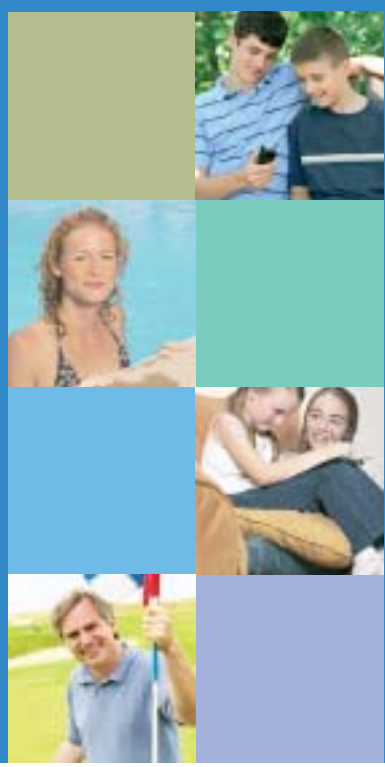
The Cystic Fibrosis Registry of Ireland

Annual Report 2005



"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 Cystic Fibrosis Registry of Ireland

Contents

Executive Summary 2

List of Tables 3

Glossary 3

List of Figures 4

Cystic Fibrosis Centres 5

Registry Management Committee 5

Introduction 6

Demographics: 8

- CF Census by Centre 8
- Consents to CFRI 9
- CF Population Projections 10
- CF Census and CFRI Enrolment Comparison 11

General Data of CF Registry of Ireland 12

- Geographical Distribution 13
- Age & Sex Distribution 15
- Ethnicity 15
- Deaths 16
- Siblings 16

Diagnosis 17

- Symptoms at Diagnosis 17
- Genotype 20
- Sweat Testing 22
- Age at Diagnosis 22

Hospitalisations & Complications 24

Cultures 28

Antibiotics 32

Pulmonary Function and BMI 36

Nutrition 39

Physiotherapy 40

Long Term Medications 41

Social Data 43

Financial 44

Acknowledgements 45

Executive Summary

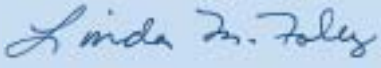
I am always struck by the sense of community that cystic fibrosis elicits. Among the professionals it brings together many types of specialist: geneticist, pulmonologist, endocrinologist, gastroenterologist, neonatologist, surgeon, paediatrician, microbiologist, and in another 10 years, the geriatrician. Then there are the allied health professionals who are so important: specialist nurses, physiotherapists, dieticians, psychologists, pharmacists, social workers: an almost endless list. Why is this? Why does this condition touch so many aspects of medicine? Perhaps the answer is found in the fundamental cause of CF: the malfunction of the chloride channel, located in the cell membrane. This is determined at conception. Competent chloride channels are necessary for normal cell function. Any tissue or organ may be affected to a greater or lesser degree. Each person with CF manifests their condition in a unique way but there are many common denominators: pancreatic insufficiency, staphylococcus colonisation, pseudomonas colonisation, diabetes, and osteoporosis. The genetic error at such a primary level of the cell may explain why there are so many possible malfunctions and why so many different specialists are required to treat one individual.

A central database with everyone's medical history on it is an essential tool for understanding this CF universe. Such an item can be used to compare and contrast conditions and complications; treatments and management. In this country, we have been working for over 4 years to develop the CF Registry of Ireland (CFRI). It is based on excellent models from Europe as well as North America and Australasia. Because of the wide dispersal of the gene, people with CF may be found anywhere in the country, so we added an internet dimension. That means that when a CF individual attends more than one hospital in different parts of the country, the internet provides the solution for bringing the records together in a central data bank. It is also the vehicle for viewing global, anonymous statistics of the CF group.

At this stage our registry is similar to a tall office building, with each floor reserved for a separate hospital. We are now seeking to fill the building with all potential tenants (PWCF - Persons With Cystic Fibrosis). We are over the half-way mark to filling our model. With continuous effort we will near the completion of the initial stage by mid-2007. Already, we are able to conduct some analyses with the data captured to date. The results have been in harmony with publications from other countries. This is another indication of the fundamental aspect of CF – there are many similarities among countries. We are also collaborating with a number of other researchers in Ireland, Europe, and America. All data that is used in studies is anonymous in nature.

During the past year we moved as tenants into space in the School of Public Health and Population Science on the Belfield campus of University College Dublin. This has afforded access to the bio-statistical resources that are required to analyse the comprehensive data from the registry. In addition, we have broadband connectivity and medical library access which we did not have in our previous offices. This adds one more speciality to the list of those who help to treat PWCF. The expert guidance from first-rate epidemiologists will lead us to new vistas in the study of CF in the community.

Finally, a word is reserved for those who are born with this problematic condition. Theirs is a strong community of individuals who support each other and stimulate the professionals to find solutions. The group graphic on the front and back covers represents the bond between the professionls and the PWCF. I hope that this publication can contribute towards finding better ways to manage and treat cystic fibrosis.



April, 2006

List of Tables

Table 1:	General data from CFRI	12
Table 2:	Ethnicity on CFRI	15
Table 3:	Families and Siblings on CFRI	16
Table 4:	Classification of Symptoms at Diagnosis	17
Table 5:	Frequency of Symptoms at Diagnosis	19
Table 6:	Common Genotypes on CFRI	21
Table 7:	'Other' Genotypes on CFRI	21
Table 8:	Age at Diagnosis, Male v. Female; Mean and Median age	23
Table 9:	Age at Diagnosis, excluding < 3 mos; Male v. Female; Mean & Median age	23
Table 10:	Hospitalisations, Paediatric v. Adult	24
Table 11:	Complication rates, Paediatric v. Adult	25
Table 12:	Culture types, Paediatric v. Adult	28
Table 13:	Twelve most frequent positive cultures	28
Table 14:	Pathogens of interest, Paediatric v. Adult	29
Table 15:	Antibiotics by route of administration	32
Table 16:	Pulmonary Function Test summary, 2004 & 05	36
Table 17:	BMI Summary; 2004 & 05	38
Table 18:	Nutrition Summary, 2005	39
Table 19:	Physiotherapy Summary, 2005	40
Table 20:	Long Term Medications Summary, 2005	41
Table 21:	Social Data Summary, 2005	43
Table 22:	Financial Summary, 2004	44

Glossary (commonly used abbreviations used throughout this publication)

CFAI:	Cystic Fibrosis Association of Ireland
CFRI:	Cystic Fibrosis Registry of Ireland
PWCF:	Persons With Cystic Fibrosis
AA:	Annual Assessment

List of Figures

Figure 1:	Number of PWCF on CFRI	6
Figure 2:	CF Census by CF Centre	8
Figure 3:	CF Census by Centre and Age	9
Figure 4:	Percentage of Consents by CF Centre	9
Figure 5:	Projected CF population to 2010	11
Figure 6:	Projected proportion Adult : Paediatric to 2010	11
Figure 7:	Proportion comparison CFRI to Census	11
Figure 8:	County of Residence on CFRI	13
Figure 9:	Province of Residence on CFRI	13
Figure 10:	CF Centre distribution on CFRI	14
Figure 11:	Province comparison CFRI vs Census	14
Figure 12:	CFRI Sex distribution	15
Figure 13:	CFRI Age band and Sex distribution	15
Figure 14:	Cause of Death, CFRI	16
Figure 15:	Symptoms at Diagnosis distribution	18
Figure 16:	Categories of Symptoms at Diagnosis	19
Figure 17:	Age at Diagnosis; Percentage Male or Female	22
Figure 18:	Cumulative Percentage at Age of Diagnosis, Male or Female	22
Figure 19:	Rate of Hospitalisations, Paediatric v. Adult	24
Figure 20:	Cardio/Pulmonary Complications, Paediatric v. Adult	25
Figure 21:	Gastrointestinal Complications, Paediatric v. Adult	26
Figure 22:	Miscellaneous Complications, Paediatric v. Adult	26
Figure 23:	Cultures: Paediatric Proportion types	30
Figure 24:	Cultures: Adult Proportion types	31
Figure 25:	Antibiotic Route in Adults or Paediatrics	32
Figure 26:	Route of Administration, Number of Days per PWCF	33
Figure 27:	Days of AB treatment, Hospital IV vs. Home IV	34
Figure 28:	Antibiotics: Paediatric Hospital IV vs. Home IV	34
Figure 29:	Antibiotics: Adult Hospital IV vs. Home IV	34
Figure 30:	Most frequently prescribed IV antibiotics	35
Figure 31:	FVC-% predicted M vs. F in Age Bands	37
Figure 32:	FEV_1-% predicted M vs. F in Age Bands	37
Figure 33:	BMI comparison M vs. F in Age Bands	38
Figure 34:	Nutrition Summary, 2005	39
Figure 35:	Physiotherapy Summary, 2005	40
Figure 36:	Long Term Medications Summary, 2005	42

Cystic Fibrosis Centres

County	Hospital	Consultant	Type of Centre
Cork	**Cork University Hospital**	Dr. Cathal Bredin Dr B Fraser	Adult Paediatric
Dublin	**Beaumont Hospital**	Prof NG McElvaney	Adult
	St Vincent's University Hospital	Dr Charles Gallagher	Adult
	The Children's University Hospital	Dr Dubhfeasa Slattery	Paediatric
	National Children's Hospital	Dr Peter Greally / Dr B Elnazir	Paediatric
	Our Lady's Hospital for Sick Children	Dr Gerry Canny	Paediatric
	Mater Misericordiae Hospital	Dr Jim Egan	Post-Transplant
Galway	**University College Hospital Galway**	Prof BG Loftus / Dr A O'Regan	Paediatric
	Merlin Park Hospital, Galway	Dr JJ Gilmartin	Adult
Kerry	**Kerry General Hospital**	Dr Fergus Leahy / Dr R.B. Fitzsimons	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 Altaf	Paediatric

Registry Management Committee

Professor N.G. McElvaney	Professor of Medicine, Royal College of Surgeons in Ireland. Beaumont Hospital, Dublin	Chairman of the Registry Management Committee
Mrs. Linda Foley	Director, CF Registry of Ireland	
Dr. Charles Gallagher	Consultant in Respiratory Medicine, St. Vincent's University Hospital, Dublin	Committee Member
Dr. Peter Greally	Consultant in Paediatric Respiratory Medicine, National Children's Hospital in Tallaght, Dublin	Committee Member
Dr. Gerry Canny	Consultant in Paediatrics & Paediatric Respirology Our Lady's Hospital for Sick Children, 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. Carl Rainey	Vice Chairperson, Cystic Fibrosis Association of Ireland	Committee Member
Mr Godfrey Fletcher	CEO, Cystic Fibrosis Association of Ireland	Committee Member
Mr. Martin Wickham	IT Director, BT - Ireland and Representative of CFAI	Committee Member

Introduction

The CF Registry of Ireland has again increased its' enrolment for 2005. The increase is 34% over 2004 (Figure 1).

We have now passed the 50% mark in enrolment. This is based on the estimated CF Census of 1182 PWCF taken in October, 2005. Once we have nearly 100% enrolment we will be able to verify the annual census figures.

Until now, we have relied on the thirteen CF Centres to return their attendance once annually. There may be PWCF who are counted in more than one centre. We have tried to control this by asking the centres to report *only* those numbers of PWCF who attend for Annual Assessment. This is presuming that an Annual Assessment is carried out in only one centre for each patient.

To the end of 2005, we collected data for both diagnosis and annual clinical data for each person. This means that only 4-5 complete records can be gathered each day. In order to increase the speed of data uptake, we have decided to collect registration and diagnosis information first, for the remainder of PWCF. Later, we will go back to collect clinical data in the form of annual assessments. This has advantages in terms of having the ability to calculate survival curves. Other interesting analyses can be carried out on the registration and diagnosis data as well.

Apart from the time factor, the other limiting issue to full ascertainment of the CF Registry is the rate at which consent forms are signed. The consenting process involves full understanding of the Registry and a detailed booklet is provided for this purpose. Often, one receives the booklet at one clinic visit, but does not sign until the next clinic visit. A period of 3-6 months may elapse before a PWCF has actually signed up.

If all PWCF were enrolled, we would be in a much better position to calculate survival rates (that is, the *projected* likelihood of survival for a baby born today with CF) for the Irish CF population.

At this time, we cannot make these calculations as we do not have enough data. If we did, we would also be able to compare the Irish CF population with other countries' survival curves.

This is the second year that we have provided each consultant with comprehensive reports of his/her patients who are on the CFRI. These include basic data on birth dates and diagnosis dates, genotype for each person, diagnosis details for each centre; complications suffered in the last 12 months; hospitalisations in the last 12 months; the microbiology of the consultants' patients; the research treatments that the consultants' patients are on; reports on

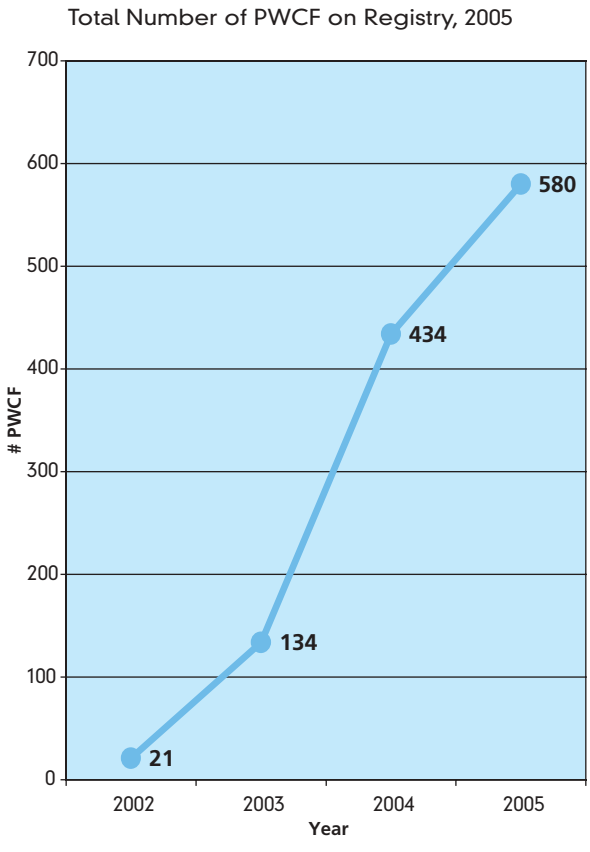


Figure 1: Number of PWCF on CFRI

pulmonary function tests, plus growth throughout the year; the nutritional status; the physiotherapy status and other drug therapy that patients are taking. These reports are available to the consultant on an individual patient basis as well as the group basis.

Regarding the accumulation of Annual Assessment records, we have a total of 583 Annual Assessments recorded on the CFRI. There are 20 PWCF with four assessments, 101 have three assessments, 168 have two assessments, and 294 have one assessment.

For the next number of months we will concentrate on enrolment as much as possible with increased emphasis on Consent forms. Full ascertainment will bring a number of benefits:

(1) we will have a much better idea of our population distribution and CF Centre attendance;

(2) we will be able to perform statistical analysis on the 'age at diagnosis' to determine whether there are differences between sexes and/or genotypes;

(3) we will be able to move towards producing survival statistics for this population in this country and compare them with other countries.

Demographics: Census from CF Centres; Census from CFRI

Cystic Fibrosis Census by Centre

The CF Census is compiled every year from the CF Centres in Ireland. Additionally, one centre which does not have a CF Nurse Specialist contributes census figures.

The CF Nurse Specialists are asked to return figures from their centre for people who attend their hospital for an Annual Assessment. They are also asked for information regarding attendance of their PWCF at other centres. We have attempted to remove the error of counting the same person in two different centres. Since 2003, we feel that the returning figures have been quite accurate.

Figure 2 shows the 2005 census, by CF Centre. The figure of 1182 PWCF is an increase of 3.4% on 2004. The last three years have shown an increase of 3-5% over the previous year.

The census from the CF Centres does not give the ages of the PWCF. Thus, when census data is used to show a Paediatric/ Adult relationship as in Figure 3, it is not as accurate as the data on the Registry, which is based on the exact age of a PWCF.

