Cystic Fibrosis Registry of Ireland Annual Report 2008

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Preface

The 2008 Annual Report is dedicated to Linda Foley who tragically passed away in November 2009 while working on this Report. The following Executive Summary was written by Linda and is left unedited as a mark of respect for a truly remarkable person. Linda is sorely missed and will never be forgotten for her contribution to cystic fibrosis care in Ireland and internationally.

Linda has left the cystic fibrosis community with a valuable resource with a near ninety percent ascertainment level of the CF population in the Republic of Ireland. The data that is now available can be maintained on a year by year basis and can be used to support cystic fibrosis research into the future.

I would like to thank the staff at all the CF hospitals for assisting the CFRI in the collection of patient data. I would also like to thank our Clinical Research Associates, Mary Harrington and Shijun Zhou for the long hours that they put in manually collecting data from patient charts, particularly when strict deadlines for completion of data collection were imposed upon them. A special thank you also goes to Abaigeal Jackson for cleaning the data and for preparing this Annual Report.

We are now at a very important phase in the development of cystic fibrosis services. Considerable investment has been made in the development of cystic fibrosis services, new units are under construction, additional staff have been recruited, and neonatal screening for cystic fibrosis is about to be introduced. CFRI has a very important role to play into the future by providing data that can be used to support CF service audit and accreditation, assist in service planning, and maintaining a valuable repository of data for use by the research community.

The registry looks forward to working with all parties so that we can meet our mission “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.”

Godfrey J. Fletcher

Executive Summary

The year, 2008, was a watershed year for the CFRI. It was the first full year of new governance with a new Executive Council, Constitution, and Charitable Status operating as an "unincorporated association with a constitution". It was also the first full year that the CFRI received realistic funding so that many objectives that had formerly been aspirational were now achievable.

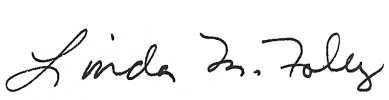
Also in 2008, a Postdoctoral Researcher, sponsored by the Health Research Board, started work on many projects that will define our registry. It was the first full year that we had a second Clinical Research Associate who was dedicated to informed consent and enrolment of new patients. As a direct result of this, ascertainment levels jumped from 63% to 88%.

There are several research opportunities that are being explored by 'mining' the data contained in the CFRI. Among the most important is an accurate survival analysis for Ireland. This will be completed during 2009. Following that there will be a number of projects that will assess the services available to PWCF to see if survival improves with increased services and access to those services.

We are also in a unique position to fully describe our CF population prior to the introduction of newborn screening (NBS) for CF. This will allow comprehensive analysis of data that will show the effect of the introduction of NBS.

The HSE should be congratulated for their continued support of the CFRI and I hope that this registry will demonstrate the usefulness of such databases for many conditions.

This annual report reflects many recent improvements and I hope that the reader will be able to see that when a vision is recognised and properly funded, many positive benefits result.



Linda M. Foley

Summary Statistics for 2008

	2007	2008
Number of patients consented	762	1065
Median age (years)	17	17.9
Number diagnosed during the year	32	19
Number of patients with genotype information	97%	96%
Number of enrolled patients deceased during the year	17	17
Median age at death (years)	24	23
Number of consented individuals alive at end of year	718	1004
% alive at end of year who were male	53.5%	57.4%
% adults (≥18 years) alive at end of year	45.5%	49.4%
Number of live patients identified by annual census	1170	1142
% ascertainment of the live CF population by the CFRI	61.4%	87.9%
Number of patients for whom annual clinical data was collected	143	813
% of patients alive at end of year for whom annual clinical data was collected	20.6%	81.0%

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Cystic Fibrosis Specialist Centres, 2008

County	Hospital	Consultant	Type of Centre
Cork	Cork University Hospital	Dr Barry Plant /	Adult
		Dr Cathal Bredin	
		Dr. Michael Henry/	Paediatric
		Dr Muireann ní Chroínín	
Dublin	Beaumont Hospital	Prof NG McElvaney /	Adult
		Dr Cedric Gunaratnam	
	St Vincent's University Hospital	Prof Charles Gallagher/	Adult
		Dr Ed McKone	
	The Children's University Hospital	Dr Dubhfeasa Slattery	Paediatric
	National Children's Hospital	Dr Peter Greally /	Paediatric
		Dr Basil Elnazir	
	Our Lady's Children's Hospital	Dr Gerry Canny /	Paediatric
		Dr Barry Linnane	
	Mater Misericordiae University Hospital	Prof Jim Egan	Heart/lung transplant
Galway	University College Hospital Galway	Dr Mary Herzig	Paediatric
	Merlin Park Hospital, Galway	Dr JJ Gilmartin	Adult
Kerry	Kerry General Hospital	Dr Fergus Leahy	Paediatric
Limerick	Midwestern Regional Hospital	Dr MJ Mahony	Paediatric
		Dr Eithne Mulloy /	Adult
		Dr TH Peirce	
Louth	Our Lady of Lourdes Hospital	Dr David Vaughan	Paediatric
		Dr John Kiely	Adult
Mayo	Mayo General Hospital	Dr Michael O'Neill	Paediatric
Sligo	Sligo General Hospital	Dr R Tummaluru	Paediatric
Waterford	Waterford Regional Hospital	Dr A Das	Paediatric
		Dr S Foley	Adult

CFRI Executive Council: 2008-2011

Prof C Gallagher	Consultant in Respiratory Medicine, St. Vincent's University Hospital, Dublin	Chairperson
Dr G Canny	Consultant in Paediatrics, Our Lady's Children's Hospital, Dublin	Vice-Chairperson
Dr P Greally	Consultant in Paediatric Respiratory Medicine, Adelaide and Meath National Children's Hospital, Dublin	Honorary Secretary
Mr G Fletcher	Non medic council member	Honorary Treasurer
Prof NG McElvaney	Professor of Medicine, Royal College of Surgeons in Ireland & Consultant in Respiratory Medicine Beaumont Hospital, Dublin	Immediate Past Chairman, ex-officio
Mrs L Foley	Chief Executive, CFRI	
Dr B Linnane	Consultant in Paediatrics, Our Lady's Children's Hospital, Dublin	Council Member
Dr E McKone	Consultant in Respiratory Medicine, St. Vincent's University Hospital, Dublin	Council Member
Dr B Plant	Consultant in Respiratory Medicine, Cork University Hospital, Cork	Council Member
Dr M Rowland	UCD School of Medicine, Medical Sciences, Children's Research Centre, Crumlin, Dublin	Council Member
Dr D Slattery	Consultant in Paediatric Respiratory Medicine, Children's University Hospital, Dublin	Council Member
Mr. M Wickham	Non medic council member	Council Member

Glossary

AA	Annual Assessment
ABPA	Allergic Bronchopulmonary Aspergillosis
Adult	Aged 18 years or older (≥18)
BAL	Bronchoalveolar lavage
BMI	Body Mass Index
CF	Cystic Fibrosis
CFAI	Cystic Fibrosis Association of Ireland
CFRI	Cystic Fibrosis Registry of Ireland
CFTR	Cystic Fibrosis Transmembrane conductance Regulator
CRA	Clinical Research Associate
CSO	Central Statistics Office of Ireland
DEXA	Dual Energy X-ray Absorptiometry
DIOS	Distal Intestinal Obstruction Syndrome
FH	Family history
FEV_1	Forced Expiratory Volume in one second
FVC	Forced expiratory Vital Capacity
GI	Gastrointestinal symptoms
HRB	Health Research Board
H2RA	H2-receptor antagonists
IV	Intravenous
MI	Meconium ileus
MRSA	Methicillin Resistant *Staphylococcus aureus*
NBS	Newborn screening
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

Hospital Abbreviations

AMNCH	National Children's Hospital at the Adelaide & Meath Hospital, Tallaght, Dublin 24
BMT	Beaumont Hospital, Dublin 9
Cavan GH	Cavan General Hospital, Cavan
CUH	Cork University Hospital, Wilton, Cork
CUHTS	Children's University Hospital, Temple Street, Dublin 1
Kerry GH	Kerry General Hospital, Tralee
Mayo GH	Mayo General Hospital, Castlebar
MWRH	Midwest Regional Hospital, Limerick
MMUH	Mater Misericordiae University Hospital, Dublin 7
OLCH	Our Lady's Children's Hospital, Crumlin, Dublin 12
OLLH	Our Lady of Lourdes Hospital, Drogheda
Sligo GH	Sligo General Hospital, Sligo
SVUH	St Vincent's University Hospital, Dublin 4
UCHG	University College Hospital Galway (including Merlin Park Hospital)
WRH	Waterford Regional Hospital, Waterford

