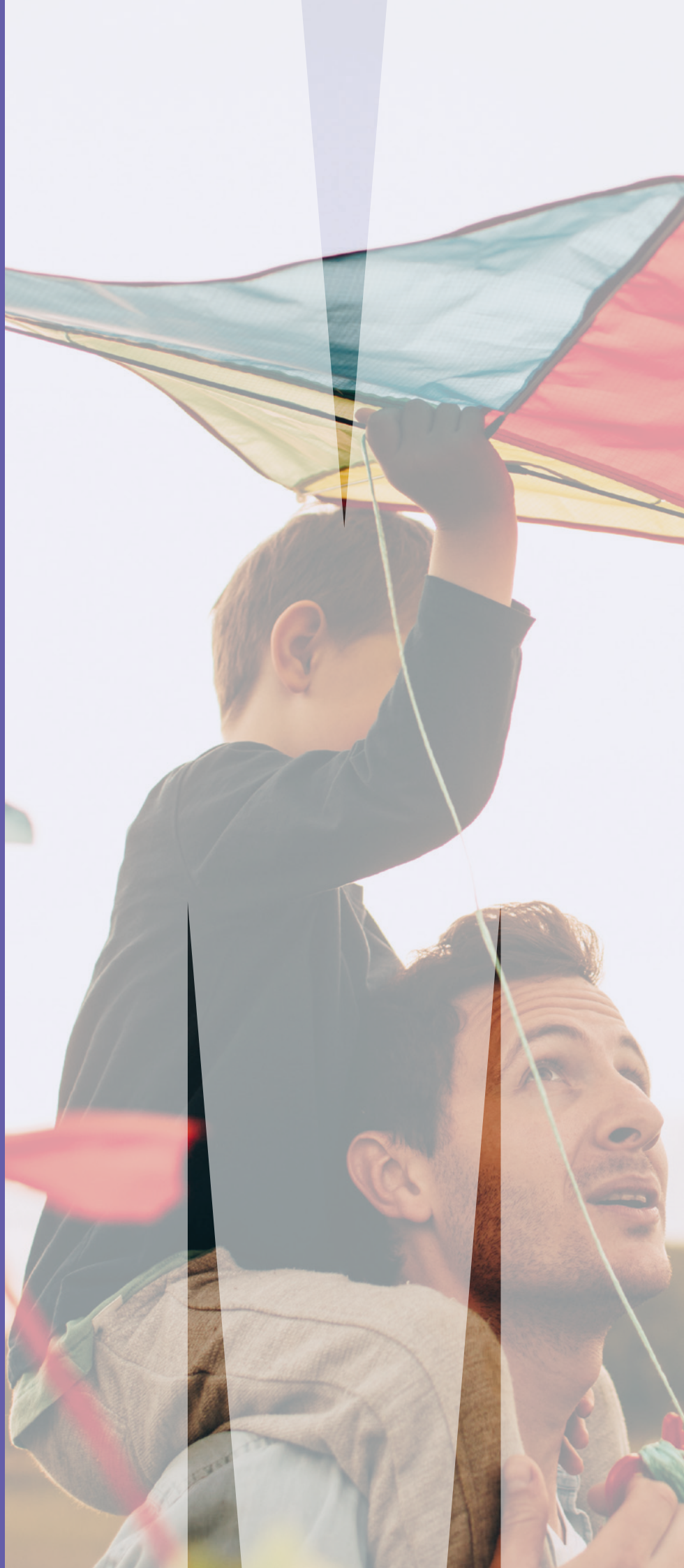
MONASH University

AUSTRALIAN CYSTIC FIBROSIS DATA REGISTRY

ANNUAL REPORT 2015

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



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Australian Cystic Fibrosis Data Registry
Monash University
Level 2, 553 St Kilda Rd,
Melbourne Vic 3004
Phone +61 3 9903 1656
Email: med–acfdregistry@monash.edu

FOREWORD

It is a great pleasure to deliver this 18th Annual Report from the Australian Cystic Fibrosis Data Registry (ACFDR) for the year 2015.

This Annual Report is a testament to the large amount of information gathered by Cystic Fibrosis Centres and the innovative science surrounding the treatment of cystic fibrosis (CF). As treatment discoveries continue to make lives better for people with cystic fibrosis the ACFDR will provide us with a clinical perspective and the important statistics that will continue to improve patient care.

This report has noted a steady upward trend in the age of Australians with CF. In 2014, the proportion of individuals with CF who were adult was 51.1 per cent, however in 2015 the proportion has grown to 52 per cent. This increase is a tribute to people with CF, their families and support networks who participate in the vigorous treatment regimens and the clinical teams who provide the highest standards of care and patient commitment.

The exceptional treatment provided by CF Centres and the introduction of life extending treatments and drugs means that people with CF can live a life like any other. Furthermore, some CF Centres recorded details such as family and marital status, education and activity in the community of CF patients. It's additional detail like this that helps us gain a greater understanding of the less readily apparent but crucial flow on effects CF has in our community.

Cystic Fibrosis Australia is well aware of the burdens this disease imposes and we plan to support mental health services for families, partners, siblings and support networks and this is something that motivates me. One significant step forward is Consumer Connect, CFA's new online forum, there to provide information and connectivity for the whole CF community.

Over the past 12 months Monash University Registry Sciences Unit has managed the ACFDR professionally and with a real commitment to improving CF lives and I have enjoyed working with them. The ACFDR Steering Committee is a talented and knowledgeable group who can guide the ACFDR into a great future.

I thank all the CF teams throughout the country who are not only committed to providing exceptional care to their patients, but for their time spent contributing data to the ACFDR.

Finally, CFA is genuinely grateful to the families and individuals who selflessly share their health outcomes and information. I thank you for your unrelenting commitment to our mission to improve lives for people with cystic fibrosis.

The steady upward trend in the age of Australians with CF… is a tribute to people with CF, their families and support networks… and the clinical teams who provide the highest standards of care

Nettie Burke
Chief Executive Officer
Cystic Fibrosis Australia
October 2017.

CYSTIC FIBROSIS Australia

INTRODUCTION

It is with great pleasure that I present the Annual Report of the Australian Cystic Fibrosis Data Registry (ACFDR) for the year 2015.

Funded by Cystic Fibrosis Australia (CFA) and endorsed by the Thoracic Society of Australia and New Zealand (TSANZ), the ACFDR collaborates with the Centre Directors of Australia's twenty–three cystic fibrosis centres to collect and analyse data relating to Australia's cohort of patients with cystic fibrosis. The overarching aim of the ACFDR is to monitor patients with cystic fibrosis to increase understanding of their disease and best practice management, with the aim of improving health service delivery, quality of care and patient outcomes.

The ACFDR has been assisted and informed since its inception in 1996 by a committed Advisory Committee, most recently chaired by Dr Peter Cooper. In September 2016, the operational management of the ACFDR was transferred to the Department of Epidemiology and Preventive Medicine, Monash University. It was also decided to broaden the governance of the ACFDR and establish a multi–disciplinary Steering Committee for the Registry. As chair of the new Steering Committee I would like to thank my predecessor, Peter, and previous members of the Advisory Committee for their strong stewardship of the ACFDR over nearly two decades.

The overarching aim of the ACFDR is… improving health service delivery, quality of care and patient outcomes

I would like to thank the members of the Monash University ACFDR team for their assistance in the preparation of this report, including the Registry's long–serving Director and Data Manager, Geoff Sims; Academic Lead, Susannah Ahern; Registry Data Analysts, Mark Tacey and Michael Esler and many others. This 2015 report introduces the new Steering Committee membership, describes developments in the progress of the ACFDR, and like its predecessors provides an annual snapshot of clinical information relating to Registry participants with cystic fibrosis in Australia.

I give sincere thanks to CFA and their financial contributors for their ongoing funding, interest and support in this important Registry. Additionally, I gratefully acknowledge the contribution from clinical staff from hospitals that participate in the ACFDR, and from their patients who have also agreed to participate. This report would not have been possible without the support from committed physicians, nursing staff, data managers and the many cystic fibrosis patients for whom this seeks to provide better care.

Professor Scott Bell, MBBS, FRACP, MD
Clinical Lead, Australian Cystic Fibrosis Registry

Executive Director – Research
Metro North Hospital and Health Service

Senior Physician, Department of Thoracic Medicine
The Prince Charles Hospital

Data Period

The data contained in this document was extracted from the Australian Cystic Fibrosis Data Registry on 29th August 2017 and pertains to data that relates to patient events from January 1st to December 31st 2015. 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
FEV_1	Forced expiratory volume (litres) in 1 second
GLI	Global Lung Initiative
MRSA	Methicillin–resistant Staphylococcus aureus
TPN	Total parenteral nutrition
WHO	World Health Organisation

EXECUTIVE SUMMARY

Governance & Management

- The Australian Cystic Fibrosis Data Registry (ACFDR) commenced data collection in 1998 under management of its funder, Cystic Fibrosis Australia and with the support of an Advisory Committee of senior cystic fibrosis physicians until mid–2016. From September 2016, operational management of the Registry was transferred to the Department of Epidemiology and Preventive Medicine, Monash University.
- In accordance with the Australian Commission on Safety and Quality in Healthcare's Operating Principles and Technical Standards for Clinical Quality Registries (2008) and Framework for Clinical Quality Registries (2014), the ACFDR has transitioned to a centralised ethics and governance process. The ACFDR received ethics approval for this from the Alfred Hospital Human Research Ethics Committee (HREC) in February 2017.
- In December 2016 the previous Advisory Committee was transitioned to a multidisciplinary Steering Committee comprising cystic fibrosis physicians, an allied health representative, a consumer representative, a health service representative, the CEO of Cystic Fibrosis Australia, and Monash University academics. A revised ACFDR Protocol and new Data Access Policy was endorsed by the Steering Committee at its first meeting.
- The new Protocol reflects extended aims for the Registry including to support ongoing review and development of the ACFDR's dataset and clinical indicators; to review and monitor trends in patient outcomes as measured by key indicators over time; to facilitate clinical trial data collection; and to undertake data linkage studies with other significant datasets, registries and biobanks.
- The ACFDR has enhanced its communication with stakeholders through initiation of a quarterly newsletter.

Registry Demographics & Diagnosis

- At the end of 2015, the ACFDR held records of 3,379 Australians with cystic fibrosis (CF), believed to capture over 90% of the eligible population of patients with CF. This includes 98 new diagnoses since 2014.
- The median age of the Registry population was 18.8 years at 31 December 2015, an increase from 18.4 years reported in 2014. Similarly, the proportion of the Registry population that is adult (18 years and over) increased to 52.0 percent in 2015, from 51.1 percent in 2014.
- CF diagnosis was generally reported (73%) within the first 3 months of age, and was determined following neonatal screening in approximately 50% of reported cases.
- The proportion of patients who were pancreatic insufficient was 82.2%, and the proportion with sweat chloride levels of ≥ 60 mmol/L was 71%.
- The most common genetic mutation remains F508del which is present in 92.1% of participants.

Clinical Measures

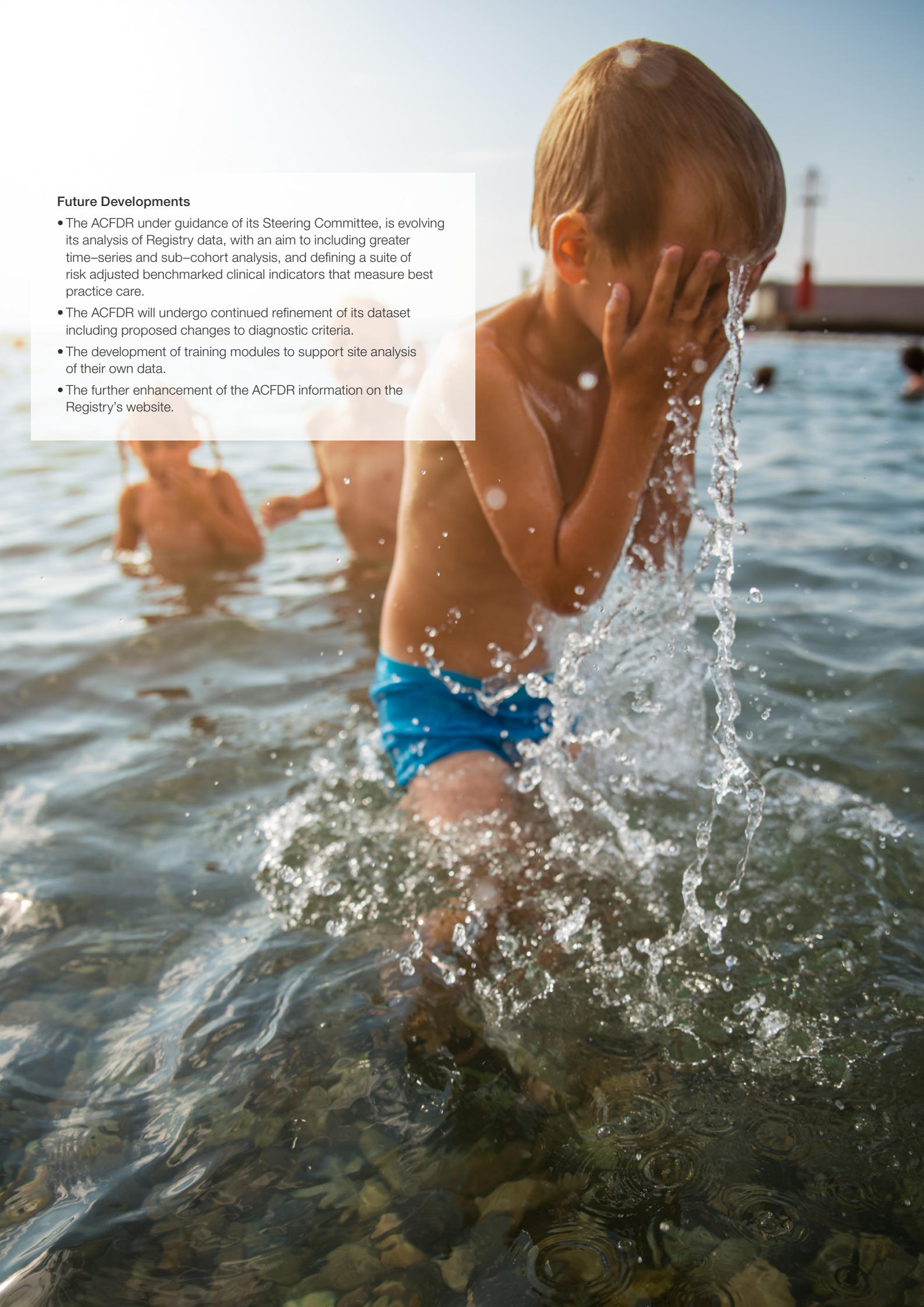
- Clinical information collected by the ACFDR included respiratory infections, medical complications, lung function and nutritional measures.
- Summary of lung function findings:
  - Approximately 5% of 6–11 yr age group have FEV_1 values < 70% predicted
  - Approximately 13% of 12–17 yr age group have FEV_1 values < 70% predicted
  - 16% of adult (18+ yr) males and 12% of adult females have FEV_1 values < 40% predicted
  - Only 16.2% of adults have FEV_1 values ≥ 90% predicted (normal).
- Summary of nutritional findings:
  - Median height percentile for 2–5 yr children is above 60%, but falls below 50% for 6–11 yr and below 45% for 12–17 yr age groups;
  - 45.4 percent of males and 46.7 percent of female children and adolescents were below the 50th percentile for BMI;
  - Approximately 56–7% of adults had an average BMI score in the 20 to 25 range;
  - 25% of adult females and 15% of males had an average BMI score < 20.
- The proportion of CF patients with gastro–oesophageal reflux, insulin–dependent diabetes or osteoporosis is 33.4%, 20.5% and 5.9% respectively.

