The Brazilian Cystic Fibrosis Patient Registry

2015

GRUPO BRASILEIRO DE ESTUDOS DE FIBROSE CÍSTICA

ANNUAL REPORT 2015

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. With the publication of this report, this initiative will have been ongoing for 7 years, with growing participation by colleagues and an increasing number of CF Centers operating in the country. There is still much to do for Brazilian patients who lack access to diagnostic and therapeutic resources in several regions of the country. The continuity and integrity of REBRAFC is of paramount importance in this scenario because it represents the main documented resource for the current situation of patients with CF in Brazil and their evolution over the years, thus demonstrating how CF is being diagnosed and treated in the country.

We believe that this initiative can contribute to changes in the public agenda, resulting in better health assistance to individuals with CF in Brazil.

Cystic Fibrosis and the 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 that remain little known in Brazil, despite the existence of various 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; however, access to drugs is not uniform in the country.

The Brazilian Cystic Fibrosis Study Group (GBEFC) is a non-profit organization, created on November 5, 2003, and composed of health professionals working in the area of CF. The activities of the GBEFC include dissemination of research, training of personnel, assistance with the establishment of centers for the treatment of CF in Brazil, organization of congresses in the country on CF (six Brazilian CF Congresses have already been held), and working with the Ministry of Health to define a national protocol for the treatment of CF. Recently, the First Brazilian Guidelines on the Diagnosis and Treatment of Cystic Fibrosis was published, an initiative of the GBEFC with support from the Brazilian Society of Pneumology and Phthisiology (SBPT) and the Brazilian Society of Pediatrics (SBP), uniting the efforts of several professionals working in the area.

The GBEFC maintains a website (www.gbefc.org.br) that provides information on CF; the present report and previous reports are available as free downloads on the site in Portuguese and English language versions.

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REBRAFC HIGHLIGHTS IN 2015

01 The patient registry is increasingly representative:

- **A total 3,857 registered patients,** 97.6% with annual follow-up data.
- **About 50%** of patients have 4 years or more of follow-up data.

02 Cystic fibrosis is diagnosed increasingly earlier in Brazil:

- **There is consistent and increasing** neonatal screening.
- **Median age** at diagnosis is around 4 months.

03 Patients with cystic fibrosis in Brazil are living longer:

- **The median age** is 12 years and growing every year.
- **Adult patients** account for about 27% of the total.

04 There are still many challenges ahead:

- **Most patients have** inadequate nutritional status.
- *Pseudomonas aeruginosa* was identified in respiratory secretion samples of **37% of patients aged under 5 years.**
- **About one-third of patients between** ages 6 and 17 years have moderate or severe disturbances in pulmonary function.

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1. INTRODUCTION

This report describes data from the Brazilian Cystic Fibrosis Registry (REBRAFC), which contains demographic, diagnostic, and treatment data of patients with cystic fibrosis (CF) in Brazil. Follow-up data of 2015 were included in the Registry during the calendar year of 2016. By the time these data were generated for analysis, 3,857 patients had been registered in the database, of which 3,767 (99%) had some follow-up data.

The number of records and follow-ups has been increasing annually, as shown in Figure 1. In this report, 346 new records were registered. Although fewer new cases were recorded than in 2015, the annual number of follow-ups continues to increase. More than 60% of patients have at least 3 years of follow-up and nearly half (48.6%) have at least 4 years of follow-up (Table 1). These data clearly illustrate the continuous updating of the REBRAFC database regarding the follow-up of registered cases.

Figure1

Growth in the number of registrations and follow-ups between 2009 and 2015.

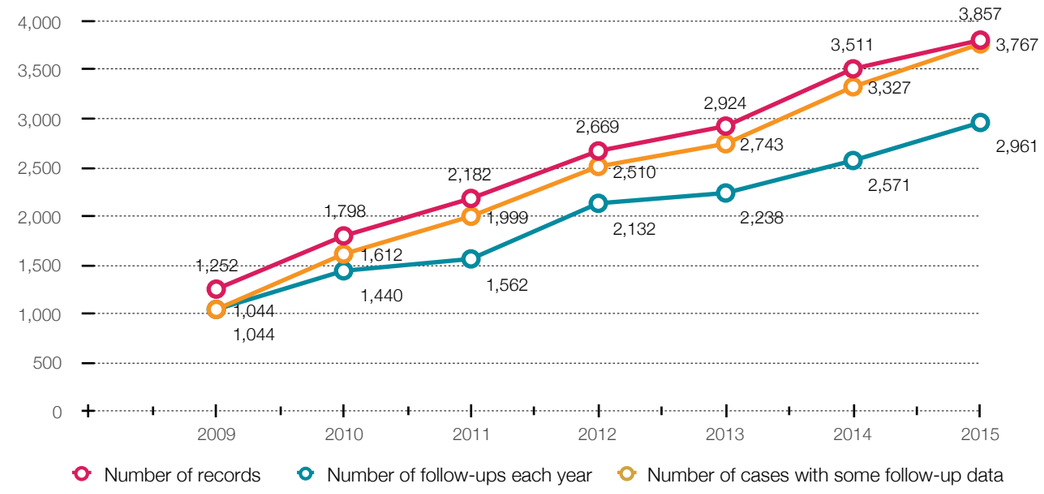


Table 1

Distribution of patients according to follow-up time.

Follow-up time	N	%	Accumulated %
7 years	418	10.8%	10.8%
6 years	468	12.1%	23.0%
5 years	455	11.8%	34.8%
4 years	532	13.8%	48.6%
3 years	515	13.4%	61.9%
2 years	699	18.1%	80.0%
1 year	680	17.6%	97.7%
No follow-up	90	2.3%	100.0%
Total	**3,857**	**100**	

n = number of patients

In the description of personal and diagnostic data, all registered patients (n = 3,857) were taken into account. For analysis of the follow-up data, only data with reference year 2015 (inserted in 2016), which included data of a total 2,961 patients, were taken into account.

2. DEMOGRAPHIC DATA

Table 2

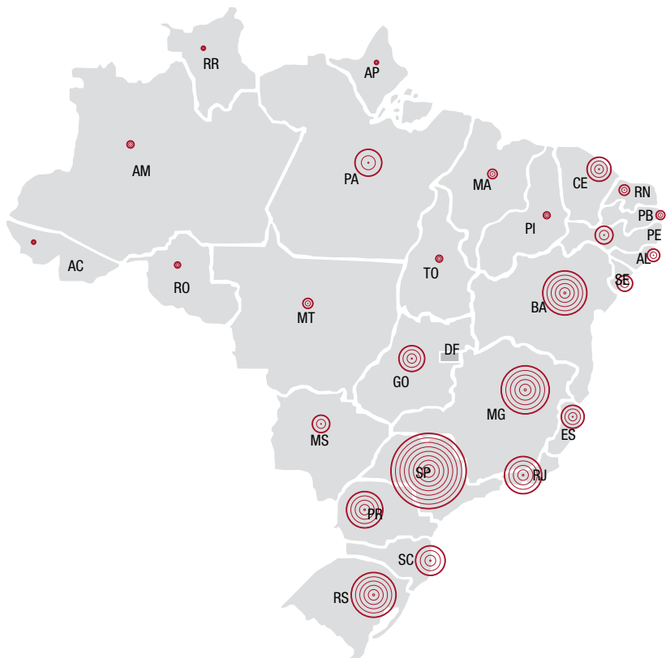
Distribution of patients according to state of birth, 2015.

State of birth	n	%
São Paulo	1,027	27.0
Minas Gerais	427	11.2
Rio Grande do Sul	408	10.7
Bahia	406	10.7
Rio de Janeiro	262	6.9
Paraná	231	6.1
Santa Catarina	182	4.8
Pará	140	3.7
Espirito Santo	125	3.3
Ceará	107	2.8
Goiás	67	1.8
Distrito Federal	66	1.7
Pernambuco	66	1.7
Mato Grosso do Sul	40	1.1
Sergipe	36	0.9
Alagoas	26	0.7
Rio Grande do Norte	24	0.6
Mato Grosso	20	0.5
Maranhão	16	0.4
Paraíba	15	0.4
Piauí	8	0.2
Tocantins	8	0.2
Amazonas	7	0.2
Rondônia	4	0.1
Acre	3	0.1
Amapá	3	0.1
Roraima	3	0.1
Não informado	130	3.4
Total	**3,857**	**100**

n = number of patients

Figure 2

Distribution of patients according to state of birth, 2015.



State	n
São Paulo	1,027
Minas Gerais	427
Rio Grande do Sul	408
Bahia	406
Rio de Janeiro	262
Paraná	231
Santa Catarina	182
Pará	140
Espirito Santo	125
Ceará	107
Goiás	67
Distrito Federal	66
Pernambuco	66
Mato Grosso do Sul	40
Sergipe	36
Alagoas	26
Rio Grande do Norte	24
Mato Grosso	20
Maranhão	16
Paraíba	15
Piauí	8
Tocantins	8
Amazonas	7
Rondônia	4
Acre	3
Amapá	3
Roraima	3

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Table 3

Distribution of patients according to region of birth, 2015.

Region of birth	n	%
Southeast	1,841	47.7%
South	821	21.3%
Northeast	704	18.3%
Midwest	193	5.0%
North	168	4.4%
Not reported	130	3.4%
Total	**3,857**	**100%**

Table 4

Distribution of patients according to state of the care center, 2015.