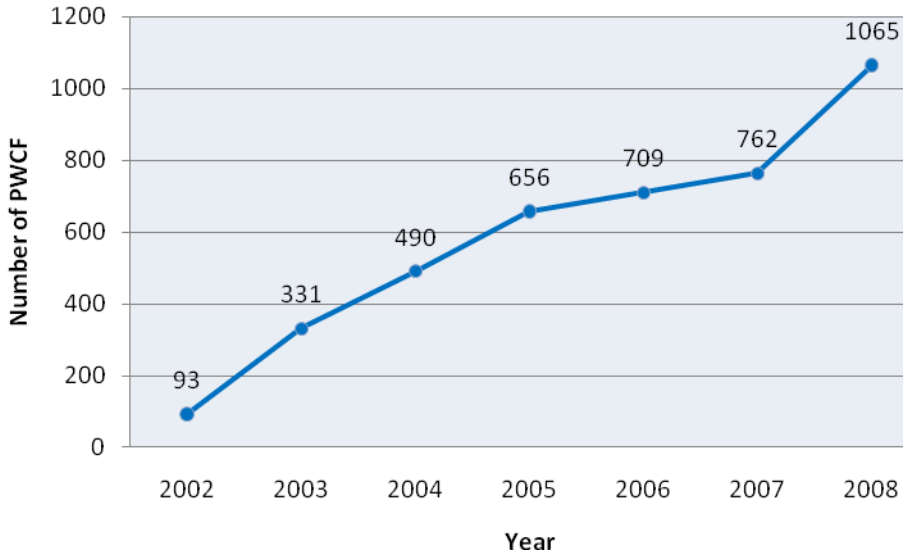
CFRI Enrolment

Since the start of the CF registry project we have been striving to enrol as many persons with CF (PWCF) that attend CF centres as possible. By the end of 2008, we enrolled 1,065 PWCF. A major boost in our figures occurred during 2008 by dedicating a new CRA to the task of enrolling PWCF. Her job was to ensure that PWCF were fully informed of the benefits of enrolling on the CFRI and to assure PWCF and their guardians that their data was protected using advanced encryption technology. There have been very few refusals to join the registry as most people realise that by being a part of this research vehicle there is ultimately benefit for all.

Figure 1 shows the number of PWCF enrolled in the CFRI based on date of PWCF consent. In previous annual reports, enrolment figures were based on date of collection of diagnostic data. The changeover to date of consent in this year's report means that enrolment figures presented here differ from previous years.

Over 300 PWCF were enrolled during 2008. Of the 1,065 PWCF enrolled by the end of 2008, 56.1% were male and 43.9% were female. Seventeen enrolled PWCF were known to have died in 2008. Of the 1004 enrolled patients alive at the end of 2008, 49.4% were aged 18 years and older, while 50.6% were under 18 years.

Figure 1: CFRI enrolment 2002 – 2008



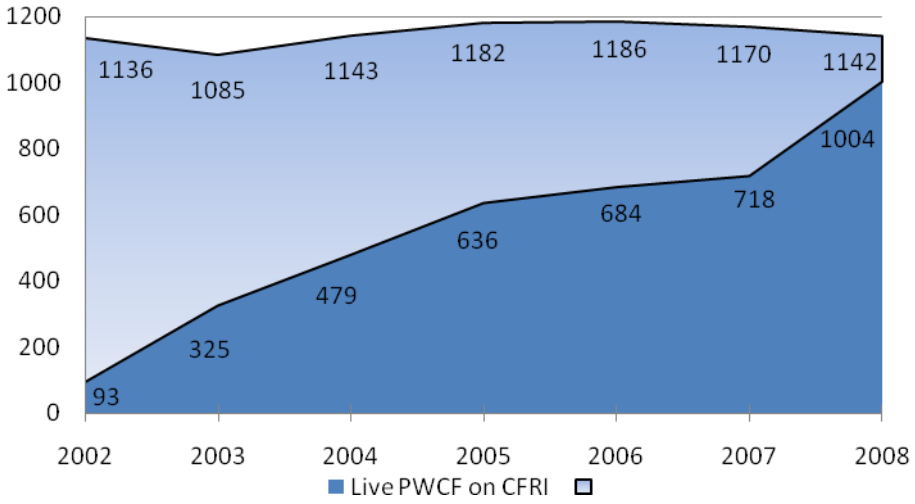
CF Centre & Clinic Census 2008

Through careful tracking of the numbers of PWCF who attend CF centres and clinics, and comparing those figures with the number of live CFRI enrolees we can confidently say that by the end of 2008, we achieved a coverage level of 87.9% of persons with a known CF diagnosis (Figure 2). This is a substantial increase in ascertainment since 2007 (just under 62%).

In addition to increased enrolment, the accuracy of our annual census of live PWCF has been enhanced. As named patients are now reported on the census, it is now possible to avoid duplication of patients who attend more than one centre. This has most likely caused a decline in census figures since 2006, rather than a decline in the CF population.

The CFRI will continue to enrol new and existing PWCF during 2009 and beyond, however as we near complete ascertainment, we expect year-on-year increases in enrolment to level off. One hundred percent enrolment of census-identified PWCF will not be possible for several reasons. Firstly, 0.8% (n=8) of census-identified PWCF have previously opted not to participate in the CFRI. Secondly, CF centres may not always be able to identify those who have left their service to attend another in Northern Ireland or abroad. This may lead to an overestimation of PWCF counted during the census by CF centres. Finally, a small proportion of PWCF identified by the census may not easily be enrolled by CFRI staff as some PWCF are hard to contact due to infrequent clinic attendance.

Figure 2: Gap in CFRI enrolment and CF centre census of living PWCF

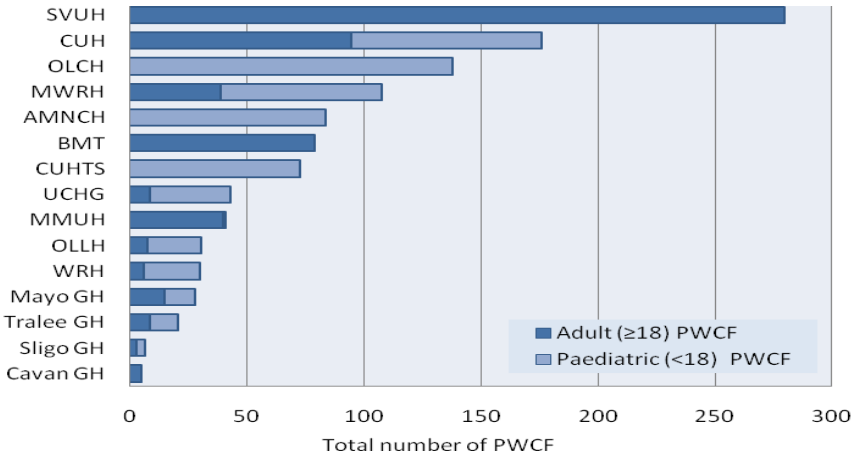


Within the international CF community, an ascertainment level of approximately 90% is considered a significant achievement. Adequate representation of the CF population is required to ensure statistics generated by analysis of registry datasets are valid. However, ascertainment rates are not always reported in international CF registries' annual reports. Anecdotal information suggests that the CFRI's coverage level of 87.9% compares favourably to leading CF registries, which include the United States and United Kingdom.

For the first time in 2008, the Mater Misericordiae University Hospital (MMUH) was invited to participate in the census. The participation of the MMUH health/lung transplant unit has improved the identification of PWCF who have undergone transplant. Figure 3 shows census figures by CF centre and by PWCF age band. As in previous annual reports, we define paediatric PWCF as those aged under 18

years. St Vincents University Hospital (SVUH), Cork University Hospital (CUH) and Beaumont Hospital (BMT) had the largest adult CF services in 2008. Our Lady's Children's Hospital (OLCH), the Adelaide and Meath National Children's Hospital (AMNCH) and Cork University Hospital (CUH) had the largest paediatric CF services.