Patient Management

- Antibiotic therapy use summary
  - 93.6% of CF patients were prescribed continuous or PRN antibiotic therapy in 2015, and more than 88% of patients in each age group;
  - Half of antibiotic users used inhaled antibiotics, with this proportion generally greater in older age groups.
- Lung transplantation data
  - 44 patients were accepted for lung transplants, and 30 patients actually received a lung transplant.
- Mortality
  - 17 patients were reported to have died in 2015.

Registry Quality Assurance

- Similar to international Registry comparisons, completeness of ACFDR data varies depending on the data item, but also varies by hospital. Interpretation of data analysis should therefore be undertaken with this in mind.
- ACFDR data completeness ranged from a high of 95–100% for Demographic, Clinical Measurement, and Genotype data; but was much lower for Complications and Social data, at < 50%.



Future Developments

- The ACFDR under guidance of its Steering Committee, is evolving its analysis of Registry data, with an aim to including greater time–series and sub–cohort analysis, and defining a suite of risk adjusted benchmarked clinical indicators that measure best practice care.
- The ACFDR will undergo continued refinement of its dataset including proposed changes to diagnostic criteria.
- The development of training modules to support site analysis of their own data.
- The further enhancement of the ACFDR information on the Registry's website.

BACKGROUND

Cystic Fibrosis (CF) is a chronic, inherited, multisystem disease affecting primarily the lungs and digestive system. It is an autosomal recessive disorder caused by mutations in the cystic fibrosis transmembrane regulator (CFTR) gene, and manifests as dysfunction of the exocrine system responsible for producing saliva, sweat, tears and mucus. The defect results in a range of clinical conditions across multiple organs including chronic obstructive lung disease, exocrine pancreatic insufficiency, liver disease, sinusitis, intestinal obstruction, failure to thrive and malnutrition, and dehydration due to abnormally high sweat sodium and chloride levels. Although the symptoms and conditions of CF are variable between patients, lung disease and progressive respiratory impairment are the primary causes of morbidity and mortality.

CF is a common inherited disorder with birth prevalence in Australia reported herein to be approximately 1:3700. Approximately 1 in 25 Australians are carriers of a genetic mutation responsible for CF. In Australia, all babies are screened for CF and the most common genetic mutation is the F508del mutation.

The treatment and management of CF is life–long and intensive. Due to its complexity and multi–systemic involvement there is a need for a range of specialists for the overall management of CF patients. A dedicated centre with a multi–disciplinary team provides the best outcome for patients with CF. Studies have reported improved clinical outcomes due to pulmonary function preservation and improved nutritional status for CF patients managed in specialist CF centres. There are currently twenty–three specialist CF centres in Australia. These sites are the mainstay of CF treatment and provide the source of patient information from which Australian Cystic Fibrosis Data Registry (ACFDR) data is derived.

The ACFDR is a long standing Registry which commenced in 1996. Since 1998 it has collected diagnostic and treatment data on over 90% of the population of cystic fibrosis patients in Australia, leading to a greater understanding of the disease's characteristics and the standard and type of care provided to patients across Australia.

Patients diagnosed with CF are invited to participate in the Registry through their treating site. Patients less than 18 years of age will consent to participate through their parent or legal guardian. Data about a CF patient's diagnosis, treatment and related complications are collected regularly with the aim to improve health service delivery and better understand the treatment of CF and outcomes for patients. The ACFDR dataset enables reporting in a manner generally consistent with other CF registries, such as in Europe, the United Kingdom and the United States.

Registry Governance

Until recently the ACFDR operated with Cystic Fibrosis Australia (CFA) as the data custodian and operator of the Registry. Following a tender process, as of 1st September, 2016 the ACFDR is being managed by the Department of Epidemiology and Preventive Medicine (DEPM), Monash University in Melbourne. Monash University is responsible for the management of the operational, governance and reporting aspects of the Registry under a shared data custodianship arrangement with CFA.

Clinician oversight of the ACFDR has since its inception been by an Advisory Committee, comprised of senior respiratory physicians. In 2016 it was agreed to transition to a broad–based Steering Committee that now includes in addition to respiratory physicians, an allied health representative, a health service representative, a consumer, representatives of Monash University, and the CEO of CFA. The role of the Steering Committee is to lead the strategic direction of the ACFDR, to review requests for access to ACFDR data, to develop and review relevant ACFDR policies and procedures, and to review the quality of outputs from the Registry. Additionally, the Chair of the Steering Committee participates in a monthly Management Committee meeting with Monash University staff to provide regular clinical input into the operations of the Registry.

The ACFDR conforms to the national operating principles for clinical quality registries, as set out by the Australian Commission of Safety and Quality in Healthcare (ACSQHC). It received ethical approval that reflected the new management of the Registry by Alfred Health in February 2017. Patient recruitment is by the specialist CF centres, utilising opt–in consent for paediatric patients, and opt–in consent or opt–out process for adult patients.

Data collection is generally submitted by most sites by direct data entry using the ACFDR web–based interface. Additionally, the ACFDR has been working closely with those health services utilising electronic patient systems for their Registry data collection. Though these systems are complex and their use still evolving, the ACFDR recognises their potential for high quality data capture that will reduce the data collection burden for health service staff in the future.

The ACFDR provides a publicly–available Annual Report and Jurisdictional Reports. It also provides annual reports to centres regarding centre data trends and comparisons. The ACFDR data may also be accessed by or analysed and provided to researchers and other interested parties. A new Data Access Policy endorsed by the Steering Committee outlines this process. The ACFDR has also commenced a quarterly newsletter publication to its key stakeholders including participating sites and physicians, and which is made available on the CFA website.

1. PEOPLE WITH CYSTIC FIBROSIS

1.1 Overview

At 31 December 2015 the Australian Cystic Fibrosis Data Registry (ACFDR) held records of 3,379 people with cystic fibrosis, 81 more than at the end of 2014.

The mean age of the Registry population was 20.9 years at 31 December 2015. This was up from 20.5 years reported in 2014. Reflecting a steady upward trend in age of Australians with CF, the proportion of the Registry population that is adult (18 years and over) increased to 52.0 percent in 2015, from 51.1 percent in 2014. For the second year running, more than half of the Australian CF population as recorded by the Registry is adult. Only one third of patients were adult in 1999, when all major adult centres first contributed data to the Registry.

The median age of 18.8 years at 31 December 2015 is also higher than at the end of previous years, having been 18.4 in 2014 and 17.9 in 2013. Median age for males (19.7 years) remained higher than that for females (18.0 years) in 2015, although both increased by approximately six months.

An increase of 81 in the overall number of registrants in 2015 is approximately equal to the excess of new diagnoses in (98) over deaths (17) reported.

1.2 Age distribution

Figure 1.1 and Table 1.1 show the age distribution of patients in the ACFDR for 2015. The lower table area shows age alternative CF age groupings that have been recommended for international comparison of CF data. All of the tables and charts later in this report use this age dissection.

Figure 1.1: ACFDR 2015: Age distribution by sex

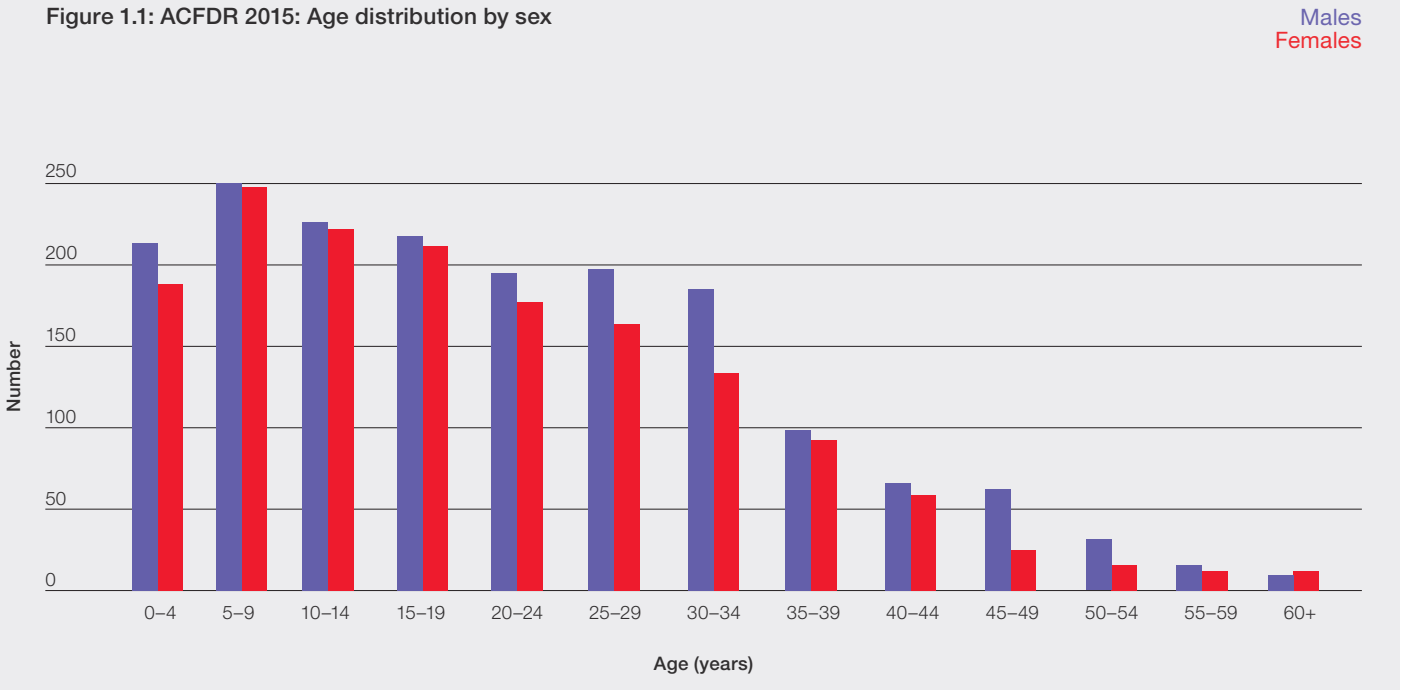


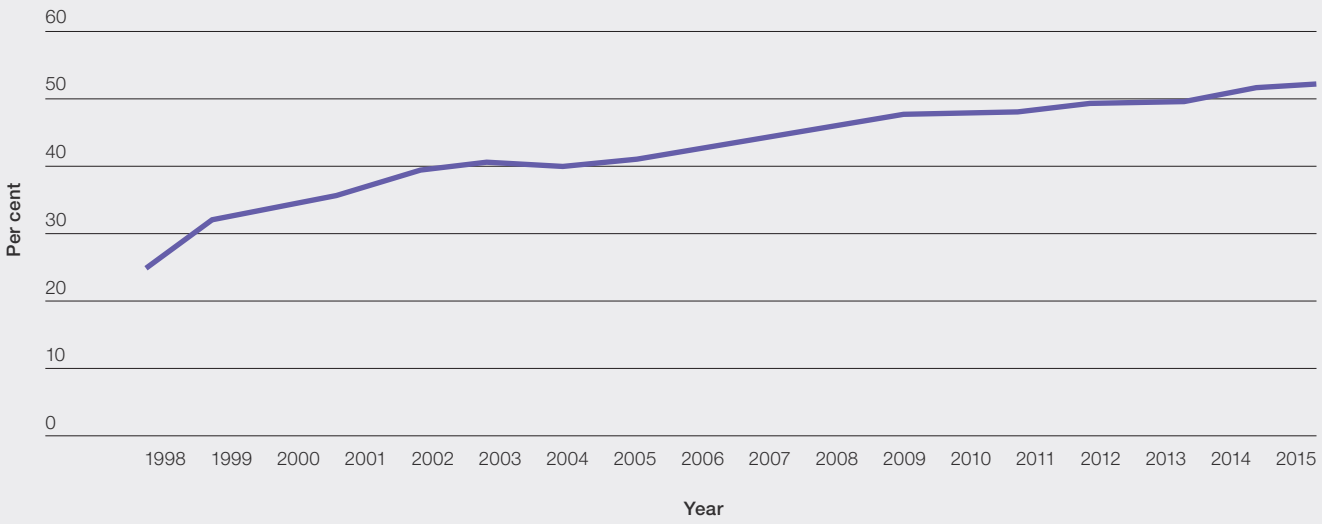
Table 1.1 – ACFDR 2015: Age and sex of registrants at 31 December 2015

Age group	Males	Females	Persons	Percent male
Standard demographic age groups:				
0 – 4 years	213	190	403	52.9
5 – 9 years	250	249	499	50.1
10 – 14 years	229	225	454	50.4
15 – 19 years	219	212	431	50.8
20 – 24 years	197	174	371	53.1
25 – 29 years	199	161	360	55.3
30 – 34 years	187	137	324	57.7
35 – 39 years	100	95	195	51.3
40 – 44 years	71	63	134	53.0
45 – 49 years	69	32	101	68.3
50 – 54 years	36	18	54	66.7
55 – 59 years	17	13	30	56.7
60 + years	11	12	23	48.8
Alternative CF age groups and totals:				
0 – 1 years	81	67	148	54.7
2 – 5 years	182	160	342	53.2
6 – 11 years	292	311	603	48.4
12 – 17 years	275	255	530	51.9
Children and adolescents	830	793	1,623	51.1
18 – 29 years	477	418	895	53.3
30 + years	491	370	861	57.0
Adults	968	788	1,756	55.1
Total, all ages	**1,798**	**1,581**	**3,379**	**53.2**

Consistent with international data, the proportion of males in the Australian CF population shows generally better survival of males compared to females with CF. At 31 December 2015, males made up 53.2 percent and females 46.8 percent of the ACFDR population. This has remained a consistent proportion since establishment of the Registry in 1998. The proportion of males is higher amongst the adult population (55.1%) than in the child and adolescent population (51.1%).

