

Annual Report 2007



CFRI 
The Cystic Fibrosis Registry of Ireland

Glossary (commonly used abbreviations in this report)

CFRI	Cystic Fibrosis Registry of Ireland
CFAI	Cystic Fibrosis Association of Ireland
PWCF	Persons with Cystic Fibrosis
NBS	Newborn Screening (for CF)
AA	Annual Assessment

Hospital Abbreviations

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

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Executive Summary

The year, 2007, was a year of transition for the Cystic Fibrosis Registry of Ireland. It changed its governance policy and with that came changes in its structure which were affirmed in early 2008. In July, 2007 the Revenue Commissioners approved of the CF Registry of Ireland as an “unincorporated association with a constitution” and issued a Charity number to the CFRI. This confirmed the CFRI as an independent entity.

In August of 2007, the HSE granted a sum in keeping with the amount recommended by the CF Working Party that was set up as a result of the Pollack report recommendations published in 2005. This money made it possible for the CFRI to hire a third employee to help with the enrolment and registration of new PWCF. By the end of 2007 the impact of the third employee had already been established. In 2008, this permitted us to move ahead with accurate census figures and to increase the ascertainment levels on the Registry.

The additional grant sum also provided for much-needed re-structuring of the registry database. Not only is there continuous necessary maintenance of such a large database, it also needs regular technical upgrading.

Near the end of 2007, we began recruitment of a Research Fellow whose employment was made possible through a 3-year grant from the Health Research Board. The Research Fellow has the primary responsibility of completing several epidemiological studies that will, for the first time, give us reliable statistics regarding survival of PWCF in the Republic of Ireland. Once these initial studies are complete we will be able to compare survival predictions for Irish PWCF with other countries' published results.

Later in the grant period, the Research Fellow will analyse the factors that influence morbidity and mortality and compare them with those of other countries. A policy analysis is also planned, comparing PWCF in Ireland to Northern Ireland and the USA. Finally, in the third year of the grant subsidy, we will audit health service resources for PWCF in the Republic and evaluate best practices with a view to devising recommendations for service improvements. The HRB grant also covers bio statistical support from the School of Public Health and Population Sciences at UCD.

The Research Fellow will submit findings to relevant academic journals. For this reason, we will continue to publish a descriptive rather than an interpretive annual report for the CFRI. The academic references will ultimately enhance the credibility of the CFRI as well as placing Irish findings on an international footing.

Thus, during 2007 there were many changes to incorporate into the operation of the CFRI, bringing an expanded and more comprehensive registry for persons with CF.



Cystic Fibrosis Centres

County	Hospital	Consultant	Type of Centre
Cork	Cork University Hospital (CUH)	Dr. Barry Plant/Dr. Michael Henry	Adult
		Dr Muireann Ní Chróinín	Paediatric
Dublin	Beaumont Hospital	Prof NG McElvaney/ Dr Cedric Gunaratnam	Adult
	St Vincent's University Hospital	Prof. Charles Gallagher/ Dr Ed McKone	Adult
	The Children's University Hospital	Dr Dubhfeasa Slattery	Paediatric
	National Children's Hospital (AMNCH)	Dr Peter Grealley/Dr Basil Elnazir	Paediatric
	Our Lady's Children's Hospital	Dr Gerry Canny/Dr Barry Linnane	Paediatric
	Mater Misericordiae University Hospital	Dr Jim Egan	Post-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/Dr TH Peirce	Adult
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

Registry Management Committee

Professor N.G. McElvaney	Professor of Medicine, Royal College of Surgeons in Ireland. Beaumont Hospital and R.C.S.I., Dublin	Chairman of the Registry Management Committee
Mrs. Linda Foley	Director, CF Registry of Ireland	
Professor Charles Gallagher	Consultant in Respiratory Medicine, St. Vincent's University Hospital, Dublin	Committee Member
Dr. Peter Grealley	Consultant in Respiratory Medicine, National Children's Hospital in Tallaght, Dublin	Committee Member
Dr. Gerry Canny	Consultant Paediatrician, Our Lady's Children's Hospital Crumlin, Dublin	Committee Member
Dr. R Tummaluru	Consultant Paediatrician, Sligo General Hospital, Sligo	Committee Member
Ms. Gerardine Leen	CF Specialist Nurse, National Children's Hospital in Tallaght, Dublin	Committee Member
Ms. Anne Marie Lyons	CF Specialist Nurse, Beaumont Hospital, Dublin	Committee Member
Mr. Sean O'Kennedy	Chairperson, Cystic Fibrosis Association of Ireland	Committee Member
Mr Godfrey Fletcher	CEO, Cystic Fibrosis Association of Ireland	Committee Member
Mr. Martin Wickham	Representative of CFAI	Committee Member

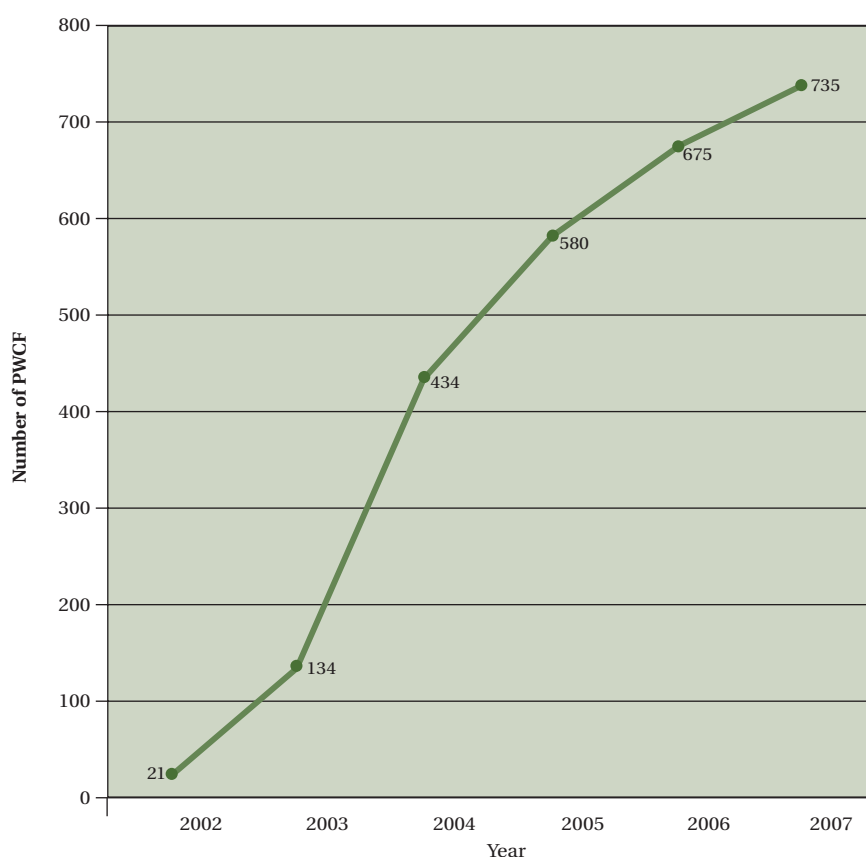
Introduction

During 2007 there were 60 additional PWCF enrolled on the CFRI, including their Registration and Diagnostic details. Of the 735 PWCF members at the end of 2007, 48% are female; 52% male; and 54% are 18 years of age or older, while 46% are less than 18 years of age. This illustrates the changing demographic pattern of the CF population in Ireland. During 2007, there were 19 PWCF enrolees who died.

The ascertainment level for the CFRI at the end of 2007 was up to 63%. As this level of 63% was still unsatisfactory, an additional Clinical Research Associate was hired in early November, 2007. Her sole responsibility was to speak directly to PWCF and parents regarding informed consent and to increase enrolment. This proved a successful strategy as over half of the total enrolment for 2007 (i.e., 35 PWCF) signed consent forms during November and December of that year.

The CRA responsible for enrolment is also the custodian of the CF census. Her task is to liaise with the CF Centres and keep track of the number of PWCF throughout the country.

