

Cystic Fibrosis Registry of Ireland

2014 Annual Report



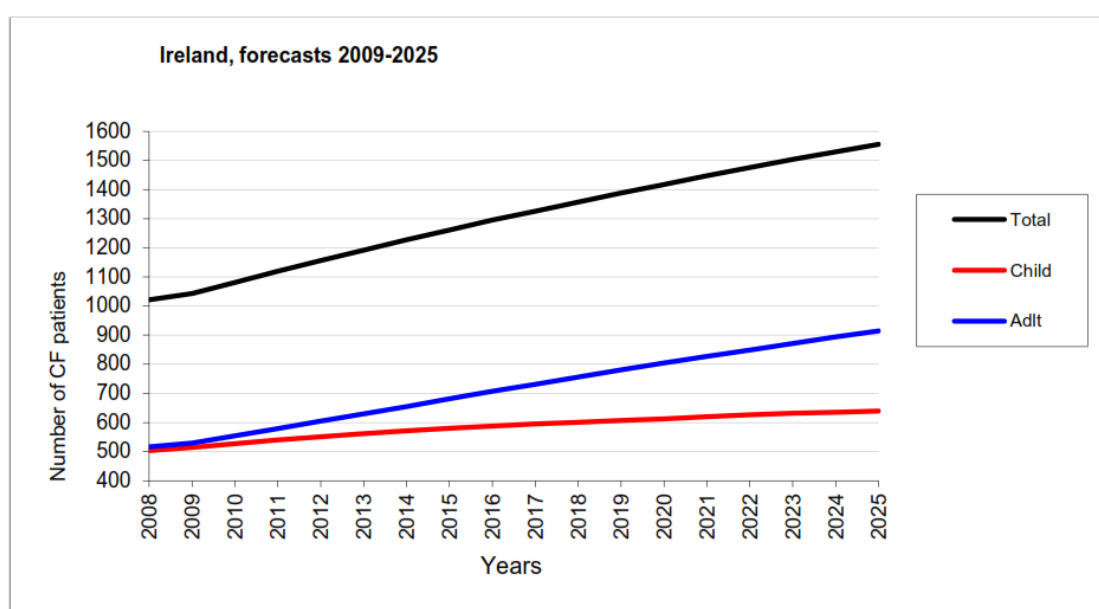
CFRI 

The Cystic Fibrosis Registry of Ireland

Preface

We are delighted to share with you the 2014 Annual Cystic Fibrosis Registry of Ireland Report. The Irish cystic fibrosis population continues to grow year on year with participants in the registry at the end of 2014 standing at 1,183, representing 90.7% of the known population. As our numbers continue to grow, it is interesting to note that the registry collected data from 200 more individuals in 2014 than it did 6 years previously without additional data collection resources. This is a huge feat considering that approximately 400 variables are manually collected from each patient's record.

It is anticipated that the Irish CF population will continue to grow, particularly our adult population. A recent study published in the European Respiratory Journal¹ analysed longitudinal data from 34 European registries and forecasted that in 16 countries including Ireland that by 2025 that the number of patients will increase by approximately 50%. The number of CF adults will increase by approximately 75% with children showing an increase of 20%. This highlights the fact that for the registry to continue to provide high quality data, it needs to be adequately resourced to cope with these increased demands.



The data presented in this report is 2014 data. It is hoped that over the coming years, the registry will be adapted to provide more current data, aiming to be a resource available to the clinical team to be used in hospitals at each patient encounter. A recent article published in the Lancet² stated that the high cost of most orphan drugs threatens the sustainability of public health care and that registries should be used as tool to assess efficacy and safety of newer treatments. They stated that the launch of collaborative disease registries that are independent from the pharmaceutical industry was essential to promote the appropriate use of orphan drugs and the management of costs. The CF community is fortunate in that it has well established national and international registries that are data rich and are already sharing de-identified data and are collaborating on common standards and on research. CFRI has already shown in research that it recently carried out in 2013 & 2014 that it was possible to use Irish registry data to inform financial planning required to support the adequate resourcing of CF services and treatments into the future. For this to

¹ Reproduced with permission of the European Respiratory Society ©: European Respiratory Journal July 2015, 46 (1) 133-141; DOI: 10.1183/09031936.00196314.

² Hollak *et al.* (2015). Post-authorisation assessment of orphan drugs. The Lancet. 386: 1940-1941.

be meaningful we need our core data to be as near to live as possible. Our new technology will allow for any hospital based encounters to be captured live. Additional resources will be required to facilitate speedy and accurate collection of data. If we can get data close to live then the Registry could become an important tool in the day to day management of CF and CF services.



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



Table of Contents

I.	Summary CFRI data, 2008-2014	5
II.	Demographics	6
	Age group and gender, 2014	
	Age distribution, 2014	
	Age by gender, 2014	
III.	Diagnosis	8
	New CF diagnoses, 2008-2014	
	Age at diagnosis, 2008-2014	
	National Newborn Bloodspot Screening Programme Statistics, 2014	
IV.	Gene mutations	11
	CFTR mutations, 2014	
	Genotype by age-band, 2014	
V.	Lung function	13
	Median FEV1% predicted, 2008-2014	
	Median FEV1% predicted by age, 2008-2014	
	Median FEV1% predicted by gender, 2014	
	Lung disease severity, 2014	
VI.	Microbiology	15
	Prevalence of respiratory organisms by age-band, 2014	
	<i>P. aeruginosa</i> infection by age-band, 2008 & 2014	
VII.	Nutrition	17
	Height Z scores in individuals under 20 years, 2014	
	Median weight Z scores in children under 20 years	
	Median BMI Z scores in children <20 years	
	Median BMI in individuals ≥20 years	
VIII.	Pulmonary exacerbations	19
	Intravenous antibiotic use, 2014	
	Hospitalisation, 2014	
IX.	Maintenance therapies	20
X.	Feeding	21
XI.	Airway clearance	22
XII.	Complications	23

XIII.	Deaths.....	25
	Deaths and median age at death	
	Median age at death by gender	
	Cause of death, 2002-2014	
	Survival in individuals born 1980-2009	
XIV.	Transplantation	27
XV.	CFRI data requests, 2013-2015	28
XVI.	CFRI research, 2014-2015	29
XVII.	Financial information.....	30
XVIII.	Technical notes	31
XIX.	Acknowledgements	32
XX.	CFRI executive council membership 2014	33

Summary CFRI data, 2008-2014

Information describing the CF population are shown below. The numbers of newly diagnosed individuals exceeds those dying in each reporting year.

	2008	2010	2012	2014
CFRI-registered individuals¹				
Number (% of CF population)	1,004 (87.9%)	1,044 (90%)	1,140 (92.7%)	1,183 (90.7%)
Adults ≥18 yrs (%)	50.6%	52.7%	52.2%	642 (54.3%)
Children <18 yrs (%)	49.4%	47.3%	47.8%	541 (45.7%)
% Males	56.1%	57.1%	57.3%	682 (57.7%)
% Females	43.9%	42.9%	42.7%	501 (42.3%)
Median age in years	17.9	18.8	19.1	19.5
Diagnosis²				
Newly diagnosed persons ²	38	43	46	31
Number of patients born each year detected by Irish NBS programme ³	-	-	26	28
Mortality				
Deaths in CFRI-registered individuals	17	16	18	20
Median age at death in years	23.5	28.1	25.9	26.9

¹calculated from all CFRI-registered individuals alive on the last day of each reporting year.

²calculated from all CFRI-registrants (alive and dead) on the database. Some diagnosis data are added after the reporting year has ended, therefore figures from previous years have been updated.

³National Newborn Bloodspot Screening Programme for CF commenced July 2011.

Demographics

The Registry has collected data on consenting individuals with CF since 2002. In 2014, it contained data on 1,348 individuals, 1,183 (87.8%) of which were alive on the last day of 2014. These 1,183 individuals represent 90.7% of CF patients known to Irish CF care teams in 2014. The Registry collected data on two hundred more individuals in 2014 than it did six years previously (2008). This has resulted in the Registry data collection team experiencing a 20% increase in workload.

Age group and gender, 2014

(n=1,183)

In recent years, improvements in care have resulted in improved life expectancy for individuals with CF. Nowadays, most patients reach adulthood, and the Registry reported that adults outnumbered children for the first time in 2009. In 2014, 54.3% of patients (n=642) were aged 18 and older (or 59.3% of patients aged 16 and older). Most patients start to transition to adult CF specialist services at around age 16 years, with most completing the transition by age 18 years. In any given year, there are approximately 60 patients aged 16-17 years. In 2014, there were between 642 (54.3%) and 702 (59.3%) patients receiving care in adult CF centres. As in other years, there were more male than female CF patients in Ireland in 2014. Fifty-five percent of children and 60% of adults were male.