State of center	n	(%)
São Paulo	1,090	28.3%
Rio Grande do Sul	443	11.5%
Minas Gerais	429	11.1%
Bahia	408	10.6%
Rio de Janeiro	263	6.8%
Paraná	249	6.5%
Santa Catarina	160	4.1%
Pará	144	3.7%
Espírito Santo	135	3.5%
Distrito Federal	108	2.8%
Ceará	107	2.8%
Pernambuco	72	1.9%
Goiás	68	1.8%
Mato Grosso	39	1.0%
Mato Grosso do Sul	34	0.9%
Sergipe	31	0.8%
Alagoas	26	0.7%
Rio Grande do Norte	25	0.6%
Maranhão	14	0.4%
Paraíba	12	0.3%
Total number of patients	**3,857**	**100%**

n = number of patients

Table 5

Distribution of patients according to sex and ethnic group, 2015.

Sex	n (%)
Male	1,985 (52.2%)
Female	1,821 (47.8%)
Total	**3,806 (100%)**
No information	*51*

n = number of patients

Ethnic group	n (%)
White	2,616 (68.7%)
Mulato	957 (25.1%)
Black	223 (5.9%)
Asian	7 (0.2%)
Indigenous	3 (0.1%)
Total	**3,806 (100%)**
No information	*51*

Table 6

Distribution of patients according to current age (last spirometry/anthropometry), 2015.

Age (years)	
Mean (standard deviation)	14.25 (11.95)
Median (p25; p75)	12.02 (6.02 – 18.39)
Total number of patients	**3,562**
Total of patients who died	**190**
Patients without spirometry/anthropometry	**105**

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

Figure 3

Distribution of patients according to current age (last spirometry/anthropometry), 2015.

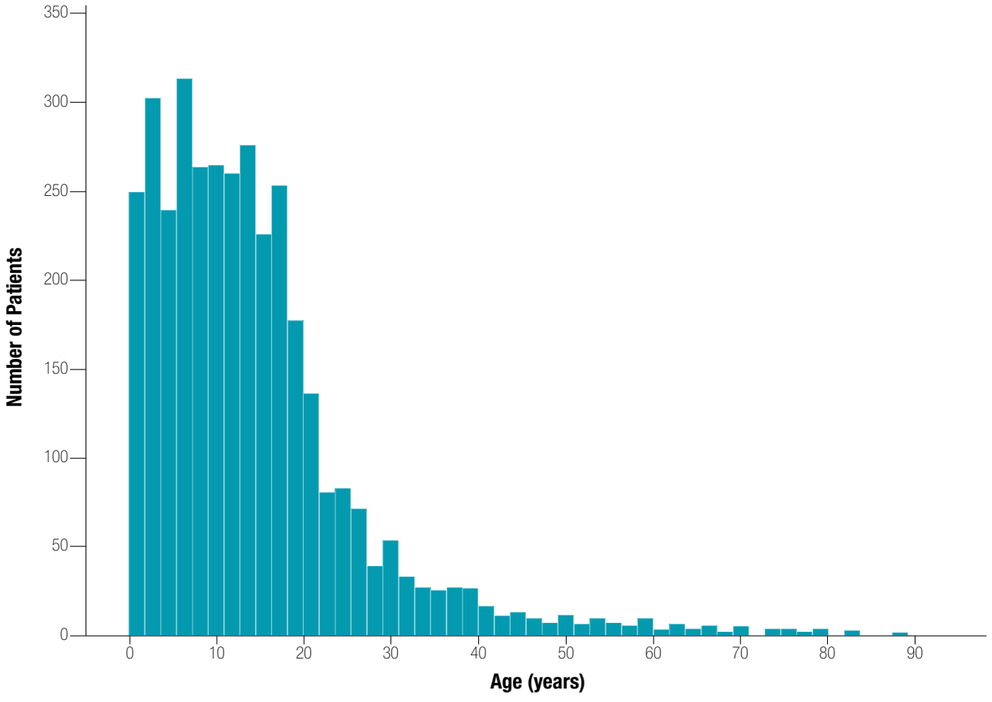

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Figure 4

Distribution of patients according to current age (last spirometry/anthropometry) and sex, 2015.

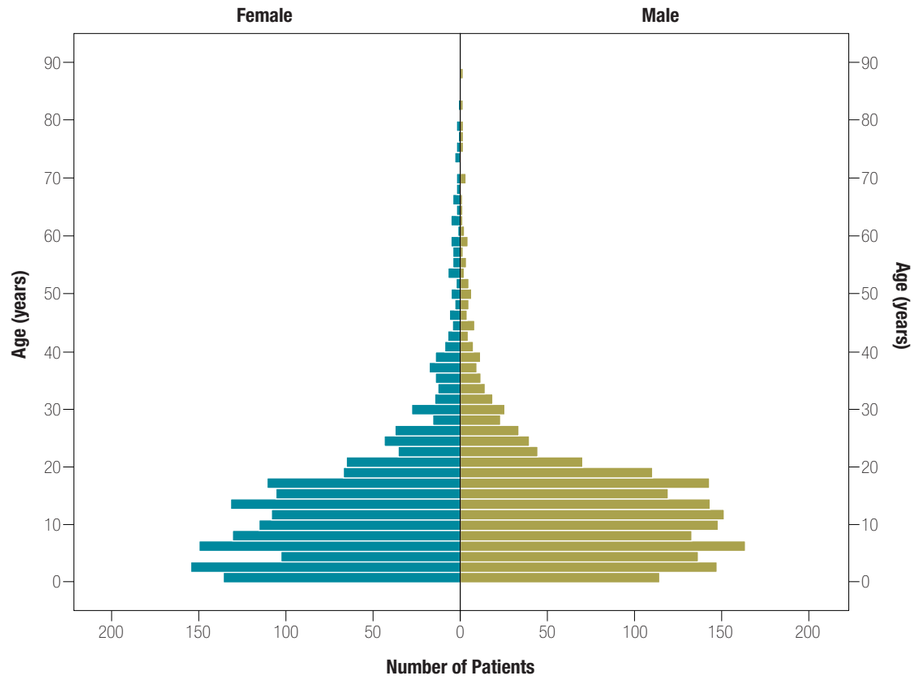


Table 7

Distribution of patients according to current age group, 2015.

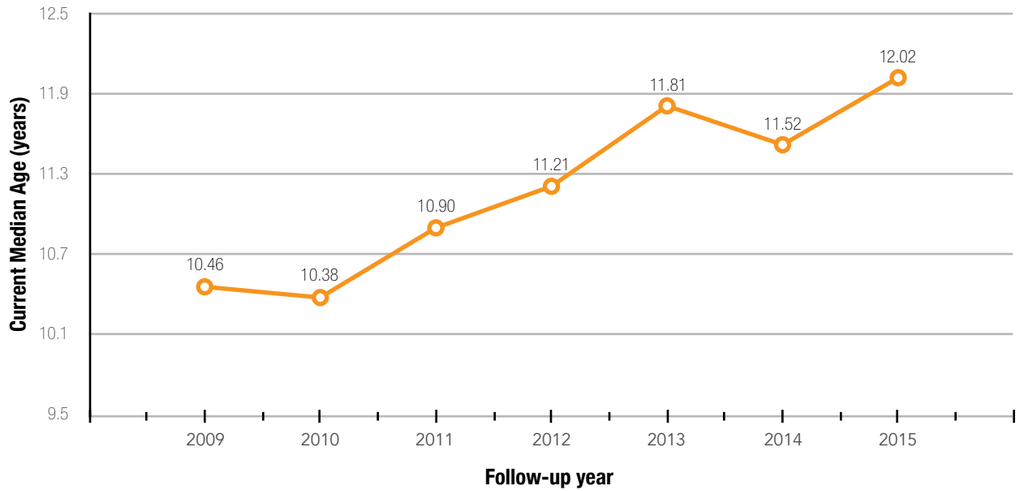
Age group (years)	n (%)
Up to 5	727 (20.4%)
> 5 to 10	778 (21.8%)
>10 to 15	721 (20.2%)
>15 to 20	595 (16.7%)
>20 to 25	282 (7.9%)
>25 to 30	159 (4.5%)
>30 to 35	84 (2.4%)
>35 to 40	75 (2.1%)
>40 to 45	36 (1.0%)
>45 to 50	26 (0.7%)
>50	79 (2.2%)
Total number of patients	**3,562 (100%)**
No information	**105**

Age group (pediatric, adult)	n (%)
Less than 18 years	2,612 (73.3%)
18 years and over	950 (26.7%)
Total number of patients	**3,562 (100%)**
No information	**105**

n = number of patients

Figure 5

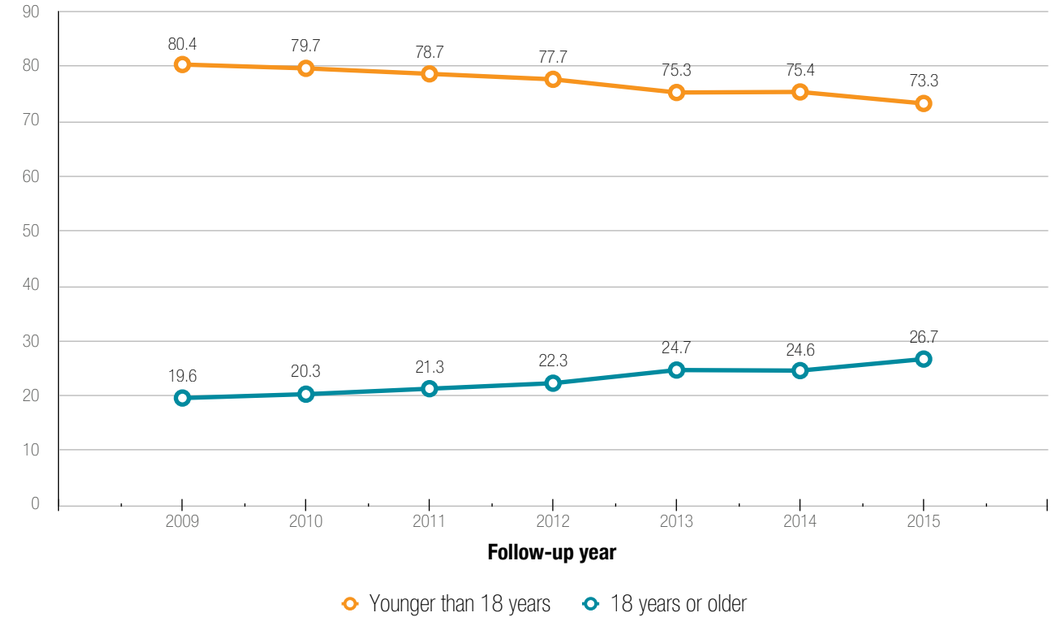
Evolution of current age from 2009 to 2015.



