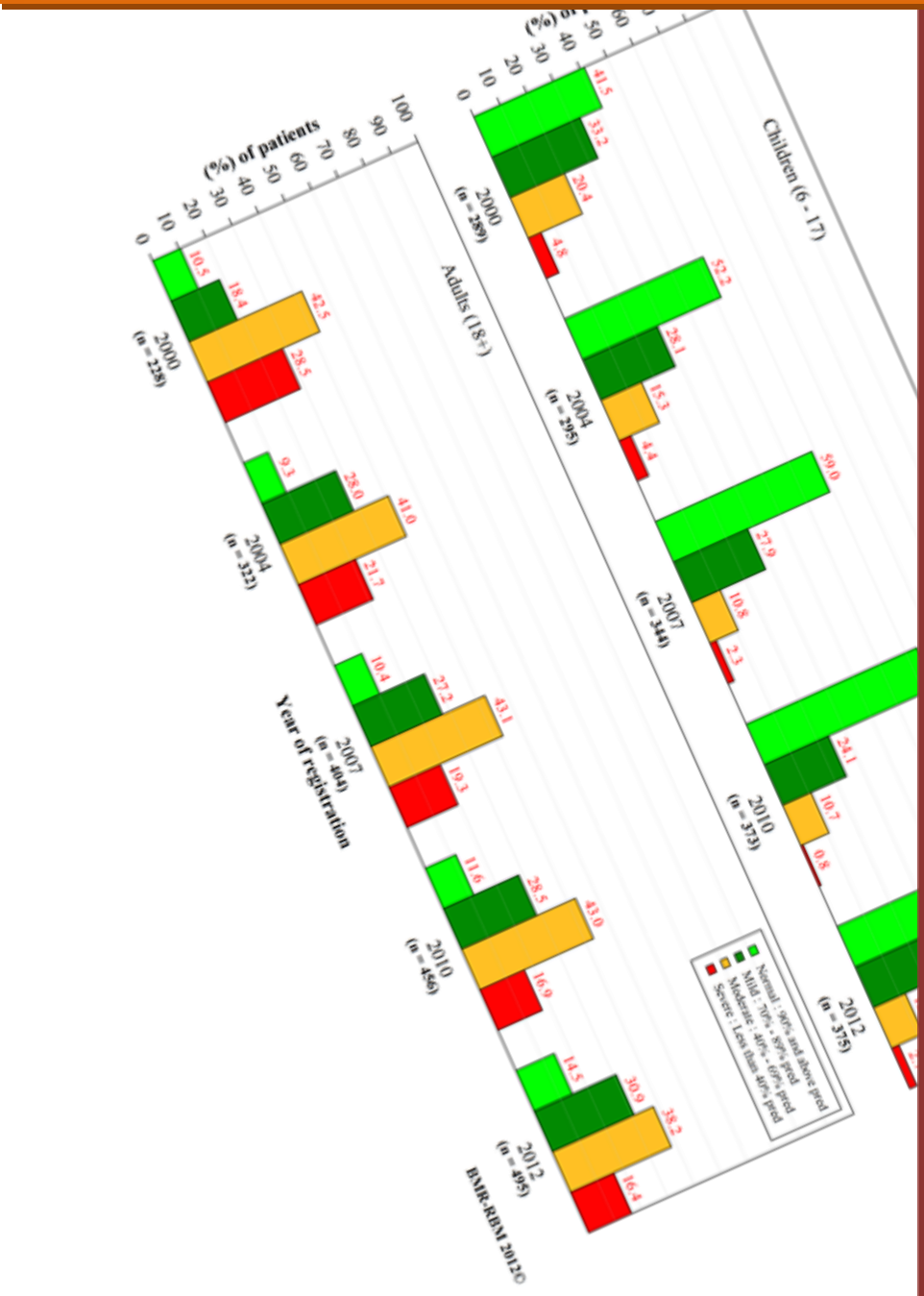
2012

WETENSCHAPPELIJK INSTITUUT VOLKSGEZONDHEID
INSTITUT SCIENTIFIQUE DE SANTÉ PUBLIQUE

ANNUAL REPORT
BELGIAN CYSTIC FIBROSIS REGISTRY
(Public version)



The Belgian Cystic Fibrosis Registry
(BCFR 2012)

Partners and Collaborators

© Scientific Institute of Public Health, Brussels 2014.
This report may not be reproduced, published or distributed without the consent of the IPH.

Public Health and Surveillance| October 2014
Brussels, Belgium
Editor: Dr Johan Peeters | General Director | Rue J. Wytsmanstraat 14 | 1050 Brussels
Internal reference Nr: PHS report/2014-037
Deposit Nr: D/2014/2505/57

Authors :
Simeon Situma WANYAMA
Muriel THOMAS

Contributors, members of the board of the BMR-RBM:
A. Malfroot (UZ - Brussel, Brussel)
E. De Wachter (UZ - Brussel, Brussel)
S. Verhulst (UZ - Antwerpen, Antwerpen)
M. Lequesne (UZ - Antwerpen, Antwerpen)
F. De Baets (UZ - Gent, Gent)
S. Van Daele (UZ - Gent, Gent)
K. De Boeck (UZ - Gasthuisberg, Leuven)
F. Vermeulen (UZ - Gasthuisberg, Leuven)
P. Lebecque (Cliniques Universitaires St-Luc, Bruxelles)
J.-P. Sacré (CHR de la Citadelle, Liège)
D. Baran (Hôpital Erasme, Bruxelles)
C. Knoop (Hôpital Erasme, Bruxelles)
V. Van Casteren (WIV-ISP, Brussel)

Research funded by the National Institute for Health and Disability Insurance (RIZIV-INAMI)

Accredited Belgian CF Reference centres

Mucoviscidose referentiecentrum UZ Brussel
UZ-Brussel — Laarbeeklaan, 101 — 1090 Brussel
A. Malfroot, E. De Wachter, E. Vanderhelst

Muco-Referentiecentrum Antwerpen
St Vincentiusziekenhuis — St Vincentiusstraat, 20 — 2018 Antwerpen
V. Nowé, I. Stappaerts
UZ-Antwerpen — Wilrijkstraat, 10 — 2650 Antwerpen
M. Lequesne, S. Verhulst

Referentiecentrum voor Mucoviscidose UZ Gent
UZ-Gent — De Pintelaan, 185 — 9000 Gent
F. De Baets, G. Joos, S. Van Daele

Muco-Referentiecentrum Gasthuisberg Leuven
UZ-Leuven – Campus Gasthuisberg — Herestraat, 49 — 3000 Leuven
K. De Boeck, F. Vermeulen, L. Dupont, M. Moens

Centre de référence de la Mucovicidose UCL
Cliniques Universitaires St-Luc — Avenue Hippocrate, 10 — 1200 Bruxelles
P. Lebecque

Centre Liégeois de rééducation fonctionnelle pour la Mucoviscidose
CHR La Citadelle — Boulevard du 12ème de ligne, — 4000 Liège
J.P. Sacré
Clinique de l'Espérance — Rue St-Nicolas, 447-449 — 4420 Montegnée
F. Piérart

Institut de Mucoviscidose ULB
Hôpital Universitaire des Enfants Reine Fabiola — Avenue J.J. Crocq, 15 — 1020 Bruxelles
G. Casimir, L. Hanssens
Hôpital Erasme — Route de Lennik, 808 — 1070 Bruxelles
C. Knoop

Registry Management

Scientific Institute of Public Health (WIV - ISP)
OD Public Health and Surveillance
Rue J. Wytsman, 14
1050 Brussels

V. Van Casteren	**: Programme responsible**	☎ **02/642.50.30 (54.07)**	🖷 **02/642.54.10**
M. Thomas	**: Project responsible**	☎ **02/642.50.23**	
S. S. Wanyama	**: Biostatistician**	☎ **02/642.57.67**	
Y. Pirson	**: Administrative**	☎ **02/642.57.41**	

http://www.wiv-isp.be/epidemio/epien/index20.htm

Suggested reference:
Annual Report Belgian Cystic Fibrosis Registry (BCFR - Public version 2012) , Brussels, Belgium.

CONTENTS

SUMMARY **13**

CHAPTER 1: BACKGROUND **14**

1.1 WHAT IS CYSTIC FIBROSIS? 14

1.2 CF PATIENT CARE IN BELGIUM 16

1.3 THE BELGIAN CYSTIC FIBROSIS REGISTRY (BMR-RBM) 16

1.4 OBJECTIVES OF THE CYSTIC FIBROSIS PATIENT REGISTRY 16

CHAPTER 2: POPULATION AND METHODOLOGY **17**

2.1 STUDY POPULATION 18

2.2 DATA COLLECTION 18

2.3 SOFTWARE 18

2.4 FEEDBACK 18

2.5 DATA FLOW 19

DEMOGRAPHIC SUMMARY OF DATA REPORTS 2009 - 2012 20

CHAPTER 3: DEMOGRAPHIC DATA **21**

3.1 AGE ON DECEMBER 31 2012 22

3.2 PREVALENCE OF CYSTIC FIBROSIS PER DISTRICT OF RESIDENCE 23

3.3 PWCF UNDER FOLLOW-UP PER DISTRICT OF RESIDENCE 24

3.4 CASES BY DISTRICT OF RESIDENCE 25

CHAPTER 4: DIAGNOSIS **26**

4.1 SYMPTOMS AND CLINICAL REASONS SUGGESTING CF 27

4.2 DOCUMENTATION OF CF DIAGNOSIS 28

4.3 AGE AT DIAGNOSIS 29

4.4 GENOTYPE 30

CHAPTER 5: ANTHROPOMETRY (HEIGHT, WEIGHT AND BMI) **31**

5.1 BMI PERCENTILES USING CACHERA REFERENCES 32

5.2 BMI PERCENTILES USING THE CDC GROWTH CHARTS 32

5.3 HEIGHT PERCENTILES USING THE CDC GROWTH CHARTS 33

5.4 WEIGHT PERCENTILES USING THE CDC GROWTH CHARTS 33

CHAPTER 6: SPIROMETRY (LUNG FUNCTION) **34**

6.1 PERCENTAGE OF PREDICTED FEV_1 35

6.2 FEV_1 CATEGORIES BY AGE GROUP 36

CHAPTER 7: MICROBIOLOGY **39**

7.1 ANNUAL PREVALENCE OF ISOLATED PATHOGENS 40

7.2 ANNUAL PREVALENCE OF CHRONIC INFECTIONS 40

CHAPTER 8: COMPLICATIONS 43
8.1 RESPIRATORY COMPLICATIONS 44
8.2 GASTRO-INTESTINAL AND ENDOCRINE COMPLICATIONS 45
8.3 MISCELLANEOUS COMPLICATIONS 46
CHAPTER 9: THERAPY, MEDICATION AND HOSPITALIZATION 47
9.1 VISITS TO CF CARE CENTERS AND HOSPITALIZATION 48
9.2 RESPIRATORY THERAPIES 49
9.3 DIGESTIVE AND NUTRITIONAL THERAPIES 50
9.4 OTHER TREATMENTS 50
9.5 INTRAVANEOUS ANTIBIOTICS 51
9.6 ORAL ANTIBIOTICS 51
CHAPTER 10: TRANSPLANTS AND CYSTIC FIBROSIS 52
10.1 TRANSPLANT STATUS 53
10.2 TYPE OF TRANSPLANT 54
CHAPTER 11: REPORTED DEATHS 55
11.1 AGE AT DEATH 56
11.2 PRIMARY CAUSE OF DEATH 57
CHAPTER 12: EDUCATION AND EMPLOYMENT 58
12.1 EDUCATION 59
12.2 SOCIAL ALLOWANCES AND EMPLOYMENT 59
REFERENCES 60
APPENDIX I 62
BMR-RBM DIGITAL QUESTIONNAIRE VERSION 1.0 REGISTRATION 2012 62
APPENDIX II 73
LIST OF ABBREVIATIONS AND DEFINITIONS 73

LIST OF TABLES

Table 1: A comparison of demographic data for years 2009 - 2012 ..... **20**
Table 2: Age on December 31 2012 by gender **22**
Table 3: District of residence **25**
Table 4: Symptoms and clinical reasons for CF diagnosis **27**
Table 5: Documentation of CF diagnosis including sweat tests, clinical symptoms, genotyping and family history **28**
Table 6: Genotype mutation pairs **30**
Table 7: Most frequently reported alleles and mutations **30**
Table 8: Proportions in each FEV_1 severity category for children and adults **36**
Table 9: Isolated pathogens and microbes 2009 - 2012 ..... **40**
Table 10: Chronic infections and colonisation 2009 - 2012 ..... **40**
Table 11: Prevalence of respiratory complications **44**
Table 12: Prevalence of gastro-intestinal and endocrine complications **45**
Table 13: Other complications reported **46**
Table 14: Physiotherapy, inhalation therapy , oral anti-inflammatory and antibiotics **49**
Table 15: Digestive and nutritional therapies **50**
Table 16: Other treatments **50**
Table 17: Type of transplant by year **54**
Table 18: Categorized age at death **56**
Table 19: Primary causes of death for reported cases **57**
Table 20: Education level **59**
Table 21: Social allowances or benefits and employment **59**

LIST OF FIGURES

Figure 1: Data flow chart **19**
Figure 2: Age on Dec 31, 2012 by gender **22**
Figure 3: Captured prevalence per 100,000 inhabitants based on district of residence in January 2012 ..... **23**
Figure 4: Number of PWCF per district of residence in January 2012 ..... **24**
Figure 5: Age at Diagnosis **29**
Figure 6: Median BMI percentile by age group and year **32**
Figure 7: CDC BMI Z-Score percentiles by age **32**
Figure 8: CDC height percentile by age category **33**
Figure 9: CDC Weight percentiles by age **33**
Figure 10: Mean percentage of predicted FEV_1 by age **35**
Figure 11: Mean percentage of predicted FEV_1 by age and gender **36**
Figure 12: Percentage of predicted FEV_1 groups by age group **37**
Figure 13: Percentage of predicted FEV_1 groups by age group for selected years **37**
Figure 14: Mean percentage of predicted FEV_1 by age group for selected years **38**
Figure 15: Prevalence of *Burkholderia cepacia complex* infections by year and age **41**
Figure 16: Prevalence of *Pseudomonas aeruginosa* infections by year and age **41**
Figure 17: Prevalence of *Pseudomonas aeruginosa, Achromobacter xylosoxidans and Burkholderia cepacia complex* by age group and year **42**
Figure 18: Prevalence of *Achromobacter xylosoxidans* by age group and year **42**
Figure 19: Number of hospitalization days **48**
Figure 20: Proportion of patients hospitalized for more than two weeks by age and year **48**
Figure 21: Proportion that used IV antibiotics treatment by age category **51**
Figure 22: Days of oral antibiotics **51**
Figure 23: Number of reported deaths since 1998 by age category **57**

ACKNOWLEDGMENTS

We would like to most sincerely thank all the partners involved in the provision of various services that go toward better care of the people with CF. We single out the National Institute for Health and Disability Insurance (RIZIV-INAMI) for their continued financial support and the CF reference centres and their multidisciplinary teams of health care professionals for their continued support to the registry and care to the patients. We also seek to recognize the contributions of the Belgian Cystic Fibrosis patients' Association (BCFA) for their continued support through project grants to various researchers for CF related themes. Finally, we also thank the patients and their parents or care givers for their willingness to participate in the annual data collection processes. This report, and the outcomes of various research questions, enhances the continued monitoring of CF disease by providing a better understanding of disease progression to researchers while stimulating ideas for research into novel treatments and disease management strategies.

The registry team

SUMMARY

This report presents the data collected in 2012. It is our hope that the report will continue to enlighten the general public about Cystic Fibrosis in general and the care available to the Belgium CF population in particular.

Since its establishment, the Belgium CF registry (BMR-RBM) has grown steadily and had 1184 patients registered in 2012. This number excludes 8 whose diagnosis for CF was revoked. There were 27 newly diagnosed patients in 2012, among them three adults, with a median age at diagnosis of 2.3 months and age range 0.1 – 35.9 years. Most of the new patients were genotyped.

Among the patients in follow-up in 2012, 51.4% were male and 56.4% adults with a median age of 20.3 years. This can be compared to the start of the registry 13 years ago when 39.0% were adults with a median age of 14.9 years. 45.4% of the patients are homozygous for the F508del mutation while 40.2% are F508del heterozygous. The main reasons for diagnosis of CF remained acute or recurrent respiratory problems (43.1%) and failure to thrive (24.5%). About 17.0% were diagnosed via neonatal screening even though there is no national neonatal screening program in Belgium as yet. Within the year, 10 deaths were reported (5 of them in transplanted patients) with age at death range of 9.3 – 52.0 years while 8 patients benefitted from a lung transplant.

Among the adults, the proportion of patients with BMI < 18.0kg/m² continues to decline from about 36.3% in 1998 to 17.4% in 2010 and 13.4% in 2012; this decline was noted even amongst the F508del homozygous patients. Amongst the patients up to 20 years, the proportion with BMI below the tenth percentile has also been declining over the years. The above suggests better nutritional management in the patients. The patient population continues to record an improvement in lung function expressed as the mean percentage of predicted FEV_1. Among the F508del homozygous patients, 38.0% of the children and 5.1% of the adults had $FEV_1 \geq 90.0\%$ of predicted in 1998 compared to 52.9% and 7.0% in 2010 and 59.4% and 10.5% respectively among the children and adults in 2012.

The overall annual prevalence of *Pseudomonas aeruginosa* reported in 2012 was 42.4% and was stable compared with a prevalence of 41.6% reported in 2009 . The prevalence of the *Burkholderia cepacia* complex on the other hand had remained lower than 3.0% over the years till 2010 where a 2.4% prevalence was reported. In 2011 the prevalence was 3.6%, an increase (though not statistically significant) while in 2012 it was 4.0%. There has been a steady increase in the prevalence of an emerging infection *Achromobacter xylosoxidans* from 5.9% in 2009 to 10.7% in 2012.

CHAPTER 1: BACKGROUND

This section defines and briefly describes what CF is, its care in Belgium, the history, role and objectives of the Belgian Cystic Fibrosis Registry (BMR-RBM) and the important contributions of the Belgian Cystic Fibrosis patients' Association (BCFA), the National Institute for Health and Disability Insurance (INAMI - RIZIV) and the CF reference centers in the provision of care and management of CF.

1.1 WHAT IS CYSTIC FIBROSIS?

Cystic Fibrosis (CF) is a progressive hereditary disease with autosomal recessive transmission: only subjects who have inherited two disease causing mutations – one from each parent - are affected. Parents who are both carriers for a CFTR mutation associated with classical CF have a 1 in 4 chance of having a child with CF, in each pregnancy. It is commonly found in populations of white Caucasian descent, such as those of Europe, North America and Australasia. Prevalence is however different from country to country and is 1/2850 live births in Belgium [1]. The earliest clear medical descriptions of CF date from the 1930s [2, 3] . CF obviously existed prior to this dates even though it remained largely unrecognized and so went undiagnosed. In these early times, it was even thought of to be a result of witchcraft [1] (http://www.cfmedicine.com/history/earlyyears.htm).

The disease is caused by the alteration (mutation) of the *CFTR* (Cystic Fibrosis Transmembrane Conductance Regulator) gene which is located on the long arm of chromosome 7. More than 1800 (http://www.genet.sickkids.on.ca/SearchPage.html) mutations have been identified in the *CFTR* gene since its discovery in 1989 [4], but not all are associated with classical CF . The *CFTR* gene codes for the CFTR protein. This is an ion channel involved in the regulation of chloride ion transport across the cell membrane. It is mainly found in the cell membranes of the respiratory and digestive tract, the sweat glands and the reproductive tract. The dysfunction of the *CFTR* protein leads to the production of sweat with a high salt content and mucus secretions with an abnormal viscosity causing dysfunction of many organs such as the lungs, pancreas and liver.

In the respiratory tract, thick mucus production results in persistent cough caused by chronic infection and inflammation leading to severe bronchial obstruction and finally lung destruction. In the pancreas, the sticky exocrine pancreatic secretions lead to obstruction and blocking of the ducts with secondary damage to the secretory gland tissue. Diminished secretion of pancreatic enzymes leads to fat and protein malabsorption causing steatorrhoea (fatty stools) and failure to thrive. Fat malabsorption also causes deficiency of fat soluble vitamins (A, D, E and K).

Most of the children with CF have a history of recurrent chest infections, steatorrhoea and failure to thrive. New-borns with CF can be affected by meconium ileus: intestinal obstruction with vomiting, abdominal distension and delay in passing the first meconium stools. The spectrum of presenting features is very wide and can vary with the age at time of clinical presentation. The diagnosis is usually made in early childhood but in some patients with late or milder symptoms it can occur later into adulthood.