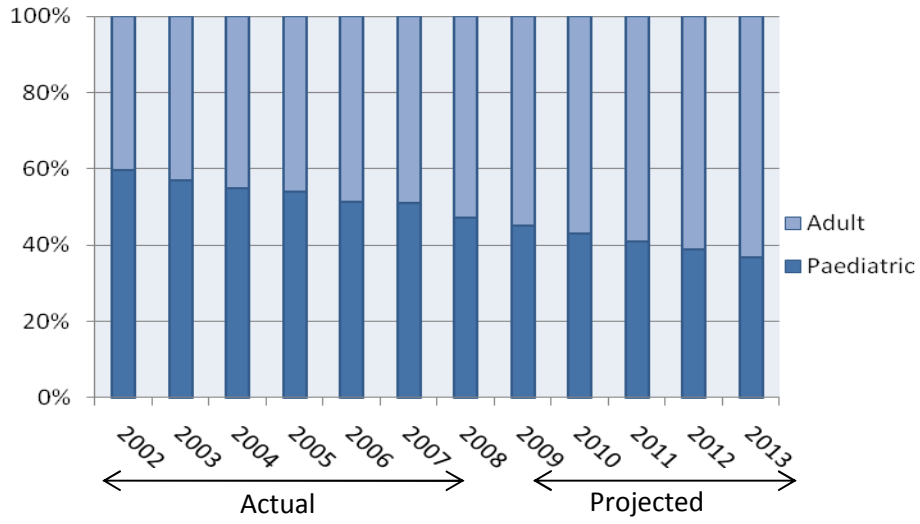
Figure 3: CF centre census of live patients in 2008, n=1142



Census figures continue to highlight the growth of the adult PWCF population and in 2008, 53% of census-identified PWCF were aged 18 years or older. Since 2002, the adult census population has increased annually by an average of 2% (or approximately 20 PWCF), with a corresponding 2% reduction in the paediatric population. Although we show a linear projection in growth of the adult population to 2013 in Figure 4, we cannot be certain when the growth in the adult population will stabilise. This will depend on whether the life expectancy of PWCF continues to improve and the trend in annual numbers of new CF diagnoses.

As CFRI ascertainment of the CF population has reached a high level, more than ever, it is capable of providing important information which can inform decisions about service reconfiguration, which is required to meet the growing needs of this population. In particular, as adult numbers increase, so too do the number of other CF-related co-morbidities requiring treatment, such as osteoporosis and diabetes.

Figure 4: Projected ratio of adult to paediatric CF patients to 2013

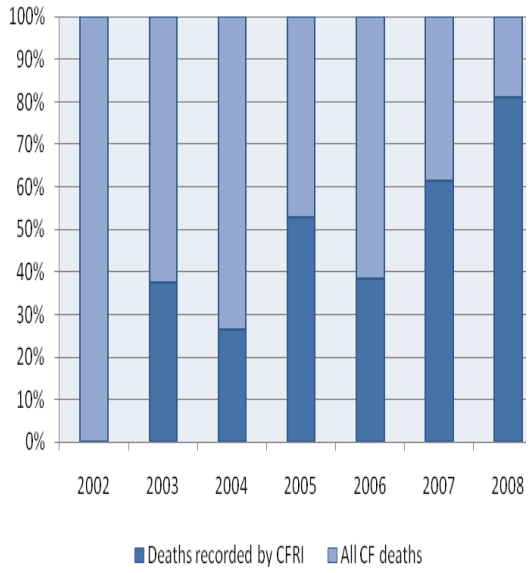


CF Survival

As part of the CFRI's Health Research Board (HRB) funded research programme of epidemiological research (2008-2011), an analysis of CF survival has been undertaken. Data on CF deaths were sourced from the Central Statistics Office (CSO) dating back to 1980) as well as the Cystic Fibrosis Association of Ireland (CFAI), which date back to 1986. As these datasets contained patient identifiable information, we were able to compare the deaths recorded by the CFRI, the CFAI and CSO. A comprehensive record of deaths due to CF from 1980 to 2008 was compiled and is reported on here.

Figure 5 shows deaths recorded by the CFRI (dark blue) as a proportion of all identified CF deaths. This has improved over time, and in 2008, 81% of all known deaths (or 17 of the 21 deaths) in that year occurred in patients enrolled on the CFRI. The absence of data on recorded deaths in the early years of the registry was an inevitable consequence of the registry being in its infancy, and being unable to provide some PWCF with an opportunity to enrol before they died.

Figure 5: Deaths recorded by the CFRI vs all known deaths.



SURVIVAL STATISTICS

Predicting how long an individual newborn PWCF will live is not possible. Yet, there are statistics that can be used, which will allow us to estimate an 'average' age at which a group of persons with CF might die. Importantly, when we are using these statistics to examine life expectancy, we can only base our estimates on information on those who have died.

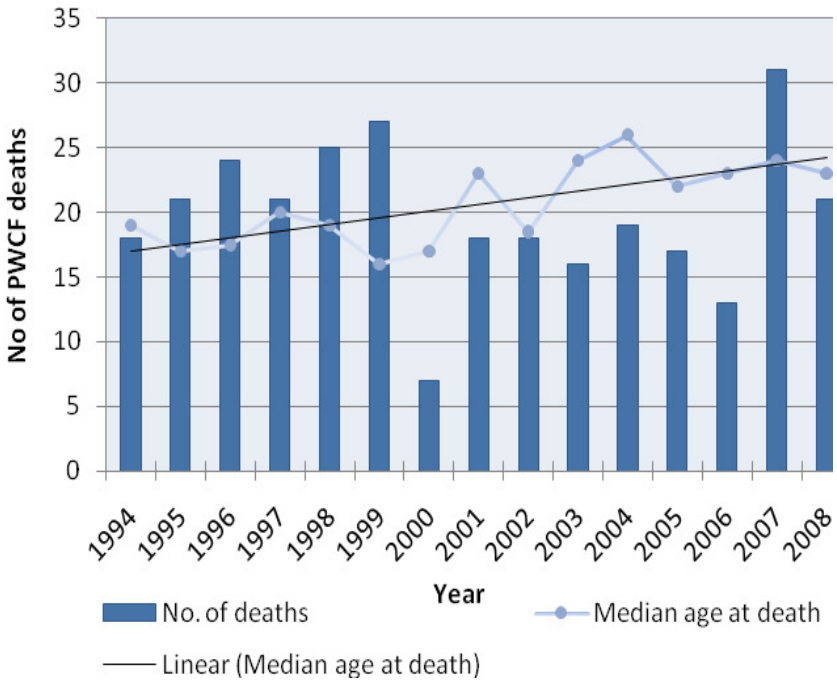
In CF, 'median age at death' and 'median survival' are used to describe life expectancy and often lead to confusion because they have different meanings. In a given CF population, we cannot be sure how long those who are alive will continue to live, but we know how long the deceased population lived before their death.

Median age at death is calculated using information from the deceased portion of the population only. The median value indicates that half of the population lived to the specified age and half lived past it. The problem with using median age at death as a measure of survival is that it only considers the survival of those who have died, but not the survival of those who are still alive. For this reason, the median age at death value is usually lower than an estimate of life expectancy derived by following an entire population until all have died.

Median survival estimation takes an entire CF population and follows them until half have died and can be performed using either of two techniques; annual current lifetables and birth cohort follow-up.

Figure 6 shows that the total number of deaths fluctuates from year to year (range: 7-31 from 1994 to 2008), however the overall trend in numbers of deaths remains stable. By contrast, the median age at death (see definition in the table entitled 'Survival statistics') has continued to increase. In 2008, the median age at death was 23 years. Since 2000, there have been four deaths in PWCF <5 years of age, which suggests that CF is no longer a common cause of childhood death in the Republic of Ireland.

Figure 6: Total number of deaths and median age at death of PWCF, 1994-2008



When we look at numbers of deaths and median age at death by gender (Figure 7) we find that there have been more deaths in females than males almost every year since 2000. Also, every year since 2002, females have had a poorer median age at death than males. This gender gap has long been observed in many CF communities, yet reasons for this disparity still remain unclear.