For the purposes of this exercise, we adopt the following convention: if a PWCF is still attending a paediatric centre, they are deemed to be less than 18 years of age. And, if they are attending an adult centre, they are considered to be at least 18 years of age. This may not always be so. Some adolescents have turned 18 but still have not made the transition to an Adult centre, and that figure, according to the CFRI data, is currently 59. Those 59 PWFC who are ≥18 but still attending a Paediatric centre will be distributed amongst the paediatric hospitals on the 'Census' and

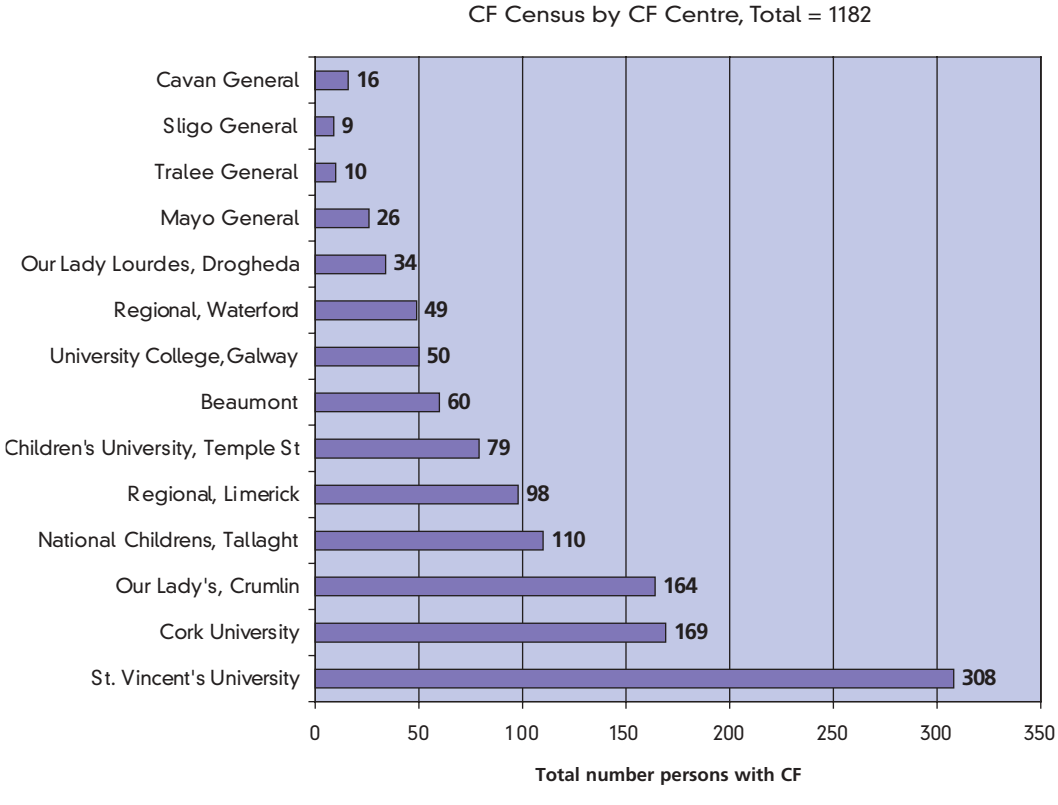


Figure 2: CF Census by CF Centre

'Projection' graphs. All of the figures based on the 'Census' have used this convention.

In contrast all of the figures from CFRI data showing an age difference reflect actual ages.

Figure 3 shows the ratio of paediatric to adult PWCF in each of those centres that cater for both populations.

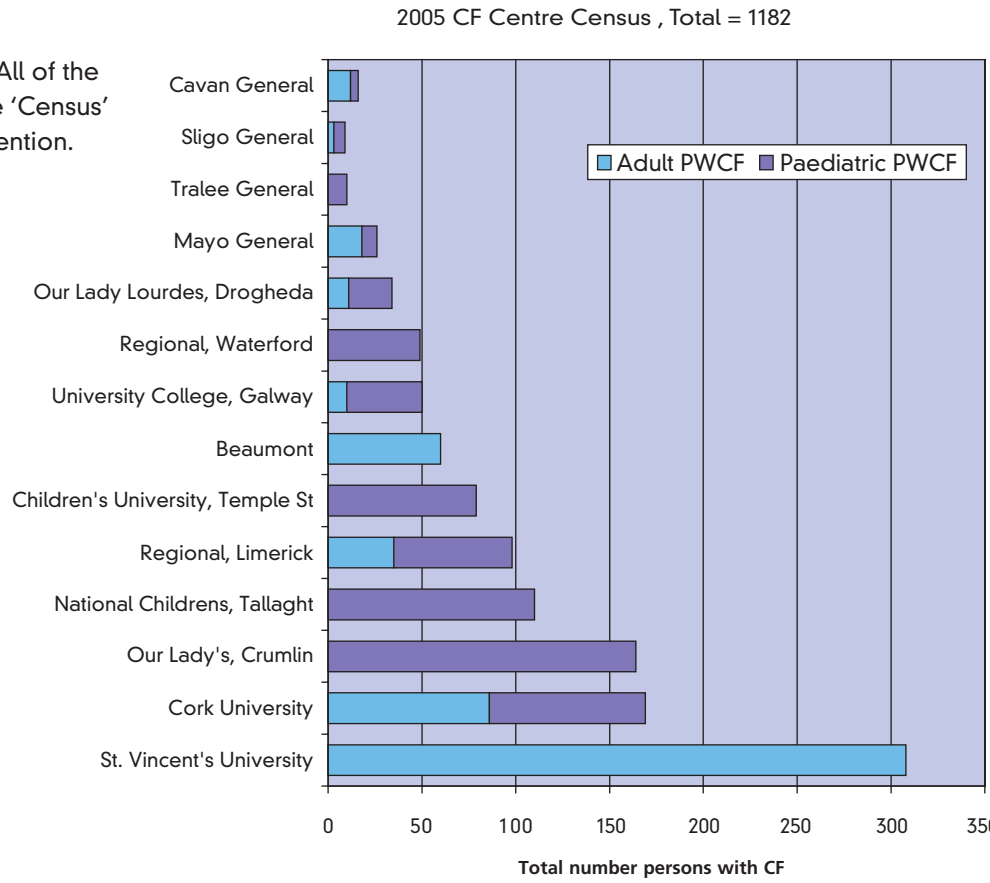


Figure 3: CF Census by Centre and Age

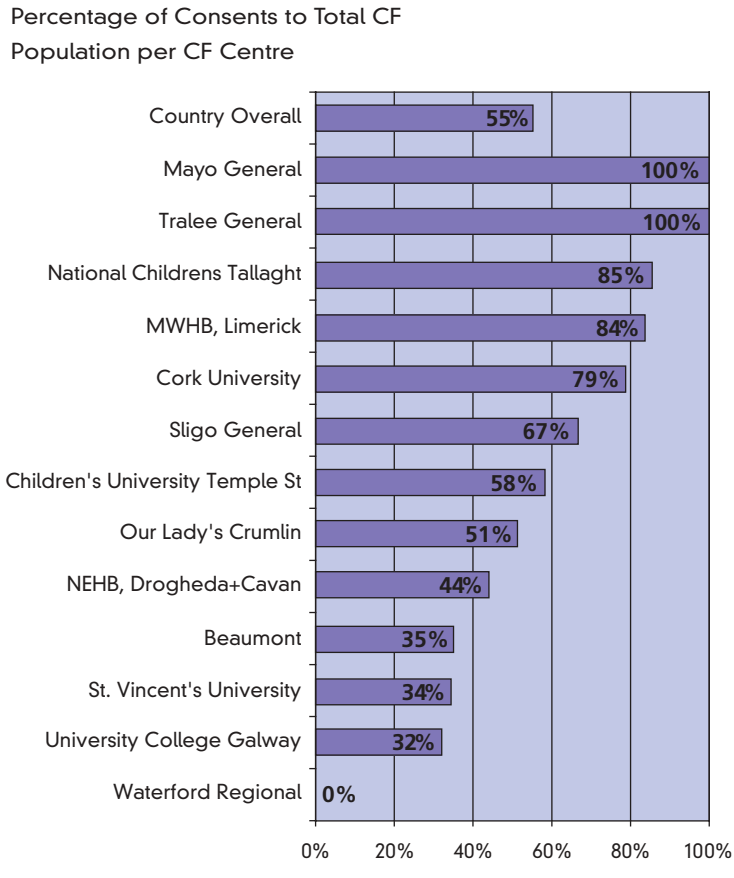


Figure 4: Percentage of Consents by CF Centre

Consents to CFRI

All enrolees must have a consent form on file in the CFRI office. Furthermore, each person who turns 18 and who is already on the CFRI because a parent had previously signed the form, must sign a form in their own right.

We can show the number of consent forms signed as a percentage of the total census in each unit (Figure 4). The overall rate for the country is 55%. Several of the major units have close to or over 80% of their patients signed up. Major efforts will be devoted to obtaining the remainder of consents in 2006. Vital data such as survival statistics cannot be calculated unless the entire population is enrolled.

CF Population Projections

Projections of the future CF population are made to show the changing relationship between adult and paediatric PWCF (Figures 5 and 6). This will assist in estimating requirements for services for PWCF. Generally, as PWCF grow older their reliance on hospital services increases. Our first estimate of the adult CF population in 2001 was 36% of the total. Now, at the end of 2005, this has increased to 46% of the total CF population. By 2010 we expect the adults to be 50% of the total and the adult portion of the population will continue to increase after that. This is primarily because there are more people who are surviving longer, while the number moving into the adult sector is close to the number being diagnosed each year. Thus, the paediatric group remains nearly static, while the adult group grows.

The population projection graphs are created based on the following assumptions:

- Birth rate of 62,000 per year
- 1 CF birth per 1400 live births
- Assume 49 New diagnoses per year; all <18; [44 Newborns, plus 5 in older age groups]
- Assume 40 matriculate to >18 group each year
- Assume 3 deaths from <18 group (average number of deaths in < 18 group for last 5 years)*
- Assume 13 deaths from Adult group each year (average number of deaths in > = 18 group for last 5 years)*

*Information supplied by the CF Association of Ireland [The CF Association of Ireland has kindly shared their statistics of deaths in each year. It is thought that the membership in the CFAI is approximately 85-90% of the total CF population. Since the deaths reported to the CFAI come directly from the CF Centres and are not restricted to members of the CFAI, we feel that these numbers reflect a true picture of the overall population changes. Comparisons have been made between the number of deaths from the CFAI data with those from the Central Statistics Office, and do not show large variations.]

They show A) the projected population increase to 2010; and B) this projection reflects the changing relationship between adults and paediatric PWCF. By 2010 the Adult group will be 50% of the total CF population.

Based on these projections, the Paediatric group will grow by 7% between 2005 and 2010; while the Adult group will grow by 25% in the same period. Overall, the increase in population over the next five years is 15%, or approximately 3% per year; which is in the region of 35 per year. This is considered to be a conservative estimate.

These projections are based on the census figures as opposed to Registry figures. They should become more accurate as enrolment approaches 100% on the CFRI.

Projected Population Increase to 2010

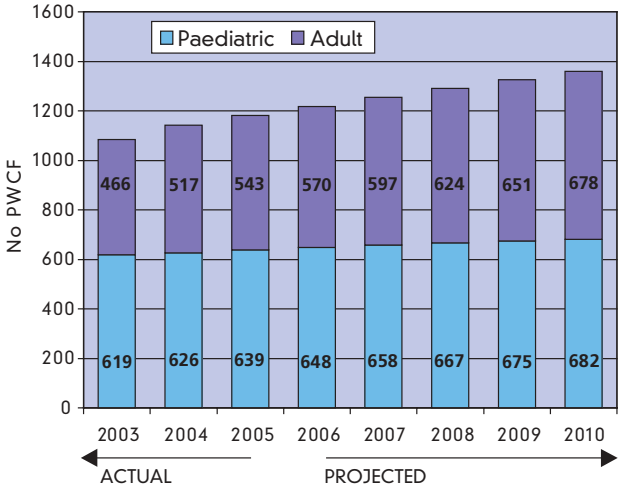


Figure 5: Projected Population Increase to 2010

Projected Percentage Change in CF Population

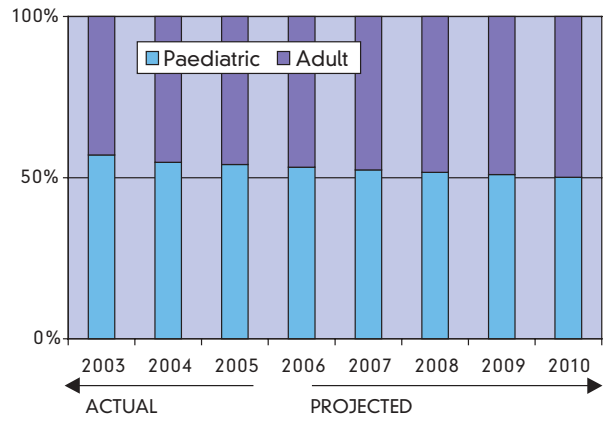


Figure 6: Projected proportion Adult: Pediatric to 2010

CF Census and CFRI Enrolment Comparison

Finally, a comparison may be made between the CFRI age groups and the census for 2005 (Figure 7).

This shows the comparison of proportions of the two age groups in both the CFRI population and the CF Census.

In the case of the CFRI, the paediatric portion is 59%, whereas in the CF Census the paediatric portion is 54%. As much of the data shown in the rest of the annual report presents comparisons between the paediatric and adult populations, it is important to see how closely the CFRI reflects the total CF population.

Comparison of CF Census with CFRI, Under 18's with >=18's

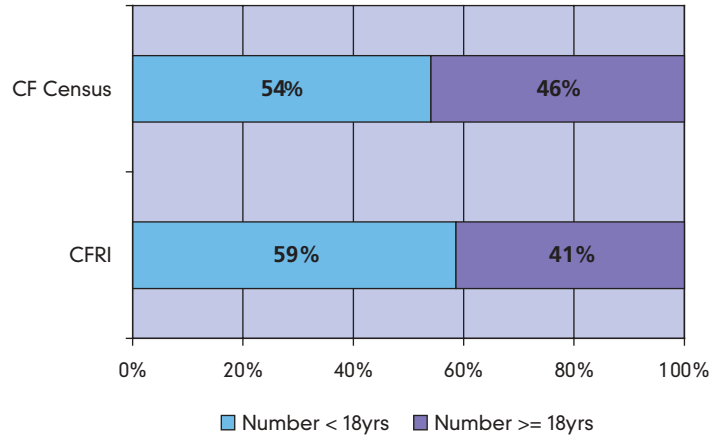


Figure 7: Proportion comparison CFRI to Census

General Data of CF Registry of Ireland

General Data of CF Registry of Ireland

Our table of general data (Table 1) is a summary of several sets of data. Firstly, the cumulative number of PWCF who are enrolled is shown. This total is 580 at the end of 2005. Then, the age range of all PWCF is displayed; from less than one year to 53 years old. The number of new enrolees for each year is shown next; followed by the mean and median ages of all PWCF, the sex and age distribution and their percentages. Finally, the number of deaths that have been recorded for each year is shown.

This CFRI report is from the set of reports known as Global Reports and is constantly updated. That is, as soon as a new person is added, the appropriate total will increase by one.

There has been a 34% increase in the registry population since 2004.

Of the 580 enrolees, 294 have one Annual Assessment; 168 have two Annual Assessments; 101 have 3 Annual Assessments, and 20 have four Annual Assessments. So, there is some longitudinal data for many patients and we can select their test results and look at them over time.

GENERAL DATA						
Year:	**2002**	**2003**	**2004**	**2005**	**Total**	
	Number	**Number**	**Number**	**Number**	**Number**	**Percentage**
Total # Pts on Registry	21	134	434	580	580	
Age Range					<1 - 53	
Patients Registered in the Year	21	113	300	146	580	
Mean Age Pts on Registry					16.4	
Median Age Pts on Registry					15	
# Males					301	51.8%
# Females					279	48.2%
# < 18 yrs					333	57.5%
# >= 18 yrs					247	42.5%
# Males >= 18					122	21%
# Females >= 18					125	21.5%
Deaths during year	0	6	5	4	15	2.6%
Total # PWCF on Registry who are alive at end of 2005					565	97.4%

Table 1: General data from CFRI

CF Registry: Distribution by County of Residence
n = 565

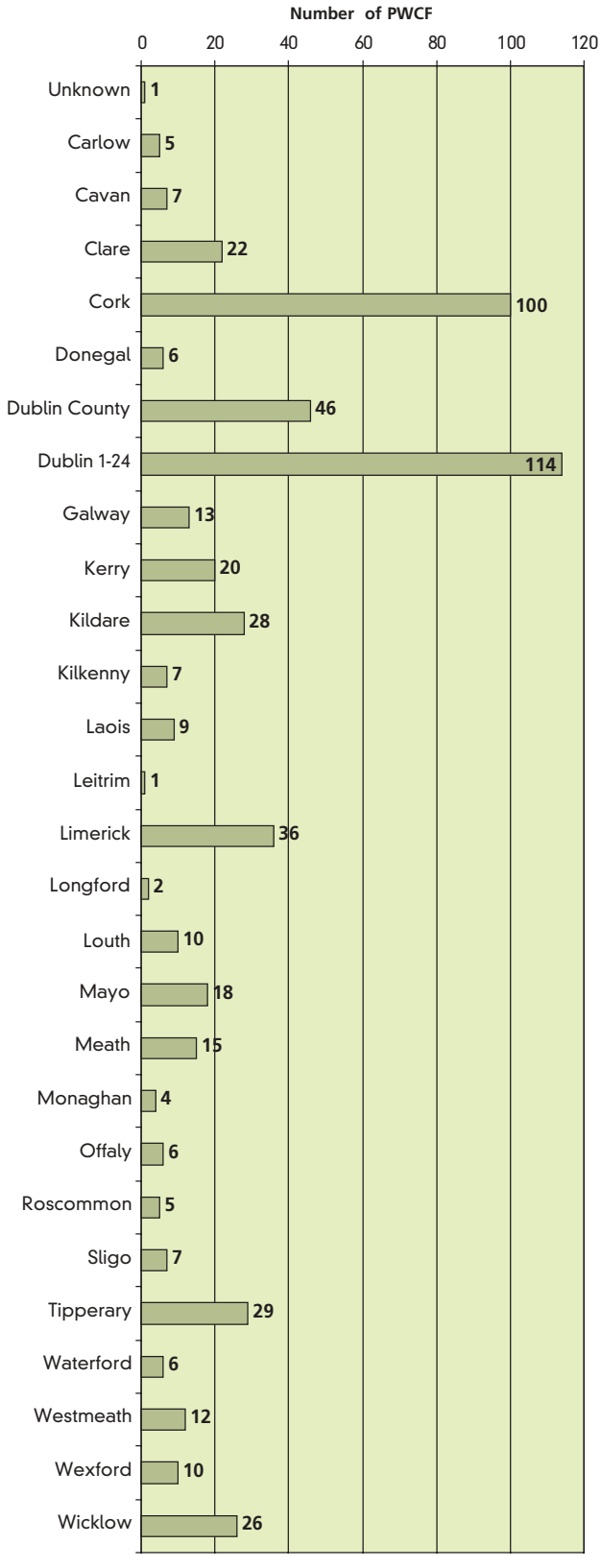


Figure 8: County of Residence on CFRI

Geographical Distribution

Figure 8 shows the number of PWCF residing in each county

The county CF populations may be aggregated into their respective provinces and these proportions are shown in Figure 9. Note that this represents 50% of the CF population, and is merely an illustration of the geographical distribution of the population at this moment in time. This picture may not be the same once all or most PWCF are enrolled.

