2013 Annual Report

CFRI

The Cystic Fibrosis Registry of Ireland

Preface

We are delighted to share with you the 2013 Annual Cystic Fibrosis Registry of Ireland Report. This report is compiled using information that has been collected from medical records for 1158 consenting CF patients. This represents 92.5% of the total CF population attending clinics in the Republic of Ireland. We are ever grateful to those patients for their willingness to participate in the Registry. Without access to their data we would not exist and would not be able to contribute towards improving CF care and outcomes not just in Ireland, but across the globe. Over 350 variables per patient are manually collected each year. This task is onerous to say the least and a sincere thanks needs to be expressed to all those who methodically abstract data from patient charts, interpret and record the relevant information onto paper forms and then convert that into digital information that can be stored and analysed.

In our 2012 Annual Report it was stated that we hoped to build a new encounter-based technology platform using new software being commissioned by the European Cystic Fibrosis Society Patient Registry. The new European platform was developed during 2013 by an Irish company and was launched at the European Cystic Fibrosis Society's meeting in June 2014. As data collected by the Irish Registry is more extensive than that collected for the European Registry, further software development commissioned by CFRI took place during 2014 to allow the migration of the complete Irish dataset across to the new platform. This was being quality checked during December 2014 and it is hoped that we will go live with Phase 1 early in 2015. Phase 1 will still require the capture of data by registry staff and possibly by specific centres on a test basis. Phase 2 is at the conceptual stage and will require considerable input from members of the multi-disciplinary teams. Our goal for Phase 2 is to have a user-friendly interface that can be used in each clinic and become a valued tool in patient management and quality control without increasing the workload of already overstretched hospital personnel.

In 2012, the Medical Research Charities Group published a report on Patient Registries in Ireland. In this report it identified 47 registries of which 69% had less 3 staff members (of which CFRI would have been one) and the majority operated with limited funding. The European Commission openly recognises that disease registries are "an indispensable infrastructure tool for translating basic and clinical research into improved care and therapeutic solutions." As our patient numbers grow, it is becoming increasingly challenging to manually collect and import patient medical data into our database. Scale has become an issue especially with the increase in requests we are receiving to use registry data. This increase in registry data requests is very welcome and reinforces the value of the registry. In 2014 we received applications for both domestic and international research, Health Technology Assessment submissions, Phase IV pharmacovigilance studies for the European Medicines Agency, as well as data requests to contribute to Government and HSE reports. We are very fortunate that CFRI has a good reputation in Ireland and is often referred to as a registry model that others should follow. The time is fast approaching where new models for disease/patient registries will need to be employed to avoid duplication of scarce resources and we would hope that CFRI would play an important role in developing a sustainable model for patient centric disease registries in Ireland into the future.

Dr Edward McKone MD, MSc, FRCPI, FCCP
Chairperson
Cystic Fibrosis Registry of Ireland

Godfrey J. Fletcher BA mod, MBA
CEO
Cystic Fibrosis Registry of Ireland

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Glossary

Abbreviation	
AA	Annual Assessment
ABPA	Allergic Bronchopulmonary Aspergillosis
Adult	Aged 18 years or older (≥18)
BAL	Bronchoalveolar lavage
BMI	Body Mass Index
CF	Cystic Fibrosis
CFI	Cystic Fibrosis Ireland
CFRI	Cystic Fibrosis Registry of Ireland
CFTR	Cystic Fibrosis Transmembrane conductance Regulator (mutation)
CRA	Clinical Research Associate
DIOS	Distal Intestinal Obstruction Syndrome
FH	Family history
FEV_1	Forced Expiratory Volume in one second
FVC	Forced expiratory Vital Capacity
GORD	Gastro-oesophageal Reflux Disease
GI	Gastrointestinal symptoms
H2RA	H2-receptor antagonists
IRT	Immunoreactive trypsinogen
IV	Intravenous
MI	Meconium ileus
MRSA	Methicillin Resistant Staphylococcus aureus
NBS	Newborn screening
NCMG	National Centre for Medical Genetics
NSAID	Non-steroidal anti-inflammatory drug
Paediatric	Aged under 18 years (<18)
PEP mask	Positive expiratory pressure mask
PPI	Proton pump inhibitors
PWCF	Persons with cystic fibrosis
RESP	Respiratory symptoms

Summary data

On the last day of 2013, the number of live persons registered with the CFRI was 1158. The number of adults registered with the CFRI exceeded 600 for the first time in 2013, increasing in number by approximately 100 since 2009. Adults accounted for 53.8% of live PWCF on the last day of 2013, and 46.2% were children. The median age of adult PWCF was 28.5 years. Median age of living patients continues to increase year-on-year. Annual variation in the number of deaths and median age at death is common in the Irish CF population. Fewer deaths occurred in 2013 than in recent years. The 8 PWCF who died in 2013 had a median age of 22.8 years (range: 10-40 years).

Organ Donation and Transplant Ireland reported a record number of lung transplants performed in Ireland in 2013, increasing from 14 in 2012 to 32 in 2013. This included a number of CF double lung transplants, which increased from 4 in 2012 to 9 in 2013.

Summary of 2013 CFRI dataset

	2013	2012	2011	2010	2009
CF persons registered (n)[1]					
Children (<18 years)	535	545	516	494	496
Adults (≥18 years)	623	595	558	550	531
Total (% census)	1158 (92.5%)	1140 (92.7%)	1074 (90.9%)	1044 (90.0%)	1027 (89.2%)
Median age (years)					
Children	9.9	9.6	9.9	10.2	9.9
Adults	28.5	27.9	27.2	26.6	26.0
Overall	19.6	19.1	18.8	18.8	18.6
Gender (%)					
Female	42.1%	42.7%	43.0%	42.9%	42.4%
Male	57.9%	57.3%	57.0%	57.1%	57.6%
Deaths in CFRI-registered persons (n)	8	18	26	16	17
Median age at death in years (n)	22.8	25.9	23.5	28.1	25.6
Recorded annual clinical data (%)					
Children (% all children)	487 (91.0%)	476 (87.3%)	468 (91.1%)	454 (91.9%)	454 (91.5%)
Adults (% all adults)	392 (62.9%)	405 (72.5%)	388 (69.4%)	412 (74.9%)	411 (77.4%)
Overall	879 (75.9%)	881 (77.3%)	856 (79.7%)	866 (83.0%)	865 (84.2%)

[1] CFRI-registered PWCF, alive on the last day of each respective year.

Gender & age

Of the PWCF alive on the last day of 2013, males outnumbered females (57.6% were male). Over half of male and female PWCF were aged 18 years or older, and the proportion of male adults was larger than female adults (55.4% vs. 51.6%). The difference in proportion of adult males compared with adult females was not statistically significant (χ^2=1.58, p=0.21).

