2013 Brazilian Cystic Fibrosis Patient Registry

GRUPO BRASILEIRO DE ESTUDOS DE FIBROSE CÍSTICA

BRAZILIAN CYSTIC FIBROSIS PATIENT REGISTRY (REBRAFC) 2013 ANNUAL REPORT

To all those interested in cystic fibrosis,

The Brazilian Cystic Fibrosis Registry (REBRAFC) contains demographic, diagnostic, and treatment data for patients with cystic fibrosis (CF) in Brazil, with the aim of increasing the attention given to this disease in our country. There is certainly still much to do for these patients. However, regional differences reflect the Brazilian public health system (SUS) model, which mandates universal access to health care, but has a decentralized structure that hinders access to diagnostic and therapeutic resources in various regions of Brazil. At a time of severe economic crisis, there is cost-cutting and decreased investment in research and health care in many regions of the country, which makes the situation seem even bleaker. On the other hand, a global effort provides support to Brazil in the form of new drugs and therapies, such as the work on the underlying defect of the CFTR protein, which gives hope to patients, caregivers, and health professionals involved in CF care.

The professional healthcare community that provides CF services, through participation in the REBRAFC initiative, expresses its involvement by reporting the realities of health care for patients, with the hope that this initiative may contribute to changes in official agendas, and result in increased assistance for individuals with CF in Brazil.

About Cystic Fibrosis and the GBEFC:

Cystic fibrosis (CF) is an inherited, autosomal recessive, multisystem disorder that affects the respiratory, gastrointestinal, hepatic, and genitourinary systems. It is a complex disease that is still little known in Brazil, although some health centers and professionals are dedicated to CF study, and have provided care for patients for some years. The treatment is also complex, and involves high cost drugs. Some of these are funded by the Ministry of Health and other state health agencies, but access to the drugs is not uniform across the country.

The Brazilian Cystic Fibrosis Study Group (GBEFC) is a non-profit organization established on November 5, 2003, and is comprised of locally-employed healthcare professionals. GBEFC activities include dissemination of research results, training of personnel, supporting the implementation of CF treatment centers, organizing conferences about the disease in Brazil (5 Brazilian conferences on CF have already been conducted), communicating with the Ministry of Health in order to establish national guidelines for CF care assistance, and implementation of neonatal screening in all Brazilian states.

The GBEFC maintains a website (www.gbefc.org.br) that provides information on cystic fibrosis; current and previous reports (2009, 2010, 2011, and 2012) are available for free download from the website in Portuguese and English language versions.

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2013 Brazilian Cystic Fibrosis Patient Registry

REBRAFC Highlights in 2013:

A total of 2,924 registered patients. Of these, 2,743 (93.8%) had at least some follow-up data (spirometry and/or anthropometry).

Average age of patients was 13.8 years.

Less than 50% of patients had results of genetic tests.

Only about 25% of patients were 18 years or older.

There were 158 newly diagnosed cases, and neonatal screening was responsible for 48% of the new cases in Brazil. The median age at diagnosis was 1.47 years.

Patients with CF were seen in 9,872 outpatient visits and were hospitalized for 13,256 days in 2013.

81% of CF patients in Brazil used pancreatic enzymes, but only 63% used nutritional supplements.

Thirty patients died in 2013, and the average age at death was 19 years.

Of the patients who had genetic testing, nearly one-quarter were homozygous for the DF508 mutation (Phe508del).

37% of patients aged up to 5 years old had *P. aeruginosa* in their respiratory secretion samples; this proportion reached 63% of patients aged 25 to 35 years.

Nearly one-third of the patients between 6 and 17 years old already had moderate or severe changes in pulmonary function; only a third of young adults (18 to 30 years old) had preserved pulmonary function.

The proportion of patients with strains with *P. aeruginosa* identified in their respiratory secretion samples was 21% (in 2009 this value corresponded to 31%).

Many Brazilian patients with CF have inadequate nutritional status (BMI below the 50th percentile), a proportion that increases in adolescence.

1. INTRODUCTION

This report describes data from the Brazilian Cystic Fibrosis Patient Registry, and comprises demographic, diagnostic, and treatment data for patients with cystic fibrosis in Brazil. In contrast with previous years, the 2013 report contains more comparative graphs in order to show progress over the years. By the time the data were extracted for analysis (December 29, 2014), a total of 2,924 patients had been registered in the database, with 2,743 (93.8%) patients with some follow-up data, and 2,238 (76,5%)with follow-up (spirometry and/or anthropometry) data from the year 2013. The number of registrations and follow-up cases has increased annually as shown in Figure 1.

Figure 1

Increase in registrations and follow-ups between 2009 and 2013.

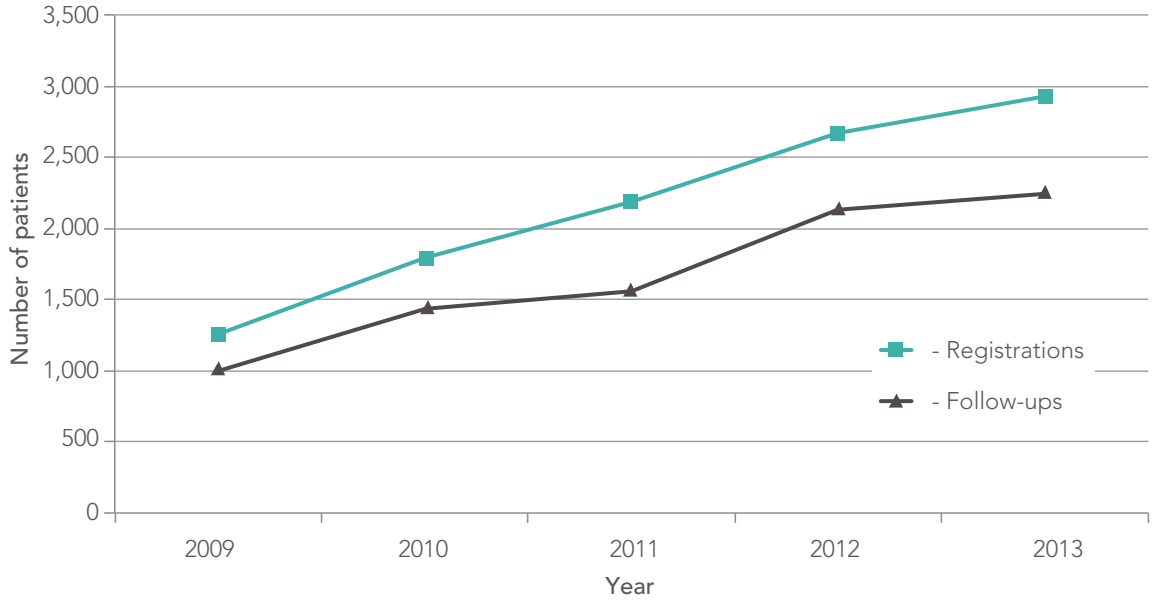


Table 1

Distribution of patients by time of follow-up.

Follow-up years	N	%	% Totals
5 years	513	17.5	17.5
4 years	565	19.3	36.8
3 years	566	19.3	56.1
2 years	620	21.2	77.3
1 year	479	16.4	93.7
No follow-up	181	6.2	100
Total	**2,924**	**100**	

n = number of patients.

Table 1 shows that more than half of patients have at least three years of follow-up.

In the description of demographic and diagnostic data, all patients were included (2,924).

To analyze the follow-up data, only 2013 was considered, which corresponded to a total of 2,238 patients

2. DEMOGRAPHIC DATA

Table 2

Distribution of patients by Brazilian state of origin (birthplace).

State of origin	n (%)
São Paulo	884 (30.2%)
Bahia	361 (12.3%)
Rio Grande do Sul	348 (11.9%)
Minas Gerais	286 (9.8%)
Rio de Janeiro	187 (6.4%)
Santa Catarina	164 (5.6%)
Paraná	153 (5.2%)
Espirito Santo	103 (3.5%)
Ceará	87 (3.0%)
Pernambuco	74 (2,.%)
Pará	56 (1.9%)
Distrito Federal	38 (1.3%)
Alagoas	28 (1.0%)
Rio Grande do Norte	24 (0.8%)

State of origin	n (%)
Goiás	22 (0.8%)
Mato Grosso	15 (0.5%)
Mato Grosso do Sul	9 (0.3%)
Tocantins	7 (0.2%)
Amazonas	6 (0.2%)
Piauí	6 (0.2%)
Paraíba	5 (0.2%)
Sergipe	4 (0.1%)
Acre	3 (0.1%)
Rondônia	3 (0.1%)
Maranhão	2 (0.1%)
Roraima	1 (0%)
Not known	48 (1.6%)

Total	**2,924 (100%)**

n = number of patients

Figure 2

Distribution of patients by Brazilian region of origin (birthplace), 2013.