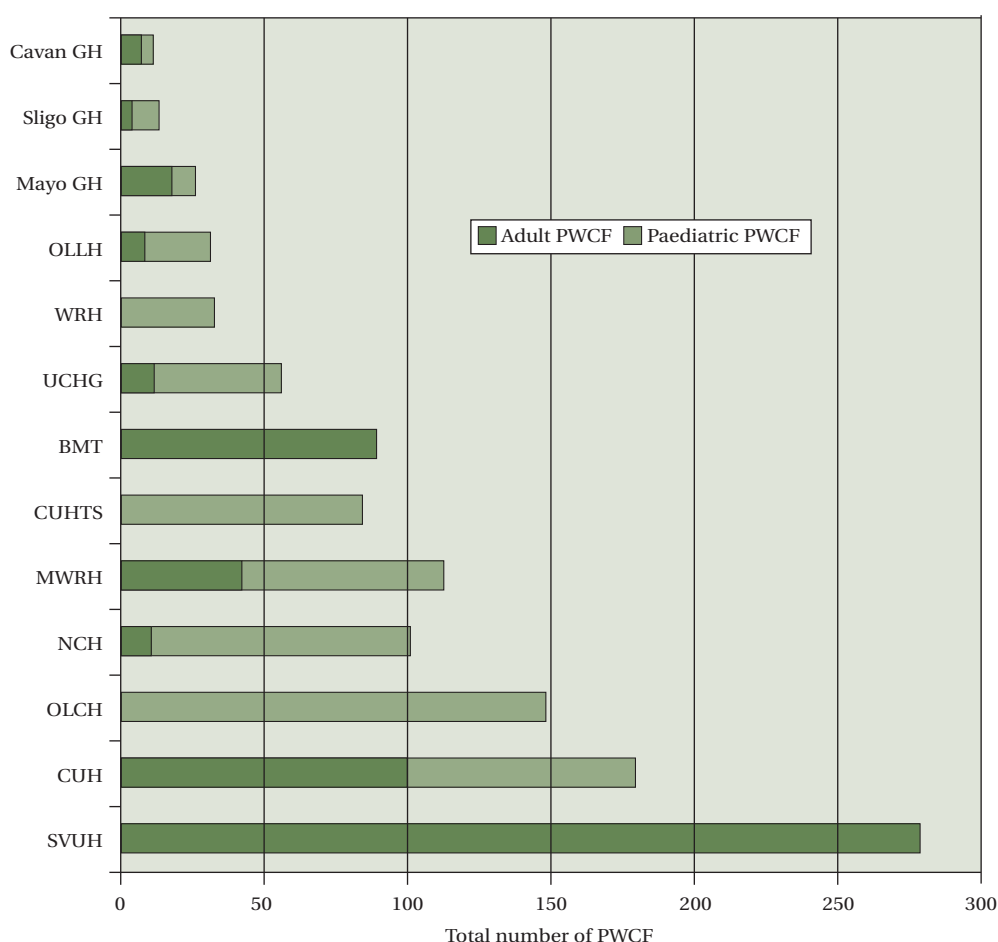
Figure 1: CFRI Enrolment 2002-2007



CF Census, 2007

During the month of October in every year since 2001, the registry has conducted a census through the CF Centres. We have tried to eliminate 'double-counting' of PWCF but this is not always possible because we do not require the submission of the names of patients. The 2007 census of 1170 (Figure 2) compares with a census of 1186 in 2006; but the difference is more likely due to a change of counting practices, rather than a reduction of CF population.

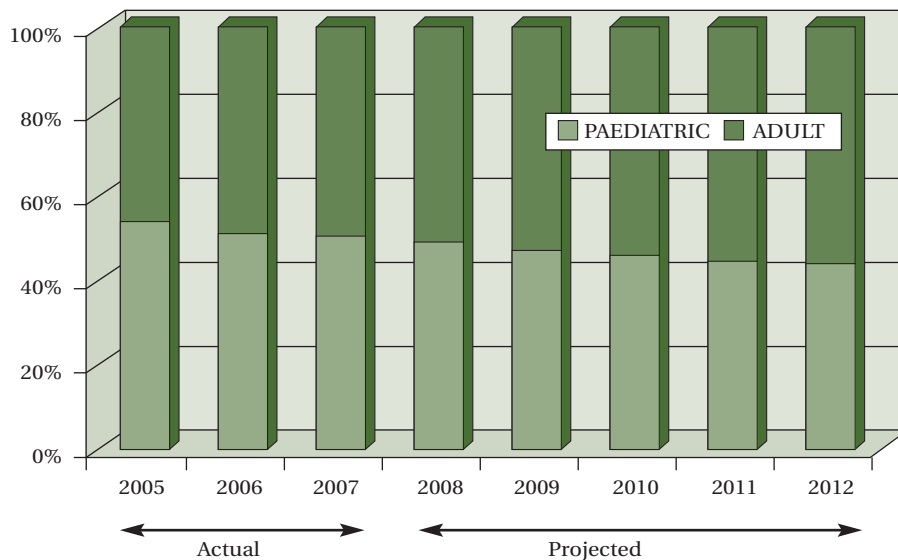
Figure 2: CF Centre Census, 2007; n=1170



Of more interest is the fact that the CF population changed in 2007 and the adult segment became more dominant (see Figure 3). This trend will continue into the future as the Adult group will grow to dominate the CF population. As long as the Irish ethnic population remains relatively static we can expect 35-40 newly diagnosed paediatric patients each year. By the same token, an equal number of PWCF would be expected to 'graduate' into the Adult group each year. Since the number of deaths in the past several years has averaged out at 19 since 1994 (and their average age at death has been above 18 since 2001), there will be a net gain in the adult group of approximately 20 PWCF per year. We can now describe the CF population in Ireland as being predominantly adult in nature. So, it is time to carefully assess adult services to ensure that they meet necessary requirements.

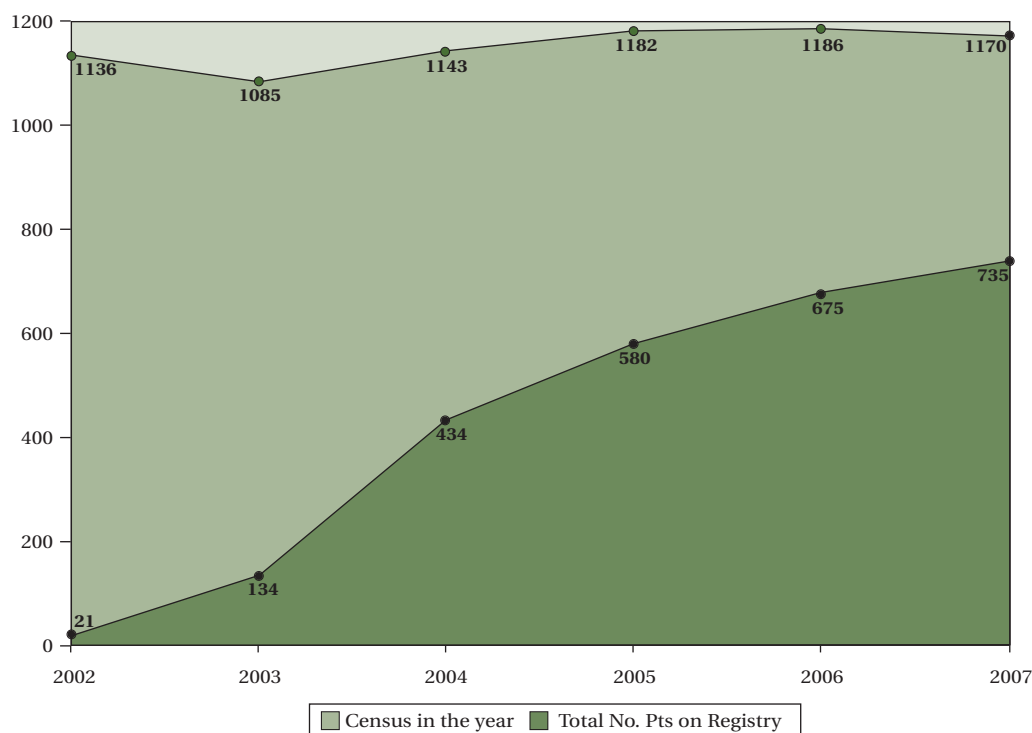
The remainder of this report describes the CF population in relation to those requirements on resources as it tabulates the number and type of complications, hospitalisations, the number of infections and the types of long-term medications, etc.

Figure 3: Projected ratio of adult to paediatric CF population to 2012



At the end of 2007 the enrolment on the CFRI had reached 735 patients. This represented an ascertainment level of 63%, based on the estimated census of 1170 (Figure 4). Although it is worthwhile to describe this population in terms of the various data parameters, the data would be far more useful if an ascertainment level of over 90% was obtainable. That is why the CFRI prioritised enrolment from late 2007.