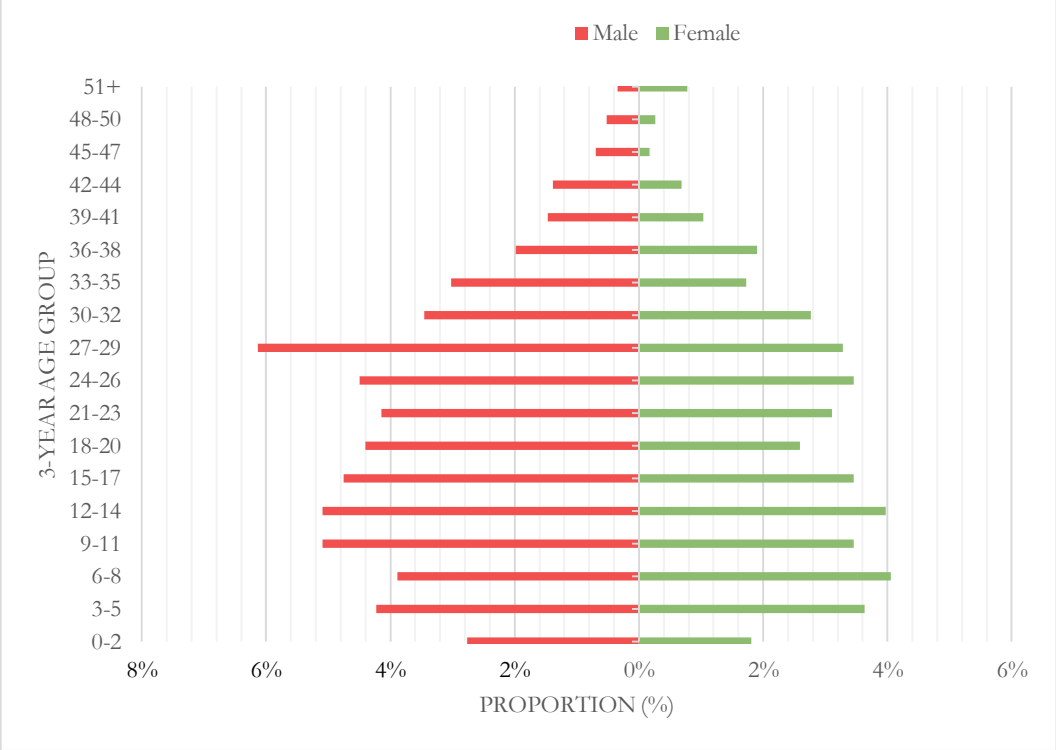
Gender of children and adults

	Females N=488	Males N=670
Children	48.4%	44.6%
Adults	51.6%	55.4%
All	42.1%	57.6%

Twenty-seven percent of PWCF were aged in their twenties at the end of 2013, and 22% were aged 30 years or older. The oldest registered PWCF was 69 years of age.

The age distribution of the CF population is illustrated below using a population pyramid. It shows the proportions of the CF population (X-axis) in three-year age cohorts (Y-axis). Males appear in red on the left of the pyramid, and females in green on the right. The overall shape is that of a pyramid; a wide base that narrows across the older age cohorts. This reflects the natural pattern of births and deaths in the CF population. Normally, it would be expected that the youngest age cohort would comprise the largest proportion of the population, however a lag in the registration of newly diagnosed PWCF means that the youngest cohort is narrower than expected.

CF population pyramid



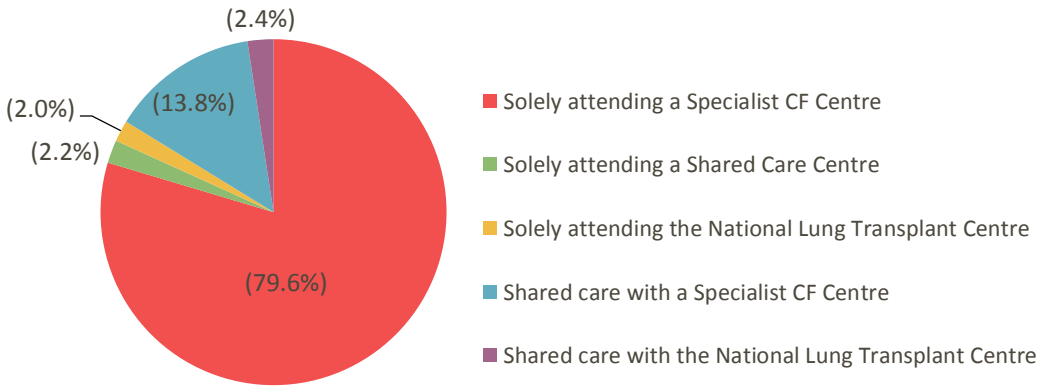
Services for people with cystic fibrosis

Health services for people with CF are provided at National Referral Centres (adult and paediatric), Specialist CF Centres, and Shared Care Centres (offering shared care to PWCF under the supervision of a Specialist CF Centre). There at eight approved specialist CF centres, which are located at: Beaumont Hospital (adults) St Vincent's University Hospital (adults – also the adult National Referral Centre), Adelaide and Meath Hospital Dublin, Incorporating the National Children's Hospital (children), Our Lady's Children's Hospital, Crumlin (children - also the paediatric National Referral Centre), Temple Street Children's University Hospital (children), University College Hospital, Galway (children and adults), Cork University Hospital (children and adults), and University Hospital Limerick (children and adults). CF care is also provided at Shared Care Centres. In 2013, data was collected from Shared Care Centres located at Cavan General Hospital, Mayo General Hospital, Our Lady of Lourdes Hospital, Drogheda, Sligo Regional Hospital, and Waterford Regional Hospital. Finally, care of PWCF is provided at the National Lung Transplant Centre at the Mater Misericordiae University Hospital.

Most PWCF (95.9%) attended a specialist CF centre for either all or some of their care (as part of a shared care arrangement). A small proportion (2.2%) opted to receive all of their CF care from a Shared Care Centre. All others (2.0%) solely attended the National Lung Transplant Centre.

Of those PWCF who had a lung transplant and were alive on the last day of 2013, 54.9% attended both the National Lung Transplant Centre and their specialist CF centre. Therefore, approximately half of PWCF who underwent a lung transplant were lost to follow-up at a specialist CF centre.

CF service provision



Diagnosis

Of the 1158 PWCF alive at the end of 2013, 85% were diagnosed before 5 years of age, 72% were diagnosed by the age of two years, 64% were diagnosed by the age of one year, and 42% were diagnosed by 3 months.

Age at diagnosis was examined separately for children and adults. One in two children were diagnosed with CF by three months (48%). Of those adults alive in 2013, 36% were diagnosed by 3 months, while 20% were diagnosed after their fifth birthday. The latter group of adults may represent a distinct genetic subgroup that are associated with mild clinical manifestations and low mortality.

Age at diagnosis

Age-band	All N=1158	Children N=535	Adults N=623
Birth - 2 months	41.6%	48.0%	36.1%
3 - 5 months	11.7%	12.2%	11.4%
6 - 11 months	10.6%	10.7%	10.6%
1 year	8.1%	10.5%	6.1%
2 years	6.0%	5.4%	6.6%
3 years	3.8%	5.1%	2.7%
4 years	2.8%	2.4%	3.1%
5+ years	13.1%	5.2%	19.9%
Not known	2.2%	0.6%	3.5%

Symptoms leading to a CF diagnosis in CFRI-registered patients alive on the last day of 2011, 2012 and 2013 respectively are shown in the table below. The proportion of PWCF diagnosed following neonatal (and antenatal) screening has increased annually since 2011. The introduction of a Neonatal Cystic Fibrosis Screening Programme in July 2011 has contributed to this increase. By 2013, 4.4% of PWCF were diagnosed as a result of either the Irish Neonatal CF Screening Programme, a screening programme overseas or antenatal screening overseas.

Over the last three years, the proportion of the live CF population who presented with respiratory and/or gastrointestinal symptoms leading to a diagnosis of CF has decreased. In addition, the proportion of PWCF with a family history of CF (with/without symptoms) has increased slightly (from 21.7% in 2012 to 22.8% in 2013).