Figure 7: Number of CF deaths and median age at death by gender, 1994-2008

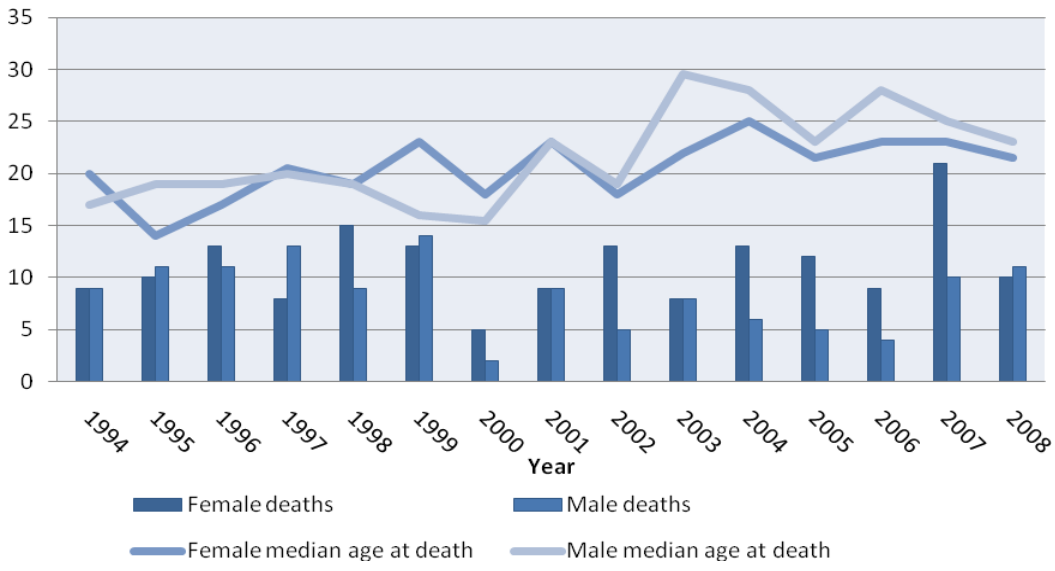
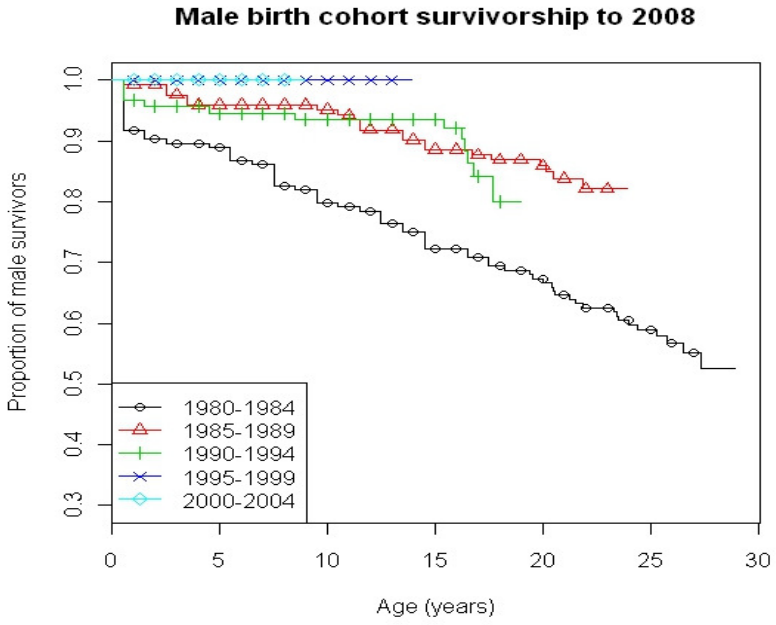
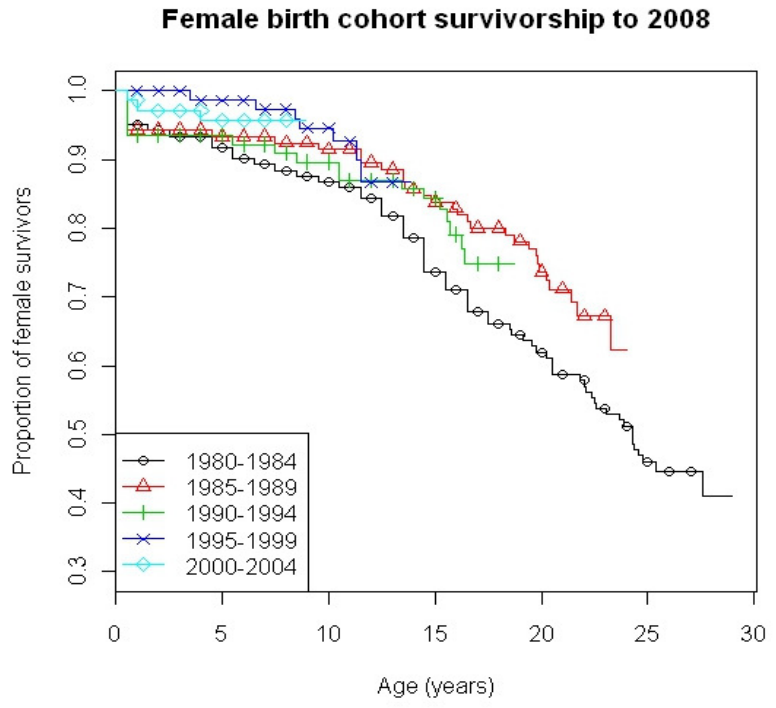


Figure 8 shows birth cohort lifetable (Kaplan-Meier) survivorship curves for males and females born between 1980 and 2004 up to 2008. Using the birth cohort lifeable approach, PWCF born in a particular time period can be followed until all have died. The point at which half the population die is called the median survival estimate, and is a more accurate measure of how long PWCF will live on average, compared with median age at death. The Figure shows that survival for both male and female PWCF has improved in succesive birth cohorts. Childhood mortality has become increasingly rare. Also, fewer deaths have been observed (up to 2008) in males than in females born from 1995 onwards.

Figure 8: Birth cohort survivorship to 2008 for PWCF born 1980-2004 by gender

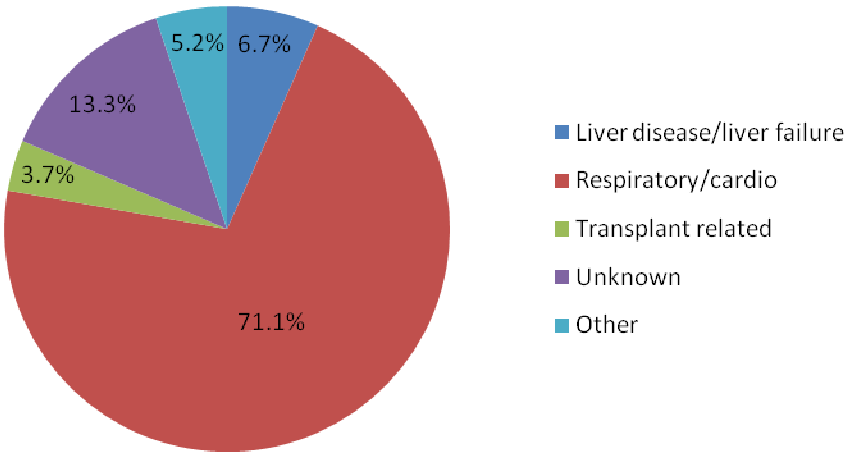




Cause of Death

Of the 135 deaths that occurred between 2002 and 2008 (Figure 9), the cause of death for 71% of PWCF was due to respiratory/cardiac failure. In previous annual reports, very few PWCF had an unknown cause of death, but this year, we do not have information for 13.3% of decedents. As CSO data has been included in this year's report for the first time, we are reliant on the cause of death noted on the death certificate. For PWCF described here as having an 'unknown' cause of death, CF was cited as the principle cause of death on the death certificate and no further detail was provided about the circumstances of death.

Figure 9: Principle cause of death, 2002-8, n=135



Demographics of the CFRI

A description of general demographic data is provided in Table 1. The average age of enrolled PWCF on the last day in 2008 was 18.3 years, and the longest living individual was aged 58 years. There were almost equal numbers of adult and paediatric PWCF on the Registry at the end of 2008. A greater proportion of males were on the registry at the end of 2008 (57%) compared with the 2007 CFRI dataset (54%). This may be due to a disproportionately large number of deaths occurring in females.