Figure 4: Gap in CFRI enrolment and CF Centre census



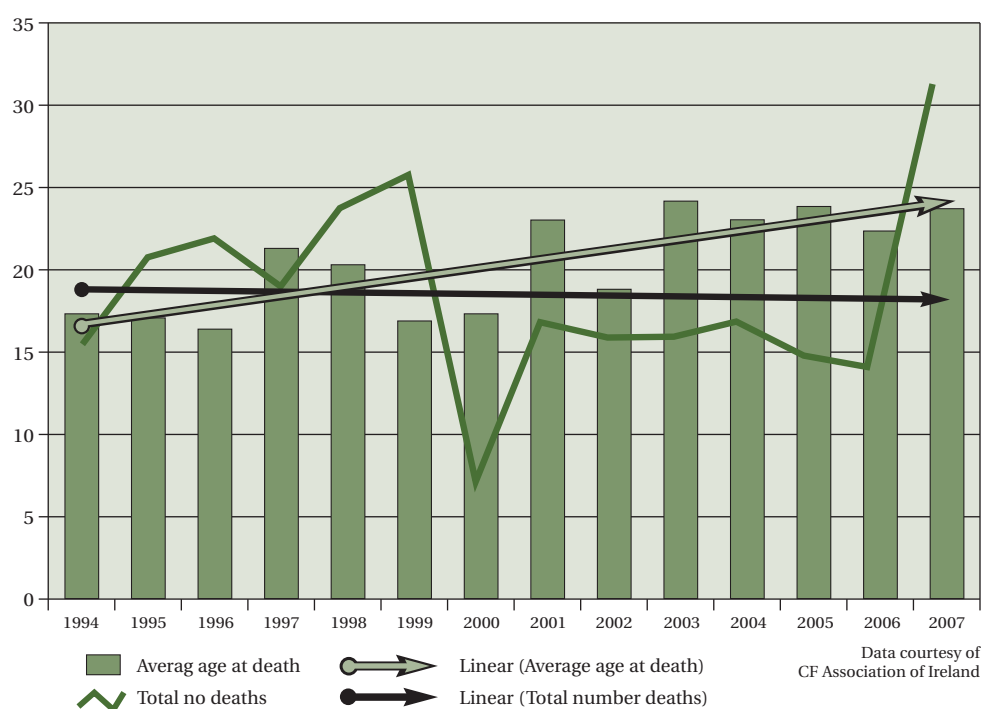
Descriptive Data from CFAI

The CF Association of Ireland (CFAI) has been keeping records of death outcomes of its members since 1986. This year we have put the total number of deaths and the average age at death over a 14-year period (1994-2007) on the same chart; and have added simple linear trend lines to the chart. Figure 5 shows that the total number of deaths has varied over the years with peaks in 1999 and 2007 and troughs in the years 2000 and 2006. The average number of deaths per year throughout the period was 19 and the range was 7-31. In other words in the year 2000, the total number of deaths recorded was 7, while the year 2007 had the highest recorded number of deaths at 31. This is a large variance. But the interesting thing is that when a trend line is added to the chart [the trend line takes into account the peaks and troughs and smoothes them out to show a general trend, or pattern over the time period] the number of deaths per year appears to be declining; or at least it has reached a plateau.

The average age at death in this period had a much smaller variance, ranging from 16 years to 24 years. The encouraging thing to note is that the trend line over this period is on an incline. In other words, the average age at death is increasing. These two observations are the subject of further study and will form the basis of the survival analysis that the CF post-doctoral Research Fellow will undertake in 2008 and beyond.

It is tempting to compare some of these figures with those from other countries. Unfortunately, such an exercise is fraught with complications and does not add to our fund of knowledge. In other words it is statistically misleading to make comparisons of national registry reports even in the same years. In order to compare countries and their CF populations, a prospective study is in order, rather than a retrospective comparison of some of the same calculations. It is important to start with the same raw data from several sources and put it into one data set and then work through the comparisons; performing full statistical analysis. Plucking similar figures from annual reports of other countries is not a rigorous method of comparison and would not stand up to scrutiny.

Figure 5: Total number of deaths and average age at death of PWCF, 1994-2007



Demographics of the CFRI

General Data

The basic parameters of the CFRI at the end of 2007 are in Table 1. The increase in enrolment over 2006 was just 60. As this left us at 63% of the estimated census, we felt that more emphasis should be placed on informed consent and registration.

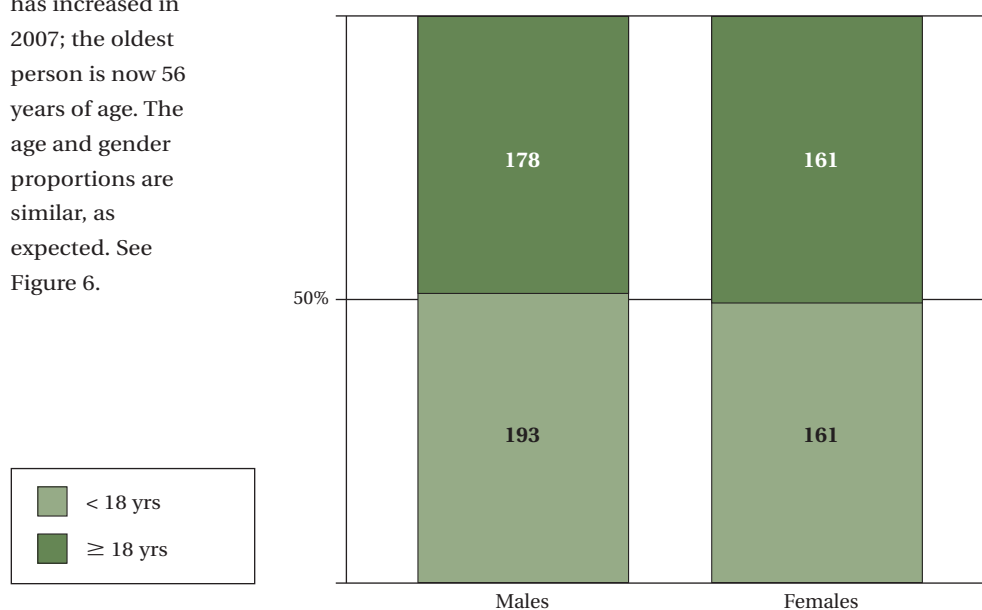
Table 1: Summary data from CFRI

General Data								
Year:	2002	2003	2004	2005	2006	2007	Total	%
PWCF Registered in the Year	21	113	300	146	95	60	735	100%
Age Range						< 1–56		
Mean Age Pts on Registry						18		
Median Age Pts on Registry						17		
Number Males						371		54%
Number Females						322		46%
Number < 18 yrs						354		51%
Number ≥ 18 yrs						339		49%
Number Males ≥ 18						178		26%
Number Females ≥ 18						161		23%
Deaths during year	0	6	5	9	5	17	42	
Total no. PWCF on Registry who are alive at end of Year							693	94%

A new CRA began in November, 2007 and was highly effective from the start. Of the 60 PWCF registered in 2007, over half of them signed consent after 1st November 2007. The strategy of devoting one member of staff to registration was deemed successful.

The age range has increased in 2007; the oldest person is now 56 years of age. The age and gender proportions are similar, as expected. See Figure 6.

Figure 6: Age and gender proportions enrolled on CFRI, 2007



If we break down the genders into age bands we see a very similar pattern to previous years.