Note: Values are expressed as medians.

Figure 6

Distribution of patients according to pediatric age group from 2009 to 2015.



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3. DADOS DO DIAGNÓSTICO

Table 8

Description of patients according to age at diagnosis.

Age (years)	
Mean (standard deviation)	5.82 (10.54)
Median (p25; p75)	1.11 (0.20 – 7.20)
Total number of patients	**3,799**
Patients with no information*	**58**

n = number of patients; p25, 25th percentile; p75, 75th percentile.
Birthdates/diagnosis incorrectly completed.

Figure 7

Distribution of patients according to age at diagnosis, 2015.

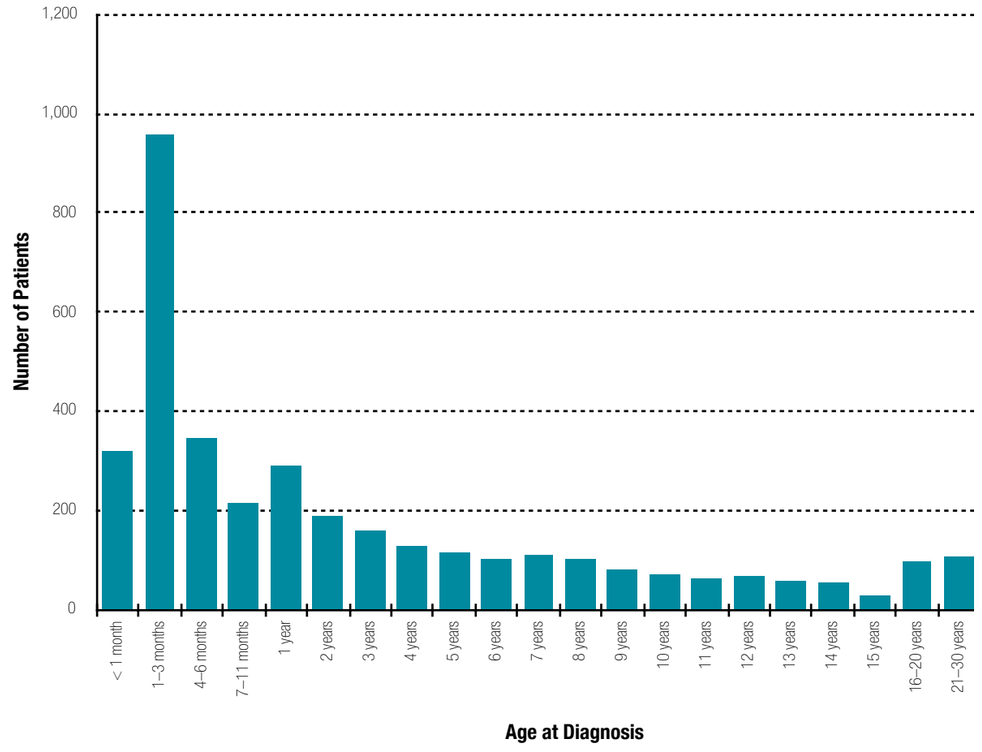
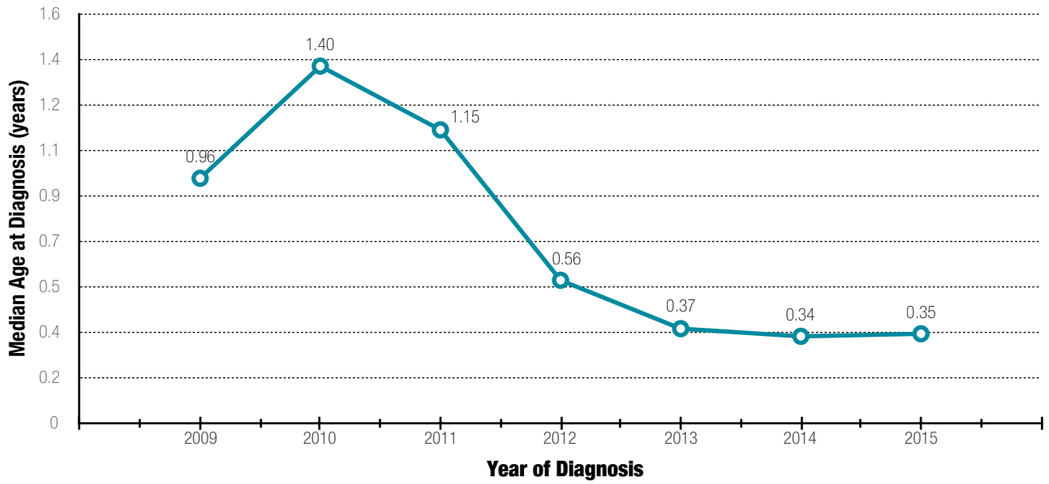


Figure 8 shows the median age at diagnosis according to the year in which cases were diagnosed, for the period between 2009 and 2015. It can be observed in the graph that in the last 3 years, the median has remained around 4 months of age.

Figure 8

Variation in age at diagnosis over the years.



Notes: Values are presented as medians.
Year of diagnosis was used instead of follow-up year (extracted from the date of diagnosis).

Table 9

Distribution of patients according to conditions for diagnosis, 2015.

Conditions for diagnosis	n	(%)
Persistent respiratory symptoms	2,294	59.5%
Growth deficit/malnutrition	1,448	37.5%
Steatorrhea or malabsorption	1,313	34.0%
Neonatal screening (IRT)	1,159	30.0%
Family history	312	8.1%
Clinical or surgical meconium ileus	292	7.6%
Sinusal disease and/or nasal polyp	222	5.8%
Metabolic disorder	213	5.5%
Edema/anemia	144	3.7%
Rectal prolapse	33	0.9%
Prolonged jaundice	35	0.9%
Infertility	15	0.4%
Other	199	5.2%
Unknown condition	143	3.7%
Total number of patients	**3,857**	**100%**

n = number of patients

Table 10

Description of patients according to sweat test results.

	Chloride (mEq/L)	Mass (mg)	Conductivity (mmol/l)
Mean (standard deviation)	90.17 (26.67)	147.94 (78.45)	103.9 (18.7)
Median (p25; p75)	91.00 (71,0; 106,0)	135.00 (100; 187)	105.0 (96; 115)
Total number of patients	**3,257**	**2,299**	**452**

n = number of patients; p25, 25th percentile; p75, 75th percentile.
For chloride and mass, the average of two measurements was taken into account.

Table 11

Diagnosis by newborn screening with immunoreactive trypsinogen (IRT).

IRT dosage (ng/ml)	1st dose	2nd dose
Mean (standard deviation)	205.1 (125.6)	205.0 (134.6)
Median (p25; p75)	176.0 (122; 257)	171.0 (116; 249)
Total patients	**1,005**	**785**

Table 12

Other diagnostic tests reported.

	n (%)
Measurement of nasal potential difference	102 (2.7%)
Rectal biopsy	72 (1.9%)
Total number of patients	**3,806 (100%)**
No information	*51*

n = number of patients

As in previous years, it was found that the age at diagnosis was significantly lower among patients who underwent neonatal screening ($p < 0.001$; Table 13 and Figure 9).

Table 13

Description of patients in relation to age at diagnosis according to neonatal screening.

	Neonatal screening		
Age at diagnosis (years)	**No**	**Yes**	**Total**
Mean (standard deviation)	8.19 (11.86)	0.43 (1.22)	5.82 (10.54)
Median (p25; p75)	3.91 (0.72; 10.37)	0.14 (0.09; 0.29)	1.11 (0.20; 7.20)
Total number of patients	**2,641**	**1,158**	**3,799**
Patients with no information	**6**	**1**	**58**

p25, 25th percentile; p75, 75th percentile.

Figure 9

Distribution of patients according to age at diagnosis and whether newborn screening was performed, 2015.