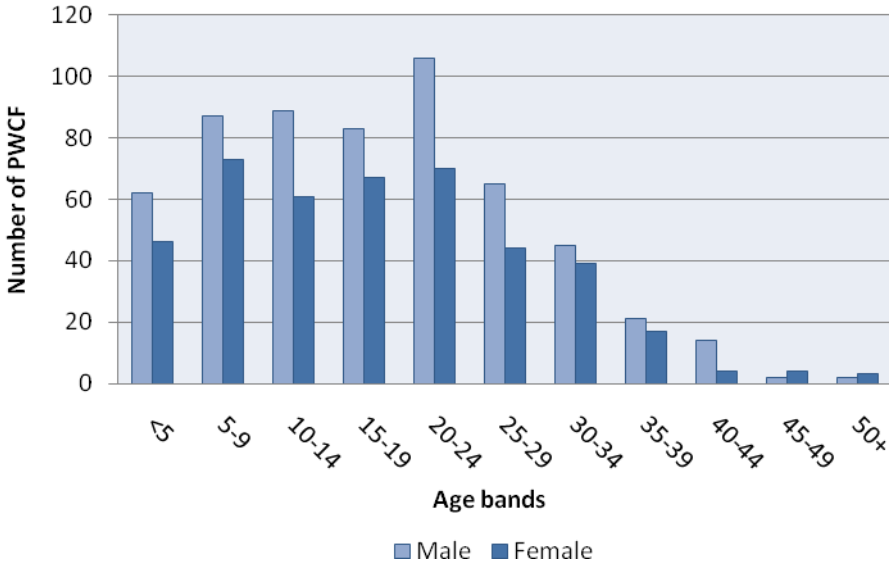
Table 1: Demographic data from the Cystic Fibrosis Registry of Ireland (CFRI)

Year	2003	2004	2005	2006	2007	2008	Total	%
PWCF consented	238	159	166	53	53	303	1065	
Age range*						<1 - 57		
Mean age (yrs)*						18.3		
Median age (yrs)*						17.9		
Number diagnosed during year						19		
Number of males*						576		57.4%
Number of females*						428		42.6%
Number <18 yrs*						508		50.6%
Number ≥18 yrs*						496		49.4%
Number males ≥18 yrs*						288		28.7%
Number females ≥18yrs*						208		20.7%
Irish ethnicity*						981		97.8%
Deaths during year	6	5	9	5	19	17	61	
Total PWCF on Registry who are alive at end of year							**1004**	**94.3%**

* of the 1004 PWCF on the Registry who are alive at end of 2008

Figure 10 shows the age distribution of PWCF alive at the end of 2008 by gender. The numbers of male and female PWCF decrease notably after the 20-24 year age band.

Figure 10: Age and gender distribution by age band, 2008 (n=1004)



The place of residence of enrolled PWCF is summarised by county in Table 2. It shows that approximately 1 in 4 patients reside in the county of Dublin, however, the vast majority of PWCF requiring CF services are distributed across the rest of the country.

Table 2: PWCF by county of residence

	Number of PWCF	%
Dublin	275	27.4%
Cork	128	12.7%
Limerick	53	5.3%
Kildare	52	5.2%
Tipperary	49	4.9%
Galway	45	4.5%
Kerry	38	3.8%
Wicklow	38	3.8%
Meath	35	3.5%
Mayo	32	3.2%
Clare	31	3.1%
Wexford	25	2.5%
Louth	21	2.1%
Westmeath	19	1.9%
Cavan	18	1.8%
Kilkenny	18	1.8%
Laois	18	1.8%
Waterford	18	1.8%
Carlow	15	1.5%
Offaly	15	1.5%
Donegal	13	1.3%
Sligo	13	1.3%
Monaghan	12	1.2%
4 counties with <10 patients	23	2.3%
Total	**1004**	**100.0%**

Patients' place of residence have been mapped for the first time using 'Health Atlas Ireland', which is a geospatial analysis tool developed by the HSE's Health Information Unit to provide health professionals with access to maps, data and statistical analysis tools. The CFRI are currently working with the Health Intelligence Unit to plan analyses which are hoped will inform decisions as to where to locate centres/clinics to provide optimal CF services.

Siblings

The CFRI is unique amongst CF registries in that it captures and reports information about the familial and sibling status of its enrolled PWCF (Table 3). In 2008, there were 937 families represented on the CFRI, who had at least one family member with CF. Thirteen percent of these families had 2 or more family members with CF. These estimates are likely to underestimate the actual number of CF families with 2 or more PWCF, because family members belonging to some enrolled PWCF may have died before they could be invited to enrol, or before the registry was initiated.

Table 3: CFRI families and siblings, 2008

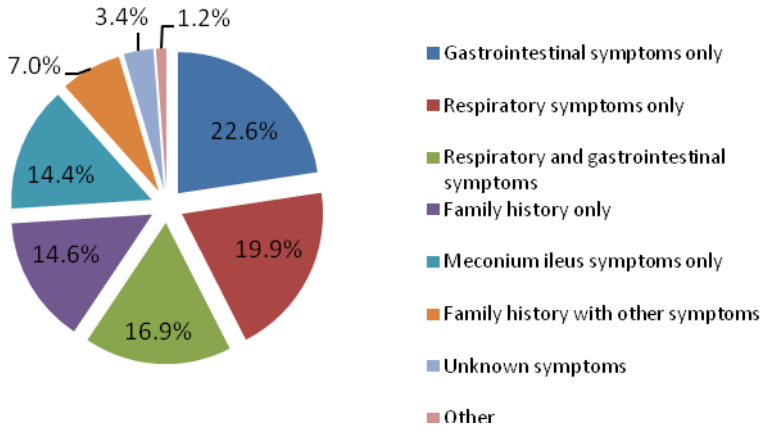
Irish CF families	
1065	Total number of PWCF enrolled
937	Families represented
13.3%	125 of 937 families had 2 or 3 members with CF
118	Number of families with 2 members with CF
7	Number of families with 3 members with CF

Diagnosis

In the absence of CF newborn screening in the Republic of Ireland, PWCF are diagnosed as a result of presentation to medical services with symptoms, or if they are required to undergo investigation for CF if there is a known family history (FH) in the immediate or extended family. As CF is a multi-system disease, there are many types and combinations of symptoms which may precede a CF diagnosis. For the purposes of presenting diagnostic data, symptoms have been categorised under the following headings: meconium ileus (MI), respiratory (RESP) and gastrointestinal (GI) symptoms (Figure 11).

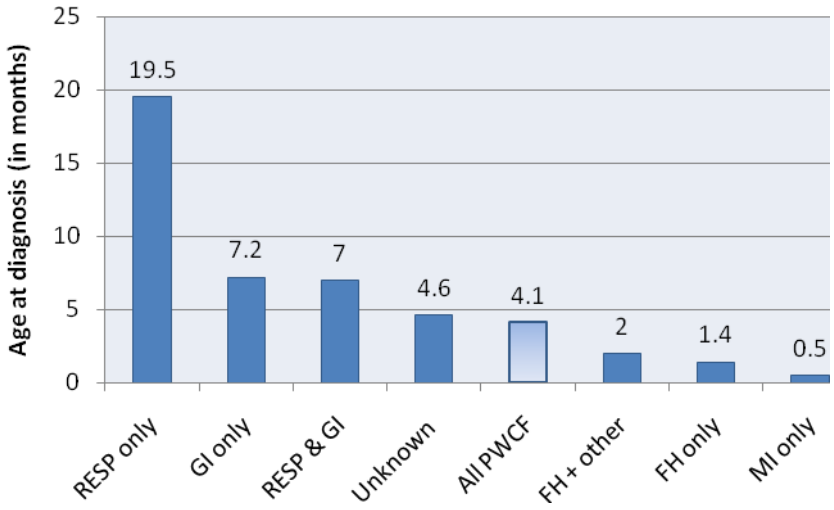
Gastrointestinal symptoms alone were the most commonly reported symptom resulting in a CF diagnosis (22.6%), followed by respiratory symptoms alone (19.9%), and both respiratory and gastrointestinal symptoms (16.9%). Nearly 22% of patients in total had a family history of CF. A proportion of these PWCF had no clinical signs or symptoms of CF (14.6% of all PWCF) and if clinical investigations for a family history had not been pursued, diagnosis could have been delayed. Finally, mode of diagnosis was unknown for 3.4% of PWCF. These PWCF were adults when invited to enrol on the CFRI, and could not remember the circumstances leading to their CF diagnosis, which occurred during childhood.