Although there is no neonatal CF screening program in Belgium yet, infants with CF can be identified in the first weeks of life by assessing their blood immunoreactive trypsin (IRT) combined with the most frequent CFTR mutations. The sweat test remains the gold standard for the diagnosis of CF. In the majority of patients with typical features, the sweat test is diagnostic. It will reveal an excessive quantity of chloride (salt) (> 60 mEq/L). In atypical forms, the sweat test chloride levels can fall into the intermediate range (30-60 mEq/L).

It is advised to perform genotyping in all patients with CF, to identify the CF causing mutations. The most common mutation in Belgium is F508del.

Today there is no causal cure for CF, treatment is symptomatic and is essentially based on respiratory (e.g. physiotherapy, inhalation therapy, antibiotics), digestive and nutritional management (e.g. pancreatic enzymes and hypercalorie diet). Due to medical progress and intensification of the care for patients with CF, the quality of life and the life expectancy have increased. The first therapy aimed to correct the basic defect has been approved for use in a subset of patients carrying the G551D mutation [5] and is evaluated for patients carrying other gating mutations.

1.2 CF PATIENT CARE IN BELGIUM

Since 1999, 7 CF reference centres have been accredited by the National Institute for Health and Disability Insurance (INAMI - RIZIV) and receive financial support. An annual care and revalidation agreement (CF convention) for patients with CF is signed between each of the 7 CF reference centres and the RIZIV-INAMI[6, 7]. Each centre has specific expertise in CF care and ensures multidisciplinary follow-up of the patients in order to provide optimal medical, paramedical, psychological and social care to the patient and their relatives. Most of the persons with CF in Belgium are followed in one of the national CF reference centres and are registered in the national CF Registry (BMR-RBM).

1.3 THE BELGIAN CYSTIC FIBROSIS REGISTRY (BMR-RBM)

The intent of a registry is to include, in a single database, the entire population of people with a given condition (or meeting a certain criteria), say chronic illness, within a defined geographical area.

The BMR-RBM was started in 1999 as a scientific project initiated by the Medical Committee of the Belgian Cystic Fibrosis Association (BCFA[1]) and the 7 CF-reference centres in Belgium collecting data of 1998. It was coordinated by the Vrije Universiteit Brussel (VUB). The main sponsor was the CF-Patient organisation; the cosponsor was the Fund Alfonse and Jean Forton of the King Baudouin Foundation. The VUB sponsored the overheads. After 5 years the scientific project came to an end and new sponsors were contacted.

In 2006, the RIZIV-INAMI became the principal sponsor and the Registry was transferred to the section of Public Health and Surveillance of the Scientific Institute of Public Health (WIV - ISP). Since then, the WIV - ISP ensures the collection and the management of the data under the supervision of the board of the BMR-RBM and the guidance of a scientific steering group. The board consists of a physician from each CF centre and the scientific collaborators of the WIV - ISP. The scientific steering group holds all stakeholders (representatives of the INAMI-RIZIV, patient association, CF Centers and scientific collaborators of the Scientific Institute).

The Belgian CF Registry lies since 2006 within the framework of the CF convention described above. Participation in collection of data for the CF Registry is one of the obligatory tasks of the CF reference centres.

1.4 OBJECTIVES OF THE CYSTIC FIBROSIS PATIENT REGISTRY

The aims of the CF patient registry are to study epidemiological aspects of the disease among people with CF in Belgium and to provide an evaluation tool for the assessment of the management and quality of care for patients with CF. It also provides a database for scientific research to CF researchers both at the Scientific Institute and the CF reference centres. The registry also participates in activities organized by and contributes to the European Cystic Fibrosis Society Patient Registry (ECFSPR)[8] and other international projects.

[1] BCFA or BVSM-ABLM : Belgische Vereniging voor Strijd tegen Mucoviscidose – Association belge de Lutte contre la Mucoviscidose

CHAPTER 2: POPULATION AND METHODOLOGY

In this section, we describe the target population and methodology used. We briefly describe the data collection procedures and its evolution over the years and give the general structure of the database by listing some of its components. We look at the reporting procedures and use a flow chart to summarize the entire process.

2.1 STUDY POPULATION

The target population for the registry is people with cystic fibrosis who are living in Belgium. In 2012, there were 1246 patients who were registered as members of the patient's association (BCFA), 721 Flemish and 525 French speaking. About 56.0% of these were adults ≥ 18 years. For the moment, the registry is estimated to have a coverage of more than 90% of all people with CF (PWCF) living in Belgium.

Prior to the registration, the physicians (at the accredited CF reference centre) provide each patient and their parents (or legal representative) information about the objectives of the Registry. The patients are only included in the Registry after signing an informed consent. They are identified by their national registry number at the centre level. This number is then encrypted into a unique code by a trusted third party (eHealth) before the data are transmitted to the registry. The patients' names are never transferred to the Registry.

2.2 DATA COLLECTION

The clinical and demographic data is collected for all patients once each year by the treating physician from medical records and consists of more than 200 recorded items.

These data are divided into two sections:

a) The core data which contains demographic data, age of CF diagnosis and initial symptoms, genotype (mutations), sweat test results and nasal transepithelial potential difference results including information on neonatal screening. These data are collected when the patient enters the Registry and is updated if necessary during follow-up years.

b) Yearly follow-up sheets collect clinical data (height, weight), lung function (forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), forced expiratory flow 25-75% (FEF_{25-75})), complications that occurred or still active during the registration year, microbiology results, treatments and medications taken as well as social data.

2.3 SOFTWARE

Until 2010, the data was collected via an Access based computer application on CD-Rom. A new web-based application which works with a trusted third party (eHealth) was developed and has been used for data collection since year 2011. The procedures for data collection, including the digital questionnaire and some definitions, are provided in the appendix.

2.4 FEEDBACK

Each of the seven reference centres (ten clinics) gets a copy of the national annual report. Since 2006, they receive a centre report made using data from patients within the individual centre. Starting 2008, a feedback report has been provided with analyses that compare the results of each centre with data from the other centres in order to improve the quality of care provided to the patients with CF in their respective centres through benchmarking. These analyses are corrected for some known factors such as patient age and gender with further corrections planned as more confounding data are collected by the registry, including socioeconomic data.

2.5 DATA FLOW

Following the development and use of a new web-based program from registry year 2012, the schema below shows various stages from data entry and processing to reporting and publication.

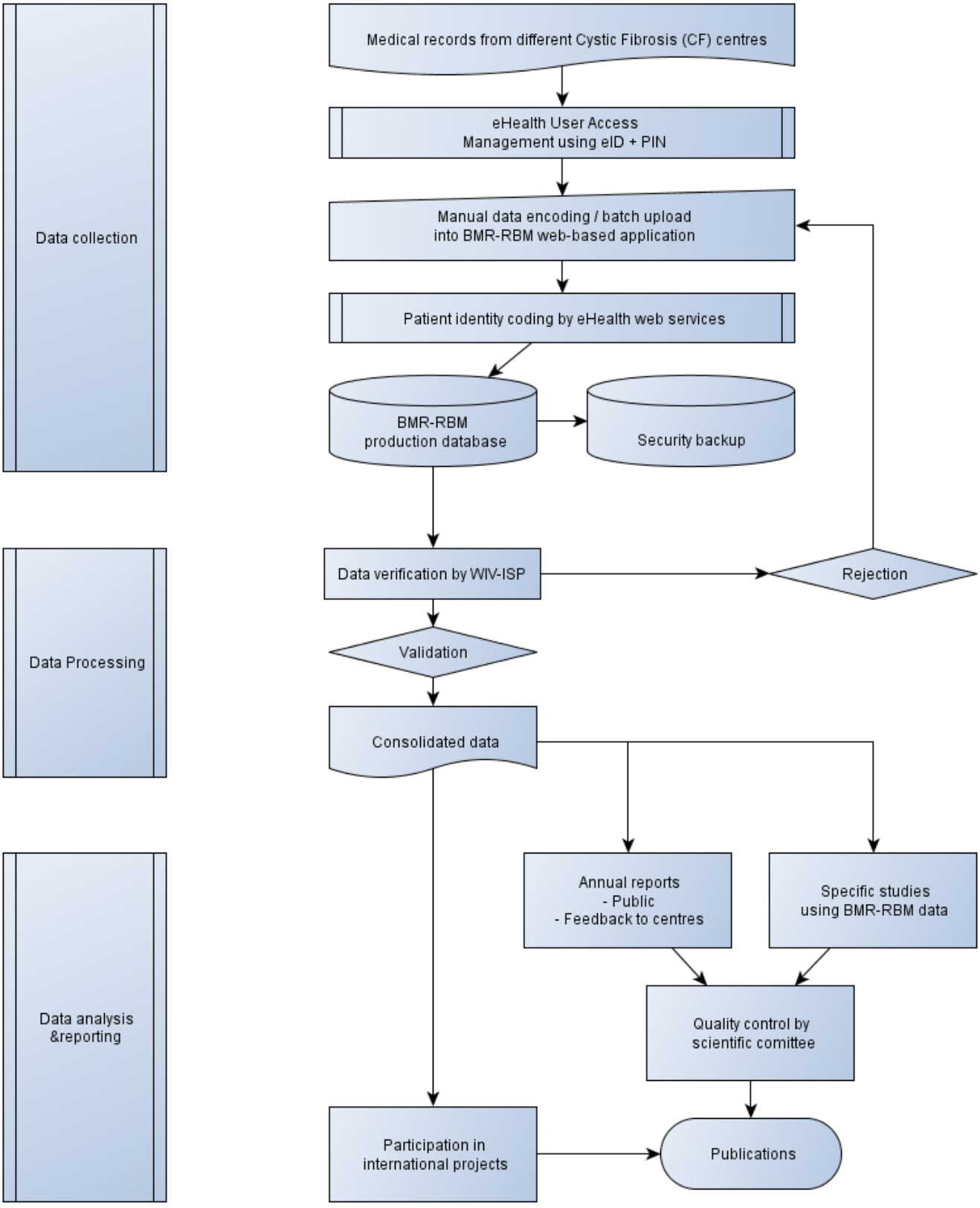


Figure 1: Data flow chart

DEMOGRAPHIC SUMMARY OF DATA REPORTS 2009 - 2012

Table 1: A comparison of demographic data for years 2009 - 2012

	2009	2010	2011	2012
Number of CF patients♈	1129	1138	1171	1184
Number of CF patients with complete records	1122	1132	1161	1154
Number of CF patients without observation♉	7	6	10	30
Number of CF patients with a transplant	118	128	134	141
Number of patients without a confirmed diagnosis♊	-	-	20	11
Number of CF patients who were not seen	-	-	9	16
New CF diagnoses	39	26	36	27
Median patient age in years (range)*	18.4 (0.0 - 68.2)	18.9 (0.2 - 69.4)	19.7 (0.0 - 70.4)	20.3 (0.1 - 71.5)
Median patient age male (range)*	17.9 (0.1 - 62.1)	18.5 (0.2 - 63.0)	19.6 (0.2 - 64.2)	20.2 (0.1 - 65.2)
Median patient age female (range)*	18.9 (0.0 - 68.2)	19.3 (0.2 - 69.4)	19.8 (0.0 - 70.4)	20.4 (0.1 - 71.5)
Males (%)	52.0	51.5	51.8	51.4
Adults ≥ 18 years (%)	51.0	52.9	54.7	56.4
Median age at diagnosis (months)	6.8	6.6	6.5	6.1
Age range at diagnosis (years)	0.0 - 65.0	0.0 - 65.0	0.0 - 65.0	-0.4 - 65.0
Median age at diagnosis, male (months)	6.5	6.3	6.5	6.2
Age range at diagnosis, male (years)	0.0 - 55.7	0.0 - 55.7	0.0 - 49.2	-0.4 - 46.9
Median age at diagnosis, female (months)	7.0	7.0	6.7	6.0
Age range at diagnosis, female (years)	0.0 - 65.0	0.0 - 65.0	0.0 - 65.0	-0.2 - 65.0
Median age at diagnosis new cases in years (range)	0.4 (0.0 - 39.1)	0.9 (0.0 - 32.8)	0.2 (0.0 - 49.2)	0.2 (-0.1 - 35.9)
Number of transplants performed	11	16	16	8
Total number of deaths reported	10	7	8	10
Number of deaths among transplant patients	5	5	2	5
Median age at death in years (range)	26.6 (14.0 - 46.7)	32.5 (22.7 - 59.5)	27.7 (9.3 - 45.8)	30.2 (9.3 - 52.0)
Overall mean FEV_1 % Predicted[15,12]	77.4 (25.4)	76.3 (25.1)	77.8 (25.6)	77.6 (26.3)
Mean FEV_1 % predicted (male)	80.0 (25.9)	79.5 (24.9)	80.9 (26.3)	80.5 (26.5)
Mean FEV_1 % predicted (female)	74.4 (24.4)	72.6 (24.7)	74.5 (24.5)	74.4 (25.8)

♈Patients with revoked diagnosis excluded (n = 8 in 2012)

♊Are excluded from analyses starting 2012

*Patient's age at the last consultation

♉Patients without at least four filled-in clinical items, postulated alive or registered as deceased, and are not used in the analysis of clinical data

The new CF diagnoses are patients with the earliest diagnosis date from amongst the clinical diagnosis date, TEPD date, genotype date or the sweat test date done within the registry data year.

Prenatal diagnosis is considered without setting to zero the age at diagnosis allowing negative values since 2012

CHAPTER 3: DEMOGRAPHIC DATA

In this section, the age at the end of the year by gender is presented in five-year categories. Information on the district of residence is provided, including maps of residence districts with estimated prevalence based on population in January 2012.

3.1 AGE ON DECEMBER 31 2012

Table 2: Age on December 31 2012 by gender

	Males			Females			All Patients		
Age years (on 31 Dec 2012)	**n**	**cum n**	**cum %**	**n**	**cum n**	**cum %**	**n**	**cum n**	**cum %**
0 -< 5	51	51	8.4	53	53	9.2	104	104	8.8
5 -< 10	56	107	17.6	81	134	23.3	137	241	20.4
10 -< 15	107	214	35.2	68	202	35.1	175	416	35.1
15 -< 20	87	301	49.5	78	280	48.6	165	581	49.1
20 -< 25	62	363	59.7	65	345	59.9	127	708	59.8
25 -< 30	73	436	71.7	80	425	73.8	153	861	72.7
30 -< 35	60	496	81.6	50	475	82.5	110	971	82.0
35 -< 40	49	545	89.6	38	513	89.1	87	1058	89.4
40 -< 45	27	572	94.1	24	537	93.2	51	1109	93.7
45 -< 50	21	593	97.5	16	553	96.0	37	1146	96.8
≥ 50	15	608	100.0	23	576	100.0	38	1184	100.0
Total	**608**			**576**			**1184**		

The overall median age on 31, December 2012 was 20.3 years; 20.2 for male and 20.4 for female patients respectively

There are more female patients above the age of 55 than there are men.

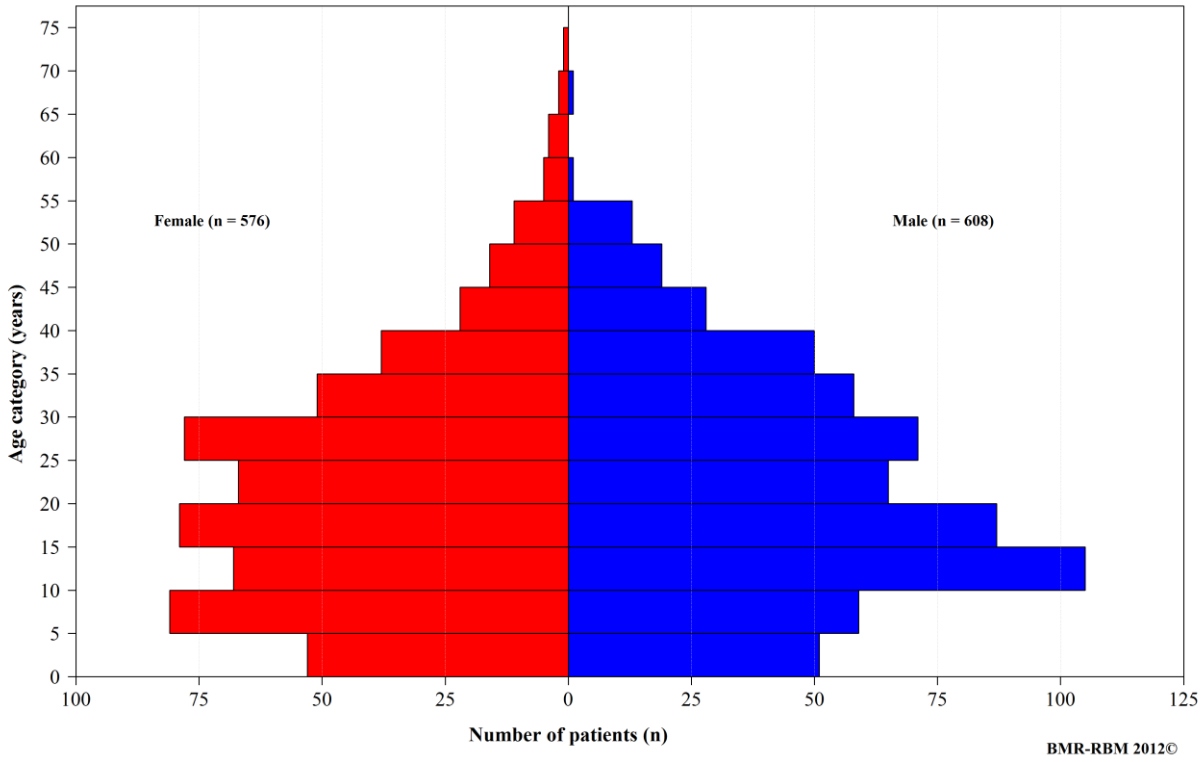


Figure 2: Age on Dec 31, 2012 by gender

3.2 PREVALENCE OF CYSTIC FIBROSIS PER DISTRICT OF RESIDENCE

The figure below illustrates the prevalence of Cystic Fibrosis in each district of residence in Belgium based on the population as at the beginning of 2012. A list with the district names and exact number of people with cystic fibrosis residing in each district is provided on page 25.

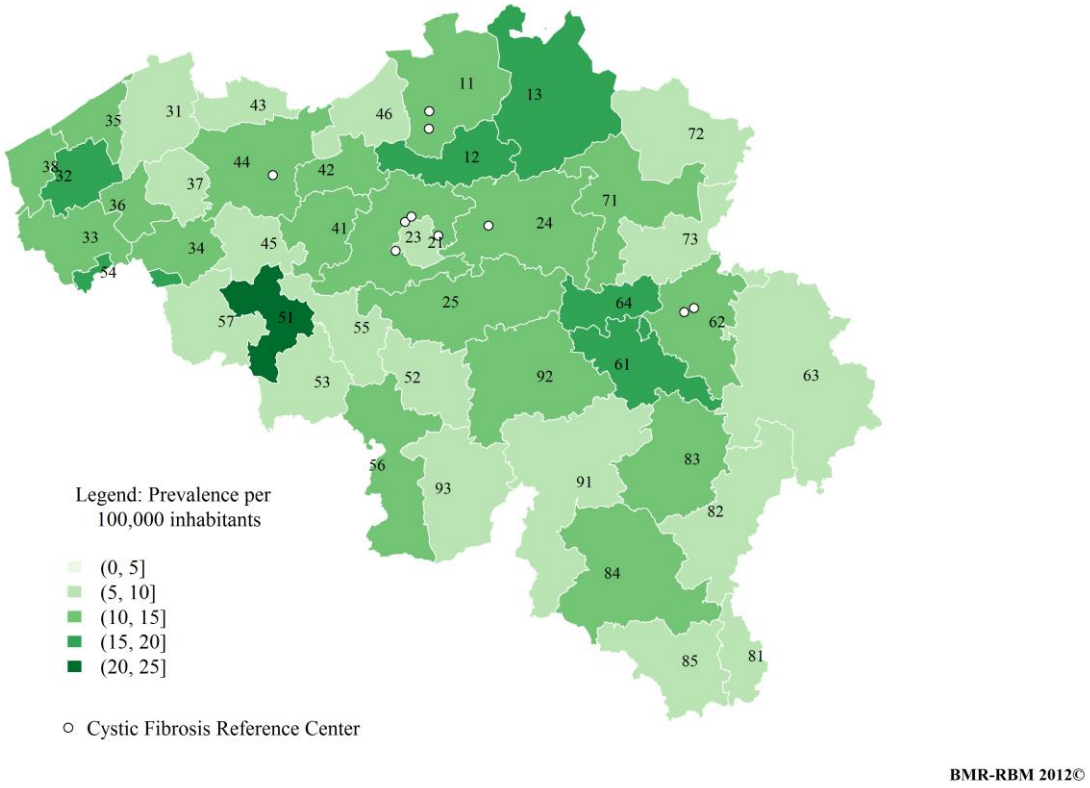


Figure 3: Captured prevalence per 100,000 inhabitants based on district of residence in January 2012

The figure above indicates that the highest prevalence of 20.0 in 100,000 is in Aat (Ath) District, code 51, with 17 patients in a population of 84,958 at the beginning of the year. District 73, Tongeren (Tongres) had the lowest prevalence of 5.0 in 100,000 given that there were 10 patients in a population of 199,698 during the reference period.