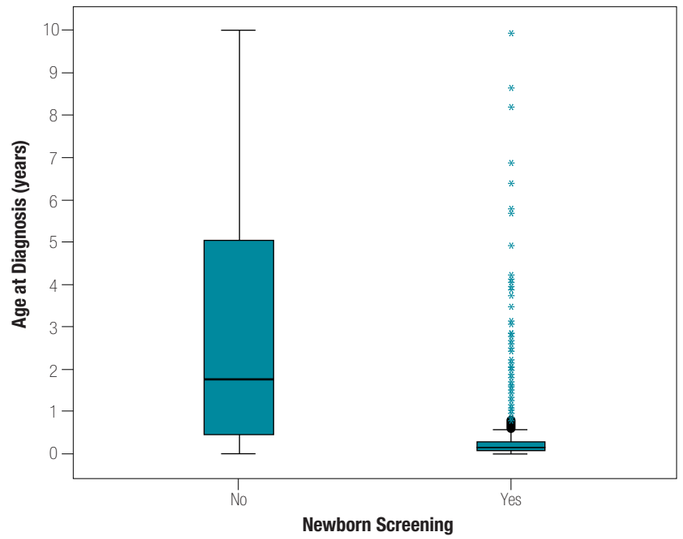
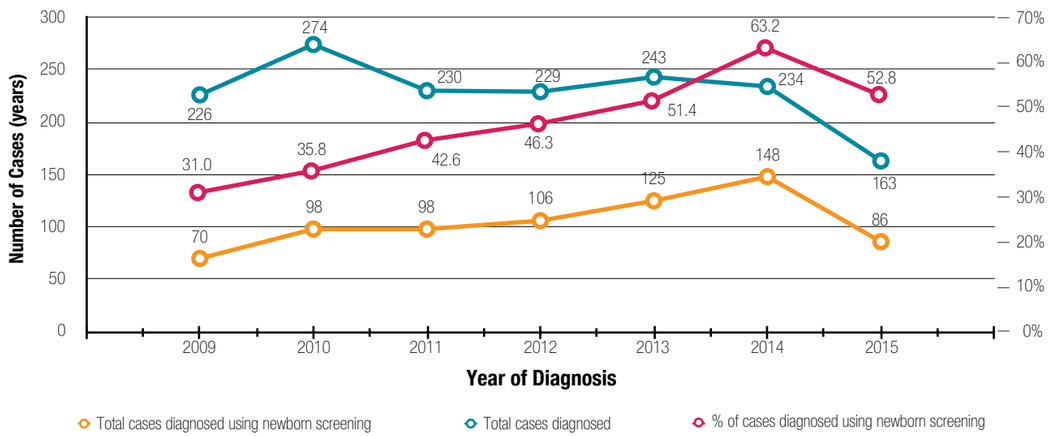


Figure 10

Diagnosis by neonatal screening from 2009 to 2015.



From 2009 to 2015, 1,599 cases of cystic fibrosis were diagnosed, of which 731 (45.7%) were diagnosed using neonatal screening. (Figure 10).

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4. GENETIC DATA

The genetic data contained in this report should be interpreted with caution, as there is no uniformity in genetic testing for CF in Brazil. Some Centers conduct only F508del mutation assessment whereas others perform mutation panels or sequencing of the CFTR gene.

Of the 3,857 registered cases, 1,760 (46%) had undergone genotype assessment. However, of these, 282 had no information; they were genotyped as "yes", but the mutation fields were blank.

Table 14

Description of patients according to cystic fibrosis genetic study results.

Genotype performed	n (%)
No	2,046 (53.8%)
Yes	1,760 (46.2%)
Total number of patients	**3,806 (100%)**
No information	*51*

Number of mutations identified	n (%)
None	282 (16.0%)
One	550 (31.3%)
Two	928 (52.7%)
Total patients with genotyping	**1,760 (100%)**

Genotype / Description	n (%)
F508del / DF508del	466 (26.5%)
F508del / Other mutation	320 (18.2%)
F508del / Unidentified	464 (26.4%)
Other mutation / Other mutation	142 (8.1%)
Other mutation / Unidentified	86 (4.9%)
Not identified / Not identified	282 (16.0%)
Total patients with genotyping	**1,760 (100%)**

Figure 11

Distribution of patients according to results of the genetic study (n = 1,760), 2015.

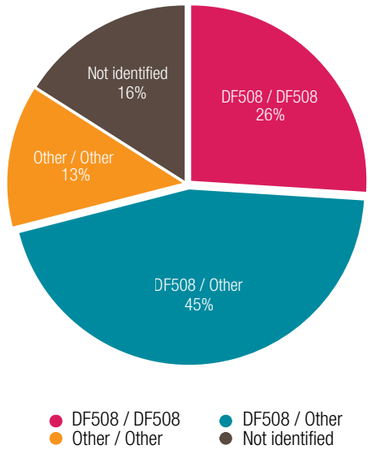

Table 15

Description of a portion of the identified mutations (1,760 patients, 3,520 alleles), 2015.

Mutation	Frequency	% of total alleles
F508del	1718	48.75%
G542X	152	4.32%
R334W	43	1.22%
3120+1G>A	42	1.19%
R1162X	39	1.11%
G85E	37	0.97%
N1303K	33	0.94%
W1282X	16	0.45%
S549R	14	0.40%
R553X	13	0.31%
S4X	12	0.31%
3849+10kbC>T	11	0.31%
2183AA>G	10	0.28%
R1066C	9	0.23%
G551D	8	0.20%
Y1092X	8	0.20%
1812-1G>A	6	0.17%
D1152H	6	0.17%

Mutation	Frequency	% of total alleles
1078delT	5	0.14%
1717-1G>A	5	0.14%
2789+5G>A	5	0.14%
711+1G>T	5	0.14%
I507del	5	0.14%
P205S	4	0.11%
R347P	4	0.09%
A561E	4	0.06%
3272-26A>G	3	0.09%
711+5G>A	3	0.09%
L206W	3	0.09%
R347H	3	0.09%
S549N	3	0.09%
2347delG	2	0.06%
3132delTG	2	0.06%
G1244E	2	0.06%
W1089X	2	0.06%
R117H	2	0.06%

Note: The table includes only mutations found at frequencies higher than one allele, with a record identified in the CFTR2 database, excluding non-pathogenic polymorphisms or dependent on combinations with pathogenic mutations resulting in protein dysfunction.

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FOLLOW-UP DATA

Only the year 2015 was considered (n = 2,961) to describe the follow-up data.

5. ANTHROPOMETRIC DATA

Anthropometric data were obtained on the day of the pulmonary function test or the last visit of the year in situations in which the pulmonary function test was not performed.

In the calculations of percentiles and Z-scores of the anthropometric data, data of the US Centers for Disease Control and Prevention (CDC) were used as reference, available from http://www.cdc.gov/growthcharts/.

Table 16

Description of patients according to anthropometric data.

WEIGHT (kg)	NCHS percentile	Z-score
Mean (standard deviation)	33.01 (29.34)	-0.72 (1.26)
Mediana (p25;p75)	25.00 (7; 54)	-0.67 (-1.51; 0.10)
Total patients	**2,169**	**2,169**

HEIGHT (cm)	NCHS Percentile	Z-score
Mean (standard deviation)	33.31 (28.79)	-0.65 (1.17)
Mediana (p25;p75)	26.00 (8; 54)	-0.65 (-1.41; 0.10)
Total patients	**2,139**	**2,139**

BMI (kg/m2)	Absolute value (patients ≥ 18 years old)	NCHS percentile (patients < 18 years old)
Mean (standard deviation)	21.45 (3.97)	43.47 (31.99)
Mediana (p25;p75)	20.84 (18.75;23.34)	40.00 (13.5; 71)
Total patients	**758**	**1,508**

p25, 25th percentile; p75, 75th percentile.

Analyzing the nutritional parameters by age, one can observe that the percentile values and Z-scores of the anthropometric measures tend to fall over the years in patients under the age of 18 years (Figures 12 and 13). In adult patients, body mass index (BMI) tends to increase with age (Figure 14). This increase in BMI among adults over time may be related to a survival effect, in which pancreatic-sufficient patients tend to have a longer life expectancy and better nutritional status.

Figure 12

Evolution of median percentiles of weight, height, and BMI according to age, among patients 2–18 years old, 2015.

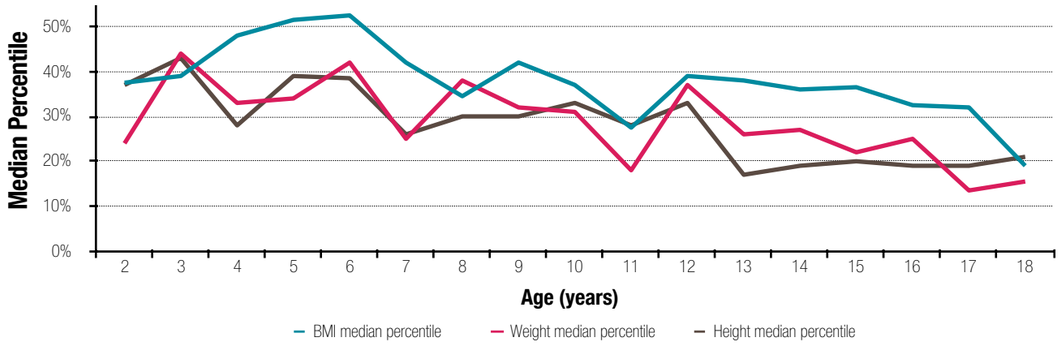


Figure 13

Evolution of Z-scores for weight and height according to age, among patients 2 –18 years old, 2015.