Figure 1.2 shows that the proportion of adults in the Registry as a whole was 52.0 percent at 31 December 2015, a trend that continues to gradually increase since the Registry commenced.

Figure 1.2: ACFDR 1998–2015: Proportion who are adult



The proportions for states and territories are shown in Table 1.2, although those for smaller jurisdictions should be interpreted in the context of their smaller populations.

Table 1.2 – ACFDR 2015: Adult status by State/Territory of residence

State or Territory of residence	Child/adolescent	Adult	Total	Percent adult
New South Wales	465	495	960	51.6
Victoria	324	398	722	55.1
Queensland	427	442	869	50.9
Western Australia	201	184	385	47.8
South Australia	137	152	289	52.6
Tasmania	47	56	103	54.4
Australian Capital Territory	19	21	40	52.5
Northern Territory	2	7	9	77.8
Overseas	1	1	2	50.0
Total	**1,623**	**1,756**	**3,379**	**52.0**

1.3 Adult marital status, education and activity

The following needs to be interpreted in the light of under–reporting (or complete non–reporting) of social characteristics by some CF centres, as noted for each set of data below.

Regarding marital status, as shown in Table 1.3, 37.2 percent of male adult patients and 42.8 percent of adult female patients for whom marital status was reported were in a formal or informal marriage relationship. All patients at five adult centres that did not report marital status for more than one third of their patients are excluded from this analysis.

Table 1.3 – ACFDR 2015: Marital status of adults [(a)]

	Males		Females	
Marital status	**Number**	**Percent**	**Number**	**Percent**
Married (includes de facto)	167	37.2	155	42.8
Not married	282	62.8	207	57.2
		100.0		*100.0*
Unknown or missing	94	17.3	78	17.7
Total	**543**		**440**	

(a) Centres with missing data for more than one third of adult patients were excluded from analysis. These comprised five centres, three large and two medium sized.

Thirteen percent of adult male CF patients and 20 percent of adult females had at least one child. These calculations exclude patients at two large adult CF centres that comprise around 44 percent of the adult CF population.

Many people with cystic fibrosis continue with education beyond senior secondary school level, with 16.8 percent of adult CF patients for whom educational attainment was reported having university qualifications and a further 24.5 percent having completed other study beyond high school. Data presented in Table 1.4 excludes six adult centres that did not report education attainment for more than half of their patients, representing about half of the adult patients in the Registry.

Table 1.4 – ACFDR 2015: Educational attainment of adults [(a)]

	Number	Percent
Junior Secondary (Year 10)	97	14.1
Senior Secondary (Year 12)	300	43.5
Tertiary Certificate or Diploma	169	24.5
University Degree	116	16.8
Left school prior to Year 10	7	1.0
Total reported	*689*	*100.0*
Unknown/not reported (incl. as % of total below)	273	28.4
Total	**962**	**100.0**

(a) CF centres with educational attainment reported for less than 50 percent of patients were excluded from analysis. These comprised six centres, three large, two medium and one small sized.

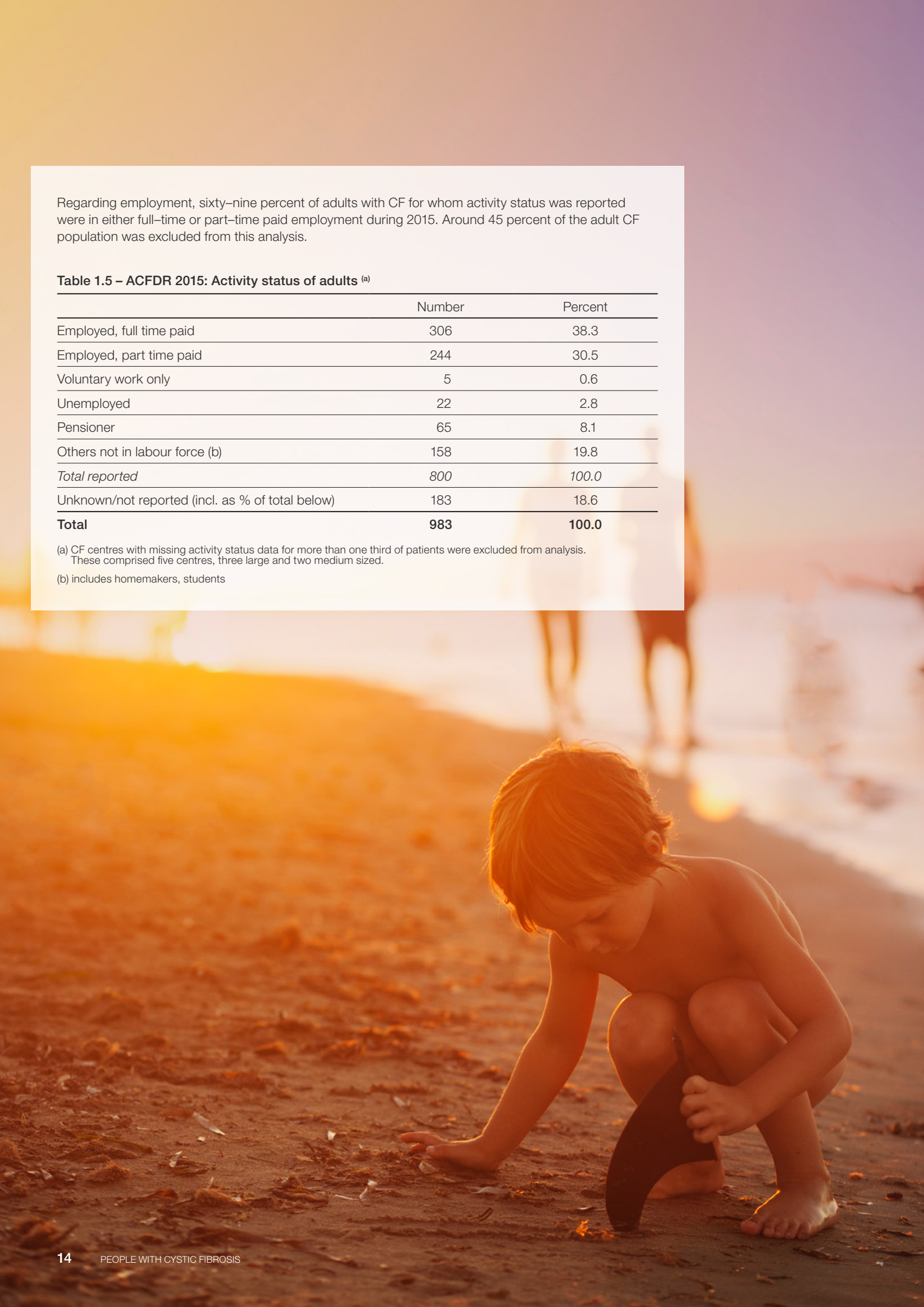
Regarding employment, sixty–nine percent of adults with CF for whom activity status was reported were in either full–time or part–time paid employment during 2015. Around 45 percent of the adult CF population was excluded from this analysis.

Table 1.5 – ACFDR 2015: Activity status of adults [a]

	Number	Percent
Employed, full time paid	306	38.3
Employed, part time paid	244	30.5
Voluntary work only	5	0.6
Unemployed	22	2.8
Pensioner	65	8.1
Others not in labour force (b)	158	19.8
Total reported	*800*	*100.0*
Unknown/not reported (incl. as % of total below)	183	18.6
Total	**983**	**100.0**

(a) CF centres with missing activity status data for more than one third of patients were excluded from analysis. These comprised five centres, three large and two medium sized.

(b) includes homemakers, students

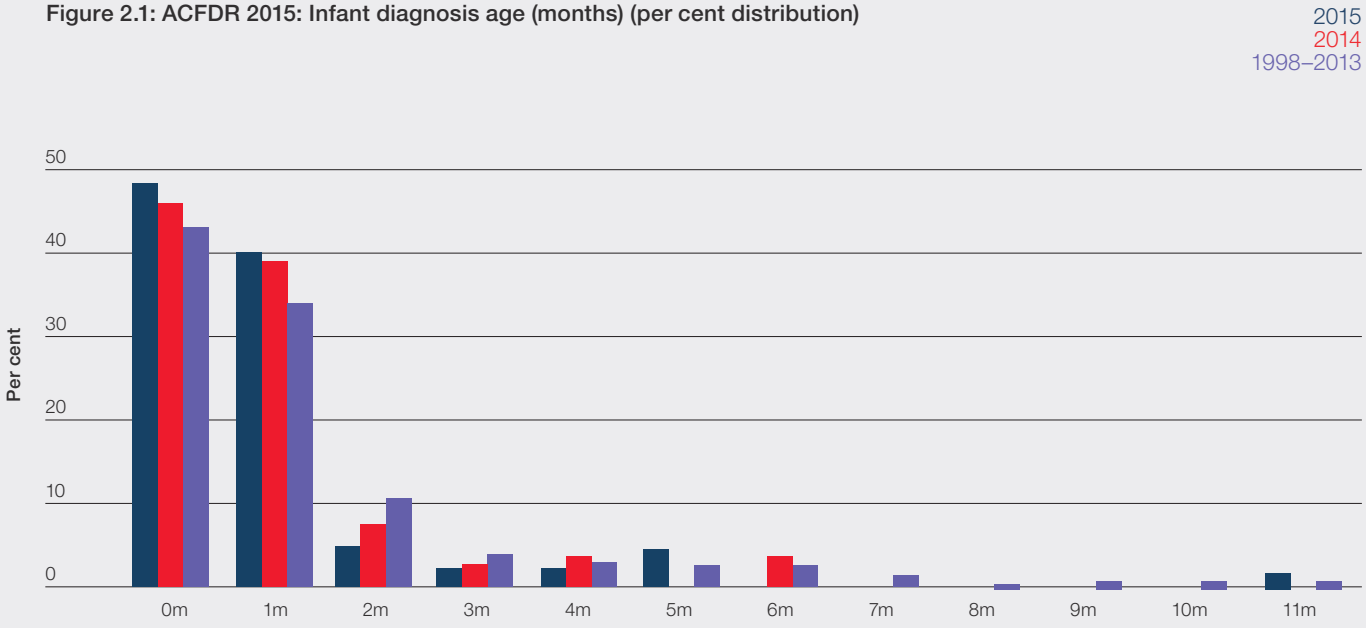


2. DIAGNOSIS

2.1 Age at diagnosis

The number of new diagnoses of cystic fibrosis (CF) notified to the Registry for 2015 was 98, including 73 diagnosed at less than one year of age (Figure 2.1).

Figure 2.1: ACFDR 2015: Infant diagnosis age (months) (per cent distribution)



All but 5 of the infant diagnoses where a diagnosis date was reported (68 out of the 73 new infant diagnoses) were completed by three months of age, assisted by neonatal screening programs that operate in all States and Territories of Australia. There were 12 infant diagnoses in 2015 where a diagnosis date was not reported but where the fact of infant diagnosis was inferred from their age being less than 12 months at the end of the year.

Australian CF centres reported 4 new cases that were diagnosed in early childhood (1 to 4 years), 3 aged from 5 to 9 years, 4 in the age group 10 to 24 years and 2 diagnosed at ages 35 years and over.

Infant diagnoses are not always made or reported in the year of birth and numbers vary across years. An estimate of CF birth incidence can be made using birth cohorts from earlier birth years, say 2010 to 2014, to avoid the reporting lag and to allow for annual variation. Using the average number aged from 1 to 5 years in 2015 (84) and the average number of births reported by the Australian Bureau of Statistics for their birth years (304,500 across years 2010 to 2014), an estimate of Australian birth incidence for CF is 27 per 100,000, or 1 in 3,650 births.

2.2 Presentation and diagnosis

Approximately 74 percent of new cases of CF diagnosed in 2015 included neonatal screening as a mode of presentation, and 12 percent reported meconium ileus, as indicated in Table 2.1. Gastrointestinal symptoms were reported in 8 percent, and respiratory symptoms in 4 percent.

Table 2.1 – ACFDR 2015: Mode of presentation [(a)] by year of diagnosis

	All years	2015	All years	2015
	Number		*Percent*	
Neonatal screening	1,664	71	51.7	74.0
Respiratory symptoms	461	4	14.3	4.2
Gastrointestinal symptoms	351	8	10.9	8.3
Meconium ileus	401	11	12.5	11.5
CF sibling	242	4	7.5	4.2
Minor manifestations	29	2	0.9	2.1
Pre–natal diagnosis	44	4	1.4	4.2
Infertility	19	0	0.6	0.0
Other	332	5	10.3	5.2
Unknown	159	1	5.2	1.0
Total	**3,379**	**98**	**100.0**	**100.0**

(a) More than one mode of presentation can be recorded for a patient so numbers in this section add to more than the total number of registrants and percentage columns add to more than 100.0.

2.3 Phenotype

The proportion of patients who are pancreatic insufficient is 82.3 percent, based on consolidated data across all years of reporting and excluding just under 23 percent of patients for whom pancreatic status is unknown or is missing.

Sweat chloride values have been reported for over half (42%) of patients in the Registry. Of these, there were 231 patients for whom sweat chloride values were below or equal to 60 mmol/L, 56 (27%) of whom had at least one copy of the R117H mutation. Of the 36 patients whose sweat chloride values were below 30 mmol/L, 25 (69%) had a copy of the R117H mutation.

2.4 Genotype

Mutation information consolidated across reporting years was available for 3,087 patients, or 91.7 percent of all patients in the Registry at the end of 2015.

As shown in Table 2.2, the genetic mutation F508del has been identified as at least one of the paired mutations responsible for the inheritance of cystic fibrosis in 92.2 percent of patients for whom genotype details have been reported. Over half of the total, 1,551 patients (50.2%) are reported as homozygous for F508del, with 1,053 of these being aged 12 years and over.

G551D was the next most prevalent mutation, with 239 or 7.7 percent of the CF population reporting genotype data having this mutation, mostly in combination with F508del or another mutation. Of these patients, 213 were aged 6 years and over.