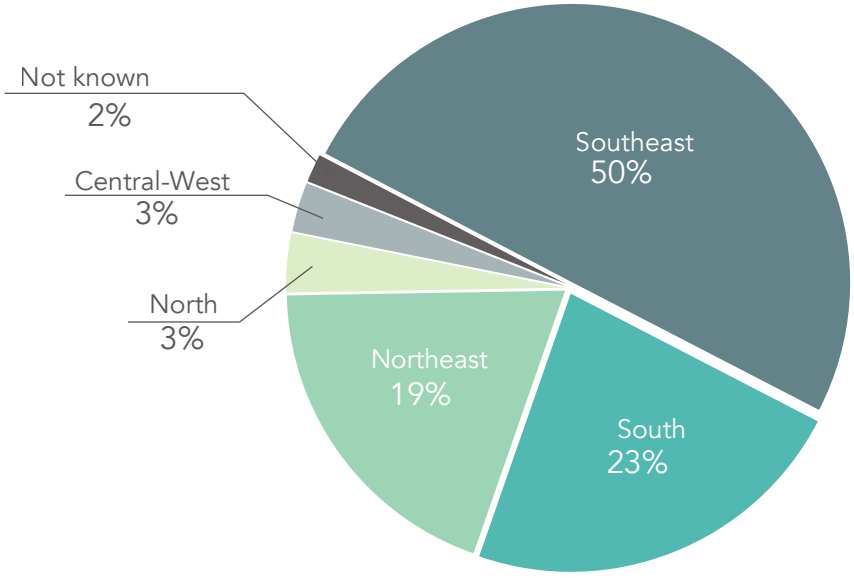


Table 3

Distribution of patients by the state where they are treated, 2013.

State where the centre is located	n (%)
São Paulo	943 (32.3%)
Rio Grande do Sul	378 (12.9%)
Bahia	365 (12.5%)
Minas Gerais	276 (9.4%)
Rio de Janeiro	183 (6.3%)
Paraná	167 (5.7%)
Santa Catarina	145 (5.0%)
Espírito Santo	109 (3.7%)
Ceará	89 (3.0%)

State where the centre is located	n (%)
Pernambuco	71 (2.4%)
Distrito Federal	68 (2.3%)
Pará	55 (1.9%)
Alagoas	28 (1.0%)
Rio Grande do Norte	25 (0.9%)
Goiás	19 (0.6%)
Mato Grosso do Sul	2 (0.1%)
Paraíba	1 (0.04%)

Total of patients	**2,924 (100%)**

n = number of patients

Figure 3

Distribution of patients by the state where they are treated, 2013.

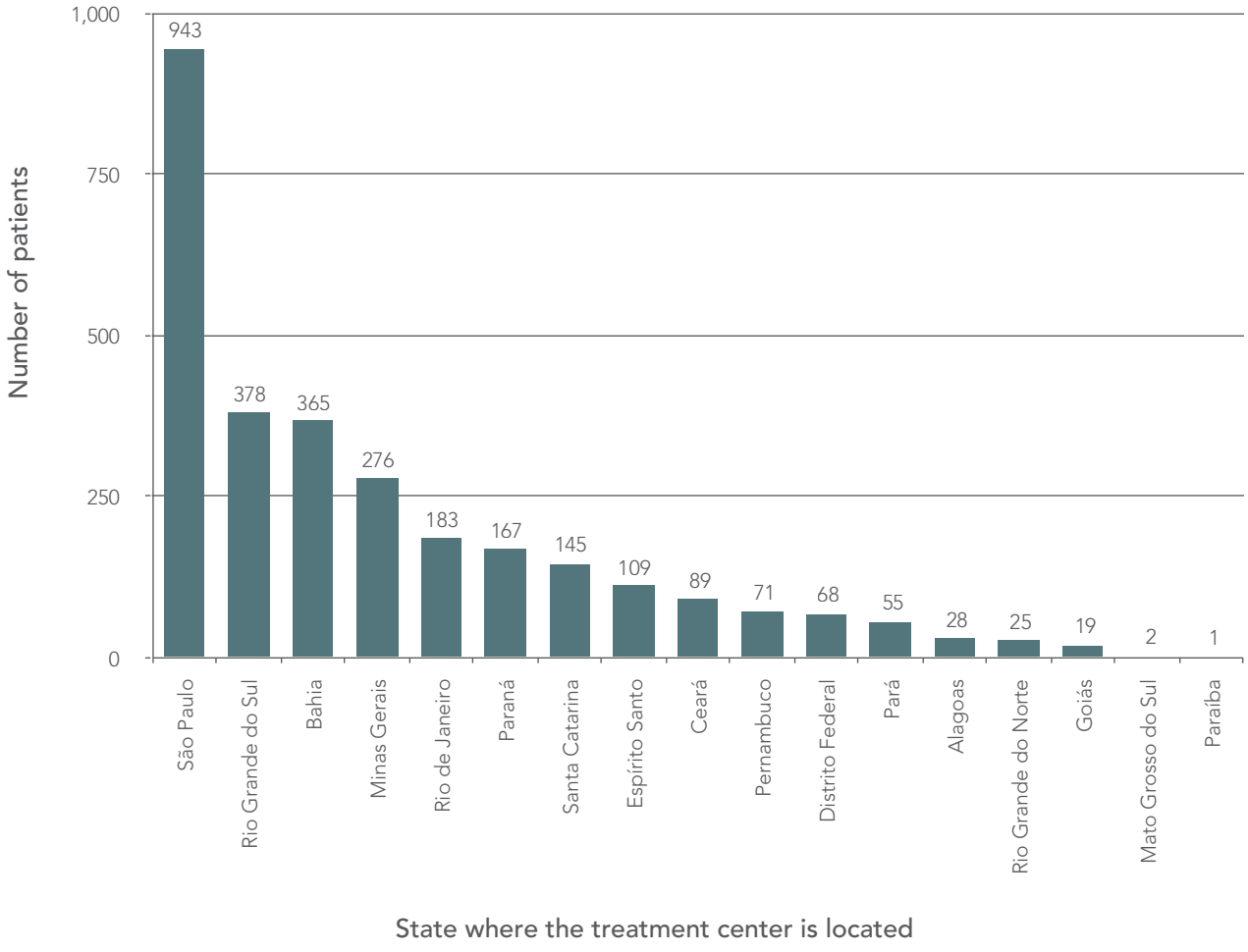


Figure 4

Distribution of patients by the state where they are treated, 2013.