Symptoms leading to a CF diagnosis

Symptom	2013 % N=1158	2012 % N=1140	2011 % N=1074
Gastrointestinal symptoms	19.9%	20.5%	22.6%
Respiratory symptoms	18.9%	19.7%	19.9%
Respiratory and gastrointestinal symptoms	17.7%	17.3%	17.1%
Family history	14.3%	14.5%	15.3%
Meconium ileus	12.9%	13.8%	14.2%
Family history and ≥1 symptom	8.5%	7.2%	6.8%
Neonatal & antenatal screening	4.4%	3.2%	0.9%
Unknown	2.9%	3.2%	3.2%
Other	0.5%	0.5%	-
Total			

Statistics from the national newborn bloodspot screening programme for 2013 are presented below. Approximately 70,000 newborns were screened for CF. Following further testing by the National Centre for Medical Genetics and sweat testing at CF specialist centres, 34 newborns were diagnosed with CF in 2013.

National Newborn Bloodspot Screening Programme Statistics

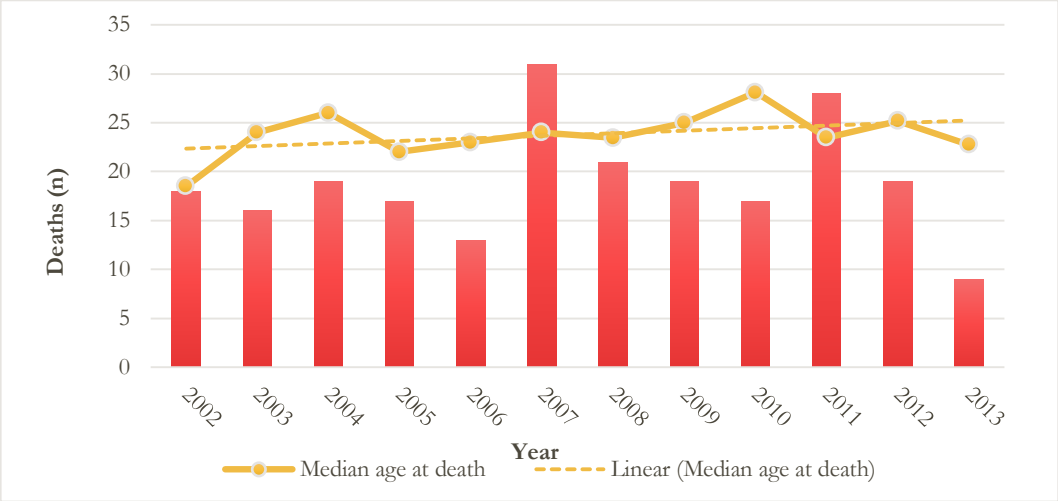
	N (%)
Number of newborns screened in 2013	69,128
Number of samples with raised IRT sent to National Centre for Medical Genetics (NCMG)	753 (1.08%)
Number of newborns with one mutation identified	61
Number of newborns with two mutations identified	28
Number of newborns referred to a CF Specialist Centre	89
Number of initial sweat tests performed	87*
Number of sweat test failures	24
Number of newborns with negative sweat test	37
Number of newborns with borderline sweat test	8
Number of newborns requiring repeat sweat test	28
Number of newborns who had further /repeat IRT	4
Number of newborns diagnosed with CF	34
Number of newborns diagnosed with variant CF	3
Number of newborns diagnosed as carriers	52

Data provided on the 3rd December 2014 by Prof Philip Mayne, Director, National Newborn Bloodspot Screening Laboratory, Temple Street. *2 newborns died prior to sweat testing

Deaths

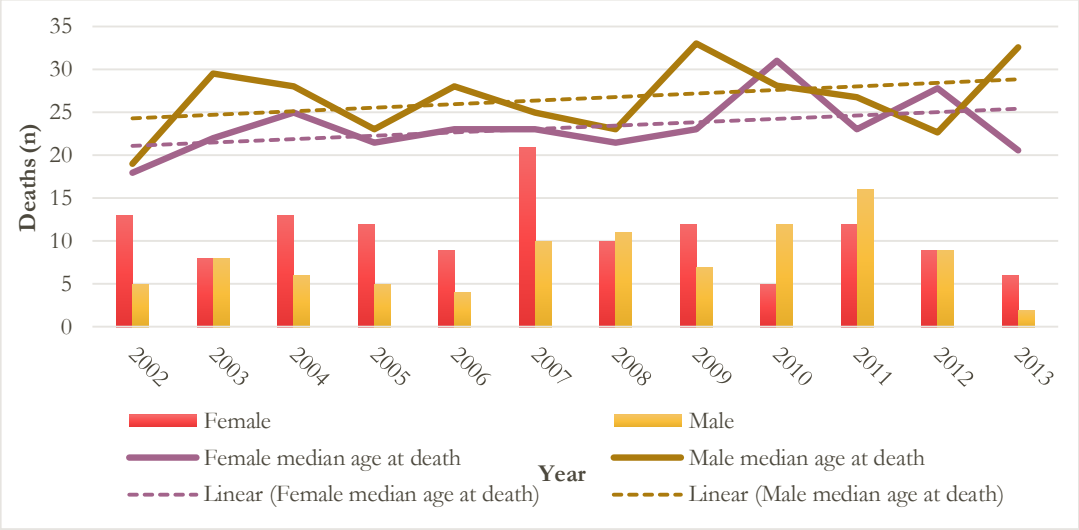
A total of 9 deaths occurred in individuals with CF in 2013, 8 of which were registered with the CFRI. Cause of death was known for five of the eight CFRI-registered deaths; all five were due to respiratory-cardiac failure. Six of the eight decedents were female. Age at death ranged from 10 to 40 years. There have been a total of 227 deaths in PWCF between 2002 and 2013.

Number of deaths and median age at death



In any small population such as the Irish CF population, there is a natural variation in the number of deaths recorded in each calendar year. Eight is the smallest number of deaths recorded by the CFRI to date, and it is unlikely that such a small number will be reported in forthcoming years. The average number of annual deaths in PWCF is nineteen.

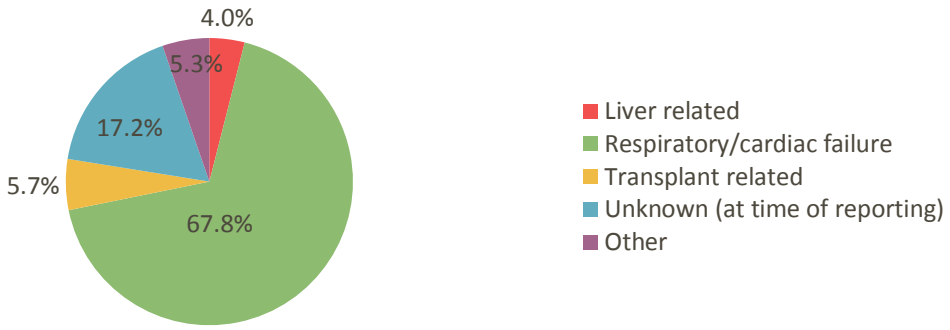
Number of deaths and median age at death by gender



There were more deaths in female PWCF than in males in 2013. Median age at death in females was 20.6, compared with 32.6 in males. This difference may appear greater than in previous years, but year-to-year variation can be expected with median age at death as well as number of deaths. Overall trends suggest that median age at death in males and females continues to improve.