Figure 7: Age and gender distribution by age bands

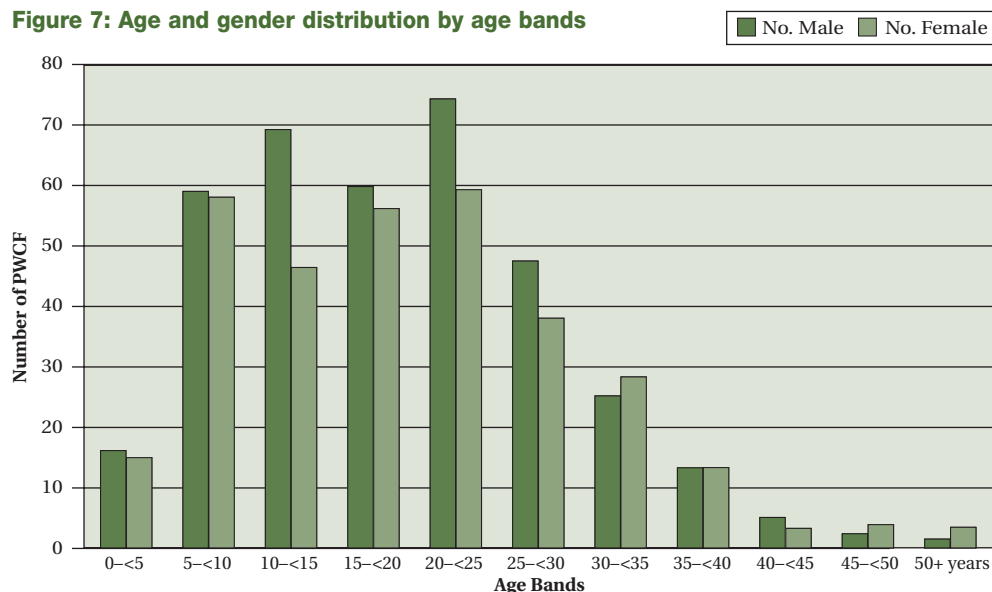


Table 2: PWCF by county of residence

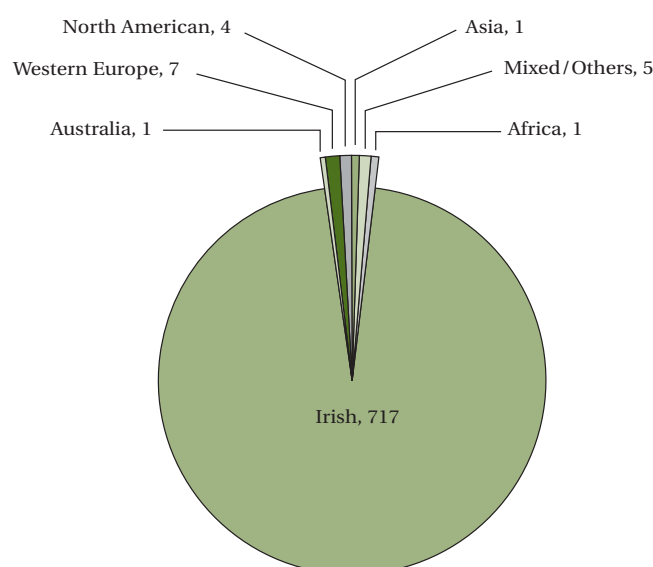
The county of residence of the PWCF (Table 2) enrolled on the CFRI reflects the general census of the country. This also reflects the need for several CF Centres to be concentrated in the Dublin area. The table can also be used to plan for CF centres outside of the Dublin area. And this distribution will become far more useful when we have the full complement of PWCF enrolled.

County of Residence		
County	No. of PWCF	Percentage
Dublin 1-24	147	21.2%
Cork	97	14.0%
County Dublin	55	7.9%
Limerick	48	6.9%
Kildare	36	5.2%
Kerry	32	4.6%
Tipperary	32	4.6%
Wicklow	30	4.3%
Clare	27	3.9%
Galway	24	3.5%
Mayo	22	3.2%
Meath	19	2.7%
Wexford	17	2.5%
Westmeath	16	2.3%
Louth	12	1.7%
Laois	9	1.3%
Sligo	9	1.3%
Kilkenny	8	1.2%
Offaly	8	1.2%
Waterford	8	1.2%
Cavan	7	1.0%
Donegal	7	1.0%
Carlow	5	0.7%
Leitrim	5	0.7%
Monaghan	5	0.7%
Roscommon	5	0.7%
Longford	3	0.4%
Total	693	100.0%

Ethnicity

The ethnicity makeup of the CFRI has not changed since we began to enrol patients and is over 97% Irish by ethnic group. Parents from England, Scotland, Germany, Netherlands, and North America are listed. There is one child of Asian parents; one of Australian parents; and one of South African parents. The criteria that we use to assign ethnic groups will be reviewed so as to harmonise with the Central Statistics Office.

Figure 8: Ethnic groups represented on CFRI



Siblings

The CFRI has 657 families represented (See Table 3). These families have an average of 2.96 children per family. The percentage of families with 2 or more CF offspring is 11%.

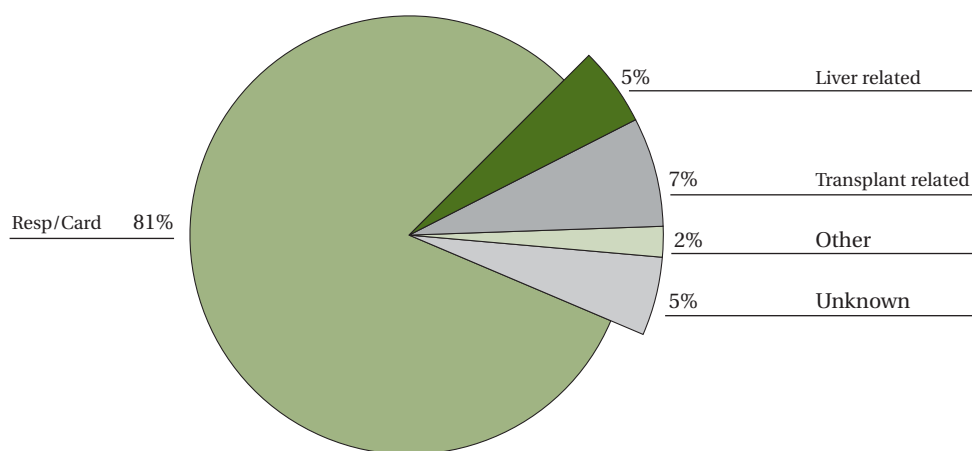
Table 3: CFRI families and siblings

Irish CF Families	
736	Total number of PWCF enrolled
657	Families Represented
11%	75 families with 2 or 3 children with CF
2.96	Average Number of children per family (with and without CF)
1.12	Average number of children with CF per family
71	Number of families with 2 siblings with CF (includes 3 sets of twins)
4	Number of families with 3 siblings with CF

Reported Deaths on CFRI

Since the CFRI began recording information, we have registered 42 deaths on the system. The vast majority, over 80%, are due to cardiac/respiratory causes which is expected due to the nature of the condition (See Figure 9). There are a small number of deaths due to transplant related problems and liver disease. During 2007 there were 2 deaths that did not report the cause and one death of unknown cause. We hope to determine these missing data and will amend the database when full information has been verified.

Figure 9: Cause of death summary, 2002-07; n=42



Diagnosis

Ireland has not yet instituted newborn screening (NBS) for cystic fibrosis. This means that nearly all patients are diagnosed due to symptom presentation. The exception to this is in families where a person already has a CF diagnosis. In those cases, all successive children are tested at birth.

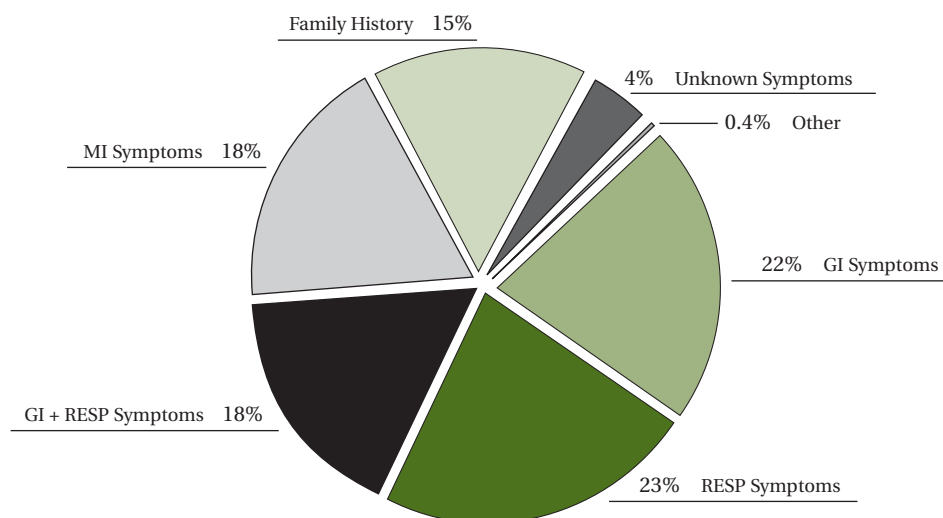
When a person is registered with the CFRI we try to obtain information about their symptoms prior to their diagnosis. Once the diagnosis is confirmed, we record the confirmatory tests that were conducted. Generally, we are finding consistent patterns of symptoms that bring the person to the attention of a doctor. These patterns are ear-marked for future analysis.

We divide the symptoms into five general categories: gastrointestinal symptoms (GI); respiratory symptoms (RESP); a combination of both gastrointestinal and respiratory (GI + RESP); a meconium ileus condition (MI); or Family History (FAM HIST). Figure 10 shows the relative proportions of symptom type among the PWCF in Ireland.

Meconium ileus is generally noted soon after birth and often, but not always requires surgery. So, it would be expected that the PWCF in the MI category would have an early date of diagnosis; and this is confirmed by measuring the median age at diagnosis on the CFRI (See Figure 11). For the MI category, the median age at diagnosis is 0.5 months. In a similar fashion, if a child is diagnosed because an older sibling has CF, then they are noted as FAM HIST; and these infants also tend to have an early date of diagnosis.