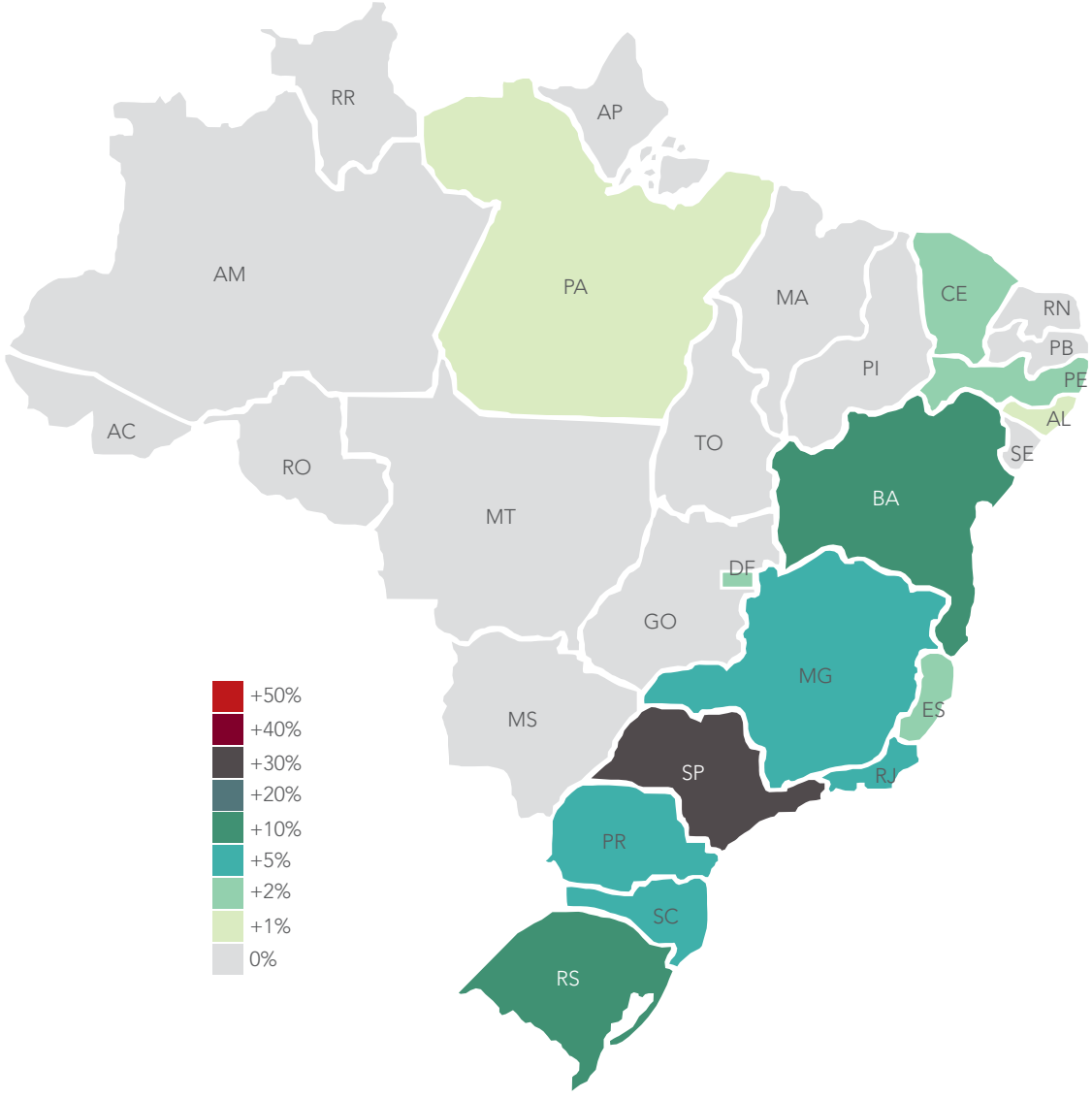


Table 4 shows the number of patients according to the state where they were treated from 2009 to 2013, and considered only those with follow-up during the reference years. In the states of São Paulo, Rio Grande do Sul, Minas Gerais, Pernambuco, Parana and Distrito Federal, there was an increase in the number of patients being followed compared to the previous year. On the other hand, in the states of Bahia, Rio de Janeiro and Alagoas, the number of patients being followed in 2013 was lower than that in 2012.

Table 4

Distribution of patients by state where they are treated, including only follow-up data for 2009 (993 patients), 2010 (1,440 patients), 2011 (1,562 patients), 2012 (2,132 patients), and 2013 (2,238 patients).

	Reference year				
State where patients are treated	**2009 n (%)**	**2010 n (%)**	**2011 n (%)**	**2012 n (%)**	**2013 n (%)**
São Paulo	392 (39.5)	612 (42.5)	570 (36.5)	764 (35.8)	821 (36.7)
Rio Grande do Sul	240 (24.2)	268 (18.6)	285 (18.2)	283 (13.3)	300 (13.4)
Bahia	216 (21.8)	210 (14.6)	202 (12.9)	227 (10.6)	176 (7.9)
Minas Gerais	28 (2.8)	122 (8.5)	167 (10.7)	208 (9.8)	240 (10.7)
Santa Catarina	5 (0.5)	88 (6.1)	106 (6.8)	114 (5.3)	104 (4.6)
Paraná	40 (4)	53 (3.7)	41 (2.6)	115 (5.4)	121 (5.4)
Rio de Janeiro	-	39 (2.7)	18 (1.2)	133 (6.2)	121 (5.4)
Pará	55 (5.5)	-	-	-	-
Ceará	1 (0.1)	3 (0.2)	49 (3.1)	54 (2.5)	59 (2.6)
Alagoas	-	22 (1.5)	23 (1.5)	24 (1.1)	3 (0.1)
Rio Grande do Norte	16 (1.6)	22 (1.5)	23 (1.5)	23 (1.1)	23 (1.0)
Pernambuco	-	1 (0.1)	-	32 (1.5)	54 (2.4)
Espírito Santo	-	-	77 (4.9)	100 (4.7)	102 (4.6)
Distrito Federal	-	-	1 (0.1)	46 (2.2)	63 (2.8)
Goiás	-	-	-	9 (0.4)	6 (0.3)
Mato Grosso do Sul	-	-	-	-	2 (0.1)
Total of patients	**993 (100%)**	**1,440 (100%)**	**1,562 (100%)**	**2,132 (100%)**	**2,238 (100%)**

n = number of patients.

Table 5

Distribution of patients according to gender and ethnicity.

Gender	n (%)
Male	1,545 (52.8%)
Female	1,379 (47.2%)
Total patients	**2,924 (100%)**

Ethnicity	n (%)
Caucasian	2,028 (69.4%)
Mulatto	698 (23.9%)
Black	188 (6.4%)
Asian	7 (0.2%)
Native American	3 (0.1%)
Total patients	**2,924 (100%)**

n = número de pacientes.

Table 6

Distribution of patients according to current age (age at the last spirometry/anthropometry).

Age (in years)	
Mean (standard deviation)	13.87 (11.81)
Median (p25-p75)	11.81 (6.15 – 17.97)
Minimum-Maximum	0.09 – 86.24
Total patients	**2,786**
Patients without spirometry/ anthropometry	138

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

Figure 5

Distribution of patients by gender.

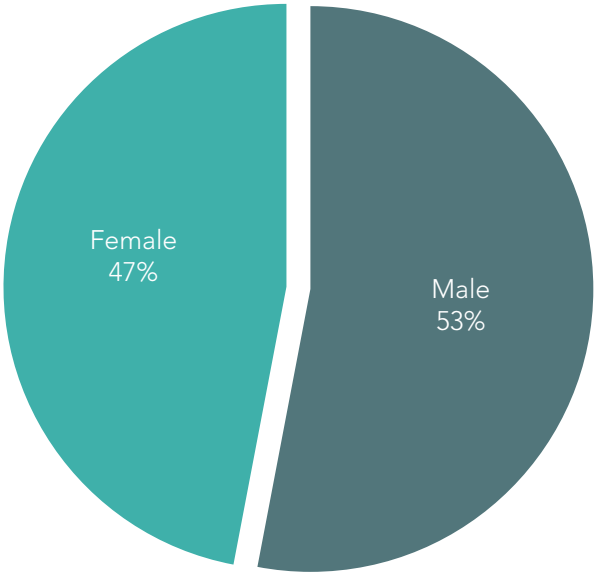


Figure 6

Distribution of patients by ethnic group.

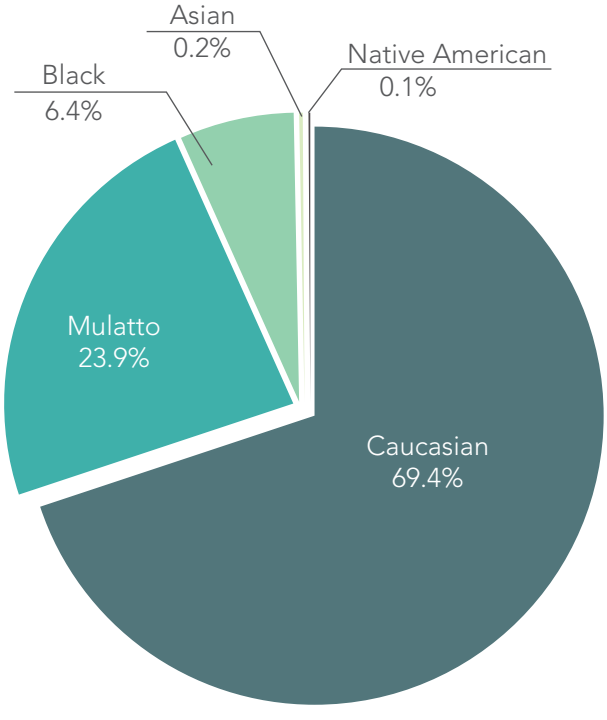


Figure 7

Distribution of patients according to current age (age at the last spirometry/anthropometry).