3.3 PWCF UNDER FOLLOW-UP PER DISTRICT OF RESIDENCE

The figure below illustrates the number of Cystic Fibrosis patients resident in each district in Belgium at the beginning of 2012. A list with the district names and exact number of people with cystic fibrosis residing in each district is provided on page 25.

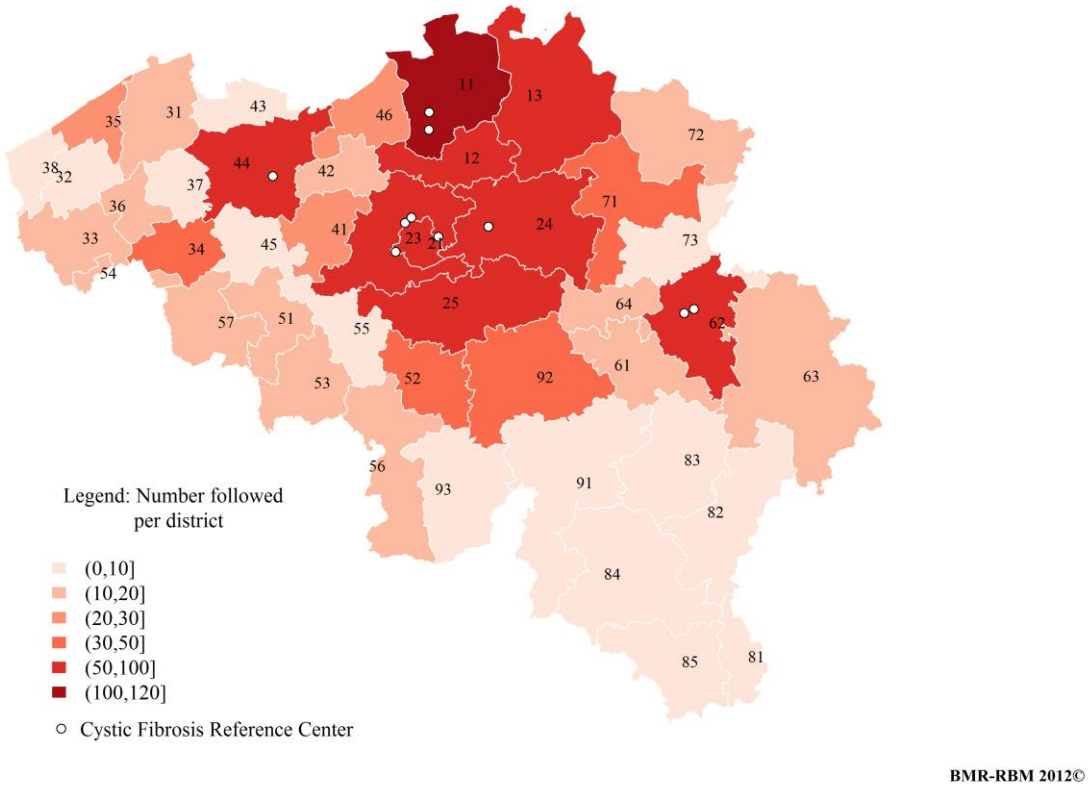


Figure 4: Number of PWCF per district of residence in January 2012

In the figure above, we see more patients concentrated in the central and northern sides of the country. Due to its populous nature though, Antwerp district with 103 patients in a population of about a million had a prevalence of 10.2 in 100,000 inhabitants.

3.4 CASES BY DISTRICT OF RESIDENCE

Table 3: District of residence

	District / Arrondissement	n	%
11	Antwerpen	103	8.7
12	Mechelen	59	5.0
13	Turnhout	72	6.1
21	Brussels Hoofdstedelijk Gewest Région Bruxelles Capitale	93	7.9
23	Halle-Vilvoorde	73	6.2
24	Leuven	51	4.3
25	Nivelles	53	4.5
31	Brugge	19	1.6
32	Diksmuide	10	0.8
33	Ieper	12	1.0
34	Kortrijk	31	2.6
35	Oostende	21	1.8
36	Roeselare	17	1.4
37	Tielt	7	0.6
38	Veurne	9	0.8
41	Aalst	29	2.4
42	Dendermonde	20	1.7
43	Eeklo	8	0.7
44	Gent	58	4.9
45	Oudenaarde	10	0.8
46	Sint-Niklaas	23	1.9
51	Ath	17	1.4
52	Charleroi	32	2.7
53	Mons	20	1.7
54	Mouscron	13	1.1
55	Soignies	10	0.8
56	Thuin	16	1.4
57	Tournai	11	0.9
61	Huy	20	1.7
62	Liège	75	6.3
63	Verviers	20	1.7
64	Waremme	12	1.0
71	Hasselt	43	3.6
72	Maaseik	15	1.3
73	Tongeren	10	0.8
81	Arlon	3	0.3
82	Bastogne	4	0.3
83	Marche-en-Famenne	8	0.7
84	Neufchâteau	8	0.7
85	Virton	5	0.4
91	Dinant	10	0.8
92	Namur	32	2.7
93	Philippeville	6	0.5
subtotal		**1168**	
Foreign country		-	
missing		16	1.4
total		**1184**	

CHAPTER 4: DIAGNOSIS

In this section, we present the symptoms and clinical reasons suggesting a CF diagnosis. Most of the patients present with either **acute or recurrent respiratory problems** (43.1%) or **failure to thrive** (24.5%). We also present a table of the procedure used for CF diagnosis which classifies the people with CF into two groups depending on whether or not they meet the **minimum conditions set for inclusion** into the European Cystic Fibrosis Society Patient Registry for (ECFSPR). Also presented is the age at diagnosis and the mutations found after genotyping. The most prevalent mutation is the F508del with about 45.4% of the patients homozygous. About 5.1% (60 patients) of those registered in 2012 had either missing, unknown or non-identified genotype information on at least one allele.

4.1 SYMPTOMS AND CLINICAL REASONS SUGGESTING CF

In a patient with suggestive symptoms, a family history of cystic fibrosis or a positive neonatal screening test, the diagnosis of CF is confirmed by an abnormal sweat test (chloride > 60 mEq/L) and/or the identification of two mutations in the CFTR gene. Although no national neonatal screening program was implemented in Belgium, some children were screened for CF. Most patients present with a combination of respiratory and/or gastrointestinal symptoms. Chronic cough, recurrent chest infections, chronic sinusitis are the most common presenting respiratory signs. Common gastrointestinal symptoms include meconium ileus (obstruction of the bowel with sticky secretions in the new-born infant), chronic diarrhoea and failure to thrive due to malabsorption. Less frequently, salt loss, jaundice or a rectal prolapse are the first diagnostic signs. In some cases, the diagnosis of cystic fibrosis is delayed until adulthood. Most of these patients are expected to have had a milder clinical course, or to present with atypical symptoms, such as infertility.

The diagnostic signs or clinical presentation are illustrated in table 4. In the Belgian CF registry, it is possible to report more than one diagnosis sign or symptom for the same patient. Over the years, the commonest clinical presentation of CF remains acute or recurrent respiratory problems. Other common features on presentation were failure to thrive, chronic diarrhoea / steatorrhoea and meconium ileus. About 17.0% of the patients were diagnosed via neonatal screening test.

Table 4: Symptoms and clinical reasons for CF diagnosis

			Newly diagnosed			
	Data 1998 – 2012		2011		2012	
	n	%	n	%	n	%
Acute or Recurrent Respiratory Problems	485	43.1	9	36.0	11	40.7
Failure to thrive	276	24.5	4	16.0	7	25.9
Chronic diarrhoea/streatorrhea/ malabsorption	231	20.5	4	16.0	4	14.8
Neonatal screening test	187	16.6	3	12.0	4	14.8
Meconium ileus	164	14.6	3	12.0	4	14.8
Family history	111	9.9	1	4.0	4	14.8
Nasal polyposis / chronic sinusitis	49	4.4	2	8.0	1	3.7
Rectal prolapse	32	2.8	1	4.0	0	0.0
Intestinal obstruction (other than meconium ileus)	27	2.4	1	4.0	0	0.0
Prenatal diagnosis	34	3.0	3	12.0	2	7.4
Dehydration / electrolyte imbalance	19	1.7	1	4.0	1	3.7
Neonatal jaundice	1	0.1	0	0.0	0	0.0
Infertility	14	1.2	1	4.0	0	0.0
Diagnosis other	84	7.5	2	8.0	0	0.0
*No diagnosis reasons given	58		1			

* The overall percentages are based on 1126, 58 patients did not have information on any of the above reasons given in the 2012 data and were excluded from the calculations. There were 27 newly diagnosed in 2012, percentages are based on 27 patients.

Note: Reasons for diagnosis are not mutually exclusive.

4.2 DOCUMENTATION OF CF DIAGNOSIS

Patients are included in the registry if CF is diagnosed. According to the European Cystic Fibrosis Society Patients Registry (ECFSPR), for a patient to be included, he/she must meet at least one of the following three criteria below:

1). Have two sweat tests done returning results of sweat chloride > 60 mmol/L.
2). If only one sweat test with chloride > 60 mmol/L is available then a DNA Analysis/Genotyping should be done identifying two disease causing CF mutations.
3). If, however, the sweat chloride values are ≤ 60 mmol/L then at least two of the conditions below should be fulfilled: -
- **i. A DNA Analysis/Genotyping identifying two disease causing CF mutations**
- **ii. A Trans epithelial (Nasal) Potential Difference value –** consistent with a diagnosis of CF .
- **iii. Clinical Presentation – documenting** typical features of CF .

The table below gives a summary of documented CF diagnosis information based on the above stated criteria.

Table 5: Documentation of CF diagnosis including sweat tests, clinical symptoms, genotyping and family history

Procedure	Data 1998 - 2012		Newly diagnosed Patients 2012	
	n	%	n	%
Patients meeting inclusion criteria for the European Cystic Fibrosis Society Patient Registry				
Clinical symptoms and/or family history, sweat test and genotyping	677	57.2	17	63.0
Clinical symptoms and/or family history and sweat test	39	3.3	2	7.4
Clinical symptoms and/or family history and genotyping	205	17.3	4	14.8
Neonatal screening test, sweat test and genotyping	101	8.5	2	7.4
Clinical symptoms and/or family history, neonatal screening test, sweat test and genotyping	56	4.7	1	3.7
Sweat test and genotyping	15	1.3	.	.
Clinical symptoms and/or family history, neonatal screening test and genotyping	11	0.9	.	.
Subtotal	**1104**	**93.2**	**26**	**96.3**
Patients not meeting inclusion criteria for the European Cystic Fibrosis Society Patient Registry				
Clinical symptoms and/or family history only	18	1.5	.	.
Genotyping only	41	3.5	.	.
Neonatal screening test and genotyping	18	1.5	1	3.7
Clinical symptoms and/or family history and neonatal screening test	1	0.1	.	.
Missing	2	0.2	.	.
Subtotal	80	6.8	1	3.7
Total	**1184**	**100.0**	**27**	**100.0**

Important Information: The data in the table above refers to documentation of CF diagnosis. The clinical diagnosis was considered if at least one of a set of symptoms was identified (see page 27; excluding neonatal screening); the sweat chloride had to be at least 60mmol/L while genotyping was considered confirmatory if two mutations were reported.

4.3 AGE AT DIAGNOSIS

The figure gives the cumulative percentage of age at diagnosis for data 2012. The median age at diagnosis was 6.1 months; 6.2 months for male and 6.0 months for female patients respectively. At the age of 18 years 92.9% of the patients were diagnosed. The median age at diagnosis was 3.3 months for the F508del homozygous patients, 9.4 months for the F508del heterozygous while for patients with other mutations it was 16.8 months.

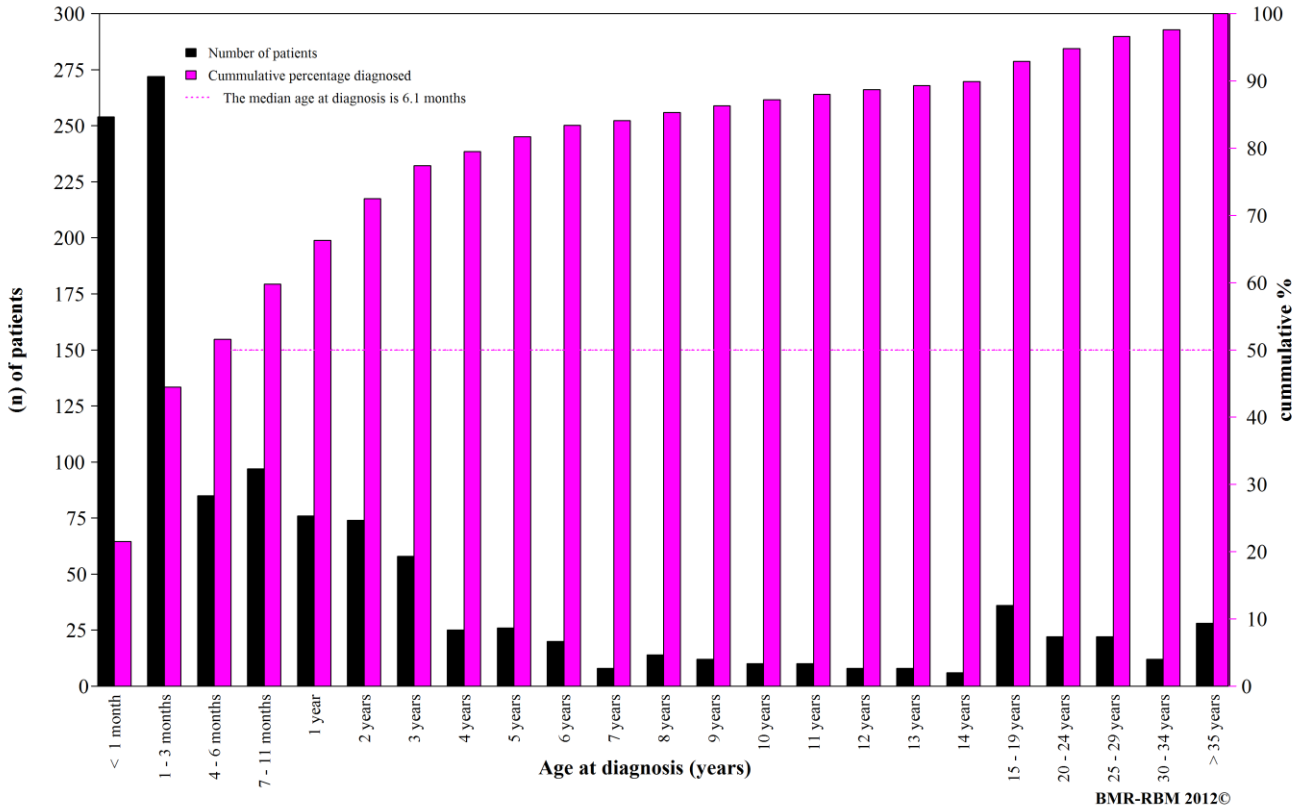


Figure 5: Age at Diagnosis

The median age at diagnosis for the 27 newly diagnosed patients in 2012 was 2.3 months; 2.5 months for male and 1.6 months for female patients respectively.

4.4 GENOTYPE

About 99.7% of the patients registered in 2012 had undergone a genetic analysis. Almost half (45.4%) were homozygote for F508del and 86% of the patients had this mutation on at least one of their alleles (table 7).

Table 6: Genotype mutation pairs

Mutation pair	n	%	cumulative %
F508del --- F508del	538	45.4	45.4
F508del --- OTHER	443	37.4	82.9
F508del --- NI	33	2.8	85.6
OTHER --- OTHER	143	12.1	97.7
OTHER --- NI	9	0.8	98.5
NI --- NI	15	1.3	99.7
subtotal	**1181**		
missing	3	0.3	
total	**1184**		

NI = Not Identified
The mutation "*Poly-T tract variations*" was treated as "Other"

Table 7: Most frequently reported alleles and mutations

	patients		alleles	
Mutation	**n**	**%**	**n**	**%**
F508del	1014	85.6	1552	65.5
N1303K	64	5.4	70	3.0
G542X	62	5.2	69	2.9
1717-1G->A	35	3.0	35	1.5
3272-26A->G	34	2.9	34	1.4
S1251N	31	2.6	31	1.3
A455E	28	2.4	28	1.2
R117H	25	2.1	25	1.1
2789+5G->A	23	1.9	23	1.0
R553X	18	1.5	18	0.8
W1282X	18	1.5	18	0.8
L927P	17	1.4	17	0.7
R1162X	14	1.2	17	0.7
2183AA->G	16	1.4	16	0.7
3849+10kbC->T	16	1.4	16	0.7
[delta]I507	10	0.8	10	0.4
3659delC	9	0.8	9	0.4
306insA	8	0.7	8	0.3
394delTT	6	0.5	7	0.3
D1152H	7	0.6	7	0.3
E60X	7	0.6	7	0.3

	patients		alleles	
Mutation	**n**	**%**	**n**	**%**
L227R	4	0.3	7	0.3
W401X	7	0.6	7	0.3
R334W	6	0.5	6	0.3
Y1092X	6	0.5	6	0.3
G178R	5	0.4	5	0.2
G551D	4	0.3	5	0.2
G85E	5	0.4	5	0.2
G970R	5	0.4	5	0.2
L165S	5	0.4	5	0.2
Q493X	5	0.4	5	0.2
R347H	5	0.4	5	0.2
3905insT	4	0.3	4	0.2
4218insT	4	0.3	4	0.2
IVS8	4	0.3	4	0.2
S1255P	4	0.3	4	0.2
Others	186	16.4	196	7.7
Not identified	54	4.6	67	2.8
subtotal			**2357**	
missing	8	0.7	11	0.5
Total			**2368**	

The alleles detected in less than four patients were summarized into the "others" category for this purpose.

CHAPTER 5: ANTHROPOMETRY (HEIGHT, WEIGHT AND BMI)

Persons with CF are known to be prone to nutritional deficiencies. Because of thick mucus, the pancreas is unable to produce and/or carry digestive enzymes to the gut. This leads to poor absorption of proteins, fats and fat soluble vitamins resulting in poor weight gain and growth. Nutritional care is of great importance for patients with CF. Maintaining or achieving a better nutritional status has a positive impact on lung function.

We present classifications of the patients into BMI, height and weight percentiles, compared to their healthy peers. The analysis of the height, weight and BMI z-scores is based on CDC [9] and Cachera[10] reference equations. An evolution of BMI and height data from selected years is also presented by age category.

In this section, data from 141 patients with a transplant (**62 male**, **74 female**) were excluded from the analysis.

5.1 BMI PERCENTILES USING CACHERA REFERENCES

The Cachera reference equations that cover BMI z-scores for ages 0.0 - 58.0 years for male (56.0 for female) patients. In 2012, data from 998 patients was analysed. The figure below shows the median BMI percentile in each age category recorded over selected years. The lines show a general trend of better BMI over the years with the lines moving symmetrically upwards.

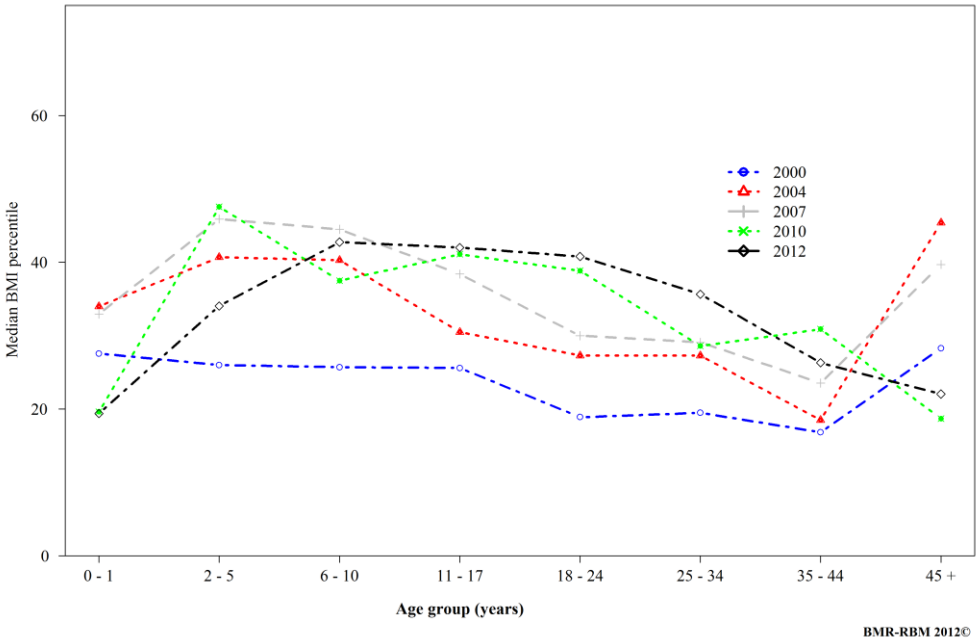


Figure 6: Median BMI percentile by age group and year

5.2 BMI PERCENTILES USING THE CDC GROWTH CHARTS

CDC growth charts cover BMI for ages 2.0 – 20.1 years. The trend depicted is quite similar to the Cachera references above. In 2012 data from 526 patients was analysed. The figure below displays the proportion in each group.