Table 2.2 – ACFDR 2015: Genotype [(a)]

Mutation 2	Mutation 1										
	F508del	G542X	G551D	N1303K	W1282X	R117H	1717–1G–>A	621+1G–>T	Other NEC	Unknown	Total
	Percent										
F508del	50.2										50.2
G542X	1.9	0.1									2.0
G551D	6.0	0.2	0.2								6.4
N1303K	1.1	0.1	0.1	0.1							1.3
W1282X	0.6	0.0	0.0	0.0	0.2						0.8
R117H	3.1	0.0	0.1	0.0	0.0	0.1					3.4
1717–1G–>A	1.3	0.0	0.0	0.0	0.0	0.0	0.0				1.4
621+1G–>T	1.2	0.1	0.0	0.0	0.0	0.0	0.0	0.0			1.3
Other NEC	15.1	0.3	0.6	0.1	0.1	0.2	0.2	0.2	1.5		18.3
Unknown	10.9	0.3	0.4	0.0	0.0	0.1	0.0	0.0	1.0	1.3	14.1
Total	**92.2**	**1.1**	**1.6**	**0.2**	**0.3**	**0.5**	**0.2**	**0.3**	**2.6**	**1.3**	**100.0**

(a) Patients with missing genotype data for both alleles were excluded from analysis

The most common genotypes identified in the Registry are homozygous 508del (50.2%), then heterozygous 508del (42.0%) then other (7.8%) (Figure 2.2). The genotypes also vary somewhat by state/territory, with the ACT and Queensland having the highest proportion of patients with the homozygous 508del genotype, and Tasmania, South Australia and Western Australia the lowest (Table 2.3).

Figure 2.2: ACFDR 2015: Genotype, major categories

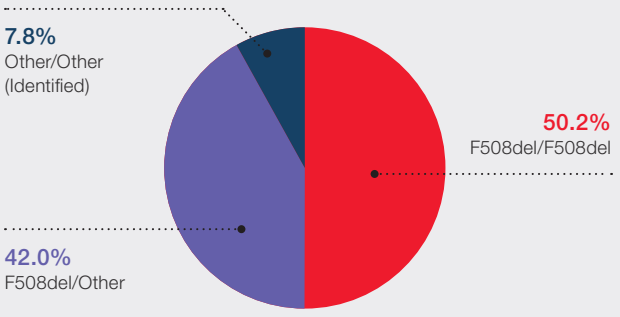


Table 2.3 – ACFDR 2015: Genotype resolved by State/Territory [(a)]

	NSW	VIC	QLD	WA	SA	TAS	ACT	All
	Percent							
Homozygous F508del	50.7	50.5	54.0	45.1	43.4	43.5	52.9	50.2
Compound heterozygous F508del	41.4	40.0	39.8	45.8	47.6	50.0	41.2	41.9
Other mutations (Identified)	7.9	9.5	6.2	8.2	9.1	6.5	5.9	7.8
Total	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
	Number of patients							
Total	**921**	**578**	**811**	**356**	**286**	**92**	**34**	**3,087**

(a) Patients with missing genotype data for both alleles were excluded from analysis

Table 2.4 shows population and allele prevalence of the most common CFTR mutations found in the Australian CF population. A more extended list is available on request. Just 21 mutations have a population prevalence of 10 or more.

Table 2.4 – ACFDR 2015: Patients and alleles – most common CFTR mutations [(a)] in Australian CF population

CFTR Mutation	Patient Number	Patient Percent	Homozygous Patient Number	Allele Number
F508del	2,858	92.1	1,560	4,418
G551D	238	7.7	7	245
R117H	116	3.7	3	119
G542X	94	3.0	3	97
1717–1G–>A	48	1.5	0	48
621+1G–>T	47	1.5	1	48
N1303K	43	1.4	2	45
W1282X	27	0.9	5	32
R553X	24	0.8	2	26
5T;TG	21	0.7	0	21
D1152H	18	0.6	0	18
P67L	18	0.6	0	18
Q493X	14	0.5	0	14
2789+2insA	14	0.5	0	14
G85E	11	0.4	0	11
E60X	11	0.4	1	12
V520F	11	0.4	0	11
I507del	10	0.3	0	10
3272–26A–>G	10	0.3	0	10
R334W	10	0.3	0	10
1078delT	10	0.3	0	10
2789+5G–>A	9	0.3	0	9
3849+10kbC–>T	9	0.3	0	9
R1162X	9	0.3	0	9
1898+1G–>A	9	0.3	0	9
3659delC	9	0.3	0	9
R560T	9	0.3	0	9
A455E	9	0.3	0	9
R347P	8	0.3	0	8
2184delA	8	0.3	0	8
1154insTC	8	0.3	0	8
S549N	8	0.3	0	8
2183AA–>G	5	0.2	3	8
R1066C	5	0.2	0	5
R117C	5	0.2	0	5
711+3A–>G	5	0.2	0	5
CFTRdele2,3	4	0.1	0	4
394delTT	4	0.1	0	4
R347H	4	0.1	0	4
R352Q	4	0.1	0	4
I1027T	4	0.1	0	4
2622+1G–>A	4	0.1	0	4
R75Q	4	0.1	1	4
3791delC	4	0.1	0	4
3121–1G–>A	4	0.1	1	4
Other mutations, not listed above	293	9.4		
Unknown mutation	434	14.0		
Total patients genotyped	**3,103**	**100.0**		

(a) More than one CFTR mutation can be recorded for a patient so numbers in this section add to more than the total number of patients genotyped and percentage columns add to more than 100.0.


The genetic mutation F508del, G551D or G542X is present in nearly 95% of cystic fibrosis patients

3. HEALTH AND FUNCTIONING

Information in this chapter covers respiratory infections, medical complications, lung function and nutritional measures. Two adult centres did not submit any microbiology information for their patients in 2015 and are excluded from the analysis. Two paediatric centres, whose 2015 data was substantially incomplete, are also excluded. All other centres submitted data for multiple occasions where clinical measures of height, weight and lung function were taken.

3.1 Respiratory infections

Patients who were tested for respiratory infections in 2015 had a mean of 4.2 tests of all types during the year. The median number of tests was 4 overall, and 5 in the age groups between 6 and 17 years. Two adult centres and two paediatric centres were excluded from this analysis.

Table 3.1 shows the distribution of CF patients according to the number of both sputum and BAL/bronchoscopy samples examined during 2015. The latter method is used mainly on smaller children.

Taking sputum samples alone, approximately three quarters (74 percent) of the patients tested had at least two sputum samples in 2015. Respiratory cultures were not performed for one quarter of patients with either no test results or 'not tested' reported. It can also be seen that respiratory culture information was not reported at all for around 25% of patients.

Table 3.1 – ACFDR 2015: Number of sputum and BAL/bronchoscopy cultures [a]

	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
				Per cent of patients tested (b)			
Sputum cultures:							
None	46.9	44.5	16.8	6.4	0.6	2.3	13.3
1	10.2	7.5	9.8	8.6	18.4	19.9	13.0
2	5.1	4.7	8.3	9.4	22.3	18.7	13.0
3	4.1	8.3	10.9	10.1	14.0	14.7	11.5
4	9.2	13.0	9.8	13.8	10.3	14.1	11.8
5	7.1	6.7	11.6	10.4	6.2	6.3	8.4
6	9.2	3.5	10.3	9.6	8.4	6.1	8.1
7 or more	8.2	11.8	22.5	31.6	19.8	17.9	20.9
Total	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
BAL/bronchoscopy:							
None	62.2	72.4	91.5	96.8	99.0	98.0	91.7
1	28.6	21.7	5.5	3.0	0.8	1.7	6.3
2	9.2	3.9	2.8	0.3	0.2	0.0	1.7
3 or more	0.0	2.0	0.2	0.0	0.0	0.3	0.3
Total	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
				Number of patients			
Patients tested (b)	*98*	*254*	*458*	*405*	*485*	*347*	*2,047*
Culture not done	47	84	139	123	186	205	784
Total reported	*98*	*254*	*459*	*409*	*487*	*352*	*2,059*
Not reported	47	84	138	119	184	200	772
Total patients	**145**	**338**	**597**	**528**	**671**	**552**	**2,831**

(a) Two adult and two paediatric centres were excluded from analysis. (b) By any method of obtaining culture

The most commonly identified organisms in respiratory specimens are various species and forms of Pseudomonas. It can be seen in Table 3.2 that 50.1 percent of patients tested produced positive Pseudomonas aeruginosa cultures, with the mucoid form showing in 22.2 percent. Its prevalence is greater in adult patients, with 42.3 percent of tested adult CF patients producing samples indicating the mucoid form of Pseudomonas aeruginosa, three times the corresponding proportion for adolescents and much higher than that for children.

Table 3.2 – ACFDR 2015: Pseudomonas infection by age group [(a)] [(b)]

	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
				Per cent			
Pseudomonas aeruginosa:							
Mucoid	0.0	2.1	4.4	14.8	38.8	46.6	22.2
Rough/non–mucoid	3.5	3.9	8.9	14.4	24.7	25.0	15.9
Not differentiated	4.1	9.5	12.9	13.5	12.1	13.2	12.0
Any Ps aeruginosa	7.6	15.5	26.2	42.7	75.6	84.8	50.1
Pseudomonas other species	1.4	1.5	3.7	3.8	2.2	0.9	2.4
				Number of patients			
Patients tested	**145**	**338**	**597**	**528**	**671**	**552**	**2,831**

(a) Two adult and two paediatric CF centres were excluded from analysis.
(b) Patient may have had more than one type of Pseudomonas infection. Percentages for individual types may add to more than totals.

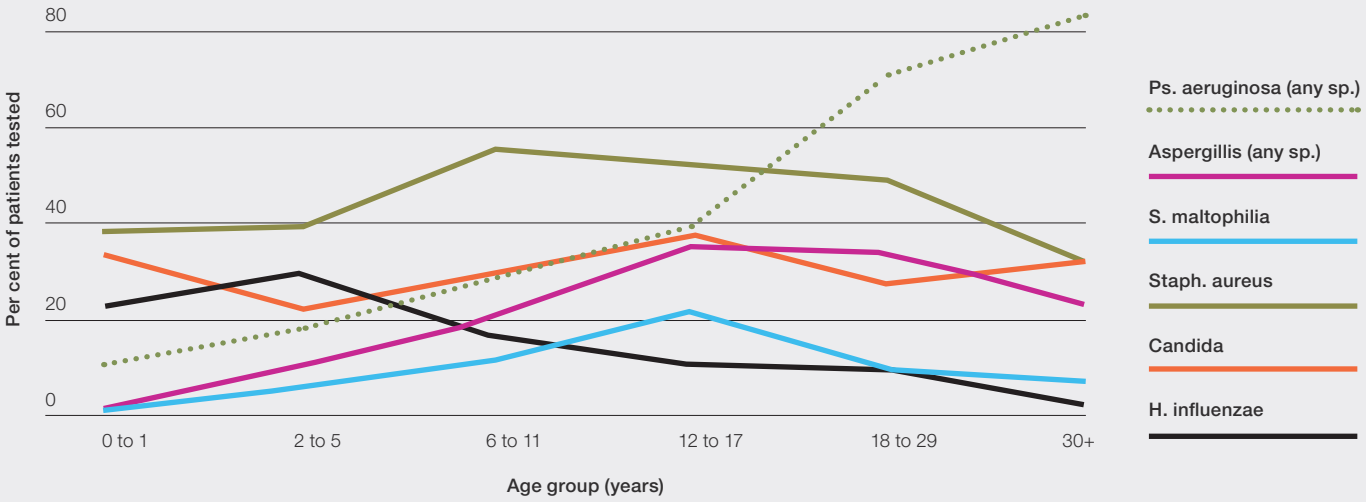
While prevalence of Pseudomonas organisms is lower in children than in adults, young children are just as likely as adult patients to produce cultures showing presence of Staphylococcus aureus (Table 3.3). Over 40% of all child/adolescent and adult patients had this bacterial infection. Haemophilus influenzae is evident in relatively high proportions of child patients, highest in children aged from 2 to 5 years, where this organism was cultured for around one fifth of children. The youngest age groups also had the highest proportions with positive cultures of the bacteria Escherichia coli; 13 percent, for those in the age group less than 2 years, being the highest. The prevalence of these major organisms in the lungs by age group is shown in Figure 3.1.

Table 3.3 – ACFDR 2015: Other respiratory culture by age group [a]

	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
				Per cent of patients tested (b)			
Bacteria:							
Staphylococcus aureus	26.2	30.5	42.2	40.7	35.6	20.5	33.9
Haemophilus influenzae	15.9	22.2	12.9	8.9	7.2	1.8	9.9
Burkholderia cepacia (Ps cepacia)	0.0	0.0	1.0	2.5	3.3	2.2	1.9
Stenotrophomonas maltophilia	1.4	4.4	9.2	16.5	7.9	4.4	8.3
Escherichia coli	16.6	6.2	3.5	3.0	1.0	0.5	3.3
MRSA (c)	2.8	1.5	1.5	4.0	3.1	2.5	2.6
Alcaligenes xylosoxidans	0.0	0.6	1.5	3.0	4.0	2.9	2.5
Serratia marcescens	1.4	2.7	1.0	3.2	0.8	0.5	1.2
Klebsiella (any species)	11.0	1.5	1.2	1.0	1.0	1.1	1.6
Non–tuberculous mycobacterium	0.0	0.3	2.4	6.4	2.8	2.2	2.8
Fungi:							
Candida	22.1	16.9	23.1	28.6	21.0	19.9	22.2
Aspergillus (any species)	0.7	7.7	15.9	27.3	24.4	15.4	18.2
Scediosporium (any species)	0.0	1.2	3.5	7.4	2.7	2.5	3.4
Other organisms not listed above	29.7	35.5	30.3	32.6	20.6	13.4	25.7
Normal flora only	60.0	68.9	70.7	68.6	22.7	12.3	46.8
No growth/sterile culture	9.7	10.7	10.9	8.9	4.2	2.4	7.2
				Number of patients			
Patients tested	**145**	**338**	**597**	**528**	**671**	**552**	**2,831**

a) Two adult and two paediatric CF centres were excluded from analysis.
(b) Note: Patients may have multiple infections during the year. Percentages may add to more than 100.0.
(c) Methicillin–resistant Staphylococcus aureus

Figure 3.1: ACFDR 2015: Prevalence of major organisms in lungs



3.2 Other medical complications

Table 3.4 shows that the prevalence of medical complications increases with age in CF patients. For instance, 48 percent of adult patients suffer gastro–oesophageal reflux, over one quarter of patients aged 30 years and over experience chronic insulin–dependent diabetes and over 40 percent of the same age group have osteoporosis or osteopenia.