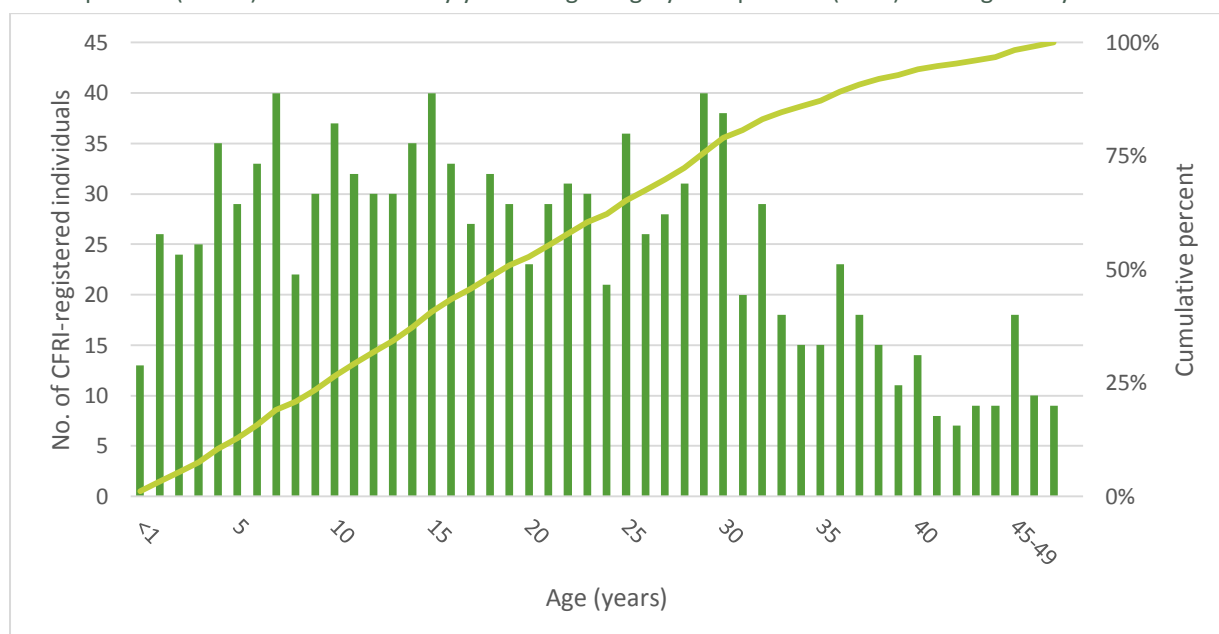
	Child <18 yrs (%)	Adult ≥18 yrs (%)
Female	243 (44.9%)	258 (40.2%)
Male	298 (55.1%)	384 (59.8%)
All	541	642

	Child <16 yrs (%)	Adult ≥16 yrs (%)
Female	219 (45.5%)	282 (40.2%)
Male	262 (54.5%)	420 (59.8%)
All	481	702

Age distribution, 2014

(n=1,183)

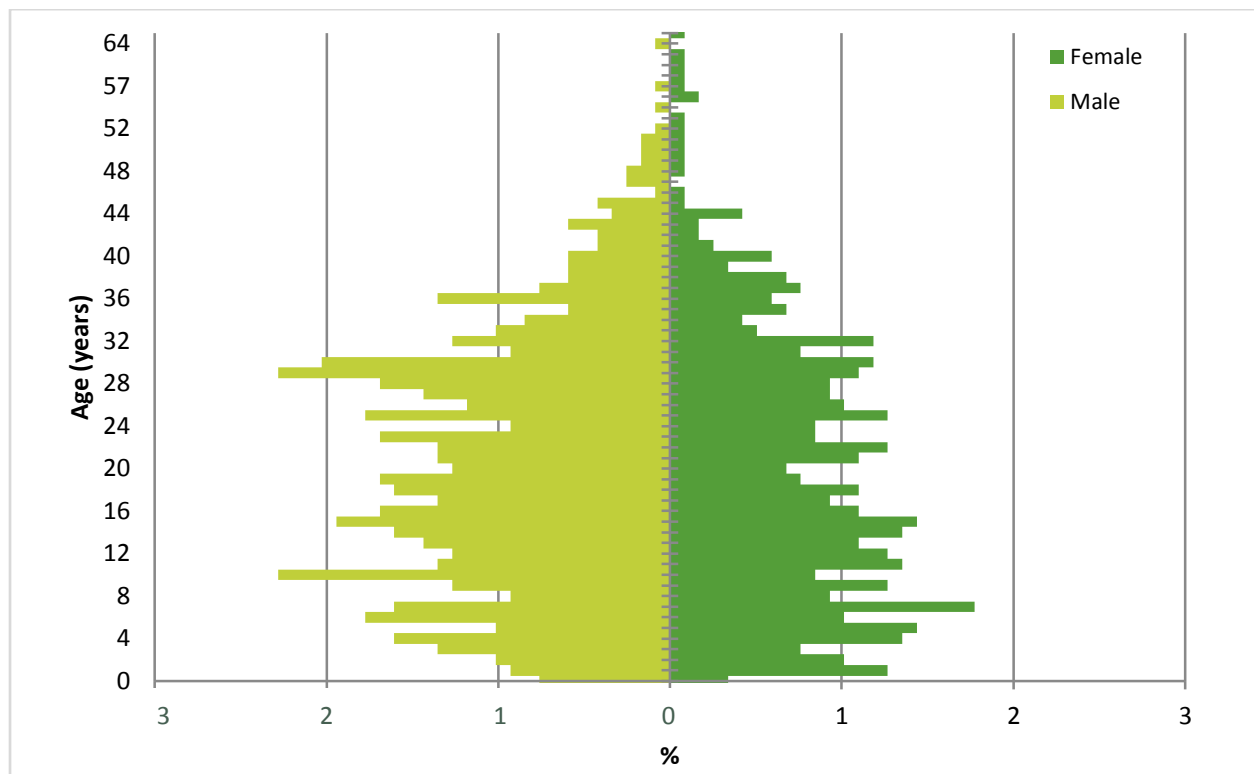
In 2014, the mean and median age of patients was 20.8 years and 19.5 years (interquartile range: 10.5-29.8) respectively. Approximately one quarter (23.4%) of patients were under age ten, half (52.8%) were under twenty and three-quarters (75.8%) were under thirty years of age. Eighty-four patients (7.1%) were aged 40 years or older.



Age by gender, 2014

(n=1,183)

The proportion of patients at each age in 2014 is presented in the population pyramid below as horizontal bars (showing males on the left and females on the right). The shape of the pyramid indicates that in 2014, the majority of both males and females were under the age of thirty years. There was a higher proportion of males than females at most ages, particularly around age ten and thirty. The narrow base of the pyramid suggests there were few CF individuals registered with the CFRI under age one at the end of 2014. Many individuals diagnosed in 2014 were registered in 2015, and these diagnoses will be included in subsequent CFRI reports.



Diagnosis

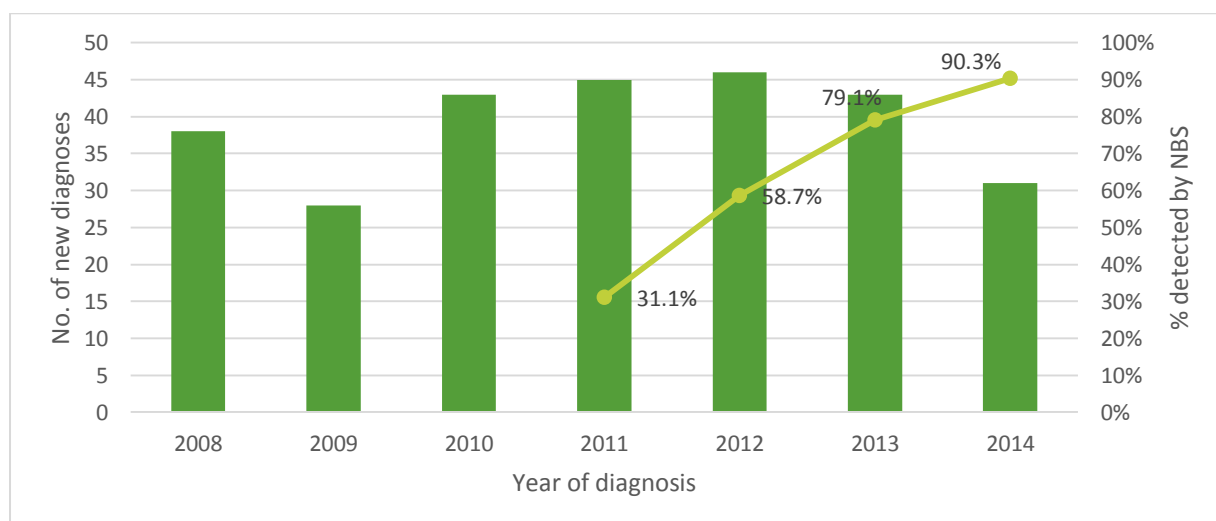
Seventeen individuals diagnosed with CF in 2014 were registered with the CFRI by the end of 2014. Additional 2014 diagnoses were registered in 2015, increasing the number of individuals diagnosed in 2014 to 31 in total. Delays in registration are not uncommon in patient registries operating on an opt-in basis, as is the case with the CFRI.

Individual's informed consent is required before the CFRI can collect their relevant CF information. Newly diagnosed individuals are invited to participate either by CFRI staff or their CF care team. The timeliest registration of newly diagnosed children occurs in those paediatric CF centres seeking patient informed consent on behalf of the CFRI.