Province Percentage CF Residents

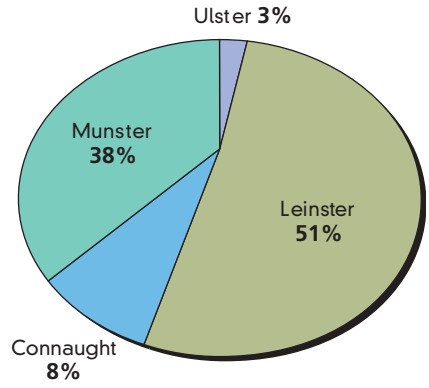


Figure 9: Province of residence on CFRI

The number of PWCF enrolled on the CFRI distributed among the CF Centres that they attend is shown in Figure 10.

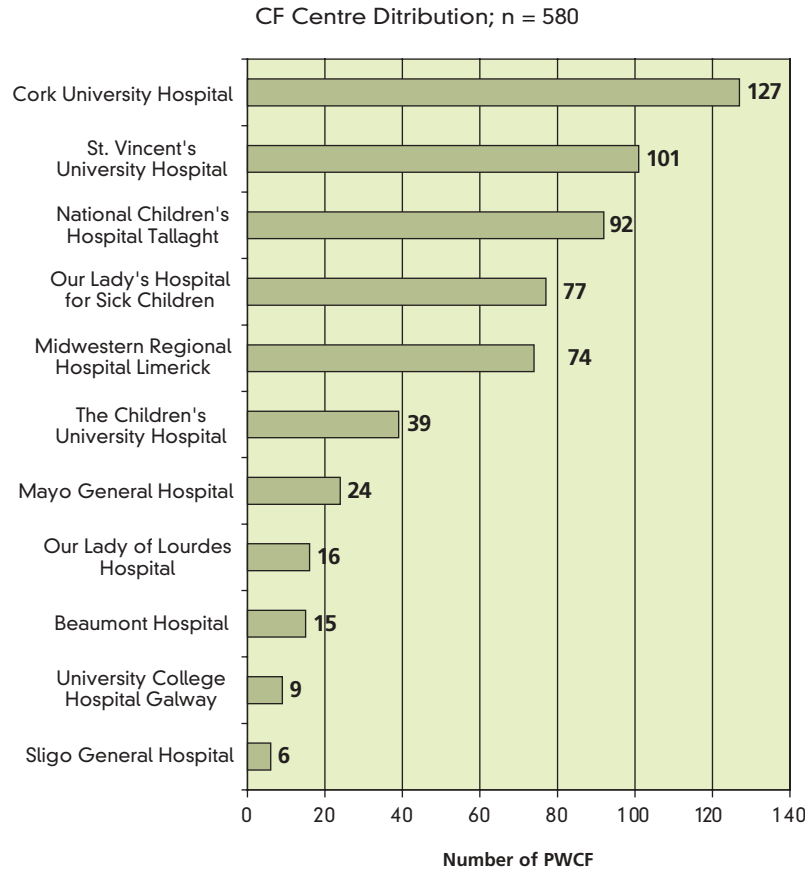


Figure 10: CF Centre distribution on CFRI

Proportional relationship between CFRI (Residence) and CF Census (CF Centre attended) by Province

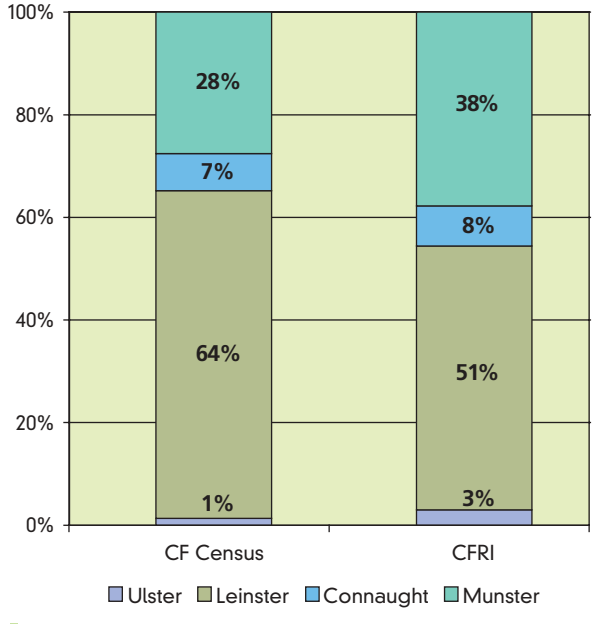


Figure 11: Province comparison between Registry (by residence) and CF Centre attendees

We might expect that PWCF would attend a CF Centre close to their residence. This does not appear to be the case. In Figure 11, the proportion of people who attend hospitals in Leinster (64%) is larger than the proportion of people who reside in Leinster (51%). In a reverse fashion, Munster shows that 28% of the total census attend hospitals in Munster (primarily CUH and Limerick Regional), whereas nearly 40% of the total number of people reside in Munster. This excess of PWCF probably attend hospitals in Leinster, rather than Munster. Similar proportions of each population live in Connaught (8%) and attend a CF Centre in Connaught (7%), while a very small proportion of the CF population are from the Ulster counties of Donegal, Monaghan, and Cavan. The census figure for Ulster is taken from Cavan General Hospital, which reports annual figures for the census but is not a full CF Centre. The majority of PWCF from the Ulster counties attend CF Centres in Drogheda and Dublin.

Age & Sex Distribution

The total number of males and females on the CFRI is fairly evenly split between males (52%) and females (48%) (Figure 12).

Figure 13 describes the CFRI population in age bands and by sex.

It is encouraging to see that over 10% of the CFRI population are now over 30 years of age. The majority of PWCF (59%) on the CFRI are under 18 years of age. This is slightly larger than what we believe the actual CF census to be (Paediatric = 54%). The average age of all enrolees is 16.4 years.

Proportion Males & Females enrolled, n = 565

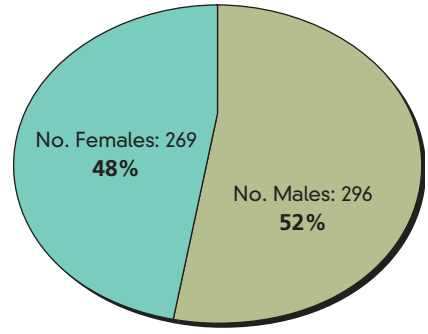


Figure 12: CFRI Sex distribution

Ethnicity

The Irish nationality and ethnicity dominate the CF population (97.9%) who live in this country, but there are some other ethnic groups who are found on the database. It is likely that other minorities will be recorded in future. Table 2 illustrates the ethnic distribution of the CFRI at the end of 2005. The 'Nationality' column describes the country of birth of the PWCF, while ethnicity is described in the "Parents' Country of origin" column. This information may be used in analysing the genetic origins of our CF population.

Age Band Distribution, by Sex; n = 565

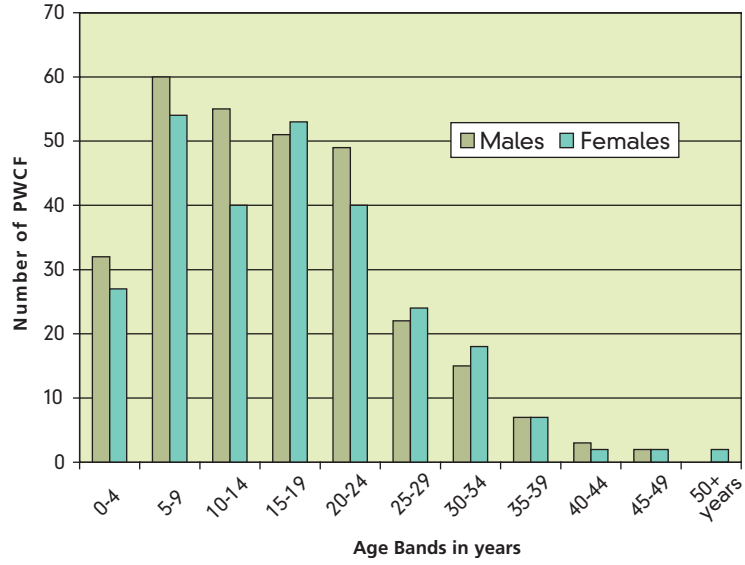


Figure 13: CFRI Age band and Sex distribution

Nationality: Country of Birth	Parents' Country origin	# PWCF On Registry	% PWCF on Registry
Ireland	Ireland	568	97.9%
United Kingdom	Ireland	1	0.2%
Canada	Ireland	1	0.2%
Ireland	Mixed	2	0.3%
Germany	Irish & German	1	0.2%
United Kingdom	England	2	0.3%
Canada	USA/North & South America	1	0.2%
United States	USA/North & South America	2	0.3%
Ireland	USA/North & South America	2	0.3%

Table 2: Ethnicity on CFRI

Deaths

There were five deaths during 2005 involving PWCF who were enrolled on the Registry. They were all female. To date, there have been 15 deaths, 10 of whom are female. These are all represented in Figure 14. The proportion of 'cause of death' is dominated by "respiratory/cardiac" causes.

Siblings

Ireland occupies a unique position in the world in terms of cystic fibrosis. It has the highest incidence of cystic fibrosis, but also may have the largest proportion of families with more than one child with CF. We are well on the way to documenting this exceptional characteristic.

In 2005, we have documented many sibling pairs and triples (Table 3). From 580 PWCF, there are 527 families represented. Our data collection allows for the total number of children in each family to be recorded and this information yields 3.3 children per family. (This is more than twice the average number of children per family in the Irish population as a whole, of 1.6.) There are 45 sibling pairs, including 3 sets of twins. There are also 4 families with three siblings with CF.

This is very interesting from an international viewpoint. These families could provide informative data about infections, the rate of cross infection within family units, and other complications.

Cause of Death, 2003-2005

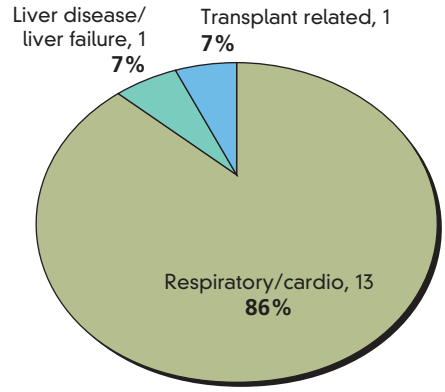


Figure 14: Cause of Death, CFRI

Families with CF Siblings	
580	total PWCF
527	Families represented
3.3	children (with and without CF) per family
1.1	children with CF per family
45	Sibling Pairs including 3 sets of twins
4	Sibling Triples

Table 3: Families and Siblings on CFRI

Diagnosis

Symptoms at Diagnosis

It is important to record a person's symptoms at diagnosis, or when first seen by a consultant. We use a list of 23 symptoms and each person may have several symptoms. Our list may be roughly divided into symptoms that brought a person to the attention of the consultant (for example "failure to thrive") and those that confirmed a diagnosis of CF (for example, a "positive sweat test"). The symptoms in the first category may be further divided into different types depending on the body system affected, say 'gastrointestinal' or 'respiratory'. Analysis can then be done to link symptoms to the 'age at diagnosis' or to the genotype.

Table 4 describes the classification of symptoms into categories.

Method of Diagnosis	Category
Meconium Ileus needing surgery Meconium Ileus managed medically Meconium Ileus equivalent Meconium Plug Syndrome BM Meconium Test Positive	Meconium Ileus
Failure to thrive and/or malnutrition Steatorrhoea and/or abnormal stools and/or malnutrition Prolonged Jaundice Hepato-biliary Disease Pancreatitis Rectal Prolapse Electrolyte imbalance / Dehydration Diabetes Mellitus	Gastrointestinal
Lower Respiratory infection/persistent lower respiratory symptoms Sinus Disease and/or Nasal polyps Clubbing	Respiratory
Family History Screening	Family
Delayed puberty Infertility	Fertility
Borderline Sweat Test Positive Sweat Test	Sweat Test
Other reasons	Other
Unknown	Unknown

Table 4: Classification of Symptoms at Diagnosis

The frequency of the various symptoms in ascending order is shown in Figure 15.

The most frequently recorded symptoms are *Lower Respiratory infections, Family History, Failure to thrive and Steatorrhoea.* Taking all of the meconium conditions together, their total is 110; so they would be the fourth most frequently recorded symptoms.

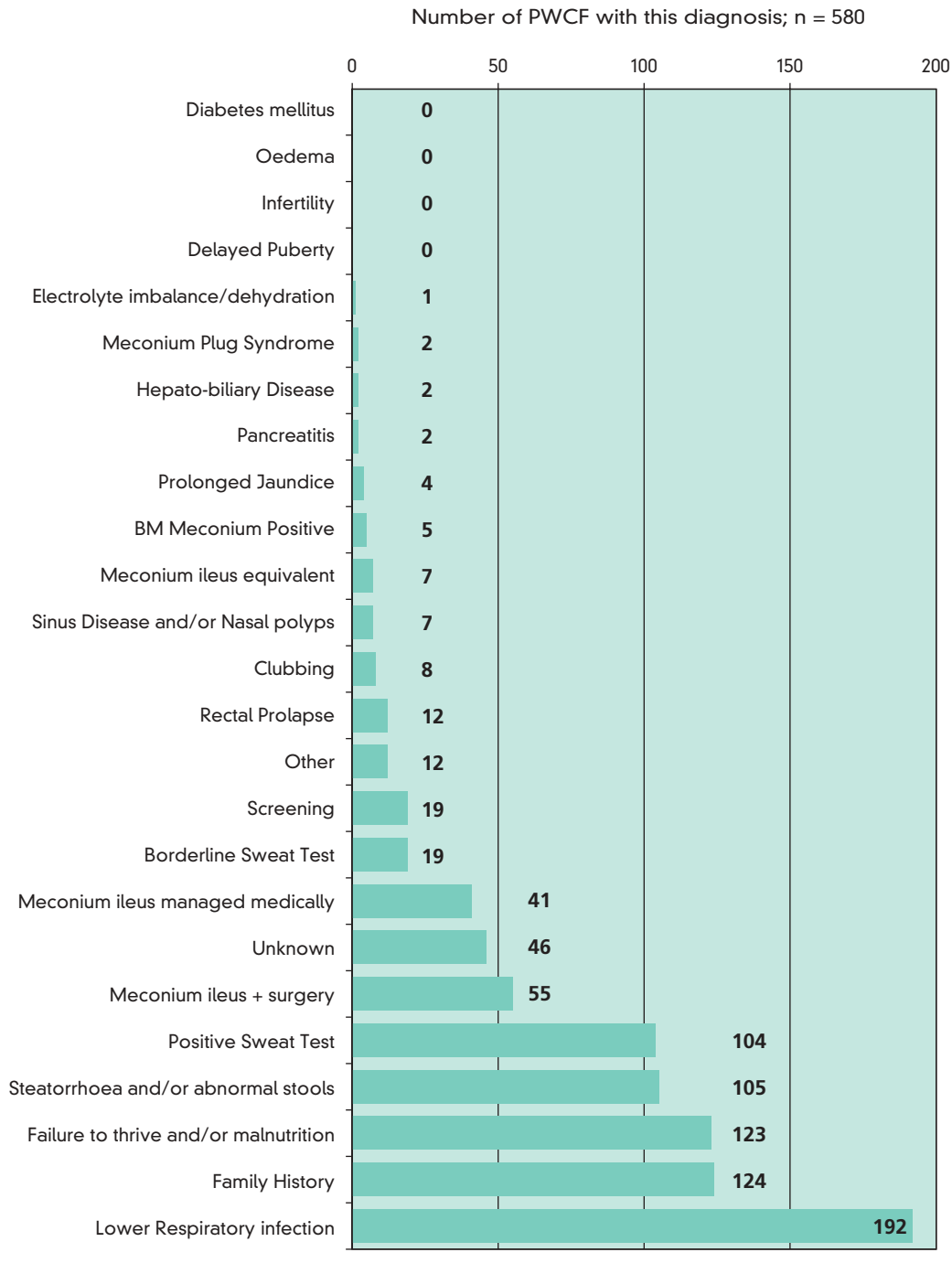


Figure 15: Symptoms at Diagnosis distribution

Table 5 shows the number of symptoms from 580 PWCF sorted into categories. On average, for each PWCF we have recorded 1.5 symptoms.