The proportion for whom none of the selected complications shown in the following table have been reported is over 79 percent for children under 6 years, but declines to 14 percent in CF patients aged 30 and over.

Table 3.4 – ACFDR 2015: Medical complications [(a)]

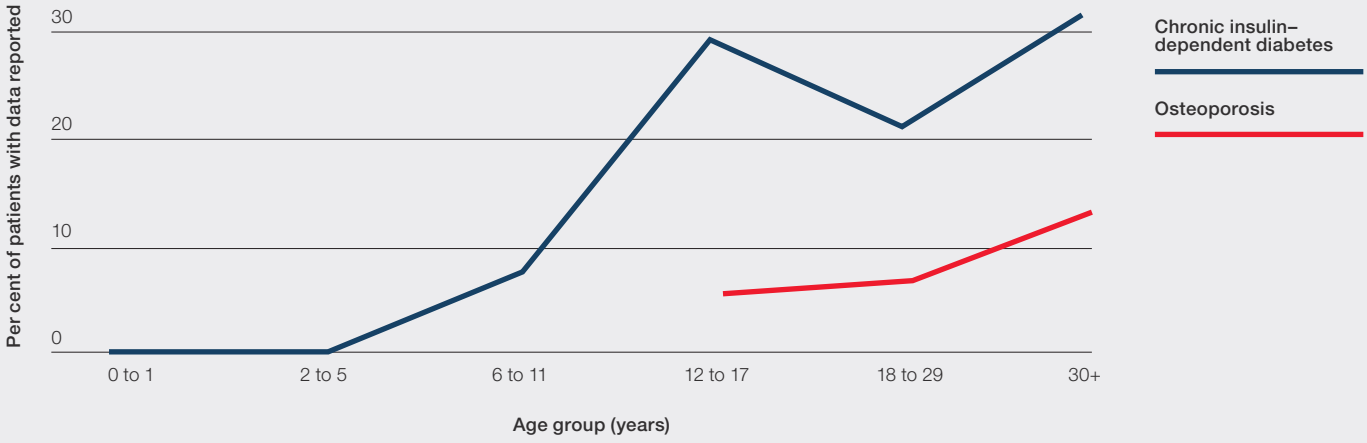
	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	**Total**
				Per cent			
Pulmonary:							
Major haemoptysis	0.0	0.0	0.0	1.2	6.1	8.0	**3.7**
Massive haemoptysis	0.0	0.0	0.0	0.4	0.2	0.9	**0.3**
Therapeutic bronchial artery embolisation	0.0	0.0	0.0	1.2	1.0	3.0	**1.1**
Pneumothorax	0.0	0.0	0.0	0.0	1.0	0.9	**0.5**
Any pulmonary above	0.0	0.0	0.0	2.0	7.5	9.8	**4.6**
Gastro–intestinal:							
Gastro–oesophageal reflux	13.0	13.5	18.6	27.4	42.6	50.9	**33.4**
– proven at endoscopy	0.0	0.8	0.7	2.0	3.9	8.3	**3.5**
Abnormal liver function test	11.6	14.3	22.9	32.5	21.3	19.8	**22.1**
Cirrhosis or portal hypertension	2.9	0.8	2.1	7.5	5.1	3.0	**4.0**
Pancreatitis	0.0	0.0	0.7	1.2	4.6	4.1	**2.6**
Any Gastro–intestinal above	20.3	24.8	36.8	49.6	57.9	62.4	**48.8**
Endocrine:							
Chronic insulin–dependent diabetes	0.0	0.0	7.1	29.0	20.6	30.2	**18.9**
Intermittent insulin–dependent diabetes	0.0	0.0	1.1	1.2	2.7	2.1	**1.6**
Other glucose abnormality	*0.0*	*0.8*	*11.1*	*23.4*	*15.7*	*16.9*	***14.3***
Any Endocrine above	0.0	0.8	17.9	51.2	37.0	48.2	**33.4**
Osteo:							
Osteoporosis	0.0	0.0	1.4	5.6	6.5	12.4	**5.9**
Osteopenia	0.0	0.0	2.5	15.1	18.6	34.0	**16.0**
Fracture this year	0.0	0.8	1.1	1.6	1.0	2.7	**1.4**
Any Osteo above	0.0	0.0	2.9	15.9	24.0	45.0	**20.1**
Other:							
Cancer	0.0	0.0	0.0	0.0	0.2	1.8	**0.5**
None of the above	79.7	74.4	50.4	20.6	23.7	13.6	**33.1**
Total reported (b)	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	***100.0***
				Number			
Total reported	*55*	*133*	*280*	*252*	*413*	*338*	***1,485***
Unknown or not stated	69	209	323	277	272	296	**1,456**
Total patients (a)	*148*	*342*	*603*	*529*	*685*	*634*	***2,941***

(a) Two adult and two paediatric CF centres were excluded from analysis.
(b) Patient may have had more than one complication. Percentages add to more than 100.0.

Fifty-one percent of male and 49.5% of female children and adolescents had lung function at or above 90% of predicted FEV_1

Although some prevalence of osteoporosis at younger ages is reported in the Table 3.4, this is not displayed in Figure 3.2 because of uncertainty about diagnosis at younger ages.

Figure 3.2: ACFDR 2015: Prevalence of major complications

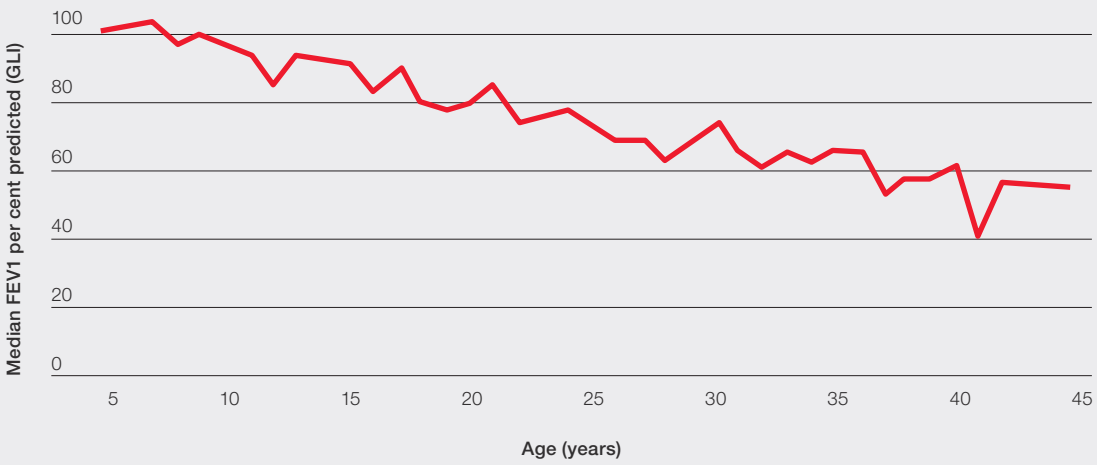


3.3 Lung function

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 patient is the average of the highest FEV_1 percent predicted value recorded in each quarter of the year.

Median CF lung function, measured as FEV_1 percent predicted, is within the normal range for young children, but is lower than 70 percent of predicted, the level at which moderate lung function impairment is experienced, in adult patients aged from around 25 years. Just over 5 percent of children aged 6 to 11 years have FEV_1 values that are below 70 percent of predicted values, but 13 percent of older children and adolescents are in this category (Figure 3.3).

Figure 3.3: ACFDR 2015: Median lung function by age



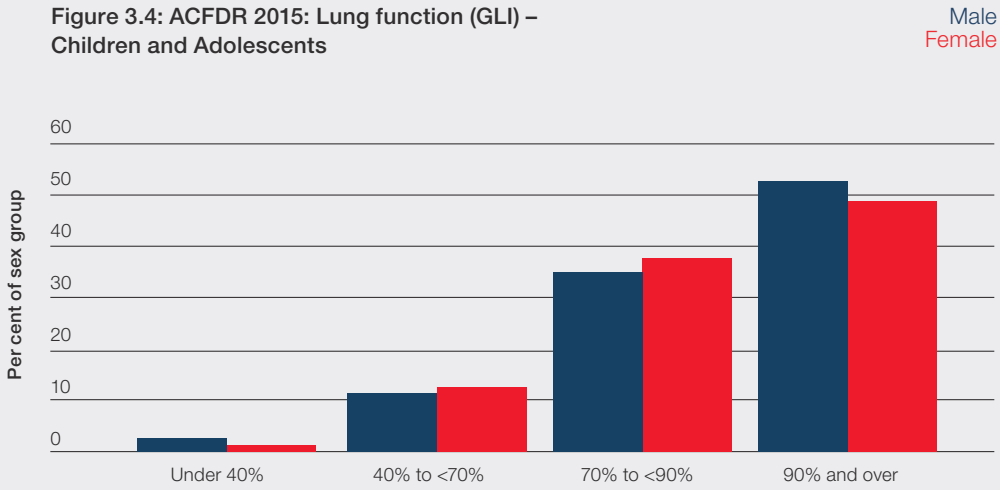
Generally greater proportions of patients have severe lung function impairment in successive older age groups, as described in Table 3.5.

Table 3.5 – ACFDR 2015: Lung function impairment by age group and sex

	<40	≥40–70	≥70–90	≥90	Total	<40	≥40–70	≥70–90	≥90	Total
	Number					*Per cent*				
Males:										
6 – 11 years	1	9	38	115	163	0.6	5.5	23.3	70.6	100.0
12 – 17 years	2	22	66	95	185	1.1	11.9	35.7	51.4	100.0
18 – 29 years	39	100	101	74	314	12.4	31.9	32.2	23.6	100.0
30 + years	68	117	59	15	259	26.3	45.2	22.8	5.8	100.0
Total measured	*110*	*248*	*264*	*299*	*921*	*11.9*	*26.9*	*28.7*	*32.5*	*100.0*
Females:										
6 – 11 years	0	10	47	117	174	0.0	5.8	27.0	67.2	100.0
12 – 17 years	1	21	65	91	178	0.6	11.8	36.5	51.1	100.0
18 – 29 years	26	105	84	60	275	9.5	38.2	30.6	21.8	100.0
30 + years	28	94	46	18	186	15.1	50.5	24.7	9.7	100.0
Total measured	*55*	*230*	*242*	*286*	*813*	*6.8*	*28.3*	*29.8*	*35.2*	*100.0*
Persons:										
Total measured	*165*	*478*	*506*	*585*	*1,734*	*9.5*	*27.6*	*29.2*	*33.7*	*100.0*

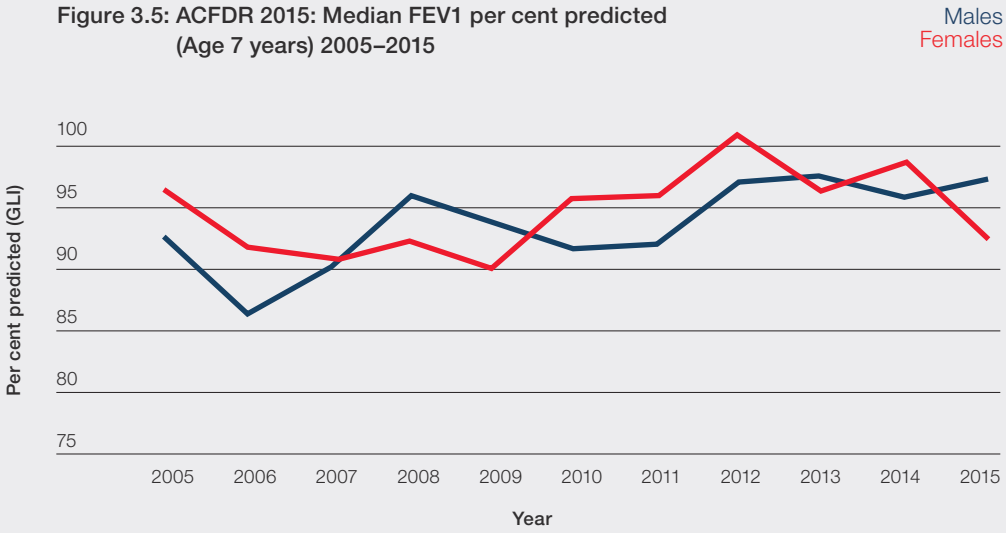
Figure 3.4 shows categories of lung function impairment experienced by the child and adolescent CF population as a whole. Fifty–one percent of male and 49.5 percent of female children and adolescents had lung function at or above 90% of predicted FEV_1.

Figure 3.4: ACFDR 2015: Lung function (GLI) – Children and Adolescents



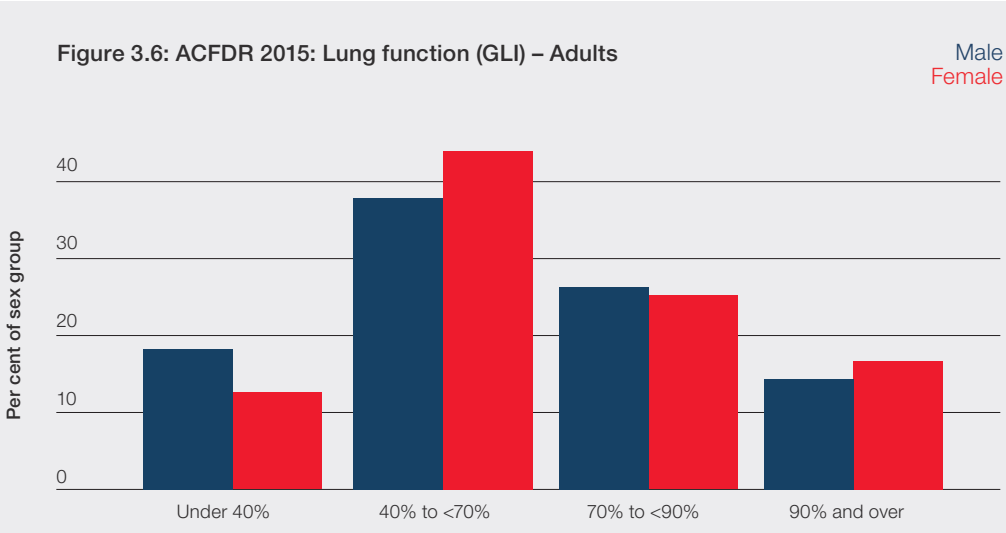
Upward trends over recent years in child and adolescent age groups were charted in the 2014 Annual Report. The following view, from cross–sectional data for 7 year old children suggests, however, that there may have been a plateauing of improvement since 2012 (Figure 3.5).