New CF diagnoses, 2008-2014

(n=274)

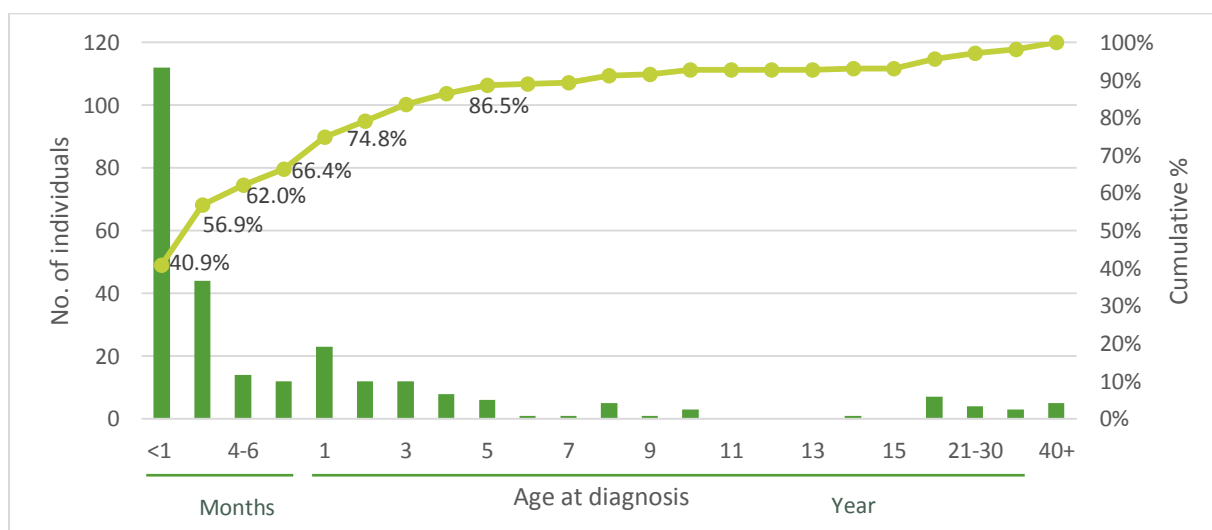
An average of 39.1 patients (range: 28-46) were diagnosed each year between 2008 and 2014. Following the introduction of the National Newborn CF Screening Programme ((NNBSP) in July 2011, the proportion of CFRI-registered individuals diagnosed annually as a result of newborn screening has increased (31.1% in 2011 - 90.3% in 2014).



Age at diagnosis, 2008-2014

(n=274)

Of the 274 individuals diagnosed with CF between 2008 and 2014, 40.9% were diagnosed before 1 month of age, 66.4% were diagnosed before 1 year and 86.5% were diagnosed before age 5.



Diagnosis in the first few months of life is more common in children born since the introduction of National Newborn CF Screening Programme, than in those born prior to its introduction (July 2011). The table below compares the age at diagnosis for children and adults in 2014. In 2014, 58.2% of children under 16 were diagnosed before 4 months of age, compared with 42.3% of adults.

Age at diagnosis	All CFRI-registered individuals in 2014 n=1,348	Patients <16 years in 2014 n=481 (%)	Patients ≥16 years in 2014 n=702 (%)
Unknown	<5	-	<5
<1 month	316 (23.5%)	173 (36%)	117 (16.7%)
1-3 months	340 (25.3%)	107 (22.2%)	179 (25.6%)
4-6 months	137 (10.2%)	30 (6.2%)	76 (10.9%)
7-12 months	82 (6.1%)	44 (9.1%)	39 (5.6%)
1 year	110 (8.2%)	50 (10.4%)	45 (6.4%)
2 years	86 (6.4%)	27 (5.6%)	44 (6.3%)
3 years	50 (3.7%)	21 (4.4%)	25 (3.6%)
4 years	39 (2.9%)	12 (2.5%)	22 (3.1%)
≥5 years	184 (13.7%)	17 (3.5%)	152 (21.7%)
Median (interquartile range) in months	4 (1-25.8)	2 (<1-12)	6 (1-46)

One in five adults was diagnosed at age five or older, compared with 3.5% of children. Those adults had a smaller proportion of the p.Phe508del homozygous CFTR genotype compared with the overall 2014 CFRI population (29.6% and 56.3% respectively).

	Adults aged ≥ 16 years in 2014 diagnosed ≥ 5 years n=152	All patients in 2014 n=1,183
p.Phe508del homozygous	29.6%	56.3%
p.Phe508del heterozygous	53.3%	35.1%
Non-p.Phe508del mutation/mutations unknown	17.1%	8.6%

In 2014, the National Newborn Bloodspot Screening Programme (NNBSP) reported that 32 newborns were diagnosed with CF. The statistics from the NNBSP are as follows:

National Newborn Bloodspot Screening Programme Statistics, 2014

	N (%)
Number of newborns screened in 2014	67,565
Number of samples with raised IRT sent to National Centre for Medical Genetics (NCMG)	670
Number of newborns with one mutation identified	44
Number of newborns with two mutations identified	29
Number of newborns referred to a CF Specialist Centre	72
Number of initial sweat tests performed	70
Number of sweat test failures	20
Number of newborns with positive sweat test	16
Number of newborns with negative sweat test	27
Number of newborns with borderline sweat test	7
Number of newborns requiring repeat sweat test	7
Number of newborns diagnosed with CF	32
Number of newborns diagnosed with variant CF	1
Number of newborns diagnosed as carriers	40

Source: Prof P Mayne, Director, National Newborn Bloodspot Screening Laboratory, Temple Street. Figures based on baby's date of birth

Gene mutations

The first mutation-specific gene therapy became available to individuals with CF in 2013, and more treatments for other common CF-causing mutations are in the development pipeline or seeking marketing authorisation. This is one reason why it is important that each individual's CF genotype is determined and recorded. CFTR mutations were determined for 97.7% of CFRI-registered individuals in 2014.

In September 2015, the European Medicines Agency Committee for Medicinal Products for Human Use recommended the granting of marketing authorisation for the medicinal product lumacaftor/ivacaftor (OrkambiTM) for the treatment of CF patients aged 12 years and older who are homozygous for the p.Phe508del mutation in the CFTR gene. In 2014, 56.3% of CFRI-registered individuals had the p.Phe508del homozygous genotype, 38.7% (n=458) were aged 12 years or older.

In respect of ivacaftor (KalydecoTM), marketing authorisation was first granted in 2012, and was initially indicated in CF patients aged six years and above who have one of nine mutations in the CFTR gene (G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N and S549R). In 2014, there were 148 CFR-registered individuals with at least one p.Gly551Asp mutation, 16 of which were aged between two and five years. In September 2015, the marketing authorisation for KalydecoTM was extended to include CF children aged 2 years and older who weigh less than 25 kg and who have one of the above listed CFTR mutations.

In addition, marketing authorisation of KalydecoTM was extended to include treatment of CF patients aged 18 years and older who have a p.Arg117His mutation. In 2014, there were 53 patients aged ≥18 years with a p.Arg117His mutation.

A positive recommendation was made by the Irish Health Service Executive Corporate Pharmaceutical Unit, supporting the provision of KalydecoTM for Irish CF patients in 2013. The recommendations for providing KalydecoTM to p.Gly551Asp patients aged 2-5 years and p.Arg117His patients aged ≥18 years, as well as providing OrkambiTM to p.Phe508del homozygous patients aged ≥12 years are awaited.

CFTR mutations, 2014

(n=1,183)

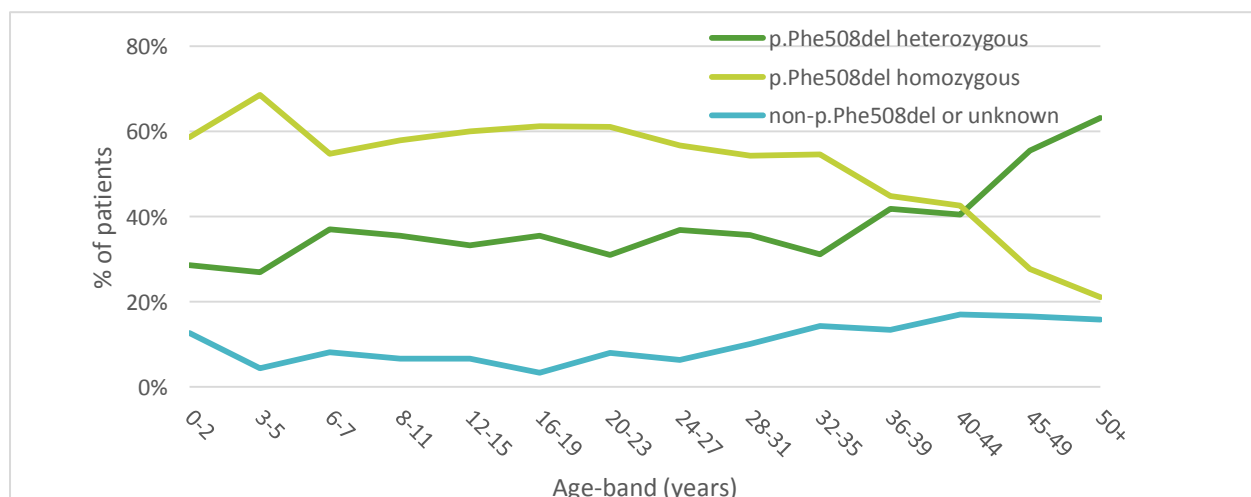
Mutation	n	%	FEV1 percent predicted median (interquartile range)
p.Phe508del homozygous	666	56.3%	81 (59.8-98)
p.Phe508del heterozygous			
p.Phe508del, p.Gly551Asp	134	11.3%	93 (75-107)
p.Phe508del, p.Arg117His	50	4.2%	86 (76.8-105.5)
p.Phe508del, p.Arg560Thr	33	2.8%	98 (78-102)
p.Phe508del, c.489+1G>T	20	1.7%	93 (77-118.5)
p.Phe508del, p.Gly542X	17	1.4%	76 (58.8-88)
p.Phe508del, c.1585-1G>A	16	1.4%	84 (62.5-93.5)
p.Phe508del, p.Ile507del	10	0.8%	80 (53.8-111)
p.Phe508del, p.Val520Phe	10	0.8%	68 (50.5-98.5)
p.Phe508del, other	125	10.6%	80 (58-99)
All other non-p.Phe508del mutations	75	6.3%	88 (55-100)
Mutation not recorded/pending	27	2.3%	90 (71.3-93.3)
Total	1183		84 (61-100)

Median FEV1% predicted values (and interquartile range) are presented by genotype for the first time. Median values range from 68% predicted for CF individuals with a p.Phe508del, p.Val520Phe genotype, to 93% predicted in CF individuals with a p.Phe508del, p.Arg560Thr or p.Phe508del, p.Gly551Asp genotype.