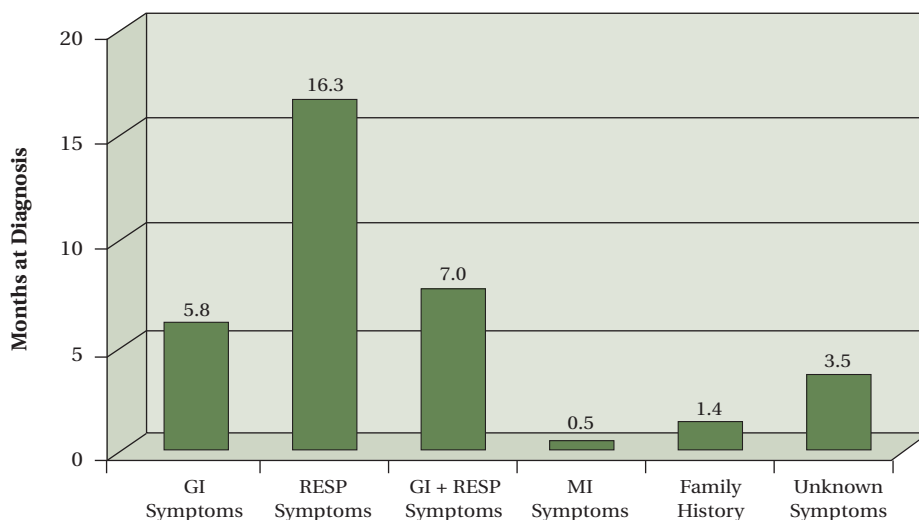
An early date of diagnosis is important so that the person can be followed at a CF Centre. The CF Centre will ensure that recommended treatments are instituted as early as possible and the child will not miss out on early growth. It is a worldwide recommendation that PWCF are followed in a specialist centre; and this is the reason that newborn screening is in place in many countries.

Figure 10: Primary symptoms at diagnosis, n=735



For the 735 PWCF who are enrolled on the CFRI, the breakdown of categories of the primary symptom is interesting (Figure 10). There are very similar numbers of persons who have GI, RESP, GI + RESP, MI, and FAM HIST as their primary symptom. When we look at the 'date of diagnosis' for the different categories (Figure 11) we see an interesting pattern emerging. For the MI, FAM HIST, GI, and GI + RESP categories; half of those PWCF are diagnosed in less than seven months. But, if we look at the RESP-only group, half of those present for investigation after 16 months of age. This "late diagnosis" can have deleterious effects on their development and on the course of their CF. We are currently examining this data to see if there are other important differences in the diagnostic groups; such as gender differences or genotype differences. This will be reported in the medical literature in subsequent years.

Figure 11: Median age at diagnosis in months, by symptom category, n=735



Genotype

During 2007 we made some improvements to the database; one of those included the ability to add additional mutations to the drop-down list on the CFRI. This means that when the National Centre for Medical Genetics (Ireland) adds a new mutation to the standard list, we can attribute all PWCF with that mutation immediately. We now have over 50 mutations represented in Ireland and we have genotype information on over 97% of enrolees. [This compares with the most recent UK annual report of 95% of their CF population characterised, and the Australian 2004 report of 75% characterised; and the 2006 report of the US Foundation, showing a figure of 85.6% genotyped.]

The seven most frequently occurring alleles reported in the Irish CF population are: $\Delta F508$, G551D, R117H, R560 T/K, G542X, 1717-1 G→A, and 621+1 G→T. Sixty-four percent of the Irish CF population is homozygous for $\Delta F508$; while 94% of the Irish CF population carries the $\Delta F508$ mutation on at least one chromosome. The mutation, G551D, is the second most frequently occurring mutation and 87 PWCF (12%) carry that on at least one chromosome; while five people are homozygous for G551D. Finally, R117H, the third most frequently occurring mutation in the Irish CF population, appears in 4% of PWCF; all of whom are heterozygous.

There are still a number of people who require further testing. These samples are sent abroad, either to England or France. Referring to Table 4, there is one person whose genotype for both alleles is under further testing (called “Result pending”); and there are 39 PWCF for whom we know at least one allele; while the other allele is listed as “Result pending”. Once those alleles have become characterised, we will add any new mutations to the list.

This data will be analysed together with the symptom data to show possible differences in phenotype as part of the on-going HRB sponsored research.

Table 4: Frequency of CF mutations on CFRI

2007 LIST	← Allele 1 →														
Allele 2 ↓	Result Pending	DeltaF508	G551D	R117H	1717-1 G->A	1154insTC	1471delA	1525-1 G->A	3007delG	3272-26A->G	621+1, G->T	Delta1507	P547H	R560 T/K	TOTAL
Result Pending	1	26	5	4	1				1	1	1				40
DeltaF508		458													458
1154insTC						1									1
1461ins4		2													2
1471delA							2								2
1525-1 G->A								1							1
1717-1 G->A		11													11
1898+1 G->A		2													2
2184delA		6													6
2622+1G->A		1		1											2
2623-2A->G													1		1
2798+2 insA		1													1
3007delG		1													1
3120 G->A		1													1
3272-26A->G		3													3
3659delC		1	1												2
3849+10KbC->T		3													3
3849+4G->A				1											1
4279insA		1													1
621+1, G->T		10													10
A209s		1													1
Delta1507		6													6
E60X		3													3
G542X		11	2												13
G551D		68	5		1										74
G85E		1													1
L1335P		1													1
M1105R		1													1
N1303K		3													3
P67L			1												1
Q493X		1													1
R1162x		1													1
R117H		21	2		2							1			26
R352Q		2													2
R553X			1												1
R560 T/K		17	2	1							1			1	22
R851X		1													1
V520F		4													4
Y563N		2													2
Total	1	671	19	7	4	1	2	1	1	1	2	1	1	1	713

Hospitalisations and Complications

The rate of hospitalisation of adults in 2007 is higher than for the paediatric population (Table 5). This is in agreement with other studies and previous annual reports.

Table 5: Hospitalisations, exacerbations and complications, paediatric vs adult groups

2007 Annual Assessments					
Age	< 18		≥ 18		Ratio of Episode rate Adult to Paed
Total No. in group	81		62		
Ave age of group in yrs	8		27		
	No.	Per PWCF	No.	Per PWCF	
Hospitalisations	18	0.22	20	0.32	1.45
Respiratory Exacerbations	23	0.28	41	0.66	2.33
Other Exacerbations	77	0.95	69	1.11	1.17
Complications	149	1.84	172	1.15	0.63

The rate of respiratory exacerbations is over twice as common in the Adult PWCF group and the rate of complications in general is more than 1.5 times the rate in the paediatric group. These are an indication that the CF condition tends to grow more serious as PWCF grow older.

If we breakdown the complications, and look at the rates in terms of the different body systems, this is shown in Table 6. Again, the picture is more serious in the Adult group and overall, there is a rate of 1.84 complications per paediatric PWCF; versus 2.73 complications in the Adult group.

Pseudomonas infection increases from 20% of patients affected in the paediatric group to 56% in the Adults; while *Staphylococcus* remains at a similar level in both age-groups.

Table 6 shows that pancreatic insufficiency has decreased in the Adult group, but this difference is more than likely due to errors of transcription rather than a difference between age groups. Once a person is described as pancreatic insufficient, that should be a 'default' complication for that person from then onwards. Also, it is from birth, so the paediatric rate is probably more accurate. This is a system fault that will be changed.

There are two conditions that do appear with greater frequency in the older age groups: diabetes and osteopenia/osteoporosis. The CFRI bears this out, showing a rate of 19% of the Adult group (versus 1% of paediatric group) reporting diabetes and 26% of the Adults reporting osteopenia/osteoporosis (versus 2% of paediatric group).

These differences between age groups are very similar to those reported in previous years when fewer patients were enrolled.

Table 6: Complication rates by system; paediatric vs. adult groups

2007 Annual Assessments				
	< 18		≥ 18	
Total # in group	81		62	
Ave age of group in yrs	8		27	
Complication	#	% of group	#	% of group
Had No Complications	1	1%	0	0%
Card/Pulmonary Complications				
Chronic Pseudomonas	16	20%	35	56%
Chronic Staphylococcus	23	28%	17	27%
Burkholderia	0	0%	1	2%
MRSA	5	6%	2	3%
Nasal Polyps	1	1%	0	0%
ABPA	0	0%	2	3%
Asthma	3	4%	1	2%
Total Cardio/Pulm	49		58	
GI Complications				
DIOS	3	4%	3	5%
Rectal Prolapse	1	1%	0	0%
Pancreatic Insufficiency	71	88%	50	81%
Abnormal LFTs	4	5%	4	6%
Liver Disease Other Than Cirrhosis	1	1%	5	8%
Cirrhosis With Portal Hypertension	1	1%	1	2%
Total GI	81		63	
Miscellaneous Complications				
Diabetes Requiring Insulin	1	1%	12	19%
Clubbing	16	20%	20	32%
Osteopenia / Osteoporosis	2	2%	16	26%
Other Morbidity	0	0%	0	0%
Total Miscellaneous	19		48	

Cultures

Both the type of culture sample as well as the type of microbiological specimen are recorded in the CFRI. In 2007, the rate (or the number of samples per person) of sputum samples recorded by the Paediatric group was 3.5 per person, while the rate in the Adult group was 4.3 per person. The number and rate for cough swabs was higher in the Paediatric group which reflects current practice. The number and rate of BAL (bronchoalveolar lavage: taken during bronchoscopy) samples is only slightly higher in the Adult group. But this rate is likely to increase in both age groups as the bronchoscopy rate increases.