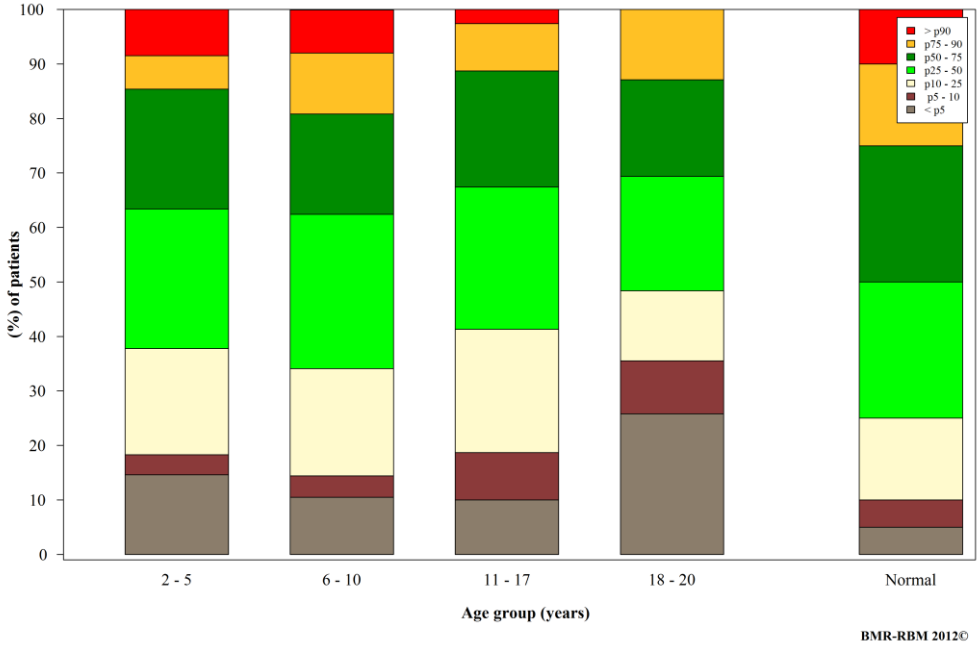


Figure 7: CDC BMI Z-Score percentiles by age

5.3 HEIGHT PERCENTILES USING THE CDC GROWTH CHARTS

The CDC growth charts cover height from 0.0 – 20.1 years. The values for patients older than 20.1 years are based on the extrapolated reference at age 20.0 years In 2012 data from 1006 patients was analysed. The figure below shows the proportion of patients in each percentile category.

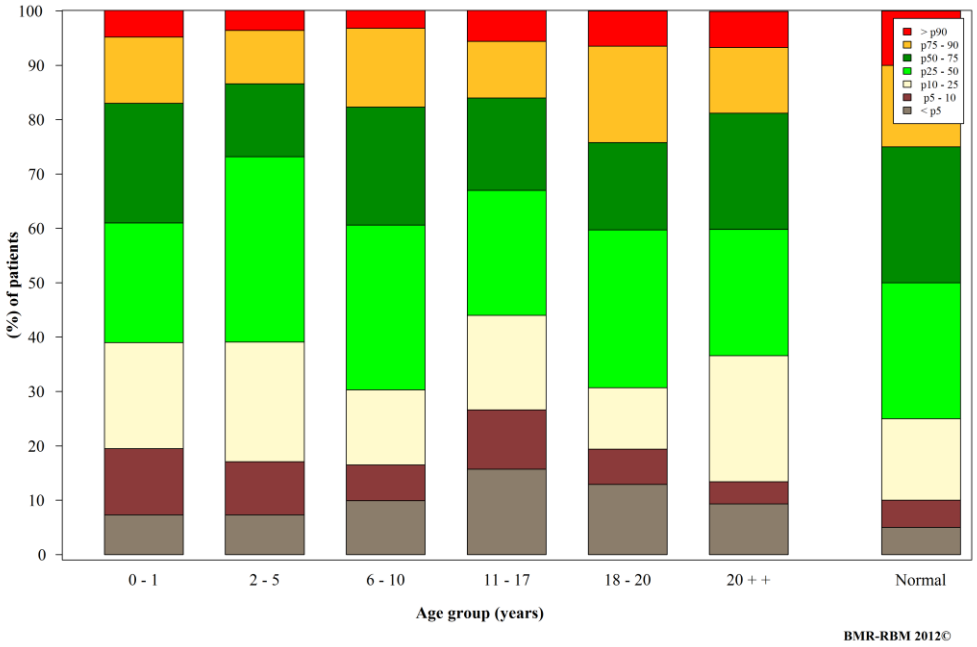


Figure 8: CDC height percentile by age category

5.4 WEIGHT PERCENTILES USING THE CDC GROWTH CHARTS

The CDC growth charts cover weight from 0.0 – 20.1 years. In 2012 data from 567 patients was analysed. The figure below indicates the proportion in each percentile group. A higher proportion with weight for age below the 5th percentile is seen in patients up to one year. This then declines in the years thereafter and increases again in those over the age 11 years. In general more than 60% of the patients in each age category have weight below the 50th percentile (0.0 SDs). This pattern has been observed in the registry over the years.

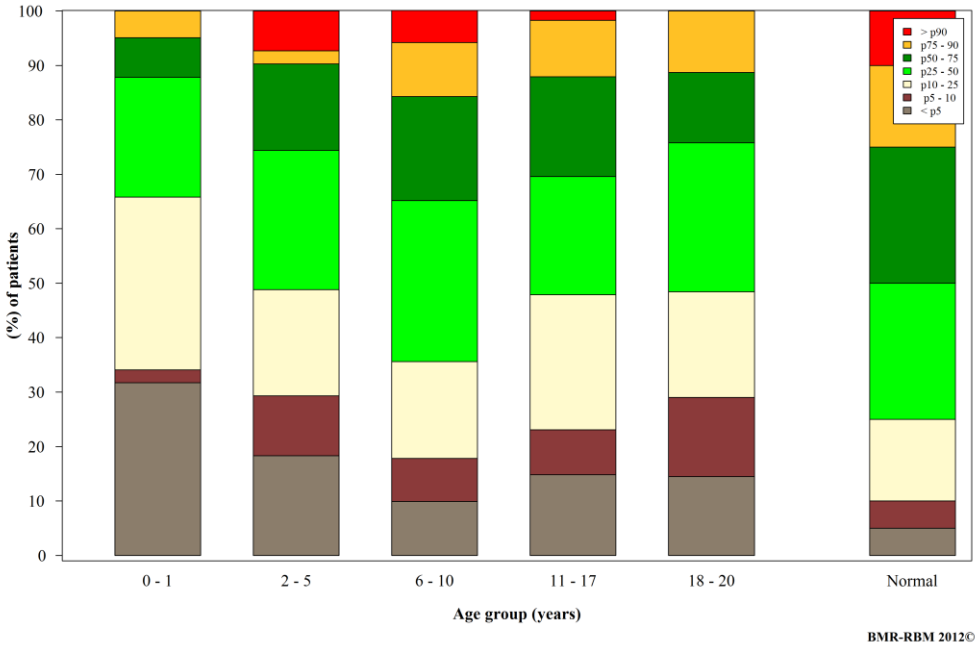


Figure 9: CDC Weight percentiles by age

CHAPTER 6: SPIROMETRY (LUNG FUNCTION)

Because most patients with CF develop progressive pulmonary disease, measures of pulmonary involvement, in particular FEV_1, have been used as markers of disease severity and to predict survival, [11] . However, considerable heterogeneity exists in prognosis and severity, even among patients of the same genotype [12].

The forced expiratory volume in 1 second (FEV_1) is the amount of air that a person is able to expire forcefully in one second, following full inspiration. The percentage of predicted FEV_1 is a clinical parameter to monitor lung function impairment and is expressed as a percentage of the predicted value for a reference population with same age, gender and height.

FEV_1% predicted values are divided in four classes for the CF population corresponding to different degrees of lung function impairment: normal lung function (≥ 90%), mild (70-89%), moderate (40-69%) and severe (< 40%) impairment.

Since lung function measurements below the age of 6 years are not reliable, data from those patients (**61 male**, **62 female**) was excluded from the lung function analysis. Those with a transplant (**62 male**, **74 female**) were also excluded. The values obtained at the last consultation of the year, pre or post bronchodilator, were analysed. An evolution of lung function from selected years by age category is also presented.

6.1 PERCENTAGE OF PREDICTED FEV_1

Wang's equations [13] were used for male, 6 – 17 years and female patients 6 – 15 years, while Hankinson's [14] were used for predictions for the male 18 years and above and female patients from 16 years onwards.

In 2012 data from 870 patients was analysed. The overall mean % predicted FEV_1 is 77.6 (SD = 26.3). The mean % predicted FEV_1 was 80.5 % (SD = 26.5) and 74.4 % (SD=25.8) respectively for 459 male and 411 female patients. The mean % predicted FEV_1 was 92.9 % (SD = 21.8) and 65.9 % (SD=23.3) respectively for 375 children and 495 adult patients.

Amongst the 393 F508del homozygous, the means were 77.5% (SD = 27.9) and 72.8% (SD = 25.3) respectively for the 207 male and 186 female patients. The means were 92.7% (SD = 23.2) and 62.6% (SD = 21.7) respectively for the 165 children and 228 adults F508del homozygous.

The figure below shows a scatter plot of FEV_1 (% of predicted) with the means calculated at yearly intervals. It shows on average declining values with age, with a steeper slope up to about 35 years of age when it levels off.

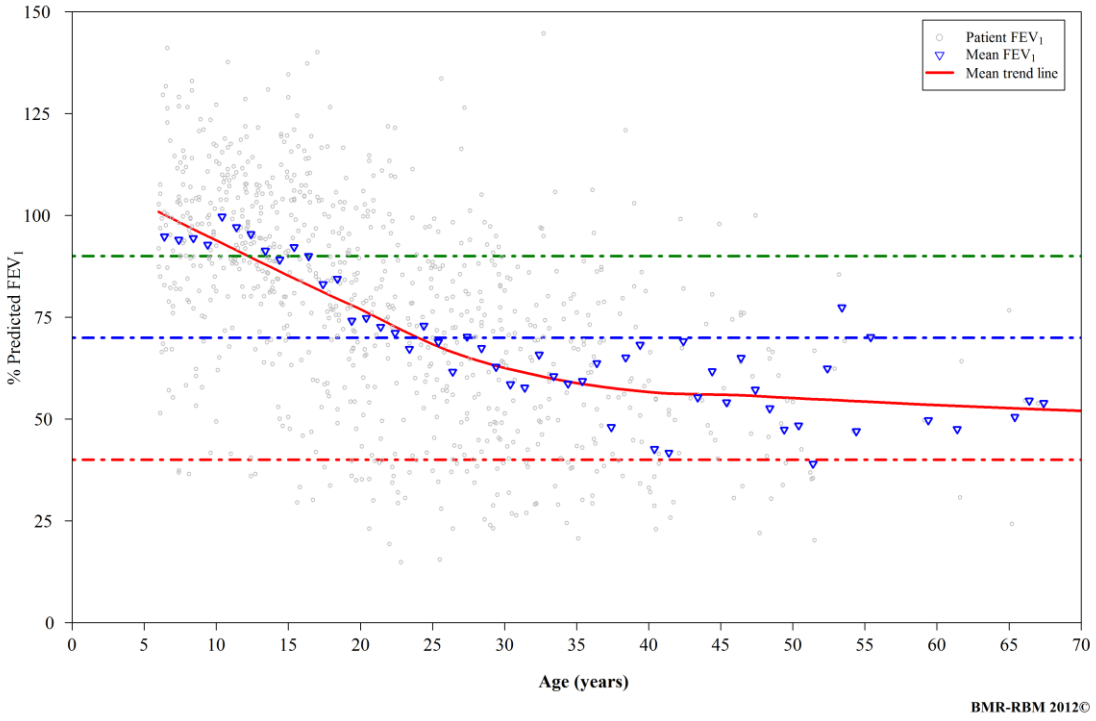


Figure 10: Mean percentage of predicted FEV_1 by age

The figure below is a scatter plot of mean FEV_1 according to gender.

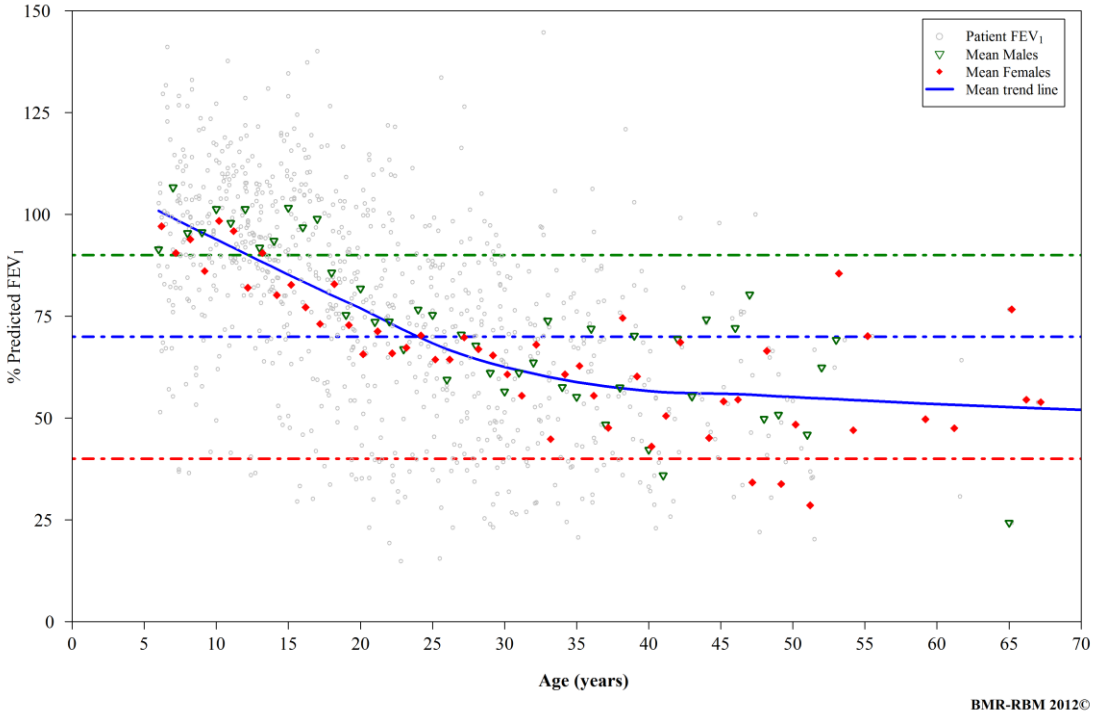


Figure 11: Mean percentage of predicted FEV_1 by age and gender

6.2 FEV_1 CATEGORIES BY AGE GROUP

FEV_1% predicted values were divided in four classes for the CF population corresponding to different degrees of lung function impairment: normal lung function (≥ 90%), mild (70-89%), moderate (40-69%) and severe (< 40%) lung function impairment. The table below shows the classification for children and adults based on the data collected in 2012.

Table 8: Proportions in each FEV_1 severity category for children and adults

	Children (6-17) years		Adults (≥ 18) years		Total	
Group	**n**	**%**	**n**	**%**	**n**	**%**
Normal : ≥ 90% predicted	224	59.7	72	14.5	296	34.0
Mild : 70% - 89% predicted	96	25.6	153	30.9	249	28.6
Moderate : 40% - 69% predicted	45	12.0	189	38.2	234	26.9
Severe : < 40% predicted	10	2.7	81	16.4	91	10.5
subtotal	**375**		**495**		**870**	
transplants	6		130		136	
< 6 years	123		.		123	
missing	9	.	16	.	25	
total	**513**		**641**		**1154**	

FEV_1 was higher than 70.0% of predicted in 62.6% of the patients :- in 85.3% of the children (6 – 17 years) and in 45.4% of the adults (18 years and above).

The figure below represents the lung function severity groups for children and adults in 2012. Using the Wang – Hankinson equations, 10.5% of the patients had FEV_1 below 40%, 34.0% had FEV_1 of at least 90% in 2012, compared to 2011 where 35.7% of the patients had FEV_1 of at least 90%.; 64.6% of the children and 13.4% of the adults.

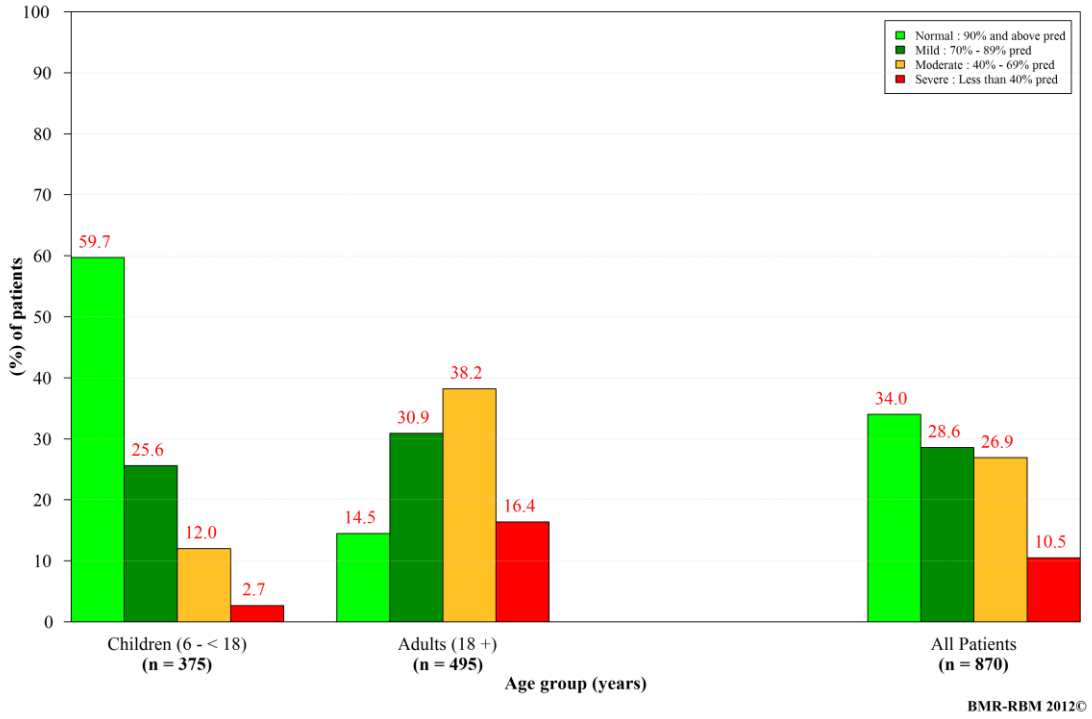


Figure 12: Percentage of predicted FEV_1 groups by age group

In this figure, a comparison of the proportion in each severity group over selected years is given. There has been a general increase in children with normal lung function and a reduction in the proportion of adults with severe lung function impairment over the years.