Figure 11: Symptoms leading to a diagnosis of CF, n=1065



There is a broadly similar pattern to previous years with regards to median age at diagnosis (Figure 12). As expected, PWCF presenting with meconium ileus had the earliest median age at diagnosis, as this would be noted soon after birth. Also, those presenting with respiratory symptoms alone experienced the greatest delay in being diagnosed. However, there were two notable changes in median age at diagnosis since 2007. Median age at diagnosis for patients presenting with respiratory symptoms alone increased from 16.3 in 2007 to 19.5 months in 2008, and gastrointestinal symptoms alone increased from 5.8 to 7.2 months. Median age at diagnosis for PWCF with respiratory and gastrointestinal symptoms remained the same (7 months). The overall median age of diagnosis for all PWCF was 4.1 months.

Figure 12: Median age at diagnosis in months by symptom category



Genotype

Genotyping was performed for 96% of enrolled PWCF, which is a similar rate to that reported by the United Kingdom in the same year (93.7%). The range of alleles detected by the National Centre for Medical Genetics at Our Lady's Children's Hospital continues to grow, so this year we have opted to summarise genotype data (Table 4). Eighty-eight percent of enrolled PWCF carry a minimum of one ΔF508 allele. ΔF508 homozygous is the most commonly detected genotype (58%).

Table 4: Frequencies of the most common CF mutations

	Number of PWCF	%
ΔF508 homozygous	621	58.3%
ΔF508 G551D	114	10.7%
ΔF508 R117H	35	3.3%
ΔF508 1717-1 G-->A	15	1.4%
ΔF508 R560 T/K	23	2.2%
ΔF508 621+1 G-->T	15	1.4%
ΔF508 G542X	14	1.3%
All other ΔF508 heterozygotes	107	10.0%
ΔF508 allele 2 unknown	17	1.6%
G551D G551D	8	0.8%
Other genotypes	48	4.5%
Not genotyped	43	4.0%
Pending	5	0.5%
Total	**1065**	

Hospitalisations and Complications

Now that we have primary information such as diagnostic data on most PWCF we can proceed to capture the year-on-year information that will tell us the long-term story on each group of PWCF. Having two CRA's to gather 2008 annual clinical assessment data meant that information on PWCF hospital-based encounters were captured for a substantially larger proportion of enrolled PWCF than reported on in previous annual reports. Table 5 indicates that such data was captured for 86.2% of paediatric patients and 75.6% of adults. Statistics on hospital-based encounters are now more reliable than ever.

Table 5: Annual assessment data collected, 2008

2008 Annual Assessments (AAs)		
	Paediatric	**Adult**
PWCF with 2008 AA data collected	438	375
Proportion of live PWCF with completed 2008 AAs (N=1004)	86.2%	75.6%

Table 6 shows the total numbers of hospitalisations, exacerbations and complications in the paediatric and adult group. The average number of hospitalisations and complications was slightly higher in the adult population, and as in previous years, and the number of respiratory exacerbations in adults was twice that experienced by paediatric patients.

Table 6: Number of hospitalisations, exacerbations and complications, paediatric vs adult groups

2008 Annual Assessments (AAs)				
	Paediatric		**Adult**	
	Number	**Average per PWCF**	**Number**	**Average per PWCF**
Number of hospitalisations	256	0.58	271	0.72
Number of respiratory exacerbations	268	0.61	470	1.25
Number of other exacerbations	73	0.17	50	0.13
Number of complications	982	2.24	1121	2.99

Table 7 examines complications in greater detail. Nearly 2 in every 3 adult PWCF had chronic *Pseudomonas aeruginosa* infection (defined as 3 or more *P. aeruginosa* culture isolates in a year) in 2008 and an estimated 2.1% had *Burkholderia cepacia* complex infection. Forty percent of paediatric patients had chronic *Staphylococcus* infection in 2008, an increase of 12% since 2007 (likely due to the improved collection of annual assessment data). MRSA was detected in 13.2% of paediatric PWCF and 8.8% of adults.

Liver disease affected 3% of paediatric and 13.3% of adult PWCF in 2008. Ninety-six percent of paediatric patients and 84.8% of adults were known to be pancreatic insufficient and requiring pancreatic enzymes. This difference may be artefactual, perhaps reflecting better recording of pancreatic status in paediatric medical charts, as it seems unlikely that adults have better pancreatic function than paediatric patients. Diabetes (requiring insulin) and osteopenia/osteoporosis are common in adults, and affect 22.4% and 40.5% of adult PWCF respectively.

Table 7: Complication rates by system; paediatric vs. adult groups

2008 Annual Assessment				
	Paediatric		Adult	
No of PWCF with completed AAs	438		375	
PWCF with no complications	4		6	
Total number of complications	982		1121	
Cardiac/Pulmonary Complications				
	Number of paediatric PWCF	**% of group**	**Number of adult PWCF**	**% of group**
Chronic *Pseudomonas*	100	22.8%	237	63.2%
Chronic *Staphylococcus*	177	40.4%	89	23.7%
Burkholderia	2	0.5%	8	2.1%
MRSA	58	13.2%	33	8.8%
Nasal polyps	10	2.3%	3	0.8%
ABPA	11	2.5%	12	3.2%
Asthma	3	0.7%	2	0.5%
Total card/pulm complications	*361*		*384*	
Gastrointestinal Complications				
DIOS	2	0.5%	8	2.1%
Rectal Prolapse	0	0.0%	0	0.0%
Pancreatic Insufficiency	421	96.1%	318	84.8%
Abnormal LFTs	14	3.2%	14	3.7%
Liver disease	13	3%	46	12.3%
Total gastro complications	*429*		*359*	
Miscellaneous Complications				
Diabetes requiring insulin	9	2.1%	84	22.4%
Clubbing	132	30.1%	109	29.1%
Osteopenia/osteoporosis	18	4.1%	152	40.5%
Other morbidity	33	7.5%	33	8.8%
Total misc complications	*192*		*378*	

Cultures

Data on >6,500 sputum swabs were collected in 2008. Due to improved collection rates of annual assessment data in 2008, the average number of positive cultures per PWCF has increased since 2007. In 2008, an adult PWCF had 9 sputum swabs tested on average (Table 8). When cough and sputum swabs are summed, paediatric PWCF had a similar number of swabs taken on average, compared with adults.

Table 8: Culture types, paediatric vs. adults

2008 Annual Assessment				
	Paediatric		Adult	
Sample type	**Number**	**Average number of positive cultures per paediatric PWCF**	**Number**	**Average number of positive cultures per adult PWCF**
Sputum samples	3115	6.5	3436	9.0
Cough swabs	1326	2.8	74	0.2
Throat swabs	751	1.6	17	<0.1
BAL swabs	40	0.1	23	0.1
Nasal swabs	126	0.3	8	<0.1

Focussing on organisms detected in sputum samples only, we find that *P. aeruginosa* was detected in 36.4% of cultures in 2009 (Table 9). (This statistic differs from that of 'chronic *Pseudomonas'* status in Table 7, which refers to having 3 or more *P. aeruginosa* culture isolates in a 12 month period). In order of decreasing frequency, other commonly detected organisms were *Staphylococcus aureus* (17.7%), *Candida* (15.3*%)* and *Aspergillus fumagatus (7.4%).*

Table 9: Twelve most frequently detected organisms in sputum cultures

	Number of positive sputum cultures	% of positive sputum cultures
***Pseudomonas aeruginosa* (Mucoid status not reported)**	1420	21.7%
Staphylococcus aureus	1164	17.7%
All *Candida* species	1009	15.3%
***Pseudomonas aeruginosa* (Mucoid)**	811	12.3%
Aspergillus fumagatus	485	7.4%
MRSA	364	5.5%
Haemophilius influenza	261	4.0%
***Pseudomonas aeruginosa* (Non-mucoid)**	157	2.4%
Stenotrophomonas maltophilia	154	2.3%
Gram positive cocci	99	1.5%
Gram negative bacilli	52	0.8%
Haemophilius parainfluenzae	46	0.7%
Other*	529	8.1%
Total	6551	

*Contains 26 *Burkholderia cepacia* complex positive sputum cultures; 10 *multivorans*, 13 *cenocepacia* and 3 *stabilis*.

Antibiotics

Figure 13 shows the total number of days PWCF received IV treatment by antibiotic during 2008. Tobramycin was the most frequently prescribed IV antibiotic, and ceftazidime was ranked second, falling from first position in 2007. Meropenem (third most commonly prescribed) and colistin sulphomethate (fourth) moved up the rankings in 2008. It is unclear whether these patterns reflect a change in practice, but with improved completion of annual assessment data, it will be possible to examine longitudinal trends in the future.