Figure 3.5: ACFDR 2015: Median FEV1 per cent predicted (Age 7 years) 2005–2015



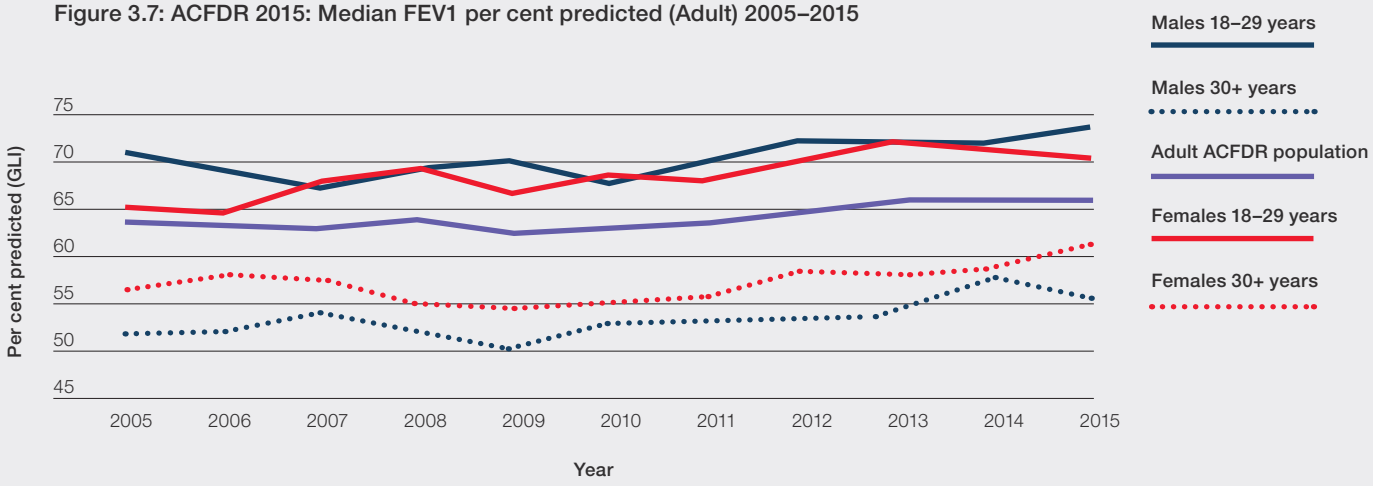
For adults with cystic fibrosis, a different pattern of lung function impairment is evident, with just 16.2 percent of both adult males and females having FEV_1 at or above 90% predicted in 2015. Lung function of less than 40% of FEV_1 per cent predicted was experienced by 16 percent of male adults and 12 percent of female adults (Figure 3.6).

Figure 3.6: ACFDR 2015: Lung function (GLI) – Adults



Trend data for adult lung function indicate improvement for the 18 to 29 years age group since 2005, for both males and females (Figure 3.7). A flatter trend for adults aged 30 and over may be confounded by possible increased survival.

Figure 3.7: ACFDR 2015: Median FEV1 per cent predicted (Adult) 2005–2015



3.4 Nutrition: weight, height and body mass index

Methodological note

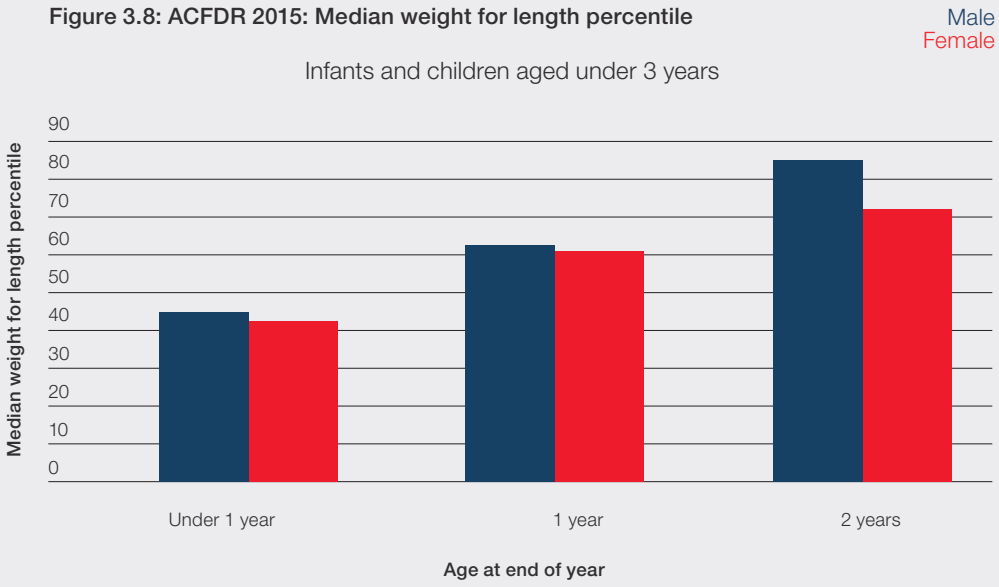
As for lung function measures reported in Section 3.3, values reported in this section are the average of the highest value recorded in each quarter of the year.

Infants and young children aged under 3 years

Nutritional outcomes for children aged under 3 years were introduced for the first time in the 2013 report. Figure 3.8 shows the median weight for length percentile for infants and children up to 1 and 2 years. For 2015, the median value of weight for length is at the 43rd percentile for female infants but for males it is at the 46th percentile. This difference may be cohort–specific.

Percentiles are derived from World Health Organisation Child Growth Standards (WHO 2006).

Figure 3.8: ACFDR 2015: Median weight for length percentile



Children and adolescents

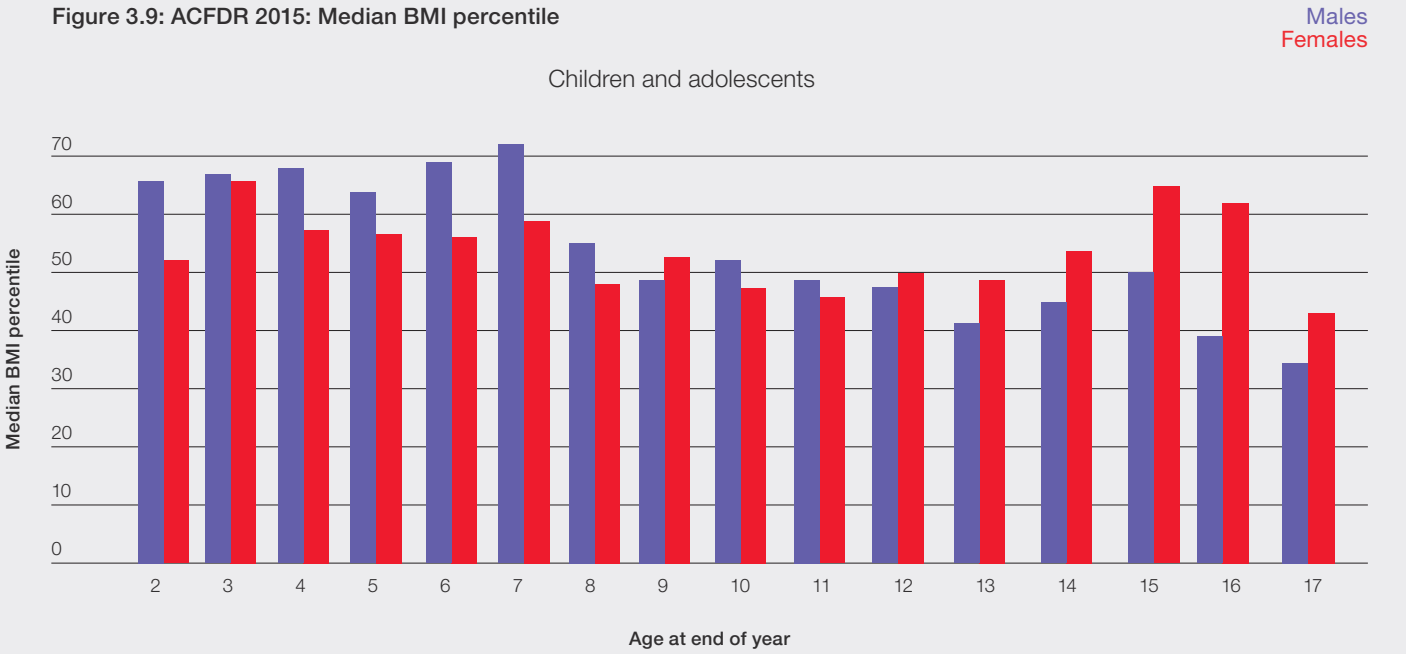
As shown in Table 3.6, Median height percentile for young children is higher than the reference population, but is below the 50th percentile in older child and adolescent age groups in 2015, for both males and females. BMI percentiles are higher than height percentiles for each age and sex group, with the exception of male adolescents (43.5th percentile). All the age and sex groups fit a pattern of lower percentiles for both height and BMI indicators in successively higher age groups, with the exception of adolescent females for the BMI percentile.

Table 3.6 – ACFDR 2015: Child and adolescent height and BMI: median percentiles by age group and sex

	Height	BMI
Males		
2–5 years	65.6	66.8
6–11 years	47.7	56.0
12–17 years	41.2	43.5
Females		
2–5 years	50.5	57.7
6–11 years	48.3	50.7
12–17 years	43.4	52.7

As shown in Figure 3.9, BMI percentiles across individual year ages show a generally consistent pattern of lower values at higher ages. The youngest (aged 2 years) cohort in 2015 appears to have returned to a pattern of younger males having higher median BMI percentiles than their female counterparts, after departing from this pattern in 2014.

Figure 3.9: ACFDR 2015: Median BMI percentile



Overall, somewhat under half (45.4 percent of males and 46.7 percent of females) children and adolescents were below the 50th percentile for BMI in 2015. The distribution is shown in Table 3.7.

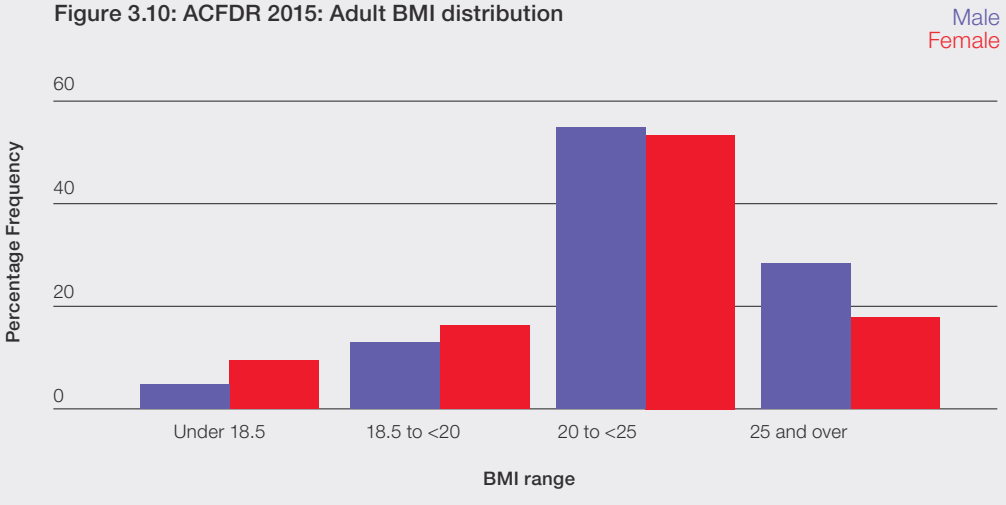
Table 3.7 – ACFDR 2015: Child and adolescent height and BMI percentile distributions by sex

	Height			BMI		
	Males	**Females**	**Persons**	**Males**	**Females**	**Persons**
		Per cent			*Per cent*	
< 3rd	2.6	3.1	2.8	0.9	1.1	1.0
3rd – 4.99th	2.2	2.4	2.3	1.3	0.9	1.1
5th – 9.99th	6.9	7.0	6.9	2.8	3.3	3.0
10th – 24.99th	15.8	15.1	15.4	15.3	12.3	13.8
25th – 49.99th	24.0	25.6	24.8	25.1	29.1	27.1
50th – 74.99th	27.2	25.4	26.3	30.9	32.2	31.5
75th – 89.99th	12.9	14.7	13.8	17.7	16.6	17.2
90th – 94.99th	3.2	3.5	3.4	3.2	3.3	3.3
95th – 96.99th	2.4	1.8	2.1	1.3	0.4	0.9
>= 97th	2.8	1.5	2.2	1.5	0.9	1.2
Total	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
		Number			*Number*	
Total	**463**	**457**	**920**	**463**	**457**	**920**

Adult body mass index

Adult Body Mass Index (BMI) scores show 57.05 percent of males and 56.42 percent of females had an average quarterly BMI score in the range 20 to less than 25 kg/m^2 (Figure 3.10). The proportion of females who had BMI scores below 20 (25.0 percent) is higher than the proportion of males (15.1 percent). Over a quarter (28.0 percent) of adult males had a BMI above 25.

Figure 3.10: ACFDR 2015: Adult BMI distribution



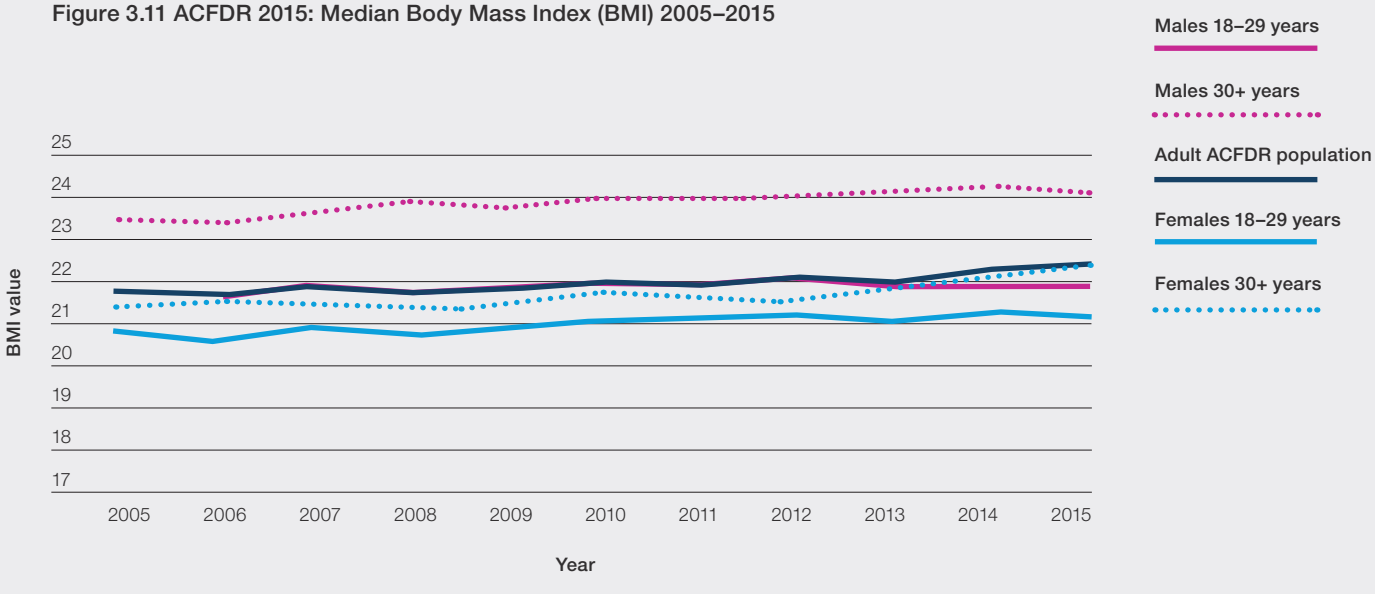
The distribution of adult BMI is further described in Table 3.8.