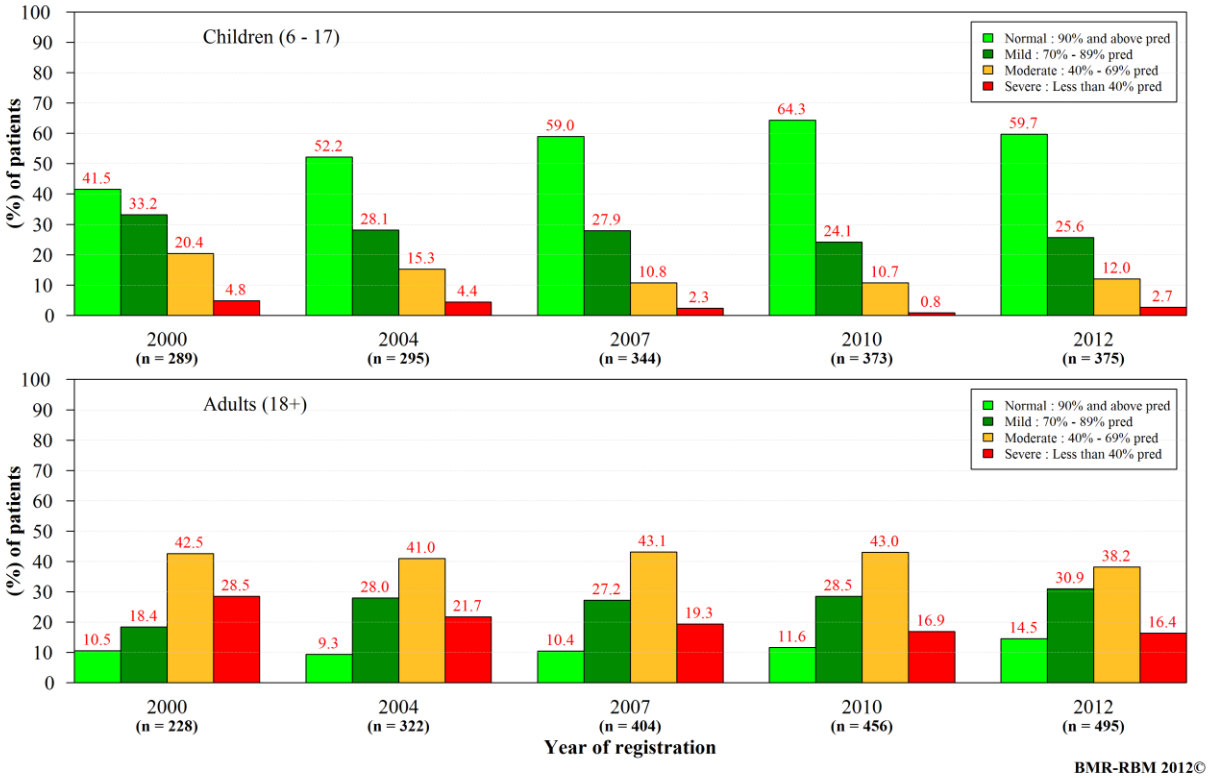


Figure 13: Percentage of predicted FEV_1 groups by age group for selected years

In the figure below, the mean % of predicted FEV_1 calculated cross-sectional shows improving lung function over time in all age categories.

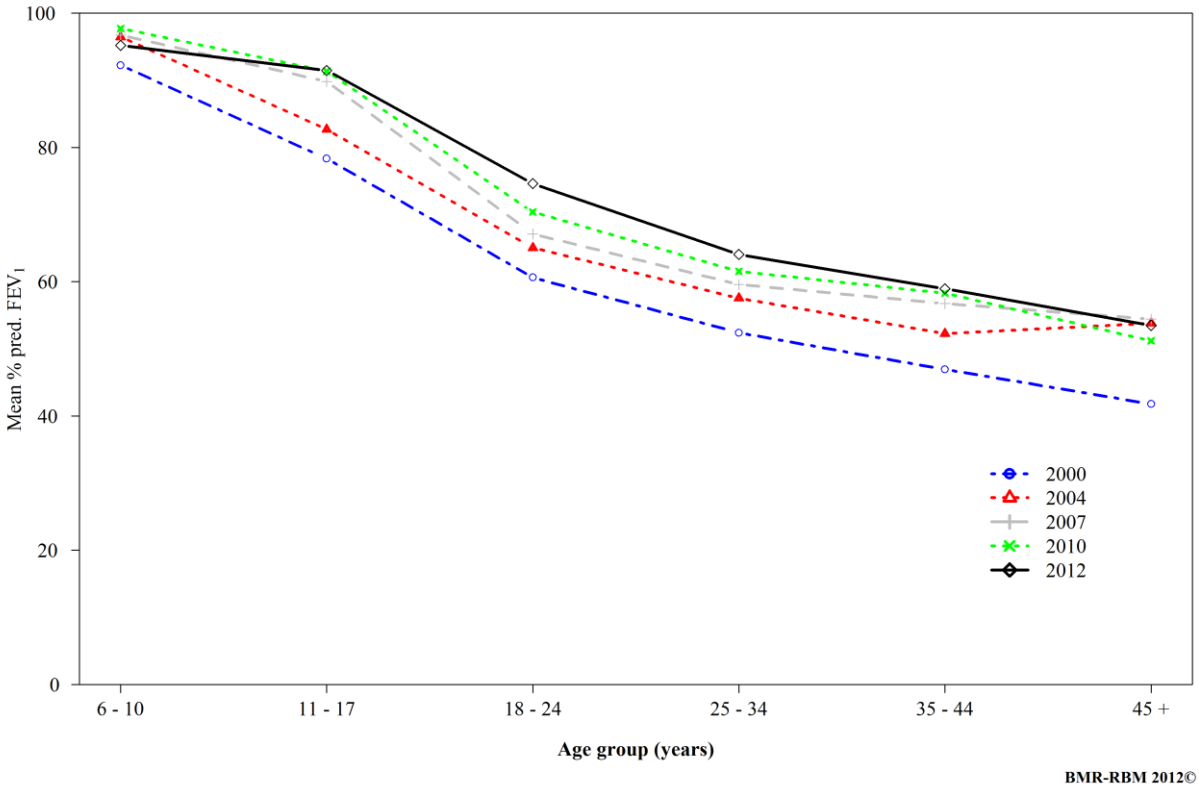


Figure 14: Mean percentage of predicted FEV_1 by age group for selected years

CHAPTER 7: MICROBIOLOGY

The production of thick mucus in the lung increases the likelihood of bacterial infections and decreases the ability to protect against infection. Over time, inflammation and infection are responsible for lung damage.

Bacterial colonisation occurs very early in the natural history of the disease. In children common bacteria such as *Staphylococcus aureus* and *Haemophilus influenzae* infect the lungs [17] . They can precede from a few months to several years the colonization by *Pseudomonas aeruginosa*. The airways of patients with CF may also be chronically colonized by fungi like *Aspergillus fumigatus* [18].

One of the main goals of CF care is to prevent or postpone by all possible means infections with the above named pathogens and to reduce the risk of chronic infection which increases respiratory morbidity and treatment burden.

In this section, we present the annual prevalence of recorded pathogens including the prevalence of chronic infections. Data from transplant patients was excluded from the respiratory microbiology analysis.

The analysis presented is based on the pathogens found at least once during the whole year (annual prevalence). The prevalence is also compared over a selected period in children and adults or by age category.

7.1 ANNUAL PREVALENCE OF ISOLATED PATHOGENS

During the year 2012, 991 (97.3%) of the 1018 non-transplant patients had at least one culture done. The median number of exploitable months was 5 with the lower and upper quartiles at 4 and 7 respectively. About 78.9% of the patients had at least four exploitable months during the year. Sputum samples were done in 785, throat swabs in 348 while 28 patients had a bronchoalveolar lavage.

The annual prevalence shown in the tables below refers to pathogens ever found during the year.

Table 9: Isolated pathogens and microbes 2009 - 2012

	2009		2010		2011		2012	
	n	%	n	%	n	%	n	%
Methicillin Resistant Staphylococcus aureus (MRSA)	83	8.5	86	8.7	97	9.5	87	8.8
Methicillin Sensitive Staphylococcus aureus (MSSA)	567	58.4	564	56.8	598	58.7	612	61.8
Pseudomonas aeruginosa	404	41.6	385	38.8	426	41.8	420	42.4
Aspergillus	303	31.2	283	28.5	329	32.3	346	34.9
Haemophilus influenzae	257	26.5	269	27.1	276	27.1	294	29.7
Stenotrophomonas maltophilia	90	9.3	90	9.1	91	8.9	118	11.9
Achromobacter xylosoxidans	57	5.9	74	7.5	91	8.9	106	10.7
Burkholderia cepacia complex	26	2.7	24	2.4	37	3.6	40	4.0
Scedosporium spp.	5	0.5	6	0.6	8	0.8	9	0.9
Non – tuberculous mycobacterium (NTM)	2	0.2	6	0.6	8	0.8	11	1.1
Other pathogen	185	19.1	200	20.1	160	15.7	147	14.8

Percentages are based on 971, 993, 1019 and 991 patients with a culture respectively for the years 2009 through 2012

While 6.4% of the children (32) and 11.2% of the adults (55) had MRSA, 27.5% (137) and 57.4% (283) respectively had a *Pseudomonas aeruginosa* infection. *Burkholderia cepacia complex* infection was found in 12 (2.4%) children and 28 (5.7%) adults. The prevalence of *Achromobacter xylosoxidans* in 2012 (10.7%) is significantly higher ($P < 0.0001$) than the value in 2009 (5.9%).

7.2 ANNUAL PREVALENCE OF CHRONIC INFECTIONS

Table 10: Chronic infections and colonisation 2009 - 2012

	2009		2010		2011		2012	
	n	%	n	%	n	%	n	%
Chronic *Pseudomonas aeruginosa*	299	30.8	294	29.6	287	28.2	276	27.9
Chronic *Burkholderia cepacia* complex	16	1.6	15	1.5	23	2.3	27	2.7
Chronic *Stenotrophomonas maltophilia*	27	2.8	23	2.3	30	2.9	27	2.7
Chronic *Achromobacter xylosoxidans*	24	2.5	29	2.9	39	3.8	54	5.4
Chronic MRSA	50	5.1	46	4.6	45	4.4	51	5.1

Percentages are based on 971, 993, 1019 and 991 patients with a culture respectively for the years 2009 through 2012

About 11.0% of the children (54) and 45.0% of the adults (276) had chronic *Pseudomonas aeruginosa* infection.

The figures below show the annual prevalence of infections over selected periods. Prevalence up to 2006 was based on a positive culture at the last consultation of the year. Since 2007, prevalence is based on any positive culture for a given pathogen among those collected during the year. In the interpretation of the graphs below, this should be taken into account.

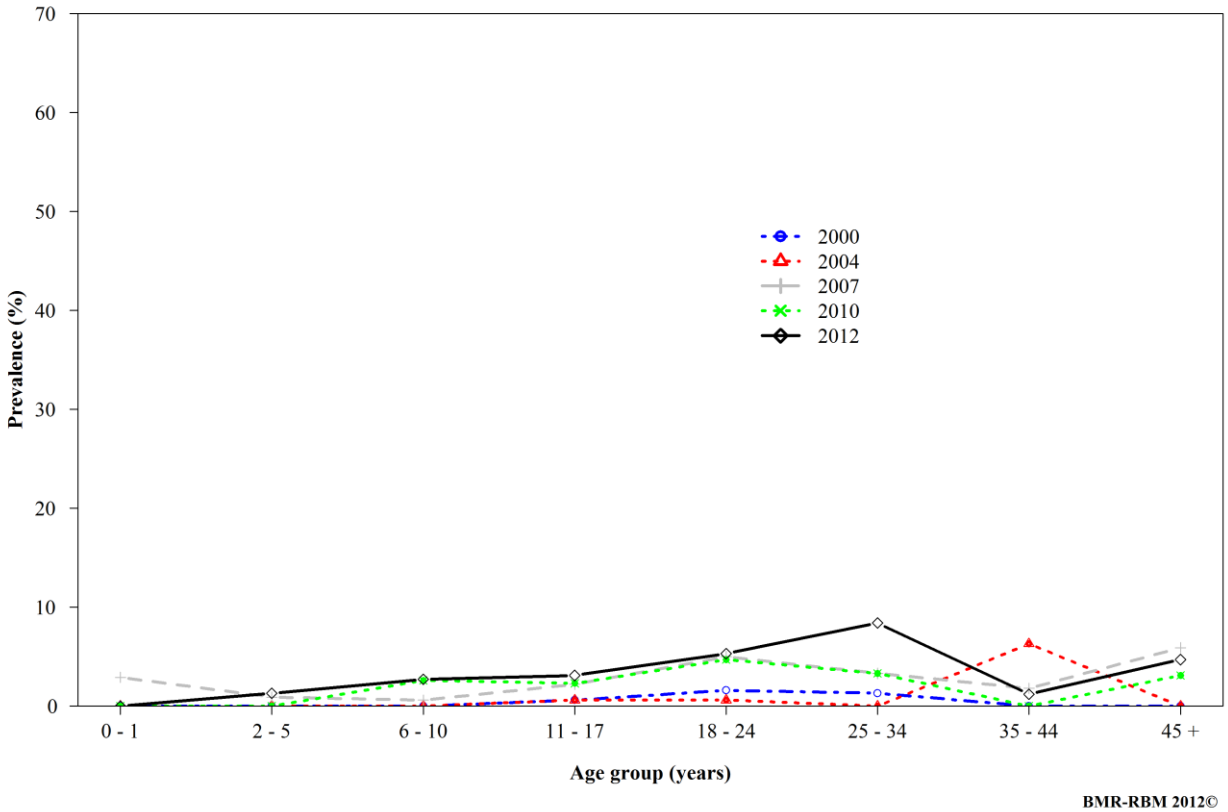


Figure 15: Prevalence of *Burkholderia cepacia complex* infections by year and age

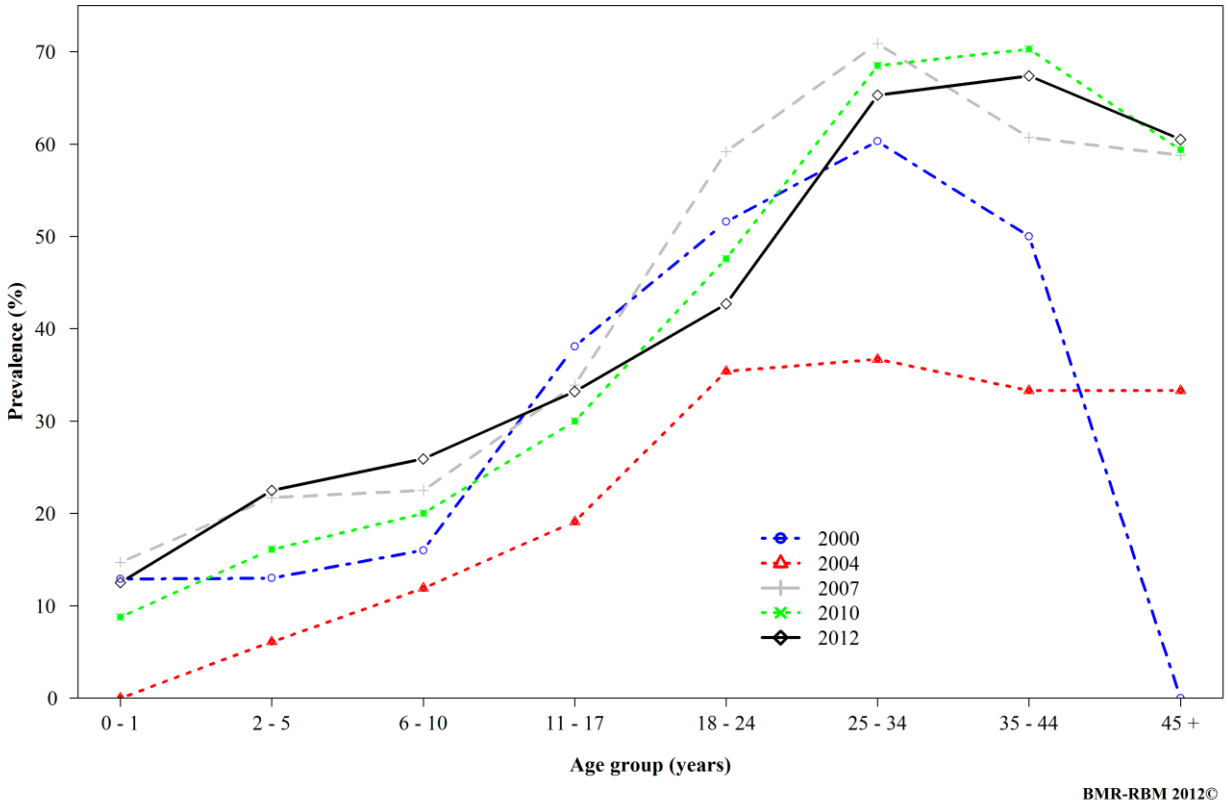


Figure 16: Prevalence of *Pseudomonas aeruginosa* infections by year and age

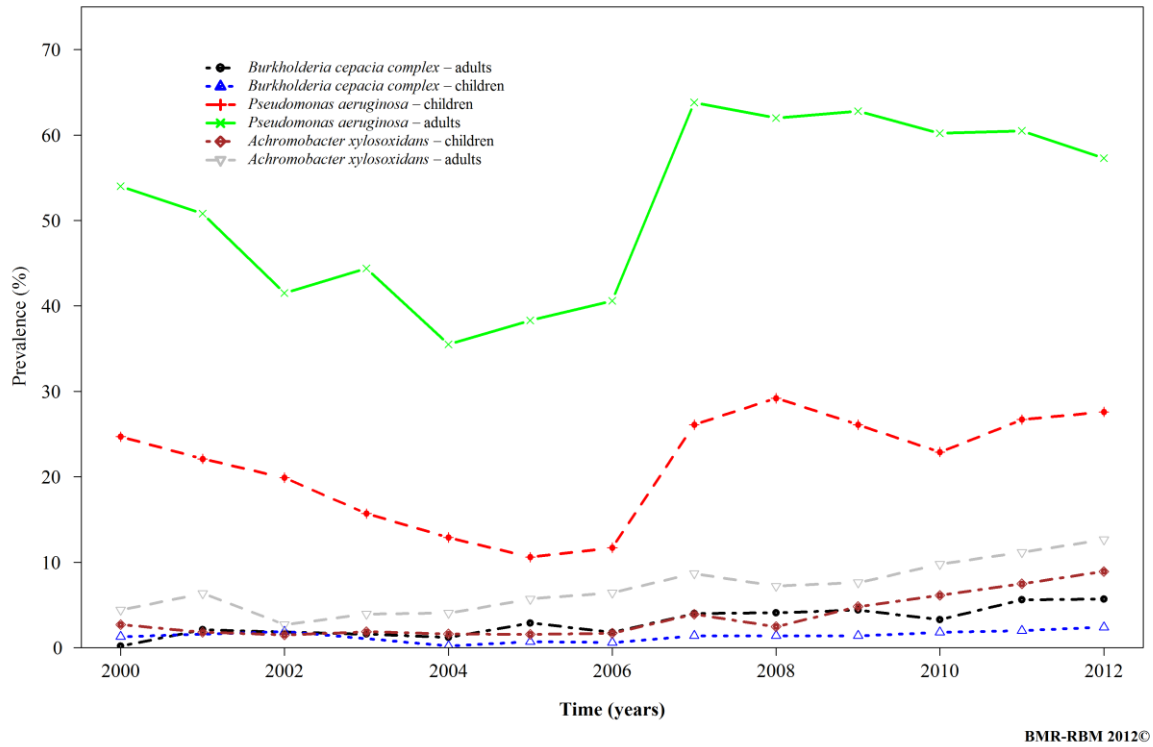


Figure 17: Prevalence of *Pseudomonas aeruginosa, Achromobacter xylosoxidans and Burkholderia cepacia complex* by age group and year

Note: The change in the prevalence over the period 2006 – 2007 is due to the change in the reporting system from a positive test at the last culture of the year to any positive ever found among the cultures done during year.

There has been an increase in the importance of some pathogens such as *Achromobacter xylosoxidans*, figures 17 - 18, which have shown an increase in the prevalence over the years.

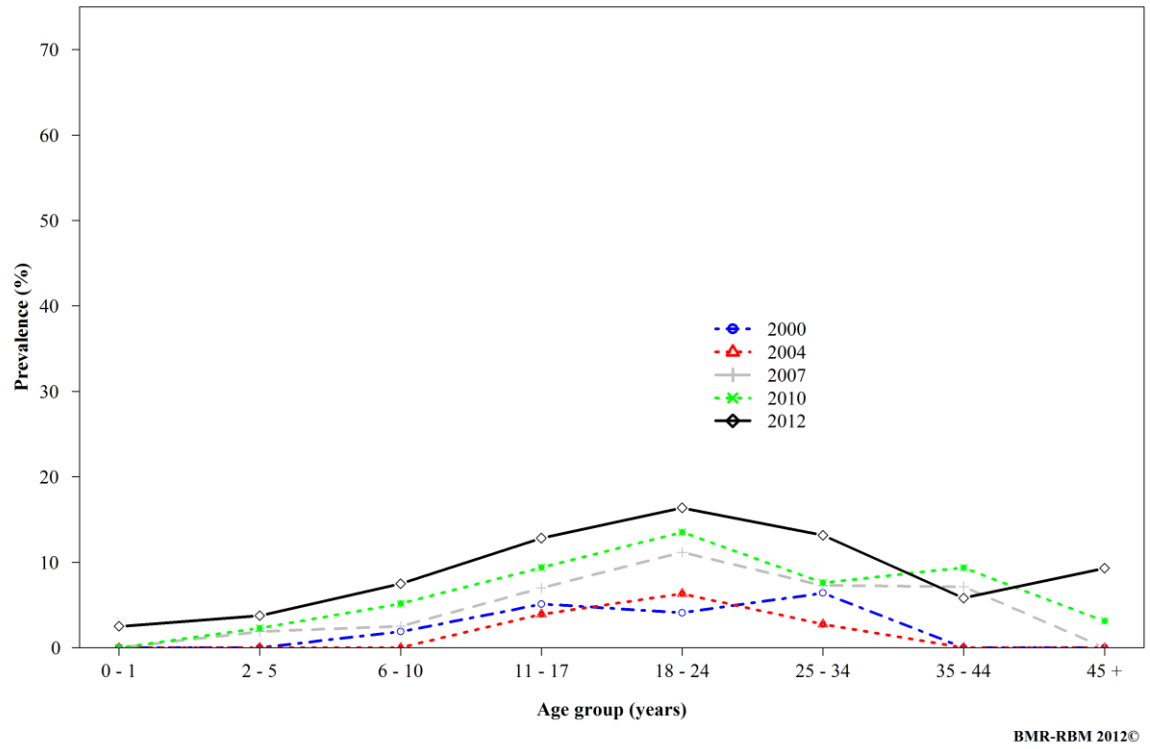


Figure 18: Prevalence of *Achromobacter xylosoxidans* by age group and year

CHAPTER 8: COMPLICATIONS

Cystic Fibrosis affects the respiratory[19], digestive[20,21], and reproductive[22,23], systems with variable degrees of severity. The defective chloride channel in CF causes a range of disturbances within the human body. Chloride channels are needed to regulate fluids within the cells. Complications in CF are mainly found in organs where mucus linings are needed (airways, intestines) and glands which need fluid to excrete their substances (pancreas, testis..).