Figure 13: Rank of order of IV antibiotics, 2008

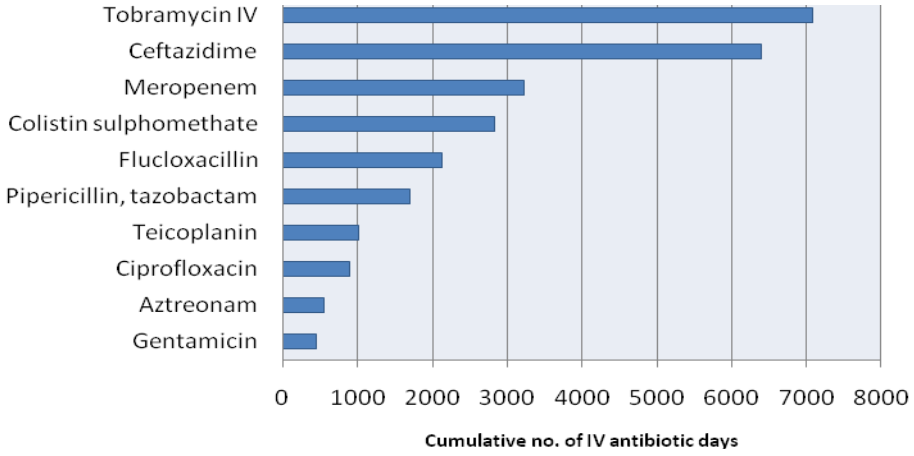
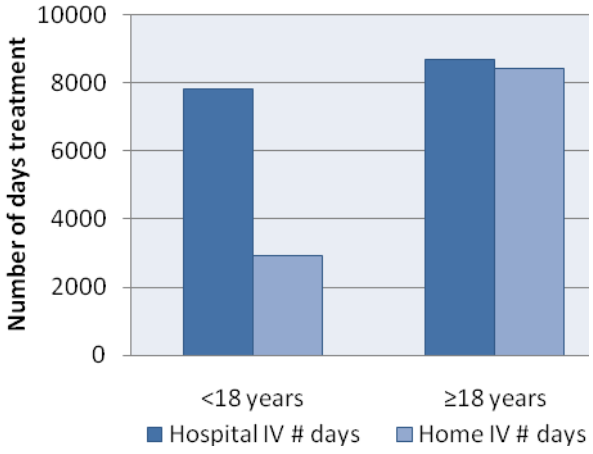


Figure 14 shows that in the paediatric population, there is a preference to hospitalise PWCF requiring antibiotic therapy. This may be due in part to facilitate training of parents in IV administration, so that subsequent treatment can be administered by the parents at home. In the adult CF population, home and hospital IV treatment were administered in equal proportion. With over 8,000 days spent in hospital on IV antibiotic treatment alone, t his highlights the importance of having appropriate in-patient facilities at adult CF services across the country.

Figure 14: Days of treatment by hospital and home IV antibiotics, adults vs. paediatrics in 2008



Pulmonary Function

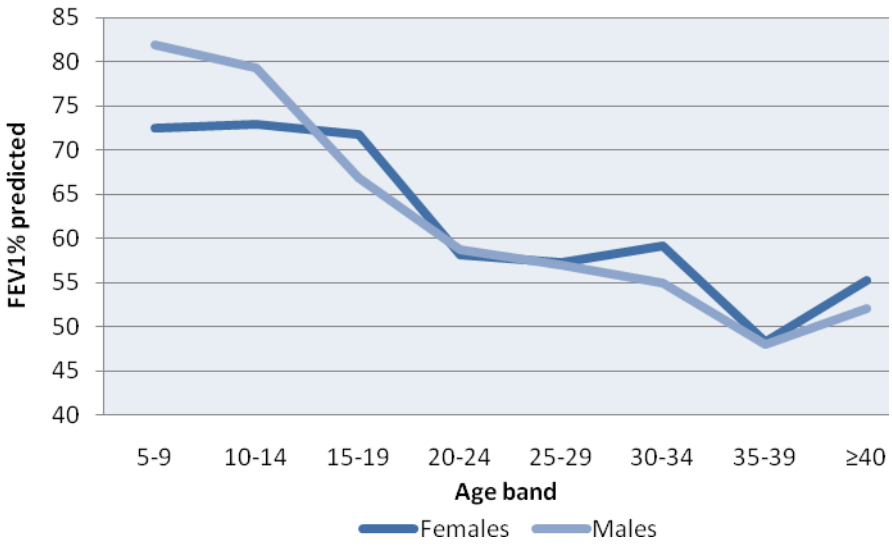
Pulmonary function data for PWCF aged five years and older is presented in table 10. Results from over 2,600 pulmonary function tests which were performed on 704 patients in 2008 were gathered (3.7 per PWCF on average). As expected, mean FEV_1 percent predicted declines across the five-year age bands. The greatest decline occurs between the 15-19 and 20-24 year age band (a decline of 10.7 FEV_1 percent predicted). This is followed by a period of relative stability across two age bands; 25-29 and 30-34 years. The overall pattern in FVC percent predicted values is similar; the greatest decline occurs between the 15-19 and 20-24 year age group and stabilises thereafter.

Table 10: Pulmonary function test summary, 2008

Age bands	Number of PFTs	Mean FEV_1 % predicted	Mean FVC % predicted
5-9	455	77.3	80.6
10-14	509	76.7	84
15-19	436	69.2	81.1
20-24	485	58.5	71.7
25-29	326	57.1	74.2
30-34	237	57.1	74.5
35-39	91	48.1	72.6
≥40	66	53.7	75.5
Total	**2605**		

FEV_1% predicted mean values are presented by age band and gender in Figure 15. The first notable trend is that males aged 5-9 and 10-14 years have much better mean FEV_1 percent predicted than females. In terms of the pattern of decline observed in both sexes, male FEV_1 percent predicted declines gradually from age 5, whereas FEV_1 percent predicted remains stable until the 15-19 age band in females and declines dramatically in the 20-24 age category. From the 20-24 age band onwards, mean FEV_1 percent predicted values in males and females converge.

Figure 15: FEV_1% predicted mean values by age band and gender, 2008



Body Mass Index

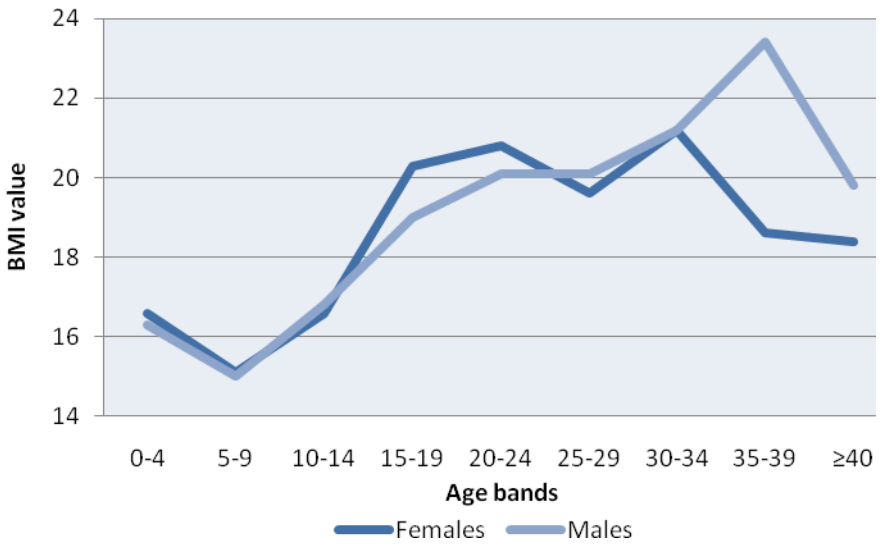
There were 2,679 BMI (body mass index) values recorded in the 2008 CFRI dataset. Table 11 shows that BMI increased gradually with increasing age, ranging from a mean BMI value of 15.1 in PWCF aged 5-9 years to a value of 21.5 in those aged 35-39 years.