In total we have 844 symptoms (disregarding the 46 "unknowns") recorded by 534 PWCF.
Many have symptoms recorded in more than one category.

Categories of Symptoms	Total
Gastrointestinal	249
Respiratory	207
Meconium Ileus	110
Family	143
Sweat Test	123
Unknown	46
Other Symptoms	12
Total	890

Table 5: Frequency of Symptoms at Diagnosis

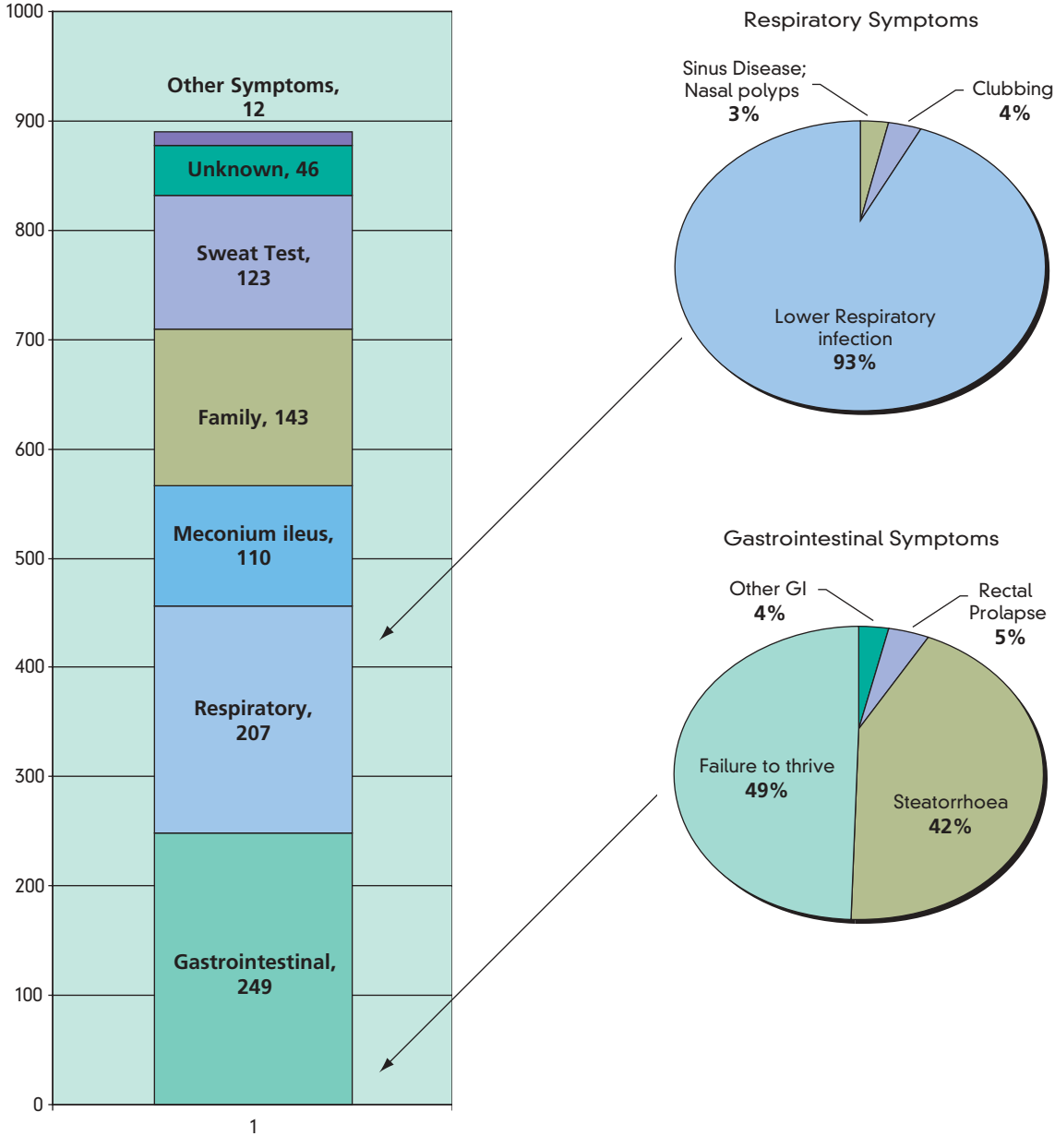


Figure 16: Categories of Symptoms at Diagnosis

If we stack these symptoms (Figure 16) in terms of their frequency and then expand the two largest categories (Gastrointestinal and Respiratory) we can see that *failure to thrive* and *steatorrhoea* are recorded with equal frequency within the GI category, and when their totals are combined, the GI symptoms are slightly more frequent than respiratory symptoms. The respiratory symptoms are almost exclusively *lower respiratory infection.* Thus, these three symptoms categories, together with *meconium ileus* (any type) account for 64% of all the symptoms noted. Then, if you also include those symptoms classified under 'Family', 80% of all symptoms are accounted for. In rank order, the following list comprises 80% of all symptoms recorded at diagnosis:

- Lower & Persistent Respiratory tract infections
- Failure to thrive
- Steatorrhoea
- Family History
- Meconium Ileus – all types

Unfortunately, not all symptoms are apparent at birth. Most of the meconium ileus category are present at birth [the exception is 'Meconium ileus equivalent', which is descriptive of the obstructed ileum but developing in the late neonatal period]. Most of the PWCF having 'family' or 'screening' symptoms are often investigated at birth. Many of the gastrointestinal symptoms are present early, and are likely due to the high rate of pancreatic insufficiency present in the Irish CF population. The respiratory symptoms generally take longer to manifest themselves. We are currently analysing our data to determine if there are differences in the Age at Diagnosis, and whether this depends on the type of symptoms one has. We are also looking at any differences between males and females and their respective ages at diagnosis.

The CFRI also allows us to examine (and link) these 'symptom' observations to one's genotype. So, this is another avenue of inquiry which we are currently analysing.

Genotype:

During the past 12 months we have gathered additional genotype data as well as increasing the total number of PWCF on the database. The new genotype data covers 565 PWCF whereas in the 2004 report we had data for only 355 PWCF. Much of the additional data is from further characterisation of less frequent genotypes. We now have at least one allele characterised for 565 PWCF, or 97% of the people on the registry.

Interestingly, the major points are similar to the 2004 data:

- 96% (n=540) are heterozygous for ΔF508; that is, in 540 people at least one chromosome carries the ΔF508 mutation.
- 66% (n=371) are homozygous for ΔF508; that is, both chromosomes carry the ΔF508 mutation.

Thus, Ireland displays a fairly homogeneous CF population with respect to genotype. Two other mutations are of interest as they are the second and third most frequently occurring mutations: G551D (the so-called 'Celtic' allele) and R117H.

The National Genetics Laboratory in Crumlin is now pursuing many of the other mutations in order to fully characterise Irish CF patients.

This year's genotype data is displayed in two tables: 1) Most Frequent CF Mutations (Table 6); and 2) Expanded detail of the 'Other' category listed in (Table 7).

MOST FREQUENT CF MUTATIONS							
	← Allele 1 →						
Allele 2 ↓	Δ1507	ΔF508	G551D	R117H	R560 T/K	Other	TOTAL
Result Pending		31	3	2		1	37
Δ1507		5					5
ΔF508		371					371
G551D		55	2		1		58
R117H	1	20					21
R560 T/K		10	1		1		12
1717-1 G->A		9		1			10
621+1, G->T		9					9
G542X		7	2				9
N1303K		3					3
R352Q		1					1
R553X			1				1
Other		19	2	2		5	28
Total	1	540	11	5	2	6	565

Table 6: Common Genotypes on CFRI

Detail describing 'Other' mutations found in Irish CF population:

'OTHER' MUTATIONS										
	← Allele 1 →									
Allele 2 ↓	ΔF508	G551D	R117H	R560 T/K	3007delG	1154insTC	1471delA	1525-1 G->A	P574H	TOTAL
3849+10KbC->T	3									3
E60X	3									3
IVS1-5842_IVS4+401del		2								2
V520F	2									2
1471delA							2			2
2622+1G->A	1		1							2
3849+4G->A			1							1
A209s	1									1
c.2052delA	1									1
c.262_263del TT	1									1
L1335P	1									1
M1105R	1									1
Q493X	1									1
R1162X	1									1
1154insTC						1				1
1461ins4	1									1
1525-1 G->A								1		1
2184delA	1									1
2623-2A->G									1	1
3120 G->A	1									1
TOTAL	19	2	2	0	0	1	2	1	1	28

Table 7: 'Other' Genotypes on CFRI

Sweat Testing:

Data on sweat testing is stored on the database. Currently, we have 43% of enrolees with a Sweat Chloride result. The rate of genotyping is higher and we see the genotype as a priority over sweat test results. However, we will continue to record sweat test results so that analysis may be carried out sometime in the future, to correlate sweat tests with genotypes.

Age at Diagnosis:

As more PWCF accumulate onto the CFRI, it still appears that there may be a difference between males and females in terms of their "age at diagnosis".

This is important and may be crucial to early growth and development.

This can be shown in a number of ways. Firstly, if we compare those who were diagnosed in less than three months or less than twelve months there is a difference favouring males. Figure 17 shows that 49% of males (versus 45% of females) are diagnosed in less than 3 months; and that 74% of males (versus 67% of females) are diagnosed in less than one year.

Using the same data, and plotting the percentage of males versus females over time; there still appears to be a lag in the female population (Figure 18). These differences may not be significant overall, but if we then look at sub-groups defined by genotypes or symptoms at diagnosis, it might emerge that certain groups of females are less likely to be diagnosed early.

This analysis is on-going and we hope to be able to show which sub-groups in the CF population are less likely to be diagnosed in less than 3 or 12 months, in the absence of newborn screening.

Comparison of Males and Females diagnosed in under 3 months or under 12 months

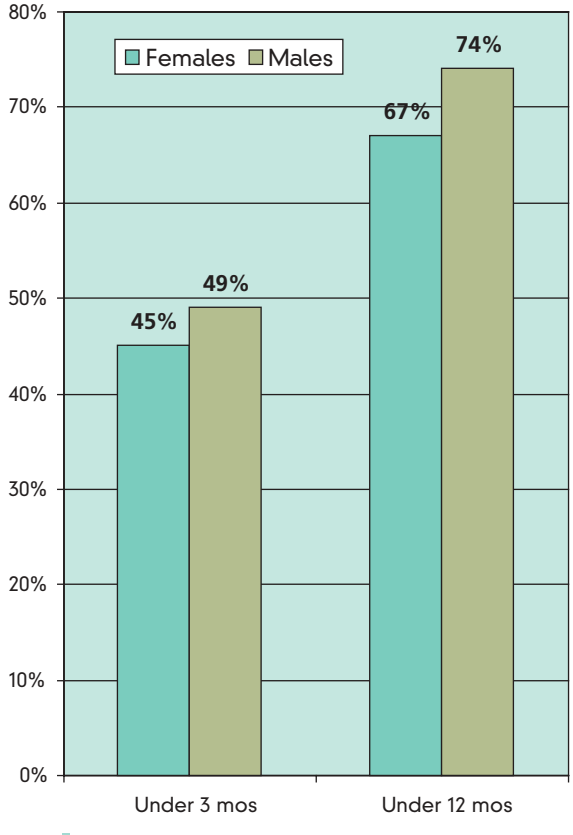


Figure 17: Age at Diagnosis; Percentage Male or Femle

Cumulative %age of PWCF at Age of Diagnosis, M v F

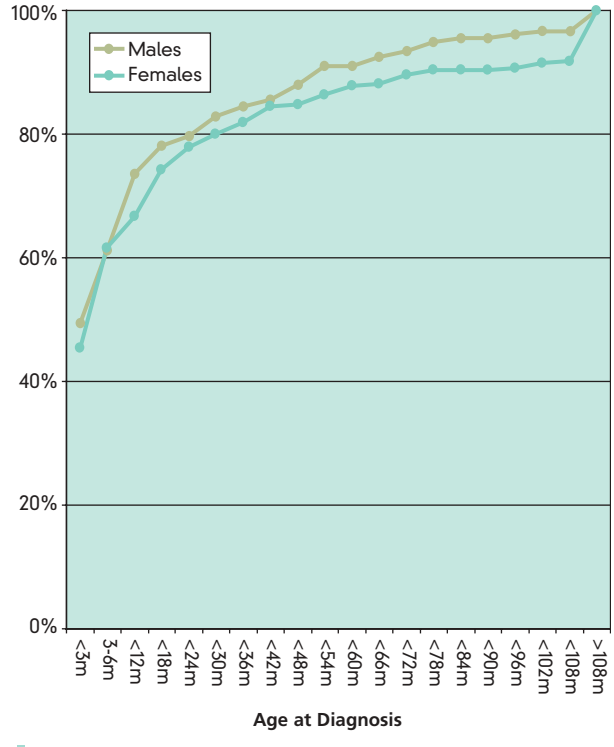


Figure 18: Cumulative percentage at Age of Diagnosis, Male or Female

We are actually looking for small differences so we will need a larger population to study before definitive results are known.

Presently we can calculate the mean and median ages at diagnosis for the two sexes.

AGE AT DIAGNOSIS, ALL	Males n=289	Females n=271
Median Age in Months	3.1	3.3
Mean Age in Months	19	29.4

Table 8: Age at Diagnosis, Male v. Female; Mean and Median age

The median age at diagnosis is similar in both sexes but the mean age at diagnosis is not the same.

We know that there is a similar incidence of meconium ileus in both sexes and this should be picked up in the first 3 months. So, if we do the same exercise, excluding all those who are diagnosed before three months, we might see if there is a difference in age at diagnosis which is based on symptoms other than meconium ileus.

This same comparison for those excluding diagnoses in less than 3 months:

AGE AT DIAGNOSIS, EXCLUDING THOSE DIAGNOSED IN < 3 MONTHS	Males n=146	Females n=148
Median age after 3 months	13.1	16.6
Mean age after 3 months	36.4	53

Table 9: Age at Diagnosis, excluding < 3 mos; Male v. Female; Mean & Median age

We are now seeing a difference in the median age as well as in the mean age. As well as that, the two groups are nearly equal in numbers indicating that more males in our sample are diagnosed in less than 3 months.

It would appear then, that if there is a difference in the age at diagnosis between males and females (favouring males) that this difference becomes more apparent after 3 months of age. This difference may reflect a difference between the sexes in relation to the emergence of clinical symptoms.

This requires further study and the significance of these trends will become apparent as we accrue more PWCF onto the CFRI. This will remain a focus of study.

Hospitalisations & Complications

This year we have looked at only those Annual Assessments that were completed in 2005. There are more than three times as many AA's entered on the database for those PWCF under 18 years of age. The trends are similar to those reported in the 2004 Annual Report. This data is particularly helpful in assisting planning of hospital service requirements.

Table 10 shows a rate of 0.8 hospitalisations in the Adult group versus a rate of 0.5 hospitalisations in the Paediatric group. The rate of respiratory infections that required IV antibiotics was nearly 3 times higher in the Adult group (1.4 to 0.5). And the rate of 'Other exacerbations' was also three times higher in the Adult group; although it is important to note that the overall number of 'other exacerbations' is far lower in both groups. Finally, the overall rate of 'complications' in the adult group is almost twice that of the paediatric group.

This is represented graphically in Figure 19.