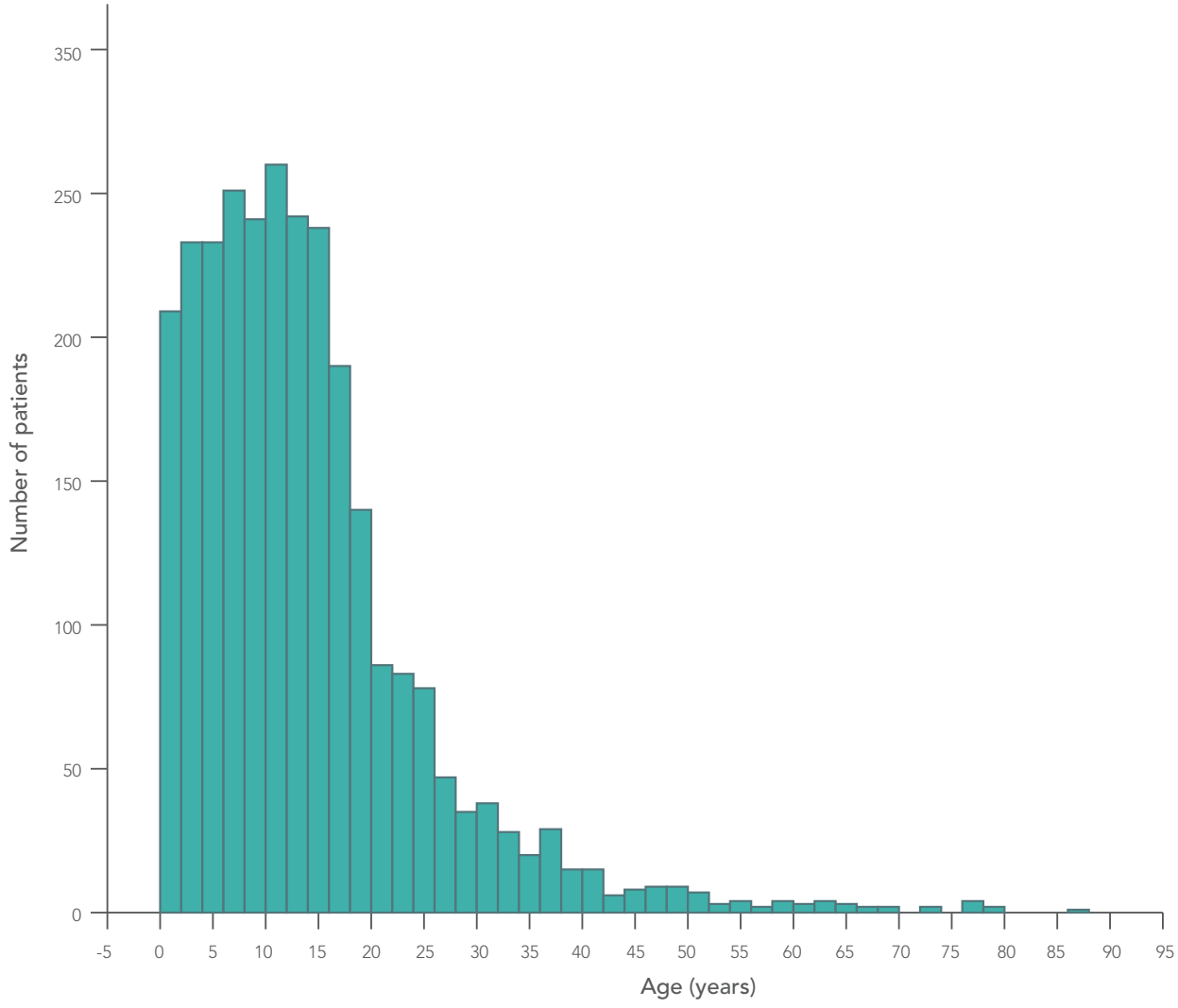


Figure 8

Distribution of patients by age group.

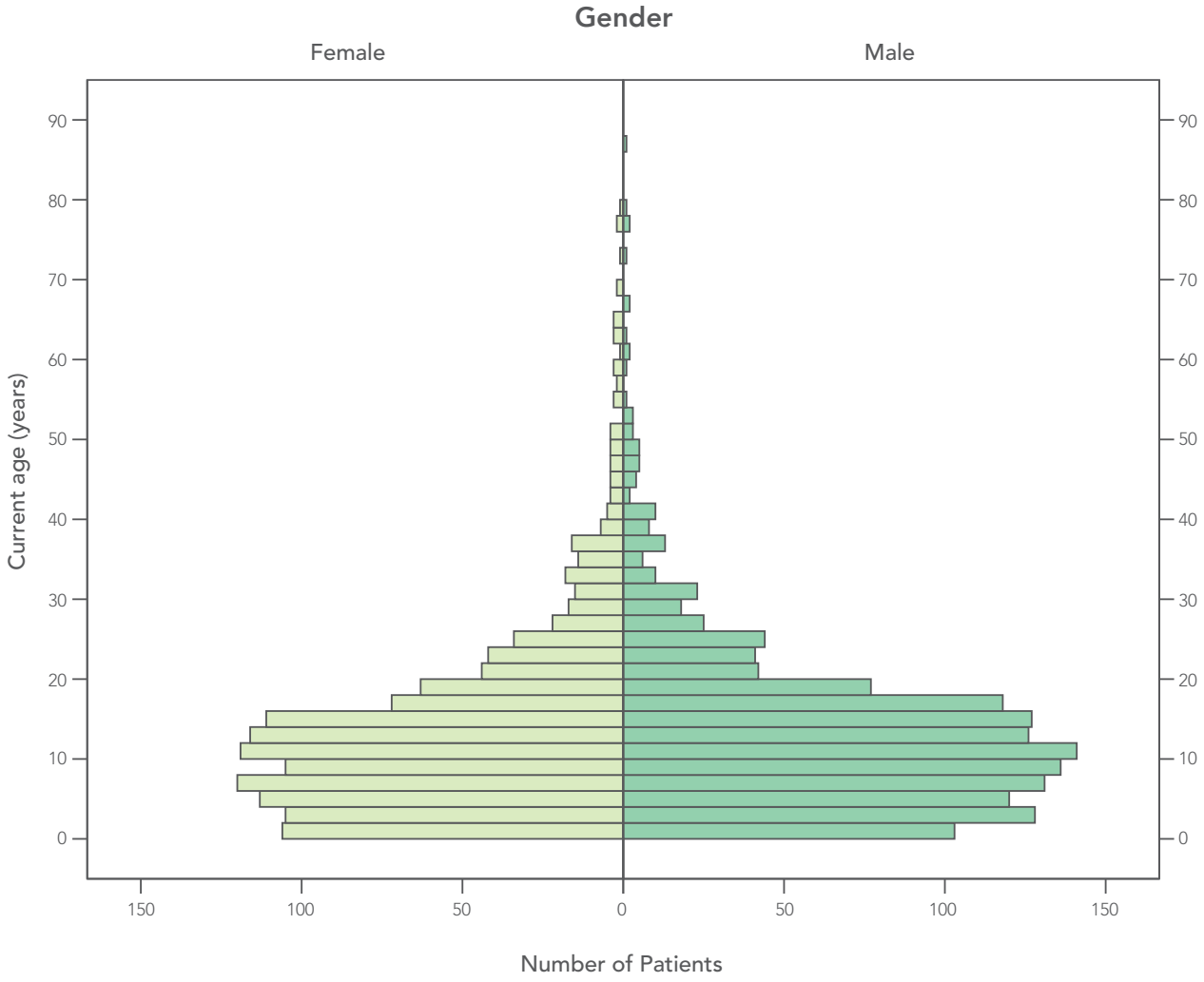


Table 7

Distribution of patients by current age group.