Table 3.8 – ACFDR 2015 Adult BMI distribution

	BMI range				
	Less than 18.5	**From 18.5 to <20**	**From 20 to <25**	**25 and over**	**Total**
			Males: per cent		
18 – 29 years	6.1	14.7	60.7	18.5	100.0
30 + years	1.2	7.0	52.3	39.5	100.0
Male adults measured	3.9	11.2	56.9	28.0	100.0
			Males: number		
Male adults measured	22	64	325	160	787
			Females: per cent		
18 – 29 years	10.3	17.3	57.4	15.1	100.0
30 + years	6.5	15.1	54.6	23.8	100.0
Female adults measured	8.8	16.4	56.2	18.6	100.0
			Females: number		
Female adults measured	*40*	*75*	*257*	*85*	*457*

Figure 3.11 shows general increases in median BMI values for grouped adult age data since 2005.

Figure 3.11 ACFDR 2015: Median Body Mass Index (BMI) 2005–2015



In 2015, antibiotic therapy was prescribed for 93.6% of cystic fibrosis patients

4. TREATMENT OF CYSTIC FIBROSIS

This Chapter describes the treatments and therapies recorded for patients in the Australian Cystic Fibrosis Data Registry.

4.1 Visits to clinics

The average number of clinic visits during 2015 was 2.2 for children and adolescents and 2.0 for adults. These figures should be treated with some caution as they may have been affected by different practices in recording clinic visits at contributing centres. The median number of visits to clinics is less likely to be so affected, and stood at 2 for children and adolescents and 1 for adults in 2015.

4.2 Therapy for cystic fibrosis patients

Antibiotic therapy was prescribed for 93.6 percent CF patients overall, and for more than 88 percent of patients in each age group. These proportions, and the numbers and proportions that follow in this section, were compiled from therapy usage information supplied for 1,995 patients, 59.0 percent of all patients in the Registry. Missing data affected two paediatric centres, three adult centres and one combined centre in 2015. Proportions of child/adolescent and adult patients for whom therapy data were missing were 25.1 and 46.3 percent respectively.

Oral antibiotic therapy was prescribed for 83.9 percent of antibiotics users (Table 4.1). Both PRN (as needed) and continuous usage was prescribed for these patients at some time during 2015, as shown in the following table. Higher proportions of adolescents (29.2%) and very young children (51.9%) than those in other age groups were prescribed oral antibiotics for continuous use.

Table 4.1 – ACFDR 2015: Oral antibiotic therapy – mode of use by age group [(a)]

	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
				Per cent			
Mode of use							
As needed (PRN)	56.7	90.4	90.0	74.7	84.9	89.3	83.9
Continuous	51.9	13.6	15.2	29.2	31.6	30.4	26.2
Mode of use unknown	1.0	1.3	0.7	1.4	0.7	0.0	0.8
Total oral antibiotics users (b)	100.0	100.0	100.0	100.0	100.0	100.0	100.0
				Number			
Total oral antibiotics users	**104**	**228**	**408**	**360**	**431**	**336**	**1,867**

(a) Patients for whom no treatment information was provided (46 percent of total) were excluded from analysis.
(b) More than one mode of use can be recorded so numbers add to more than 100.0.
As well, mode of use was not recorded for all patients where oral antibiotics were reported.

Just under one half (48.3%) of antibiotics users used inhaled antibiotics in 2015, with proportions generally greater in successively older age groups (Table 4.2).

Table 4.2 – ACFDR 2015: Inhaled antibiotics by age group [(a)]

	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
				Per cent			
Inhaled antibiotics							
Yes	13.2	22.8	41.8	54.7	57.5	62.8	48.3
No	79.2	69.8	53.2	34.4	26.9	22.5	40.8
Unknown	0.0	0.0	0.7	0.3	0.2	0.3	0.3
Total antibiotics users	100.0	100.0	100.0	100.0	100.0	100.0	100.0
				Number			
Total antibiotics users	**106**	**232**	**419**	**369**	**487**	**382**	**1,995**
Mode of use							
As needed (PRN)	85.7	75.5	65.7	41.6	66.1	69.6	62.6
Continuous	14.3	20.8	32.0	58.4	40.7	33.8	39.6
Mode of use unknown	7.1	2.5	1.1	0.0	0.0	0.4	0.5
Total inhaled antibiotics users (b)	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
				Number			
Total inhaled antibiotics users	**14**	**53**	**175**	**202**	**280**	**240**	**964**

(a) Patients for whom no treatment information was provided (46 percent of total) were excluded from analysis.
(b) More than one mode of use can be recorded so numbers add to more than 100.0.
As well, mode of use was not recorded for all patients where oral antibiotics were reported.

Almost all CF patients use a range of other therapies to manage conditions other than infections, and many take nutritional supplements (Table 4.3). Therapies used by the highest proportion of patients include pancreatic enzymes (50.5% of children/adolescents and 65.9% of adults), vitamin supplements (53.7% and 60.2% respectively), bronchodilators (24.9% and 58.4%) and salt tablets (26.6% and 17.7%).

Table 4.3 – ACFDR 2015: Other therapy by type [(a)] [(b)]

	Child/adolescent		Adult	
	Number	*Percent*	*Number*	*Percent*
Dornase alpha	447	36.8	385	40.8
Pancreatic enzymes	613	50.5	621	65.9
Vitamin supplements	652	53.7	568	60.2
Bronchodilators	303	24.9	551	58.4
Corticosteroids inhaled	165	13.6	335	35.5
Corticosteroids oral	74	6.1	64	6.8
Mannitol	33	2.7	38	4.0
Insulin	73	6.0	174	18.5
Macrolides	102	8.4	455	48.3
Salt tablets	323	26.6	167	17.7
Antihypercalcaemics	3	0.2	14	1.5
Gastric acid secretion reducers	226	18.6	309	32.8
Other	543	44.7	355	37.6
Patients with therapies reported	**1,215**	**100.0**	**943**	**100.0**

(a) Patients for whom no treatment information was provided (46 percent of total) were excluded from analysis.
(b) Individuals may use more than one type of therapy; percentages by type of therapy add to more than 100.0.

Nutritional supplement information is provided in Table 4.4. The usage of nutritional supplements increases from 8.9% for infants to a peak of 36.5% for adolescents, before reducing to 29.6% for adults aged 30 and above. The majority of those taking nutritional supplements take the supplements orally, with the exception of the infant age group, with a higher proportion of infants receiving the supplements via TPN or via gastrostomy tube.

Table 4.4 – ACFDR 2015: Nutritional supplements by age group [(a)] [(b)]

	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
				Per cent			
Oral (prescribed)	2.7	8.2	14.0	15.7	25.1	24.3	17.5
Nasogastric	0.9	0.9	1.4	1.7	0.7	1.9	1.3
Total Parenteral Nutrition (TPN)	1.8	0.0	0.0	0.3	0.0	0.0	0.2
Gastrostomy tube/button	1.8	2.6	3.7	8.6	4.8	1.7	4.2
Nutritional supp. type unknown	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total using nutritional supplements	8.9	17.7	32.4	36.5	35.6	29.6	30.3
Not using nutritional supplements	91.1	82.3	67.6	63.5	64.4	70.4	69.7
Patients with nutritional supplements reported	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
				Number			
Total with nutritional supplements reported	*112*	*232*	*429*	*362*	*458*	*362*	*1,955*
Nutritional supplements not reported	8	16	19	37	69	54	203
Patients with therapies reported	*120*	*248*	*448*	*399*	*527*	*416*	*2,158*

(a) Patients for whom no treatment information was provided (36 percent of total) were excluded from analysis.
(b) Individuals may use more than one type.

Of the 1,908 patients for whom treatment data were reported in 2015, 19 were reported to have commenced oxygen therapy during 2015 and 25 remained on oxygen therapy commenced in a previous year. The majority in each category (14 and 24 respectively) were adults.

Nine patients commenced using non–invasive ventilation in 2015, and 15 had commenced in earlier years. Three of those commencing during 2015 were children/adolescents and all patients who had commenced earlier were adults.

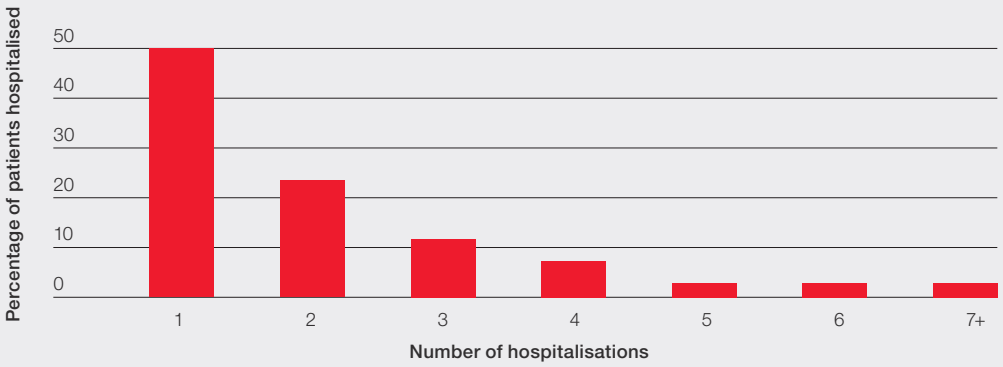
For both non–invasive ventilation and oxygen therapy, it is likely that the numbers reported are less than complete, as the full patient population of two adult CF centres is missing from reported data.

4.3 Hospital treatment

The manner of collection of hospitalisation data for the Registry does not allow a clear distinction to be drawn between 'no hospitalisation' and missing data in relation to a patient. Three paediatric hospitals (all large in patient numbers) and three adult hospitals (two large and one medium) were excluded from the analysis of hospitalisation because no data or incomplete data were provided. This excluded 39 percent of patients in the Registry from this analysis.

Of the 2062 patients attending hospitals that provided adequate data, 42.9 percent experienced at least one hospitalisation for any indication during 2015. Half of these had more than one period in hospital during the year (Figure 4.1).

Figure 4.1: ACFDR 2015: Hospitalisations



The distribution of hospitalisations by age is shown in Table 4.5.

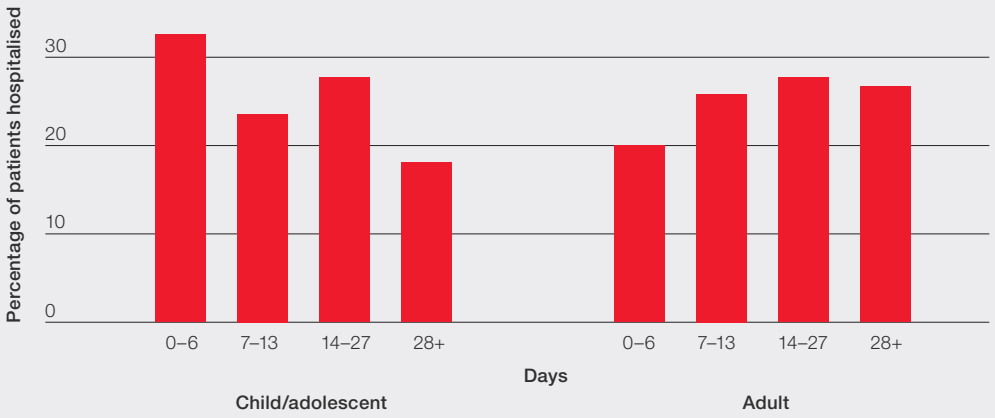
Table 4.5 – ACFDR 2015: Hospitalisation related to cystic fibrosis, respiratory causes [(a)]

	Persons aged						
	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
	Per cent of persons in age group						
Number of hospitalisations							
None or none reported	40.9	49.4	56.6	50.9	58.0	64.4	57.1
1	31.0	25.0	24.0	18.4	20.9	19.7	21.4
2	12.7	15.3	11.2	11.3	10.0	6.8	10.0
3	8.5	4.6	4.5	5.8	4.5	4.9	5.0
4	2.8	2.3	2.6	6.8	3.5	2.2	3.4
5	0.0	0.6	0.3	2.4	1.4	0.9	1.1
6	1.4	1.1	0.3	2.1	0.9	0.9	1.0
More than 6	2.8	1.7	0.6	2.4	0.9	0.2	1.0
Total	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
				Number			
Total	**71**	**176**	**313**	**293**	**662**	**547**	**2,062**

(a) Six CF centres were excluded from analysis (see text)

Of the 884 persons whose hospitalisation in 2015 experience is analysed here, half (49.8%) accumulated at least 14 admitted days through the year. Mean and median days, of 21 and 13 respectively for these people, underline the fact that some CF patients spend considerable periods of time hospitalised. Adult patients (mean 23.0 days, median 14 days) generally spent more days as admitted patients in hospital than children and adolescents (18.7 and 12 days respectively) (Figure 4.2).

