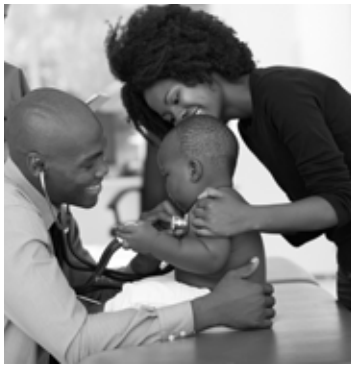
The Brazilian

Cystic Fibrosis

Patient Registry

2017



GRUPO BRASILEIRO DE ESTUDOS DE FIBROSE CÍSTICA

Annual Report 2017

To all people interested in cystic fibrosis,

The Brazilian Cystic Fibrosis Registry (REBRAFC) contains demographic data on the diagnosis and treatment of patients with cystic fibrosis (CF) in Brazil, with the aim of improving the attention given to this disease in our Country. This initiative is turning 9 years old with the publishing of the current Report, with the growing participation of colleagues and Centers acting in the Country.

This report brings more results from the genotyping project, coordinated by the Brazilian Cystic Fibrosis Study Group (GBEFC). There are already about 80% of patients with genetic study. We still have a relatively high ratio of patients with inconclusive and negative genotyping results, but strategies of diagnostic review are already underway, including new sweat tests with equipment distributed by GBEFC to many Regions of the Country.

There are also some pieces of news, specially concerning acute respiratory exacerbations. As this aspect is currently of great importance in the CF scenario and represents an important outcome of most therapeutic intervention studies, information gathering now includes oral treatments. Besides that, greater detail about hospital admissions for reasons distinct of respiratory exacerbation was included.

There are still lots to do for Brazilian patients who suffer with lack of access to diagnostic and therapeutic resources in many regions of the Country. The continuity and solidity of REBRAFC is of great importance in this scenario, because it represent the main documented resource of the real situation of Brazilian patients, and its evolution throughout the years – therefore showing how CF is being diagnosed and treated in the Country.

We proceed believing that this initiative can contribute to changes in the government agenda, resulting in a better health care for CF patients in Brazil.

About Cystic Fibrosis and GBEFC:

Cystic fibrosis (CF) is an autosomal recessive disease with multisystem involvement (respiratory, gastrointestinal, hepatic, and genitourinary systems). It is a complex disease with progressive and potentially lethal features, which remain little known in our country, despite the existence of some Centers and professionals dedicated to the study and care of patients over many years. Treatment is also complex and involves high-cost drugs, some of which are subsidized by the Ministry of Health and others by state health secretariats, in a way that access to drugs is not uniform throughout the Country.

The Brazilian Cystic Fibrosis Study Group (GBEFC) is a non-profit organization composed of health professionals working in the area, created on November 5, 2003. Among the GBEFC activities, we can mention research, personnel training, and assistance in the establishment for the CF treatment center in the Country, promoting CF Conferences and collaborating with the Ministry of Health to define a national CF treatment protocol.

The GBEFC maintains an internet website (www.gbefc.org.br) that provides various pieces of information about cystic fibrosis; the current report and previous ones are available for free download in this website in both Portuguese and English versions.

Executive Commitee of the REBRAFC:

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1 INTRODUCTION

This report describes data from the Brazilian Cystic Fibrosis Registry (REBRAFC), which contains demographic, diagnostic and treatment aspects of patients with cystic fibrosis in Brazil. **Data on patients with record and/or followed up during 2017, included in the Registry during the calendar year of 2018** are presented. By the time these data base was generated for analysis, **5,128 patients** were registered, from which 4,711 *91,9%) had some follow up data.

The number of records and follow ups has increased annually, as shown in Figure 1. In 2017 **474 new records** were observed, but the annual number of follow ups has again not increased at the same proportion as the records.

More than 60% of patients have at least 3 years of follow-ups, 76% have at least 2 years of follow-ups and **almost 40% (1,960 patients) have at least 5 years of follow-ups** (Table 1). These data clearly illustrate the continuous update of REBRAFC database regarding the follow-up of registered cases.

FIGURE 1
Evolution of records and follow-ups numbers between 2009 and 2017.

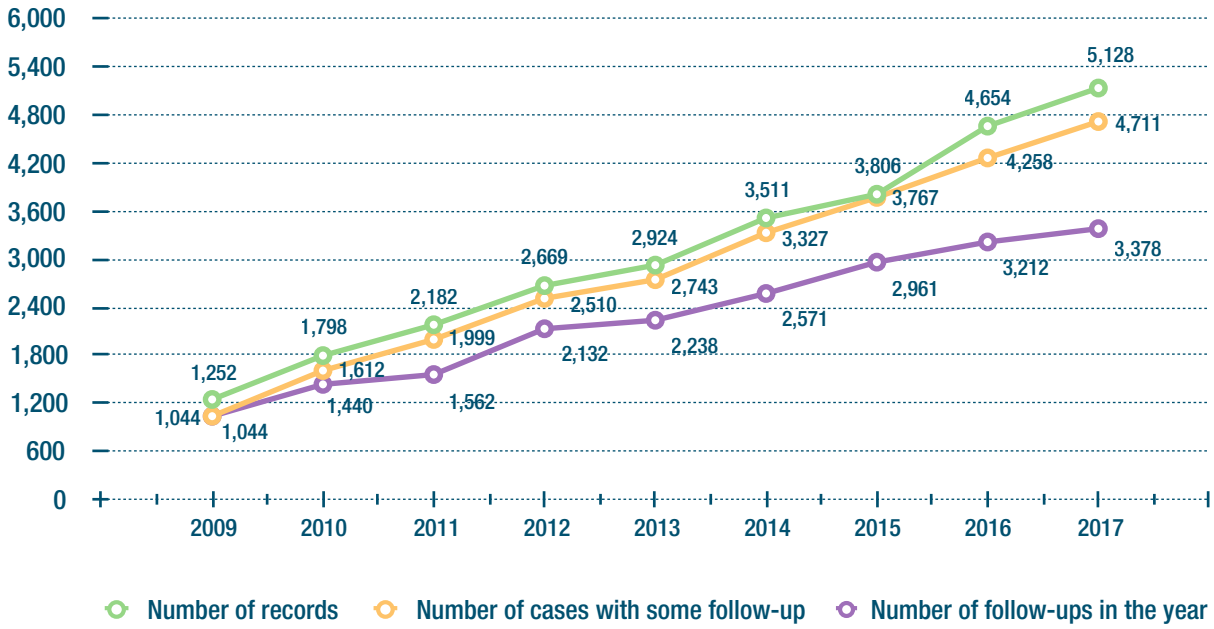


TABLE 1
Distribution of patients according to follow-up time.

FOLLOW-UP TIME	N	%	ACCUMULATED %
9 years	337	6.6%	6.6%
8 years	383	7.5%	14.1%
7 years	364	7.1%	21.2%
6 years	426	8.3%	29.5%
5 years	450	8.8%	38.3%
4 years	597	11.6%	49.9%
3 years	652	12.7%	62.6%
2 years	685	13.4%	76.0%
1 year	817	15.9%	91.9%
No follow-up	417	8.1%	8.1%
TOTAL	**5,128**	**100%**	**100%**

For the description of personal data and diagnostic, all registered patients were considered (n = 5,128). For the follow-up data analysis, only the data of the reference year 2017 were considered (inserted in 2018), which add to a total of 3,378 patients.

2

DEMOGRAPHIC DATA

From the total of 5,128 patients, 12 were foreigners (3 Americans, 2 Portuguese, 2 Austrians, 1 Spanish, 1 Lebanese, 1 Swiss, 1 Uruguayan, and 1 Paraguayan).

TABLE 2

Distribution of patients according to state of Birth, 2017.

STATE OF BIRTH	N	%	STATE OF BIRTH	N	%
São Paulo	1,311	25.6%	Mato Grosso	51	1.0%
Minas Gerais	611	11.9%	Sergipe	42	0.8%
Rio Grande do Sul	500	9.8%	Rio Grande do Norte	37	0.7%
Bahia	454	8.9%	Alagoas	36	0.7%
Rio de Janeiro	376	7.3%	Piauí	36	0.7%
Paraná	329	6.4%	Maranhão	32	0.6%
Santa Catarina	273	5.3%	Paraíba	23	0.4%
Pará	166	3.2%	Tocantins	16	0.3%
Espirito Santo	136	2.7%	Amazonas	11	0.2%
Ceará	133	2.6%	Rondônia	10	0.2%
Goiás	117	2.3%	Acre	7	0.1%
Distrito Federal	81	1.6%	Amapá	7	0.1%
Pernambuco	76	1.5%	Roraima	2	0.0%
Mato Grosso do Sul	61	1.2%	Unknown information	194	3.8%
			TOTAL	**5,128**	**100%**

n = number of patients.

FIGURE 2

Distribution of patients according to state of birth, 2017.

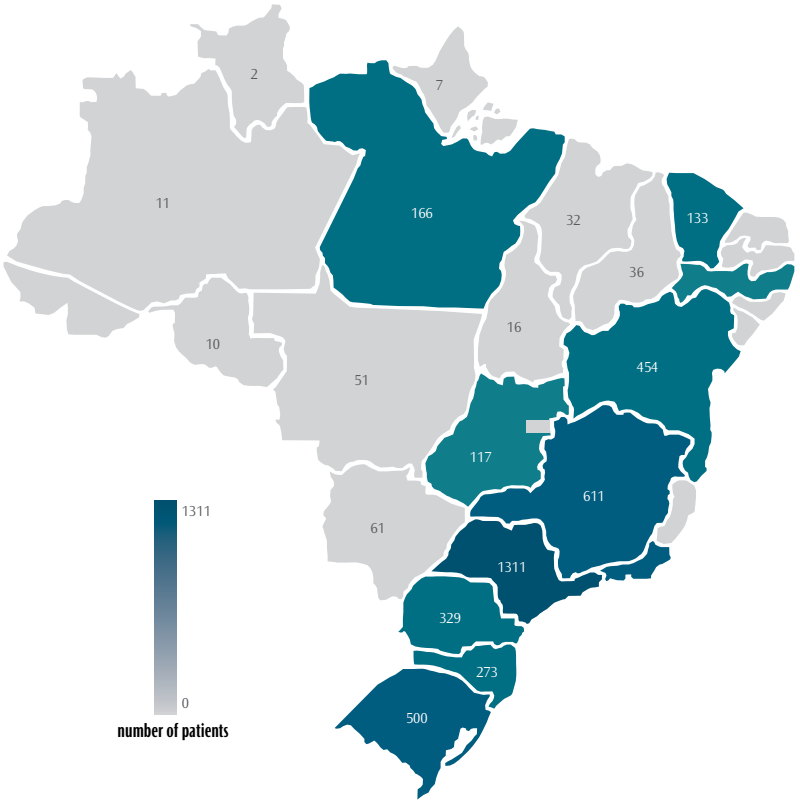


TABLE 3
Distribution of patients according to region of birth, 2017.

REGION OF BIRTH	N (%)
Southeast	2,434 (47.5%)
South	1,102 (21.5%)
Northeast	869 (16.9%)
Midwest	310 (6.0%)
North	219 (4.3%)
Not reported	194 (3.8%)
TOTAL	**5,128 (100%)**

TABLE 4
Distribution of patients according to state of one's Care Center, 2017.

STATE OF CARE CENTER	N	%
São Paulo	1,407	27.4
Minas Gerais	650	12.7
Rio Grande do Sul	552	10.8
Bahia	446	8.7
Paraná	391	7.6
Rio de Janeiro	370	7.2
Santa Catarina	249	4.9
Pará	174	3.4
Espirito Santo	148	2.9
Ceará	134	2.6
Distrito Federal	133	2.6
Goiás	123	2.4
Pernambuco	73	1.4
Mato Grosso do Sul	57	1.1
Mato Grosso	39	0.8
Sergipe	38	0.7
Rio Grande do Norte	37	0.7
Alagoas	35	0.7
Piauí	30	0.6
Maranhão	23	0.4
Paraíba	16	0.3
Amazonas	3	0.1
TOTAL OF PATIENTS	**5,128**	**100%**

TABLE 5
Distribution of patients according to sex and race, 2017.

SEX	N (%)
Male	2,664 (52.0%)
Female	2,464 (48.0%)
TOTAL OF PATIENTS	**5,128 (100%)**
COLOR / RACE	**N (%)**
White	3,521 (68.7%)
Mulatto	1,279 (24.9%)
Black	312 (6.1%)
Asian	12 (0.2%)
Indigenous	4 (0.1%)
TOTAL OF PATIENTS	**5,128 (100%)**

n = number of patients.

FIGURE 3
Distribution of patients according to state of one's Care Center, 2016 and 2017.

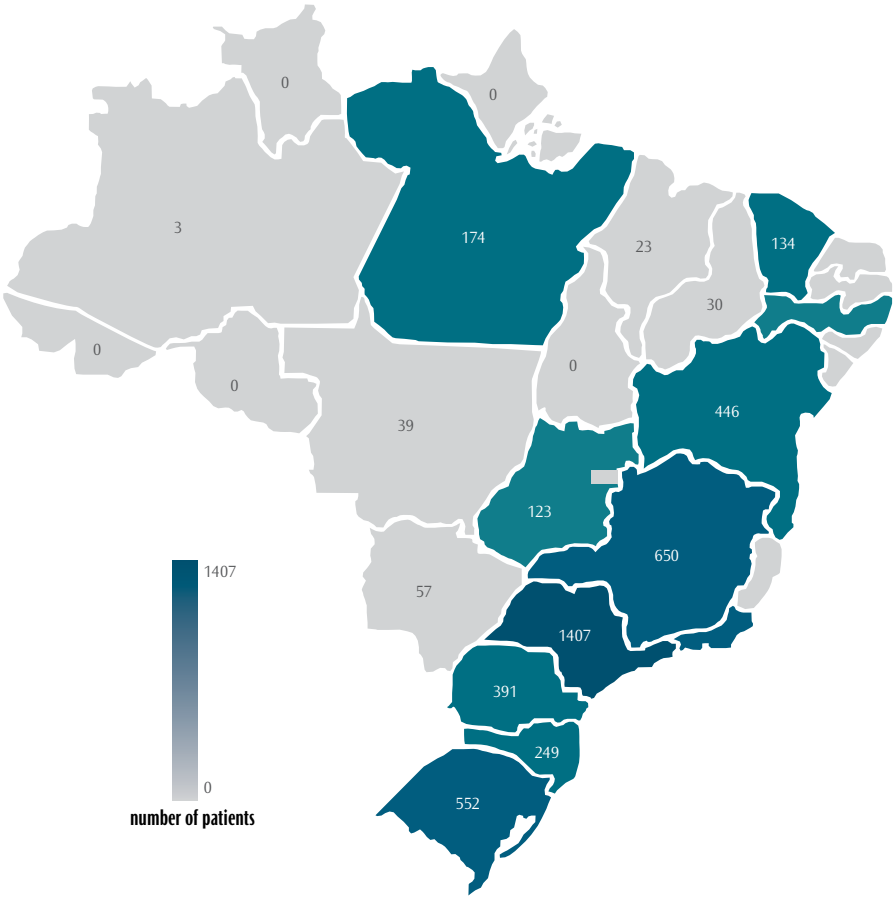


TABLE 6

Description of patients according to current age (age of last spirometry or anthropometry), 2017.

AGE (IN YEARS)	
Mean (standard deviation)	14.58 (11.94)
Median (p25-p75)	12.60 (6.11 – 18.98)
TOTAL OF PATIENTS WITH KNOWN AGE	**4,361**
PATIENTS WHO DIED	**299**
PATIENTS WITHOUT SPIROMETRY / ANTHROPOMETRY	**51**
PATIENTS WITHOUT FOLLOW-UPS	**417**
TOTAL OF PATIENTS	**5,128**

n=number of patients; p25 = percentile 25, p75 = percentile 75.

FIGURE 4

Distribution of patients according to current age (age of last spirometry or anthropometry), 2017.