In this section we cover the most frequent complications recorded during the year by age category. The overall prevalence is compared to the prevalence reported in previous years.

Data from transplant patients was excluded from the analysis of complications.

8.1 RESPIRATORY COMPLICATIONS

Allergic bronchial pulmonary aspergillosis (ABPA). ABPA is an allergic reaction to *Aspergillus fumigatus* a fungus that colonizes the airway of people with CF. Diagnosis is not always obvious as many symptoms of ABPA (cough, wheezing, shortness of breath, decline in lung function) are common symptoms of CF lung disease. Diagnosis relies on a combination of the clinical picture, blood tests and lung imaging.

Nasal polyps: In patient with CF, chronic infections of the upper airways (chronic sinusitis) may cause the formation of nasal polyps which are mucosal overgrowths. They are responsible for nasal obstruction.

Haemoptysis: When the damage within the bronchi reaches a blood vessel the patient with CF is coughing blood. Haemoptysis is mild in most cases, but sometimes the bleeding is so severe that a therapeutic embolization of the bleeding vessel is needed.

A **pneumothorax** occurs when air reaches the vacuum of the pleural space, mainly caused by destruction of the alveoli causing the leakage of air. This complication is more common in the adults who have more advanced lung disease [24,26].

Table 11: Prevalence of respiratory complications

	2009		2010		2011		2012	
Complication	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Allergic Bronchopulmonary aspergillosis (ABPA)	74	7.4	64	6.4	63	6.1	40	3.9
Pneumothorax	3	0.3	1	0.1	2	0.2	3	0.3
Nasal polyps	117	11.6	120	11.9	85	8.3	108	10.6
Sinusitis	212	21.1	210	20.9	169	16.4	177	17.4
Massive haemoptysis	27	2.7	18	1.8	10	1.0	6	0.6
Massive haemoptysis requiring embolization	2	0.2	9	0.9	7	0.7	2	0.2

Percentages are based on 1005, 1007, 1030 and 1018 non transplant patients respectively for the years 2009 through 2012

ABPA is the most frequent major respiratory complication. In 2012 it was reported in 13 (2.6%) children and in 27 (5.3%) adults.. This is a significant reduction (P = 0.0235) in the overall prevalence compared to 2011 and the previous years. A change in the criteria for reporting this complication by the centres could explain, at least partially this trend [25].

8.2 GASTRO-INTESTINAL AND ENDOCRINE COMPLICATIONS

Pancreatic insufficiency : Pancreatic enzymes are needed to digest fat and proteins. Pancreatic insufficiency is the inability of the pancreas to produce and transport enough enzymes to digest fat and proteins resulting in malabsorption with steatorhea (fatty stools), malnutrition and a deficiency in fat-soluble vitamins (ADEK).

Gastro-oesopahgeal reflux is a condition in which contents of the stomach or small intestine repeatedly move back up into the oesophagus. When repeated it causes oesophagitis and it may worsen the respiratory function.

Distal intestinal Obstruction syndrome (DIOS) : The intestinal cells with defective chloride channels produces thick intestinal mucus which in combination with stools can cause intestinal obstruction. DIOS is especially found in the terminal ileum and caecum. It can causes acute abdominal pain. DIOS usually responds to medical treatment but in a few cases a surgical intervention may be required.

Liver disease : All patients with CF present a defect CFTR protein in their biliary tract. Nevertheless some persons do develop liver disease leading to cirrhosis (replacement of the liver tissue by fibrosis) and others do not. Sometimes cirrhosis evolves in portal hypertension and in advanced cases a liver transplant can be proposed.

CF related Diabetes: Insulin is a hormone which maintains the balance of sugar in blood. Malfunctioning of the endocrine part of the pancreas leads to an insufficiency of the secretion of insulin leading to diabetes.

Table 12: Prevalence of gastro-intestinal and endocrine complications

	2009		2010		2011		2012	
Complication	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Pancreatic Insufficiency	850	84.6	847	84.1	855	83.0	830	81.5
Acute pancreatitis	11	1.1	5	0.5	11	1.1	6	0.6
CF related diabetes (CFRD)	113	11.2	122	12.1	143	13.9	128	12.6
Impaired Glucose Tolerance (IGT)	57	5.7	85	8.4	68	6.6	59	5.8
Peptic ulcers	1	0.1	2	0.2	4	0.4	2	0.2
Gastro-oesophageal reflux	189	18.8	190	18.9	179	17.4	198	19.4
Cirrhosis with portal hypertension	24	2.4	33	3.3	32	3.1	33	3.2
Gallstones	23	2.3	26	2.6	28	2.7	32	3.1
Intestinal obstruction(surgery)	10	1.0	5	0.5	5	0.5	4	0.4
Intestinal obstruction(no surgery)	91	9.1	75	7.4	55	5.3	74	7.3
Gastroparesis	4	0.4	3	0.3	2	0.2	7	0.7
Clostridium infection (treatment needed)	2	0.2	7	0.7	10	1.0	4	0.4

Percentages are based on 1005, 1007, 1030 and 1018 non transplant patients respectively for the years 2009 through 2012

The data shows that 426 (84.0%) of the children and 404 (79.1%) of the adults are pancreatic insufficient. CFRD was recorded in 16 (3.2%) of the children and 112 (21.9%) of the adults.

8.3 MISCELLANEOUS COMPLICATIONS

Reproductive system complications: Most men with cystic fibrosis are infertile because of congenital bilateral absence of the vas deferens (which allows the transport of the spermatozoids). However, as the production of spermatozoids is being preserved, techniques of assisted procreation are possible. Although women with cystic fibrosis may be less fertile than other women, it is possible for them to conceive and to have successful pregnancies. Those pregnancies require a higher surveillance.

Osteopenia and osteoporosis: Osteopenia and osteoporosis which are the result of a progressive loss of the bone mass are more frequent and earlier in cystic fibrosis due to various risk factors like malabsorption of vitamins D, use of glucocorticoids, chronic inflammation…

CF related arthritis/arthropathy: Patients with advanced lung disease sometimes develop painful inflammation of joints. The exact cause is not known and regression of joint symptoms is usually seen when respiratory disease is stabilized.

Psychiatric disease: It is difficult to define and quantify, however, the psychological repercussions of this pathology are frequent and often involve a bad compliance with the treatment.

Table 13: Other complications reported

	2009		2010		2011		2012	
Complication	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
CF related Arthritis / arthropathy	26	2.6	52	5.2	98	9.5	72	7.1
Cancer	2	0.2	2	0.2	3	0.3	2	0.2
Surgery	56	5.6	68	6.8	98	9.5	66	6.5
General anaesthesia	51	5.1	66	6.6	86	8.3	73	7.2
Others	186	18.5	138	13.7	126	12.2	143	14.0
Psychiatric disease	14	1.4	18	1.8	23	2.2	24	2.4
*Osteopenia/ Osteoporosis	133	13.2	130	12.9				
Osteopenia					107	10.4	112	11.0
Osteoporosis					24	2.3	24	2.4
Hypertension requiring treatment					16	1.6	14	1.4

Percentages are based on 1005, 1007, 1030 and 1018 non transplant patients respectively for the years 2009 through 2012

*Since 2011, data on the Osteopenia (the lowest z-score on Dual X-ray absorptiometry (DXA) between -1 and -2.5) and Osteoporosis (the lowest z-score on DXA < -2.5) complications are recorded separately.

CHAPTER 9: THERAPY, MEDICATION AND HOSPITALIZATION

Till today no definitive cure for CF exists. The problems of all cystic fibrosis patients are related to defective epithelial function with impaired production of mucus and fluids leading to complications described in the previous section. Treatment of the disease is therefore mostly based on preventing or reducing symptoms and complications.

In this section, the most common treatments and therapy used in 2012 is presented. An evolution of the proportion of patients hospitalized by age category for selected years is also presented. This analysis excludes data from the transplant patients.

Except for anti-conceptive therapy, the percentages are based on **507** children and **511** adults from a total of **1018** non transplant patients

9.1 VISITS TO CF CARE CENTERS AND HOSPITALIZATION

The median number of visits was 6 visits with the lower quartile at 4 and the upper at 7 visits respectively. Most of the patients, 84.7%, had a minimum of the four recommended visits to a CF reference centre during the year.

The figures below concern the number of days of hospitalization. In 2012, 57.6% of the patients were not hospitalized. Among the children (507) and adults (511), 65.7% and 49.6% respectively were not hospitalized.

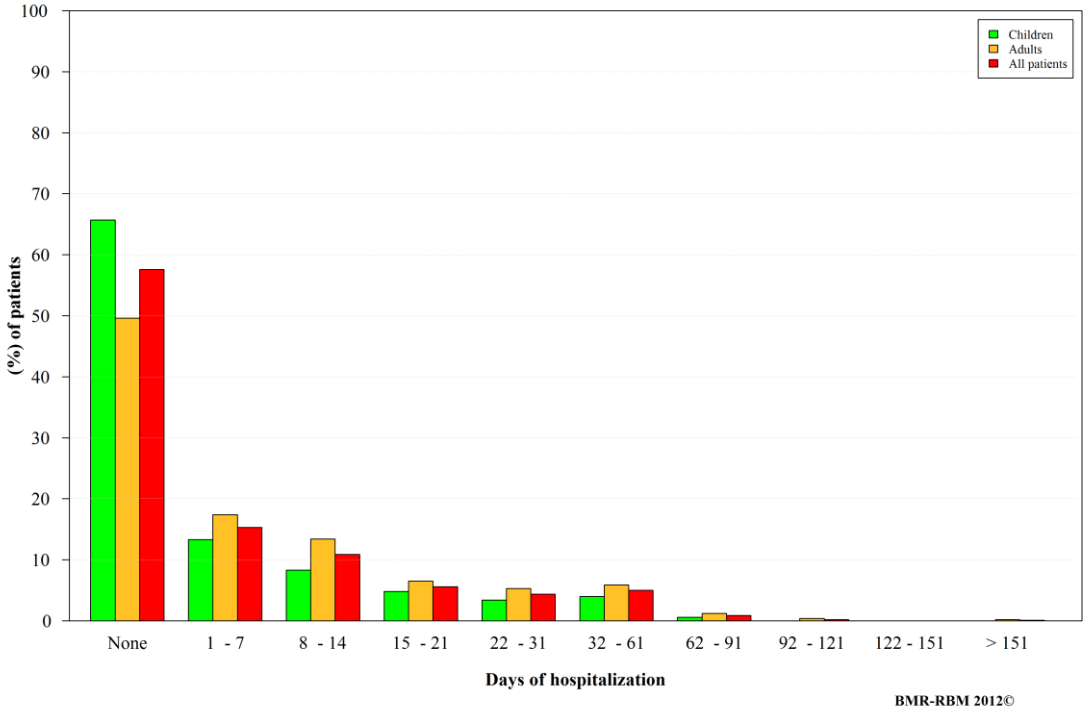


Figure 19: Number of hospitalization days

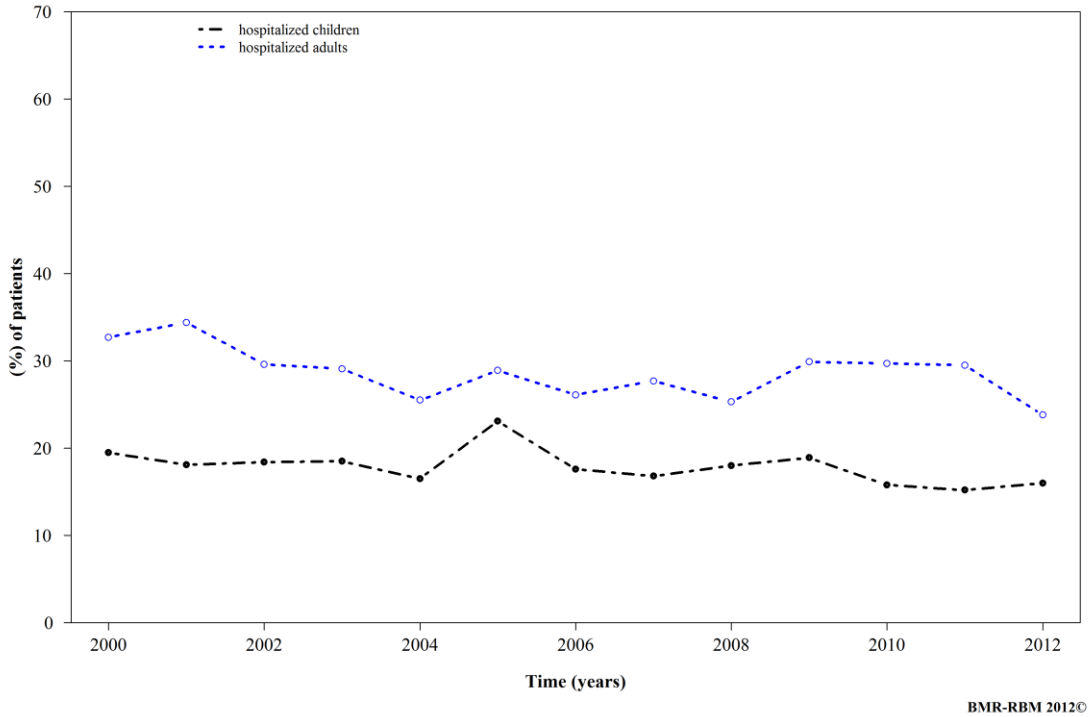


Figure 20: Proportion of patients hospitalized for more than two weeks by age and year

9.2 RESPIRATORY THERAPIES

To Prevent and treat respiratory infections: Because mucus is stuck within the bronchi, evacuating mucus is one the most important interventions. A patient with CF has regular chest physiotherapy sessions. Most of the patients also need autogenic drainage (the patients initiates physiotherapy at his own body). Maintenance inhaled medications include mucolytics that thin the sticky airway secretions such as RhDNase or hypertonic saline. Bronchodilators are given to open the bronchi. Inhaled antibiotics are used to treat infection, prevent or postpone colonization. In advanced lung disease oxygen is needed[27].

Every year, almost half of the patients with CF are hospitalized, mostly for the treatment of pulmonary exacerbations caused by an infection requiring intravenous antibiotics.
Inflammation caused by repeated infections plays an important role in the progression of lung injury. This explains the interest in the use of anti-inflammatories such as azithromycin or other anti-inflammatory drugs as complementary treatment.

Table 14: Physiotherapy, inhalation therapy , oral anti-inflammatory and antibiotics

	Children		Adults		Total	
Treatment	**n**	**%**	**n**	**%**	**n**	**%**
Regular chest physiotherapy	**487**	**96.1**	**439**	**85.9**	**926**	**91.0**
Antibiotics	**459**	**90.5**	**465**	**91.0**	**924**	**90.8**
Oral only	304	60.0	191	37.4	495	48.6
IV only	3	0.6	8	1.6	11	1.1
Oral and IV	146	28.8	254	49.7	400	39.3
Inhaled antibiotics	250	49.3	307	60.1	557	54.7
Tobramycin (300 mg)	46	9.1	117	22.9	163	16.0
Other inhaled antibiotics	236	46.5	266	52.1	502	49.3
Inhalation therapy(excluding antibiotics)	**494**	**97.4**	**479**	**93.7**	**973**	**95.6**
RhDnase	343	67.7	386	75.5	729	71.6
Other mucolytics	125	24.7	110	21.5	235	23.1
Hypertonic saline	290	57.2	285	55.8	575	56.5
Bronchodilators	386	76.1	390	76.3	776	76.2
Corticosteroids	244	48.1	329	64.4	573	56.3
Intranasal steroids	**225**	**44.4**	**231**	**45.2**	**456**	**44.8**
Oral anti-inflammatories	**186**	**36.7**	**317**	**62.0**	**503**	**49.4**
Azithromycin	167	32.9	307	60.1	474	46.6
Systemic corticosteroids	20	3.9	36	7.0	56	5.5
NSAID	7	1.4	37	7.2	44	4.3
Oxygen therapy	**6**	**1.2**	**15**	**2.9**	**21**	**2.1**

Note: Out of 895 patients aged 6 and above, 375 had FEV_1 predicted less than 75% , among these 195 also had a chronic *Pseudomonas* infection. 19 of the 195 received TOBI only, 77 used other inhaled antibiotics only and 66 used both TOBI and other inhaled antibiotics. However, 33 chronically infected patients with FEV_1 predicted less than 75% used none of the two treatments.

9.3 DIGESTIVE AND NUTRITIONAL THERAPIES

Optimizing the nutritional status: Because the nutritional status of a patient is correlated with the disease severity, every person with CF should take a well-balanced high-calorie and high-fat diet. Most individuals with CF are pancreatic insufficient [20] and must take pancreatic enzymes at every meal to digest food correctly. Also supplements of vitamins ADEK are administered routinely. Some people with CF receive supplemental feedings given overnight by a tube placed into the stomach (enteral feeding) or given intravenously (parenteral feeding).

Table 15: Digestive and nutritional therapies

	Children		Adults		Total	
Treatment	**n**	**%**	**n**	**%**	**n**	**%**
Pancreatic enzymes	433	85.4	411	80.4	844	82.9
Fat soluble vitamins (A,D,E and K)	449	88.6	392	76.7	841	82.6
Proton pump inhibitor and/or H2 receptor blocker	220	43.4	229	44.8	449	44.1
Ursodeoxycholic acid	135	26.6	121	23.7	256	25.1
Enteral feeding	13	2.6	9	1.8	22	2.2
Parenteral feeding	8	1.6	11	2.2	19	1.9
Gastrostomy tube	17	3.4	15	2.9	32	3.1

9.4 OTHER TREATMENTS

Monitoring the onset of other complications followed by appropriate therapeutic interventions: Every patient is regularly examined for possible signs of the onset of known complications of the disease. Ursodeoxycholic acid is a hydrophilic bile acid normally present in human bile which stimulates the biliary secretion and protect the hepatic cells. This therapy is usually started when clinical, biological or imaging finding point towards liver disease. Depending on complications, other medications are prescribed such as insulin therapy when a patient develops CF related diabetes or bisphosphonates for osteoporosis. The treatment burden for CF patients is high. Most CF patients spend a lot of time every day performing therapies. This imposes also a substantial burden on their family [28] .

Table 16: Other treatments

	Children		Adults		Total	
Treatment	**n**	**%**	**n**	**%**	**n**	**%**
Insulin therapy	17	3.4	88	17.2	105	10.3
Oral therapy for diabetes	1	0.2	24	4.7	25	2.5
Bisphosphonates	.	.	15	2.9	15	1.5
Anti-conceptive therapy (females aged 12 and over)	11	15.5	81	45.8	92	37.1
Prokinetics	43	8.5	43	8.4	86	8.4
Use of Psychopharmaca	11	2.2	60	11.7	71	7.0

Note: Out of 1018 non transplant patients, 128 had CFRD, among these 100 used insulin therapy only, 18 used only oral therapy for diabetes while one patient used both oral therapy for diabetes and insulin therapy. However, 9 patients with CFRD used none of the two treatments.

9.5 INTRAVANEOUS ANTIBIOTICS

In the year 2012, 40.2% (409) of the patients received IV antibiotics; 29.2% (148) amongst the children and 51.1% (261) among the adults. The figures below show the proportion that received IV antibiotics at home and/or in hospital in 2011 (top) compared to 2012 (bottom). There are fewer patients below six years taking IV antibiotics at home. Most of the adults have IV antibiotics both at home and in hospital.