Table 11: BMI summary, 2008

Age bands	N	Mean BMI
0-4	74	16.4
5-9	455	15.1
10-14	509	16.7
15-19	436	19.6
20-24	485	20.4
25-29	326	19.9
30-34	237	21.2
35-39	91	21.5
≥40	66	19.1
No of PWCF	2679	

Stratifying this analysis by gender (Figure 16), we see that females have a slightly better mean BMI in the 15-19 and 20-24 age category than males. From the 25-29 age band onwards, mean BMI is greater in male PWCF than in females, reaching 23.4 in the 35-39 age band.

Figure 16: BMI mean values by age band and gender, 2008



Nutrition

It is difficult to make comparisons between nutritional status in 2007 and 2008 CFRI datasets, because annual assessment data from 2007 were scant (89 PWCF were reported on in 2007 compared with 813 in 2008). In subsequent annual reports, we will report on year-on-year changes, which may provide some insights into changes in clinical practice over time.

The range of nutritional supplements prescribed in 2008 is shown in Table 12. The vast majority of PWCF were taking vitamins and nearly one fifth of PWCF were prescribed calorie supplements. Statistics relating to pancreatic insufficiency are reported in Table 7.

Table 12: Nutrition summary, 2008

2008 Annual Assessment				
	Paediatric		Adult	
No of PWCF	438		375	
	Number of paediatric PWCF	**% of group**	**Number of adult PWCF**	**% of group**
Calorie supplements	91	20.8%	63	16.8%
Vitamins	389	88.8%	279	74.4%
Minerals	49	11.2%	36	9.6%
Gastrostomy feeds	18	4.1%	33	8.8%
Supplemental feeding	108	24.7%	82	21.9%
Oral supplements	75	17.1%	47	12.5%
Nasogastric	5	1.1%	4	1.1%
Parenteral feeds	1	0.2%	0	0.0%
Other supplement feeds	1	0.2%	0	0.0%

Physiotherapy

As stated in previous annual reports, the absence of recorded physiotherapy data in some adult hospital medical records precludes a thorough analysis of physiotherapy data. For example, nearly three-quarters of paediatric PWCF were reviewed by a physiotherapist at an annual assessment, compared with less than half of adults. This is unlikely to reflect current practice.

The information available from hospital charts which we report on here shows that the PEP mask is the most frequently used physiotherapy modality in paediatric PWCF (28.5%), followed by acapella (21.7%) and percussion (13.5%) (Table 13). The PEP mask is also commonly used in adults (12.5%), as well as autogenic drainage (10.7%).

Table 13: Physiotherapy summary, 2008

2008 Annual Assessment				
	Paediatric		Adult	
No of PWCF	438		375	
PWCF seen by Physio at AA	319		171	
% seen by Physio	72.8%		45.6%	
	Number of paediatric PWCF	**% of group**	**Number of adult PWCF**	**% of group**
Postural drainage	27	6.2%	0	0.0%
Percussion	59	13.5%	4	1.1%
Active cycle breathing	15	3.4%	6	1.6%
Autogenic drainage	17	3.9%	40	10.7%
Flutter	19	4.3%	15	4.0%
PEP Mask	125	28.5%	47	12.5%
Acapella	95	21.7%	27	7.2%

Long-Term Medications

Beta agonists, inhaled steroids and rhDNase are the most frequently prescribed long-term medications in both in adult and paediatric CF patients (Table 14). Unlike the 2007 annual report, the ratio of beta agonist use has equalised in adult and paediatric groups, and the use of inhaled steroids and rhDNase by adults is no longer twice that of paediatric patients. As expected, there are a greater proportion of adults receiving osteoporosis treatment (42.9%) and insulin (16.8%) than paediatric patients.

Table 14: Long-term medication summary, 2008

2008 Annual Assessment				
	Paediatric		Adult	
No of PWCF	438		375	
	Number of paediatric PWCF	**% of group**	**Number of adult PWCF**	**% of group**
Beta agonist	196	44.7%	190	50.7%
Inhaled steroid	135	30.8%	177	47.2%
rhDNAse	134	30.6%	127	33.9%
H2RA/PPI	106	24.2%	123	32.8%
Other medication	68	15.5%	58	15.5%
Urso deoxycholic acid	55	12.6%	57	15.2%
Osteoporosis treatment	38	8.7%	161	42.9%
Anti-cholinergic	21	4.8%	10	2.7%
Lactulose	13	3.0%	16	4.3%
Oral steroid	12	2.7%	24	6.4%
Insulin	10	2.3%	63	16.8%
Night-time oxygen	3	0.7%	13	3.5%
Nebulised saline	9	2.1%	15	4.0%
Aminophylline/theophylline	0	-	9	2.4%
NSAID for arthropathy	0	-	1	0.30%

Financial Information

The financial summary in Table 15 lists the Income and Expenses for the CFRI in 2007 and 2008.

Table 15: Income & Expenses July 2007-December 2008

Income & Expenses	2008 €	July-Dec 2007 €
Income		
Grant income	272,000	272,000
Sundry income	1,118	
Bank deposit interest	17	
Total income	273,135	272,000
Expenses		
Wages & salary	149,049	58,408
Employer's PRSI	16,023	6,280
Rent payable	4,830	2,415
Insurance	485	0
Computer network & server costs	3,153	9,590
Database costs	12,520	0
Heat & light	662	331
Repairs & maintenance	431	0
Printing, postage and stationary	13,086	2,381
Travelling & subsistence	13,547	2,049
Audit	979	900
Bank charges	142	7
Sundry expenses	554	25
Depreciation on equipment	1,112	886
Pre entry expenses	(30,200)	116,180
Total expenses	186,373	199,452
(Deficit)/Surplus	86,762	72,548

The following points should be noted:

The 2007 accounts are reported for the period July to December 2007. This six month period accounts for the first financial period for CFRI to operate as an independent body.

The primary source of income for CFRI is the Department of Health & Children, through the Health Service Executive which was an annual grant of €272,000 in both 2007 & 2008. In 2007 funding was increased from €132,000 in 2006 as a direct result of additional funding being allocated to cystic fibrosis services in the Government's Annual Budget of 2006.

The increase in funding assisted in clearing a bank overdraft of €75,911 which had accumulated as a result of underfunding in previous years and a delayed grant payment schedule in 2007.

An outstanding loan of €30,200 from the Cystic Fibrosis Association of Ireland was written off. This loan had built up prior to 2006 and assisted in meeting annual shortfalls in working capital.

While surpluses of Income vs. Expenses were declared in 2007 and 2008, 2009 is forecast to show a deficit due to a cut back in funding to 2005 and 2006 levels of €132,000 per annum.

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 CFRI in this reporting year.

First we would like to thank the HSE for providing generous financial support to the CFRI since its inception in 2002. We would also like to thank the Health Research Board for funding a 3-year research programme (2008-2010).

Each PWCF and/or their guardian kindly agreed to share medical information with this Registry. By consenting in such large numbers, the information reported by the registry each year has become increasingly useful.

The management committee of the CFRI have provided great support during a period of growth and development within the Registry.

The Cystic Fibrosis Association of Ireland was integral in the initiation of this Registry and continues to support the work that is undertaken by the Registry.

Each CF centre and clinic provides immense assistance to CFRI staff in the collection of this important information. In particular, we thank nursing staff at each site for their continuing co-operation.

The UCD School of Public Health, Physiotherapy and Population Science has hosted the CFRI at Woodview House for five years now. Prof C Kelleher and staff have made an invaluable contribution to the CFRI research programme.

We thank Dr H Johnson and his team at the HSE Health Intelligence Unit for introducing us to HealthAtlas Ireland, and for their expert input into geospatial analysis of CFRI data.

Finally, we thank the Central Statistics Office in Cork for providing information on CF decedents, and the National Centre for Medical Genetics in Our Lady's Children's Hospital in Crumlin for providing CF genotyping information.

Publications from CFRI, 2008

Whilst research outputs from the Health Research Board-funded project (commenced March 2008) were prepared in 2008, there are inherent delays in the process of journal publication of those peer-reviewed papers. These papers will be identified in future annual reports, as will research papers presented at national and international conferences.

Delayed diagnosis of CF associated with symptomatology in a country without newborn screening.
AD Jackson, L Daly, M Harrington, S Zhou, P Fitzpatrick, C Kelleher, L Foley.
22nd North American Cystic Fibrosis Conference, Orlando, November 2008.
Pediatric Pulmonology, 43(S31), p404.

"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.

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CFRI
The Cystic Fibrosis Registry of Ireland