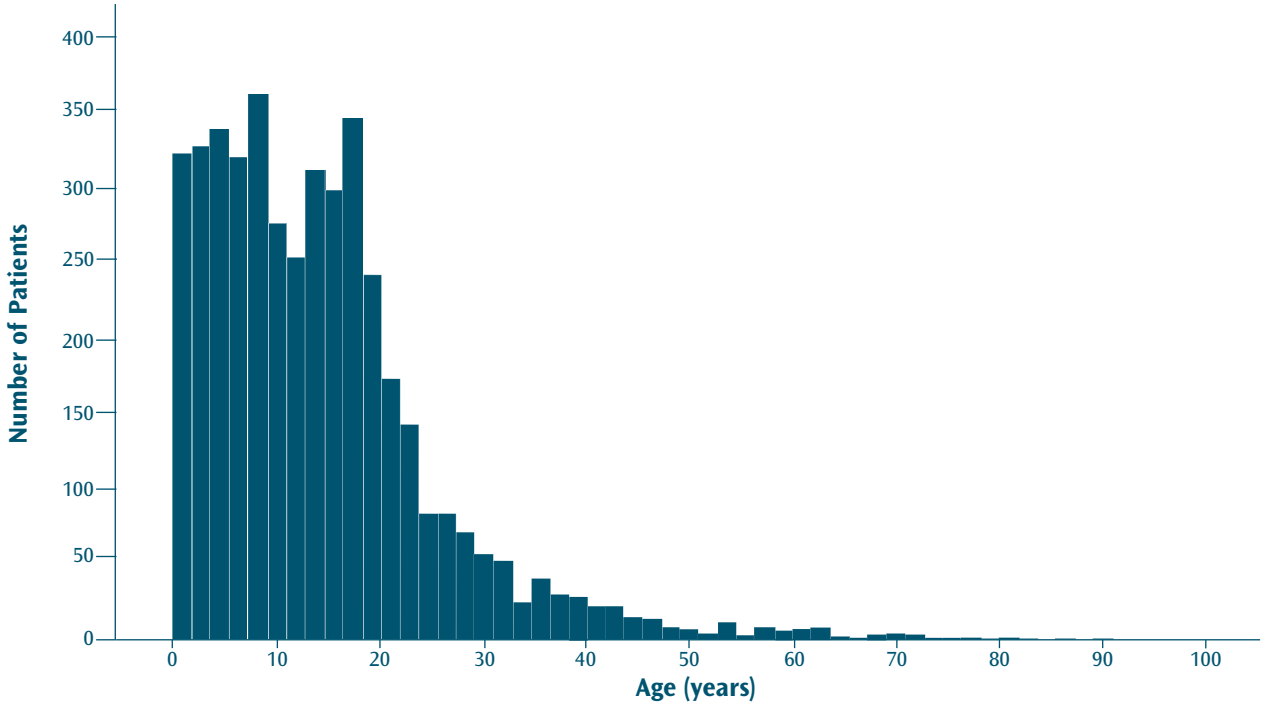


FIGURE 5

Distribution of patients according to current age (age of last spirometry or anthropometry), 2017.

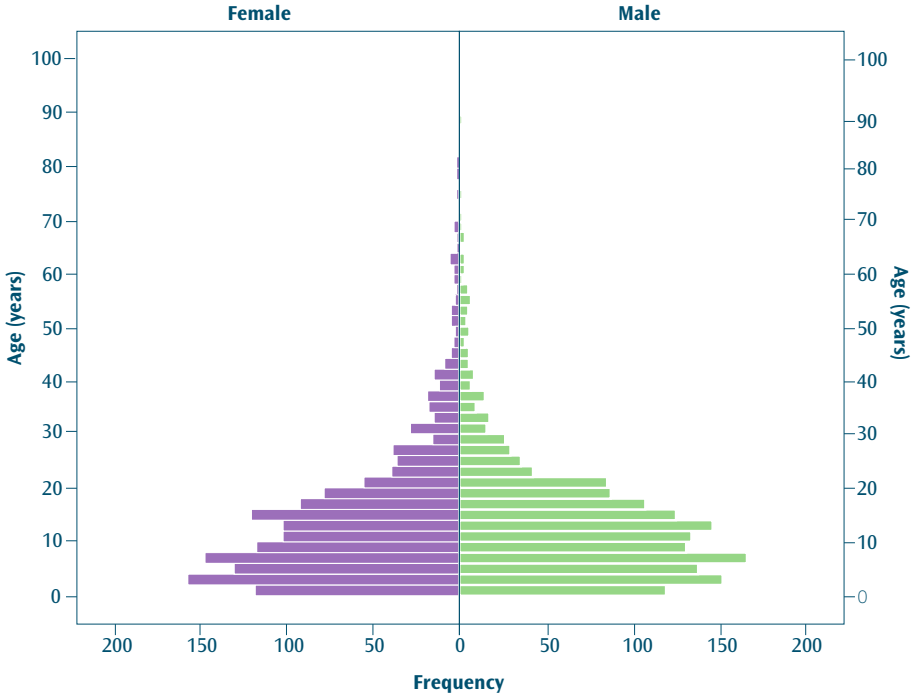


TABLE 7

Distribution of patients according to current age group, 2017.

AGE GROUP	N (%)
Up to 5	899 (20.6%)
> 5 to 10	904 (20.7%)
>10 to 15	779 (17.9%)
>15 to 20	811 (18.6%)
>20 to 25	382 (8.8%)
>25 to 30	200 (4.6%)
>30 to 35	116 (2.7%)
>35 a to 40	90 (2.1%)
>40 to 45	57 (1.3%)
>45 to 50	32 (0.7%)
>50	91 (2.1%)
TOTAL OF PATIENTS	**4,361 (100%)**
AGE GROUP (PEDIATRIC – ADULT)	**N (%)**
Less than 18 years	3,102 (71.1%)
18 years or older	1,259 (28.9%)
TOTAL OF PATIENTS	**4,361 (100%)**

n = number of patients.

FIGURE 6
Evolution of current age from 2009 to 2017.

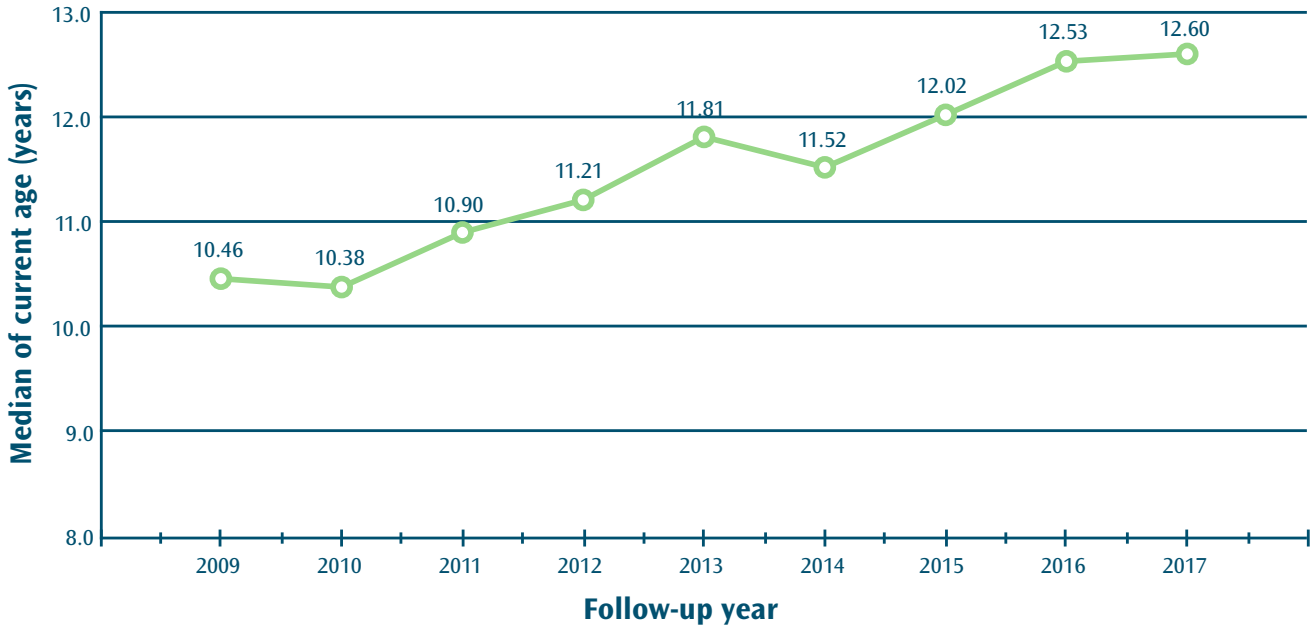
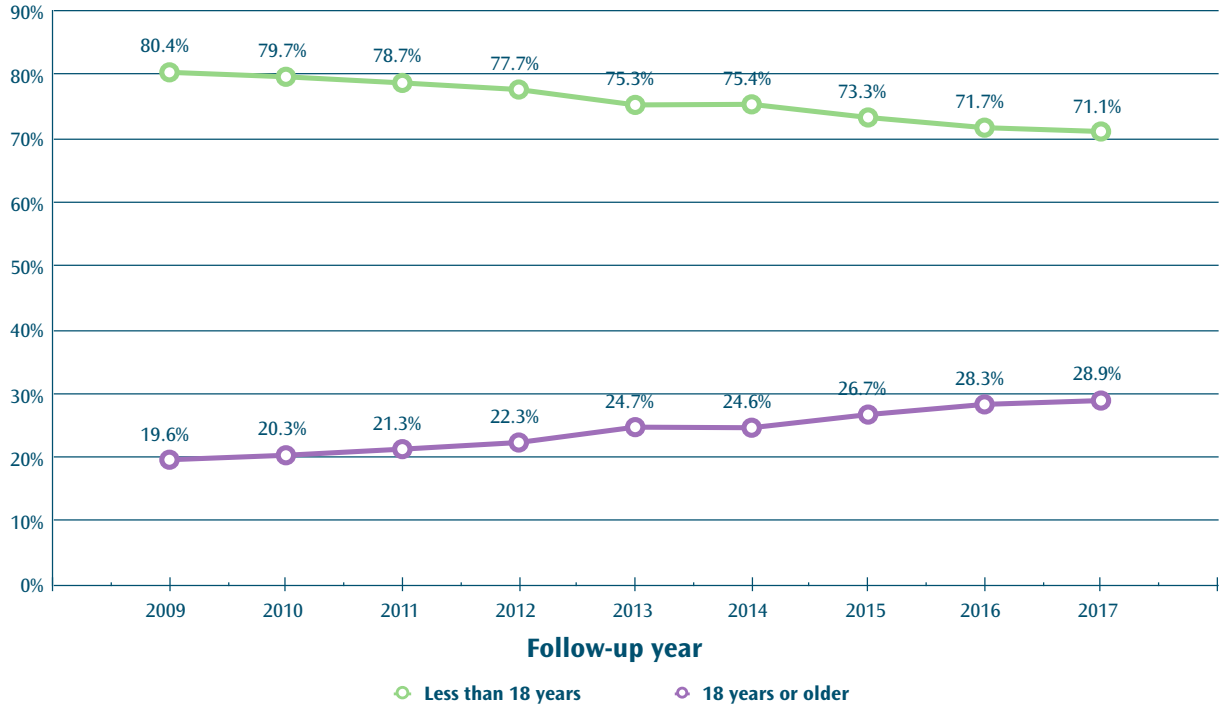


FIGURE 7
Distribution of patients according to pediatric age group from 2009 to 2017.



DIAGNOSTIC DATA

3

TABLE 8

Description of patients according to age at diagnosis, 2017.

AGE (YEARS)	
Mean (standard deviation)	5.74 (10.50)
Median (p25-p75)	0.85 (0.17 – 7.15)
TOTAL OF PATIENTS	**4,361**
PATIENTS WITH NO INFORMATION*	**299**

n = number of patients; p25 = percentile 25, p75 = percentile 75.

*birthdates/diagnosis incorrectly filled out

FIGURE 8

Distribution of patients according to age at diagnosis, 2017.

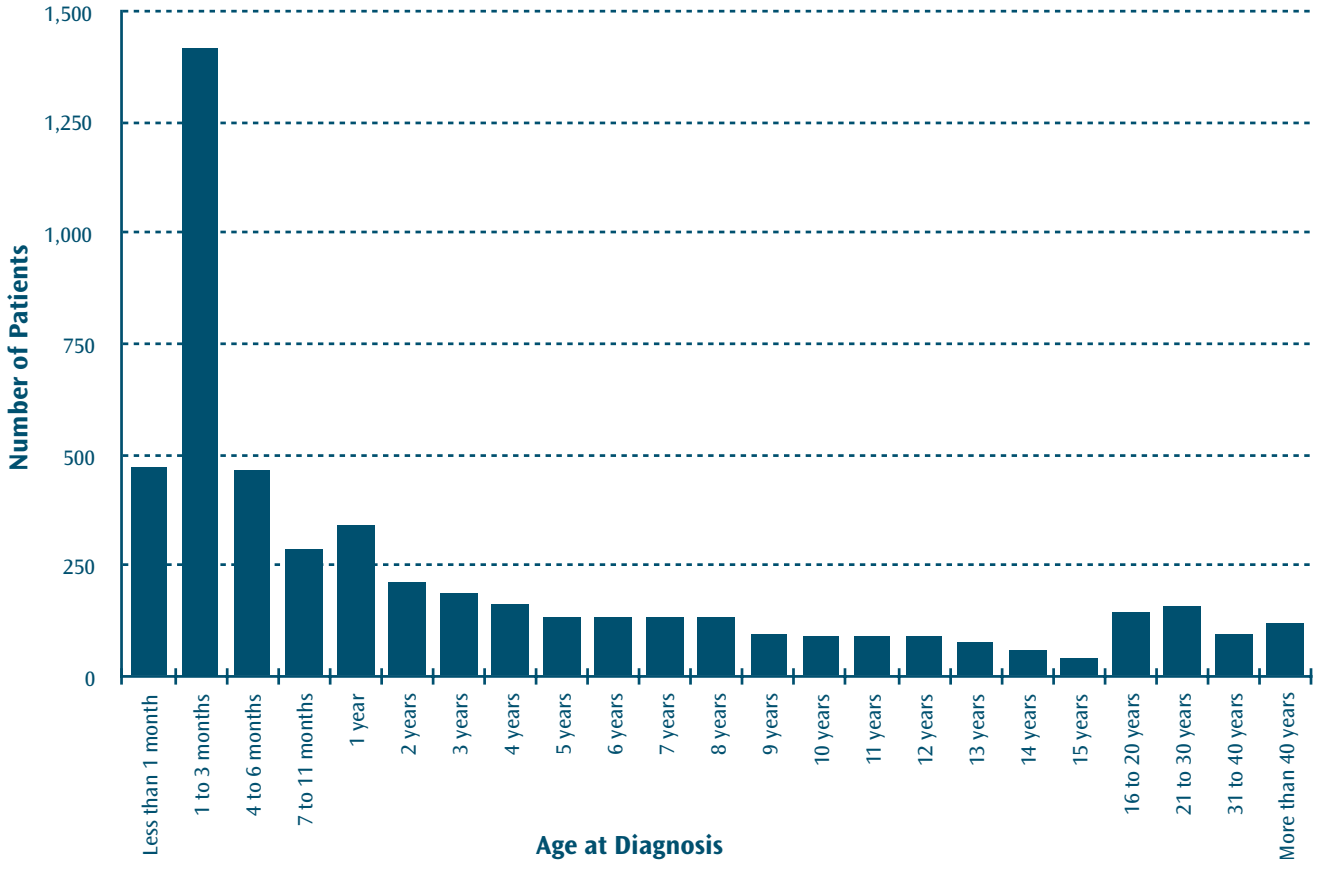


FIGURE 9

Variations of age at diagnosis over the years.

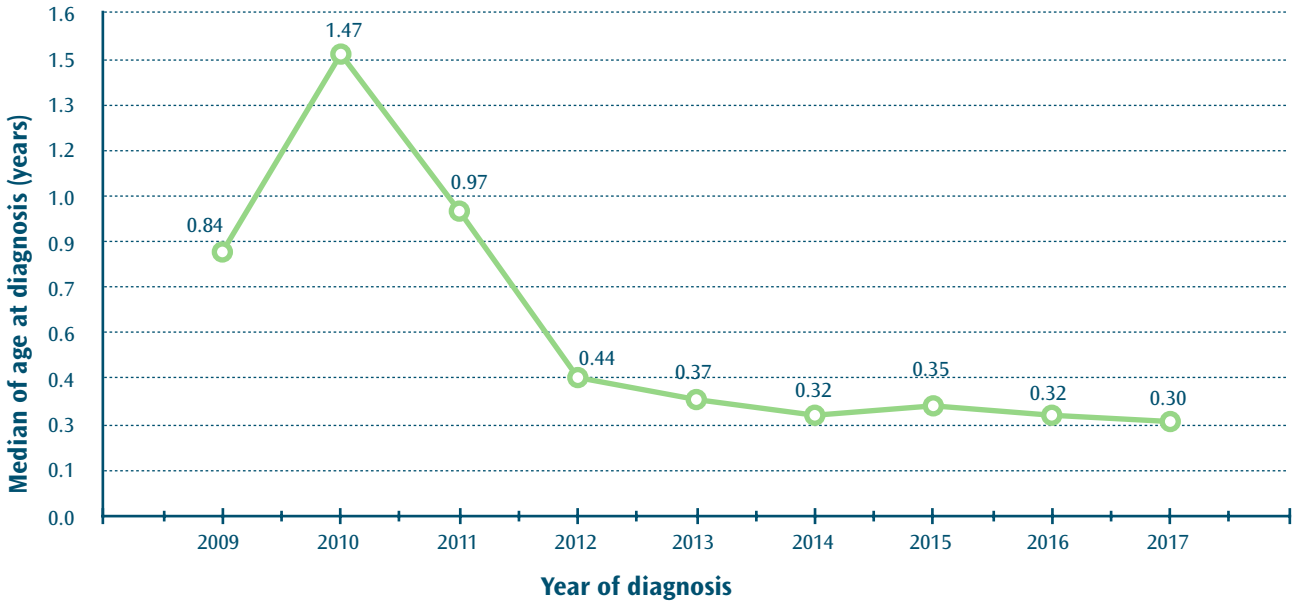


Figure 9 presents the age at diagnosis median according to the year in which cases were diagnosed, considering the period between 2009 and 2017. We can see in the graph that in the last 6 years, the median has remained below 4 months of age.