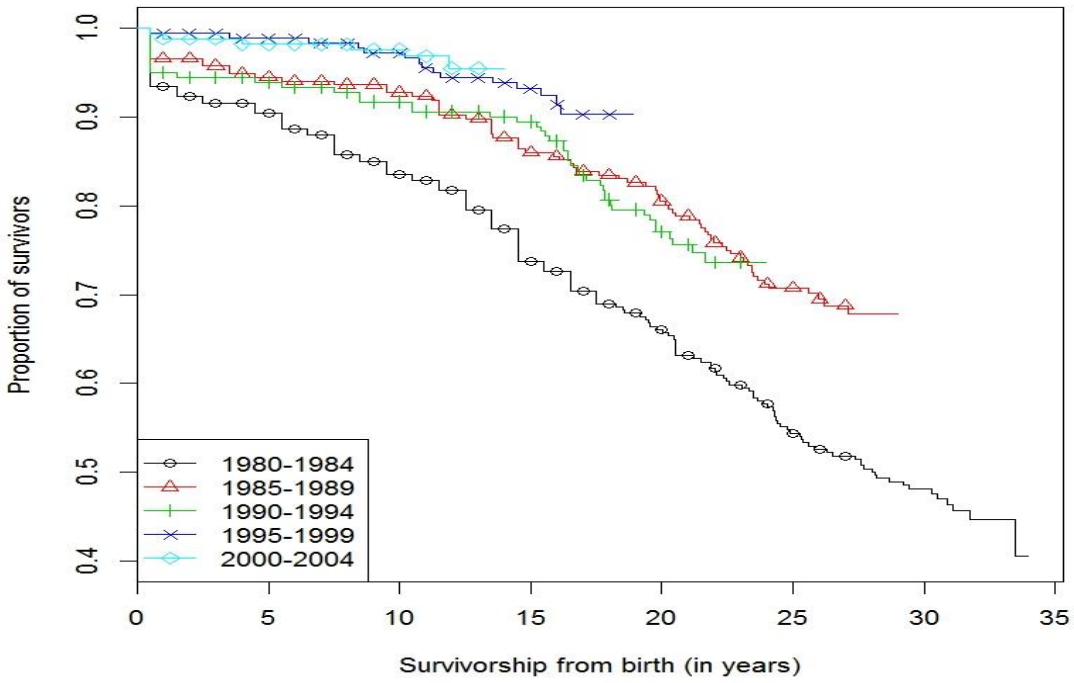
The cause of death for the 227 PWCF deaths recorded between 2002 and 2013 is shown below. Of those with a known cause of death, 81.9% died as a result of respiratory/cardiac failure.

Cause of death



Survival in consecutive birth cohort has improved. Whereas 82.8% of PWCF born 1980-1984 were alive at age ten years, the proportion of PWCF born 2000-2004 who survived to age ten years was 96.9%.

Birth cohort survival to 2013



Genotype

Ninety-eight percent of PWCF had known genotypes. Class II CFTR mutation p.F508del was detected on either one or both alleles in 91.2% of PWCF, while 14.5% had Class III mutation G551D on either one or both alleles. In March 2013, CFTR potentiator ivacaftor (Kalydeco™), an oral prescription medicine for CF, first became available for use in Ireland, for PWCF aged six years and older with a G551D mutation.

CFTR mutations

Mutation	PWCF	%
p.F508del homozygous	654	56.5%
p.F508del heterozygous		
p.F508del, p.G551D	129	11.1%
p.F508del, p.R117H	49	4.2%
p.F508del, p.R560 T/K	30	2.6%
p.F508del, c.621+1 G-->T	17	1.5%
p.F508del, c.1717-1 G-->A	16	1.4%
p.F508del, p.G542X	17	1.5%
All other p.F508del heterozygote mutations	144	12.4%
Homozygous p.G551D	14	1.2%
All other mutations	60	5.2%
Mutation not recorded	12	1.0%
Mutation identification pending	16	1.4%
Total	1158	

Annual clinical data

Annual clinical data was manually extracted from hospital medical records by CFRI staff for 75.9% of PWCF. The number of PWCF for whom annual clinical data was gathered increased slightly in 2012 and 2013 compared to previous years. However, the proportion of PWCF for whom data is collected has declined in each consecutive year, over the past five years, from 84.2% in 2009 to 75.9% in 2013. This reflects the perennial challenge of collecting annual clinical data for a growing population without a corresponding growth in resources within the CFRI.

Annual clinical data collection

	2013	2012	2011	2010	2009
Children (%)	487 (91.0%)	476 (87.3%)	468 (91.1%)	454 (91.9%)	454 (91.5%)
Adults (%)	392 (62.9%)	405 (72.5%)	388 (69.4%)	412 (74.9%)	411 (77.4%)
All (% of 1158 live PWCF)	879 (75.9%)	881 (77.3%)	856 (79.7%)	866 (83.0%)	865 (84.2%)

Clinical event summary

Hospitalisations recorded by CFRI are those which have been processed through the hospital's admission service (i.e. a day case or inpatient admission). For PWCF with available annual clinical data, 44.7% of children and 46.7% of adults had one or more recorded hospital admission in 2013. In recent years, the development of new CF units have provided opportunities to enhance the capacity to deliver care to PWCF. In August 2013, a new in-patient and out-patient facility for CF patients opened at St Vincent's University Hospital, Dublin.

The average number of hospitalisations and respiratory exacerbations per child and per adult remains similar to previous years. For adults, the actual numbers of hospitalisations and respiratory exacerbations recorded by the CFRI in 2013 were lower than in previous years. This is due to the lower rate of annual clinical data collection in 2013, for reasons previously described.

Hospitalisations and respiratory exacerbations

	Children		Adults	
	n	Average per PWCF	n	Average per PWCF
Hospitalisations	491	1.01	414	1.05
Respiratory exacerbations requiring IV antibiotics	441	0.91	615	1.57

Complications

PWCF may experience none, one or multiple complications in any given calendar year. In 2013, 1,319 complications were recorded for children (2.7 on average per child) and 1,611 for adult PWCF (4.1 on average per adult). Chronic bacterial colonisation of the respiratory tract remains the most common complication in 2013; chronic Staphylococcal infection was reported for 58.7% of children, and chronic Pseudomonal infection for 64.3% of adults.

Between 2012 and 2013, chronic *Pseudomonas aeruginosa* infection decreased in children from 24.4% to 18.7%. *Burkholderia cepacia* infection increased from 6 to 10 cases in children, and from 12 to 14 cases in adults. The number of cultures found to contain MRSA was less than in 2012. The number of PWCF with non-tuberculous mycobacterial (NTM) infection refers to those individuals with a 2013 annual assessment, who provided a specimen which was culture positive for NTM between 2008 and 2013. This differs from previous years, where only PWCF with a culture positive in that year was reported.

Proportions of PWCF with pancreatic insufficiency (93.3%), and gastro-oesophageal reflux disease (42.4%) remain unchanged from the previous reporting year. Abnormal liver function tests were reported in 3.9% of children and 5.4% of adults. The proportion of children with liver disease declined from 6.5% in 2012 to 4.1% in 2013, and from 17.8% to 12.2% in adults. We acknowledge that CFRI reporting of liver-associated complications is likely to be underestimated, and this is due to difficulties capturing and interpreting occasionally unequivocal medical information.

Cardio-respiratory complications

	No of complications	
	Children N (%)	Adults N (%)
Chronic *Pseudomonas aeruginosa* infection[1]	91 (18.7%)	252 (64.3%)
Chronic *Staphylococcus aureus* infection[1]	286 (58.7%)	146 (37.2%)
Burkholderia cepacia infection	10 (2.1%)	14 (3.6%)
MRSA	44 (9.0%)	29 (7.4%)
Non-tuberculous *Mycobacteria*	16 (3.3%)	18 (4.6%)
Nasal polyps[2]	11 (2.3%)	9 (9.0%)
Allergic Bronchopulmonary Aspergillosis[2]	21 (4.3%)	25 (6.4%)
Asthma[2]	10 (2.1%)	14 (3.6%)
All other cardiorespiratory complications[2,3]	2 (0.4%)	4 (1.0%)

[1] ≥3 cultures in a year. [2] Physician-reported. [3] Cor pulmonale, pneumothorax, haemoptysis

Gastrointestinal complications

	No of complications	
	Children N (%)	Adults N (%)
Distal intestinal obstructive syndrome[1]	5 (1.0%)	19 (4.8%)
Pancreatic Insufficiency[2]	464 (95.1%)	356 (90.8%)
Abnormal liver function tests	19 (3.9%)	21 (5.4%)
Liver disease	20 (4.1%)	48 (12.2%)
Gastro-oesophageal reflux disease[1]	156 (32.0%)	217 (55.4%)
All other gastrointestinal complications[1,3]	5 (1.0%)	7 (1.8%)

[1] Physician-reported. [2] Reported use of pancreatic enzymes. [3] Haematemesis, colonic stricture, gallbladder disease.