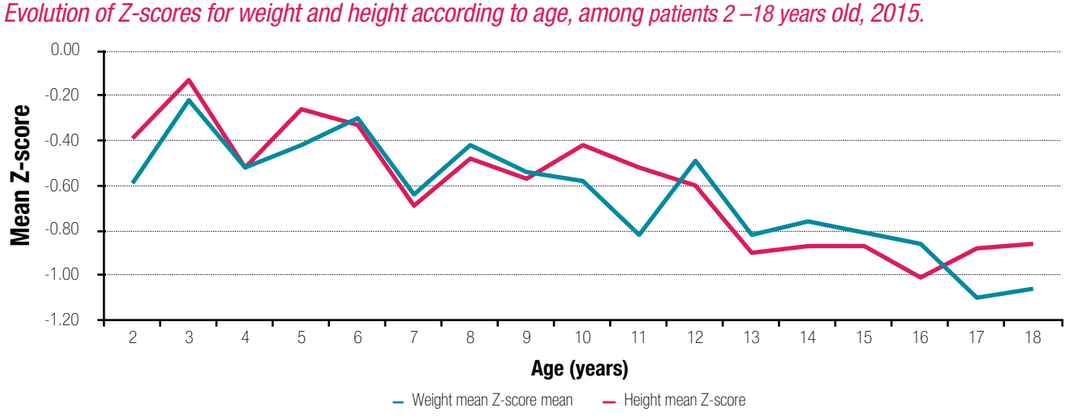
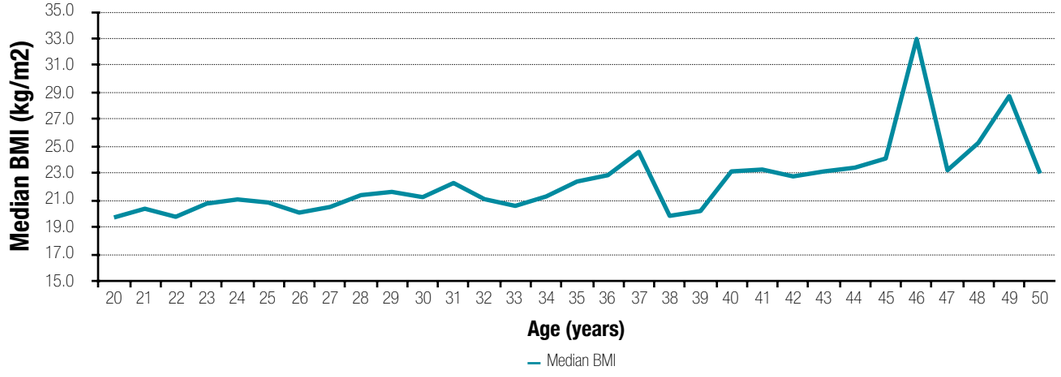


Figure 14

Evolution of BMI according to age, among patients 19–50 years old, 2015.



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6. PULMONARY FUNCTION DATA

Spirometry data were available for 1,512 patients (51.1%). In the case of patients with more than one lung function test in the year, test data with the best pulmonary function values were reported. The predicted lung function values used as reference were from Stanojevic et al., Spirometry Centile Charts for Young Caucasian Children: The Asthma UK Collaborative Initiative. American Journal of Respiratory and Critical Care Medicine 2009;180(6):547-552

Table 17

Description of patients according to pulmonary function data.

Z-score, FVC	
Mean (standard deviation)	-1.59 (2.03)
Median (p25; p75)	-1.40 (-2.88; -0.24)
Total number of patients	**1,461**

Z-score, FEV1	
Mean (standard deviation)	-2.18 (2.17)
Median (p25; p75)	-1.98 (-3.81; -0.61)
Total number of patients	**1,461**

Percentage of predicted FVC	
Mean (standard deviation)	81.48 (23.53)
Median (p25; p75)	83.14 (65.95; 97.20)
Total number of patients	**1,461**

Percentage of predicted FEV 1	
Mean (standard deviation)	72.66 (27.24)
Median (p25; p75)	75.34 (52.07; 92.67)
Total number of patients	**1,461**

FEV1 / FVC	
Mean (standard deviation)	0.76 (0.14)
Median (p25; p75)	0.78 (0.67-0.87)
Total number of patients	**1,507**

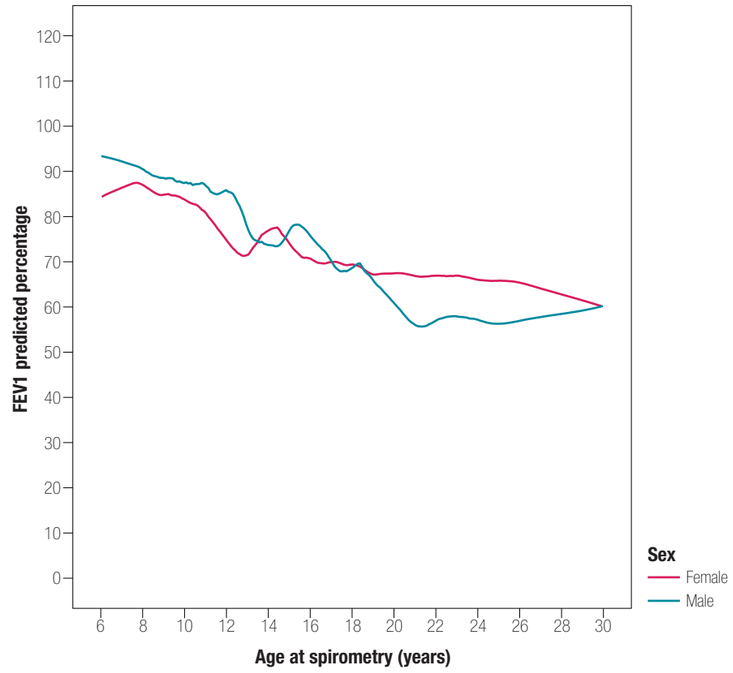
Z-score, FEV 1 / FVC	
Mean (standard deviation)	-1.42 (1.59)
Median (p25; p75)	-1.39 (-2.63; -0.27)
Total number of patients	**1,461**

n = number of patients; p25, 25th percentile; p75, 75th. FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second.

Analyzing the pulmonary function data by age, there is a progressive and marked decrease in the values of FEV1 according to age.

Figure 15

Percentage of predicted FEV1 according to age, among patients 6–30 years old, 2015.



Note: Correlations: r = –0.274 for females, r = –0.384 for males.

In the age group 6 to 17 years, a significant proportion of patients with established functional alterations is observed (more than 30% of patients with predicted FEV1 less than 70%). However, greater functional loss occurs in adults, in which about 60% of patients have moderate or severe obstruction. There was a significant difference between children/adolescents and adults ($p < 0.001$). From the age of 18 years, there were no significant differences ($p = 0.480$ for the comparison between patients aged up to 30 years and over 30 years).

Table 18

Degree of obstruction according to age group, 2015.

	Age group			
Degree of obstruction	**6–17 years**	**18–30 years**	**> 30 years**	**Total**
Normal (predicted FEV1 % ≥ 90%)	334 (37.7%)	55 (14.6%)	29 (14.7%)	418 (28.6%)
Normal/mild (predicted FEV1 % ≥ 70% and < 90%)	277 (31.2%)	100 (26.5%)	43 (21.8%)	420 (28.7%)
Moderate (predicted FEV1 % ≥ 40% and < 70%)	187 (21.1%)	136 (36.1%)	70 (35.5%)	393 (26.9%)
Severe (predicted FEV1 % < 40%)	89 (10.0%)	86 (22.8%)	55 (27.9%)	230 (15.7%)
Total number of patients	**887 (100%)**	**377 (100%)**	**197 (100%)**	**1,461 (100%)**

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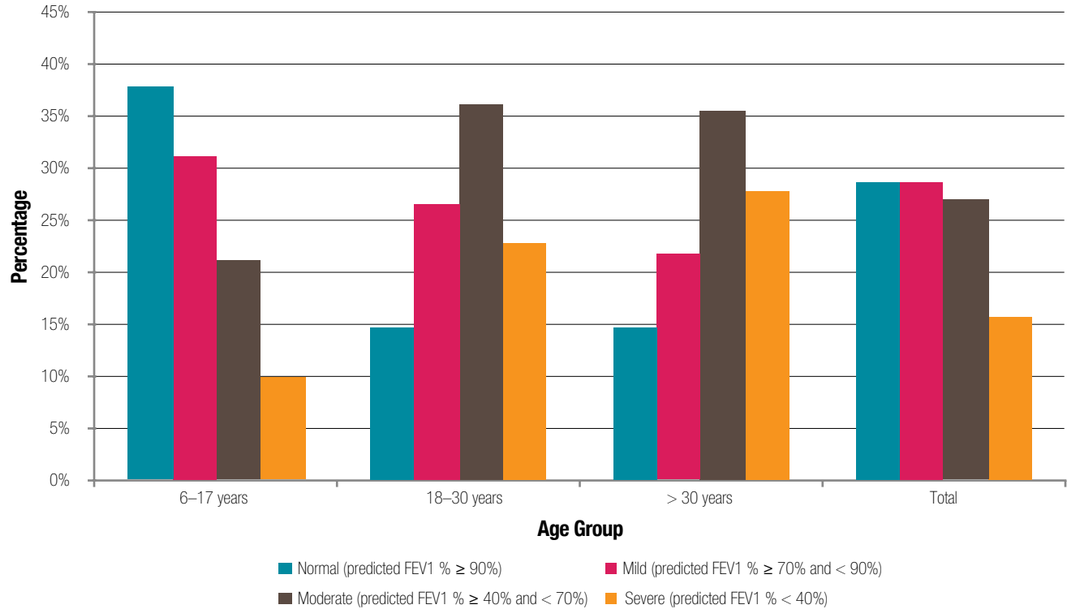
Figure 16