The twelve most frequently occurring samples are listed in Table 8. All the *Pseudomonas aeruginosa* specimens are listed at the top of the table and the percentage of the total sputum samples are given in the right column. The proportion of *P. aeruginosa* of the total number of sputum samples is 35%.

Table 7: Culture types, paediatric vs adult

2007 Annual Assessments				
	< 18		≥ 18	
Total # in group	81		62	
Ave age of group in yrs	8		27	
Sample Type	#	Rate	#	Rate
Sputum samples	284	3.5	269	4.3
Cough swabs	357	4.4	1	0.02
Throat swabs	0		0	
BAL samples	0		2	0.03
Nasal swabs	11	0.1	0	

Table 8: Twelve most frequent positive cultures

Total Twelve Most Frequently Occurring Positive Sputum Cultures, 2007			
Culture	Name	Number cultures	% of total sputums
1	<i>Pseudomonas aeruginosa</i> (Mucoid status not reported)	265	20%
2	<i>Pseudomonas aeruginosa</i> (Mucoid)	119	9%
3	<i>Pseudomonas aeruginosa</i> (Non-mucoid)	73	6%
4	<i>Staphylococcus aureus</i>	281	22%
5	<i>Haemophilus influenza</i>	91	7%
6	All <i>Candida</i>	185	14%
7	MRSA	88	7%
8	<i>Aspergillus fumigatus</i>	62	5%
9	<i>Stenotrophomonas maltophilia</i>	34	3%
10	<i>Streptococcus pneumoniae</i>	14	1%
11	<i>Moraxella catarrhalis</i>	9	1%
12	Beta haemolytic streptococcus Group B	8	1%
	OTHER*	70	5%
	Total	1299	100%

* Includes 4 *B cepacia* complex positive sputums: 3 of *Multivorans*, 1 of *Cenocepacia*.
There were also 3 of '*Burkholderia* not specified'

Antibiotics

Most Frequently Prescribed IV Antibiotics

The nine most frequently prescribed IV antibiotics are shown in Figure 12. This figure shows the antibiotics that have been prescribed for at least 100 days, taken from 143 annual assessments.

The rank order of antibiotics has changed somewhat since the previous report. Ceftazidime and Tobramycin IV are still in the first and second positions; flucloxacillin has moved to third position (from position 7 in 2006) and piperacillin is in fourth position as it was in 2006. The two new antibiotics on this list are teicoplanin and cefuroxime. Colistin sulphomethate has moved from seventh position to fifth; while gentamicin has moved from third position to eighth position. Finally, ciprofloxacin was in eighth position in 2006 but has moved to tenth position (not shown) in 2007. These variations may or may not reflect a change in practice due to a change in sensitivities of the microbiological specimens; but, it is worth investigating over time. It is possible to map the changes using data from the CFRI, in order to correlate with clinical practice.

Figure 12: Rank order of IV antibiotics, 2007

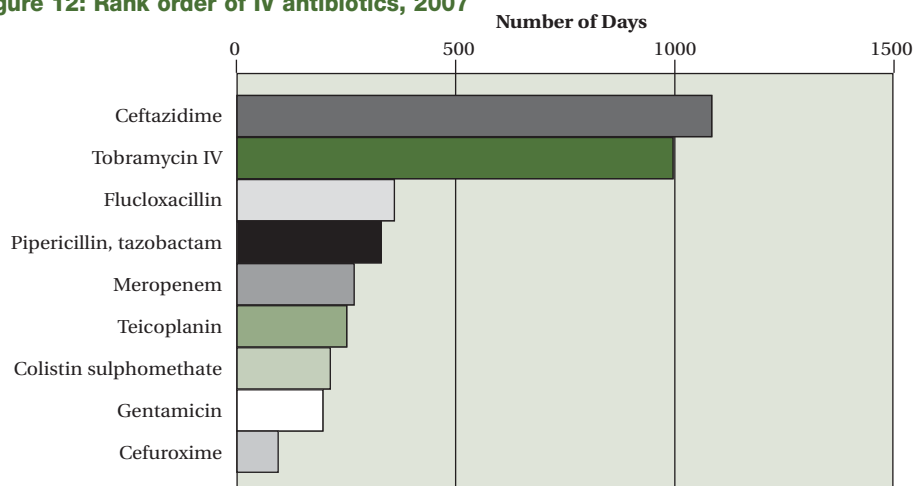
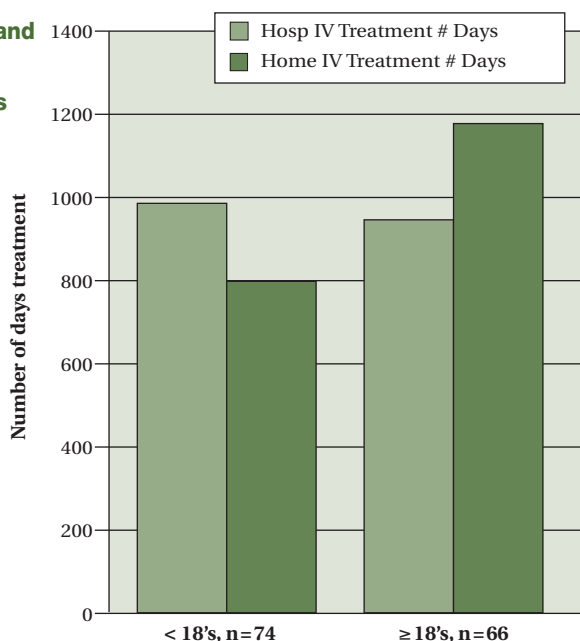


Figure 13: Hospital and Home IV antibiotics, adults vs paediatrics

When we compared similar numbers of adult and paediatric PWCF we found that total IV days were slightly higher in the adult group (2,132 days vs 1,796 days). The differences in the two groups was in the place of administration; home IV is more favoured by the adult group.



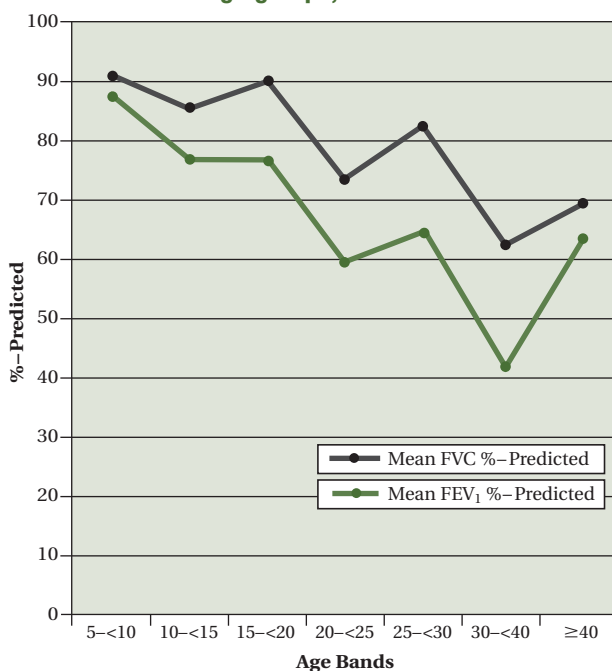
Pulmonary Function and BMI

Due to the small numbers of 2007 Annual Assessments available we have combined the gender data and have charted the age groups only, for pulmonary function and BMI.

**Table 9: Pulmonary function test summary, 2007
(both genders combined)**

Age Bands	N	Mean FEV ₁ %-Predicted	Mean FVC %-Predicted
5 – <10	39	88	91.7
10 – <15	35	77	85.9
15 – <20	24	77	90.6
20 – <25	27	60	73.8
25 – <30	12	65	82.9
30 – <40	14	42	62.9
≥40	3	64	69.7
Total in data set	154		

**Figure 14: Pulmonary function test averages
within age groups, 2007**



The mean FVC-% predicted and the mean FEV₁-% predicted both show a gentle decline (Figure 14) over the age groups until the 30-40 year age group. Then, in the over 40 year age group, there is an improvement in these two parameters.