Age group	n (%)
Up to 5 years	566 (19.4%)
> 5 to 10	601 (20.6%)
>10 to 15	621 (21.2%)
>15 to 20	449 (15.4%)
>20 to 25	215 (7.4%)
>25 to 30	114 (3.9%)
>30 to 35	76 (2.6%)
>35 to 40	54 (1.8%)
>40 to 45	26 (0.9%)
>45 to 50	21 (0.7%)
>50 years	43 (1.5%)
Total of patients	**2,786 (100%)**
Patients without data	138

Age group (pediatric-adult)	n (%)
Less than 18 years	2,097 (75.2%)
18 years or more	689 (24.7%)
Total of patients	**2,786 (100%)**
Patients without data	138

n = number of patients.

Note: Patients without data comprise those who were not followed-up in 2013 or do not have recorded data (spirometry/anthropometry)

Figure 9

Distribution of patients by age group.

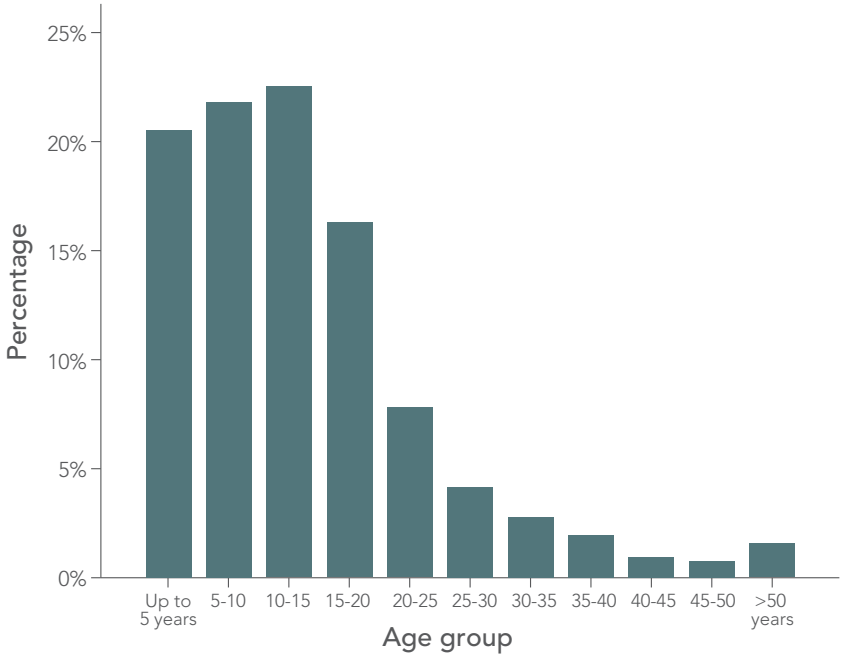


Figure 10

Distribution of patients by age group and gender.

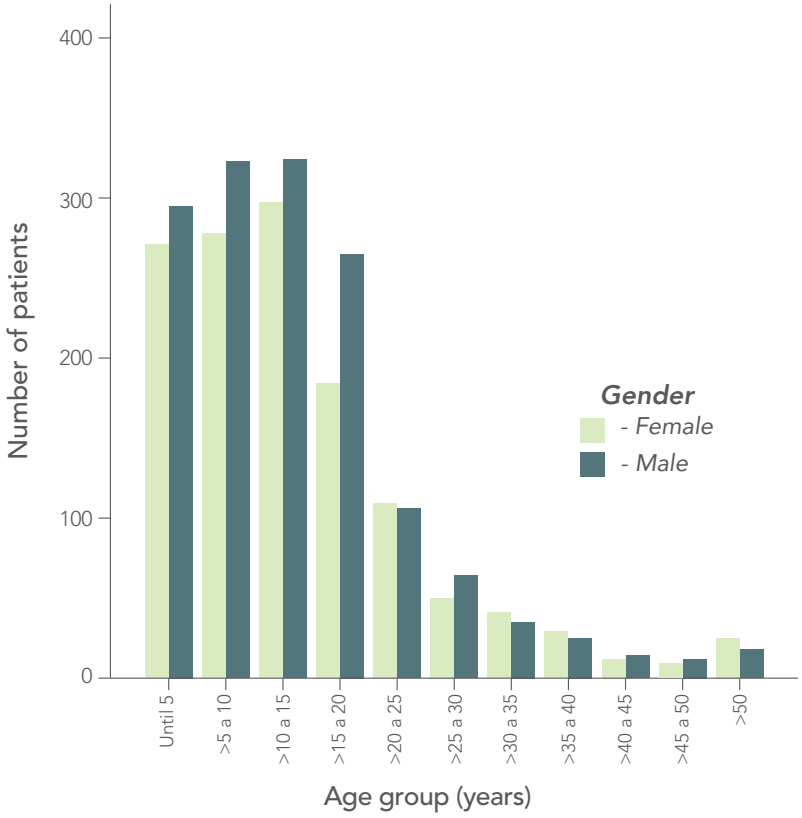


Figure 11

Change in current age of patients from 2009 to 2013. Mean age ± standard deviation.

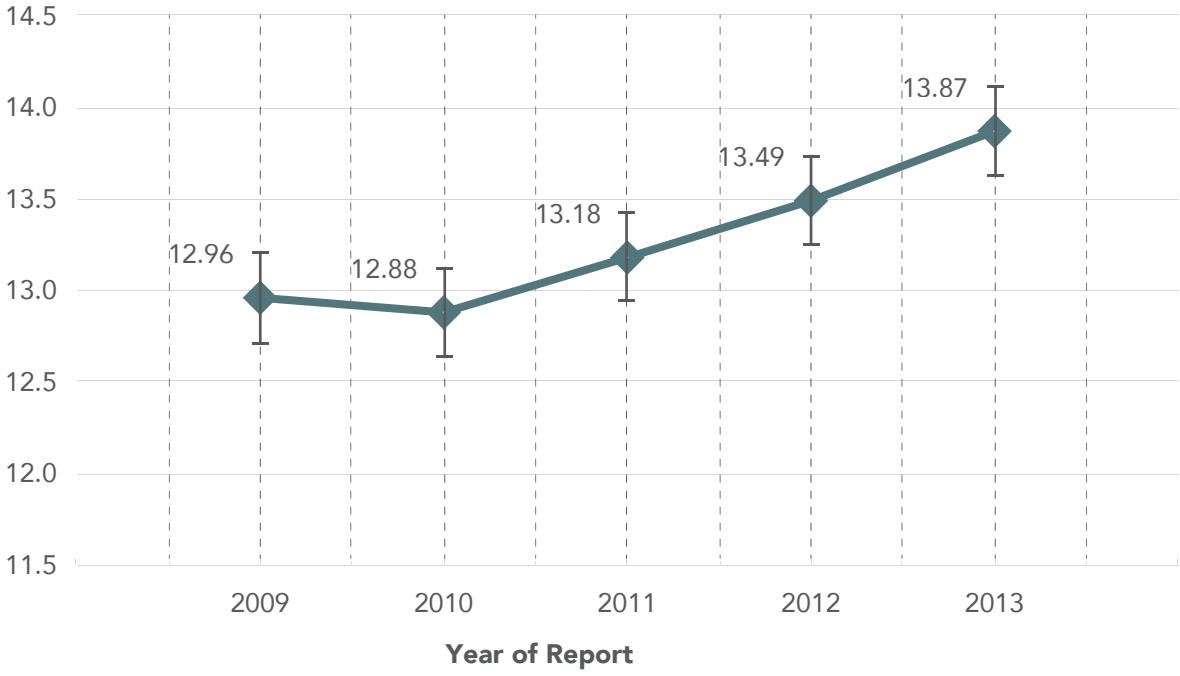


Figure 12

Distribution of patients by pediatric (< 18 years) or adult (> 18 years) age group.