TABLE 9

Distribution of patients according to conditions for diagnosis, 2017.

CONDITIONS FOR DIAGNOSIS	N (%)
Persistent Respiratory Symptoms	2,916 (56.9%)
Growth Deficit / Malnutrition	1,862 (36.3%)
Steatorrhea or Malabsorption	1,718 (33.5%)
Neonatal Screening (IRT)	1,814 (35.4%)
Family History	414 (8.1%)
Clinical or Surgical Meconium Ileus	369 (7.2%)
Sinus Disease and/or Nasal Polyp	312 (6.1%)
Metabolic Disorder	306 (6.0%)
Edema / Anemia	198 (3.9%)
Prolonged Jaundice	49 (1.0%)
Rectal Prolapse	46 (0.9%)
Infertility	30 (0.6%)
Other	249 (4.9%)
Unknown condition	120 (2.3%)
TOTAL OF PATIENTS	**5,128 (100%)**

n = number of patients.

TABLE 10

Description of sweat testing results, 2017.

	CHLORIDE (mEq/l)	CONDUCTIVITY (mmol/l)
Mean (standard deviation)	90.69 (26.30)	100.7 (20.8)
Median (p25-p75)	91.00 (72.25 - 105.50)	103.0 (92.0 - 113.0)
TOTAL OF PATIENTS	**4,347**	**770**

p25 = percentile 25, p75 = percentile 75. For chloride the means of 2 taken measurements were considered.

TABLE 11

Diagnostic via newborn screening – results of of immunoreactive trypsinogen dosage (IRT),2017.

DOSE OF IMMUNOREACTIVE TRYPSINOGEN (IRT) (ng/ml)	1st DOSAGE	2nd DOSAGE
Mean (standard deviation)	195.4 (116.5)	196.9 (124.1)
Median (p25-p75)	168.0 (119 - 240)	167.0 (114.0 - 243.0)
TOTAL OF PATIENTS	**1,571**	**1,209**

TABLE 12

Other diagnostic tests reported, 2017.

	N (%)
Measurement of Nasal Potential Difference	115 (2.2%)
Rectal Biopsy	78 (1.5%)
TOTAL OF PATIENTS	**5,128 (100%)**

n=number of patients.

TABLE 13

Description of patients according to age at diagnosis and newborn screening, 2017.

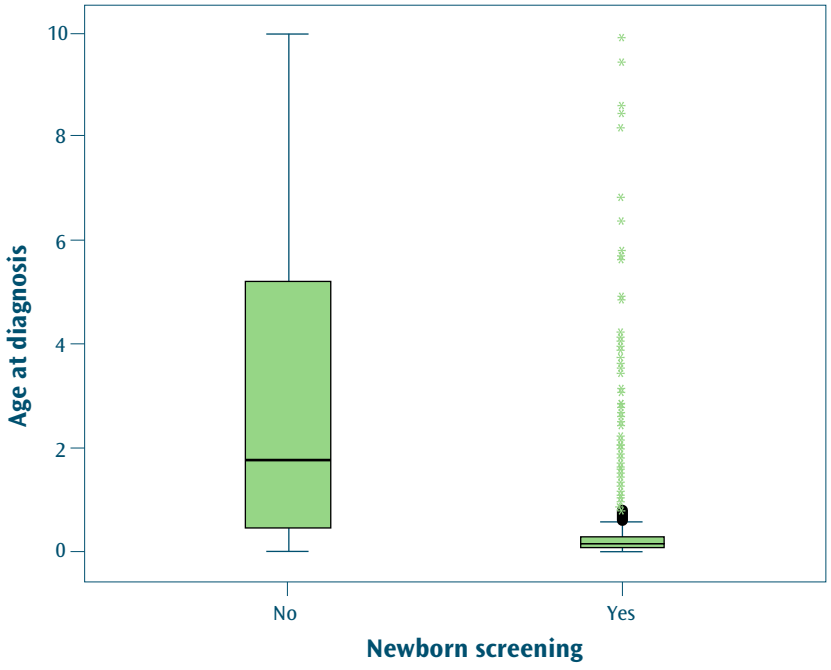
AGE AT DIAGNOSIS (YEARS)	NEWBORN SCREENING		TOTAL
	NO	YES	
Mean (standard deviation)	8.65 (12.08)	0.44 (1.29)	5.74 (10.50)
Median (p25-p75)	4.27 (0.72 - 11.27)	0.14 (0.09 - 0.28)	0.82 (0.17 - 7.15)
TOTAL OF PATIENTS	**3,307**	**1,813**	**5,120**
PATIENTS WITH NO INFORMATION	**7**	**1**	**8**

p25 = percentile 25, p75 = percentile 75.

As in previous years, it was found that the age at diagnosis is significantly lower among patients who underwent newborn screening (p<0,001, Table 13 and Figure 10).

FIGURE 10

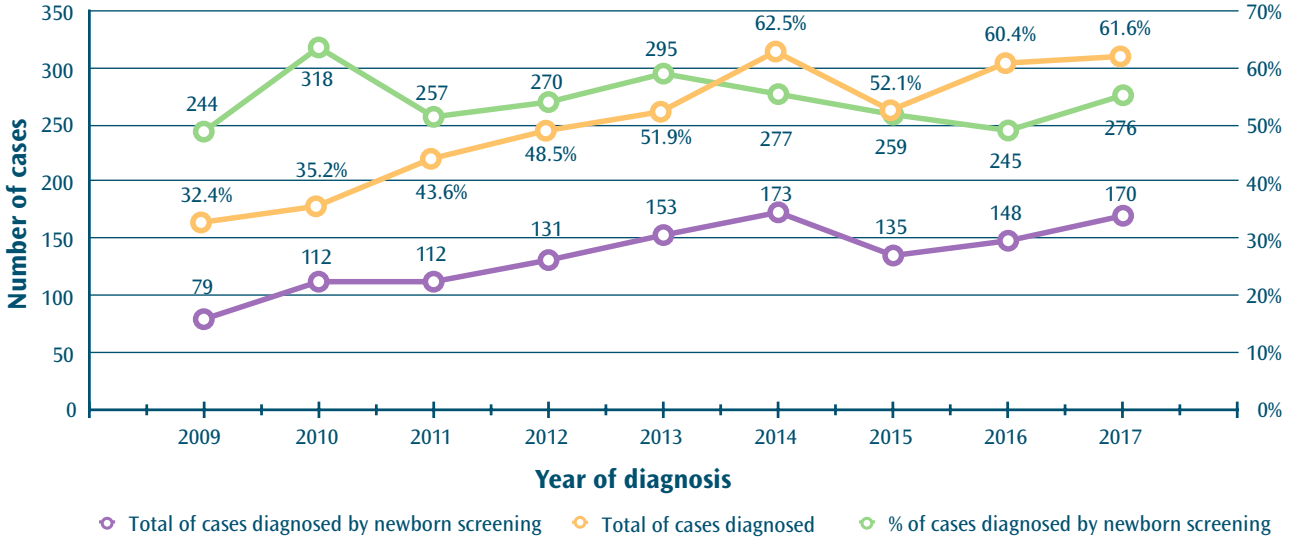
Distribution of patients according to age at diagnosis according to newborn screening, 2017 – considering only diagnosed patients up to 10 years of age.



In the period from 2009 to 2017, 2,441 cases of cystic fibrosis were diagnosed, from which 1,213 (48.7%) were diagnosed by newborn screening. In the years 2016 and 2017, newborn screening was already responsible for more than 60% of new diagnosis.

FIGURE 11

Diagnosis by newborn screening from 2009 to 2017.



4

GENETIC DATA

From the 5,128 registered cases, 4,076 (79.5%) were genotyped. From those, 2,688 (65.9%) were positive (identification of two or more pathogenic variants), 483 (11.8%) negative (no identified variant or only non CF-causing variants) and 905 (22.2%) inconclusive (only one pathogenic variant or at least one variant of uncertain/unknown significance).

TABLE 14

Description of patients according to genetic study of cystic fibrosis, 2017.

GENOTYPE PERFORMED	N (%)
No	1,052 (20.5%)
Yes	4,076 (79.5%)
TOTAL OF PATIENTS	**5,128 (100%)**
RESULTS	**N (%)**
Negative (no identified variant)	483 (11,8%)
Inconclusive*	905 (22.2%)
Positive	2,688 (65.9%)
With 1 pathogenic variant homozygous	1,098 (26.9%)
With 2 pathogenic variants	1,582 (38.8%)
With 3 pathogenic variants	8 (2.0%)
TOTAL OF PATIENTS WITH GENOTYPE	**4,076 (100%)**

* only one pathogenic variant or at least one variant of uncertain/unknown significance.

FIGURE 12

Evolution of genotyping in long term patients.

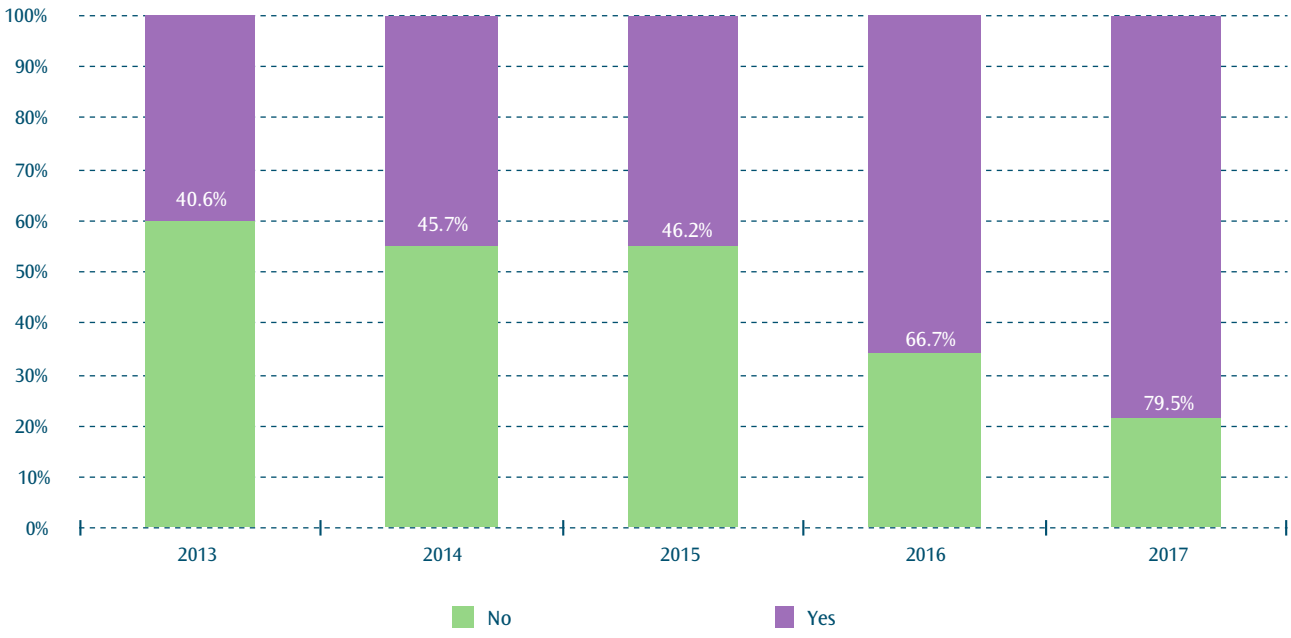


TABLE 15

Description of frequency of genetic study according to Region, 2017.

GENOTYPE PERFORMED	NORTH	NORTHEAST	MIDWEST	SOUTHEAST	SOUTH	TOTAL N(%)
No	68 (31.1%)	293 (33.7%)	62 (20.0%)	406 (16.7%)	167 (15.2%)	1,052 (20.5%)
Yes	151 (68.9%)	576 (66.3%)	248 (80.0%)	2,028 (83.3%)	935 (84.3%)	4,076 (79.5%)
TOTAL OF PATIENTS	**219 (100%)**	**869 (100%)**	**310 (100%)**	**2,434 (100%)**	**1,102 (100%)**	**5,128 (100%)**

194 patients with no information about their Region of birth.

Among the patients with a genotype study, more than half of them had at least a copy of the F508DEL mutation (2,096 patients, 51.4%). In total, 974 patients (23.9%) were homozygotes and 1,122 (27.5%) were heterozygotes for the F508del mutation.

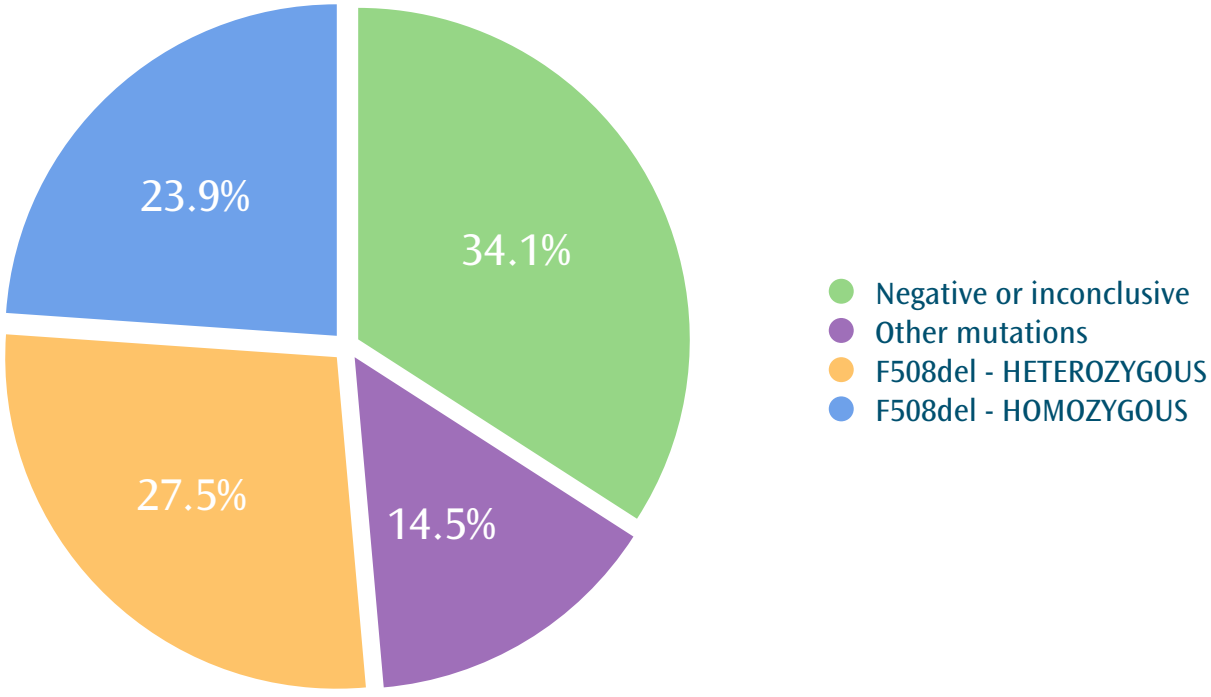
TABLE 16

Description of genotyping results according to frequency of the F508del mutation, 2017.

GENOTYPE - DESCRIPTION	N (%)
F508del - HOMOZYGOUS	974 (23.9%)
F508del - HETEROZYIGOUS	1,122 (27.5%)
Other mutations (without F508del)	592 (14.5%)
Negative or inconclusive	1,388 (34.1%)
TOTAL DE PACIENTES COM GENÓTIPO	**4,076 (100%)**

FIGURE 13

Distribution of patients according to genetic results (n = 4,076), 2017.