Genotype by age-band, 2014

(n=1,183)

In almost every three-year age-band, the most common genotype was p.Phe508del homozygous. From age forty onwards however, the proportion of p.Phe508del heterozygous patients exceeded that of p.Phe508del homozygous individuals; the former accounted for 55.6% of 45-49 year olds and 63.2% of 50+ year olds.



Lung function

Lung function is measured as FEV1, which is the volume of air that has been exhaled at the end of the first second of forced expiration. This is measured in litres, but is expressed as a percentage of the expected value from healthy individuals of the same sex, height and age – ‘FEV1% predicted’. An FEV1% predicted of 100 indicates that the lung function is the same as the mean lung function of people of the same sex, height and age. In 2014, the median value of individual’s best FEV1% predicted values was 84% (interquartile range: 61-100).

Median FEV1% predicted, 2008-2014

(n=21,519)

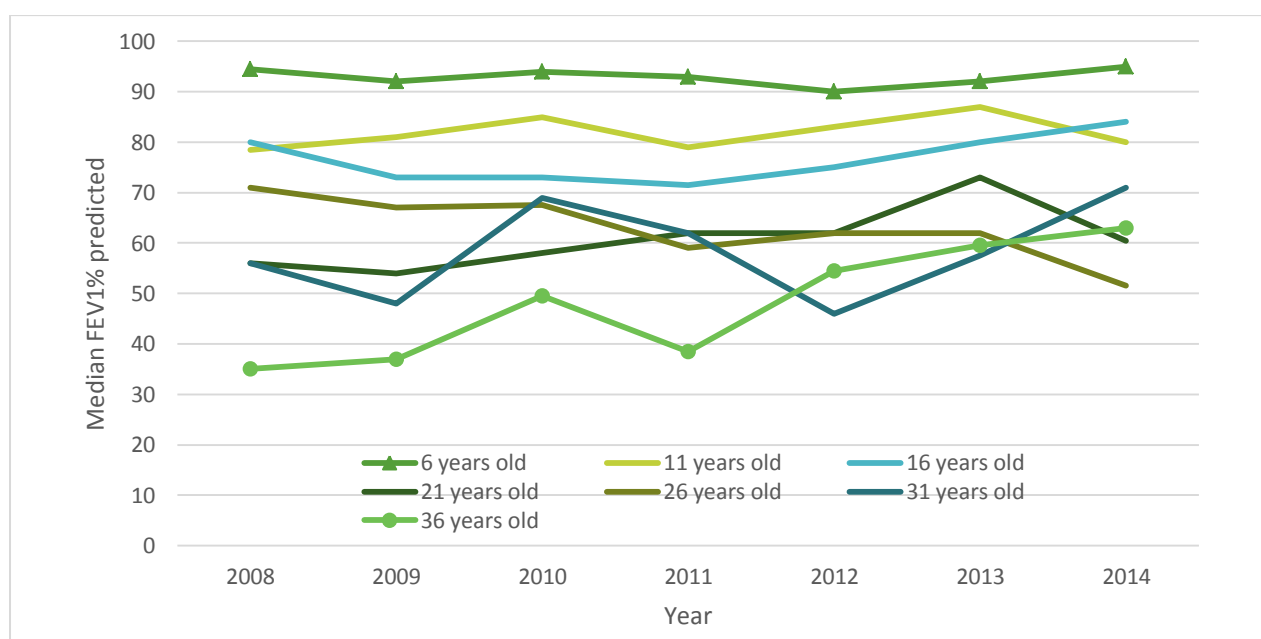
The median of every recorded FEV1% predicted value in 2014 (n=2,727) was 75% (interquartile range: 54-93). This is an improvement on median values reported 2008-2012.

Year (no. of PFTs)	2008 (n=2,755)	2009 (n=2,947)	2010 (n=3,131)	2011 (n=3,340)	2012 (n=3,344)	2013 (n=3,275)	2014 (n=2,727)
Median	70	70	71	70	70	74	75
Interquartile range	49-87	49-87	50-89	51-87	50-88	52-91	54-93
No. of patients	705	746	772	800	799	790	674

Median FEV1% predicted by age, 2008-2014

(n=4,519)

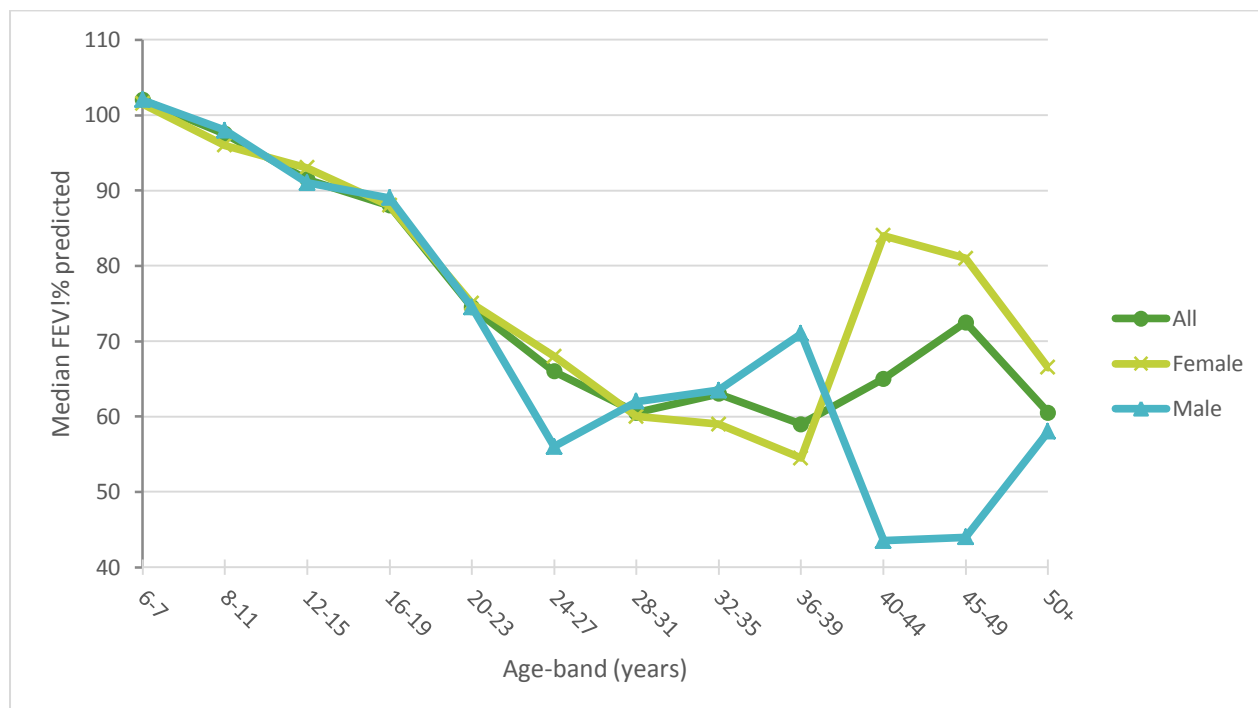
The figure below shows annual median FEV1% predicted values of individuals aged 6, 11, 16, 21, 26, 31 and 36 in each year from 2008 to 2014. A comparison between median FEV1% predicted of 36 year old CF individuals in 2014 with 36 years olds in 2008 shows that lung health at this age has improved overall. In 2014, lung health was also better for 11, 16 and 21 year olds than in previous years. In contrast, FEV1% predicted of 26 year olds has declined overall since 2008.



Median FEV1% predicted by gender, 2014

(n=649)

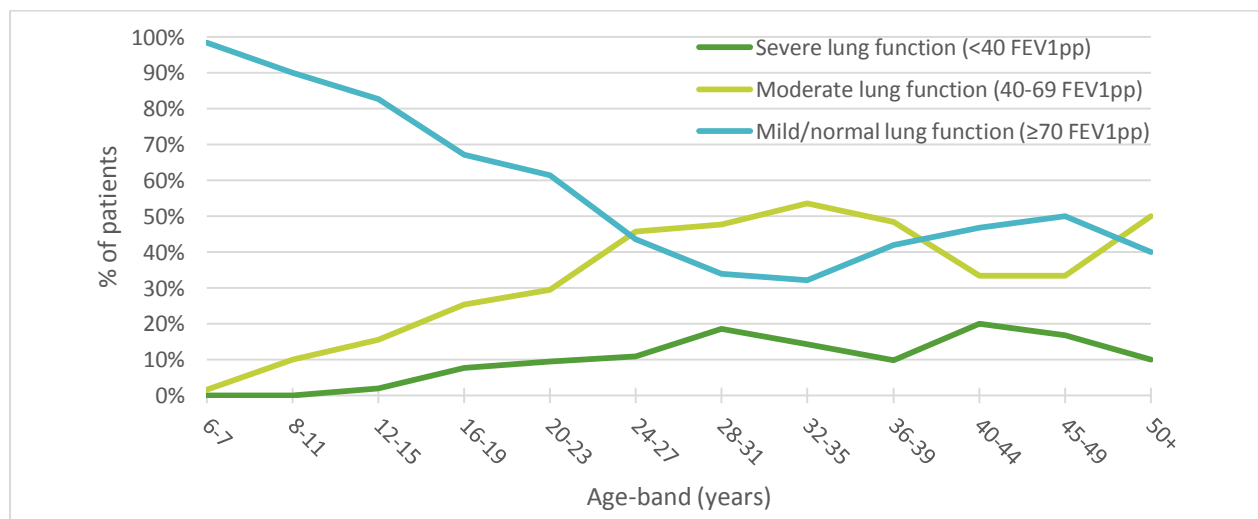
The best FEV1% predicted values of males and females in 2014 were compared. Similar values were determined for both sexes from age 6 to 23 years. Males aged 24-27 had a lower median value than females, but males aged 28-39 years had a slightly higher value than females. Females aged 40+ had a higher median FEV1% predicted value than males. The higher lung function in the older age groups reported here may be misleading, as there are a small number of patients over the age of forty, some of which had late CF diagnoses and/or are likely to have mild CFTR mutations.