2005 ANNUAL ASSESSMENTS

	< 18		>=18		Ratio of Episode rate Adult to Paed
Total # in group	159		52		
Ave age of group in yrs	9		25		
	#	Per PWCF	#	Per PWCF	
Hospitalisations	74	0.5	41	0.8	1.69
Respiratory Exacerbations	83	0.5	72	1.4	2.65
Other Exacerbations	18	0.1	18	0.3	3.06
Complications	358	2.3	207	4.0	1.77

Table 10: Hospitalisations Paediatric v. Adult

Rates of Hospitalisation and Exacerbations per PWCF, Paediatric vs Adult, 2005

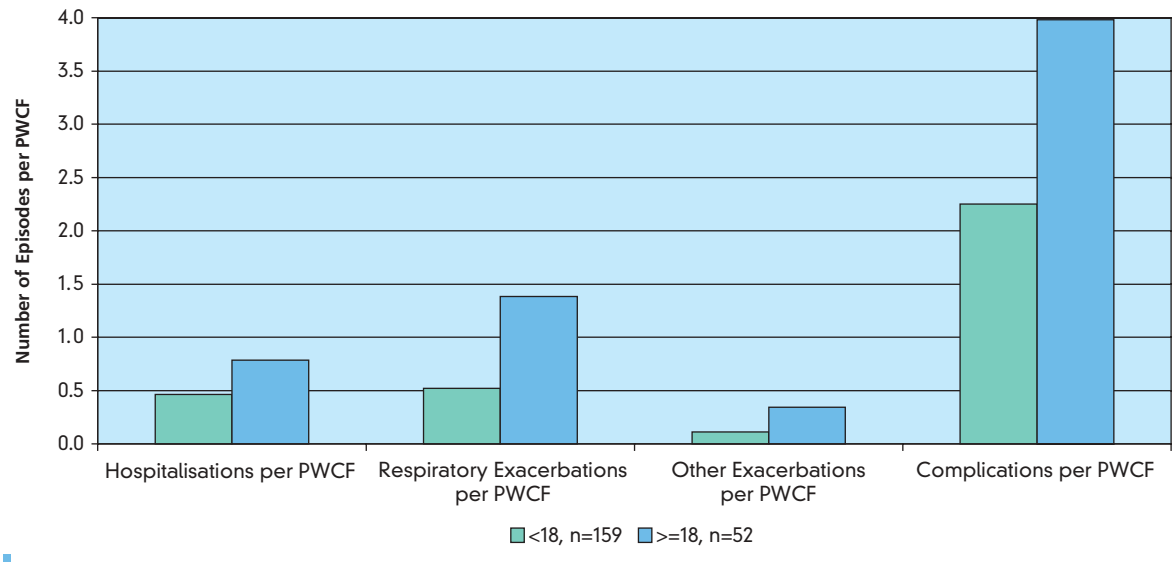


Figure 19: Rate of Hospitalisations, Paediatric v. Adult

All of these comparisons are to be expected. One might even expect the hospitalisation rate in the Adult group to be higher than it is. No doubt, the reason that it is not higher is due to a higher rate of home IV antibiotic treatment in the Adult group. This will be shown in greater detail in the antibiotic section.

Now we will examine the 'Complications' in more detail. We break them down into the following categories: "Cardio/Pulmonary", "Gastrointestinal", and "Miscellaneous". The proportion of PWCF with "No Complications" is shown on each detailed graph, for reference.

Firstly, we compare the major categories shown in Table 11.

COMPLICATION RATES PER PWCF, MAJOR CATEGORIES

	< 18		>=18		Ratio Adult rate to Paed rate
Total # in group	159		52		
Ave age of group in yrs	9		25		
Type of Complication	**Total number**	**Rate per person**	**Total number**	**Rate per person**	
Had No Complication	6	0.04	2	0.04	1.0
Cardio/Pulmonary	138	0.87	68	1.31	1.5
Gastrointestinal	161	1.01	66	1.27	1.3
Miscellaneous	55	0.35	62	1.19	3.4

Table 11: Complication rates Paediatric v. Adult

This table shows a number of things: 1) the number and rate of people having 'No complications' in a year is similar in both groups; 2) the rate of 'Cardio/Pulmonary' complications is somewhat higher in the older age group; 3) the rate of 'Gastrointestinal' complications is again somewhat higher in the Adult group; 4) the rate of 'Miscellaneous' complications is almost three and one half times higher in the Adult group.

The three charts (Figures 20, 21, and 22) showing the relative percentages in the two groups are as follows:

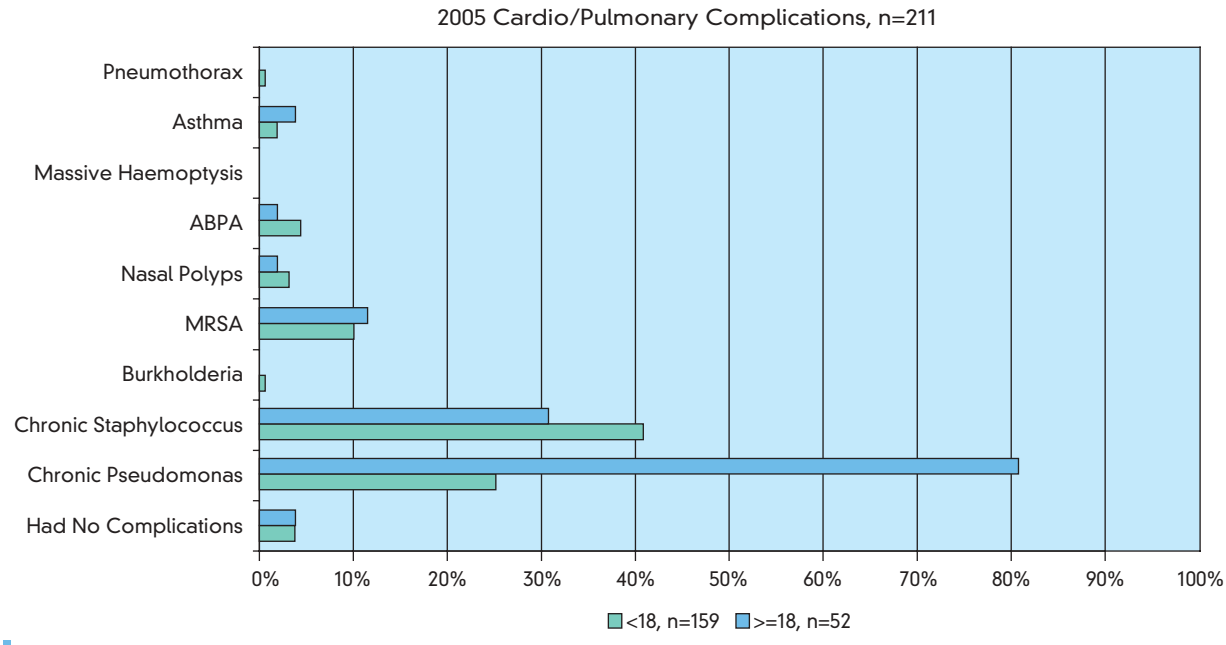


Figure 20: Cardio/Pulmonary Complications, Paediatric v. Adult

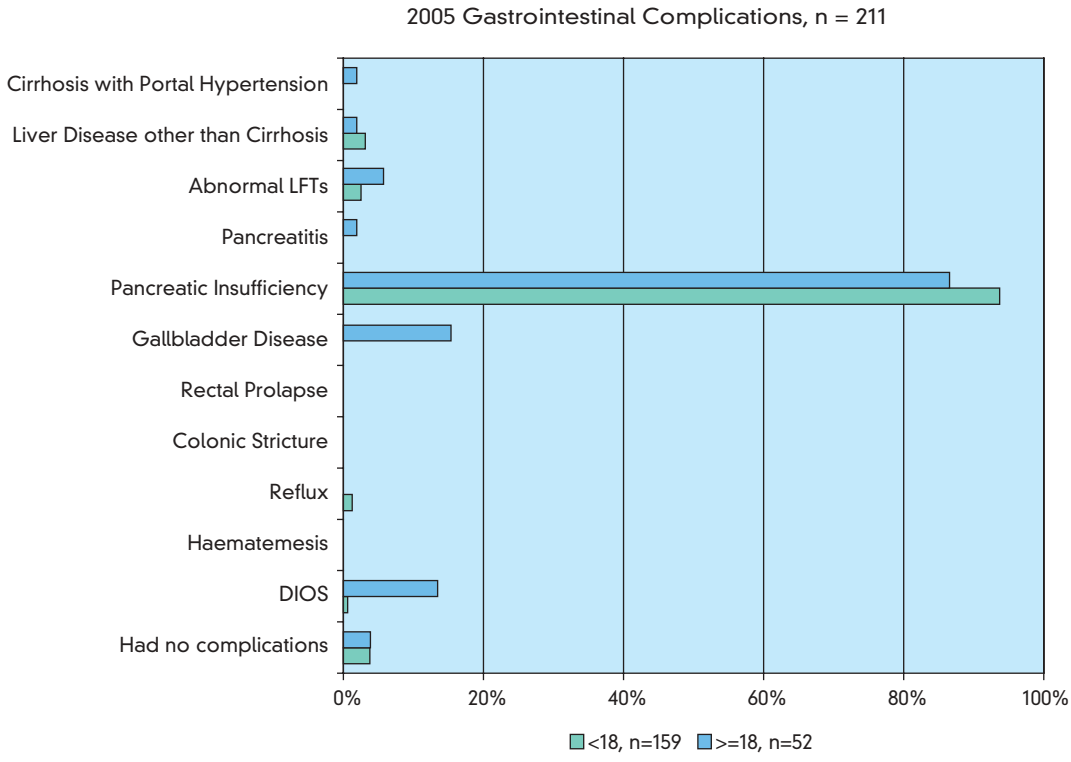


Figure 21: Gastrointestinal Complications, Paediatric v. Adult

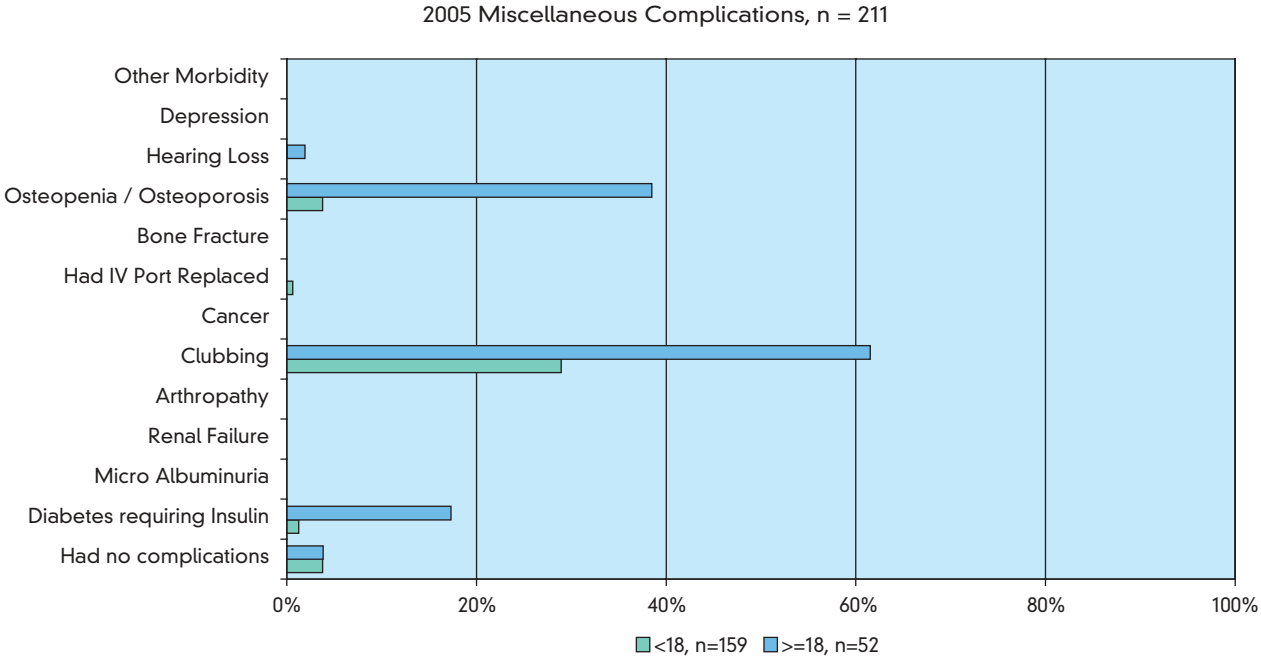


Figure 22: Miscellaneous Complications, Paediatric v. Adult

Considering all types of complications, the following points may be made:

- The rate of chronic staphylococcus infection diminishes in the Adult group (40% versus 30% in Adults).
- The rate of chronic pseudomonas greatly increases in the Adult group (80% in Adults versus 25% in Paediatric group).
- The rate of MRSA is similar in the two age groups and is about 10% for both groups.
- The rate of 'pancreatic insufficiency' is similar in both groups and is over 85%. This is by far the most frequent GI complication.
- 'Gallbladder disease' and 'Distal Intestinal Obstruction Syndrome' (DIOS) are almost unknown in the Paediatric group, but profess themselves in the Adult group. The rate of these two complications is still less than 20% in the Adult group.
- The rates of 'Diabetes requiring insulin' and 'Osteopenia/osteoporosis' are far higher in the Adult group and this is to be expected.
- The rate of 'Clubbing' is twice as high in the Adult group, but the rate in the Paediatric group is still rather high at 29%; and this may be due to late diagnosis.

This data is in agreement with many international studies. As PWCF grow older, their chances of developing more complications increase. The possibility of contracting chronic pseudomonas, DIOS, clubbing, osteopenia/osteoporosis, and diabetes all increase with age. With these occurrences, the rate of hospitalisation increases.

Cultures

During 2005, there were 710 sputum samples recorded on the CFRI, taken from 212 PWCF. After sputum samples, the culture types in order of occurrence are: cough swabs, throat swabs, nasal swabs and BAL samples. The number and type of samples is often dependent on the age of the PWCF. Thus, we see a higher rate of cough and throat swabs taken from the paediatric group; while a higher rate of sputum samples are taken from the adult group. Table 12 illustrates these comparisons. In all, there were 1140 samples sent for microbiological testing from this group of PWCF.

2005 ANNUAL ASSESSMENTS

	< 18		>=18	
Total # in group	159		53	
Ave age of group in yrs	9		25	
Type	**#**	**rate**	**#**	**rate**
Sputum samples	493	3.1	217	4.1
BAL samples	3	0.02	2	0.04
Throat Swab samples	165	1.0	7	0.1
Cough Swab samples	210	1.3	14	0.3
Nasal Swab samples	27	0.2	2	0.04

Table 12: Culture types, Paediatric v. Adult

Each sample may produce one or more types of bacterial growth. The majority (93%) of positive cultures are accounted for by 12 commonly occurring pathogens. These are listed in Table 13.

TWELVE MOST FREQUENTLY OCCURRING POSITIVE CULTURES, 2005

	CultureName	% of total number of cultures
1	Staphylococcus aureus	26%
2	Pseudomonas aeruginosa (Mucoid status not reported)	21%
3	Haemophilus influenza	11%
4	Candida not specified	10%
5	Aspergillus fumagatus	7%
6	Pseudomonas aeruginosa (Mucoid)	6%
7	MRSA	4%
8	Candida: Albicans	2%
9	Stenotrophomonas maltophilia	2%
10	E. Coli	1%
11	Moroxella catarrhalis	1%
12	Pseudomonas aeruginosa (Non-mucoid)	1%
	Total	**93%**

Table 13: Twelve most frequent positive cultures

The first 5 microbes on the list account for 75% of the culture results affecting Irish PWCF.

We looked more closely at a group of common pathogens (plus additional pathogens of interest) and determined their occurrence within the two age groups. Also, we calculated the overall Male to Female ratio for several of the pathogens to see if there was any indication of a sex difference.

Table 14 lists the numbers of PWCF who had at least one positive culture as well as the total number of cultures for that pathogen. One person may be tested several times in a year and this can distort the interpretation of the incidence within the population. For example, in the Paediatric group, 88 PWCF were positive for Staphylococcus aureus 220 times in 2005; while 13 Adult PWCF were positive for SA on 27 occasions in 2005.

We found that there were 551 positive cultures from 159 PWCF in the Paediatric group giving a rate of 3.5 infections per PWCF. While in the Adult group of 52 PWCF there were 177 positive cultures, yielding a rate of 3.4 infections per person.