Other common CF co-morbidities are shown in the table below. Osteoporosis/osteopenia was reported in 37.8% of adults and 27.3% of adults were being treated with insulin for CF-related diabetes.

Other complications

	No of complications	
	Children N (%)	Adults N (%)
Diabetes[1]	15 (3.1%)	107 (27.3%)
Clubbing	146 (30.0%)	190 (48.5%)
Osteopenia/osteoporosis	9 (1.8%)	148 (37.8%)

[1] Requiring insulin

Pulmonary function

Forced expiratory volume in one second is an important marker of lung health in PWCF aged six years and older. It is presented here as a percentage of the predicted/reference value for a healthy peer ('FEV1% predicted'). In general, an FEV1% predicted of <40% indicates severe lung disease, 40-69% indicates moderate disease, and ≥70% indicates mild lung disease in PWCF.

A total of approximately 1,800 values were collected for 670 PWCF aged ≥6 years in 2013, indicating that PWCF had on average 2.7 pulmonary function tests per PWCF in 2013. The highest recorded FEV1% predicted value was selected for each PWCF, and the median value was estimated for each age band as shown in the table below. This is a departure in approach from previous annual reports, and brings reporting of pulmonary function in line with European reporting standards.[1] As a result, median FEV1% predicted in most age bands is higher than in previous years.

Median FEV1% predicted

Age (years)	No. of PWCF	FEV1% predicted		
		Median	25th percentile	75th percentile
6-8	80	96.5%	86	107
9-11	85	91%	80	100.5
12-14	87	88%	77	100
15-17	71	84%	61	104
18-19	40	73.5%	56	95
20-24	96	71.5%	47.8	86
25-29	86	63.5%	47	82.3
30-34	57	66%	46.5	78
35-39	38	56%	40	71
≥40	30	61%	37.8	86
All ages (6+)	670	80%	57	96

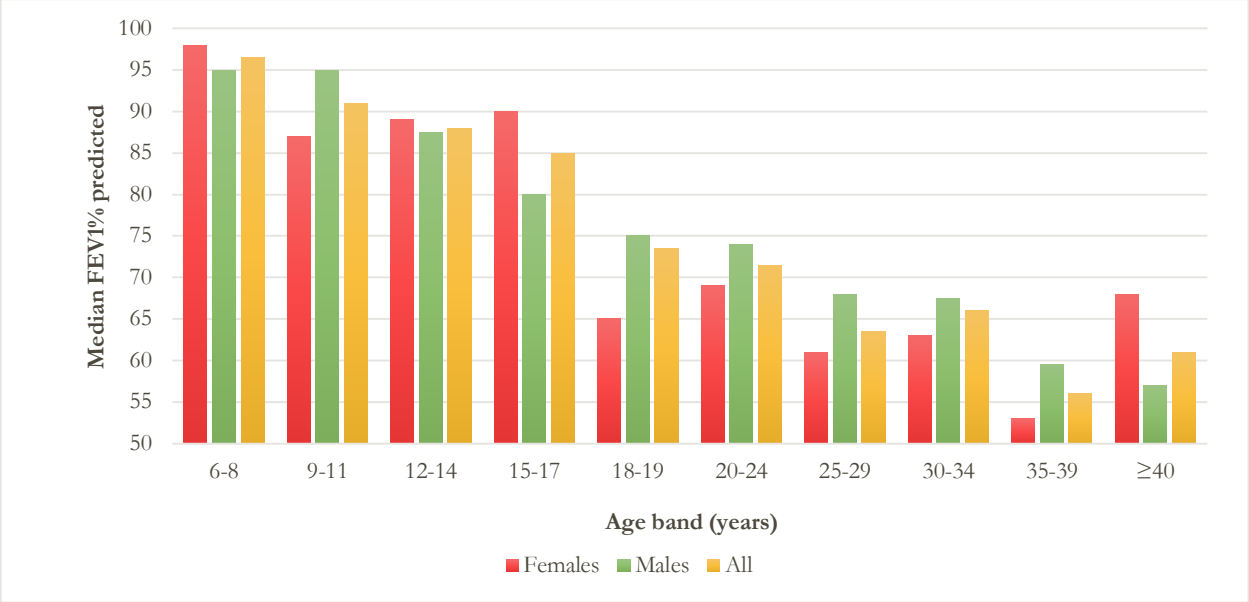
Median FEV1% predicted was 91% in children from age 6 (mean 88.2%, interquartile range 78%-102%), and 66% in adults (mean 65.8%, interquartile range 47%-84%).

Median FEV1% gradually declined across all age bands (with the exception of PWCF ≥40 years). The largest consecutive decrease in median FEV1% predicted was between the 15-17 and 18-19 year age bands (84% to 73.5%) and the 30-34 and 35-39 year age bands (66% to 56%).

The decline of FEV1% predicted across male age bands in 2013 appear to even-paced. Median values in female in 2013 were similar across the 9-11, 12-14 and 15-17 year age bands however, a notable difference in the median value of females aged 15-17 and 18-19 years exists.

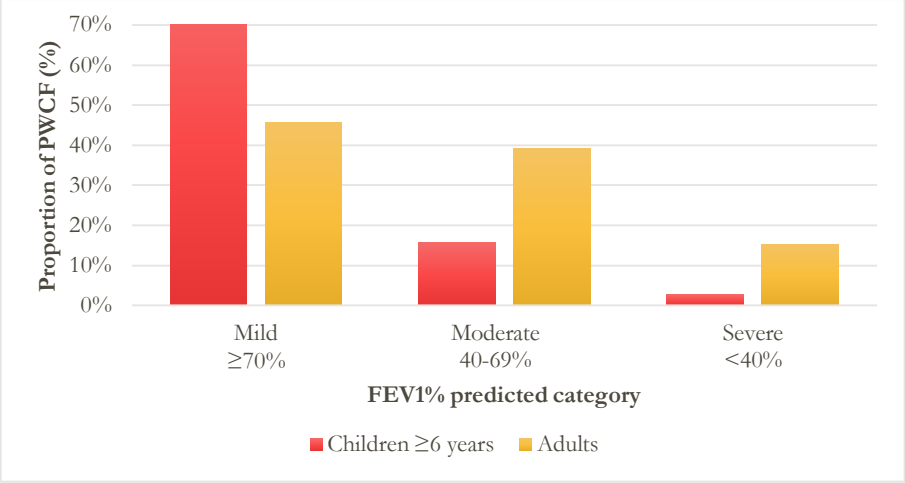
[1] Previous CFRI Annual Reports estimated median values in each age band using all FEV1% predicted values recorded in that year.

Median FEV1% predicted by age and gender



In 2013, 81.5% of children's and 45.5% of adult's best FEV1% predicted values were in the mild lung disease category. Three percent of children and 15.2% of adult PWCF had severe (<40%) lung disease.