DESCRIPTION OF MUTATIONS:

Using the CFTR2 (www.CFTR2.org) categorization as a base, the mutations were categorized as CF-causing, varying clinical consequence, unknown significance or non CF-causing. 287 distinct mutations were identified (127 new mutations compared to the previous year). In total, 118 (40.8%) were CF-causing, 19 (6.6%) were varying clinic%) were of unknown meaning and 138 (48.4%) were not in the CFTR2 base (updated in March 11,2019), Table 17.

TABLE 17

Description of identified mutations (4076 patients – 8152 alleles), 2017.

RANKING	MUTATION (LEGACY NAME OR C.DNA DESCRIPTION)	NUMBER OF ALLELES	% IN RELATION TO TOTAL OF ALLELES	CAUSALITY (CFTR2)
1	F508del	3,578	43.89%	CF-causing
2	G542X	541	6.64%	CF-causing
3	3120+1G->A	224	2.75%	CF-causing
4	R334W	174	2.13%	CF-causing
5	R1162W	163	2.00%	CF-causing
6	G85E	130	1.59%	CF-causing
7	N1303K	101	1.24%	CF-causing
8	R1066C	97	1.19%	CF-causing
9	S4X	90	1.10%	CF-causing
10	M470V	86	1.05%	Non CF-causing
11	3272-26A->G	71	0.87%	CF-causing
12	2184delA	58	0.71%	CF-causing
13	S549R	56	0.69%	CF-causing
14	Y1092X	50	0.61%	CF-causing
15	A561E	49	0.60%	CF-causing
16	P205S	45	0.55%	CF-causing
16	W1282X	45	0.55%	CF-causing
17	1812-1G->A	32	0.39%	CF-causing
18	5T;TG11	31	0.38%	Variable consequence
19	L206W	30	0.37%	CF-causing
20	2789+5G->A	28	0.34%	CF-causing
21	711+1G->T	27	0.33%	CF-causing
22	S466X	26	0.32%	CF-causing
22	V232D	26	0.32%	CF-causing
23	5T	25	0.31%	Variable consequence
23	1717-1G->A	25	0.31%	CF-causing
23	R553X	25	0.31%	CF-causing
24	711+5G->A	22	0.27%	CF-causing
24	I507del	22	0.27%	CF-causing
25	A559T	21	0.26%	CF-causing
26	2183AA->G ou 2183delAA->G	19	0.23%	CF-causing
26	2184insA	19	0.23%	CF-causing
26	3849+10kbC->T	19	0.23%	CF-causing
27	D1152H	18	0.22%	Variable consequence
28	Q1100P	17	0.21%	Missing on CFTR2
29	CFTdele2,3	16	0.20%	CF-causing
29	c.3874-1G>A	16	0.20%	Missing on CFTR2
30	R1066H	15	0.18%	CF-causing
30	c.1052C>G	15	0.18%	Missing on CFTR2

RANKING	MUTATION (LEGACY NAME OR C.DNA DESCRIPTION)	NUMBER OF ALLELES	% IN RELATION TO TOTAL OF ALLELES	CAUSALITY (CFTR2)
30	c.743+1G>A	15	0.18%	Missing on CFTR2
31	5T;TG12	13	0.16%	Variable consequence
32	CFTRdele19-21	12	0.15%	CF-causing
32	c.1766G>A	12	0.15%	Missing on CFTR2
33	G551D	11	0.13%	CF-causing
33	R347H	11	0.13%	CF-causing
33	c.2552G>T	11	0.13%	Missing on CFTR2
34	CFTRdele2	10	0.12%	CF-causing
35	L1077P	9	0.11%	CF-causing
36	V201M	8	0.10%	Unknown meaning
36	3132delTG	8	0.10%	CF-causing
36	R347P	8	0.10%	CF-causing
36	S1255X	8	0.10%	CF-causing
36	W1089X	8	0.10%	CF-causing
36	c.1045G>C	8	0.10%	Missing on CFTR2
36	c.487delA	8	0.10%	Missing on CFTR2
37	1078delT	7	0.09%	CF-causing
37	621+1G->T	7	0.09%	CF-causing
37	c.1936G>T	7	0.09%	Missing on CFTR2
37	c.2555_2556insT	7	0.09%	Missing on CFTR2
37	c.443T>A	7	0.09%	Missing on CFTR2
38	D614G	6	0.07%	Variable consequence
38	G576A	6	0.07%	Non CF-causing
38	R668C	6	0.07%	Non CF-causing
38	2143delT	6	0.07%	CF-causing
38	3120G->A	6	0.07%	CF-causing
38	M1101K	6	0.07%	CF-causing
38	c.1083_1084insTATGA	6	0.07%	Missing on CFTR2
39	L967S	5	0.06%	Variable consequence
39	R117H	5	0.06%	Variable consequence
39	1898+3A->G	5	0.06%	CF-causing
39	2307insA	5	0.06%	CF-causing
39	2347delG	5	0.06%	CF-causing
39	E92X	5	0.06%	CF-causing
39	I1234V	5	0.06%	CF-causing
39	R117C	5	0.06%	CF-causing
39	R764X	5	0.06%	CF-causing
39	R851X	5	0.06%	CF-causing
39	c.3607A>G	5	0.06%	Missing on CFTR2
39	c.484A>G	5	0.06%	Missing on CFTR2
39	c.952T>A	5	0.06%	Missing on CFTR2
40	124del23bp	4	0.05%	CF-causing
40	3659delC	4	0.05%	CF-causing

RANKING	MUTATION (LEGACY NAME OR C.DNA DESCRIPTION)	NUMBER OF ALLELES	% IN RELATION TO TOTAL OF ALLELES	CAUSALITY (CFTR2)
40	4005+1G->A	4	0.05%	CF-causing
40	4016insT	4	0.05%	CF-causing
40	H1375P	4	0.05%	CF-causing
40	Q220X	4	0.05%	CF-causing
40	R1158X	4	0.05%	CF-causing
40	Y275X	4	0.05%	CF-causing
40	c.2053_2054insAA	4	0.05%	Missing on CFTR2
40	c.580-2A>C	4	0.05%	Missing on CFTR2
40	c.772A>G	4	0.05%	Missing on CFTR2
40	CFTRdele10	4	0.05%	Missing on CFTR2
41	G1069R	3	0.04%	Variable consequence
41	P5L	3	0.04%	Variable consequence
41	2789+2insA	3	0.04%	Unknown meaning
41	S1235R	3	0.04%	Non CF-causing
41	1898+1G->A	3	0.04%	CF-causing
41	3600+2insT	3	0.04%	CF-causing
41	3791delC	3	0.04%	CF-causing
41	E831X	3	0.04%	CF-causing
41	H1054D	3	0.04%	CF-causing
41	Y913X	3	0.04%	CF-causing
41	c.1399C>T	3	0.04%	Missing on CFTR2
41	c.2089delA	3	0.04%	Missing on CFTR2
41	c.254G>T	3	0.04%	Missing on CFTR2
41	c.2997_3000delAATT	3	0.04%	Missing on CFTR2
41	c.3067_3072delATAGTG	3	0.04%	Missing on CFTR2
41	c.325T>C	3	0.04%	Missing on CFTR2
41	CFTRdele15	3	0.04%	Missing on CFTR2
41	CFTRdele4	3	0.04%	Missing on CFTR2
42	5T;TG13	2	0.02%	Variable consequence
42	D579G	2	0.02%	Variable consequence
42	P750L	2	0.02%	Variable consequence
42	7T	2	0.02%	Non CF-causing
42	I148T	2	0.02%	Non CF-causing
42	L997F	2	0.02%	Non CF-causing
42	R75Q	2	0.02%	Non CF-causing
42	V754M	2	0.02%	Non CF-causing
42	1497delGG	2	0.02%	CF-causing
42	2991del32	2	0.02%	CF-causing
42	3121-1G->A	2	0.02%	CF-causing
42	3171delC	2	0.02%	CF-causing
42	36006->A	2	0.02%	CF-causing
42	3849G->A	2	0.02%	CF-causing
42	4428insGA	2	0.02%	CF-causing

RANKING	MUTATION (LEGACY NAME OR C.DNA DESCRIPTION)	NUMBER OF ALLELES	% IN RELATION TO TOTAL OF ALLELES	CAUSALITY (CFTR2)
42	541delC	2	0.02%	CF-causing
42	711+3A->G	2	0.02%	CF-causing
42	991del5	2	0.02%	CF-causing
42	A455E	2	0.02%	CF-causing
42	CFTRdele17a-18	2	0.02%	CF-causing
42	E585X	2	0.02%	CF-causing
42	G1244E	2	0.02%	CF-causing
42	I336K	2	0.02%	CF-causing
42	Q715X	2	0.02%	CF-causing
42	Q98X	2	0.02%	CF-causing
42	1465_1466insTAAT	2	0.02%	Missing on CFTR2
42	c.137C>T	2	0.02%	Missing on CFTR2
42	c.1513G>T	2	0.02%	Missing on CFTR2
42	c.1656delA	2	0.02%	Missing on CFTR2
42	c.1680+1G>A	2	0.02%	Missing on CFTR2
42	c.1706A>G	2	0.02%	Missing on CFTR2
42	c.2057C>A	2	0.02%	Missing on CFTR2
42	c.2476G>T	2	0.02%	Missing on CFTR2
42	c.274-2A>G	2	0.02%	Missing on CFTR2
42	c.2879_2882delCTAT	2	0.02%	Missing on CFTR2
42	c.3011delC	2	0.02%	Missing on CFTR2
42	c.3367+2T>A	2	0.02%	Missing on CFTR2
42	c.3410T>G	2	0.02%	Missing on CFTR2
42	c.3425_3426insAGTA	2	0.02%	Missing on CFTR2
42	c.3746G>A	2	0.02%	Missing on CFTR2
42	c.3794G>T	2	0.02%	Missing on CFTR2
42	c.3896C>T	2	0.02%	Missing on CFTR2
42	c.4061T>G	2	0.02%	Missing on CFTR2
42	c.409_412delCTCC	2	0.02%	Missing on CFTR2
42	c.4096-1G>A	2	0.02%	Missing on CFTR2
42	c.432delC	2	0.02%	Missing on CFTR2
42	c.4333G>A	2	0.02%	Missing on CFTR2
42	c.4delC	2	0.02%	Missing on CFTR2
42	CFTRdele18-20	2	0.02%	Missing on CFTR2
42	CFTRdele19-20	2	0.02%	Missing on CFTR2
42	CFTRdele25-27	2	0.02%	Missing on CFTR2
42	E1409K	2	0.02%	Missing on CFTR2
43	621+3A->G	1	0.01%	Variable consequence
43	621+3A->G	1	0.01%	Variable consequence
43	D1270N	1	0.01%	Variable consequence
43	D443Y	1	0.01%	Variable consequence
43	F1052V	1	0.01%	Variable consequence
43	R1070Q	1	0.01%	Variable consequence

RANKING	MUTATION (LEGACY NAME OR C.DNA DESCRIPTION)	NUMBER OF ALLELES	% IN RELATION TO TOTAL OF ALLELES	CAUSALITY (CFTR2)
43	R117H;7T	1	0.01%	Variable consequence
43	R74W	1	0.01%	Variable consequence
43	R170W	1	0.01%	Non CF-causing
43	1161delC	1	0.01%	CF-causing
43	1248+1G->A	1	0.01%	CF-causing
43	1341+1G->A	1	0.01%	CF-causing
43	1609delCA	1	0.01%	CF-causing
43	1717-8G->A	1	0.01%	CF-causing
43	1782delA	1	0.01%	CF-causing
43	185+1G->T	1	0.01%	CF-causing
43	2372del8	1	0.01%	CF-causing
43	2711delT	1	0.01%	CF-causing
43	2869insG	1	0.01%	CF-causing
43	2942insT	1	0.01%	CF-causing
43	3905insT	1	0.01%	CF-causing
43	394delTT	1	0.01%	CF-causing
43	4374+1G->T	1	0.01%	CF-causing
43	4382delA	1	0.01%	CF-causing
43	712-1G->T	1	0.01%	CF-causing
43	CFTRdele19	1	0.01%	CF-causing
43	G1249R	1	0.01%	CF-causing
43	L732X	1	0.01%	CF-causing
43	M1V	1	0.01%	CF-causing
43	P67L	1	0.01%	CF-causing
43	Q2X	1	0.01%	CF-causing
43	Q493X	1	0.01%	CF-causing
43	Q552X	1	0.01%	CF-causing
43	R709X	1	0.01%	CF-causing
43	R792X	1	0.01%	CF-causing
43	S1251N	1	0.01%	CF-causing
43	S549N	1	0.01%	CF-causing
43	S912X	1	0.01%	CF-causing
43	S945L	1	0.01%	CF-causing
43	W1098C	1	0.01%	CF-causing
43	W1098X	1	0.01%	CF-causing
43	W57G	1	0.01%	CF-causing
43	c.1043T>A	1	0.01%	Missing on CFTR2
43	c.1084_1088dup	1	0.01%	Missing on CFTR2
43	c.1115delA	1	0.01%	Missing on CFTR2
43	c.1116+1G>T	1	0.01%	Missing on CFTR2
43	c.1117G>A	1	0.01%	Missing on CFTR2
43	c.1126C>T	1	0.01%	Missing on CFTR2
43	c.1135G>A	1	0.01%	Missing on CFTR2

RANKING	MUTATION (LEGACY NAME OR C.DNA DESCRIPTION)	NUMBER OF ALLELES	% IN RELATION TO TOTAL OF ALLELES	CAUSALITY (CFTR2)
43	c.1210-1Gdel	1	0.01%	Missing on CFTR2
43	c.1317T>G	1	0.01%	Missing on CFTR2
43	c.147_150delATCT	1	0.01%	Missing on CFTR2
43	c.1486delT	1	0.01%	Missing on CFTR2
43	c.1499G>A	1	0.01%	Missing on CFTR2
43	c.1505T>G	1	0.01%	Missing on CFTR2
43	c.1525G>C	1	0.01%	Missing on CFTR2
43	c.1530_1531delTT	1	0.01%	Missing on CFTR2
43	c.1547_1548delGA	1	0.01%	Missing on CFTR2
43	c.1548A>T	1	0.01%	Missing on CFTR2
43	c.1550A>G	1	0.01%	Missing on CFTR2
43	c.1559T>A	1	0.01%	Missing on CFTR2
43	c.1654C>A	1	0.01%	Missing on CFTR2
43	c.166G>T	1	0.01%	Missing on CFTR2
43	c.167_168+3insT	1	0.01%	Missing on CFTR2
43	c.1687T>C	1	0.01%	Missing on CFTR2
43	c.1760T>C	1	0.01%	Missing on CFTR2
43	c.1766+3A>C	1	0.01%	Missing on CFTR2
43	c.1853T>C	1	0.01%	Missing on CFTR2
43	c.2375G>A	1	0.01%	Missing on CFTR2
43	c.241delT	1	0.01%	Missing on CFTR2
43	c.2658-2A>G	1	0.01%	Missing on CFTR2
43	c.2658-2A>G	1	0.01%	Missing on CFTR2
43	c.2706C>G	1	0.01%	Missing on CFTR2
43	c.274-6T>C	1	0.01%	Missing on CFTR2
43	c.2989-3C>G	1	0.01%	Missing on CFTR2
43	c.2T>G	1	0.01%	Missing on CFTR2
43	c.3001G>A	1	0.01%	Missing on CFTR2
43	c.3032T>G	1	0.01%	Missing on CFTR2
43	c.3110C>A	1	0.01%	Missing on CFTR2
43	c.3115_3116insCAG	1	0.01%	Missing on CFTR2
43	c.3139G>T	1	0.01%	Missing on CFTR2
43	c.3188G>A	1	0.01%	Missing on CFTR2
43	c.319G>C	1	0.01%	Missing on CFTR2
43	c.3231_3232delGT	1	0.01%	Missing on CFTR2
43	c.3257C>T	1	0.01%	Missing on CFTR2
43	c.326A>G	1	0.01%	Missing on CFTR2
43	c.3331_3333delTTC	1	0.01%	Missing on CFTR2
43	c.3344_3345insA	1	0.01%	Missing on CFTR2
43	c.3367+1G>A	1	0.01%	Missing on CFTR2
43	c.3469-2A>G	1	0.01%	Missing on CFTR2
43	c.3486_3487delAG	1	0.01%	Missing on CFTR2
43	c.3569_3570delTT	1	0.01%	Missing on CFTR2

RANKING	MUTATION (LEGACY NAME OR C.DNA DESCRIPTION)	NUMBER OF ALLELES	% IN RELATION TO TOTAL OF ALLELES	CAUSALITY (CFTR2)
43	c.3728T>A	1	0.01%	Missing on CFTR2
43	c.3739G>A	1	0.01%	Missing on CFTR2
43	c.3841C>T	1	0.01%	Missing on CFTR2
43	c.3874-8T>A	1	0.01%	Missing on CFTR2
43	c.38C>T	1	0.01%	Missing on CFTR2
43	c.3925C>T	1	0.01%	Missing on CFTR2
43	c.3999delG	1	0.01%	Missing on CFTR2
43	c.3G>A	1	0.01%	Missing on CFTR2
43	c.4028delG	1	0.01%	Missing on CFTR2
43	c.410T>C	1	0.01%	Missing on CFTR2
43	c.4242+5G>A	1	0.01%	Missing on CFTR2
43	c.4399_4477del	1	0.01%	Missing on CFTR2
43	c.449T>G	1	0.01%	Missing on CFTR2
43	c.473G>A	1	0.01%	Missing on CFTR2
43	c.488A>C	1	0.01%	Missing on CFTR2
43	c.489C>T	1	0.01%	Missing on CFTR2
43	c.490-1G>T	1	0.01%	Missing on CFTR2
43	c.51delC	1	0.01%	Missing on CFTR2
43	c.560delA	1	0.01%	Missing on CFTR2
43	c.577G>A	1	0.01%	Missing on CFTR2
43	c.619C>T	1	0.01%	Missing on CFTR2
43	c.675T>A	1	0.01%	Missing on CFTR2
43	c.676G>C	1	0.01%	Missing on CFTR2
43	c.864_868delAAGAC	1	0.01%	Missing on CFTR2
43	c.870+1G>T	1	0.01%	Missing on CFTR2
43	c.992T>A	1	0.01%	Missing on CFTR2
43	CFTRdele10-11	1	0.01%	Missing on CFTR2
43	CFTRdele10-24	1	0.01%	Missing on CFTR2
43	CFTRdele12	1	0.01%	Missing on CFTR2
43	CFTR20-21	1	0.01%	Missing on CFTR2
43	CFTR21-27	1	0.01%	Missing on CFTR2
43	CFTR25-26	1	0.01%	Missing on CFTR2
43	F191V	1	0.01%	Missing on CFTR2
43	G314E	1	0.01%	Missing on CFTR2
43	S434X	1	0.01%	Missing on CFTR2

FOLLOW-UP DATA:

For the description of the **follow-up** data, only the year of 2017 was considered (n = 3,378 patients).