Lung disease severity, 2014

(n=649)

Lung disease is categorised for the purposes of this analysis as mild/normal lung function ($\geq 70\%$) moderate (40-69%) and severe ($< 40\%$). In 2014, individuals in younger age groups (up to 20-23 years) had predominantly mild/normal lung function. More individuals had moderate rather than mild/normal lung function from age 24-39 years. Mild to normal lung function was most common in individuals in their forties.



Microbiology

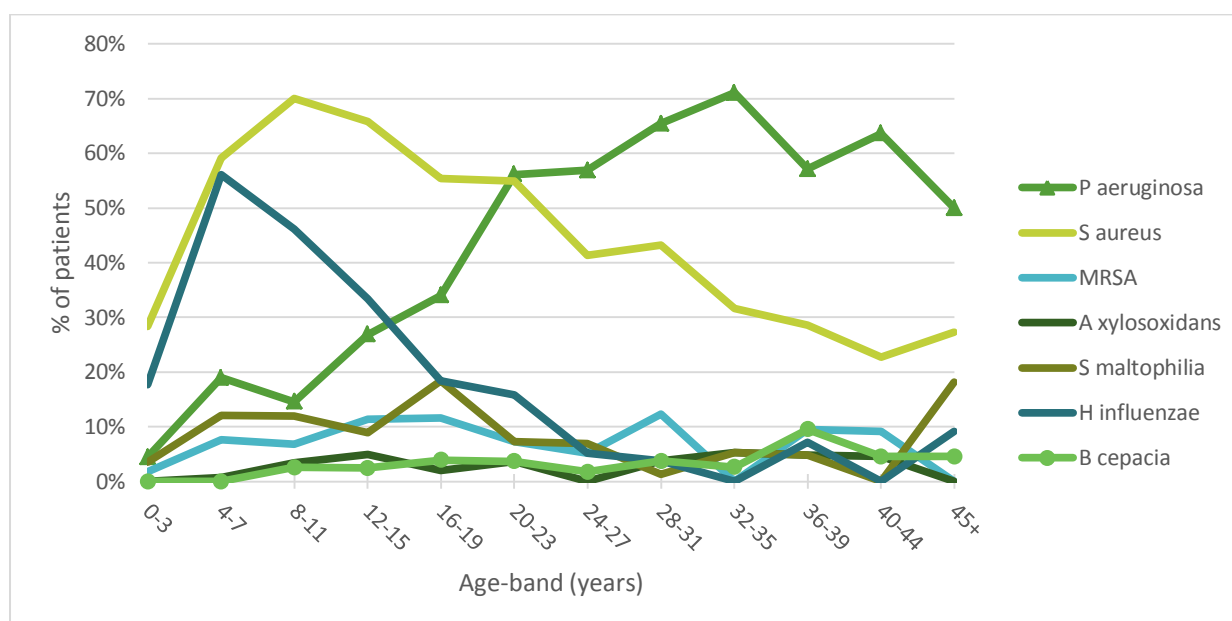
Individuals with CF may develop lung infections because bacteria tend not to be cleared easily from the thickened mucus of the lung. Infections can result in reduced lung function.

Prevalence of respiratory organisms by age-band, 2014

(n=933)

The proportion of CF individuals with detected respiratory infections are presented here as a proportion of CFRI-registered individuals with ≥ 1 recorded encounter in 2014 (n=933). A large proportion of individuals in younger age bands, particularly those aged 4 to 15 years, had *Staphylococcus aureus* infection. MRSA was detected in 11% of 12-19 year olds. Over half (56.1%) of 4-7 year olds had a *Haemophilus influenzae* infection and the proportion of individuals with a 2014 culture positive report of *Burkholderia cepacia* ranged from zero to 9.5% across all age groups. One in four 12-15 year olds had a *Pseudomonas aeruginosa* infection (defined as ≥ 1 culture positive specimen), and *P. aeruginosa* was the most commonly detected lung infection in individuals aged twenty and older in 2014 (50-71.1%).

Eleven patients had a culture positive report of non-tuberculous mycobacteria in 2014. *Burkholderia cepacia* was detected in 23 individuals; 18 had a genomovar II *B. multivorans* infection. The remainder of patients had either two *B. cepacia* genomovars reported in 2014 or had a genomovar III *B. cenocepacia* infection.

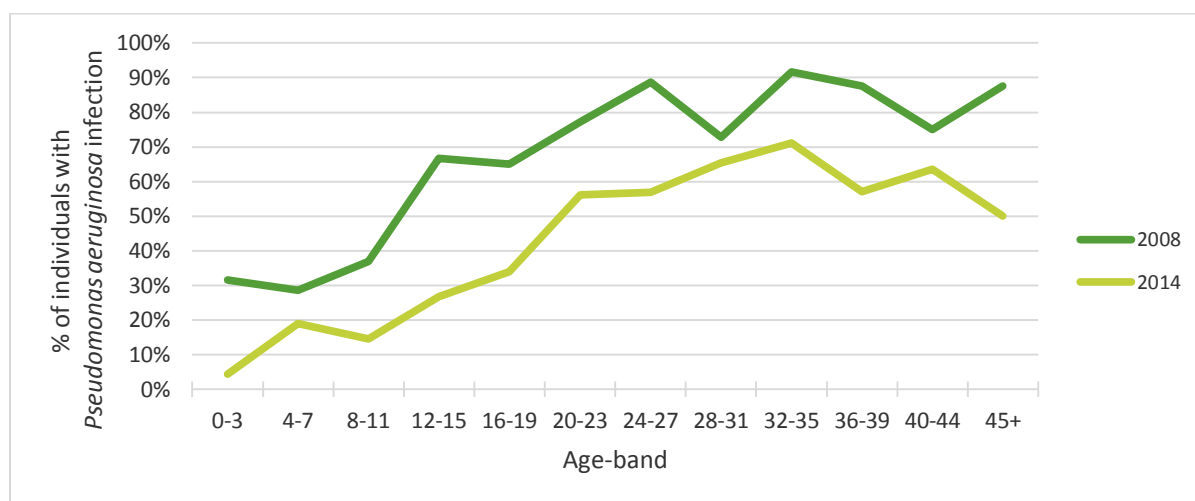


***P. aeruginosa* infection by age-band, 2008 & 2014**

(n=813 in 2008, n=933 in 2014)

The proportion of culture positive reports of *P. aeruginosa* in 2008 and 2014 were determined (for individuals in 2014 with ≥1 recorded 2014 encounter, and for individuals in 2008 with an Annual Assessment record). In 2014, 34.62% of individuals (n=933) had a culture positive report for *P. aeruginosa*, which is a marked decline from the 2008 *P. aeruginosa* prevalence estimate of 60.5%.

Sixty-five percent of 16-19 year olds in 2008 had *P. aeruginosa* infection, compared with 35% in 2014. In individuals aged ≥20 years, the proportions of individuals with *P. aeruginosa* infection ranged from 50-71.1% in 2014, compared with 72.9-91.7% in 2008.



Nutrition

Nutritional outcomes height, weight and BMI are an important measure of health in CF individuals. In analyses of patient populations, these outcomes are often expressed using Z-scores. Z scores are a statistical measurement of the relationship between an individual's height/weight/BMI, and the mean of a group of reference individuals. A z-score of 0 means that the measurement (e.g. height/weight/BMI) is equal to the mean measurement of individuals of the same age and sex in the reference (i.e. healthy population). A z-score of -2 means that the value is two standard deviations below the mean of people of the same age and sex in the reference population, and a score of +2 means that the value is two standard deviations. The average score for a healthy population is typically zero.

Height Z scores in individuals under 20 years, 2014

(n=877)

In 2014, height measurements were recorded for 877 individuals (74.1%). Compared to a healthy reference population, the median height of CF individuals was below average at every age. In 2014, individuals aged 12-15 years had the lowest median height Z score (median: -0.64, interquartile range: -1.23-0.15).

Age(years)	Median	Interquartile range
0-3	-0.03	(-0.88, 0.66)
4-7	-0.26	(-1.2, 0.57)
8-11	-0.25	(-0.85, 0.3)
12-15	-0.64	(-1.23, 0.15)
16-19	-0.43	(-0.89, 0.16)
20-23	-0.29	(-0.82, 0.48)
24-27	-0.44	(-0.96, 0.16)
28-31	-0.44	(-0.97, 0.21)
32-35	-0.26	(-1.01, 0.3)
36-39	-0.26	(-1.2, 0.57)
40-44	-0.46	(-0.97, 0.23)
45+	-0.56	(-1.18, -0.02)

Median weight Z scores in children under 20 years

(n=850)

In 2014, weight measurements were recorded for 850 individuals (71.9%). Compared to a healthy reference population, the median weight of CF individuals aged 0-11 was above the average weight of a healthy reference population.

Individuals aged 12-15 (median -0.55) and 24-27 years (median -0.63) had the poorest median weight in 2014.