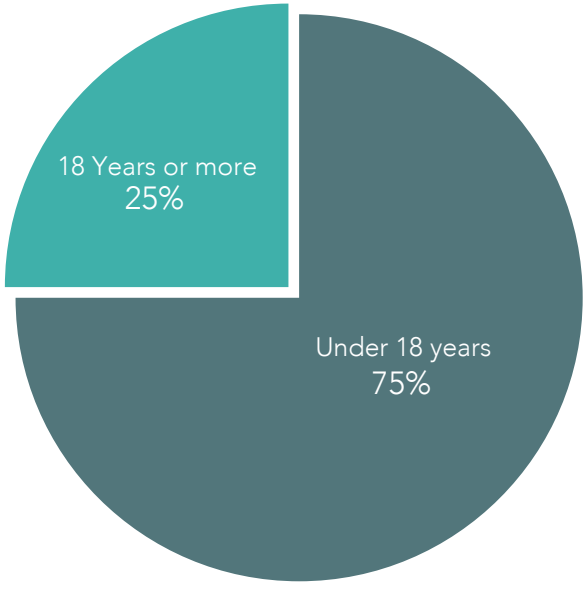
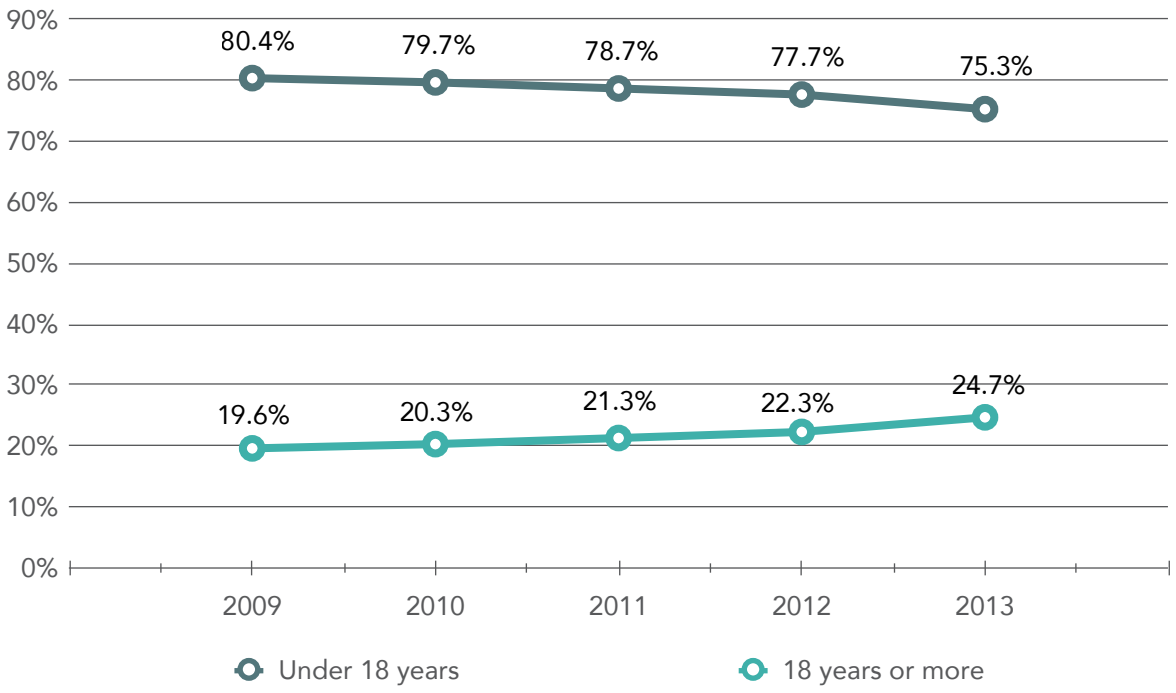


Figure 13

Distribution of patients by pediatric age group from 2009 to 2013.



This graph seems to suggest that most Brazilian patients still belong to pediatric age groups; however, there has been an increasing trend in patient age and proportion of adults in recent years.

3.DIAGNOSTIC DATA

Table 8

Age of patients at diagnosis.

Age (years)	
Mean (standard deviation)	5.74 (9.96)
Median (p25-p75)	1.47 (0.25 – 7.35)
Minimum-Maximum	0 – 82.95
Total of patients	**2,918**
Patients without data*	6

n=number of patients; p25 = 25th percentile, p75 = 75th percentile.
**birth dates/diagnosis recorded incorrectly*

Figure 14

Distribution of patients by age at diagnosis.

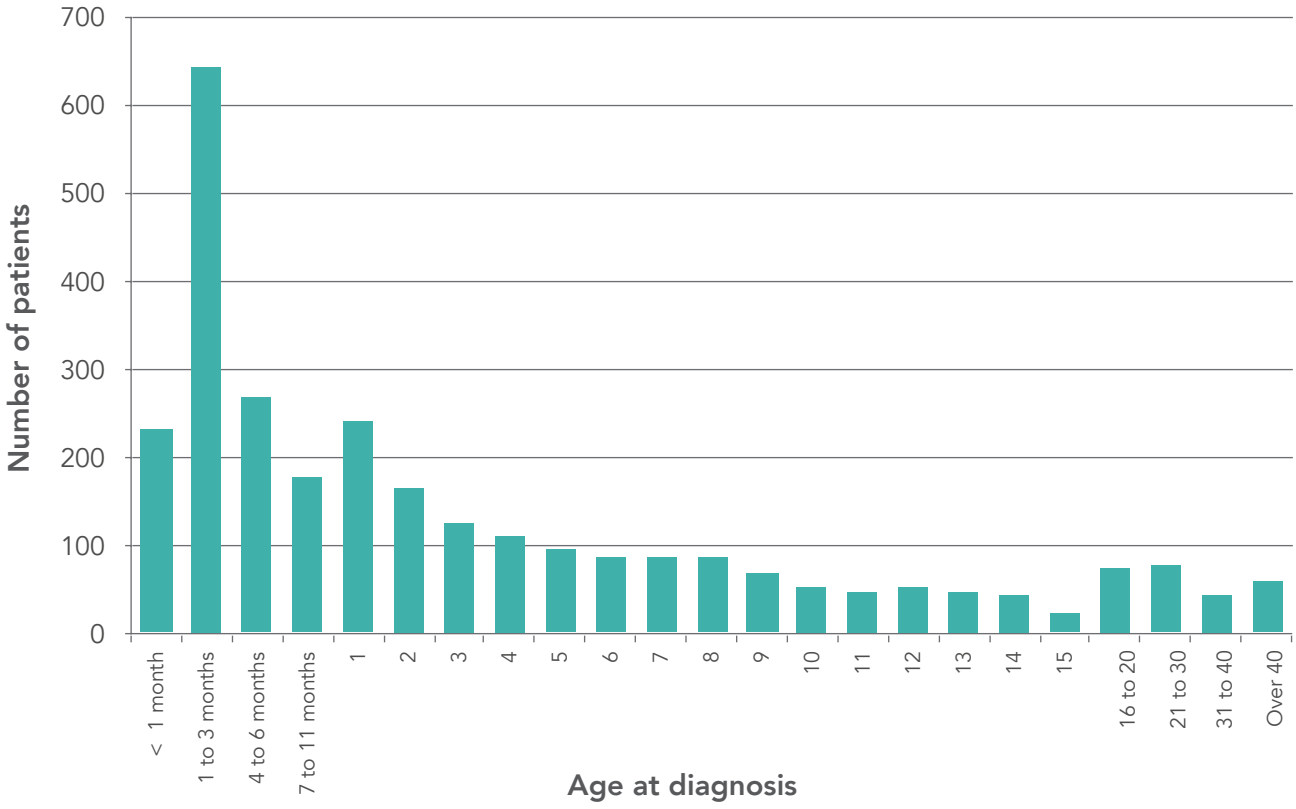
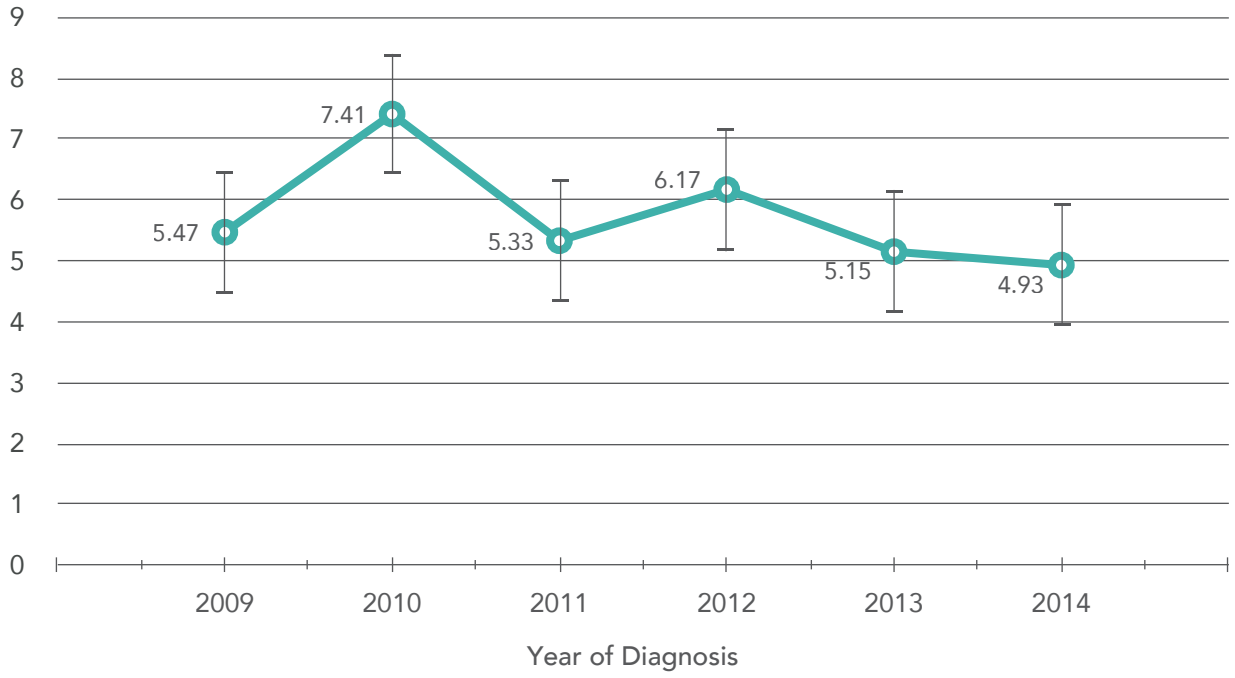