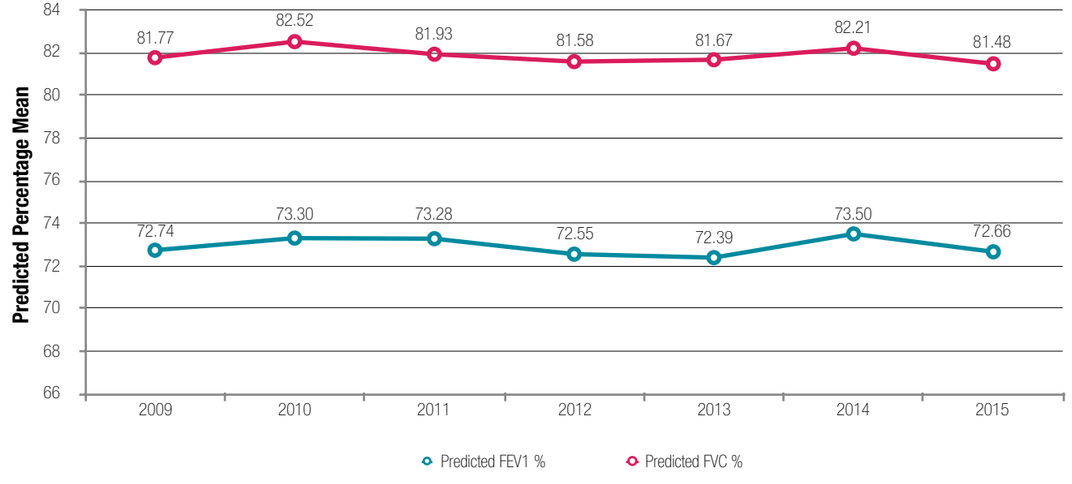
Distribution of patients according to degree of obstruction and age group, 2015.



Analyzing the evolution of pulmonary function over the years (2009 to 2015), we observed that mean values of FEV 1 and FVC of the studied population did not increase during the study period (Figure 17).

Figure 17

Variations in the percentages of FVC and FEV1 predicted values from 2009 to 2015.



The following graphs (Figures 18 and 19) show the relationship between nutritional indexes and lung function, both in the pediatric age group (BMI percentile × FEV1 values) and in adults (BMI value × FEV1).

Figure 18

FEV1 predicted percentage according to BMI percentile among patients aged 6–18 years, 2015.

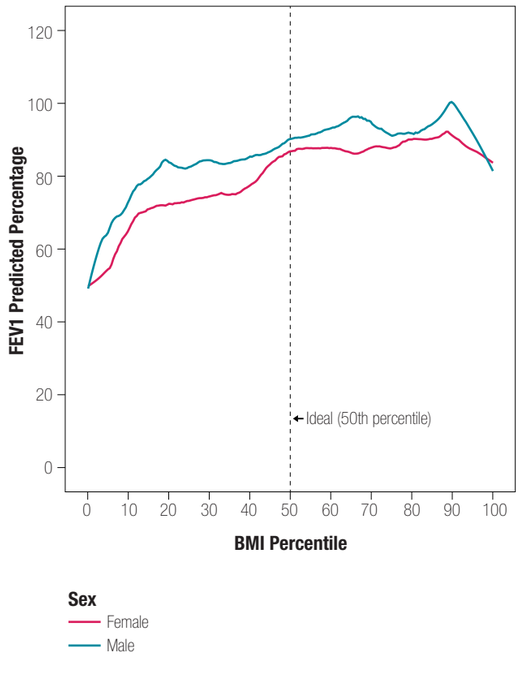
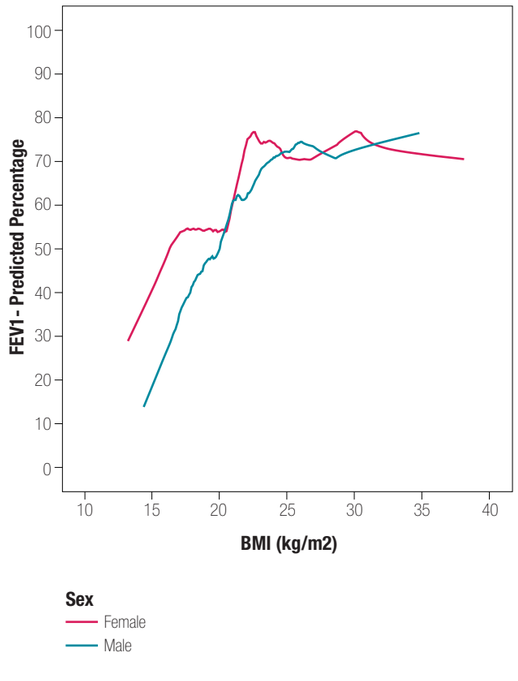


Figure 19

FEV1 predicted percentage according to BMI, in patients aged 20–40 years old, 2015.



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7. MICROBIOLOGICAL DATA

Identification of the pathogen in question is performed at least once per year. As there is no standardization regarding the techniques of processing and culture of respiratory tract samples from patients with CF in Brazil, these data should be interpreted with caution.

Table 19

Description of microorganisms identified, 2015.

Microorganisms identified	n	%
Oxacillin-sensitive *Staphylococcus aureus*	1,723	58.2%
Pseudomonas aeruginosa	1,265	42.7%
Non-mucoid *Pseudomonas aeruginosa*	885	29.9%
Mucoid *Pseudomonas aeruginosa*	611	20.6%
Burkholderia cepacia complex	228	7.7%
Haemophilus influenzae	221	7.5%
Oxacillin-resistant *Staphylococcus aureus*	222	7.5%
Stenotrophomonas maltophilia	151	5.1%
Candida sp.	149	5.0%
Klebsiella pneumoniae	125	4.2%
Aspergillus fumigatus	86	2.9%
Achromobacter sp.	71	2.4%
Serratia sp.	65	2.2%
Other *Pseudomonas*	56	1.9%
Escherichia coli	53	1.8%
Nontuberculous *mycobacteria*	13	0.4%
Mycobacterium tuberculosis	7	0.2%
Total number of patients	**2,961**	**100%**

Table 20

Microorganisms identified according to age group.

	Microorganisms identified						
Age (years)	*Oxacillin-sensitive S. aureus*	*Pseudomonas aeruginosa*	*Haemophilus influenzae*	*Burkholderia cepacia complex*	*Oxacillin-resistant S. aureus*	*Stenotrophomonas maltophilia*	n*
< 5	60.1%	37.1%	*10.4%*	*4.7%*	*5.9%*	*6.2%*	*642*
> 5 - 10	67.6%	35.3%	*10.8%*	*7.5%*	*7.2%*	*5.1%*	*641*
> 10 - 15	65.9%	44.8%	*8.4%*	*11.0%*	*10.2%*	*6.4%*	*581*
> 15 - 20	60.9%	46.5%	*4.9%*	*7.9%*	*6.7%*	*6.1%*	*445*
> 20 - 25	44.7%	47.8%	*3.5%*	*8.8%*	*7.0%*	*0.9%*	*228*
> 25 - 30	44.3%	60.0%	*2.1%*	*10.7%*	*13.6%*	*2.9%*	*140*
> 30 - 35	45.5%	58.4%	*3.9%*	*10.4%*	*9.1%*	*3.9%*	*77*
> 35	26.0%	46.9%	-	*4.2%*	*3.1%*	*2.6%*	*192*

** Total: 2,946 patients (15 patients with no information on age)*

Figure 20

Prevalence of pathogens identified, according to age group, 2015.