Age (years)	Median	Interquartile range
0-3	0.08	(-0.71, 0.82)
4-7	0.21	(-0.38, -0.75)
8-11	0.11	(-0.57, 0.6)
12-15	-0.55	(-1.3, 0.33)
16-19	-0.45	(-1.03, 0.26)
20-23	-0.48	(-1.15, 0.11)
24-27	-0.63	(-1.21, 0.43)
28-31	-0.32	(-0.8, 0.41)
32-35	-0.34	(-0.69, 0.46)
36-39	-0.02	(-0.46, 1.03)
40-44	-0.07	(-0.3, 0.69)
45+	0.24	(-0.36, 0.92)

Median BMI Z scores in children <20 years

(n=477)

BMI Z scores in children aged <1 to 11 years were above that of the average reference population.

Age-band	Median	Interquartile range
0-3	0.25	(-0.07, 1.01)
4-7	0.34	(-0.23, 0.89)
8-11	0.38	(-0.23, 0.69)
12-15	-0.24	(-1.02, 0.5)
16-19	-0.33	(-0.93, 0.19)

Median BMI in individuals ≥20 years

(n=315)

An adult with a BMI of less than 18.5 kg/m² is considered to be underweight by the World Health Organisation. The median BMI of adults of all ages fell within the normal range (18.5-25 kg/m²).

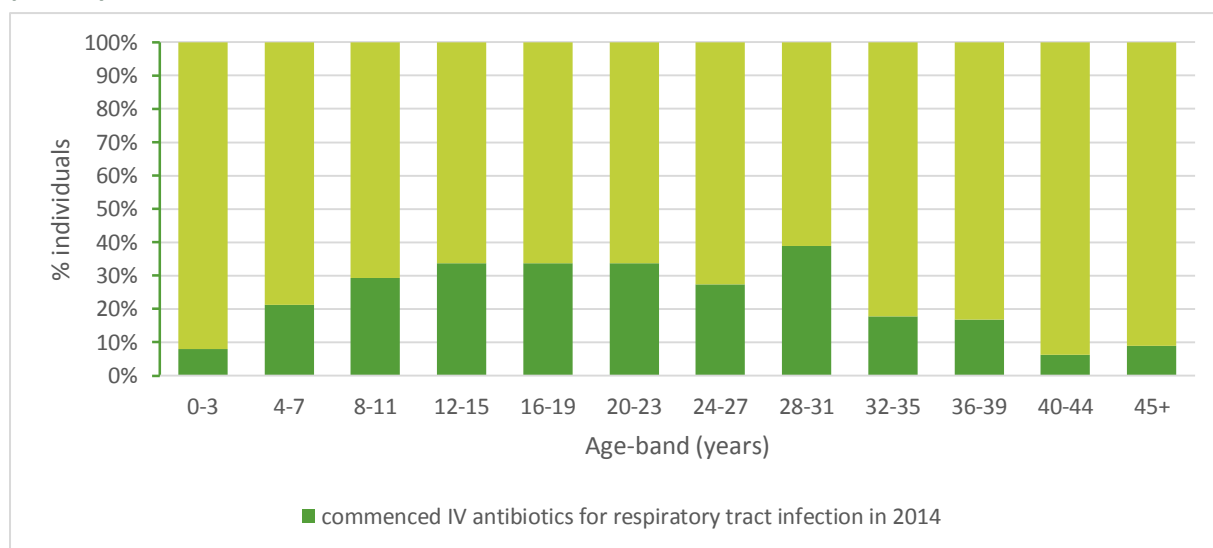
Age-band	Median	Interquartile range
20-23	19.2	(20.8, 22.8)
24-27	19.2	(21.4, 23.8)
28-31	20.6	(22.1, 24.2)
32-35	19.6	(22.1, 24.1)
36-39	21.6	(23.3, 26.3)

Pulmonary exacerbations

Pulmonary exacerbations are typically treated with an intravenous course of antibiotics, administered to individuals either in hospital, at home, and sometimes commenced in hospital and completed at home. In 2014, 311 individuals commenced at least one course of IV antibiotics to treat a respiratory exacerbation. Approximately 40% (38.9%) of individuals aged 28-31 years and one third (33.6%) of 12-23 year olds had at least one pulmonary exacerbation requiring IV antibiotics in 2014.

Intravenous antibiotic use, 2014

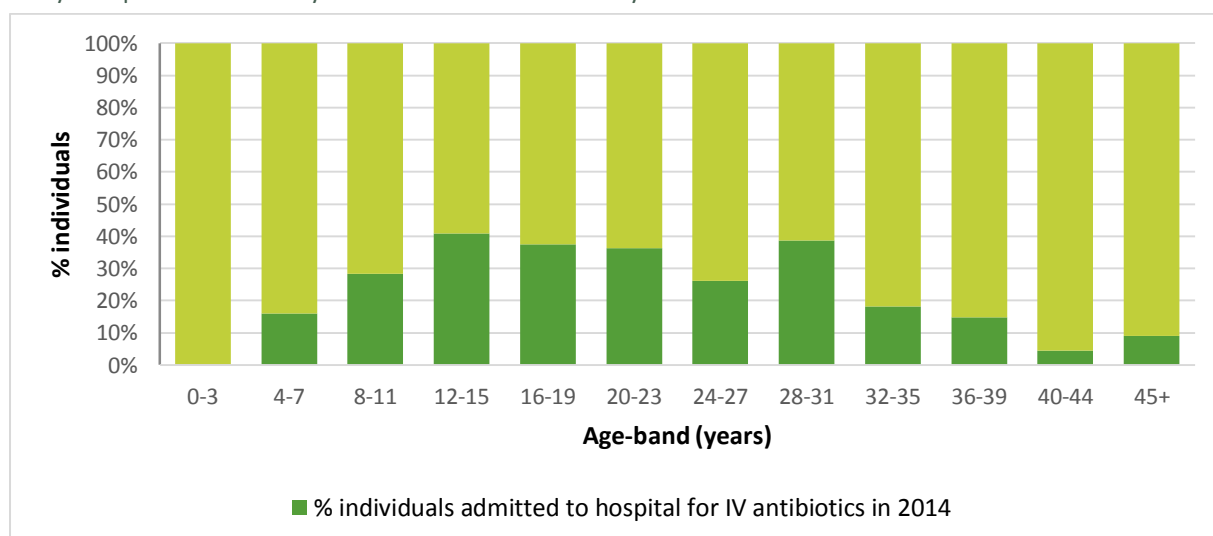
(n=933)



Hospitalisation, 2014

(n=933)

In 2014, the CFRI recorded a total of 554 hospitalisations in 290 patients. The most common reason for admission was for treatment of a pulmonary exacerbation (83.2% of hospitalisations, n=238 patients). Seven percent of admissions were for other CF-related reasons and 5.8% were for non-CF related procedures/treatments. The proportions of individuals admitted to hospital for treatment of a pulmonary exacerbation in 2014 in each age-band are shown below. Forty-one percent of 12-15 year olds and 37.5% of 16-19 year olds were admitted at least once in 2014.



Maintenance therapies

(n=931)

Maintenance therapy information recorded at individuals' annual assessments (AAs) were considered. If AA data was not collected, data from the last encounter of 2014 was considered.

	Children under <6 years (n=171)	Children 6-17 years (n=365)	Adult ≥18 years (n=395)
Pulmonary			
Oral antibiotic	47.4%	40%	65.6%
Inhaled antibiotic	12.3%	32.1%	70.1%
Mucolytic	48.5%	72.6%	40.3%
Beta agonist	31.6%	69%	63.8%
Anticholinergic	2.3%	<1%	7.6%
Combined beta-agonist-anticholinergic	-	-	2.5%
Inhaled steroid	13.5%	28.2%	31.6%
Nasal medication	2.3%	<1%	7.6%
Gastrointestinal			
H ² receptor antagonist	<1%	<1%	1.5%
Proton pump inhibitors	5.8%	5.2%	21.5%
Urso-deoxycholic acid	1.2%	8.5%	16.5%
Other			
Kalydeco ^{TM*}	-	100%	85.6%

*As a proportion of children and adults with a p.Gly551Asp mutation and alive at the end of 2014. KalydecoTM licensed in CF patients aged ≥6 years.

Feeding

(n=933)

Supplementary feeding can be required because of sustained weight loss, and can involve passing food directly into the stomach via the nose or abdomen. Feeding was supplemented in 265 individuals (28.4%), most of which opted for a nasogastric tube (19.2%).

	All	Child <16 years	Adult ≥ 16 years
Any supplemental feeding	28.4%	29.5%	27.2%
Oral supplementation	19.2%	19.8%	18.5%
Gastrostomy tube	1.6%	<1%	2.7%
Not known	7.8%	8.9%	6.7%

Airway clearance

(n=727)

Physiotherapy is an important part of CF treatment, which aids the clearance of mucus from the lungs. Techniques used by individuals at the time of their 2014 annual assessment are reported here (n=727). These techniques can be used in combination, and the figures presented in the table below are not mutually exclusive. Acapella and the Positive Expiratory Pressure mask were the most frequently employed physiotherapy modalities in children. Almost half of adults performed autogenic drainage. Secondary physiotherapy modalities such as exercise were also performed by individuals (not reported here).

	Child <16 years (n=434)	Adult ≥ 16 years (n=293)
Positive Expiratory Pressure mask	35.5%	22.2%
Autogenic drainage	8.1%	45.7%
Acapella	32.0%	22.5%
Active cycle breathing technique	3.0%	3.4%
Age appropriate activity	15.4%	0.7%
Flutter	1.8%	3.8%
High frequency chest wall oscillation	3.9%	1.0%
Postural drainage	0.2%	0.7%

Nine percent of adults with recorded physiotherapy data were using oxygen at home.