PFT and BMI explained

Pulmonary function and height/weight (from which you can calculate Body Mass Index, or BMI) are generally measured at the same time. Many studies have shown that pulmonary function and body mass index are positively associated.

The pulmonary function tests recorded are 'Forced Expiratory Volume in 1 second' and 'Forced Vital Capacity'. Both of these tests are an indication of the condition of lung functioning. These results are usually compared with other people in the same age group who are of the same sex, weight, and height. These values are then calculated as a "percent of the predicted" result for the normal population of that same age, sex, height, and weight. If a value is over 80% (for either FVC-% predicted or FEV₁-% predicted) this is considered within the normal range. [Pulmonary function tests are not normally carried out in children under 4/5 years old.]

The BMI, or Body Mass Index is an indication of the relationship between height and weight of a person. The height and weight are generally taken every time pulmonary function tests are performed, so the BMI can be calculated alongside the PFT's. BMI is an important figure to track over time, as it will give an indication of nutritional status and growth.

In our data, we have taken an average of all of the people within an age group (band).

This could be an artefact of the data, but if we look at the genotype of the three PWCF in this group, out of the three genotypes; one is not recorded; one is G551D/unknown; and one is Δ F508/R117H. This is not a typical group from the CFRI; two were not diagnosed until they were over 20 years of age; suggesting a milder course and genotype/phenotype; and consequently better pulmonary function. So, it is possible that the over-40 year age group will always have a higher proportion of those with a milder phenotype; and consequently will have better lung function than younger age groups. This is something that we will continue to monitor.

There are some interesting patterns that should be examined as we move through the age groups (Figure 14). There is a slight decline in the youngest age group (5– \leq 10 years); followed by a plateau (10– \leq 15); followed by a decline in the 20– \leq 25 group and another decline in the 30– \leq 40. So, we must pose the questions, “are there key times in a PWCF’s life when there is likely to be faster deterioration in pulmonary function, than during other times?” “If so, are these declines related to life style?” Finally, “Are there similar patterns of decline in BMI?”

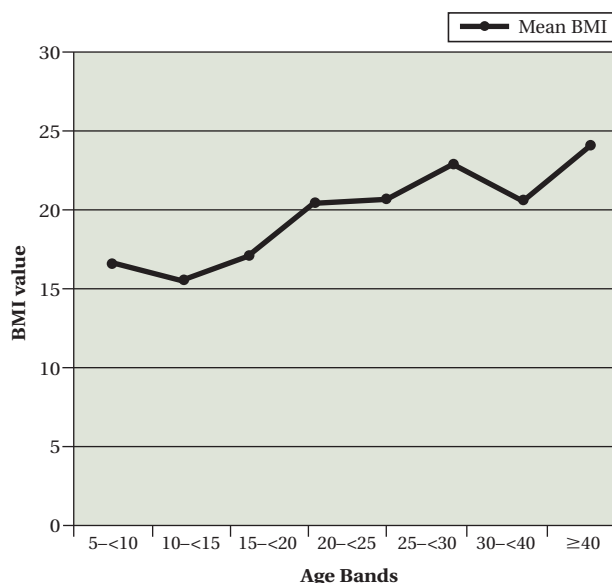
Table 10: BMI Summary, 2007 Both genders combined

Age Bands	N	Mean BMI
0 – <5	6	16.6
5 – <10	39	15.7
10 – <15	36	17.2
15 – <20	24	20.4
20 – <25	25	20.7
25 – <30	11	23
30 – <40	14	20.6
\geq 40	3	24.1
Total in data set	158	

This is worth further investigation as this pattern is similar to that reported in previous years.

By comparison, the BMI displays a slightly different pattern. This data indicates that BMI increases steadily with age. The highest mean BMI recorded is in the over-40 age group. Again, these three have different genotypes and may have milder phenotypes. If they have a milder condition, it is likely that they will have a higher BMI than some of the other groups where Δ F508 predominates.

Figure 15: BMI comparison over age groups; both genders combined



Nutrition

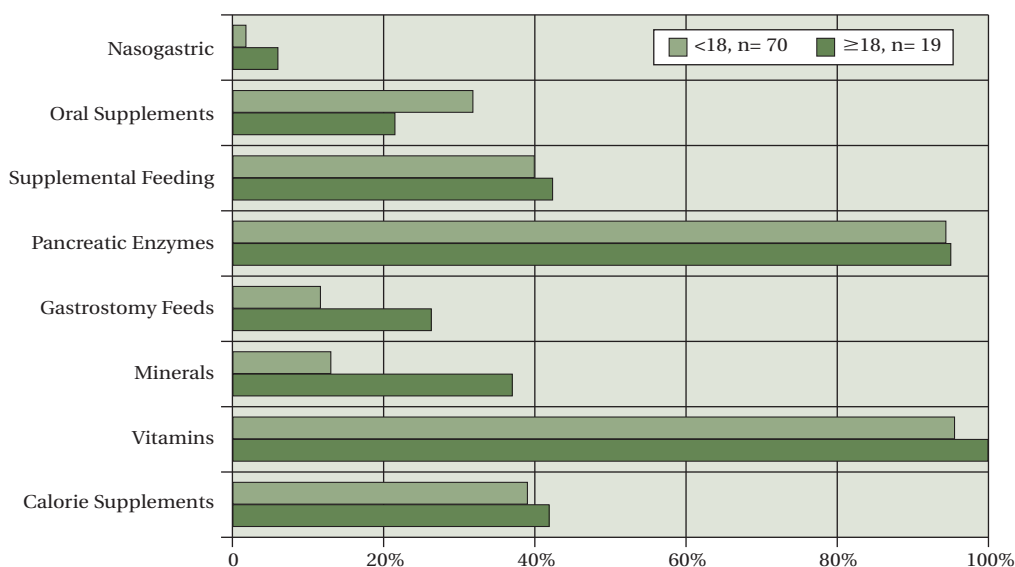
The 2007 data shows very little variance from the 2006/05 data. Both age groups show that over 90% of PWCF take pancreatic enzymes. There is now only one branded enzyme that is prescribed. The adult group shows increases in gastrostomy feeds and mineral intake over previous years.

And, there is a slight increase in the number of patients taking oral supplements now, the larger increase being in the paediatric group. Otherwise, this set of charts displays the information as we would expect it.

Table 11: Nutrition summary, 2007

2007 Annual Assessments				
	< 18		≥ 18	
Total # in group	70		19	
Ave age of group in yrs	8		26	
Type	#	% of group	#	% of group
Calorie Supplements	27	39%	8	42%
Vitamins	67	96%	19	100%
Minerals	9	13%	7	37%
Gastrostomy Feeds	8	11%	5	26%
Pancreatic Enzymes	66	94%	18	95%
Supplemental Feeding	28	40%	8	42%
Oral Supplements	22	31%	4	21%
Nasogastric	1	1%	1	5%
Parenteral Feeds	0		0	
Other Supplement Feeds	0		0	

Figure 16: Nutrition summary, 2007



Physiotherapy

It is not always clear from the main hospital chart whether a PWCF has been seen by the physiotherapist on their Annual Assessment visit. These data are taken from that chart rather than other information which may be located in the physiotherapy department. This data shows that approximately 60% of PWCF from both age groups are seen by a physiotherapist in the year. This is unlikely and probably does not reflect actual practice.

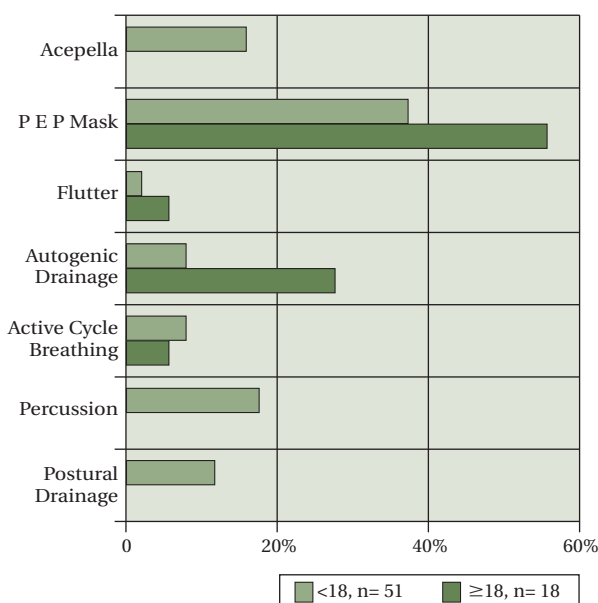
The percentages of each group that are recorded under the various modalities take this into account. Instead of using the whole group as a denominator (85 for paediatric group; and 28 for adult group) we have calculated the percentages from the number who are reported as being seen by the physiotherapist at their annual visit. Using the data we have, it shows that 22% of the paediatric group and 33% of the adult group practice two different types of physiotherapy per day.