5

ANTHROPOMETRIC DATA

Anthropometric data were obtained on the day of the pulmonary function exam or at the last visit of the year, in situations where the pulmonary function exam was not performed.

The calculation of percentiles and Z-scores of the anthropometric data used as a reference data from the US Centers for Disease Control and Prevention (available at http://www.cdc.gov/growthcharts/).

TABLE 18

Description of patients according to anthropometric data, 2017.

WEIGHT	NCHS PERCENTILE	Z-SCORE
Mean (standard deviation)	33.54 (29.79)	-0.69 (1.26)
Median (p25;p75)	26.00 (6; 56)	-0.63 (-1.52; 0.14)
TOTAL OF PATIENTS	**2,397**	**2,397**
HEIGHT	**NCHS PERCENTILE**	**Z-SCORE**
Mean (standard deviation)	34.37 (28.81)	-0.61 (1.14)
Median (p25;p75)	27.00 (9; 56)	-0.60 (-1.36; 0.15)
TOTAL OF PATIENTS	**2,408**	**2,408**
BMI (kg/m2)	**ABSOLUTE VALUE (PATIENTS AGED 18 YEARS OR OLDER)**	**NCHS PERCENTILE (PATIENTS UNDER 18 YEARS OF AGE)**
Mean (standard deviation)	21.40 (3.78)	42.72 (31.73)
Median (p25;p75)	20.94 (18.78; 23.46)	39.00 (13; 70)
TOTAL OF PATIENTS	**841**	**1,637**

p25 = percentile 25, p75 = percentile 75.

FIGURE 14

Evolution of median percentile for weight, height and BMI according to age among patients 2-18 years old, 2017.

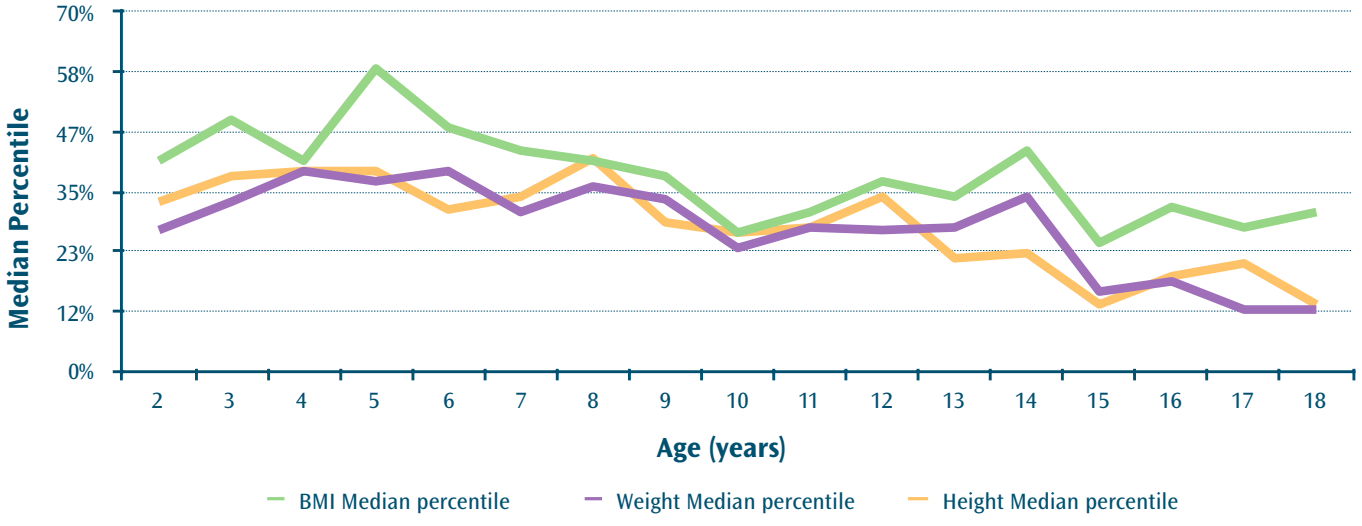


FIGURE 15

Evolution of Z-scores for weight and height according to age among patients 2-18 years old, 2017.

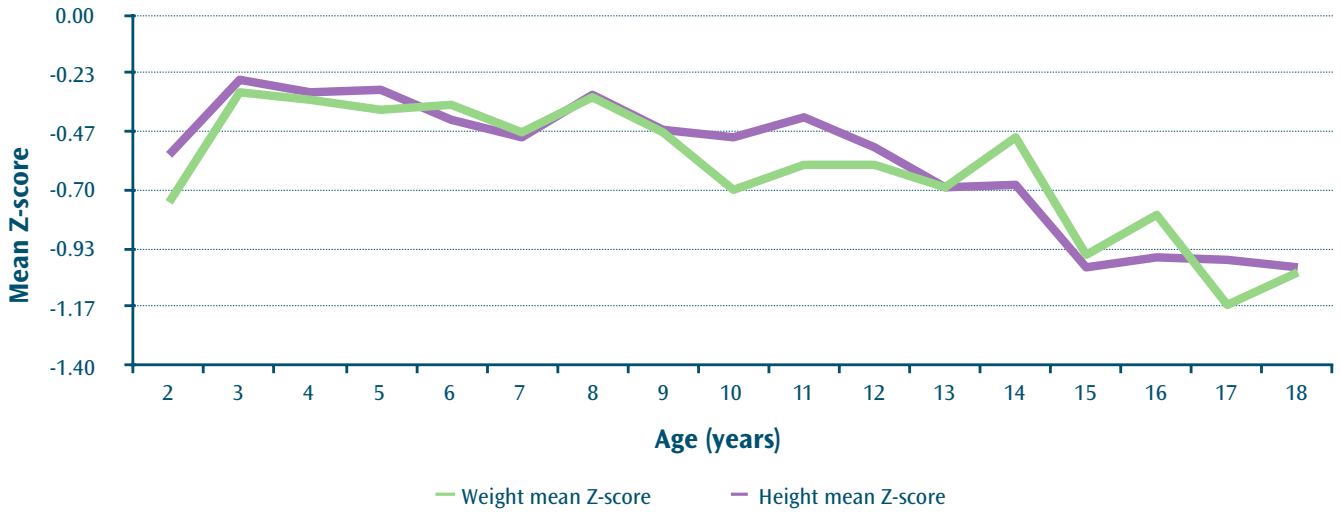
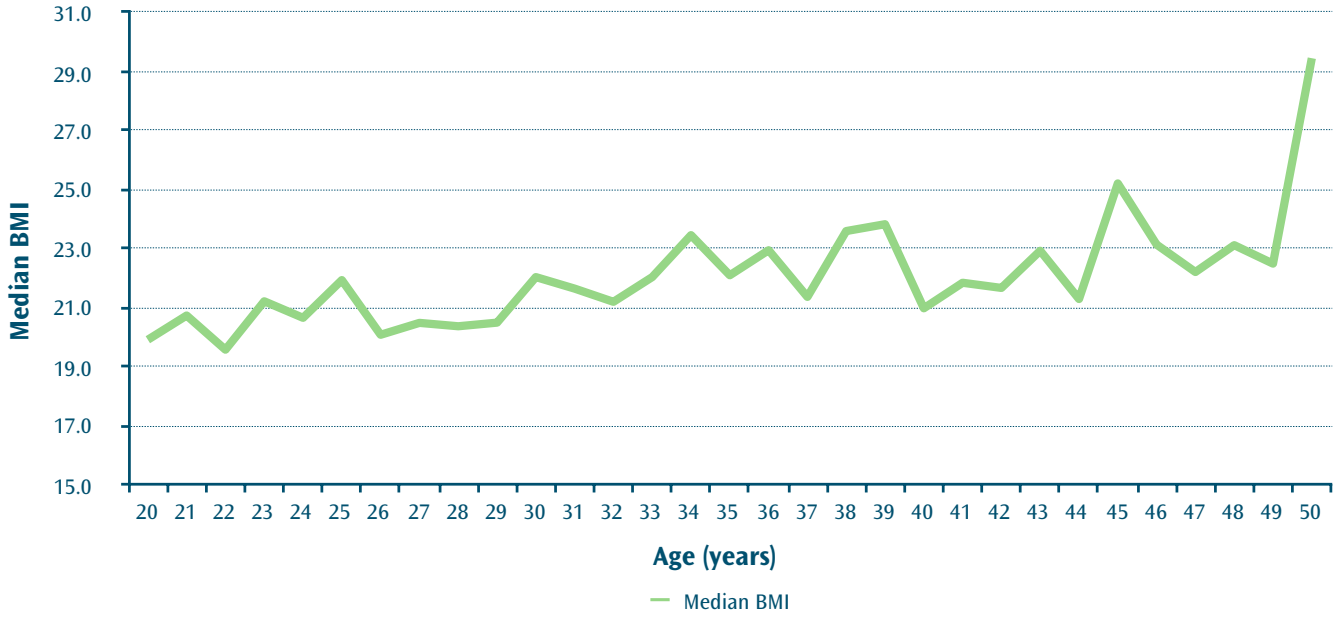


FIGURE 16

Evolution of Body Mass Index according to age among patients aged 20 years or older, 2017.



6

PULMONARY FUNCTION DATA

Spirometry data were available for 1,635 patients (48.4% of patients with follow-up). In the case of patients with more than one lung function test a year, the best pulmonary function values were inserted. The predicted lung function values used as reference were the stablished parameters by the Global Lung Function Initiative (https://www.ers-education.org/guidelines/global-lung-function-initiative.aspx)

Quanjer PH et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respir J 2012; 40: 1324–1343

TABLE 19

Description of patients according to pulmonary function data, 2017.

Z-SCORE - FVC	
Mean (standard deviation)	-1.57 (2.05)
Median (p25;p75)	-1.28 (-2.93; -0.06)
TOTAL NUMBER OF PATIENTS	**1,568**

PERCENTAGE OF PREDICTED - FVC	
Mean (standard deviation)	81.76 (23.71)
Median (p25;p75)	84.62 (65.09; 99.30)
TOTAL NUMBER OF PATIENTS	**1,568**

Z-SCORE – FEV1	
Mean (standard deviation)	-2.14 (2.18)
Median (p25;p75)	-1.97 (-3.87; -0.45)
TOTAL NUMBER OF PATIENTS	**1,568**

PERCENTAGE OF PREDICTED – FEV1	
Mean (standard deviation)	73.24 (27.52)
Median (p25;p75)	76.23 (51.38; 94.72)
TOTAL NUMBER OF PATIENTS	**1,568**

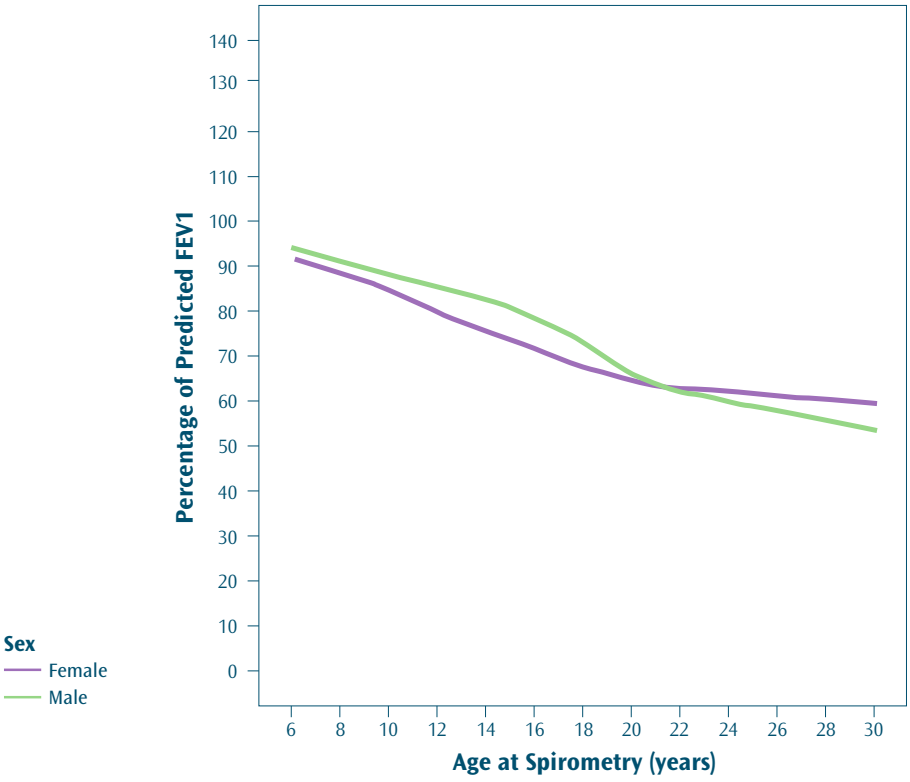
FEV1/FVC	
Mean (standard deviation)	0.76 (0.14)
Median (p25;p75)	0.78 (0.67-0.87)
TOTAL NUMBER OF PATIENTS	**1,634**

Z-SCORE - FEV1/FVC	
Mean (standard deviation)	-1.38 (1.56)
Median (p25;p75)	-1.38 (-2.59; -0.27)
TOTAL NUMBER OF PATIENTS	**1,568**

p25 = percentile 25, p75 = percentile 75. FVC: forced vital capacity, FEV1: forced expiratory volume.

FIGURE 17

Percentage of predicted FEV1 according to age among 6-30 year-old, 2017 – curves softened by the Lowess method.



More than 40% of evaluated patients in 2017 had a moderate or severe airflow obstruction (Table 20). This percentage is lower in the age group of 6 – 17 years old and higher in patients who are 18 years old or older, thus, it is during adolescence that greater airflow functional loss happens.