	Child <16 years (n=434)	Adult ≥ 16 years (n=293)
Non-invasive positive pressure ventilation	7 (1.6%)	11 (3.8%)
Home oxygen therapy	7 (1.6%)	26 (8.9%)

Complications

(n=853)

It is common for most individuals to experience complications of cystic fibrosis. These complications can have an impact on health and quality of life, as they interfere with the respiratory, gastrointestinal and hepatobiliary organs and affect bones, joints, mental health etc. The prevalence of reported complications presented here is in part influenced by screening practices for these conditions in clinical settings, as well as CFRI data collection practices. Complications were recorded in 853 individuals in 2014.

	Child <16 years (n=466)	Adult ≥ 16 years (n=387)
Respiratory		
Allergic Bronchopulmonary Aspergillosis	4.1%	6.2%
Nasal polyps	1.5%	2.8%
Asthma	1.1%	8.3%
Pneumothorax	-	<1%
Hepatobiliary & pancreas		
Pancreatic Insufficiency	93.8%	90.7%
Pancreatitis	<1%	<1%
Abnormal liver function tests	6.2%	2.3%
Liver disease other than cirrhosis	7.9%	8.8%
Cirrhosis with portal hypertension	1.3%	6.2%
CF-related diabetes requiring insulin	3.4%	26.4%
Gastrointestinal		
Gastro-oesophageal reflux disease	29.4%	54.8%
Distal intestinal obstructive syndrome	2.6%	4.9%
Rectal prolapse	<1%	-
Musculo-skeletal		
Osteoporosis/osteopenia	0.4%	23.5%
Arthropathy	<1%	<1%
Fracture	<1%	1.6%
Other		
IV port replaced	1.3%	2.1%
Depression	-	4.1%
Non-CF morbidity	30.5%	44.2%

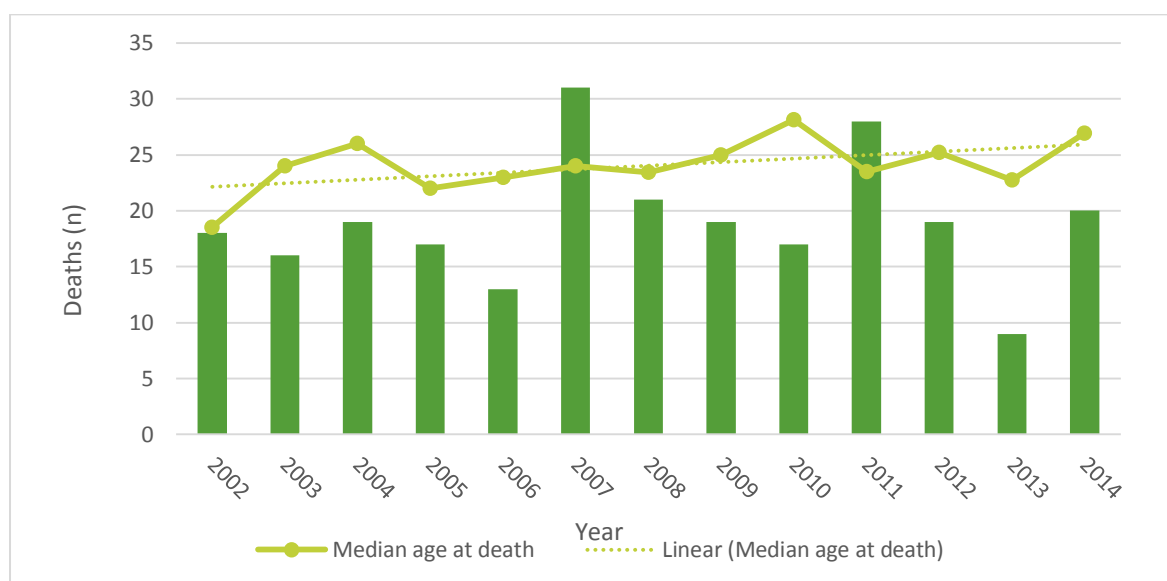
Nearly all individuals with CF experience pancreatic insufficiency, which requires pancreatic enzyme replacement medications that are taken at mealtimes. CF-related diabetes (requiring insulin) and osteoporosis/osteopenia affected approximately one in four adults in 2014. The proportion of individuals with liver disease is likely to have been underestimated by the CFRI due to difficulties interpreting occasionally equivocal medical information from hospital charts. Internationally recognised research involving Irish CF patients has shown that liver disease is an important complication in CF, which can lead to an increased risk of death.

Deaths

Deaths and median age at death

(n=249)

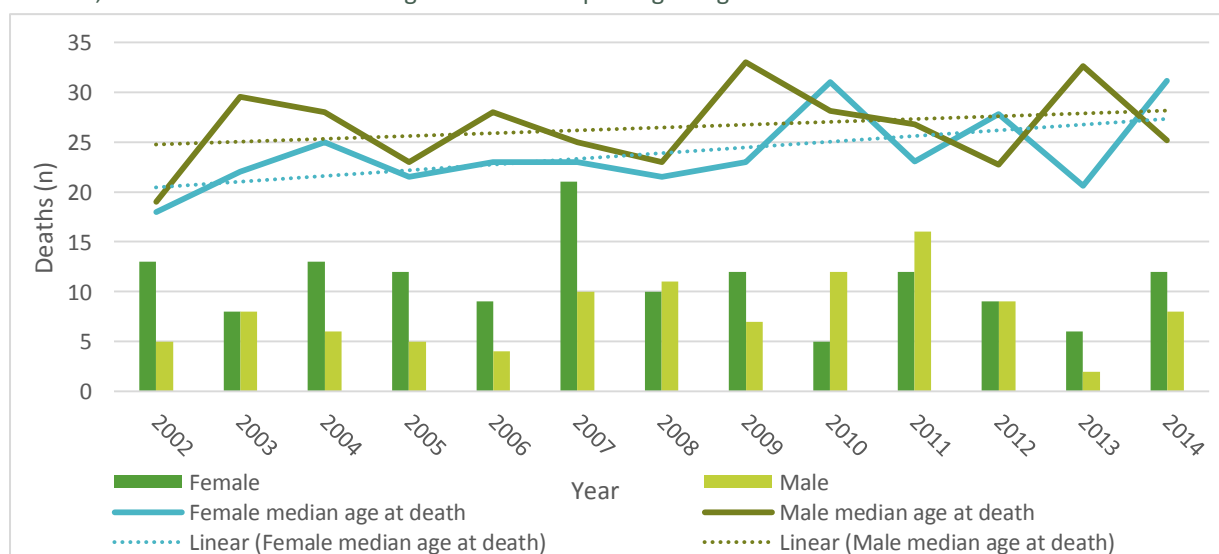
There have been 249 deaths in individuals with CF since 2002 (CFRI-registered and non-registered individuals), 22 of which occurred in 2014. Twenty were registered with the CFRI and they died at an age between 9 and 47 years. Twelve were female (60%) and six of the deaths occurred in children under eighteen years of age. The median age at death in 2014 was 26.9 years.



Median age at death by gender

(n=249)

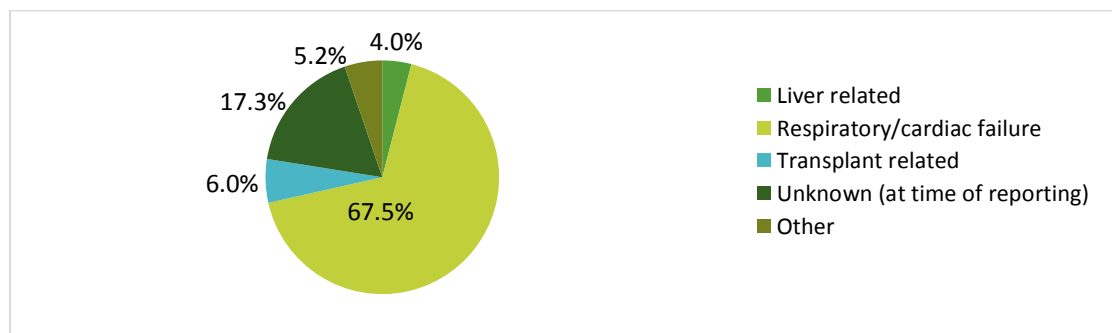
In 2014, there were more deaths in females than in males, but an older median age at death was recorded for females (31.1 years) compared with males (25.2 years). Each year between 2002 and 2009, males' median age at death was greater than that of females. Since 2010, the gender with the greater median age at death changed year-on-year. Linear trend lines for median age at death indicate that over time, median age at death has improved in males and females, and that females' median age at death is improving at a greater rate than males.