Table 12: Physiotherapy summary, 2007

2007 Annual Assessments				
	< 18	% seen by phys	≥ 18	% seen by phys
Total # in group	85		28	
Total Seen by Physio at AA	51	60%	18	64%
Ave age of group in yrs	8		26	
Type	#	% of group	#	% of group
Postural Drainage	6	12%	0	
Percussion	9	18%	0	
Active Cycle Breathing	4	8%	1	6%
Autogenic Drainage	4	8%	5	28%
Flutter	1	2%	1	6%
PEP Mask	19	37%	10	56%
Acapella	8	16%	0	
Regular Exercise	81	95%	27	96%

There are a few changes in practice that might reflect the usefulness of various forms of physiotherapy since 2006. The 'acapella' technique is used exclusively by the paediatric group and the percentage has not changed since the last report. The use of the PEP mask has increased in both groups, and this is especially noticeable in the adult group. The use of autogenic drainage is also up in both groups; as is postural drainage in the paediatric group. The adult group does not have any record of practicing postural drainage. The techniques that show a reduction in use since 2006 are the flutter technique, percussion and the active cycle of breathing. We will attempt to obtain more detailed physiotherapy information in future years.

Figure 17: Physiotherapy summary, 2007



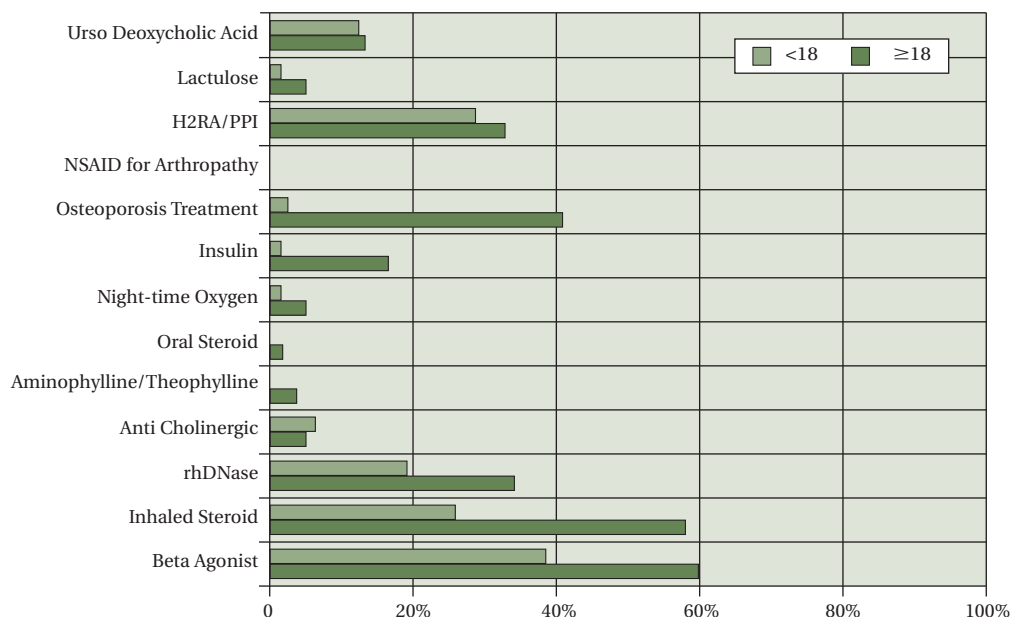
Long term Medications

As in previous years and as is expected, beta agonists, inhaled steroids, rhDNase, and H2Ra/PPI's are taken by the largest proportions of each group (Table 13 and Figure 18). The ratio of Adult consumption of the beta agonists, inhaled steroids, and rhDNase is twice that of the paediatric group. More notable differences arise between the age groups when comparing the relationship between insulin and osteoporosis medication usage. Here the ratio of adult consumption is 13 times that of paediatric consumption for insulin and 16 times that of paediatric consumption for osteoporosis products. Differences are also apparent in those taking night-time oxygen; the adults taking it more frequently than those under 18 years of age. But there is still a very low percentage in both groups. About one third of both age groups take a similar amount of H2-receptor antagonists/ proton pump inhibitors. These patterns have not changed and reflect the increase of complications in the adult group, such as the development of diabetes and osteopenia/osteoporosis.

Table 13: Long-term medication summary, 2007

2007 Annual Assessments					
Age	<18		≥ 18		Ratio Adult percentage to Paed percentage
Total No. in group	81		62		
Ave age of group in yrs	8		27		
Type	No.	% of group	No.	% of group	
Beta Agonist	31	38%	37	60%	2
Inhaled Steroid	21	26%	36	58%	2
rhDNase	15	19%	21	34%	2
Anti Cholinergic	5	6%	3	5%	1
Aminophylline /Theophylline	0	0%	2	3%	
Oral Steroid	0	0%	1	2%	
Night-time Oxygen	1	1%	3	5%	4
Insulin	1	1%	10	16%	13
Osteoporosis Treatment	2	2%	25	40%	16
NSAID for Arthropathy	0	0%	0	0%	
H2RA/PPI	23	28%	20	32%	1
Lactulose	1	1%	3	5%	4
Urso Deoxycholic Acid	10	12%	8	13%	1
Other Medication	0	0%	0	0%	

Figure 18: Long-term medication summary, 2007



Social Data

The gathering of social data is very difficult. There are no 'social templates' in the hospital chart, and very little social information is found in clinical notes. The data for 2007 was not viable enough to reproduce here. For many patients there was data from earlier annual assessments, but social questions were not completed for the 2007 annual assessment.

This will be a section that will receive further attention in coming years. We might create a questionnaire for PWCF to fill-in while they wait for their appointment; alternatively we could conduct interviews with those attending the clinic. We may also take the opportunity to ask for social worker input. All of these techniques may result in creating a sampling template rather than blanket coverage, but we would hope to present the data in the most representative way possible



Financial

The financial summary (Table 14) lists the expenses for the CFRI in 2006.

The following points should be noted:

- The only source of income for the CFRI is the Department of Health & Children, through the Health Service Executive which has been an annual grant of €132,000 beginning in 2003.
- The salary summary includes employees' salaries and employer's PAYE and PRSI.
- There is a deficit which increases each year because the present grant level is insufficient to cover the essential expenses of the CFRI. It is hoped that this will be increased in future years to sustain the CFRI.

The accounts were audited by Farrell Grant Sparks, Chartered Accountants, Molyneux House, Bride Street, Dublin 8.

Table 14: Financial Summary 2006

Financial Summary 2006	
	€
INCOME (Grant)	132,000
SYSTEM SPECIFICATION	
Hosting Fee, Domain maintenance, Security Certificate	4,138
DEVELOPMENT COSTS	
Database Application, programming	22,264
CONSULTANT'S FEES	3,267
TRAVELLING EXPENSES	6,487
ADMINISTRATION COSTS	
printing, office supplies, insurance, subscriptions, work permit	3,813
ANNUAL REPORT	
Design, printing	7,279
DEPRECIATION	681
WAGES and SALARIES	
PAYE, PRSI, Employers PRSI	105,045
TOTAL COSTS	152,974
DEFICIT	– 20,974

Acknowledgements

The Health Service Executive has very generously supported the CFRI from its inception. As we move toward full ascertainment levels the registry will be able to contribute reports and data that can influence decision-making regarding CF within the health services.

The Registry Management Committee has always supported and contributed excellent ideas for the management and structure of the registry and this is acknowledged here.

The Cystic Fibrosis Association of Ireland which was the impetus for the start of the registry continues to encourage the registry.

The CF Nurse specialists, CF physiotherapists, CF dieticians and all the other associated healthcare worker groups who participate in CF care are always keen to contribute their ideas for a more useful and informative registry.

The School of Public Health and Population Science at UCD has provided many academic and management resources to the registry and this is much appreciated. A registry of this type should be located within an academic environment and it is particularly appropriate that it have an epidemiological base.

As in previous years, this annual report is dedicated to those people who have cystic fibrosis and hopes that their voices are heard through this medium.

Publications from CFRI, 2007

Farrell P, Joffe S, Foley L, Canny GJ, Mayne P, Rosenberg M. Diagnosis of cystic fibrosis in the Republic of Ireland: epidemiology and costs. *Ir Med J.* 2007 Sep;100(8):557-60.



The Cystic Fibrosis Registry of Ireland

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

Mission Statement of the CFRI

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

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

Cystic Fibrosis Registry of Ireland

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University College Dublin

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www.cfri.ie

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Charity Number: CHY17566