Figure 15

Changes in age at diagnosis over time. Mean ± standard deviation.



Note: For the graphs above, the year of diagnosis (extracted from the diagnostic data) was used instead of the year of competence

Table 9

Distribution of patients according to criteria for diagnosis.

Conditions for diagnosis	n (%)
Persistent respiratory symptoms	1,855 (63.4%)
Growth deficit / Malnutrition	1,174 (40.2%)
Steatorrhea or Malabsorption	1,091 (37.3%)
Neonatal screening (IRT)	742 (25.4%)
Family history	244 (8.3%)
Clinical or surgical meconium ileus	229 (7.8%)
Sinus disease and/or nasal polyp	188 (6.4%)
Metabolic disorder	167 (5.7%)
Edema / Anemia	109 (3.7%)
Rectal prolapse	29 (1.0%)
Prolonged jaundice	27 (0.9%)
Infertility	13 (0.4%)
Other	153 (5.2%)
Unknown condition	78 (2.7%)
Total patients	**2,924 (100%)**

n = number of patients.

Table 10

Distribution of patients according to the sweat test.

	Chloride (mEq/l)	Mass (mg)	Conductivity (mmol/l)
Mean (standard deviation)	88.90 (26.55)	146.97 (77.29)	103.9 (18.9)
Median (p25-p75)	89.50 (69.5-105.5)	134.00 (100-184.05)	105.0 (96-115)
Minimum-Maximum	0.38-249.50	0.08-470	33-180
Total of patients	**2,466**	**1,877**	**300**

n=number of patients; p25 = 25th percentile, p75 = 75th percentile. For chloride and mass, the mean values of the two measurements were considered, excluding values above 500.

Table 11

Diagnosis by neonatal screening – Level of immunoreactive trypsinogen (IRT).

Level of immunoreactive trypsinogen(TIR) (ng/mL)	1ª result	2ª result
Mean (standard deviation)	214.1 (126.6)	208.3 (135.2)
Median (p25-p75)	183 (126-264)	174.5 (117-249.5)
Minimum-Maximum	8.6-1,255	10-1,049
Total of patients	**634**	**492**

Table 12

Other tests reported used in the diagnosis.

	n (%)
Nasal potential difference	94 (3.2%)
Rectal biopsy	69 (2.4%)
Total patients	**2,924 (100%)**

n = number of patients.

Table 13

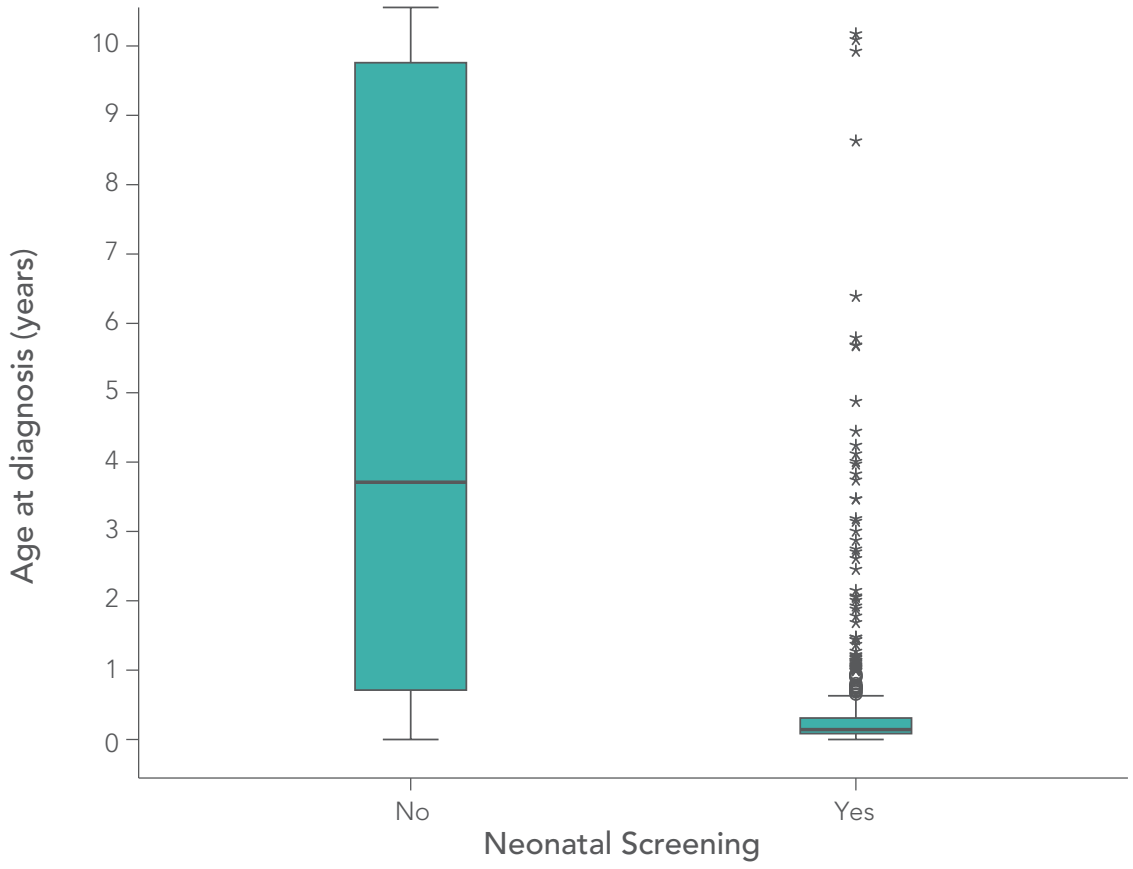
Patients grouped by age at diagnosis according to neonatal screening.