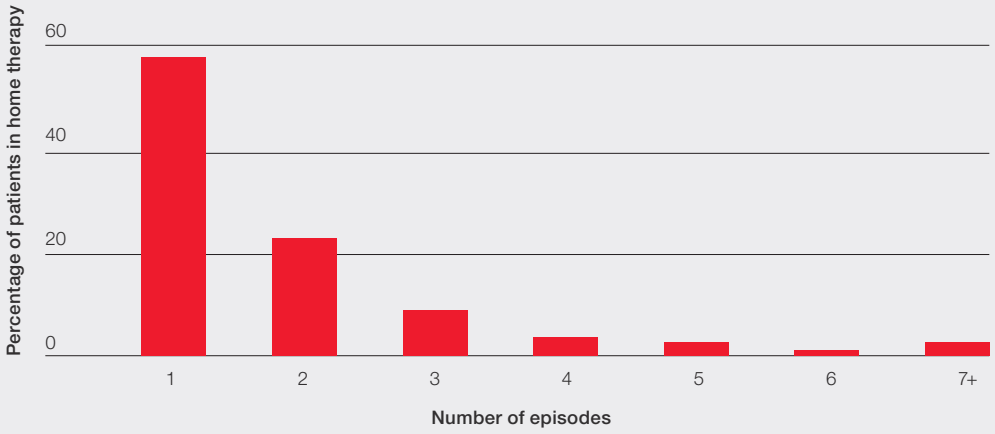
Figure 4.2: ACFDR 2015: Accumulated hospital days



4.4 Home therapy

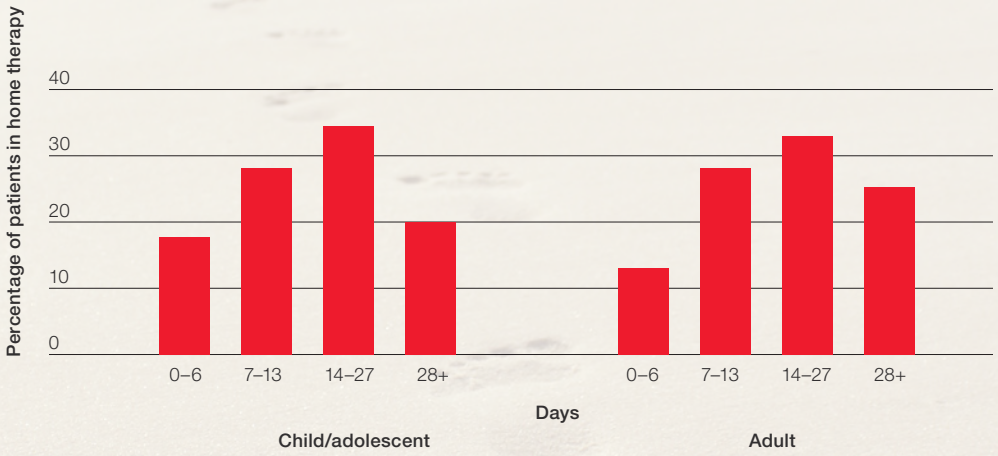
As for hospitalisation data, the manner of collection of data about intravenous antibiotic therapy administered at home does not allow a clear distinction to be drawn between 'no home therapy' and missing data in relation to a patient. Three paediatric hospitals (all large in patient numbers) and seven adult hospitals (four large and three small) were excluded from the analysis of home therapy because no data or incomplete data were provided. This excluded 46 percent of patients from the analysis.

Figure 4.3: ACFDR 2015: Home therapy



A total of 128 child or adolescent patients and 213 adult patients in the population analysed spent a mean of 19.7 days and 24.9 days respectively having intravenous antibiotic therapy at home. Median values were 14 days for each group. Figure 4.4 shows the distributions of those days.

Figure 4.4: ACFDR 2015: Accumulated home therapy days



4.5 Non–transplant surgery

Table 4.6 shows the age distribution of persons reported as having undergone selected non–transplant surgery during 2015. In view of the incompleteness of reporting, these numbers are likely to be under–estimates.

Table 4.6 – ACFDR 2015: Non–transplant surgery during the year [(a)]

	0–1 years	2–5 years	6–11 years	12–17 years	18–29 years	30+ years	All ages
IV access devices	0	0	0	1	7	0	8
Gall bladder disease	0	0	0	0	0	0	0
Gastrostomy	0	2	1	3	5	1	12
Intestinal obstruction	1	0	1	0	0	0	2
Nasal (any surgery)	0	0	4	2	3	1	10
Other	2	3	1	3	16	18	43

(a) Patients for whom no treatment information was provided (46 percent of total) were excluded from analysis.

5. ORGAN TRANSPLANTS

5.1 Patients assessed for transplant in 2015

Cystic fibrosis centres reported 49 patients had been assessed for organ transplant during 2015. Of these, 44 (42 adult) had been accepted onto transplant waiting lists (Table 5.1).

Forty–three patients had been accepted for a bilateral lung transplant and one for a liver transplant. For five other patients accepted, the organ to be transplanted was not specified.

Table 5.1 – ACFDR 2015: Patients accepted for transplants in 2015

Age group:	Males	Females	Persons
6 – 11 years	0	1	1
12 – 17 years	1	0	1
18 – 29 years	81	16	24
30 years and over	8	10	18
All ages	*17*	*27*	*44*

5.2 Transplants during 2015

Thirty bilateral lung transplants were reported by CF centres as having occurred in 2015 (Table 5.2). All but one of these transplants (29) were performed on adult patients, including 14 patients aged 30 years and over. One male aged 18–29 years of age had heart, lung and liver transplants in 2015, with another male aged 18–29 years of age having a combined lung and liver transplant.

Table 5.2 – ACFDR 2015: Patients receiving lung transplants in 2015

Age group:	Males	Females	Persons
12 – 17 years	1	0	1
18 – 29 years	7	8	15
30 years and over	6	8	14
All ages	14	18	30

One adult female patient who is not included in Table 5.2, was reported as receiving a liver transplant in 2015.

6. MORTALITY

6.1 Deaths recorded in 2015

The number of deaths reported to the Registry in 2015 was 17, fewer than 19 reported in 2014. One of the deaths reported in 2015 was of a person aged less than 18 years (Table 6.1).

Table 6.1 – ACFDR 2015: Deaths, by age and sex

Age group:	Males	Females	Persons
12 – 17 years	0	1	1
18 – 29 years	3	5	8
30 + years	2	6	8
All ages	*5*	*12*	*17*

By state and territory of residence, the highest number of deaths was reported for people residing in New South Wales (10). Two deaths were reported in Victoria, 2 in Queensland, 2 in Tasmania and 1 in Western Australia. No deaths of persons with CF in South Australia were reported in 2015 (Table 6.2).

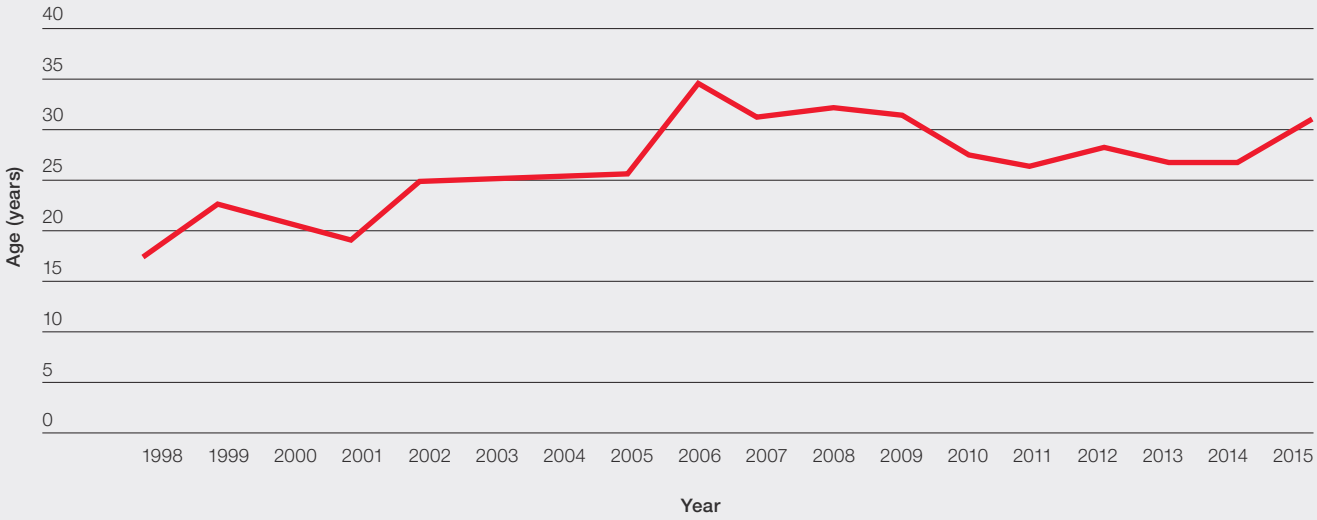
Table 6.2 – ACFDR 2015: Deaths recorded by state

	Males	Females	Persons
New South Wales	4	6	10
Victoria	0	2	2
Queensland	0	2	2
Western Australia	0	1	1
Tasmania	1	1	2
Total	*5*	*12*	*17*

The median age of death was 31.6 years in 2015, up from 27.7 in 2014.

The median age at death for patients who died on 2015 was 31.6 years, up from a median of 27.7 in 2014. A rising trend shown in this indicator from 1998 appeared to have stabilised or even reversed from around 2006, when the median age at death was 35 years. Whilst the 2015 figure may signal a return of an upward trend, the change should be interpreted conservatively, because of the relatively small number of deaths each year (Figure 6.1).

Figure 6.1: ACFDR 1998–2015: Median age at death



6.2 Causes of death

Ten of the 17 deaths reported in 2015 were due to pulmonary causes, three due to gastro–intestinal complications, with another 3 cases as a result of post–transplant complications. One cause of death was unknown or stated (Table 6.3).

Table 6.3 – ACFDR 2015: Cause of death

	Males	Females	Persons
Related to CF:			
Pulmonary	2	8	10
Gastro–intestinal	1	2	3
Other (including post–transplant)	1	2	3
Unrelated to CF	0	0	0
Cause unknown or not stated	1	0	1
All causes	*5*	*12*	*17*

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 Director/ Data Manager and Registry Co–ordinator 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 hospital. For 2015, complete or near–complete data was available for clinical data including lung function measurements, with the least complete data collected for social characteristics. Interpretation of data analysis in the latter should therefore be undertaken with caution.

The following table summarises the categories of data collection, and the percent completeness overall for 2015. This should be noted when interpreting data analysis.

Table 7 – ACFDR 2015: Data Completeness

Type of Data	% Sites near complete	% Overall Patients complete
Demographic information	100%	100%
Clinical Measurements	91%	80%
Pancreatic insufficiency	100%	93%
Genotype	96%	91%
Diagnostic information	91%	85%
Treatments	65%	59%
Microbiology	65%	61%
Hospital / Home Therapy	60%	61% / 54%
Social	48%	36%
Complications	43%	50%

Output editing of data

Duplicate patient records held in the Registry are rationalised prior to analysis for reporting. These are identified from advice about patient transfers between treatment centres and, additionally, by investigation of unreported potential duplicates from searches for patients of the same sex and date of birth.

Duplicate encounter records are removed and encounter data undergo plausibility checking, logical edits and examination of outliers to identify, remove or correct clear data entry errors before analysis for tables and charts.

8. APPENDICES

List of Figures

List of Tables

ACFDR Advisory Group members (pre–September 2016)

Advisory committee members	
Dr Peter Cooper	The Children's Hospital, Westmead, NSW
Professor Adam Jaffe	Sydney Children's Hospital, Randwick, NSW
A/Professor James Martin	Women's and Children's Hospital, Adelaide, SA
Professor Peter Bye	Royal Prince Alfred Hospital, Camperdown, NSW
Professor Scott Bell	The Prince Charles Hospital, Brisbane, QLD
A/Professor Sarath Ranganathan	Royal Children's Hospital, Melbourne, VIC
Dr Guy Marks	Liverpool Hospital, Liverpool, NSW
Dr Phil Robinson	Royal Children's Hospital, Melbourne, VIC
Dr Gerard Ryan	Sir Charles Gairdner Hospital, Perth WA
Mr Geoff Sims	Australian Clinical Registries
Ms Nettie Burke	Cystic Fibrosis Australia

Registry Steering Committee Membership (from September 2016)

Advisory committee members	Role/specialisation	Institution/Association
Dr 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	Lady Cilento Children's Hospital, Qld
Dr Andre Schultz	CF Physician – Paediatrics	Princess Margaret Hospital (to be known as Perth Children's Hospital in 2017), WA
Professor Peter Bye	CF Physician – Adults	Royal Prince Alfred Hospital, NSW
A/Professor Peter Middleton	CF Physician – Adults	Westmead Hospital, NSW
A/Professor Tom Kotsimbos (by invitation)	CF Physician Adults	Alfred Health, Vic
Ms Nettie Burke	CEO	Cystic Fibrosis Australia
Mr Geoff Sims	Data Manager – ACFDR	Monash University, VIC
Dr Susannah King	Dietitian	Alfred Hospital, VIC
Ms Lucy Keatley	Nurse/Data Entry	Westmead Hospital, NSW
Ms Morgan Gollan	Consumer Representative	NSW

List of Participating Sites

Site	
Sydney Children's Hospital (SCH)	paediatric
Royal Prince Alfred Hospital (RPA)	adult
The Children's Hospital, Westmead (CHW)	paediatric
Westmead Hospital (Adults) (WMH)	adult
Gosford Hospital (GOS)	adult
John Hunter Children's Hospital (JHC)	paediatric
John Hunter Hospital (Adults) (JHA)	adult
Royal Children's Hospital (RCM)	paediatric
The Alfred Hospital (ALF)	adult
Monash Medical Centre (MMC)	paediatric and adult
The Prince Charles Hospital (PCH)	adult
Mater Hospital (Adults) (MAH)	adult
Gold Coast University Hospital (GCH)	adult
Lady Cilento Children's Hospital (LCC)	paediatric
Royal Adelaide Hospital (RAH)	adult
Women and Children's Hospital (WCH)	paediatric
Princess Margaret Hospital for Children (PMH) (to be known as Perth Children's Hospital from 2017)	paediatric
Sir Charles Gairdner Hospital (SCG)	adult
Royal Hobart Hospital (RHH)	paediatric
Launceston General Hospital (LGH)	paediatric
North West Regional Hospital (BUR)	paediatric
Tasmanian Adults (incorporating RHH and LGH)	adult
The Canberra Hospital – adult clinic (CHA)	adult
The Canberra Hospital – children (CHC)	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 role account below

Email: med–acfdregistry@monash.edu

Registry Academic Lead: Dr Susannah Ahern

Registry Co–ordinator: Joanna Dean

Phone: +61 (0)3 9903 0101

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

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.

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