PWCF with at least one positive culture in 2005

2005 ANNUAL ASSESSMENTS

	< 18			>=18			All
Total # in group	159			52			211
Ave age of group in yrs	9			25			13
Culture Type	**# of PWCF***	**Total # cultures**	**rate per PWCF**	**# of PWCF***	**Total Cultures**	**rate per PWCF**	**M:F ratio**
Aspergillus Fumagatus	13	25	8%	5	21	10%	1.3
Burkholderia Cepacia Complex: All Genomovars	1	1	0.6%	1	1	2%	
Haemophilus Influenza	62	121	39%	5	7	10%	1.6
MRSA	14	48	9%	5	15	10%	1.7
Pseudomonas aeruginosa - Mucoid status not reported	46	92	29%	27	68	52%	1.1
Pseudomonas aeruginosa - Mucoid	12	18	8%	14	27	27%	1.9
Pseudomonas aeruginosa - Non Mucoid	2	2	1.3%	4	5	8%	
Pseudomonas fluorescens	2	2	1.3%	2	4	4%	
Pseudomonas alcaligen	1	1	0.6%	0	0		
Staphylococcus aureus	88	220	55%	13	27	25%	1.3
Stenotrophomonas maltophilia	9	14	6%	1	2	2%	1
Streptococcus pneumoniae	6	7	4%	0	0		
Total "Pathognes of Interest"		**551**			**177**		
Other Cultures	115	358	72%	19	66	37%	

*=Number of PWCF with at least one positive culture in 2005

Table 14: Pathogens of interest, Paediatric v. Adult

The ratio of males to females for each of the pathogens listed was similar (that is close to 1) with the exceptions of Haemophilus influenza (1.6); MRSA (1.7); and Pseudomonas aeruginosa-mucoid (1.9). In these cases, the ratio was in favour of males. However, it is important to note that the numbers in these examples are small and what this warrants is monitoring in the future to see if these trends continue as more samples are added to the database. It will be interesting to see if any particular infections tend to occur in one sex more frequently than the other.

The column headed "rate per PWCF" is the percentage of PWCF in the group (either Adult or Paediatric) who tested positive for that pathogen. In other words, 39% of the Paediatric group tested positive for Haemophilus influenza, while only 10% of the Adult group tested positive for that same pathogen. There is a higher proportion of the Adult group testing positive for all of the Pseudomonas categories, while the rate of Staphylococcus aureus is higher in the Paediatric group (55% to 25%). These findings are similar to published studies.

One other point to note is the comparison between the Adults and Paediatric PWCF in terms of 'Other Cultures'. The Paediatric group has a rate of 72%; in other words, almost three quarters of them reported positive cultures which were outside of the 'pathogens of interest' list. This is against 37% of the Adult group in our sample. So, there would appear to be a greater range of microbes found in the Paediatric population, but this might well be related to the numbers of PWCF in each group and may not be an actual difference.

A note of caution should be sounded: the numbers in these samples are relatively small and have been restricted to only those samples taken in 2005. As we move further into the future we will have extensive data to use for comparisons between the adult group and the paediatric group as well as between males and females.

Finally, we looked at all of the culture samples (Figures 23 & 24) to see the relationships between the major categories. The results are shown in pie charts.

These pie charts (Figures 23 &24) show us all the sputum samples and the proportion of each microbe within the overall microbial sample count.

All Cultures in Paediatric Group; Number, Type and Percentage of Positives;
Total no. PWFC: 159; Total no. Cultures: 909

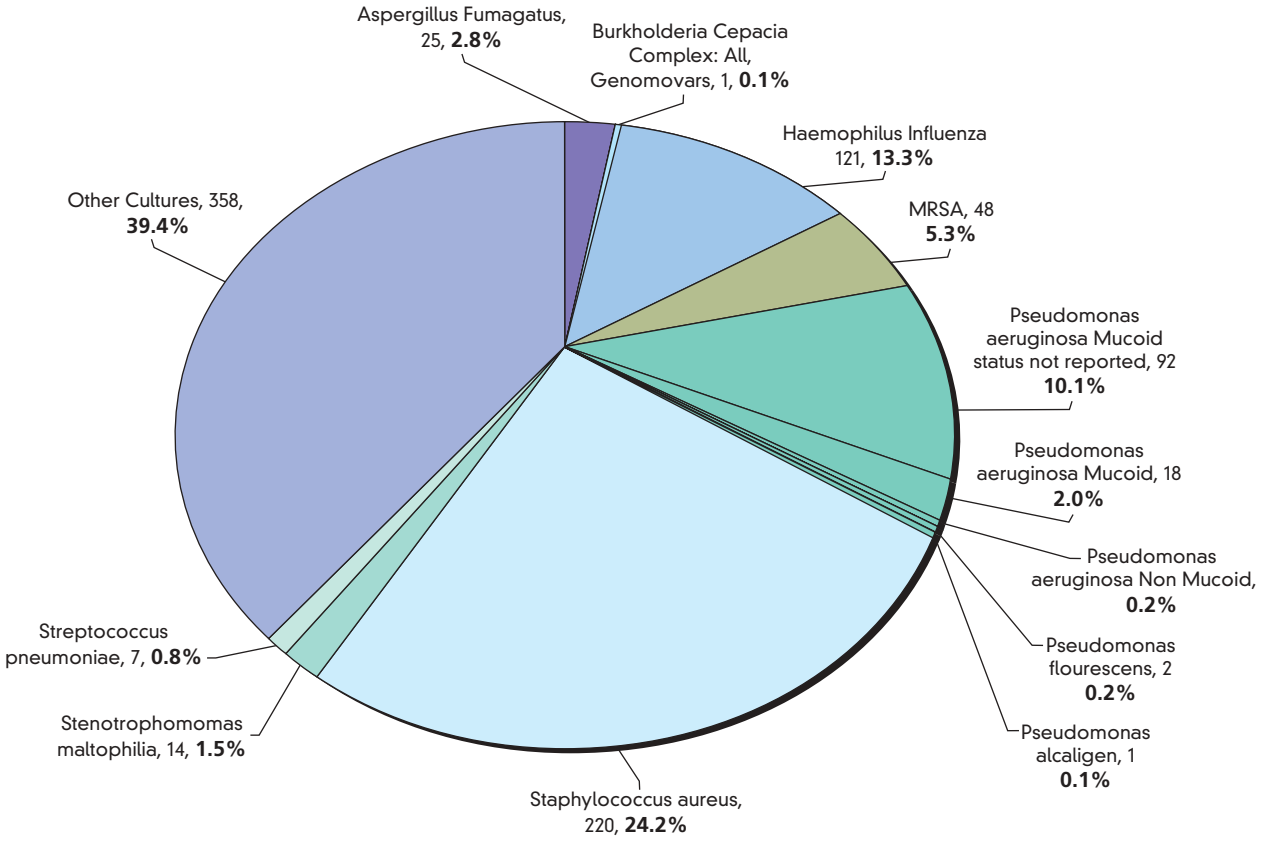


Figure 23: Cultures: Paediatric proportion types

All Cultures in Adult Group; Number, Type and Percentage of Positives;
Total no. PWCF: 52; Total no. Cultures: 243

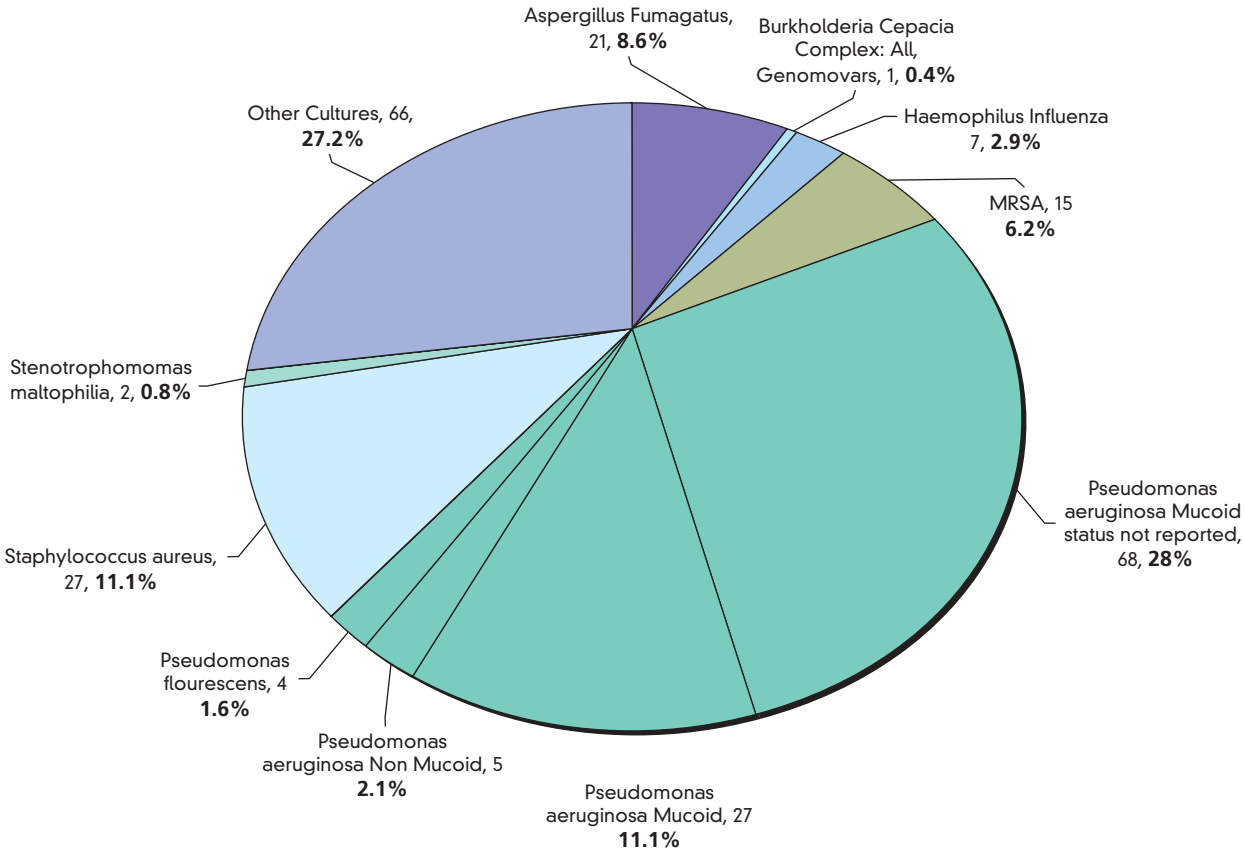


Figure 24: Cultures: Adult proportion types

There are a few items that stand out and these are in keeping with international observations:

- The dominance of Pseudomonas aeruginosa in the Adult group is obvious;
- Haemophilus influenza and all Pseudomonas strains are of approximate equal proportions in the under 18 age group while Staphylococcus aureus is the dominant microbe in this group.
- The incidence of MRSA appears to be similar in both age groups.

There were so few samples of Burkholderia cepacia in this set of data that we cannot make any comments on it.

Antibiotics

We have examined the antibiotic intake for those people who had antibiotic treatment in 2005, and report comparisons between Adult PWCF and Paediatric PWCF by the 'route of administration' and by antibiotic. The numbers of annual assessments examined in each group are 53 Adult and 159 Paediatric. The mean age for the Adult group is 25, while the mean age for the Paediatric group is 9 years of age. The cut-off age is 18; those PWCF over 18 at the time of Annual Assessment are included in the Adult group.

The summary table (Table 15) is shown below.

2005 ANTIBIOTICS BY ROUTE OF ADMINISTRATION

	n	Mean Age at AA	Number who had Oral Antibiotic (%)	Number on Cont Oral Antibiotics (%)	Number who had IV Hosp (%)	Number who had IV Home (%)	Number on Inhaled Antibiotic (%)
Adults	53	25	20 (38%)	9 (17%)	10 (19%)	11 (21%)	35 (66%)
Paeds	159	9	72 (45%)	16 (10%)	21 (13%)	4 (3%)	64 (40%)

Table 15: Antibiotics by route of administration

This table shows that there are higher percentages of Adult PWCF taking Inhaled antibiotics and who had Home IV antibiotics in 2005. The percentages of people who are on Oral, Continuous Oral, and who have had Hospital IV antibiotics in 2005 are similar in the two age groups. [There is a distinction made between 'Oral Antibiotic' and 'Continuous Oral Antibiotic': in the first case, these are people who have had discrete courses of oral antibiotics in the year; while the other group is taking oral antibiotics every day.] Figure 25 shows the route of administration of antibiotics in both the Paediatric and Adult groups.

Antibiotic route: Percentage of PWCF; Adult vs Paediatric, 2005

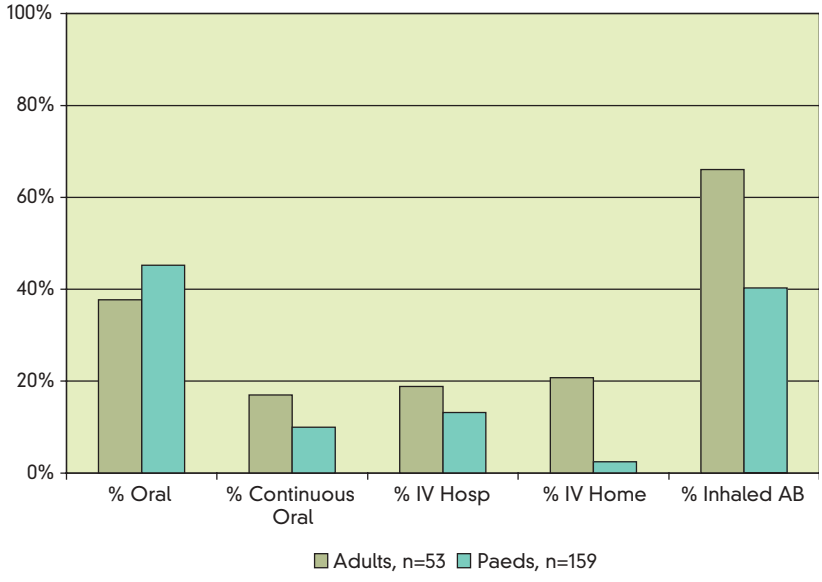


Figure 25: Antibiotic Route in Adults or Paediatrics

The database also allows us to consider the number of days treatment for each route and calculate the number of days treatment per person. By calculating the number of treatment days, we then see differences between Adult and Paediatric populations in terms of those who have had discrete courses of Oral antibiotics and IV antibiotics. See Figure 26.

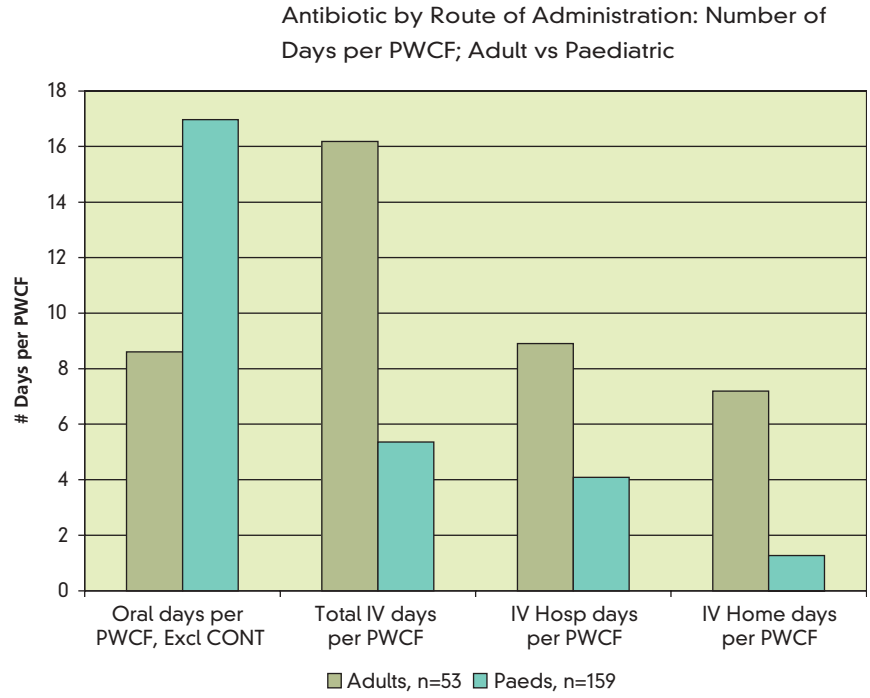


Figure 26: Route of Administration, Number of Days per PWCF

It would appear that even though the percentage of people in each group who take discrete courses of Oral antibiotics is similar (38% of Adults and 45% of Paediatrics), the number of courses (and days) is higher in the Paediatric group. This is found by calculating the number of days per person in the Oral group: the Paediatric group data yields 17 days per person, while the Adult group data yields 8.6 days per person.

This calculation also shows that the actual days of IV treatment per PWCF (both Hospital IV and Home IV) is considerably higher in the Adult group. The total number of days per person in each group is 5.4 days per person on IV antibiotics (both Home and Hospital) in the Paediatric group while the number is 16.2 days per person in the Adult group.

Now if we turn to the most frequently prescribed antibiotics, we again see differences between the two age groups.

Firstly, we calculated the total number of days' treatment for both age groups but split them between Hospital IV and Home IV. The number of days for Hospital IV is 1.8 times the number of days for IV Home antibiotics. See Figure 27.