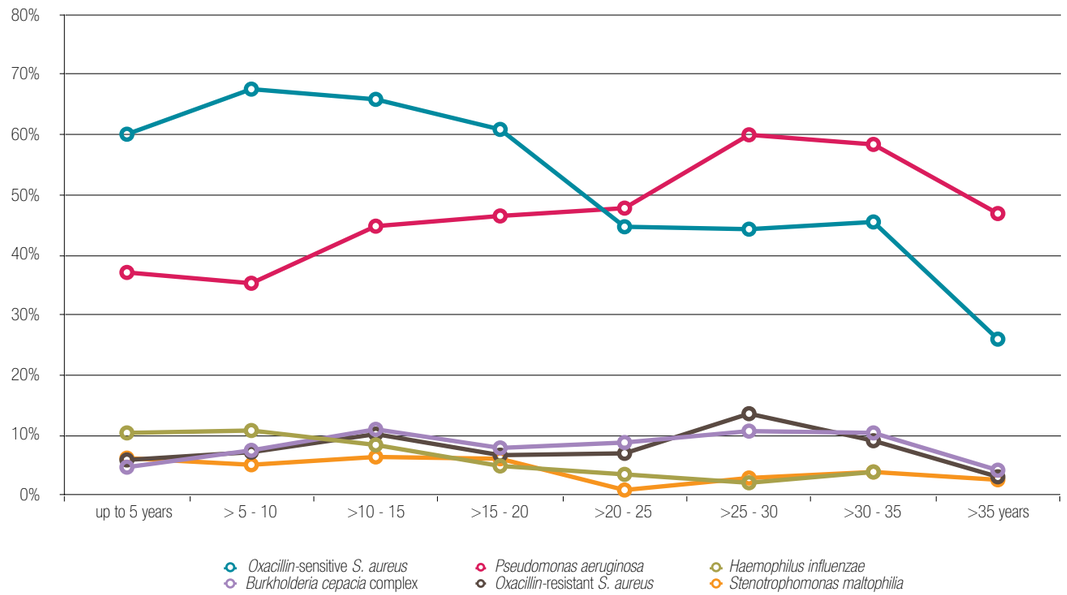
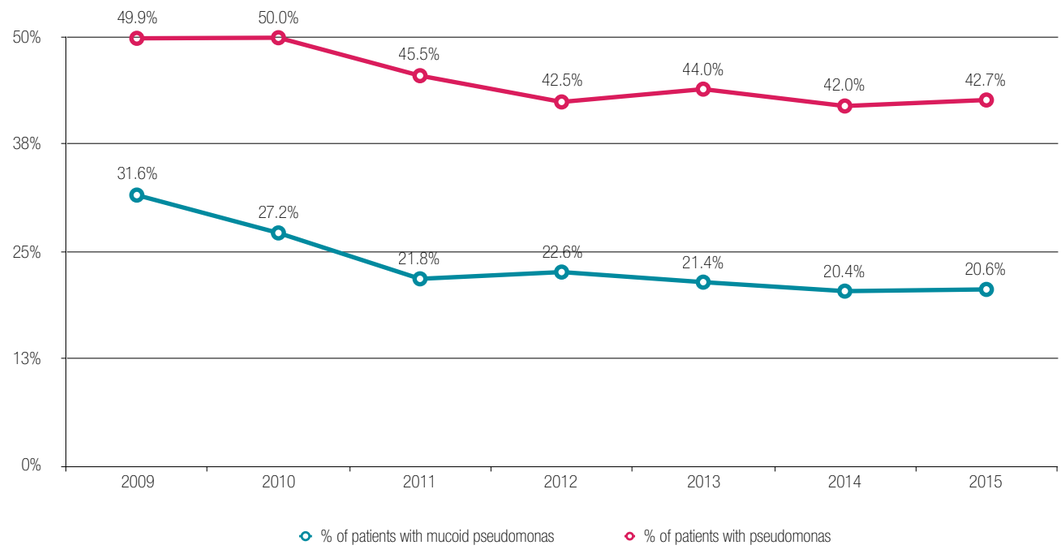


Figure 21

Percentage of patients with Pseudomonas aeruginosa, from 2009 to 2015.



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8. CLINICAL TREATMENT DATA

In 2015, 12,708 consultations were carried out, with a median value of 4 consultations per patient.

Figure 22

Distribution of patients according to the number of consultations in 2015.

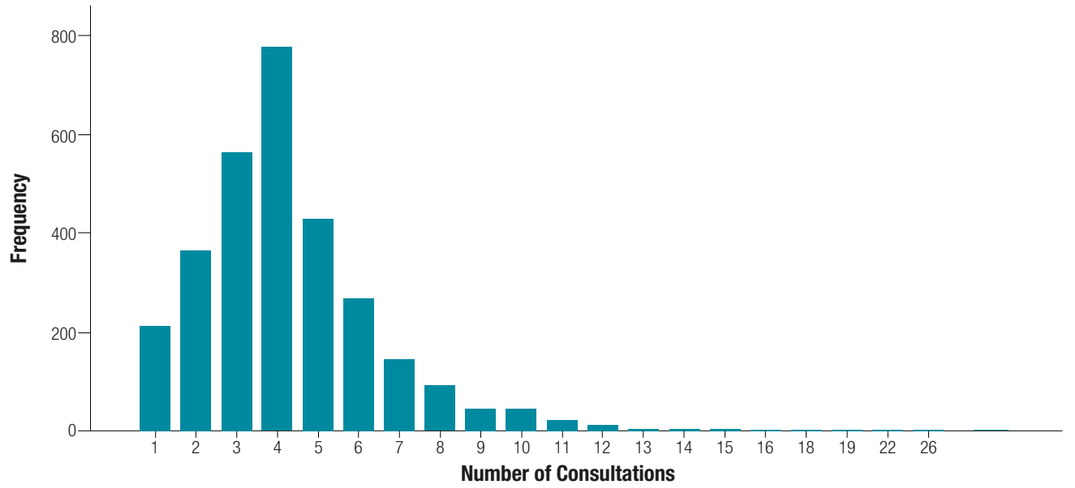

Table 21

Patient deaths, 2015.

Death	n (%)
No	2,905 (98.0%)
Yes	56 (2.0%)
Total number of patients	**2,961 (100%)**

Age at death (years)	
Mean (standard deviation)	20.20 (10.57)
Median (p25; p75)	18.38 (13.98; 27.92)
Minimum–maximum	0.29; 43.78

Note: in this report and in previous reports, the percentage of deaths was calculated by considering only the total number of patients followed up in the reference year. This estimate does not represent the patients' survival. It should be emphasized that the most adequate analysis of deaths is the one that uses median survival curves.

Cause of death	n
Respiratory cause	43
Complications of lung transplantation	5
Dehydration	0
Gastrointestinal-hepatic cause	4
Cardiovascular cause	0
Accidental or violent	1
Other causes	2
Unknown	1
Total	**56**

Table 22

Total Shwachman–Kulczycki score according to age group, among patients < 18 years old.

	Age group				
Total score	**< 5 years**	**> 5 - 10 years**	**>10 - 15 years**	**>15 - 18 years**	**Total**
Severe (≤ 40	-	5 (1.0%)	21 (4.6%)	10 (4.3%)	36 (2.2%)
Moderate (41 to 55)	9 (1.9%)	26 (5.2%)	41 (9.1%)	38 (16.2%)	114 (6.9%)
Mild (56 to 70)	43 (9.1%)	80 (15.9%)	89 (19.7%)	64 (27.2%)	276 (16.6%)
Good (71 to 85)	149 (31.4%)	176 (35.1%)	187 (41.4%)	80 (34.0%)	592 (35.6%)
Excellent (86–100)	273 (57.6%)	215 (42.8%)	114 (25.2%)	43 (18.3%)	645 (38.8%)
Total number of patients	**474 (100%)**	**502 (100%)**	**452 (100%)**	**235 (100%)**	**1.663 (100%)**

Figure 23

95% confidence intervals (CI) for mean Shwachman–Kulczycki scores according to age group (< 18 years age).

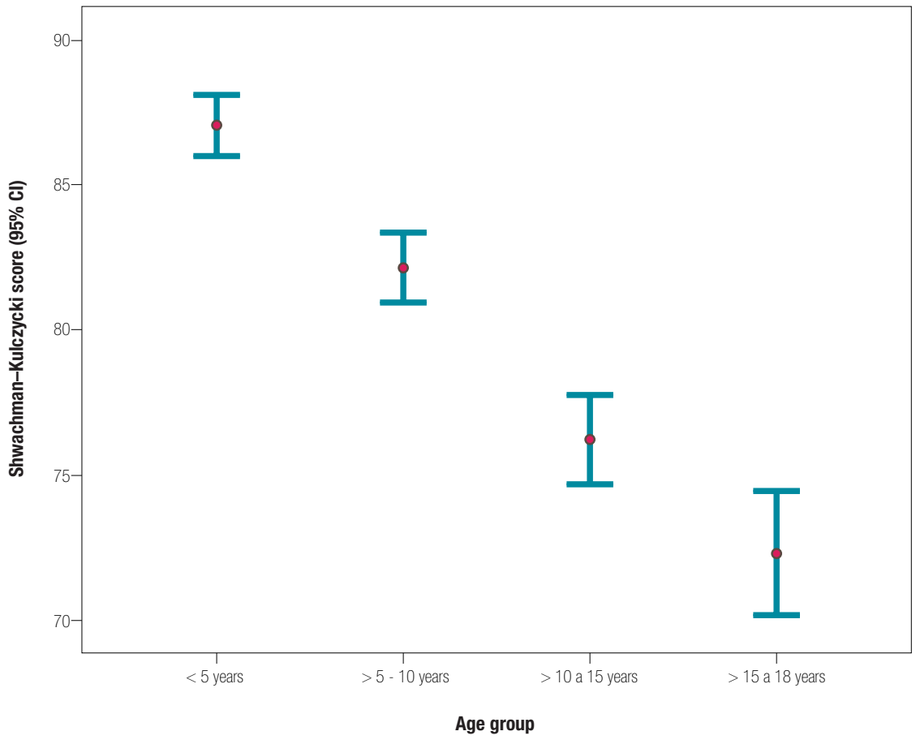

Table 23

Complications/comorbidities in the previous year.

Complications/comorbidities in the previous year	n (%)
Asthma	370 (12.5%)
Evidence of hepatic impairment	270 (9.1%)
Gastroesophageal reflux disease	181 (6.1%)
Diabetes	121 (4.1%)
Nasal polyposis	139 (4.7%)
Osteopenia / osteoporosis	104 (3.5%)
Hemoptysis	157 (5.3%)
Chronic atelectasis	66 (2.2%)
Pulmonary hypertension / cor pulmonale	30 (1.0%)
Cirrhosis with portal hypertension	19 (0.6%)
Cholelithiasis	45 (1.5%)
Allergic bronchopulmonary aspergillosis	26 (0.9%)
Distal intestinal obstruction syndrome	28 (0.9%)
Pancreatitis	15 (0.5%)
Pneumothorax	19 (0.6%)
Hematemesis	5 (0.2%)
Intestinal invagination	3 (0.1%)
Colonic stenosis	1 (0.03%)
Total number of patients	**2,961 (100%)**

n = number of patients

Table 24

Transplants received by CF patients, 2015.