Cause of death, 2002-2014

(n=249)

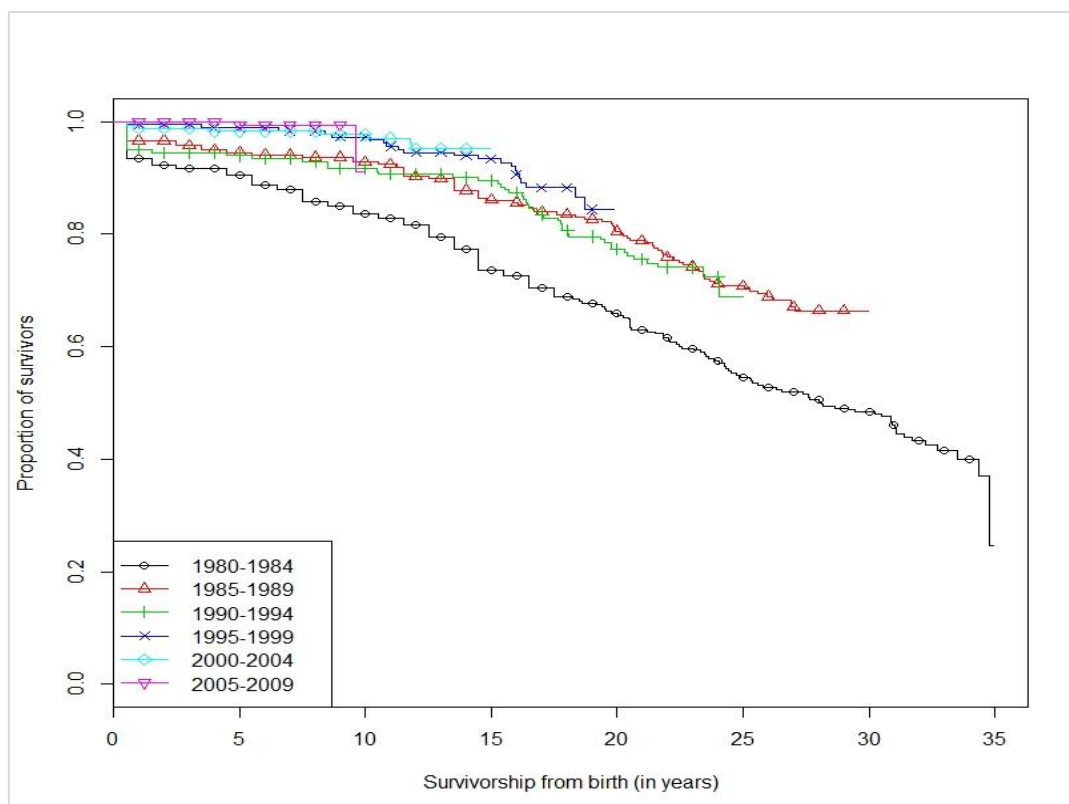
Respiratory/cardiac failure was the most common cause of death in individuals with CF between 2002 and 2014 (69%). Of those with a known cause of death, 81.9% died as a result of respiratory/cardiac failure.



Survival in individuals born 1980-2009

(n=1,197)

Improvements in survivorship of individuals with CF born between 1980 and 2009 is shown below. Half of individuals with CF born 1980-84 died before their 29th birthday. Ten percent died in the first five years of life. By comparison, every CF individuals born 2005-2009 reached their fifth birthday. Eighty-one percent of PWCF born in the nineties, and 97.2% of those born in the 2000's were alive at the end of 2014.³



³ Jackson, AD *et al.* Thorax, 2011

Transplantation

The number of individuals with CF receiving double lung transplants increased in recent years, from 4 in 2012, to 9 in 2013 and 19 in 2014 (source: Irish National Lung Transplant Programme at the Mater Misericordiae University Hospital). In 2014, the Irish National Lung Transplant Programme at the Mater Misericordiae University Hospital took over the care of all Irish adult lung transplants from the Freeman Hospital in Newcastle.

In 2014, the CFRI were not in a position to invite consent, nor gather information on CF individuals attending the Mater Misericordiae University Hospital. Despite there being no arrangement in place for data collection by the CFRI at that site, it was possible to estimate (using data collected at CFRI-participating CF specialist centres) that 78 CFRI-registered individuals had received a double lung transplant and were alive at the end of 2014.

In 2015, the CFRI and the Mater Misericordiae University Hospital initiated activities to seek the approval of appropriate agencies to allow the collection of data for the CFRI on consenting individuals with CF. It is anticipated that the quality and completeness of CFRI records on patients who have undergoing transplantation should be greatly enhanced, and we look forward to presenting more detailed transplant information in subsequent reports.

CFRI data requests, 2013-2015

Requests for CFRI data may require completion and submission of a data application form (available at www.cfri.ie). The CFRI Executive Committee review and either approve or decline the application, based on the content of the application form. Requests for data similar to what is generally published in our Annual Reports usually do not require the completion of a formal data request. Both formal and information data applications have increased in recent years, and we report on these statistics here for the first time.

	2013	2014	2015*
Data applications reviewed by CFRI Executive Committee	9	6	7
Declined	1	-	-
Approved	8	6	7
<i>CFRI-affiliated independent researchers</i>	4	1	4
<i>Other independent researchers</i>	4	4	2
<i>Other</i>	-	1	1
Data applications approved by CFRI operational staff	-	5	5
Total number of data applications	9	11	12

*provisional data

CFRI research, 2014-2015

The Cystic Fibrosis Registry of Ireland mission statement indicates that registries ‘...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.’

Anonymised registry datasets can be made available to approved doctors and researchers to allow such analyses take place. As described in the section on data requests, only approved, trusted third parties may be granted limited access to CFRI data. The table below summarises some of the approved research collaborations the CFRI are currently engaged in.

Principal Investigators	Project title	Start date	End date
Dr Patricia Fitzpatrick, UCD School of Public Health/ Dr Barry Linnane, University Hospital Limerick	Early evaluation of the clinical and economic effects of the cystic fibrosis newborn screening programme	October 2013	September 2016
Dr Kirstin Schaffer, St Vincent’s University Hospital on behalf of the Irish CF microbiology group	Epidemiology of <i>Burkholderia cepacia</i> in Ireland	September 2015	Mid-2016
Ms Emma Reece & Dr Peter Greally, the Adelaide and Meath Hospital Incorporating the National Children’s Hospital & Trinity College Dublin	Co-infecting microbes: implications for cystic fibrosis airways disease	2013	2016
Dr Marion Rowland, UCD School of Medicine and Medical Science	Cystic fibrosis liver disease	2005	Continuing
Dr Roisin Adams, National Centre for Pharmacoeconomics	Patient preferences for health	2016	2019
Ms Breda Nolan/ Dr Gerardine Doyle, UCD School of Business	The patient registry as a mediating instrument to support integrated care	2014	2017

The CFRI also leads its own in-house epidemiological and health services research programme. In 2014, the CFRI concluded a 12-month study on the patterns of cost and utilisation of CF healthcare services in Ireland. The table below highlights the principal scientific outputs from that research programme.

Scientific conference	Paper title
European Cystic Fibrosis Society Conference 2014, Gothenberg, Sweden	Can Registry Data be Used to Examine CF Health Service Utilisation? Perspectives of the Irish CF Registry
European Cystic Fibrosis Society Conference 2015, Brussels, Belgium	Direct medical cost of CF care in the Irish public healthcare system
Irish National CF Conference, Killarney, 2015	Direct costs of cystic fibrosis care in the Irish public healthcare system*

*Joint winner of poster award at the Irish National CF conference, 2015.

In 2015, the CFRI were granted a two-year Vertex Innovation Award for a project entitled ‘Evaluating outcomes in European cystic fibrosis patients with access to their health records: a randomised control trial of a Registry Patient Portal’. The anticipated first date of enrolment for participants in Ireland, Denmark and Slovenia is March 1st, 2016.

Finally, the CFRI is also currently engaged in pharmacovigilance of newly marketed CF therapies, to assist pharmaceutical companies in meeting the European Medicines Agency’s post-marketing safety requirements.

Financial information

Income & Expenses		2014 €
Income		
Core Funding		140,000
Other funding and donations		69,878
Deferred income released – Vertex Grant		24,500
Deferred income released – Dept of Health		47,232
Sundry income		102
	Total income	281,712
Expenses		
Wages & salary		161,521
Employer's PRSI		12,576
Rent payable		6,072
Service Charges		662
Insurance		464
Software development, Computer network & server costs		57,072
Telephone & fax		207
Printing, postage and stationery		1,211
Travelling & subsistence		11,136
Legal & professional fees		4,397
Audit		984
Bank charges		309
Subscriptions		120
Depreciation on equipment		527
	Total expenses	257,258
	(Deficit)/Surplus	24,454

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.

Technical notes

Data collection sites

In 2014, the CFRI gathered data from the eight HSE-designated CF specialist centres (Beaumont Hospital, St Vincent's University Hospital, the Adelaide and Meath Hospital Dublin, Incorporating the National Children's Hospital, Our Lady's Children's Hospital, Crumlin, Temple Street Children's University Hospital, University Hospital Galway, Cork University Hospital and University Hospital Limerick), and five shared care CF centres (Cavan General Hospital, Mayo General Hospital, Our Lady of Lourdes Hospital, Drogheda, Sligo Regional Hospital, and Waterford Regional Hospital).

Lung function analysis

As spirometry cannot reliably be performed until the age of 6 years, only reported values for CF individuals aged 6 and older were considered. The CF centre reported value of FEV1% predicted was considered. For individuals who were reported to have had a lung transplant in or before 2014, their FEV1% predicted values in the year of transplant and post-transplant were excluded.

Nutrition

Heights and weights recorded at the patient's best FEV1% predicted of the year were included in the analysis. Where no spirometry was performed, the nutrition record with the best weight measurements in the year was considered. The reference group used to estimate Z scores was the Centre for Disease Control (CDC) 2000 reference charts (Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC Growth Charts for the United States).

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, our industry partners who have provided us with unconditional grants, and other funded researchers who have included us in their research grant applications. 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 deserves 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. Particularly for the extra work that had to be done to assist with the development of the new registry technology.

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 Sport 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 2014 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 Abi Jackson and Larry Ungar for their hard work and dedication in preparing this report.

CFRI executive council membership 2014

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	CF Ireland
Mr Godfrey Fletcher	CEO	Chief Executive Officer Cystic Fibrosis Registry Ireland
Prof 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
Prof Paul McNally		Consultant in Paediatric Respiratory Medicine Our Lady's Children's Hospital, Crumlin
Dr Barry Linnane		Consultant in Paediatric Respiratory Medicine Midwestern Regional 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

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

©Cystic Fibrosis Registry of Ireland, 2016
Charity Number: CHY17566