Severity of lung disease



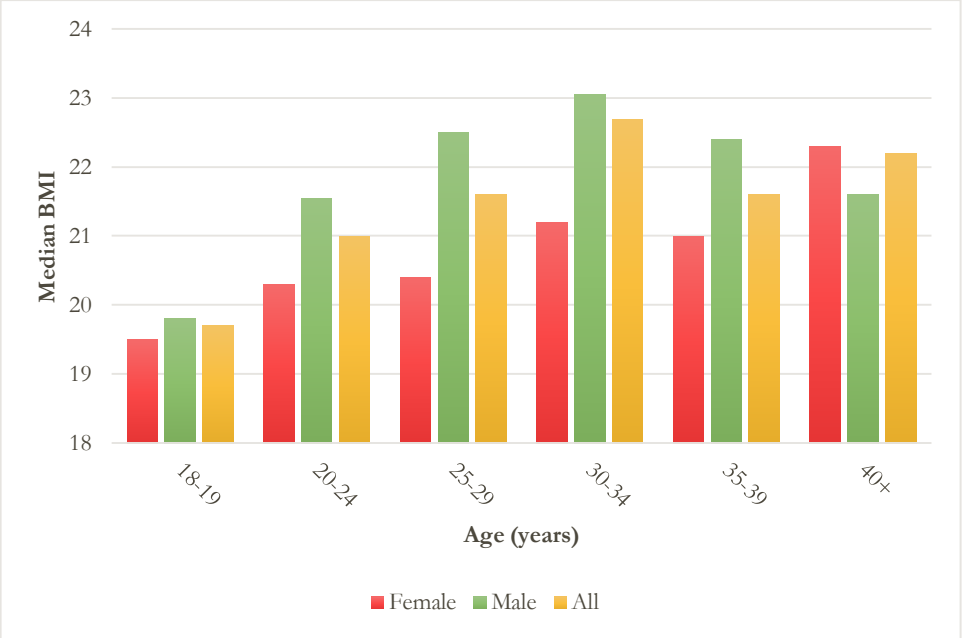
Body mass index (BMI)

Over 2,100 BMI values were collected in 2013. In this year's Annual Report, reporting of BMI has been brought in line with European reporting standards (see pulmonary function values also). Highest recorded values for each PWCF in 2013 are reported here.[2]

Of the 780 PWCF with recorded BMIs in 2013, 350 were aged 18 years and older. Median values of best BMI values were 21.8 for adult males and 20.7 for adult females.

Best BMI values are shown by age band in the bar chart below. Median BMI of males exceeded that of females in each age band (with the exception of the 40 years and older age band). Median BMIs were highest for males in the 30-34 age band (median 23.05) and 40 years and older age band for females (median 22.3).

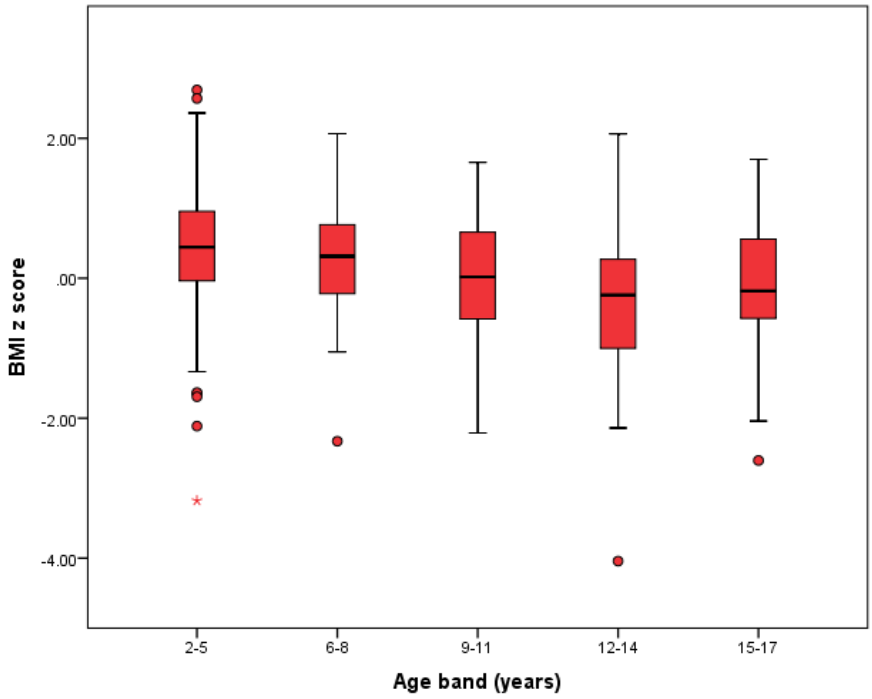
Adult median BMI values



BMI z-score is the preferred measure for examining growth in CF children. It is a measure that has been weight-adjusted for a child's age and sex, relative to an appropriate reference standard, in this case, the Centers for Disease Control and Prevention 2000 growth charts. The boxplot below shows that in 2013, the median BMI z-score for children aged 2-11 years was slightly above average, while those aged 12-17 had a value slightly below average.

[2] Previously, median values were estimated using all BMI values recorded for PWCF in that year.

Children's BMI *z*-score



Microbiology

Approximately 9,000 microbiology results were recorded in 2013, 65.5% of which were provided by children. Children had a greater number of culture results reported in 2013 (5,826 culture isolates) compared to the previous year (4,218 in 2012). On average, 6.3 sputum samples were examined for children in 2013, compared with 4.8 in 2012. An average of 7.4 sputum samples from adults were examined in 2013.

Culture isolates

	Children		Adults	
	n	Average per PWCF	n	Average per PWCF
Sputum samples	3079	6.3	2909	7.4
Throat swabs	1204	2.5	4	0.0
Cough swabs	1203	2.5	78	0.2
BAL sample	114	0.2	11	0.0
Nasal swabs	70	0.1	4	0.0
Other swabs*	156	0.3	59	0.2
Total	5826	11.9	3065	7.8

* Axilla, groin, unknown

Of the 5,988 recorded sputum cultures, 24.1% grew *Pseudomonas aeruginosa*, 17.8% grew *Staphylococcus aureus* and species of Candida were detected in 15.5% of sputum isolates. *Burkholderia cepacica* complex was identified in 1.1% of sputum samples, an increase from 0.7% in 2012. Most (59/67 isolates) were *Burkholderia cepacia* complex genomovar II *(B multivorans).*

Sputum culture

	n	%
Pseudomonas aeruginosa	1441	24.1%
P. aeruginosa (mucoid status not reported)	649	45.0%
P. aeruginosa (mucoid)	529	36.7%
P. aeruginosa (non-mucoid)	263	18.3%
Staphylococcus aureus	1067	17.8%
All Candida species	929	15.5%
Normal flora	766	12.8%
Aspergillus fumigatus complex	300	5.0%
MRSA	230	3.8%
Haemophilus influenza	229	3.8%
Stenotrophomonas maltophilia	161	2.7%
Gram positive cocci	69	1.2%
Burkholderia cepacia complex*	67	1.1%
Haemophilus parainfluenza	62	1.0%
Gram negative bacilli	47	0.8%
Other	620	10.4%
Total	**5,988**	