Transplants	n (%)
Pulmonary transplantation	35 (1.2%)
Donor corpse	*33*
Donation intervivos	*2*
Liver transplantation	1 (0.03%)
Total number of patients	**2,961 (100%)**

Table 25

Oxygen therapy among CF patients, 2015.

Oxygen therapy	n (%)
No	2,832 (95.6%)
Yes	129 (4.4%)
Continuous	78 (2.6%)
Nocturnal	51 (1.7%)
Total number of patients	**2,961 (100%)**

Table 26

Insulin use among CF patients, 2015.

Use of Insulin	n (%)
No	2,831 (95.6%)
Yes	130 (4.4%)
Total number of patients	**2,961 (100%)**

Table 27

Inhaled therapies use among CF patients, 2015.

Bronchodilators	n (%)
Short-acting beta2 agonist	1,125 (38.0%)
Long-acting beta2-agonist	665 (22.5%)
Anticholinergic 129 (4.4%)	129 (4.4%)

Antibiotics	n (%)
Inhaled tobramycin 300 mg	1,095 (37.0%)
Colimycin	517 (17.5%)
Amikacin	50 (1.7%)
Injectable tobramycin	21 (0.7%)
Gentamicin	20 (0.7%)
Vancomycin	7 (0.2%)
Aztreonam	5 (0.2%)
Others	44 (1.5%)

Mucolytics	n (%)
Alfadornase	2,132 (72.0%)
N-Acetylcysteine	97 (3.3%)

Saline solutions	n (%)
0.9% saline solution	470 (15.9%)
3% hypertonic saline solution	174 (5.9%)
5% hypertonic saline solution	163 (5.5%)
7% hypertonic saline solution	566 (19.1%)
Total number of patients	**2,961 (100%)**

n = number of patients

Table 28

Oral medications used among CF patients, 2015.

	n (%)
Pancreatic enzymes	**2,357 (79.6%)**
< 5,000 U/kg/day	783 (33.2%)
5,000-10,000 U/kg/day	1371 (58.1%)
> 10,000 U/kg/day	182 (7.7%)
Unknown	21 (0.9%)
Nutrition supplements	**1,901 (64.2%)**
Oral	1,691 (89.0%)
Gastrostomy	75 (3.9%)
Probe	18 (0.9%)
Unknown	117 (6.2%)
Azithromycin	960 (32.4%)
Proton pump inhibitors	609 (20.5%)
Ursodeoxycholic acid	504 (17%)
Corticosteroids	184 (6.2%)
H2 blockers	176 (5.9%)
Ibuprofen or other NSAIDs (arthropathy)	11 (0.4%)
Ibuprofen (pulmonary disease	6 (0.2%)
Total number of patients	**2,961 (100%)**

*n = number of patients. *Percentages for enzyme doses or type of supplement were calculated based on subgroup(s) that used enzymes or supplements.*

Table 29

Pseudomonas aeruginosa eradication treatment.

P. aeruginosa eradication treatment	n (%)
Yes	717 (24.2%)
No	1,409 (47.6%)
Unknown	835 (28.2%)
Total number of patients	**2,961 (100%)**

Table 30

Intravenous treatments and hospitalizations.

Intravenous treatments	n (%)
Home care*	118 (16.4%)
Hospital care*	566 (78.8%)
Home and hospital care*	34 (4.7%)
Total	718 (24.2%)
Total number of patients	**2,961 (100%)**

**Percentage of total number of patients in treatment.*

Cycles/year	
Mean (standard deviation	2.05 (4.36)
Median (p25; p75)	1 (1; 2)
Total number of patients	**704**

Days/year	
Mean (standard deviation	26.29 (22.85)
Median (p25; p75)	18 (14; 30)
Total number of patients	**685**

Catheter implanted	n (%)
No	2,912 (98.3%)
Yes	49 (1.7%)
Total number of patients	**2,961 (100%)**

Table 31

Intravenous antibiotics and days of hospitalization per year, according to age group.

	Age group					
Days/year	**< 5 years**	**> 5 - 10**	**>10 - 15**	**>15 - 20**	**> 20 years**	**Total**
Mean (SD)	20.87 (16.2)	20.3 (14.2)	30.0 (28.5)	30.6 (25.2)	28.0 (23.0)	*26.3 (22.9)*
median (p25; p75)	14 (14; 27)	14 (14; 21)	19.5 (14; 33)	21.0 (14; 35)	20.0 (14; 30)	*18 (14; 30)*
Total number of patients	**143**	**93**	**142**	**127**	**177**	**682**

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Table 32

Intravenous antibiotics used among CF patients, 2015.

Drugs used	n	(%)
Ceftazidime	422	14.3%
Amikacin	419	14.2%
Oxacillin	217	7.3%
Imipenem / meropenem	181	6.1%
Ciprofloxacin	157	5.3%
Sulfamethoxazole trimethoprim	132	4.5%
Vancomycin	98	3.3%
Tobramycin	86	2.9%
Cefepima	77	2.6%
Gentamicin	56	1.9%
Piperacillin / tazobactam	52	1.8%
Linezolid	22	0.7%
Colimycin	21	0.7%
Ticarcillin / Piperacillin	14	0.5%
Aztreonam	12	0.4%
Cefuroxime	8	0.3%
Chloramphenicol	1	0.03%
Other	44	1.5%
Total number of patients	**2,961**	**100%**

n = number of patients.

Table 33

Specific data of the adult population.

	Sex		
	Male	**Female**	**Total**
Azoospermia/hypospermia*	46 (11.6%)	-	46
Pregnancy	-	15 (3.9%)	15
Oral or injectable contraceptive	-	64 (16.5%)	64
Stable relationship	67 (16.8%)	91 (23.4%)	158 (20.1%)
Employed	132 (33.2%)	102 (26.2%)	234 (29.7%)
Total patients aged ≥ 18 years	**398**	**389**	**787**

** Patients who have undergone infertility testing.*

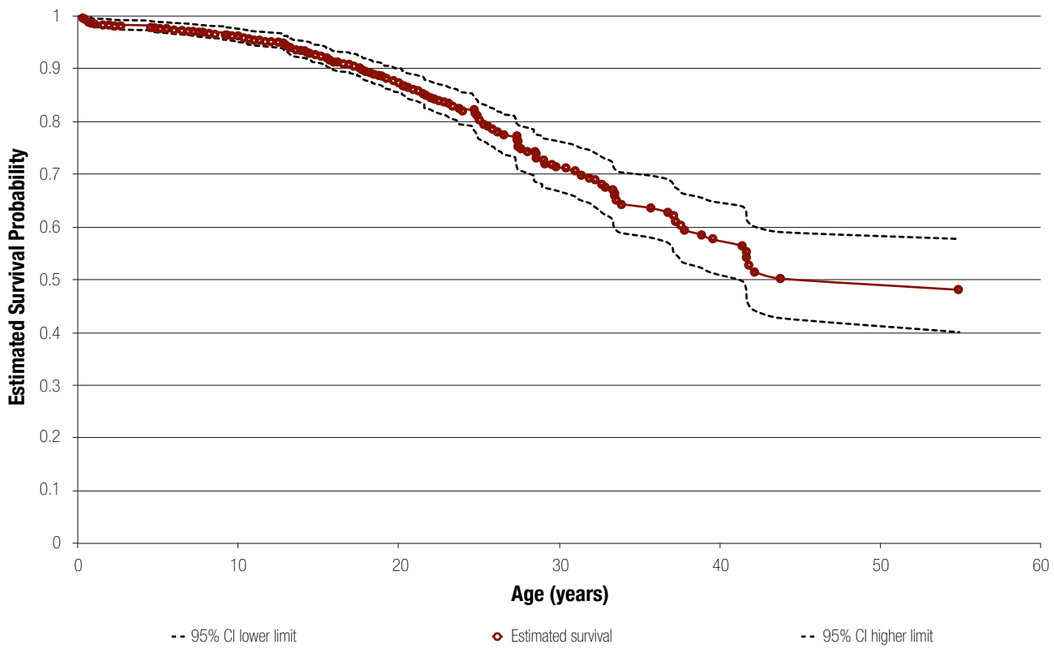
9. SURVIVAL

There were 190 deaths (5%) throughout the series; however, 7 of them were due to other causes (femoral osteosarcoma, piercing septicemia, accidental death, unknown cause, acute myocardial infarction, car accident, and violent death). These cases were excluded from the survival analysis. Using the same methodology adopted by the American organization, the Cystic Fibrosis Foundation (CFF), the survival analysis included 179 deaths, excluding the above 7 deaths from other causes and 4 deaths that occurred in 2016.

Figure 26 shows the survival curve, considering all patients observed in this period. The median survival was 43.8 years, with a lower limit at 41.4 years, the age at which the confidence interval (CI) crosses the 50% probability of survival line.

Figure 24

Survival curve by the Cox method for the total number of patients during 2009 to 2015.



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Centers that contributed to this report by providing patient follow-up data in 2015
(in alphabetical order by state)

Center	City	State	Director
Hospital Universitario da Univ Federal de Sergipe	Aracaju	SE	Daniela Gois Meneses
Hospital Especializado Otavio Mangabeira	Salvador	BA	Maria Angélica Santana
Hospital Universitário Prof. Edgar Santos	Salvador	BA	Edna Lúcia Santos de Souza
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Santa Casa de Porto Alegre	Porto Alegre	RS	Gilberto Bueno Fischer
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