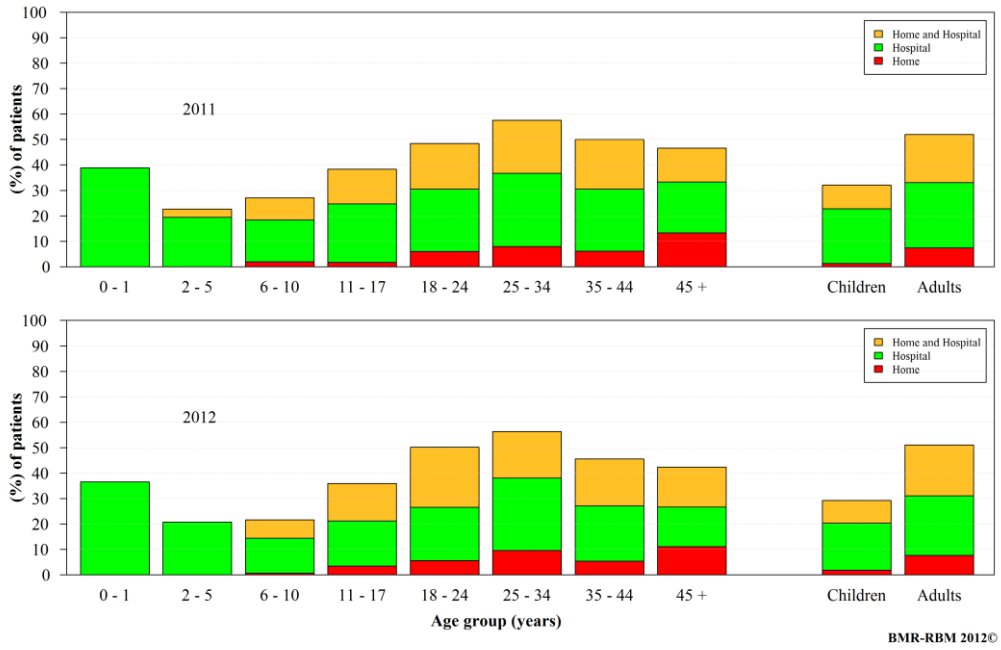


Figure 21: Proportion that used IV antibiotics treatment by age category

9.6 ORAL ANTIBIOTICS

The figures below show the days of oral antibiotics used in 2011 (top) and compared to 2012 (bottom). In 2012 about 9.1% of the patients did not take any oral antibiotics; 8.0% of children and 10.3% of the adults. These numbers are almost half of those reported in 2011. More than a quarter of both the children and adults, used oral antibiotics for over six months.

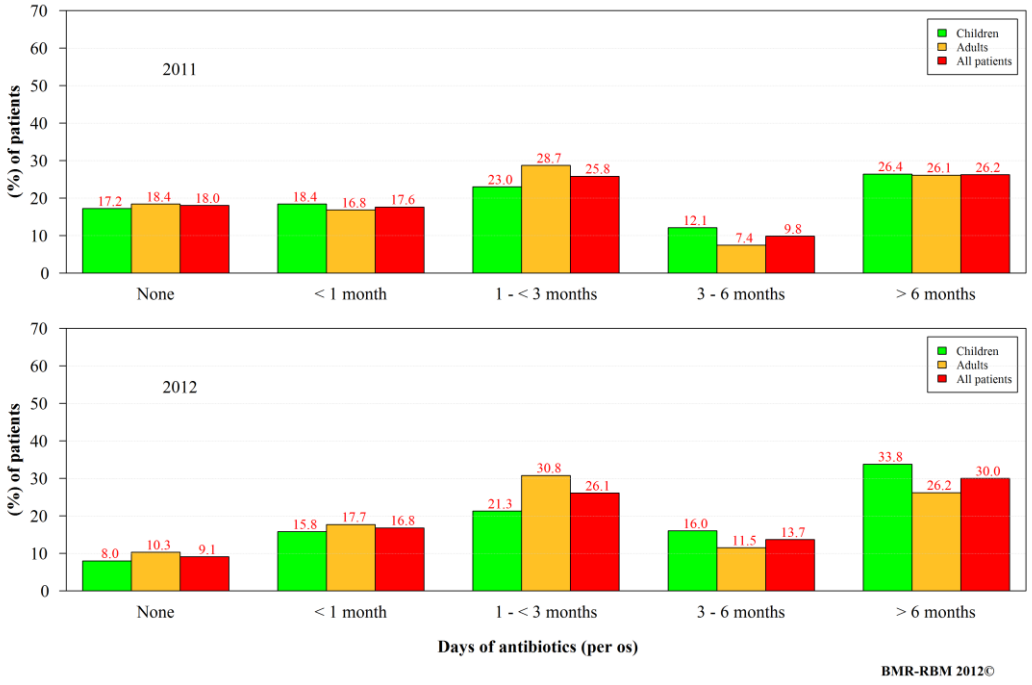


Figure 22: Days of oral antibiotics

CHAPTER 10: TRANSPLANTS AND CYSTIC FIBROSIS

When a patient with CF develops severe and progressive lung disease, lung transplantation may become an option. However, like other major surgeries, lung transplantation involves significant risks. A lung transplant is indicated only for patients who have a severe disease and who have exhausted all other forms of conventional medical treatment. For these patients, lung transplantation may offer prolonged survival and an improved quality of life; in some cases even a 'new' life.

The success rate of lung transplantation for CF patients is steadily improving. At present the actuarial survival rate is > 65 % at 3 years and > 40 % at 10 years after surgery[29]. The longest surviving patients had their transplant operations now more than 20 years ago.

The first (heart)-lung transplant in a Belgian patient with CF was performed in 1988. Since this time more than 200 patients with CF[30] (182 reported in the CF registry) have received a (heart)-lung transplant in Belgium and approximately 10 lung transplants per year are now performed for CF. Some patients with CF will need other types of transplantations such as liver transplantation for end-stage CF-related liver cirrhosis or renal transplantation for end-stage renal disease because of diabetes, antibiotic toxicity or the toxicity of immunosuppressive drugs required after lung transplantation.

This is a short analysis of data concerning the transplant patients. It includes a table with all transplants ever reported in the registry. This table shows the type and year of transplant and also the number of patients presumed still alive by the time of data collection 2012, categorized by the year of first transplant.

10.1 TRANSPLANT STATUS

The registry records show that since inception of the registry in 1998, at least **197** patients, **91** male and **106** female, have benefitted from transplantation; either single or multiple. There are 14 patients with a transplant on more than one occasion.

The age at the first transplant was estimated using the last consultation in the year of transplant where available or the last day of the year if the former was missing. The data shows that the mean (SD) and median (IQR) age of the transplant patients in the year of the first transplant was 26.8 (9.1) and 27.0 (12.0) respectively. The oldest patient at first transplant was 58.0 years. About 12.7% (25 patients) had the first transplant done before age 18 years.

In 2012, there were **141 (12.3%)** patients with a recorded transplant, 5 (0.4%) were on the waiting list while one patient declined a transplant. The mean (SD) and median (IQR) age of the transplant patients reported as alive in 2012 was 34.2 (10.1) and 33.0 (14.0) years respectively with a range of 14.0 – 63.0 years at the last consultation in 2012. 66 were male while 75 were female, more than 95.0% of the transplant patients in the 2012 data were adults. Five transplant patients died in 2012.

The data presented in table 17 concerns all recorded transplants in the registry and is compared with data on patients reported alive by the time of data collection for year 2012 (the numbers in the far right column). Slight differences may be noted with previous reports as we seek to consolidate the transplant data. In this table, the numbers of transplants performed do not add up to the number of patients.

10.2 TYPE OF TRANSPLANT

The most frequent transplant done is the Lung transplant, either single or with a liver or heart. So far, 167 isolated lung transplants have been carried out.

Table 17: Type of transplant by year

	Type of transplant							Totals	
Year	**Kidney**	**Liver**	**Lung**	**Lung-Heart**	**Heart**	**Liver-Kidney**	**Lung-liver**	**Transplants performed**	**Patients Alive**
1991	.	.	.	2	.	.	.	**2**	**1**
1992	.	.	.	.	.	.	.	**-**	**-**
1993	.	.	.	2	.	.	.	**2**	**1**
1994	.	.	.	3	.	.	.	**3**	**1**
1995	.	1	2	3	.	.	.	**6**	**1**
1996	.	.	.	1	.	.	.	**1**	**1**
1997	.	.	1	3	.	.	.	**4**	**4**
1998	.	.	8	3	.	.	.	**11**	**3**
1999	.	.	6	.	.	.	.	**6**	**2**
2000	.	.	10	.	.	.	.	**10**	**6**
2001	.	4	14	.	.	.	1	**19**	**14**
2002	.	2	9	.	.	.	.	**11**	**8**
2003	.	1	9	.	.	.	.	**10**	**9**
2004	.	.	12	.	.	.	.	**12**	**10**
2005	.	2	9	.	.	.	1	**12**	**8**
2006	1	1	14	.	1	.	.	**17**	**10**
2007	1	1	16	.	.	.	.	**18**	**8**
2008	3	.	13	1	.	.	.	**17**	**13**
2009	.	1	9	.	.	1	.	**11**	**9**
2010	.	1	13	.	.	.	2	**16**	**13**
2011	2	.	14	.	.	.	.	**16**	**11**
2012	.	.	8	.	.	.	.	**8**	**8**
Total	**7**	**14**	**167**	**18**	**1**	**1**	**4**	**212**	**141***

*** Total number of patients alive in 2012 by transplant year considering the first transplant.**

Note: Multiple transplants or grafts are counted as separate transplant occasions in the table above. A total of 212 transplants on 197 patients are so far reported in the registry. There are 14 patients who have had a transplant on more than one occasion.

CHAPTER 11: REPORTED DEATHS

This section has a summary of data on the deaths reported to the registry since inception in 1998. The number of deaths is also classified into age groups with information on the primary cause of death given in the latter part. Note that the stated causes of death are not mutually exclusive.

The data is updated each year from center reports with delays of up to two years noted in the confirmation of the data. From 2013, this background data will be automatically updated using the ConsultRN module by linking the registry data collection to the national registry database.

11.1 AGE AT DEATH

The data in the registry data shows that there have been 125 reported deaths since its inception in 1998, 64 male and 61 female. 16 (12.8%) of the deaths were in children below 18 years while 8 (6.4%) of the deaths were in children younger than ten years. The mean (SD) and median (IQR) age at death for all reported cases are 27.9 (11.0) and 27.1 (13.3) respectively with the youngest at 0.6 years and the oldest case at 59.5 years. The table below shows the year and age at death for confirmed cases.

Table 18: Categorized age at death

	YEAR															
Age at death	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**Total**
0 - 4	1	.	.	.	.	.	.	1	1	.	.	.	.	.	.	**3**
5 - 10	.	.	.	2	.	1	.	.	.	1	.	.	.	1	1	**6**
11 - 14	.	.	.	.	.	1	.	.	.	1	.	1	.	.	.	**3**
15 - 20	2	5	1	1	.	2	2	.	2	1	2	1	.	.	1	**20**
21 - 24	.	2	2	3	.	3	3	1	.	.	.	2	3	2	1	**22**
25 - 30	1	3	1	2	3	3	2	1	.	2	3	2	.	2	2	**27**
31 - 34	1	.	3	.	4	1	1	.	.	.	.	2	2	1	2	**17**
35 - 40	.	1	2	2	2	1	.	.	2	1	.	.	.	.	2	**13**
41 - 44	.	.	.	.	.	.	1	.	1	1	.	1	.	1	.	**5**
45 - 50	.	.	.	.	.	1	.	.	.	1	1	1	.	1	.	**5**
51 - 54	.	.	.	.	.	.	.	.	.	.	.	.	1	.	1	**2**
55 - 60	.	.	.	.	1	.	.	.	.	.	.	.	1	.	.	**2**
Total	**5**	**11**	**9**	**10**	**10**	**13**	**9**	**3**	**6**	**8**	**6**	**10**	**7**	**8**	**10**	**125**

The number of deaths are not consolidated for years 2011 and 2012 due to delays in reporting. The link to the national registry via ConsultRN starting with collection from 2013 will provide an automatic update of this data to reduce discrepancies in reporting.

The figure below shows the number of confirmed deceased patients by age category. Most of the deceased patients were in the age category 25 – 30 years.

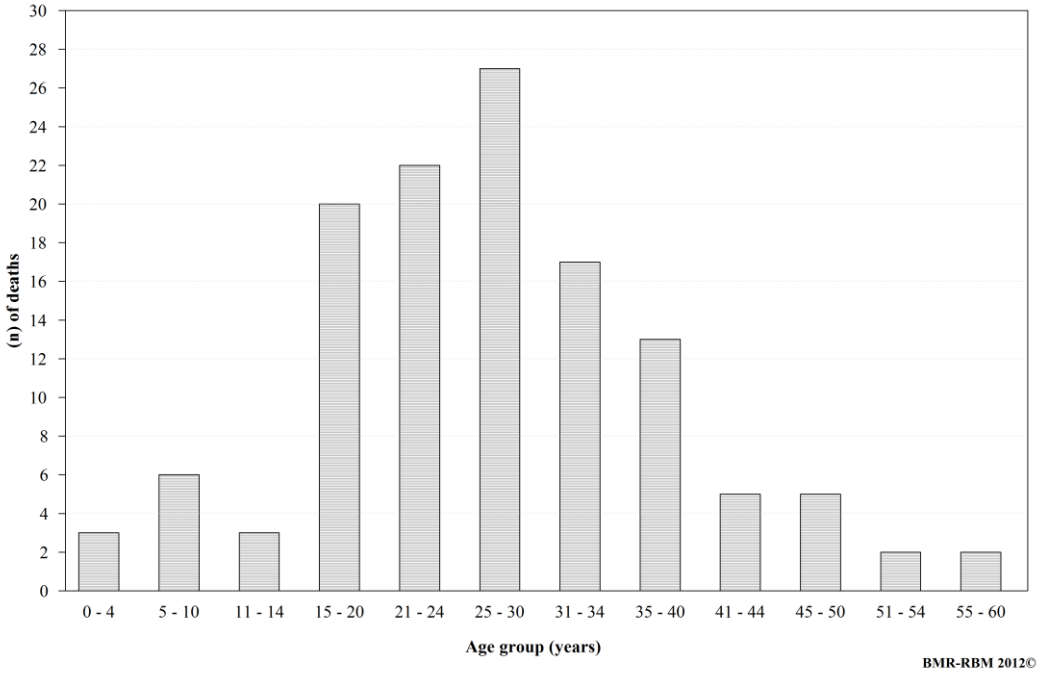


Figure 23: Number of reported deaths since 1998 by age category

11.2 PRIMARY CAUSE OF DEATH

Table 19: Primary causes of death for reported cases

Cause of death[1]	n	%*
Respiratory	50	40.0
Transplant	34	27.2
Other	19	15.2
Cardiac	5	4.0
Liver	4	3.2
Cancer	4	3.2
Suicide	3	2.4
Trauma	1	0.8
Unknown + missing	20	16

*based on the total reported deaths

[1] Causes of death are not mutually exclusive and these percentages are attributable to the specific cause of death

[2] Other causes of death include and are not limited to: - septic shock, multi-organ failure, terminal renal insufficiency, hypoglycaemic coma

Note: The most common primary causes of death are associated with the respiratory system or are as a result of post-transplant complications. Amongst the deaths reported in 2012, one was a patient less than 18 years.

CHAPTER 12: EDUCATION AND EMPLOYMENT

People with CF are living longer. According to the registry data the median patient age had increased from 14.9 in 1998 to about 20.3 in 2012 suggesting better life expectancy. Despite their therapy burden, they are now studying, graduating and taking up a career either part-time or even full-time.

This section contains an annual summary of social and economic data, including education level of the people with CF registered in 2012. It details information on social allowances and employment status. All patients with substantial data, including those with a transplant are included in this analysis.

12.1 EDUCATION

Table 20: Education level

	Children		Adults		Total	
Education level	**n**	**%**	**n**	**%**	**n**	**%**
no school	48	9.4	81	13.0	129	11.4
regular school / education attendance	460	90.4	128	20.6	588	52.0
has finished school/education	.	.	381	61.3	381	33.7
unknown	1	0.2	32	5.1	33	2.9
subtotal	**509**		**622**		**1131**	
missing	4		19		23	
total	**513**		**641**		**1154**	

12.2 SOCIAL ALLOWANCES AND EMPLOYMENT

Table 21: Social allowances or benefits and employment

	Children		Adults	
Description	**n**	**%**	**n**	**%**
additional child allowance	484	94.3	94	14.7
income support (in adults)	.	.	248	38.7
disability allowance	1	0.2	94	14.7
preferential tariff (in adults)	.	.	379	59.1
pension allowance (in adults)			13	2.0
employment*	2	0.4	262	51.1

***data excludes 128 adults still actively in school**

Amongst the 262 patients who said they were employed, 133 (50.8%) worked full time, 93 (35.5%) part-time while for 36 patients, this was unknown. Two children and 17 adults had no information on social allowances

REFERENCES

1. **Farrell PM**. *The prevalence of cystic fibrosis in the European Union*. J Cyst Fibros 2008; **7**:450-453.

2. **Dequeker, E., Accurso, F., Cabeza, S., Cassiman, J.-J., Corey, M., Davidson, A., Döring, G., Heidet, L., Heijerman, H., Kotsimbos, T., Mastella, G., Morrison, C., Pignatti, P.F., Strandvik, B., Tsui, L.-C., Dodge, J.** *Classification of cystic fibrosis and related disorders*. J Cyst Fibros 2002;**1 :** 5-8.

3. **Quinton PM** . *Physiological Basis of Cystic Fibrosis: A Historical Perspective*, Physiological Reviews 1999; **79**(1) S3-S22.

4. **Riordan, J.R., Rommens, J.M., Kerem, B.-S., Alon, N., Rozmahel, R., Grzelczak, Z., Zielenski, J., Lok, S., Plavsic, N., Chou, J.-L., Drumm, M.L., Iannuzzi, M.C., Collins, F.S., Tsui, L.-C**. *Identification of the cystic fibrosis gene: cloning and characterization of complementary DNA.* Science 1989; 245: 1066-1073.

5. **Ramsey BW., Davies J., McElvaney NG., Tullis E., Bell SC., Dřevínek P., Griese M., McKone EF., Wainwright CE., Konstan MW., Moss R., Ratjen F., Sermet-Gaudelus I., Rowe SM., Dong Q., Rodriguez S., Yen K., Ordoñez C., Elborn JS.** *VX08-770-102 Study Group. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation.* N Engl J Med 2011; **365**:1663-72.

6. http://www.inami.be/care/fr/revalidatie/convention/mucoviscidose/pdf/agreement.pdf
   http://www.inami.be/care/nl/revalidatie/convention/mucoviscidose/pdf/agreement.pdf

7. http://www.inami.be/care/fr/revalidatie/convention/mucoviscidose/pdf/avenant.pdf
   http://www.inami.be/care/nl/revalidatie/convention/mucoviscidose/pdf/avenant.pdf

8. http://www.ecfs.eu/projects/ecfs-patient-registry/information-about-ecfspr-cf-patients

9. **Kuczmarski R.J**., **Ogden C.L**., **Guo S.S**. et al. *CDC Growth Charts for the United States: Methods and Development. National Center for Health Statistics*. Vital Health Statistics 2002; **11**(246): 1-190.

10. **Rolland-Cachera MF., Cole TJ., Sempé M., Tichet J., Rossignol C., Charraud A.** *Body mass index variations: centiles from birth to 87 years.* Eur J Clin Nutr 1991; **45**: 13-21. *Rolland-Cachera MF: personal communication.

11. **Schluchter MD., Konstan MW., Drumm ML., Yankaskas JR ., Knowles MR.** *Classifying Severity of Cystic Fibrosis Lung Disease Using Longitudinal Pulmonary Function Data. Am J Respir Crit Care Med 2006;* **174**: 780–786.

12. **McKone EF., Emerson SS., Edwards KL., Aitken ML**. *Effect of genotype on phenotype and mortality in cystic fibrosis: a retrospective cohort study*, Lancet 2003, **361**: 1671–1676

13. **Wang X., Dockery DW., Wypij D., Fay ME., Ferris BG Jr**. *Pulmonary function between 6 and 18 years of age*. Pediatr Pulmonol 1993; **15**(2):75-88.

14. **Hankinson JL., Odencrantz RJ., Fedan KB.** *Spirometric Reference Values from a Sample of the General U.S. Population.* Am. J. Respir. Crit. Care Med 1999; **159**: 179-187.

15. **Cole TJ**. *The LMS method for constructing normalised growth standards*. Eur J Clin Nutr 1990; **44**: 45-60.

16. http://www.genet.sickkids.on.ca/cftr/SearchPage,$Form.direct

    http://www.cftr2.org/browse.php

17. **Hart CA., Winstanley C.** *Persistent and aggressive bacteria in the lungs of cystic fibrosis children*. Br Med Bull 2002; **61**: 81–96.

18. **de Vrankrijker AM., van der Ent CK., van Berkhout FT., Stellato RK., Willems RJ., Bonten MJ., Wolfs TF**. *Aspergillus fumigatus colonization in cystic fibrosis: implications for lung function?* Clin Microbiol Infect. 2011; **17**(9):1381-6.

19. **Flume PA**., *Pulmonary Complications of Cystic Fibrosis*, Respir Care 2009; **54**(5):618 – 625.