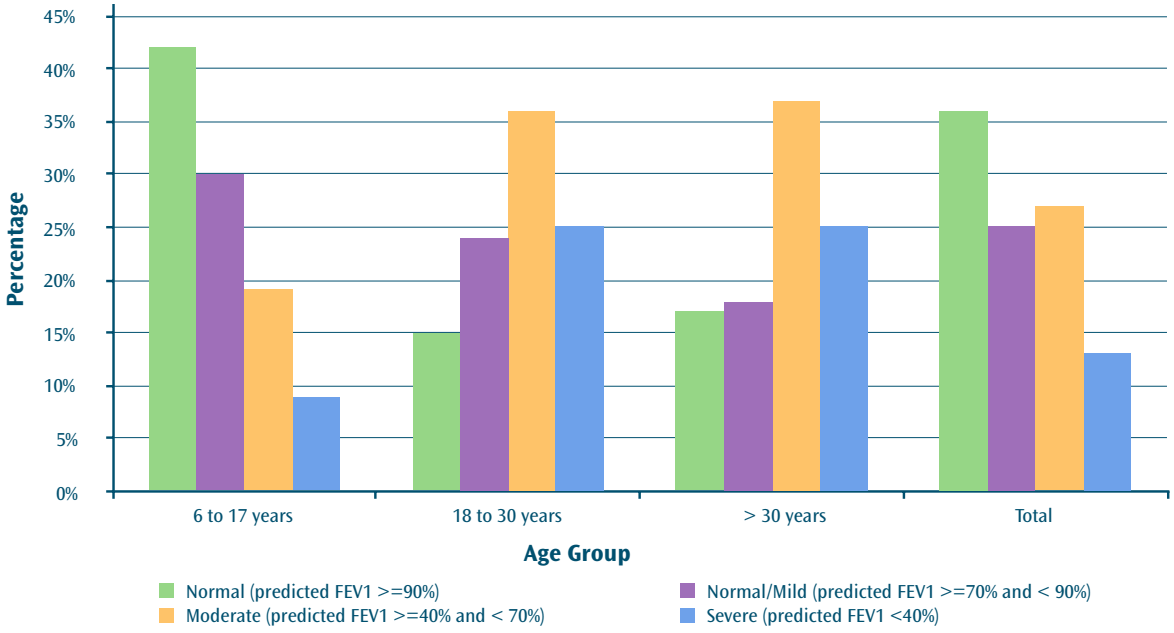
TABLE 20

Degree of airflow obstruction according to age group, 2017.

DEGREE OF AIRFLOW OBSTRUCTION	AGE GROUP			
	6 - 17 YEARS	18 - 30 YEARS	> 30 YEARS	TOTAL
Normal (predicted FEV1 >=90%)	389 (41.5%)	68 (15.5%)	32 (16.7%)	489 (31.2%)
Normal/Mild (predicted FEV1 >=70% and < 90%)	285 (30.4%)	107 (24.4%)	35 (18.2%)	427 (27.2%)
Moderate (predicted FEV1 >=40% and < 70%)	178 (19.0%)	156 (35.5%)	71 (37.0%)	405 (25.8%)
Severe (predicted FEV1 <40%)	85 (9.1%)	108 (24.6%)	54 (28.1%)	247 (15.8%)
TOTAL NUMBER OF PATIENTS	**937 (100%)**	**439 (100%)**	**192 (100%)**	**1,568 (100%)**

FIGURE 18

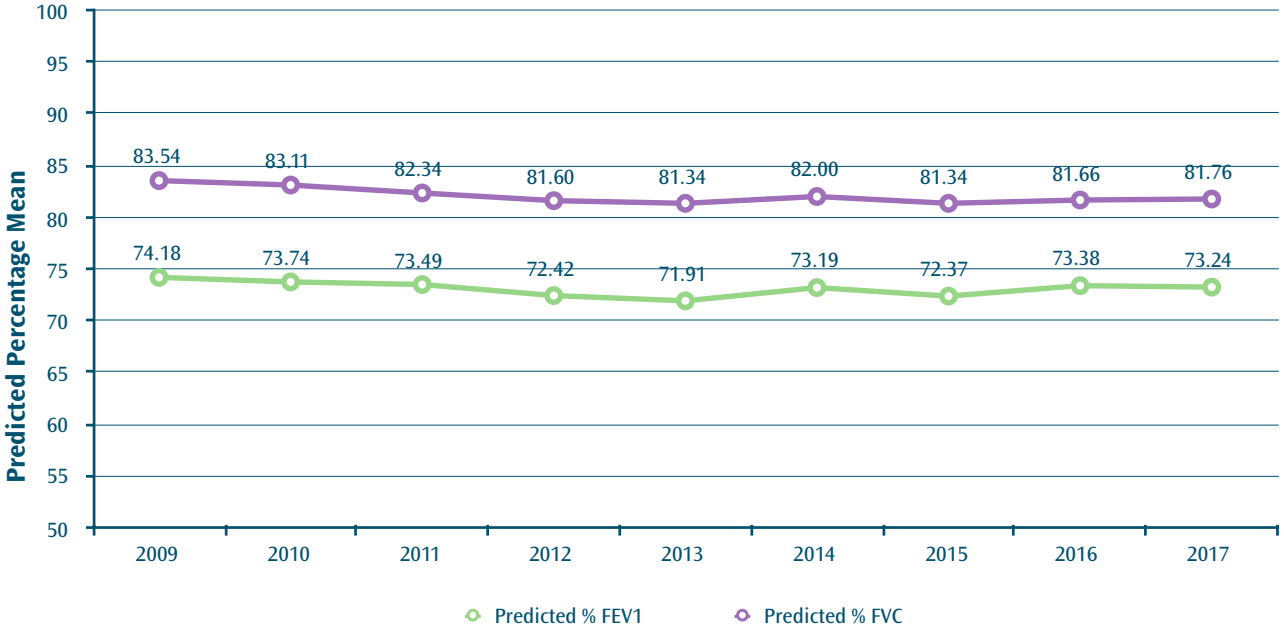
Distribution of patients according to the degree of obstruction, according to age group, 2017.



Analyzing the evolution of pulmonary function over the years (2009 to 2017), we can see that the values of FEV1 and FVC had little variations with a slight decrease over the years (Figure 19)

FIGURE 19

Variations in mean percentages of predicted values of FVC and FEV1 in 2009 to 2017.



The graphs below show the relation between nutritional indexes and pulmonary function, for both pediatric age group (percentile of BMI x FEV1 values), and adults (value of BMI x FEV1), Figures 20 and 21.

FIGURE 20

Predicted percentage of FEV1 according to BMI percentile in patients 6-18 years, 2017 – curves softened by the Lowess method.

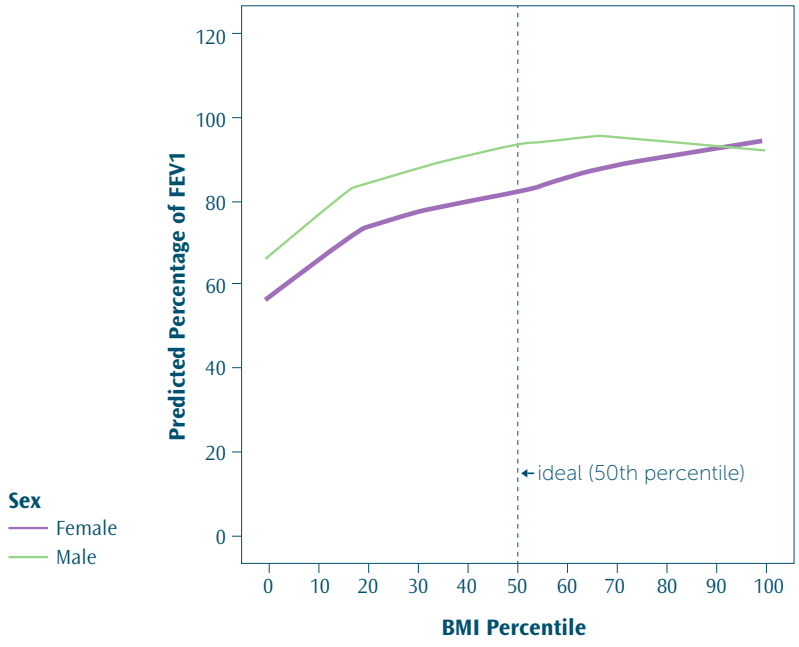
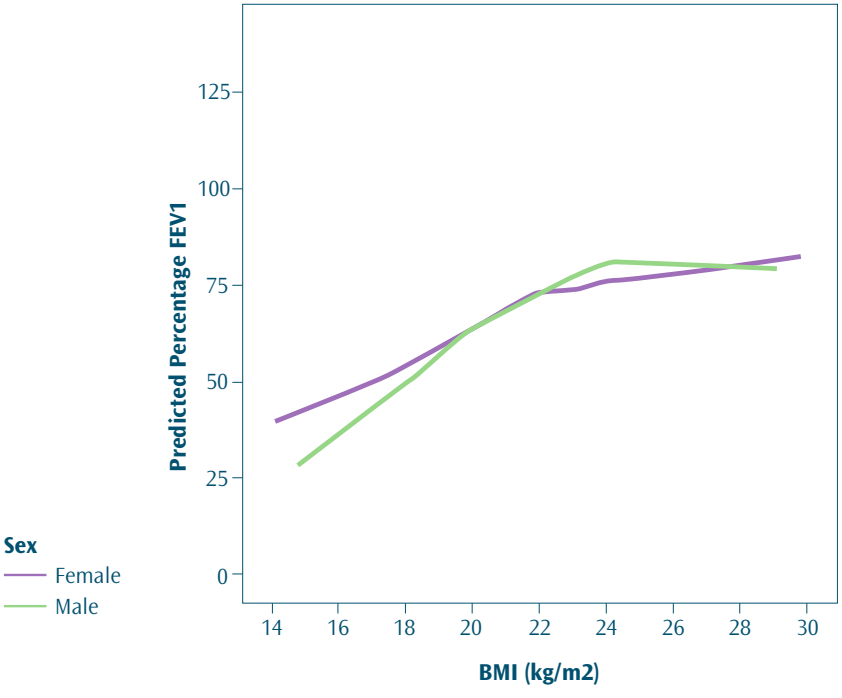


FIGURE 21

Predicted percentage of FEV1 according to BMI in patients 20-40 years, 2017 – curves softened by the Lowess method.



7

MICROBIOLOGICAL DATA

Microbiological data refer to the identification of the addressed pathogen in terms of at least once a year. The samples from respiratory tract can correspond to sputum, oropharyngeal swab, bronchoalveolar lavage or tracheal aspirate. As there is no standardization of processing techniques and sample culture of the respiratory tract of patients with cystic fibrosis, data must be interpreted with caution.

TABLE 21

Description of identified microorganisms, 2017.

IDENTIFIED MICROORGANISMS	N	%
Staphylococcus aureus Oxacillin-sensitive	1,993	59.0%
Pseudomonas aeruginosa	1,430	42.3%
Non-mucoid *Pseudomonas aeruginosa*	1,040	30.8%
Mucoid *Pseudomonas aeruginosa*	628	18.6%
Burkholderia cepacia complex	263	7.8%
Haemophilus influenzae	269	8.0%
Staphylococcus aureus Oxacillin-resistant (MRSA)	234	6.9%
Stenotrophomonas maltophilia	177	5.2%
Candida sp.	170	5.0%
Aspergillus fumigatus	117	3.5%
Klebsiella pneumoniae	98	2.9%
Achromobacter sp.	64	1.9%
Serratia sp.	59	1.7%
Escherichia coli	49	1.5%
Other *Pseudomonas*	48	1.4%
Mycobacterium tuberculosis	10	0.3%
Non-tuberculous mycobacteria	9	0.3%
TOTAL NUMBER OF PATIENTS	**3,378**	

TABLE 22

Identified microorganisms according to age, 2017.

AGE GROUP	IDENTIFIED MICROORGANISMS								
	S. aureus Oxacillin-sensitive	*Pseudomonas aeruginosa*	*Mucoid Pseudomonas aeruginosa*	*Non-Mucoid Pseudomonas aeruginosa*	*Haemophilus influenzae*	*Burkholderia cepacia Complex*	*S. aureus Oxacillin-resistant*	*Stenotro phomonas maltophilia*	N*
Up to 5 years	58.4%	34.3%	5.6%	30.5%	14.1%	4.1%	7.5%	6.6%	787
> 5 to 10	70.5%	34.7%	9.1%	29.9%	9.9%	6.4%	7.3%	5.5%	729
>10 to 15	67.3%	42.0%	16.6%	33.4%	8.7%	8.8%	6.4%	7.8%	578
>15 to 20	58.7%	48.8%	28.6%	33.9%	5.0%	9.5%	7.7%	3.4%	504
>20 to 25	52.0%	51.3%	36.9%	29.0%	2.5%	13.6%	6.5%	4.7%	279
>25 to 30	44.9%	49.0%	36.7%	27.2%	0.7%	12.9%	6.8%	2.0%	147
>30 to 35	44.3%	49.4%	36.7%	29.1%	0.0%	13.9%	5.1%	2.5%	79
>35 years	33.1%	50.3%	34.9%	27.4%	1.1%	5.1%	5.1%	2.3%	175

* total: 3.278 patients (100 patients had no information on age).

FIGURE 22

Prevalence of identified pathogens according to age group, 2017.

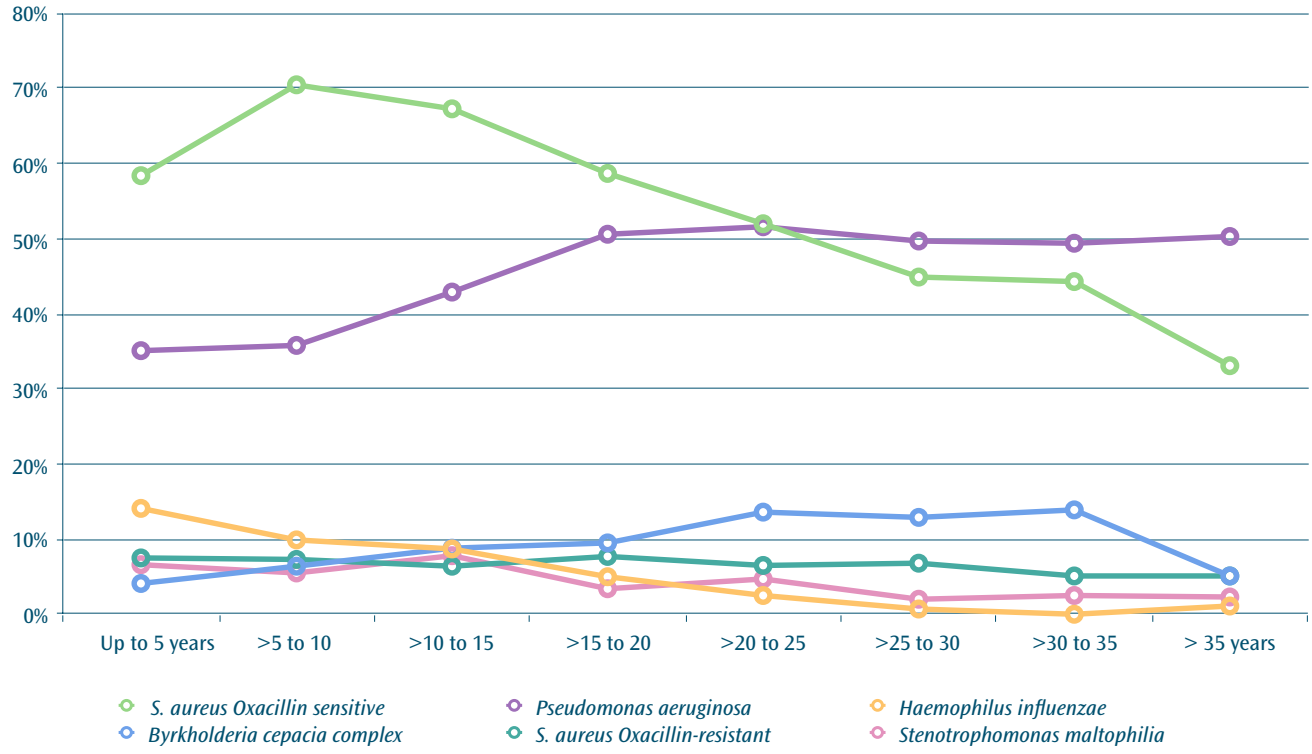
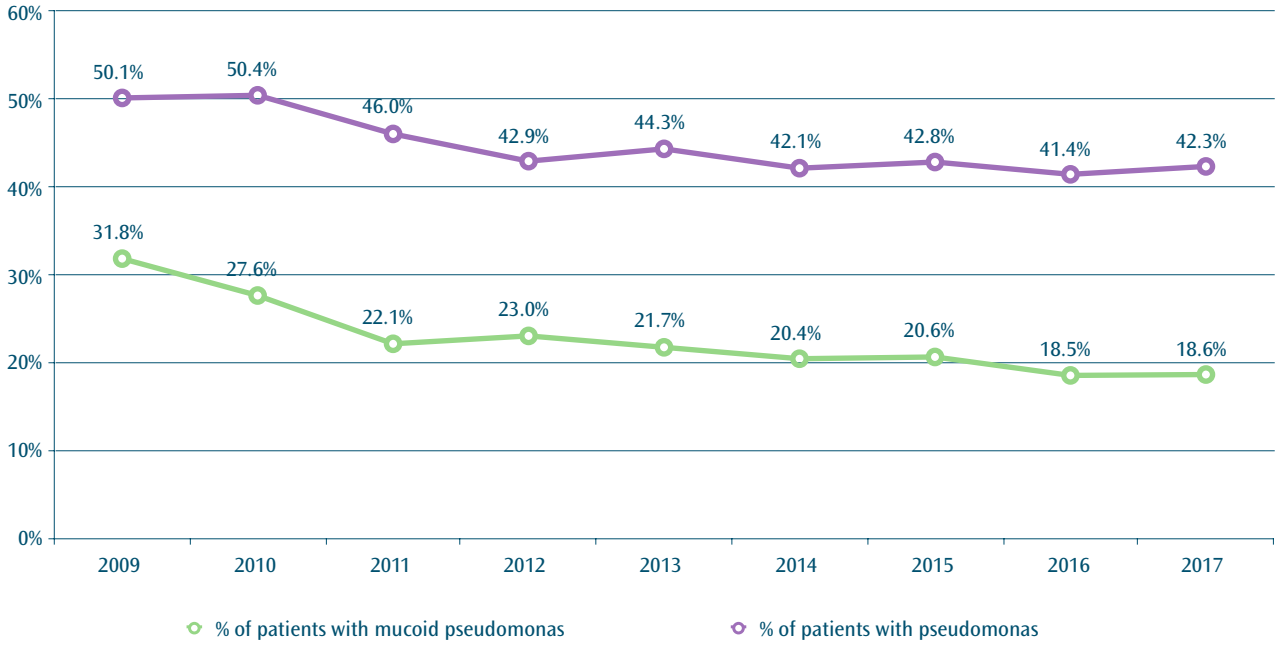


FIGURA 23

Percentages of patients with Pseudomonas aeruginosa from 2009 to 2017.