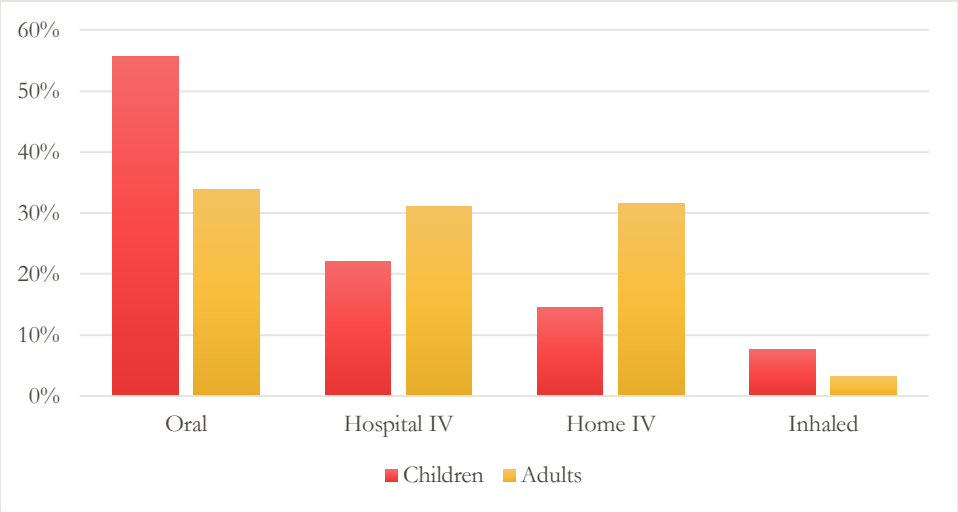
*Contains 59 *Burkholderia cepacia complex genomovar II (B multivorans), 4 genomovar III (B cenocepacia) and 4 B cepacia genomovar unspecified.*

Antibiotics

Approximately 4,000 (3,946) courses of antibiotics were commenced by PWCF in 2013. Fifty-four percent of recorded antibiotics were administered to children (for either prophylaxis or treatment of respiratory or other exacerbation). PWCF commenced 4.5 courses of antibiotics in 2013. The commonest methods of antibiotic administration were via oral medication (45.7%), hospital IV (26.3%) and home IV (22.4%).

In children, most courses of antibiotics were administered orally (55.7%). IVs were administered in hospital (2.21%) slightly more often than at home (14.5%). In adults, similar proportions of antibiotics were administered orally (33.9%), by IV in hospital (31.2%) and by IV at home (31.7%).

Route of administration



The most frequently prescribed antibiotics in 2013 were ciprofloxacin (13.2% of all antibiotics prescribed), tobramycin (12.3%), co-amoxiclav (11.3%) and ceftazidime (10.2%). The three most frequently prescribed medications for each administrative method are shown below. Of all oral antibiotics recorded, ciprofloxin was prescribed most frequently (25.3%). For hospital and home IVs, tobramycin was most commonly prescribed (26.4% and 23.7% respectively).

Frequently prescribed antibiotics

	Oral	% of oral medication
1st	Ciprofloxin	25.3%
2nd	Co-amoxiclav	23.2%
3rd	Flucloxacillin	12.5%

Hospital IV	% of hospital IV medication
Tobramycin	26.4%
Ceftazidime	19.8%
Meropenem	14.6%

Home IV	% of home IV medication
Tobramycin	23.7%
Ceftazidime	22.2%
Meropenem	15.5%

Maintenance medications

Maintenance medications comprise part of the daily treatment regimen undertaken by PWCF, which can take up to two and a half hours to complete. Maintenance medications are defined as those which taken regularly for a minimum of 3 months. Beta-agonists are part of most PWCFs regimen. Its use increased in children from 67.6% in 2012 to 74% in 2013, and from 64.4% to 69.1% in adults. Recombinant human DNase (Pulmozyme®) use has increased in adults (from 45.7% in 2012 to 505.5% in 2013). Nebulised hypertonic saline use in children declined from 55.9% to 46.4% (2012 to 2013), while adults' use remained unchanged.

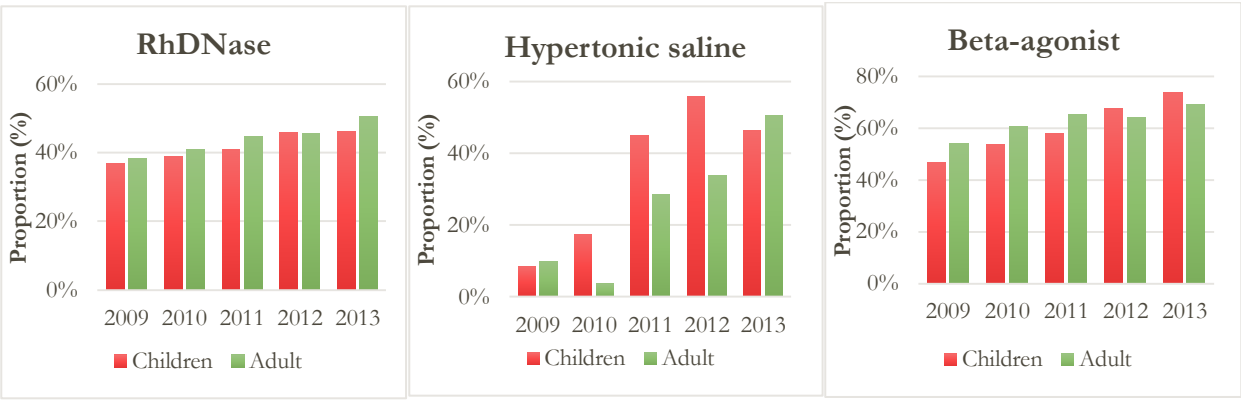
Respiratory medications

	Children n=487 (%)	Adults n=392 (%)
Inhaled		
Beta-agonist	360 (73.9%)	271 (69.1%)
Steroid	142 (29.2%)	157 (40.1%)
Anti-cholinergic	8 (1.6%)	32 (8.2%)
Nebulised		
Recombinant human DNase (rhDNAse)	226 (46.4%)	198 (50.5%)
Hypertonic saline*	226 (46.3%)	138 (35.2%)
Oxygen (continuous/night-time)	9 (1.9%)	25 (6.4%)
Oral steroid	31 (6.4%)	47 (12.0%)

*Continuous and intermittent use

The prescription of maintenance medication changes over time, as research emerges that can provide CF care teams with better information on best clinical practice. RhDNase, nebulised hypertonic saline and beta agonists are three examples of this, and as shown in the bar charts below, they have been prescribed with increasing frequency over the past five year period.

Trends in maintenance medications



Rates of use of gastrointestinal medication remain unchanged from 2012, with over a half of adults (55.1%) and nearly one-third of children (31.6%) using H2-receptor antagonists (H2RAs) or protein-pump inhibitors (PPIs) to treat gastro-oesophageal reflux disease.

Gastrointestinal medications

	<18 years n=487 (%)	≥18 years n=392 (%)
Urso-deoxycholic acid	44 (9.0%)	70 (17.9%)
H2RA/PPI	154 (31.6%)	216 (55.1%)
Lactulose/movicol	64 (13.1%)	45 (11.5%)

Use of other medication provides insight into treatment of and prophylaxis for CF-related co-morbidities in the CF population. Nearly half of adults received medication for osteoporosis/osteopenia, and 22.5% have CF-related diabetes requiring insulin treatment.

Other maintenance medications

	<18 years n=487 (%)	≥18 years n=392 (%)
Osteoporosis treatment(s)	40 (8.2%)	190 (48.5%)
Insulin	14 (2.9%)	88 (22.5%)
Kalydeco™	58 (96.7%[1])	72 (81.8%[2])

[1] % of PWCF with ≥1 G551D allele and aged 6 to 17 years. [2] % of PWCF with ≥1 G551D allele and aged ≥18 years.

Nutrition

In 2013, nearly all PWCF had their dietary and nutritional care reviewed by the dietetics service at least once a year. Vitamins are the nutritional supplement taken by most PWCF. Improved capture of information on mineral supplementation in adults has meant that the proportion of adult PWCF using minerals has increased from 5.2% in 2012 to 34.7% in 2013. One in five adults used calorie supplements.