20. **Sinaasappel M., Stern M., Littlewood J., Wolfe S., Steinkamp G., Heijerman Harry G.M., Robberecht E., Doring G.** *Nutrition in patients with cystic fibrosis: a European Consensus*, J Cyst Fibros 2002; **1**: 51–75.

21. **Goodin B.,** *Nutrition Issues in Cystic Fibrosis*, Practical Gastroenterology 2005; 76 – 94.

22. **McCallum TJ., Milunsky JM., Cunningham DL., Harris DH., Maher TA., Oates RD.** *Fertility in Men With Cystic Fibrosis: An Update on Current Surgical Practices and Outcomes*. Chest 2000; **118**:1059-62.

23. **Lyon A, Bilton D**. *Fertility Issues in Cystic Fibrosis.* Paediatr Respir Rev 2002; **3**: 263-240.

24. **Kioumis IP., Zarogoulidis K., Huang H., Li Q., Dryllis G., Pitsiou G., Machairiotis N., Katsikogiannis N., Papaiwannou A., Lampaki S., Porpodis K., Zaric B., Branislav P., Mpoukovinas I., Lazaridis G., Zarogoulidis P**. *Pneumothorax in cystic fibrosis.* J Thorac Dis. 2014 Oct;6(Suppl 4):S480-7

25. **Stevens DA., Moss RB., Kurup VP et al. Participants in the Cystic Fibrosis Foundation Consensus Conference.** *Allergic bronchopulmonary aspergillosis in cystic fibrosis--state of the art: Cystic Fibrosis Foundation Consensus Conference.* Clin Infect Dis. 2003 Oct 1;37 Suppl 3:S225-64.

26. **Schuster SR., McLaughlin FJ., Matthews WJ Jr., Strieder DJ0, Khaw KT., Shwachman H**., *Management of pneumothorax in cystic fibrosis*, Journal of Pediatric Surgery 1983; **4** : 492-497.

27. **Elphick HE., Mallory G**. *Oxygen therapy for cystic fibrosis. Cochrane Database of Systematic Reviews 2013*, Issue 7. Art. No.: CD003884. DOI: 10.1002/14651858.CD003884.pub4.

28. **Sawicki GS., Sellers DE., Robinson WM**. *High treatment burden in adults with cystic fibrosis: Challenges to disease self-management*, J Cyst Fibros 2009; **8** (2): 91-96.

29. **Christie JD., Edwards LB., Kucheryavaya AY., Benden C., Dobbels F., Kirk R., Rahmel AO., Stehlik J., Hertz MI**. *The Registry of the International Society for Heart and Lung Transplantation: 29th Adult Lung and Heart-Lung Transplant Report-2012*. J Heart Lung Transplant. 2012; **31**:1073-86.

30. **Van Raemdonck D.** on behalf of the Thoracic Committee of the Belgian Transplantation Society. (Heart-)Lung transplantation in Belgium. Annual report 2012. Personal communication.

APPENDIX I

BMR-RBM DIGITAL QUESTIONNAIRE VERSION 1.0 REGISTRATION 2012

I. BACKGROUND DATA

Patient Code : 13488
Collect year : 2011

X Variables collected in the European CF Registry (ECFSPR)

- Identification
- Diagnosis
- Sweat Test
- Genotype
- Nasal transep.pot.diff.

Identification

NISS code :

District :

Update district Missing data

X Gender : Male Female
X Birth month :
X Birth Year :
Age :
Order in the family :
Country of origin mother :
Country of origin father :
Height father : cm measured
Height mother : cm measured
X Received transplant :
X Diagnosis confirmed :
X Deceased :
X Death month :
X Death Year :

Diagnosis confirmed (ref_DiagnosisConfirmed)
1 No
2 Yes
3 To be confirmed
4 Unknown
999 Missing Data

Diagnosis

X Date of clinical diagnosis :

- Respiratory problems
- Nasal polyposis/chronic sinusitis
- Chronic dia-/steatorrhea/malabsorption
X Meconium ileus
- Intestinal obstruction (other than meconium ileus)
- Rectal prolapse
- Dehydration/electrolyte imbalance
- Failure to thrive
- Prenatal diagnosis
- Neonatal screening test
- Prolonged icterus
- Family history
- Infertility
- Other Other specify :
- Missing data

X NeoNatal Screening :

Neonatal screening (ref_NeoNatalScrTest)
0 Unknown
1 Not done
2 Performed positive
3 Performed negative
4 Performed result unknown
999 Missing Data

Sweat Test

Date of sweat test: (dd/mm/yyyy)

X Type of sweat test:

Sweat test Collected by:

X Chloride:

Sodium:

Type of sweat test (ref_SweatTestType)	
0	Unknown
1	Pilocarpine Iontoforesis
3	Conductivity
999	Missing Data

Sweat test collected by (ref_SweatTestCollection)	
0	Unknown
1	Gauze pad
2	Wescor nanoduct
3	Wescor macroduct
999	Missing Data

Genotype

List of mutations (see next page)

Date of genotype: (dd/mm/yyyy)

X Chromosome 1:

X Other:

T status 1:

X Chromosome 2:

X Other:

T status 2:

Date genotype (new nomenclature): (dd/mm/yyyy)

Chromosome 1 (new nomenclature):

Other (new nomenclature):

T status 1 (new nomenclature):

Chromosome 2 (new nomenclature):

Other (new nomenclature):

T status 2 (new

Nasal transep.pot.diff.

Date transep. pot.: (dd/mm/yyyy)

Nasal transep.pot.diff. :

Nasal transep. Pot. diff (ref_TransEpitalial)	
2	Not Executed
4	Normal
5	Evocative
999	Missing Data

Mutation (ref_GenotypeMutation)		**Mutation new nomenclature** (ref_GenotypeMutationNewNomenclature)	
0	not identified	0	not identified
1	df508	1	c.1521_1523delCTT
2	G542X	2	c.1624G>T
3	G551D	3	c.1652G>A
4	W1282X	4	c.3846G>A
5	N1303K	5	c.3909C>G
6	R553X	6	c.1657C>T
7	621+1G->T	7	c.489+1G>T
8	3849+10kbC->T	8	c.3717+12191C>T
9	1717-1G->A	9	c.1585-1G>A
10	R117H	10	c.350G>A
11	G85E	11	c.254G>A
12	R347P	12	c.1040G>C
13	[delta]I507	13	c.1519_1521delATC
14	2789+5G->A	14	c.2657+5G>A
15	R1162X	15	c.3484C>T
16	R560T	16	c.1679G>C
17	R334W	17	c.1000C>T
20	2184delA	20	c.2052delA
21	711+1G->T	21	c.579+1G>T
22	1078delT	22	c.946delT
23	A455E	23	c.1364C>A
24	3659delC	24	c.3527delC
25	S1251N	25	c.3752G>A
26	E60X	26	c.178G>T
28	394delTT	28	c.262_263delTT
35	2183AA->G	35	c.2051A>G
45	3272-26A->G	45	c.3140-26A>G
47	3120+1G->A	47	c.2988+1G>A
61	1898+1G->A	61	c.1766+1G>A
67	I148T	67	c.443T>C
74	2143delT	74	c.2011delT
90	Q552X	90	c.1654C>T
116	Del exon 2-3	116	c.54-5940_273+10250del21kb
117	3905insT	117	c.3773_3774insT
118	3199del6	118	c.3067_3072delATAGTG
119	711+5G->A	119	c.579+5G>A
999	missing data	999	Missing data
120	not done	120	not done
121	other	121	other

T status (ref_GenotypeTStatus)		**T status new nomenclature** (ref_GenotypeTStatus_New)	
0	Not applicable	0	Not applicable
1	5T	1	c.1210-12T(5)
2	7T	2	c.1210-12T(7)
3	9T	3	c.1210-12T(9)
999	Missing Data	999	Missing Data

II. DATA COLLECTION OF THE YEAR 2012

1. Observation

Observation | Microbiology | Complications | Therapy | Transplantation | Social

- Life/Death
- Cause of death
- Last consultation of the year
- The best lung function of the year

Patient status (ref_PatientState)	
1	First registration in this center
2	in follow up
4	Not seen patient
5	Revoked diagnosis
7	Moved to other center
8	No information
998	Missing Data

Life/Death

Patient alive : ☐

Patient Status :

Cause of death

- ☐ Respiratory
- ☐ Cardiac
- ☐ Hepatic
- ☐ Trauma
- ☐ Suicide
- ☐ Associated with cancer

Type :

- ☐ Associated with organ transplantation
- ☐ Other cause

Type

- ☐ Cause unknown

Last consultation of the year

Date Consultation : (dd/mm/yyyy)

Lung function executed (ref_LungFunctionExecuted)	
1	No
2	Yes
3	Impossible
999	Missing Data

Anthropometry

X Weight Kg

Height cm

Lung Function

Executed :

FVC : L

FEV1 : L

FEF25-75 : L/s

The best lung function of the year

X Date of best LungFx : (dd/mm/yyyy)

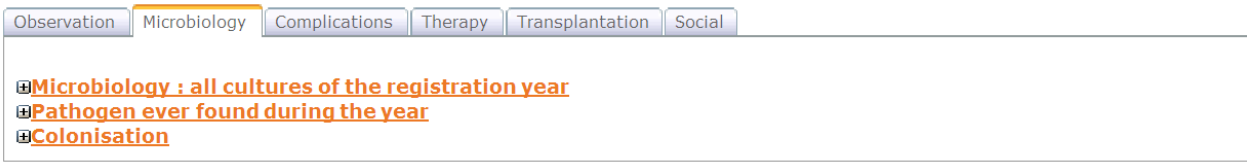
X FVC : L

X FEV1 : L

FEF25-75 : L/s

X Height : cm

2. Microbiology



Microbiology : all cultures of the registration year

Microbiology executed :

- ☐ Swabs
- ☐ Sputum
- ☐ Broncho-alveolar lavage (BAL)
- ☐ Missing values

Microbio executes (ref_Mbio_Test)
1 Executed
2 Not Executed
999 Missing Data

Pathogen ever found during the year

- ☐ Pseudomonas aeruginosa
- ☐ Burkholderia cepacia complex
- X ☐ Stenotrophomonas maltophilia
- ☐ Achromobacter xylosoxidans (Alcaligenes)
- ☐ methicillin resistant Staphylococcus aureus (MRSA)
- ☐ methicillin sensible Staphylococcus aureus (MSSA)
- ☐ Haemophilus influenzae
- ☐ Aspergillus
- ☐ Scedosporium prolificans
- X ☐ Atypical Mycobaterium (~~no~~ NTM)
- ☐ Other
- ☐ No pathogens
- ☐ Missing Values

Colonisation

- Number of exploitable months
- X Pseudomonas colonisation
- X B. cepacia compl. colonisation :
- Stenotrophomonas colonisation
- Achromobacter colonisation
- X SA MRSA colonisation

Number of exploitable months (ref_Mbio4K_Month)
0 0
1 1
2 2
… …
11 11
12 12
999 Missing Data

3. Complications

Complications (occuring or still active in the registration year)

Complications :

Respiratory causes
Digestive causes
Other complications
Surgery

Respiratory causes

X Allergic broncho pulmonary aspergillosis

ABPA Treated :

Treatment for ABPA :

X Pneumothorax

Nasal polyps (having required/requiring therapy)

Sinusitis (having required/requiring therapy)

X Massive haemoptysis

Requiring surgery

Treatment for ABPA (ref_ComplicationABPATypeTreatm)	
1	Oral steroids and antifungal
2	Omalizumab and antifungal
3	Other
4	Unknown
999	Missing Data

CFR Diabetes (ref_ComplicationDiab)	
1	No
2	IGT
3	CFRD
4	CFRD without fasting hyperglycemia
5	CFRD with fasting hyperglycemia
999	Missing Data

Digestive causes

X CF diabetes :

OGTT done this year :

Acute pancreatitis

Peptic ulcers

Gastro-oesophageal reflux

X Liver disease Cirrhosis with portal hypertension

Gallstones

Intestinal obstruction: requiring surgery

Intestinal obstruction: not requiring surgery

Gastroparesis

Clostridium

Osteopenia / Osteoporosis (ref_ComplicationOsteo)	
0	Missing Data
1	z-score>=-1
2	z-score <-1 and >-2,5
3	z-score <=-2,5
4	Not done
99	

Other complications

CF related arthritis/arthropathy

Osteopenia / Osteoporosis :

Date of most recent DEXA :

Psychiatric

X Cancer

Type :

Hypertension treated

Chronic renal insufficiency :

Other complications: specify

Type :

Chronic renal insufficiency (ref_ComplicationDiabChronRenalInsuff)	
1	No
2	Stage I GFR (Glomerular filtration rate) ≥ 90 ml/min/1.73 m²
3	Stage II GFR 60-89 ml/min/1.73 m²
4	Stage III GFR 30-59 ml/min/1.73 m²
5	Stage IV GFR 15-29 ml/min/1.73 m²
6	Stage V GFR < 15 ml/min/1.73 m²
7	Dialysis
999	Missing Data

Surgery

Surgery

General anaesthesia

Type :

4. Therapy

Therapy received during the year of registration

Number Consultations :

Days in hospital :

Respiratory system
Digestive system
Miscellaneous

Systemic antibiotics (ref_Antibiotics)
1 No
2 per os
3 iv
4 per os + iv
999 Missing Data

Respiratory system

Systemic antibiotics :

Days per os :

Days iv at home :

Days iv in hospital :

Days per os (ref_TherapyResp_ABNrDaysDomOral)
1 None
2 < 1 month
3 1 - 3 months
4 3 - 6 months
5 > 6 months
999 Missing Data

X Inhaled antibiotics :

- Tobramycine 300mg
- Other

Home O2-therapy (ref_Oxygen)	
1	No
2	At Night
3	Day and Night
999	Missing Data

X Home O2-therapy

Inhalation therapy (except antibiotics) :

X Bronchodilators
Mucolytics
X Hypertonic saline
Corticosteroids
X RhDnase

Intranasal steroids

Antiinflammatories p.o.

- Systemic Corticoids
- NSAID
X Azithromycine

Digestive system

Pancreatic sufficient :

X Pancreatic enzymes :

Fat soluble vitamins (ADEK) :

X Ursodeoxycholic acid :

Tube feeding :

Gastrostomy :

Parenteral feeding :

X

Miscellaneous

Oral therapy for diabetes :	
Insulin therapy :	
Prokinetics :	
PPI + H2 receptor blocker :	
Anticonceptive therapy :	
Psychopharmaca :	
Bisphosphonates :	
Regular chest physiotherapy :	
Randomised drug trial :	

5. Transplantation

Transplants

Transplant status :

Type of transplant :

Year of transplant :

Precise date of first entering the Tx waiting list: (dd/mm/yyyy)

Precise date of the most recent Tx : (dd/mm/yyyy)

This section contains historical data

X Transplant status 1 :

X Type of transplant 1 :

Year of transplant 1 :

Precise date of first entering the Tx waiting list : 1 (dd/mm/yyyy)

Precise date of the most recent Tx : 1 (dd/mm/yyyy)

Transplant status 2 :

Type of transplant 2 :

Year of transplant 2 :

Precise date of first entering the Tx waiting list : 2 (dd/mm/yyyy)

Precise date of the most recent Tx : 2 (dd/mm/yyyy)

Transplant status 3 :

Type of transplant 3 :

Year of transplant 3 :

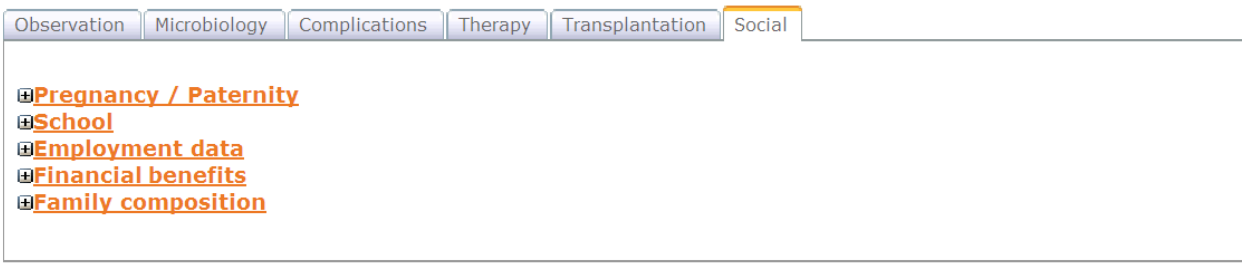
Precise date of first entering the Tx waiting list : 3 (dd/mm/yyyy)

Precise date of the most recent Tx : 3 (dd/mm/yyyy)

Transplant status (ref_Transplant)	
1	Not evaluated
2	Refused by transplant center
3	Waiting list
4	Received transplant
5	Evaluated but not on waiting list
6	Refused by patient
999	Missing Data

Transplant type (ref_TransplantType)	
0	Lung
1	Lung-Heart
2	Liver
3	Heart
4	Lung-Liver
5	Kidney
6	Liver-Kidney
999	Missing Data

6. Social



Pregnancy / Paternity

Parenthood this year

Birthdays of the biological children for this patient :

Child 1 : (mm/yyyy) / Child 4 : (mm/yyyy) /

Child 2 : (mm/yyyy) / Child 5 : (mm/yyyy) /

Child 3 : (mm/yyyy) / Child 6 : (mm/yyyy) /

School

School status :

School status (ref_SchoolType)
0 unknown
1 regular school/education attendance
4 has finished school/education
7 No school
999 Missing Data

Employment data

Patient works

Percentage :

Work percentage (ref_OccupationType)	
0	Unknown
1	Fulltime
2	Parttime
999	Missing Data

Financial benefits

Additional child allowance

Income support

Disability allowance

Preferential tariff

Pension

Integration support

Family composition

Household composition

Number of siblings including the patient

Order of the patient in the family

Number of siblings with CF

Number of siblings deceased from CF

Household composition (ref_FamilyStatus)	
1	Unchanged
2	Changed
3	First Registering
999	Missing Data

General Remark :

APPENDIX II

List of abbreviations and definitions

ABPA - Allergic bronchopulmonary aspergillosis
BCFR - The Belgian Cystic Fibrosis registry
BFCA – Belgian Cystic Fibrosis patient's Association
BMI - Body mass index is a measure of relative weight based on an individual's mass and height. It is defined as the individual's body mass divided by the square of their height – with the value universally being given in units of kg/m^2.
BMR-RBM - Belgisch Mucoviscidose Register - Registre Belge de la Mucoviscidose
Bronchoalveolar lavage - is a medical procedure in which a bronchoscope is passed through the mouth or nose into the lungs and fluid is squirted into a small part of the lung and then collected for examination.
BVSM-ABLM - Belgische Vereniging voor Strijd tegen Mucoviscidose – Association belge de Lutte contre la Mucoviscidose
CDC - The Centers for Disease Control and Prevention is the national public health institute of the United States. Its main goal is to protect public health and safety through the control and prevention of disease, injury, and disability.
CDC growth charts - These consist of a series of percentile curves that illustrate the distribution of selected body measurements in children.
CF – Cystic Fibrosis
CFRD - Cystic Fibrosis Related Diabetes refers to a form of diabetes as a direct consequence of having cystic fibrosis.
ConsultRN – a module from the eHealth platform for linking the registry data collection to the national registry database for updates of demographic data.
Dual energy X-ray absorptiometry - (DXA, previously DEXA) is a means of measuring bone mineral density (BMD).
ECFSPR - European Cystic Fibrosis Society Patient Registry
eHealth – a Belgian electronics health records processing and communication platform that acts as a trusted third party.
FEV_1 - Forced Expiratory Volume is the volume of air that can forcibly be blown out in one second, after full inspiration
FEF_{25-75} - Forced Expiratory Flow 25-75% is the flow (or speed) of air coming out of the lung during the middle portion of a forced expiration.
FVC - Forced Vital Capacity is the volume of air that can forcibly be blown out after full inspiration, measured in litres.
INAMI - Institut national d'assurance maladie-invalidité
Pseudomonas aeruginosa - is the most important pathogen in the CF airway. *P. aeruginosa* is acquired from environmental reservoirs and can cause both acute and chronic infections, depending on the clinical context.
PWCF - People With Cystic Fibrosis
rhDNase - Recombinant human deoxyribonuclease is an enzyme that breaks down DNA strands in airway secretions, hydrolyzes the DNA present in sputum/mucus of CF patients, reducing viscosity in the lungs and promoting secretion clearance.
RIZIV- Rijksinstituut voor ziekte- en invaliditeitsverzekering
TEPD - Transepithelial potential difference is the voltage across an epithelium, and is the sum of the membrane potentials for the outer and inner cell membranes used in CF diagnosis
VUB - Vrije Universiteit Brussel
WIV - ISP - IPH - Scientific Institute of Public Health

NOTES

ANNUAL REPORT
BELGIAN CYSTIC FIBROSIS REGISTRY
BELGIUM (Public version 2012)