CLINICAL TREATMENT DATA

In 2017, **14,318** healthcare visits were carried out, with a median of 4 encounters per patient.

FIGURE 24

Distribution of patients according to the number of healthcare visits in 2017.

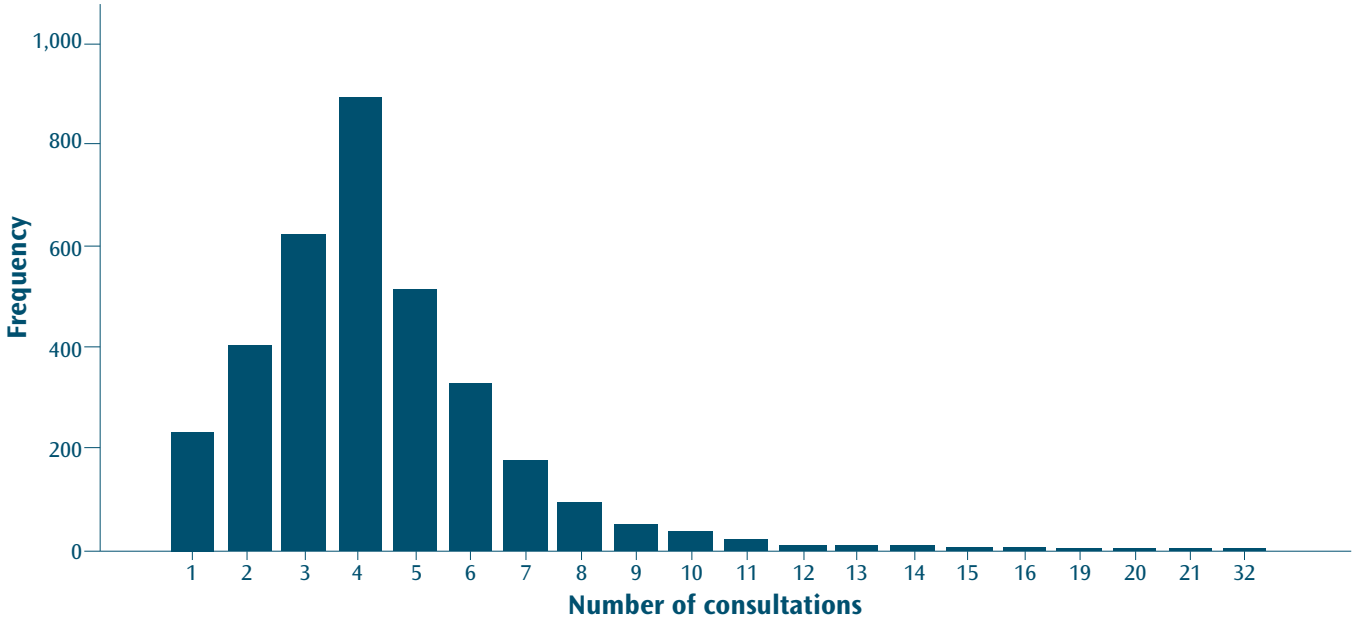


TABLE 23

Deaths.

DEATH	N(%)
No	3,328 (98.5%)
Yes	50 (1.5%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**
Age at death (years)	
Mean (standard deviation)	17.4 (9.26)
Median (p25-p75)	15.7 (10.5-22.2)
Minimum – Maximum	0.4-40.6

CAUSE OF DEATH	N	%
Respiratory cause	43	86.0%
Transplantation complications	3	6.0%
Gastrointestinal-hepatic cause	3	6.0%
Other causes	1	2.0%
TOTAL OF DEATHS	**50**	**100%**

P.S.: in this and previous reports, the percentage of deaths was calculated considering only the total of follow-up patients in the reference year. This estimate does not represent the survival of patients. It Should be emphasized that the more adequate analysis of deaths is the one that uses mean survival curves.

TABLE 24

Shwachman-Kulczycki Score: Total score per age group (patients up to 18 years old, n=1,738), 2017.

TOTAL SCORE	AGE GROUP				
	UP TO 5	>5 TO 10	>10 TO 15	>15 TO 18	TOTAL
Severe (≤ 40)	1 (0.2%)-	9 (1.7%)	16 (3.8%)	15 (5.9%)	41 (2.4%)
Moderate (41 a 55)	9 (1.7%)	25 (4.7%)	37 (8.8%)	31 (12.1%)	102 (5.9%)
Medium (56 a 70)	45 (8.5%)	83 (15.7%)	79 (18.8%)	60 (23.4%)	267 (15.4%)
Good (71 a 85)	173 (32.5%)	178 (33.6%)	163 (38.7%)	94 (36.7%)	608 (35.0%)
Excellent (86-100)	304 (57.1%)	234 (44.2%)	126 (29.9%)	56 (21.9%)	720 (41.4%)
TOTAL OF NUMBER PATIENTS	**532 (100%)**	**529 (100%)**	**421 (100%)**	**256 (100%)**	**1,738 (100%)**

FIGURE 25

Confidence intervals (95%) for mean Shwachman-Kulczycki scores according to age group (only patients > 18 years old), 2017.

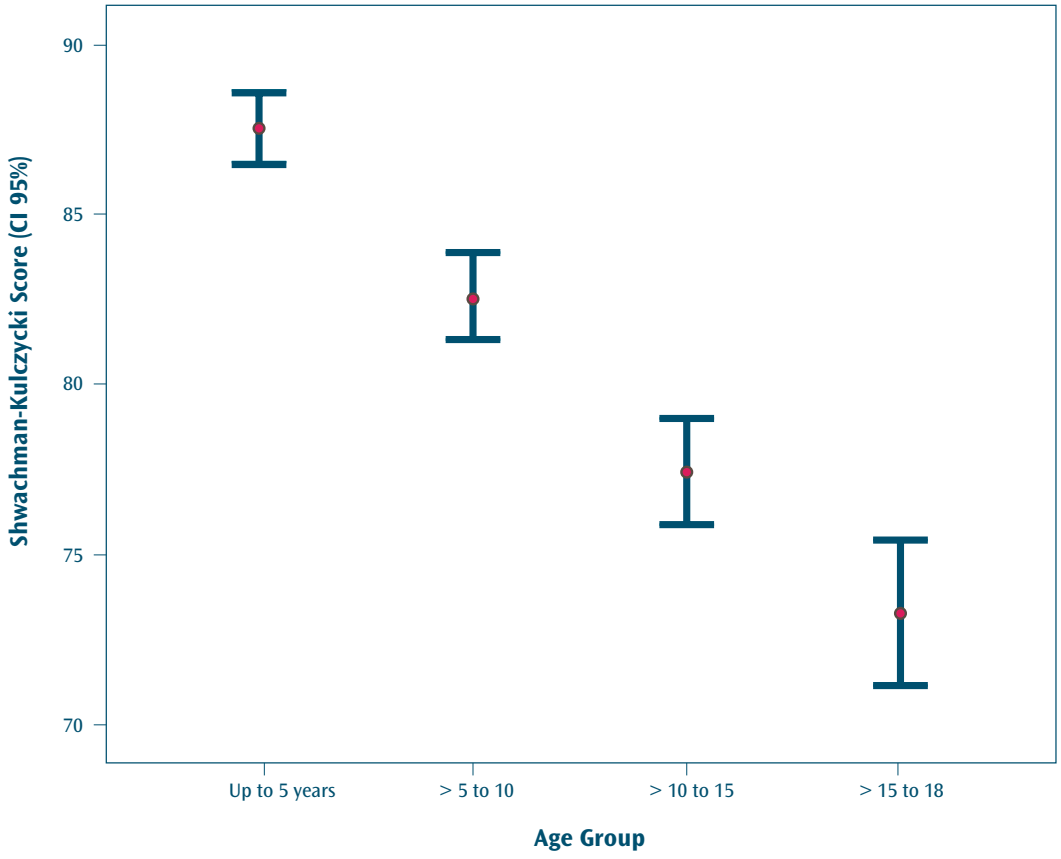


TABLE 25

Complications/comorbidities in the previous year.

COMPLICATIONS / COMORBIDITIES IN THE PREVIOUS YEAR	N (%)
Asthma	469 (13.9%)
Gastroesophageal Reflux Disease	321 (9.5%)
Evidence of hepatic impairment	267 (7.9%)
Nasal Polyposis	189 (5.6%)
Diabetes	153 (4.5%)
Osteopenia/Osteoporosis	92 (2.7%)
Chronic Atelectasis	82 (2.4%)
Cholelithiasis	43 (1.3%)
Pulmonary Hypertension / Cor pulmonale	40 (1.2%)
Cirrhosis with Portal Hypertension	39 (1.2%)
Distal Intestinal Obstruction Syndrome	27 (0.8%)
Allergic bronchpulmonary aspergillosis	25 (0.7%)
Pancreatitis	19 (0.6%)
Hematemesis	2 (0.1%)
Intestinal Invagination	2 (0.1%)
Colonic stenosis	1 (0.03%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

n = number of patients.

TABLE 26

Transplants.

TRANSPLANTS	N (%)
Pulmonary transplantation	43 (1.27%)
Deceased donor	40
Living donor	3
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

P.S.: there was no record of liver transplantation.

TABLE 27

Oxygen Therapy.

OXYGEN THERAPY	N (%)
No	3,222 (95.4%)
Yes	156 (4.6%)
Continuous	89 (2.6%)
Nocturnal	67 (2.0%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

TABLE 28
Insulin usage.

USE OF INSULIN	N (%)
No	3,212 (95.1%)
Yes	166 (4.9%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

TABLE 29
Inhaled therapies.

BRONCHODILATORS	N (%)
Short-acting beta-2 agonist	1,308 (38.7%)
Long-acting beta-2 agonist	756 (22.4%)
Anticholinergic	108 (3.2%)
INHALED CORTICOSTEROIDS	**N (%)**
Yes	974 (28.8%)
No	2,404 (71.2%)
ANTIBIOTICS	**N (%)**
Inhaled Tobramycin 300mg	1,164 (34.5%)
Colimycin	567 (16.8%)
Inhaled Tobramycin in dry powder	105 (3.1%)
Amikacin	21 (0.6%)
Gentamicin	21 (0.6%)
Injectable Tobramycin	10 (0.3%)
Vancomycin	6 (0.2%)
Aztreonam	13 (0.4%)
Others	20 (0.6%)
MUCOLYTICS	**N (%)**
Dornase alfa	2,428 (71.9%)
N-Acetyl Cysteine	111 (3.3%)
SALINE SOLUTIONS	**N (%)**
Saline solution 0.9%	502 (14.9%)
Hypertonic saline solution 3%	216 (6.4%)
Hypertonic saline solution 5%	250 (7.4%)
Hypertonic saline solution	769 (22.8%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

n = number of patients.

TABLE 30
Oral medications.

	N (%)
Pancreatic Enzymes	2,723 (80.6%)
Less than 5.000 U/kg/day	866 (31.8%)
5.000 - 10.000 U/kg/day	1,607 (59.0%)
Greater than 10.000 U/kg/day	207 (7.6%)
Unknown	43 (1.6%)
Nutritional Supplements	2,080 (61.6%)
Oral	1,816 (87.3%)
Gastrostomy	81 (3.9%)
Probe	18 (0.9%)
Unknown	165 (7.9%)
Azithromycin	1.333 (39.5%)
Protons Pump Inhibitors	777 (23.0%)
Ursodeoxycholic acid	575 (17.0%)
Corticosteroid	208 (6.2%)
H2 Blockers	238 (7.0%)
Ibuprofen or Other NSAID (Arthropathy)	6 (0.18%)
Ibuprofen (Pulmonary Disease)	8 (0.24%)
CFTR Modifying Drug (Orkambi)	4 (0.12%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

n = number of patients.*the percentages relative to enzyme doses or type of supplement were calculated based on subgroup(s) using enzymes/supplements.

TABLE 31
Treatment for *P. aeruginosa* eradication.

TREATMENT FOR *P. AERUGINOSA* ERADICATION	N (%)
Yes	791 (23.4%)
No	1,815 (53.7%)
No information	772 (22.9%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

TABLE 32
Implanted intravenous catheter.

IMPLANTED INTRAVENOUS CATHETER	N (%)
No	3,349 (99.1%)
Yes	29 (0.9%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

ACUTE RESPIRATORY EXACERBATIONS:

Almost half of the patients (49.3%) had at least one episode of acute respiratory exacerbation in 2017. In most episodes (71.5%) oral treatment was used, while 28.5% of the exacerbations were treated intravenously. The use of intravenous treatment seems to increase as the episodes become more frequent (in Figure 26 we can see that among patients with 4 or more exacerbations per year, the percentage of treated episodes intravenously surpasses 35%). The mean time of treatment was of 14 days, for both oral and intravenous treatment.

TABLE 33

Acute respiratory exacerbations.

EXACERBATIONS	N (%)
No exacerbations	1,100 (32.6%)
Determined number of episodes during the year	1,665 (49.3%)
Unknown / No information	613 (18.1%)
TOTAL NUMBER OF PATIENTS	**3,378 (100%)**

NUMBER OF EPISODES (ORAL OR INTRAVENOUS TREATMENT)	
1	687 (41.3%)
2	435 (26.1%)
3	247 (14.8%)
4	134 (8.0%)
5	82 (4.9%)
More than 5	80 (4.8%)
TOTAL NUMBER OF PATIENTS WITH EPISODES	**1,665**

TREATMENT DAYS (PER EPISODE)	ORAL	INTRAVENOUS
Mean (standard deviation)	16.3 (7.9)	15.6 (8.9)
Median (p25-p75)	14 (14-20)	14 (13-16.5)
TOTAL NUMBER OF PATIENTS THAT USED THE TREATMENT	**1,395**	**641**
TOTAL NUMBER OF PATIENTS THAT USED HOME CARE INTRAVENOUS TREATMENT		**22 (0.7%)**

FIGURE 26

Distribution of patients according to the number of acute respiratory exacerbations in 2017 (n = 2,765 patients, patients with unknown number/no information were excluded).

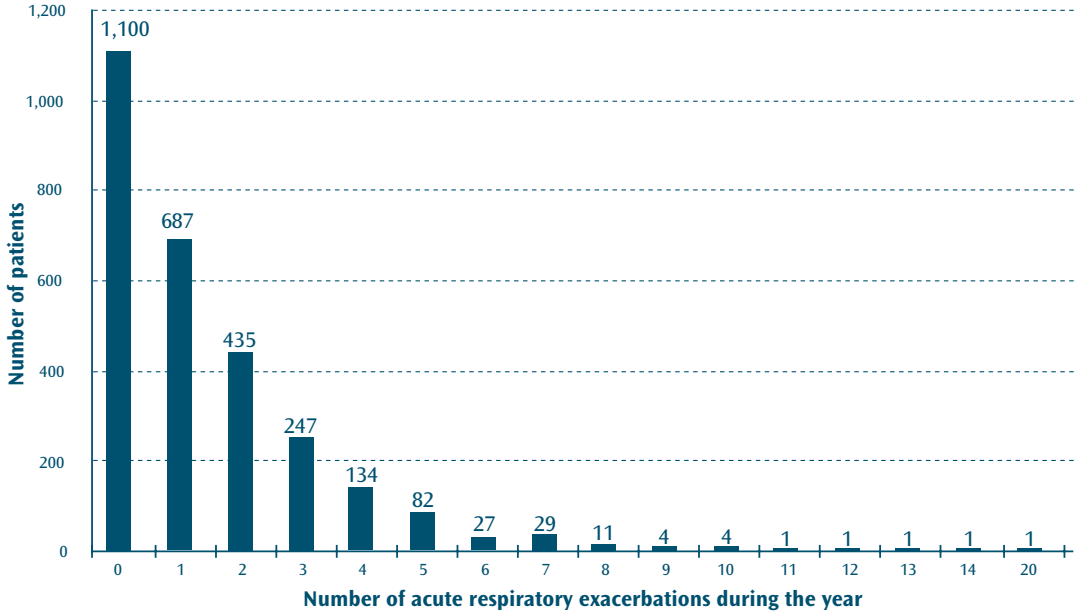


FIGURE 27

Distribution of treatment modality (oral or intravenous) according to the number of acute respiratory exacerbations in 2017 (n = 1,665 patients).