Total # Days AB treatment, Hosp IV vs Home IV,
Total # PWCF = 211

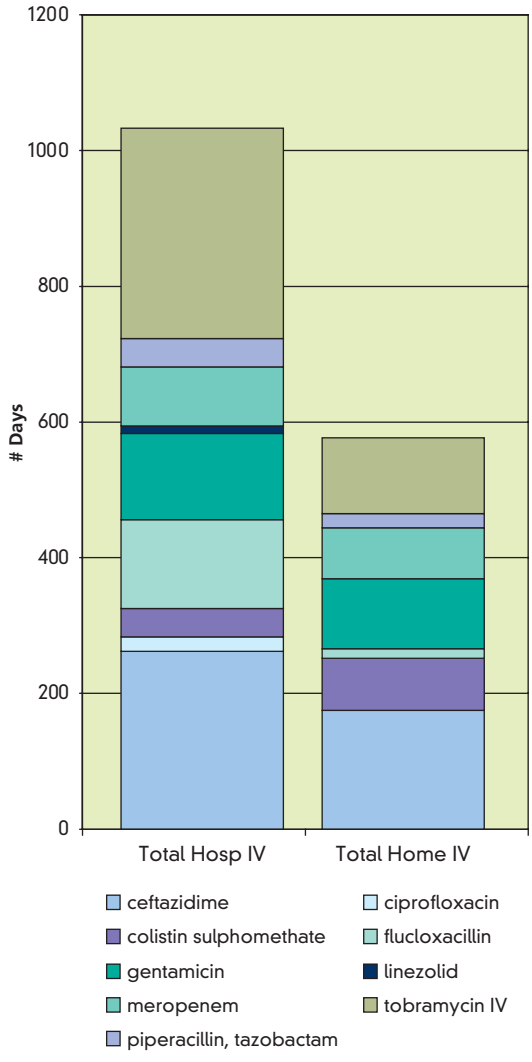
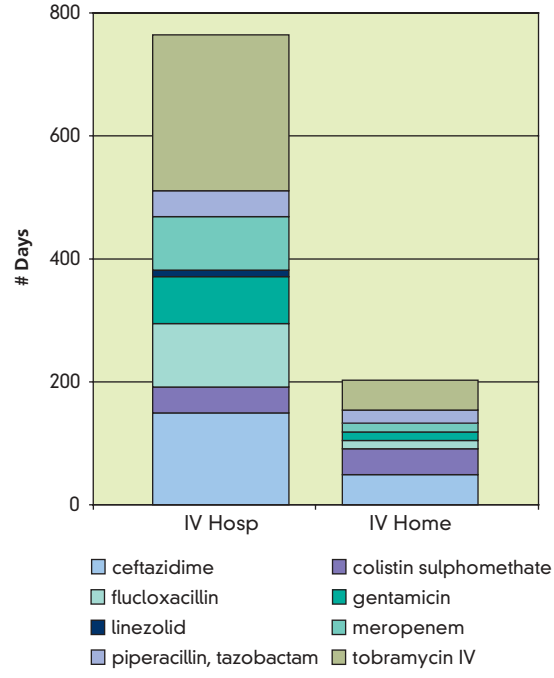


Figure 27: Days of AB treatment, Hospital IV vs. Home IV

Then if we consider each age group separately, we can see that there seems to be a preference for Home IV administration in the Adult group, while a trend towards Hospital IV shows in the Paediatric group. (See Figures 28 & 29).

Paediatric PWCF, # days AB treatment, Hosp IV vs Home IV
PWCF = 159



Adult PWCF, # days AB treatment, Hosp IV vs Home IV
PWCF = 52

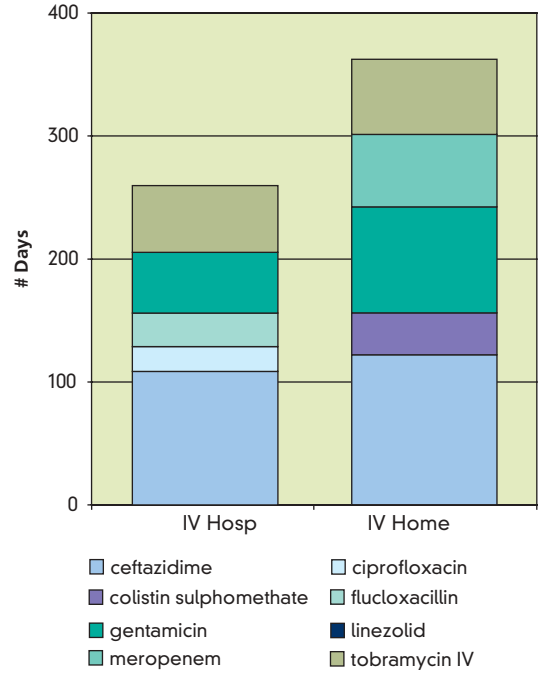


Figure 28 (top right): Antibiotics: Paediatric Hospital IV vs Home IV

Figure 29 (bottom right): Antibiotics: Adult Hospital IV vs Home IV

There are 3.8 times more Hospital IV days versus Home IV days in the Paediatric group, while there are 1.4 times more Home IV days versus Hospital IV days in the Adult group.

The types of antibiotics prescribed reflect the types of cultures found in both sets of PWCF. Ceftazidime and IV tobramycin are prescribed most often, followed by gentamicin, meropenem, flucloxacillin, colistin sulphomethate, piperacillin/tazobactam, ciprofloxacin and linezolid. See Figure 30.

Antibiotic data will be analysed in a more comprehensive fashion as the number of PWCF increases. It should be possible to calculate the cost of treating a person at home versus in hospital. But, that type of exercise is beyond the scope of this report.

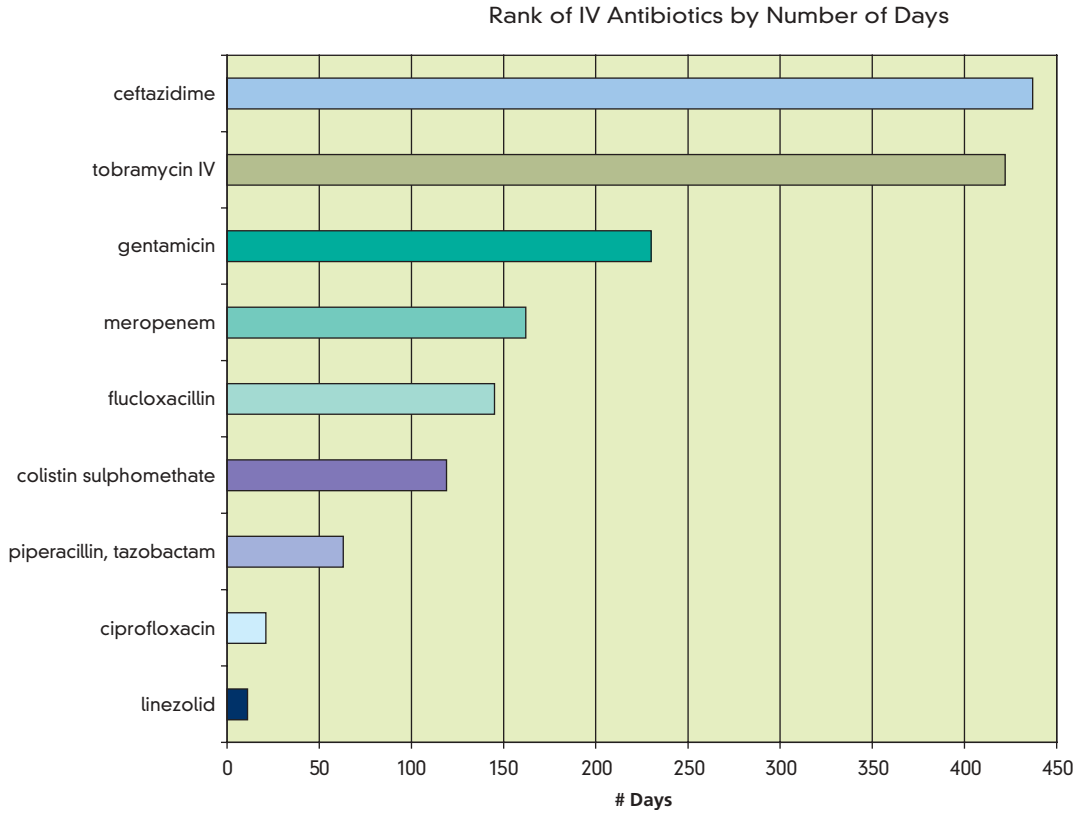


Figure 30: Most frequently prescribed IV antibiotics

Pulmonary Function and BMI

Pulmonary function and height/weight (from which you can calculate Body Mass Index, or BMI) are generally measured at the same time. We have combined data from 2004 and 2005 for summary. Many studies have shown that pulmonary function and body composition are positively associated.

The pulmonary function tests that we record are 'Forced Expiratory Volume in 1 second' (FEV_1) and 'Forced Vital Capacity' (FVC). Both of these tests are an indication of lung function. These results are usually compared with other people in the same age group who are of the same sex, weight, and height. [Pulmonary function tests are not normally carried out in children under 4/5 years old.] These values are then calculated as a "percent of the predicted" result for the normal population of that same age, sex, height, and weight. A value over 80% (for either FVC or FEV_1) is considered within the normal range.

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 pulmonary function tests. BMI is an important figure to track over time, as it will give some indication of nutritional health and growth.

In our data, we have separated the groups by sex and then taken an average of all of the people within an age group ('age bands').

Table 16 shows pulmonary function results for 176 males and 160 females. These tests were performed in either 2004 or 2005, but are all from separate PWCF.

PULMONARY FUNCTION TEST SUMMARY OF RESULTS, 2004 AND 2005 COMBINED

	Males			Females		
		Mean FEV_1 -%Predicted	Mean FVC %-Predicted		Mean FEV_1 -%Predicted	Mean FVC %-Predicted
Age Bands	**N**	**Males**	**Males**	**N**	**Females**	**Females**
5-9	52	90	92	39	81	82
10-14	44	70	79	40	71	77
15-19	40	72	86	38	70	82
20-24	25	57	71.5	19	56	68.3
25-29	8	54	60.6	10	62	81
30-39	6	32	59.3	11	56	70
>40	1	32	56	3	53	75.7
Total analysed	**176**			**160**		

Table 16: Pulmonary Function Test summary, 2004 & 05

This table is shown graphically in two charts. (See Figures 31 & 32)

FVC-% Predicted, Males v Females in Age Band Distribution

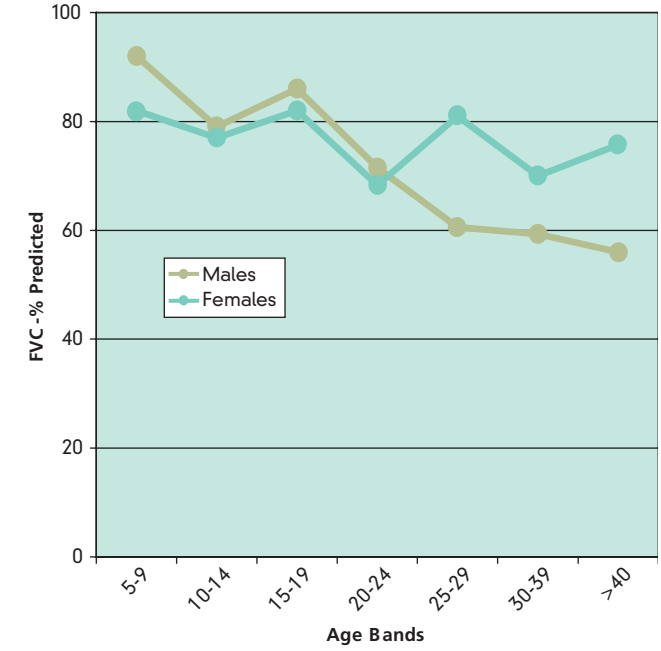


Figure 31: FVC-% predicted M vs. F in Age Bands

FEV_1-% Predicted, Males v Females in Age Band Distribution

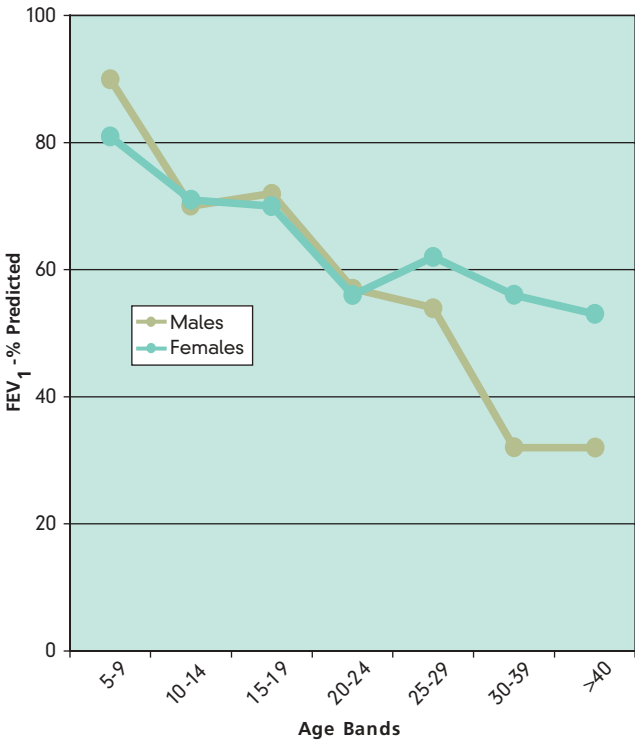


Figure 32: FEV_1-% predicted M vs. F in Age Bands

These show a similar pattern for males and females. In the youngest age group (ages 5-9 years) the males have slightly higher results than females; the next three age bands show that lung function is very similar in both sexes.

But in the PWCF who are over 25 years of age, the females show higher results than the males. This may be artefact or else it may indicate that as PWCF age, some factors come into play, which may leave females with a better outcome in later years. Whichever is the case, this should be studied further.

Finally, we calculated the average BMI score within each age band and Table 17 shows the results. This table includes the results from the children of ages 1 to 4; and again Annual Assessments from both 2004 and 2005 were combined.

BMI COMPARISON IN 2004 & 2005 COMBINED

Age Bands	N	MALES	N	FEMALES	Total in set
0-4	17	17.6	20	16.7	37
5-9	58	15.7	43	15.4	101
10-14	46	17.2	41	17.8	87
15-19	40	18.3	38	20.6	78
20-24	26	19.1	20	18.7	46
25-29	8	22.8	14	20.7	22
30-39	9	22.6	12	21.3	21
>40	1	23.7	3	22.6	4
Total analysed	**205**		**191**		**396**
BMI NOT done	**0**		**1**		**1**
Total AA's in set	**205**		**192**		**397**

Table 17: BMI Summary; 2004 & 05 combined

The figure (Figure 32) coupled with this table shows a much closer association between males and females in all age bands; with the males having a higher BMI in the older age groups.

Further study is needed to describe the relationship between body composition and pulmonary function as PWCF grow older.

Mean BMI: Age & Sex Distribution, 2004-05

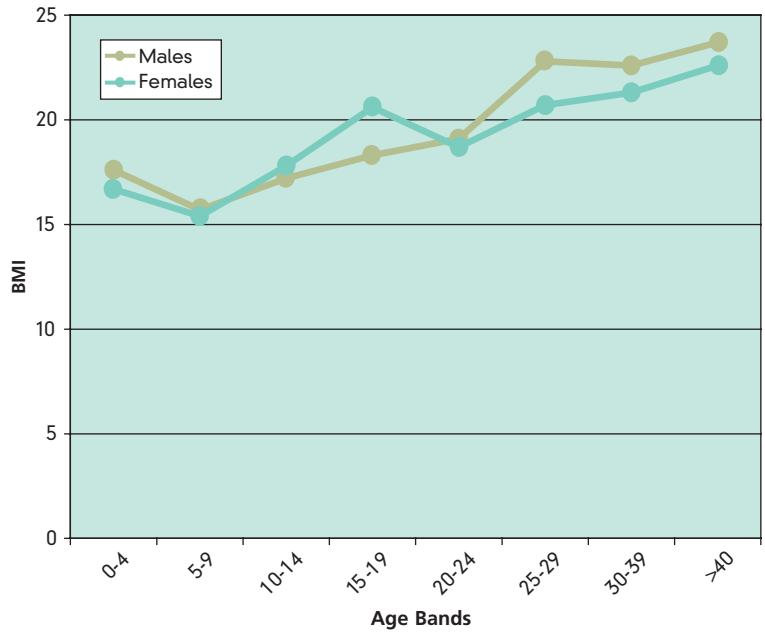


Figure 33: BMI comparison M vs. F in Age bands

Nutrition

It is extremely important for PWCF to maintain their weight and growth as this is closely linked to pulmonary function. The nutritional needs of PWCF are followed closely by the CF Centres. According to the recorded data on the CFRI, 96% of the Paediatric group attended a dietician at annual assessment; while 88% of the Adult group did as well (Table 18). Records for the group who attended a dietician in 2005 are presented. The percentage of each group is compared.