Nutritional treatment

	Children n=487 (%)	Adults n=392 (%)
Reviewed by dietician	479 (98.4%)	378 (96.4%)
Pancreatic enzymes	464 (95.1%)	356 (90.8%)
Calorie supplements	49 (10.1%)	75 (19.1%)
Vitamins	465 (95.5%)	353 (90.1%)
Minerals	50 (10.3%)	136 (34.7%)

Oral supplements include calorie only, calorie and protein only, and enteral nutritional supplements. One in four PWCF used one or more of these oral supplement types in 2013. Gastrostomy tube feeding increased slightly in children between 2012 (9.5%) and 2013 (12.3%).

Supplemental feeding

	Children n=487 (%)	Adults n=392 (%)
Oral supplements	117 (24.0%)	107 (27.3%)
Nasogastric tube feeding	3 (0.6%)	3 (0.8%)
Gastrostomy tube feeding	60 (12.3%)	41 (10.5%)

Airway clearance

The number of PWCF reviewed at least once by a physiotherapist increased during 2013. The use of airway clearance devices were common in children; 33% used the Acapella® and 23.4% used the Positive Expiratory Pressure (PEP) mask (23.4%). Over half of adults used the breathing technique autogenic drainage (51.5%). Acapella® was the second most common technique used by adult (11.2%). The CFRI did not record method of airway clearance for 16.6% of children and 25% of adults either because they did not perform any airway clearance at the time of review, or because it was not recorded in the hospital charts.

Airway clearance techniques

Children	Number of modalities(%)
Reviewed by physiotherapist	466 (95.7%)
Acapella®	156 (33.0%)
PEP mask	114 (23.4%)
Other*	49 (26.7%)
Autogenic drainage	40 (8.2%)
Percussion	29 (6.0%)
Flutter	10 (2.1%)
Active cycle breathing	8 (1.6%)
None reported	81 (16.6%)

Adults	Number of modalities (%)
Reviewed by physiotherapist	361 (92.1%)
Autogenic drainage	202 (51.5%)
Acapella®	44 (11.2%)
Other*	12 (3.1%)
PEP mask	28 (7.1%)
Active cycle breathing	8 (2.0%)
None reported	98 (25%)

*Other: Therapep, BiPAP, trampolining, huffing, postural drainage, age appropriate activities

Financial information

Financial summary for 2013

Income & Expenses		2013 €
Income		
Grant income		140,000
Other funding & donations		67,015
Deferred income released		24,500
Sundry income		299
	Total income	231,814
Expenses		
Wages & salary		127,599
Employer's PRSI		9,368
Rent payable		6,072
Service Charges		662
Insurance		468
Computer network & server costs		9,646
Printing, postage and stationery		1,738
Office costs		241
Telephone & fax		171
Travelling & subsistence		5,281
Legal & professional fees		4,000
Audit		1,000
Bank charges		192
Grants given		1,500
Subscriptions		285
Depreciation on equipment		935
	Total expenses	169,159
	(Deficit)/Surplus	62,656

The full audited accounts were prepared Hayden Brown, Chartered Accountants, Grafton Buildings, 34 Grafton Street, Dublin 2 and copies are available upon written request to CFRI.

Acknowledgements

There are many individuals and groups that have contributed to and supported the work of the Cystic Fibrosis Registry of Ireland during this reporting year.

First we would like to thank all those who have financially supported the registry. This includes the HSE (through our Service Level Agreement), Cystic Fibrosis Ireland, and our industry partners who have provided us with unconditional grants. Without your support CFRI could not survive.

Most importantly we would like to thank each PWCF and/or their guardian for consenting for their medical data to be collected and used in a de-identified form to drive research into the development of new treatments and models of care for cystic fibrosis patients nationally and internationally.

We would also like to thank every member of the CF multi-disciplinary teams in every centre who assist our Research Associates in collecting data and assist in the patient consent process.

Our CFRI staff, Dr Shijun Zhou, Ms Mary Harrington and Dr Abi Jackson deserve special thanks for working tirelessly in the collection and preparation of quality data that contributes so much to CF research, service and treatment development, and quality management.

Our management committee have been very supportive during the year and are always available when any assistance is required.

We would also like to thank UCD for supplying us with affordable accommodation through the sponsorship of the School of Public Health, Physiotherapy and Population Science. We appreciate the support and mentorship of Prof Kelleher and her colleagues who have made an invaluable contribution to our own internal research programme.

The HSE's Health Intelligence unit have been particularly supportive and special thanks go to Dr H Johnson, Dr D Beaton and Dr F Donohue.

We would to thank Prof Philip Mayne, Children's University Hospital for confirming the numbers of infants detected in 2013 with two CFTR mutations by the national screening programme. We would also like to thank Prof David Barton and his team at the National Centre for Medical Genetics at Our Lady's Children's Hospital, Crumlin for assisting in the confirmation of CFTR genotyping.

Finally, we thank Dr Abaigeal Jackson and Larry Ungar for their hard work and dedication in preparing this report.

CFRI executive council membership 2013

Dr Ed McKone	Chairperson	Consultant in Respiratory Medicine St. Vincent's University Hospital, Dublin
Dr Cedric Gunaratnam	Vice Chairperson	Consultant in Respiratory Medicine Beaumont Hospital, Dublin
Prof Charles Gallagher	Immediate Past Chairperson	Consultant in Respiratory Medicine St. Vincent's University Hospital, Dublin
Dr Marion Rowland	Secretary	Lecturer UCD School of Medicine & Medical Sciences
Mr John Coleman	Treasurer	Chairperson CF Ireland
Mr Godfrey Fletcher	CEO	Chief Executive Officer Cystic Fibrosis Registry Ireland
Dr Peter Greally		Consultant in Paediatric Respiratory Medicine The Adelaide and Meath Hospital Dublin, Incorporating the National Children's Hospital
Prof Gerry McElvaney		Professor of Medicine, Royal College of Surgeons in Ireland & Consultant in Respiratory Medicine Beaumont Hospital, Dublin
Dr Paul McNally		Consultant in Paediatric Respiratory Medicine Our Lady's Children's Hospital, Crumlin
Dr Barry Linnane		Consultant in Paediatric Respiratory Medicine University Hospital, Limerick
Prof Barry Plant		Consultant in Respiratory Medicine Cork University Hospital, Cork
Dr Dubhfeasa Slattery		Consultant in Paediatric Respiratory Medicine Temple Street Children's University Hospital, Dublin
Mr Philip Watt		Chief Executive CF Ireland
Mr Martin Wickham		Patient Representative

"The national Cystic Fibrosis Registry of Ireland will endeavour to collect and analyse information relating to cystic fibrosis in order to improve the quality of care for all of the people with cystic fibrosis in the Republic of Ireland."

Mission Statement of the CFRI

Cystic Fibrosis is an inherited condition that affects many body functions such as breathing, digestion, and reproduction. This lifelong condition usually becomes more severe with age and affects both males and females in equal proportions. The symptoms and severity of cystic fibrosis vary from person to person. The majority of people have both respiratory and digestive problems. There is no cure for cystic fibrosis. Life expectancy has increased steadily over the past 20 years, and today cystic fibrosis is no longer exclusive to childhood.

Better treatment strategies help to improve the length and quality of life of people with CF by controlling their symptoms. Improved treatments can be developed using patient registries. Cystic fibrosis registries gather information on all aspects of a patient's condition. They act as information storehouses for infection and treatment statistics. Detailed analysis of this information can yield significant findings about the most effective treatments for CF. It is through these analyses that better management of CF may be achieved.

Cystic Fibrosis Registry of Ireland
Woodview House
University College Dublin
Belfield
Dublin 4
Ireland

www.cfri.ie

CFRI

The Cystic Fibrosis Registry of Ireland