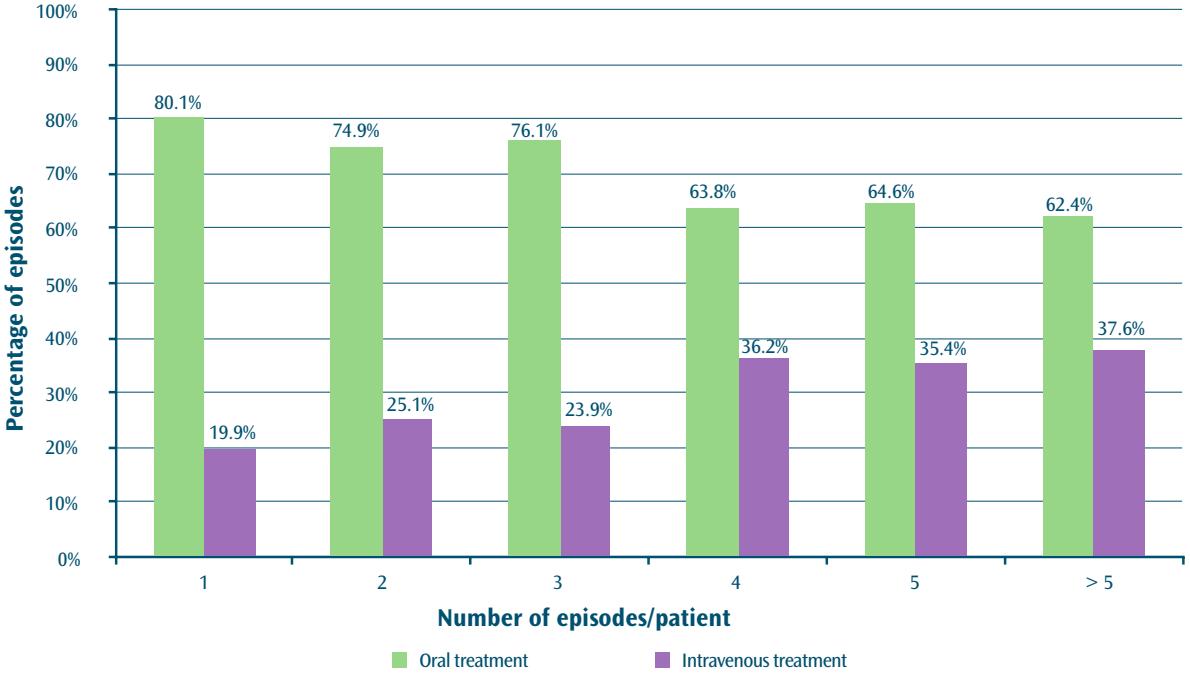


TABLE 34

Complications of cystic fibrosis - hemoptysis e pneumothorax, 2017.

HEMOPTYSIS	N (%)
Number of episodes	
One	58 (56.3%)
Two	29 (28.2%)
Three or more*	16 (15.5%)
PATIENTS WITH HEMOPTYSIS	**103 (3.0%)**

PNEUMOTHORAX	N (%)
Number of episodes	
One	8
Two	1
Three	1
PATIENTS WITH PNEUMOTHORAX	**10 (0.3%)**

There were still 181 hospitalized patients (5.4%) due to distinct reasons (not related to acute respiratory exacerbations), shown in the Table below:

TABLE 35

Hospital admissions for distinct reasons (not related to acute respiratory exacerbations), 2017.

	DEHYDRATION/ METABOLIC DISORDER	GASTROINTESTINAL CONDITION	SURGERY
Number of patients	34	52	51
Number of episodes during the year			
1	27	41	45
2	5	7	4
3 or more	2	4	2
DAYS (PER EPISODE)			
Mean (standard deviation)	11 (18.7)	9 (11.2)	9 (11.1)
Median (p25-p75)	6 (3-11)	6 (3-10)	5 (3-15)

P.S.: patients may have been admitted for more than one non-respiratory cause during the period.

TABLE 36

Intravenous Antibiotics –Drugs Used 2017.

DRUGS USED	N	(%)
Ceftazidime	411	12.2%
Amikacin	378	11.2%
Oxacillin	224	6.6%
Imipenem / Meropenem	208	6.2%
Ciprofloxacin	101	3.0%
Sulfa-Trimethoprim	98	2.9%
Cefepime	82	2.4%
Vancomycin	81	2.4%
Injectable Tobramycin	71	2.1%
Piperacillin/Tazobactam	70	2.1%
Gentamicin	43	1.3%
Linezolid	31	0.9%
Levofloxacin	30	0.9%
Colimycin	24	0.7%
Teicoplanin	24	0.7%
Ticarcillin/Piperacillin	7	0.2%
Cefuroxime	2	0.1%
Tigecycline	2	0.1%
Aztreonam	1	0.03%
Others	72	2.1%
TOTAL NUMBER OF PATIENTS	**3,378**	**100%**

n = number of patients.

TABLE 37

Specific Data on Adult Population.

	SEX		
	MALE	FEMALE	TOTAL
Azoospermia/Hypospermia*	62 (14.0%)	-	62
Pregnancy	-	9 (2.0%)	9
Oral or injectable contraceptive	-	70 (15.3%)	70
Stable relationship	65 (14.7%)	106 (23.1%)	171 (19.0%)
Employed	116 (26.2%)	99 (21.6%)	215 (23.9%)
TOTAL NUMBER OF PATIENTS AGED ≥ 18 YEARS	**442**	**459**	**901**

* Patients with investigatory report.

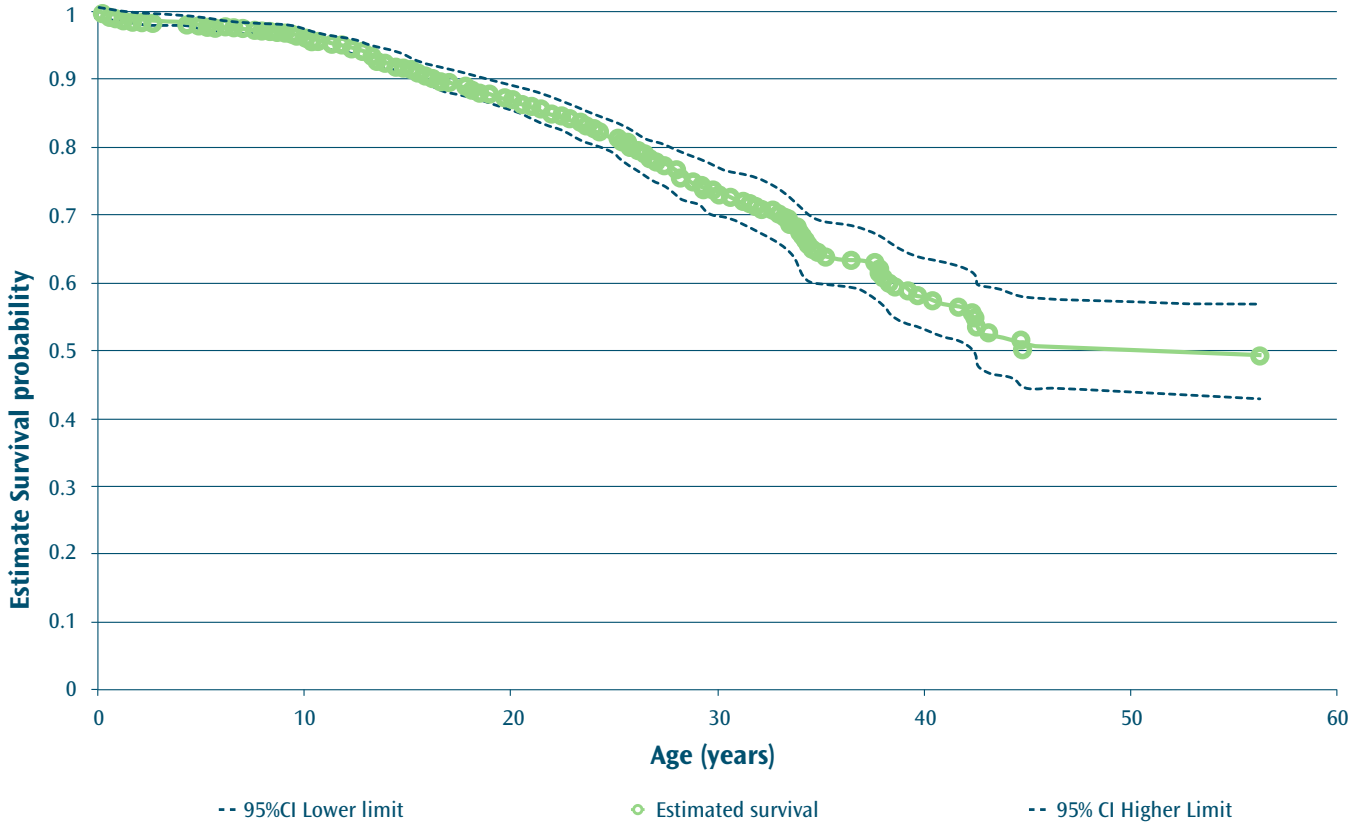
9

SURVIVAL

From the total of 4,711 cases with follow-ups, 299 deaths were observed (6.3%). However, 9 of them had an unknown cause (5 cases) or not related to the disease (4 deaths in an accidental or violent way). This cases were censured in the survival analysis. Survival analysis used the same methodology adopted by the North American Cystic Fibrosis Foundation (CFF) organization.

Figure 25 shows the survival curve considering all observed patients in this period. From 2009 to 2017, 290 deaths related to cystic fibrosis were observed. Median survival corresponds to the age where the curve (probability estimate) reaches 50%. In this case, the estimated survival at 43.8 years old was 0.05994 and at 54.9 years old was 0.49516. Thus, we know that the curve reaches 50% between those two ages. Median survival was between **43.8 years old and 54.9 years old** (lower limit – minimum estimate of the confidence interval – of 41.6 years old).

FIGURE 28
Survival curve by the Cox method, 2009 to 2017.



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This work would not have been possible without the support of the pharmaceutical companies listed below, who financially supported the initiative in an ethical and enthusiastic manner, with no privileged data collection or marketing space in the document.

- Vertex Farmacêutica do Brasil Ltda.
- Produtos Roche Químicos e Farmacêuticos S. A.

We would also like to thank all the health professionals involved in the treatment of cystic fibrosis for their cooperation in this initiative, which we are certain will bring great benefit to Brazilian patients with cystic fibrosis.

HOSPITAL	CITY	STATE	NUMBER OF FOLLOW-UPS IN 2017	DIRECTOR
PAM Codajás	Manaus	AM	1	Cláudia Mello Gonçalves
Hospital Especializado Otavio Mangabeira	Salvador	BA	146	Maria Angélica Santana
Hospital Universitario Prof. Edgard Santos	Salvador	BA	64	Edna Lúcia Santos de Souza
Hospital Infantil Albert Sabin	Fortaleza	CE	85	Claúdia de Castro e Silva
Hospital da Criança de Brasília Jose Alencar	Brasília	DF	73	Luciana de Freitas Velloso Monte
Hospital de Base do Distrito Federal	Brasília	DF	28	Clarice Guimarães de Freitas
Hospital Infantil N Sra da Gloria	Vitória	ES	92	Roberta de Cássia Melotti
Hospital Dr Dorio Silva ES	Vitória	ES	38	Daniele Menezes Torres
Hospital das Clinicas da UFGO	Goiânia	GO	36	Lusmaia Damaceno Camargo Costa
APAE Anápolis	Anápolis	GO	29	Eliane Pereira dos Santos
Hospital Universitário Materno-Infantil de São Luis	São Luis	MA	15	Denise Haidar
Hospital Infantil João Paulo II	Belo Horizonte	MG	160	Alberto Andrade Vergara
Hospital das Clínicas da UFMG	Belo Horizonte	MG	110	Elizabet Vilar
Hospital Julia Kubitschek	Belo Horizonte	MG	66	Marcelo de Fuccio
Hospital Universitário da UFJF	Juiz de Fora	MG	38	Marta Cristina Duarte
Hospital das Clínicas da UFMG - Adultos	Belo Horizonte	MG	23	Marina Nishi
Consultório Francisco Reis	Belo Horizonte	MG	19	Francisco José Caldeira Reis
Hospital de Clínicas de Uberlândia/UFU	Uberlãndia	MG	5	Erica Rodrigues Mariano de Almeida
APAE - Iped Campo Grande	Campo Grande	MS	42	Lilian Cristina Ferreira Andries
Hospital Universitário João de Barros Barreto	Belém	PA	140	Valéria de Carvalho Martins
Hospital Universitário Lauro Wanderley	João Pessoa	PB	1	Constantino Cartaxo
Instituto Materno Infantil de Pernambuco	Recife	PE	39	Murilo Carlos Amorim de Britto
Hospital das Clínicas da UFPR	Curitiba	PR	111	Carlos Antônio Riedi
Hospital Pequeno Principe	Curitiba	PR	71	Paulo Kussek
Hospital das Clínicas da UFPR - Adultos	Curitiba	PR	44	Mariane Martynychen
Instituto Fernandes Figueira	Rio de Janeiro	RJ	168	Tania Wrobel Folescu
Hospital Universitário Pedro Ernesto - UERJ	Rio de Janeiro	RJ	58	Monica Firmida
Hospital dos Servidores do Estado Rio de Janeiro	Rio de Janeiro	RJ	35	Daniela de Souza Paiva Borgli
Centro de Referência em Fibrose Cística do RN	Natal	RN	26	Vera Maria Dantas
Hospital das Clínicas de Porto Alegre - Adultos	Porto Alegre	RS	114	Paulo de Tarso Roth Dalcin
Hospital das Clínicas de Porto Alegre	Porto Alegre	RS	103	Paulo Cauduro Maróstica
Hospital São Lucas	Porto Alegre	RS	89	Leonardo Araújo Pinto
Santa Casa de Porto Alegre	Porto Alegre	RS	44	Gilberto Bueno Fischer
Hospital Infantil Joana de Gusmao	Florianópolis	SC	95	Noberto Ludwig Neto

HOSPITAL	CITY	STATE	NUMBER OF FOLLOW-UPS IN 2017	DIRECTOR
Hospital Nereu Ramos	Florianópolis	SC	18	Concetta Esposito
Hospital Infantil Jeser Amarante Faria	Joinville	SC	17	Tiago Neves Veras e Rafaela C. Benvenutti da Costa
Hospital Santa Isabel	Blumenau	SC	10	Glaunir Maria Foletto
Hospital Universitário da Univ Federal de Sergipe	Aracaju	SE	38	Daniela Gois Meneses
Santa Casa	São Paulo	SP	174	Neiva Damaceno
Instituto da Criança	São Paulo	SP	161	Joaquim Carlos Rodrigues
Unicamp	Campinas	SP	153	Antonio Fernando Ribeiro
Hospital das Clínicas da FMUSP - Adultos	São Paulo	SP	108	Rodrigo Athanazio e Samia Rached
Hospital das Clínicas da USP Ribeirão Preto	Ribeirão Preto	SP	103	Lídia Alice Gomes M. M. Torres
UNIFESP	São Paulo	SP	93	Sonia Mayumi Chiba
UNESP	Botucatu	SP	78	Giesela Fleischer Ferrari
Hospital de Base Fac Med de SJ Rio Preto	São José do Rio Preto	SP	25	Katia Izabel de Oliveira
Consultório Fabiola Adde	São Paulo	SP	22	Fabíola Vilac Adde
Centro de Puericultura - CPAP	São Paulo	SP	3	Luiz Vicente Ribeiro R. da Silva Filho
TOTAL NUMBER OF FOLLOW-UPS IN 2017			**3,378**	

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