2005 ANNUAL ASSESSMENTS

	< 18		>=18	
Total # in group	159		52	
Number seen by Dietician at AA	153		46	
Ave age of group in yrs	9		25	
Type	**#**	**% of group**	**#**	**% of group**
Calorie Supplements	44	29%	24	52%
Vitamins	148	97%	43	93%
Minerals	10	7%	5	11%
Gastrostomy Feeds	11	7%	4	9%
Pancreatic Enzymes	143	93%	38	83%
Supplemental Feeding	42	27%	24	52%
Oral Supplements	29	19%	19	41%
Nasogastric	4	3%	2	4%
Parenteral Feeds	0	0%	0	0%
Other Supplement Feeds	0	0%	0	0%

Table 18: Nutrition Summary, 2005

Since the vast majority of Irish PWCF have pancreatic insufficiency, so too do most PWCF take both pancreatic enzymes and vitamins. These two parameters do not display differences with respect to age.

Supplements, however, become more necessary as people grow older. This is shown by a greater proportion of PWCF in the adult group taking oral supplements, calorie supplements, and supplemental feeding (Figure 34).

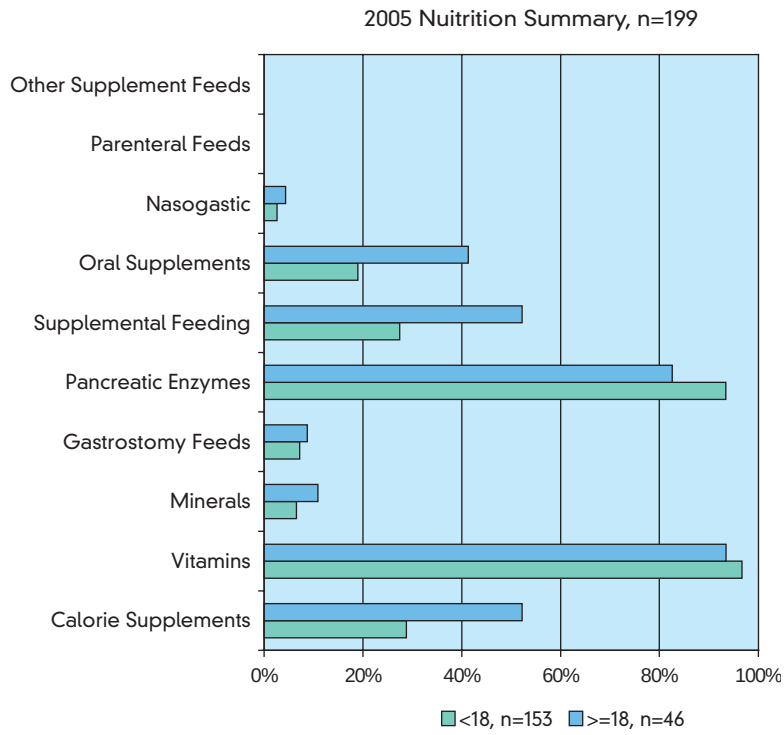


Figure 34: Nutrition Summary, 2005

Physiotherapy

The importance of continuous and consistent daily physiotherapy cannot be overemphasised. The CFRI records show very high visiting rates to the physiotherapist, although these recorded rates are not quite as high as the dietician rates (Table 19). This is more likely to be a characteristic of record keeping, rather than a description of the true situation. We have found that separate, detailed physiotherapy records are often kept in the PT department and changes in therapy regimes are not always found in the primary hospital chart. Thus, we assume that larger percentages of each group (Paediatric = 91%; Adult = 83%) are visiting with the physiotherapist regularly, but this will take further substantiation from information at the CF Centres.

Examination of the PT data reveals changes in approach when one progresses from the Paediatric group to the Adult group (Figure 35). It is important to note that most PWCF employ more than one technique on a daily basis. The PT modalities, 'percussion' and 'PEP mask' are used more frequently in the Paediatric group, while 'flutter' and 'autogenic drainage' are employed more by the Adult group. 'Acapella' as well as 'trampoline' appear to be techniques that are gaining in usage, beginning with the paediatric group. Both groups have similar proportions of PWCF utilising the 'Active Cycle of Breathing' techniques.

2005 ANNUAL ASSESSMENTS

	< 18		>=18	
Total # in group	159		52	
Total Seen by Physio at AA	145		43	
Ave age of group in yrs	9		25	
Type	**#**	**% of group**	**#**	**% of group**
PosturalDrainage	8	6%	2	5%
Percussion	45	31%	1	2%
ActiveCycleBreathing	27	19%	8	19%
AutogenicDrainage	2	1%	11	26%
Flutter	13	9%	10	23%
PositiveExpiratoryPressureMask	81	56%	14	33%
Acapella	19	13%	2	5%
Other	5	3%	0	0%

Table 19: Physiotherapy Summary, 2005

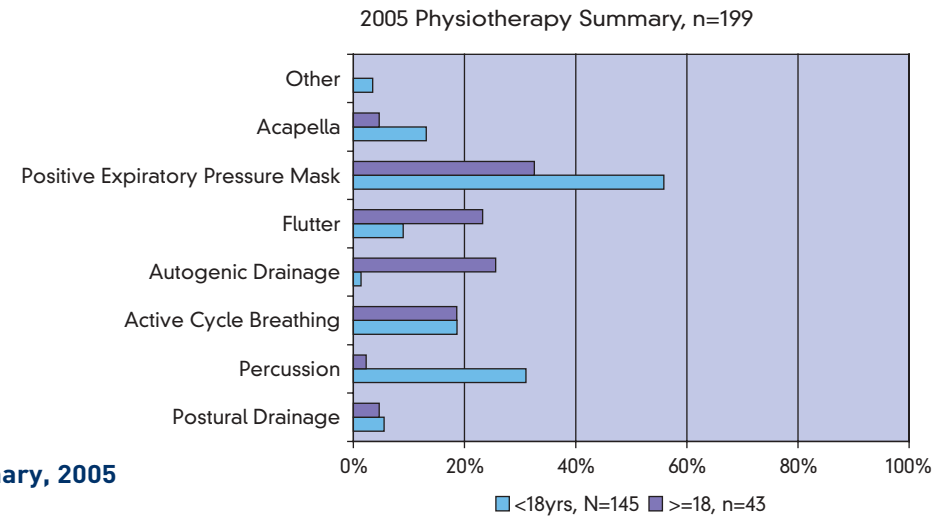


Figure 35 (right): Physiotherapy Summary, 2005

Long Term Medications

An examination of the types of long-term medications reflects the natural course of CF (Table 20 and Figure 36). First of all, there is greater usage of 'beta agonists', 'inhaled steroids', and 'rhDNase' in the adult group, reflecting the condition of the lungs. This is also reinforced by noting the larger use of 'night-time oxygen' in the adult group, although O_2 usage is still less than 4%, even in the older group. Secondly, there is an increased use of osteoporosis and diabetes treatment (i.e. insulin) in the older age group. The figure for osteoporosis treatment is 33% in the Adult group (versus 4% in the Paediatric group) and is roughly in agreement with the occurrence of osteopenia/osteoporosis complication rate of 38% (see Complications section, Miscellaneous). The figures for 'insulin' (17% in Adults versus 1% in Paediatrics) however, would indicate an increasing need for pancreatic treatment in the older group.

An interesting trend is apparent between the 'proton pump inhibitors' and the 'H_2 antagonists'. The usage of these products in the paediatric group favours the 'H_2 antagonists', while the 'proton pump inhibitor' is more widely prescribed in the adult group. One could conclude that there is a greater need for gastric acid control in the adults.

The only product which has a slightly higher proportion of usage in the paediatric group is 'ursodeoxycholic acid'. This is 13% versus 10% or a ratio of 0.7 Adult to Paediatric which is not a significant difference.

The main observation from this data is that it supports the 'Complications' data and the large ratios are related to organ systems that deteriorate over time.

2005 ANNUAL ASSESSMENTS

	< 18		>=18		Ratio Adult %age to Paed %age
Total # in group	159		52		
Ave age of group in yrs	9		25		
Type	**#**	**% of group**	**#**	**% of group**	
Beta Agonist	41	26%	32	62%	2.4
Inhaled Steroid	41	26%	27	52%	2.0
rhDNase	38	24%	21	40%	1.7
Anti Cholinergic	10	6%	3	6%	0.9
Aminophylline /Theophylline	0	-	4	8%	
Oral Steroid Every Day	0	-	2	4%	
Oral Steroid Alternate Days	2	1%	3	6%	4.6
Night-time Oxygen	2	1%	2	4%	3.1
Insulin	1	1%	9	17%	27.5
Osteoporosis Treatment	7	4%	17	33%	7.4
NSAID for Arthropathy	0	-	1	2%	
H2Antagonist	19	12%	2	4%	0.3
Proton Pump Inhibitor	17	11%	10	19%	1.8
Lactulose	5	3%	3	6%	1.8
Urso Deoxycholic Acid	21	13%	5	10%	0.7
Other Medication	2	1%	6	12%	9.2

Table 20: 2005 Long Term Medications Summary

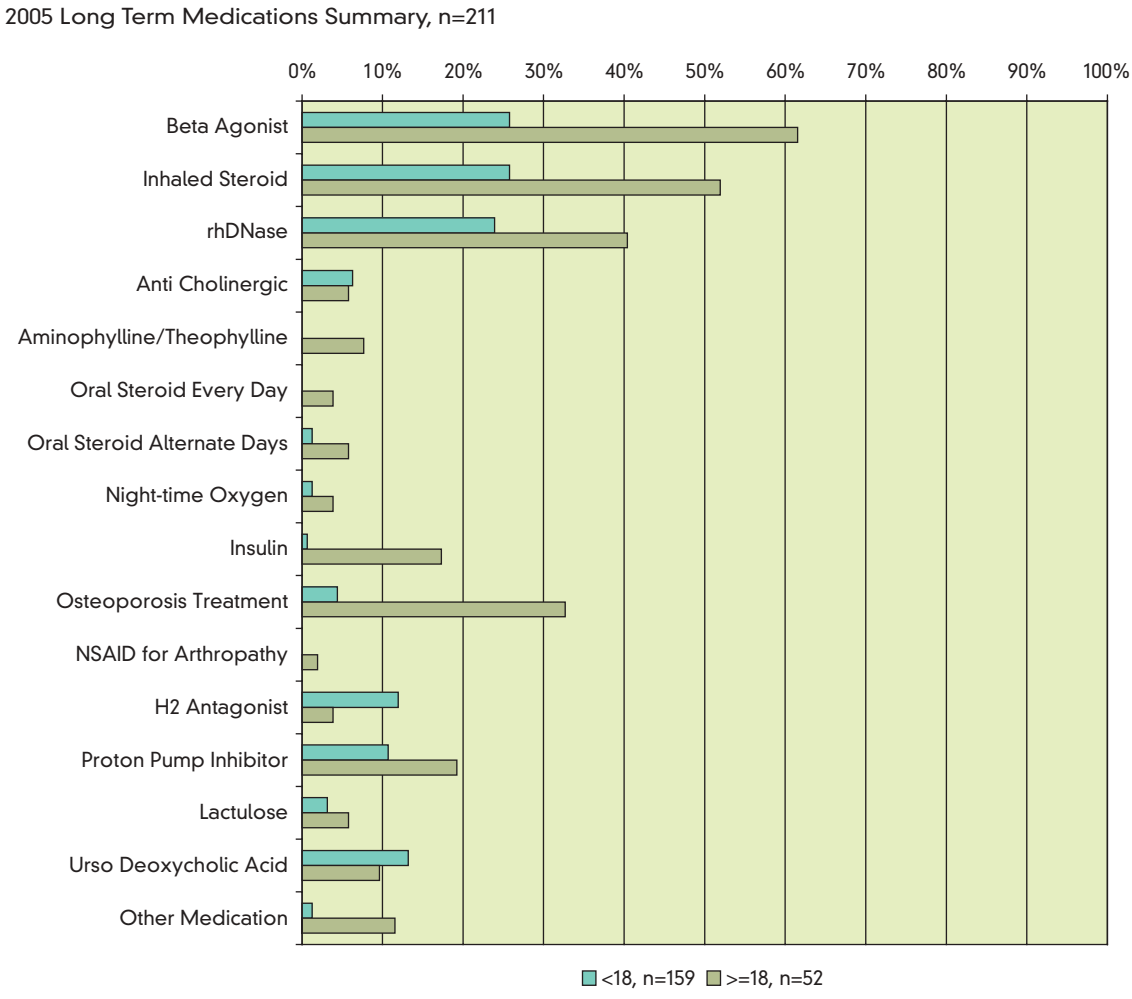


Figure 36: Long Term Medications Summary, 2005

Social Data

Social data is particularly difficult to capture. The main reason for this is that there is no specific section in the medical chart to record such information. We rely on anecdotal notes from out-patient visits or nurses' notes as sources.

In order to improve this data gathering we would probably need to carry out a proper study which would involve postal questionnaires as well as follow-up one-to-one interviews. This would be a worthwhile project as it would contribute to the growing amount of 'Quality of Life' data that is emerging from many countries.

What is very heartening is the fact that from the small amount of data that we do have (Table 21), we can see that a very small percentage of PWCF are off work or school due to illness for more than 8 weeks in a year. In fact, the vast majority are off school or work for less than two weeks each year, and this would not be different to the entire working or school-going population. And, approximately 40% take no days off due to illness. These figures probably attest to a good deal of treatment given at home, such as intravenous antibiotics.

WORK OR SCHOOL DAYS OFF IN 2005

	PWCF in Primary School	PWCF in Secondary School	PWCF Working Full or Part time
Number in Group	**18**	**8**	**10**
No days off	7	3	4
Less than 2 weeks	5	4	4
Less than 8 weeks	5	0	2
More than 8 weeks	1	1	0
Number in Group	**18**	**8**	**10**
No days off	39%	38%	40%
Less than 2 weeks	28%	50%	40%
Less than 8 weeks	28%	0%	20%
More than 8 weeks	6%	13%	0%
PWCF with No days off or Less than 2 wks	**67%**	**88%**	**80%**

Table 21: Social Data Summary, 2005

Financial

The following financial summary (Table 22) lists the major expenses for the CFRI in 2004.

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
- A second employee was taken on in January, 2004. Subsequent increases compared with previous years are shown in the 'Set-up Hardware' and 'Travelling Expenses' categories.
- The cost of the Annual Report was actually paid for in 2003, so does not appear on this statement. It was shown in the previous Annual Report.
- This summary does not show salaries for the employees.
- The accounts were audited by Kelly Murray Scollard, Stephens Lane, Dublin 2.

FINANCIAL SUMMARY 2004

INITIAL SYSTEM SPECIFICATION Hosting Fee, Domain maintenance, Security Certificate	€15,056
DEVELOPMENT COSTS Database Application, programming	€25,108
SET-UP HARDWARE Laptop, printer, software	€2,925
TRAVELLING EXPENSES	€12,927
ADMINISTRATION COSTS Telephone, Heat, electricity, printing, office supplies, insurance	€6,619
DATA ENTRY PROJECT	€5,580
ANNUAL REPORT Design, printing	
TOTAL	**€68,215**

Table 22: Financial Summary, 2004

Acknowledgements

The CFRI moved to the University College Dublin campus in Belfield in September, 2005 and is now a tenant at the School of Public Health and Population Science. This move was facilitated by Prof Muiris X Fitzgerald, Dean of Medicine and Prof Cecily Kelleher, Head of the School of Public Health and Population Science. We now have a wealth of academic resources that are much appreciated.

ECOM-Ireland continues to consult, programme, build queries, and develop the website / database to top international standards.

In early 2005 the HSE convened a multi-disciplinary working party "To review the current configuration and delivery of services to CF patients in the Republic of Ireland, across hospital and community, and to make recommendations for reconfiguration, improvement, and development." The CFRI would like to recognise this work as it includes resources and a commitment to a more permanent status for the registry. All participants should be thanked for their efforts.

The Adult group of the CFAI continues to provide support and advice whenever called upon to do so. It is heartening too, to receive so many calls from interested parents who would like to ensure that their children have been enrolled.

Without the cooperation of the CF Nurse Specialists this project could not continue. While they deliver compassionate service to their patients, they also contribute ideas and proposals to the CFRI.

The European CF Registry Board, through the ECFS has continued to give encouragement and advice to all participating countries through their extensive network. Many countries have shared their experience and contacts. The German, French, and UK databases are of gold standard quality, and represent solid, enviable targets for the remainder.

Finally, as always the Registry Management Committee has unselfishly given their support and input to the CFRI.

Cystic Fibrosis Registry of Ireland

UCD School of Public Health and Population Science

Woodview House

University College Dublin

Belfield, Dublin 4, Ireland

www.cfairegistry.org

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 with the help of patient registries. Cystic fibrosis registries gather information on all aspects of a patient's condition. They act as 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 this analysis that better management of CF may be achieved

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