	Neonatal screening		
Age (years)	**No**	**Yes**	**Total**
Median (standard deviation)	7.55 (10.94)	0.42 (1.11)	5.74 (9.96)
Median (p25-p75)	3.71 (0.71-9.76)	0.14 (0.08-0.31)	1.47 (0.25 – 7.35)
Minimum-Maximum	0-82.95	0-13.83	0 – 82.95
Total of patients	**2,177**	**741**	**2,918**
Patients without data	5	1	6

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

Figure 16

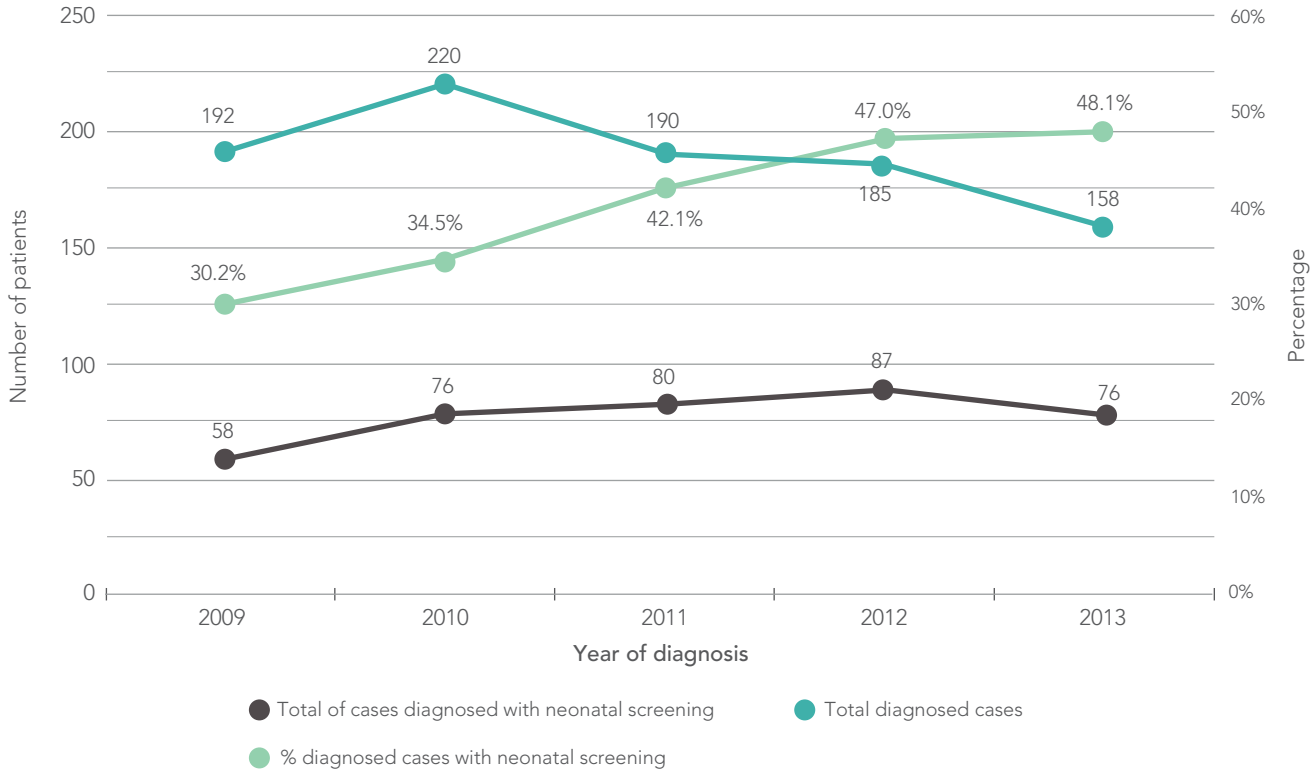
Patients grouped by age at diagnosis according to neonatal screening.



A total of 945 cases of cystic fibrosis were diagnosed from 2009 to 2013, of whom 377 (39.9%) patients had neonatal screening. The graph below shows that the percentage of cases diagnosed through neonatal screening has been increasing each year, accounting for almost half of all cases (48.1%) in 2013.

Figure 17

New diagnosis of cystic fibrosis and contribution of neonatal screening.



Despite the increase in the percentage of cases diagnosed by neonatal screening, there was no significant reduction in the average age at diagnosis (ANOVA with p=0.2).

4.GENETIC DATA

Table 14

Patients grouped according to genetic testing for cystic fibrosis.

Genotype performed	n (%)
No	1,737 (59.4%)
Yes	1,187 (40.6%)
Total patients	**2,924 (100%)**

Number of mutations	n (%)
None	255 (21.5%)
One	394 (33.2%)
Two or more	538 (45.3%)
Total patients genotyped performed	**1,187 (100%)**

Genótipo - descrição	n (%)
DF508/DF508	316 (26.6%)
DF508/Others	162 (13.6%)
DF508/Not identified	341 (28.7%)
Others/Others	59 (5.0%)
Others/Not identified	54 (4.5%)
Not identified/Not identified	255 (21.5%)
Total de pacientes com genótipo	**1,187 (100%)**

Figure 18

Distribution of patients by genetic study results (n=1,187).

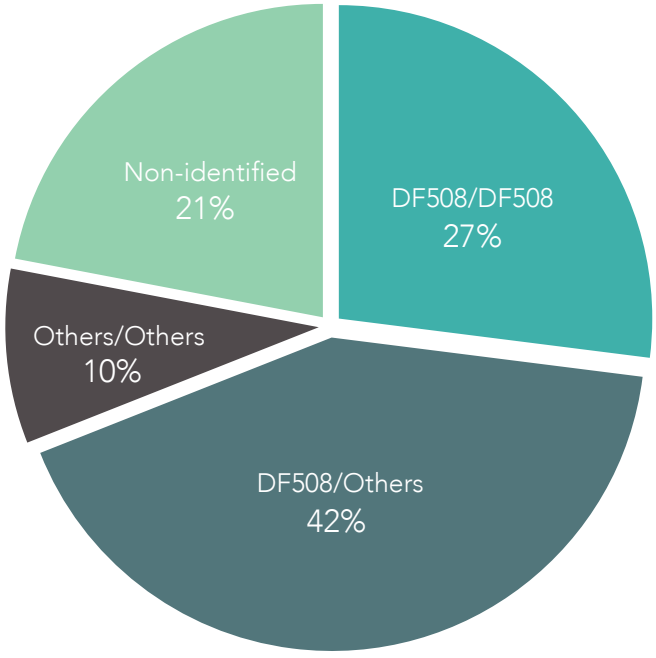


Table 15

Mutations identified (1,187 patients, 2,374 alleles).

Mutations	n	%
DF508	1,093	46.0%
G542X	98	4.1%
R334W	22	0.9%
R1162X	20	0.8%
N1303K	17	0.7%
G85E	16	0.7%
W1282X	14	0.6%
3120+1G>A	13	0.5%
G551D	6	0.3%
2183AA>G	5	0.2%
3849+10kbC>T	5	0.2%
R553X	5	0.2%
2789+5G>A	4	0.2%
711-1G>T	4	0.2%
1078delT	4	0.2%
1717-1G>A	3	0.1%
1812-1G>A	3	0.1%
S549R	3	0.1%
I507	2	0.1%
W1089X	2	0.1%
Y1092X	2	0.1%
D1152H	2	0.1%
M1101K	2	0.1%
Outra	74	3.1%
Total alleles studied (n=1,187 patients)	**2,374**	**100%**

FOLLOW-UP DATA

For the description of the follow-up data, only the year 2013 was considered

5. ANTHROPOMETRIC DATA

Anthropometric data were obtained on the day pulmonary function testing was performed, or at the last appointment of the year when pulmonary function testing was not performed.
The calculation of percentiles and Z score of anthropometric data used the data from the CDC as reference (available at http://www.cdc.gov/growthcharts/).

Table 16

Patients distributed according to anthropometric data.

WEIGHT (kg)	NCHS Percentile	Z Score
Mean (standard deviation)	33.54 (29.78)	-0.69 (1.26)
Median (p25;p75)	25 (7;57)	-0.67 (-1.50; 0.17)
Minimum; Maximum	0;100	-3.99; 3.97
Total patients	**1,687**	**1,687**

HEIGHT (cm)	NCHS Percentile	Z Score
Mean (standard deviation)	32.90 (28.17)	-0.66 (1.14)
Median (p25;p75)	26.00 (8; 52)	-0.63 (-1.41; 0.05)
Minimum; Maximum	0-100	-3.98; 3.94
Total patients	**1,683**	**1,683**

IMC (kg/m2)	Medida	NCHS Percentile
Mean (standard deviation)	17.91 (3.72)	43.47 (32.30)
Median (p25;p75)	17.09 (15.26-19.82)	38 (14; 72)
Minimum; Maximum	7.85; 38.67	0-100
Total patients	**2,173**	**1,281**

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

There was no difference between adult men and women with regard to BMI (Figure 24).
In patients less than 20 years old, the nutritional status (measured by percentiles and Z-scores of anthropometric measurements) worsens with age (Figures 20 and 21). On the other hand, in adult patients, the BMI tended to increase with age (Figure 22).

Figure 19

Distribution of adult patients (18 years or older) with regard to BMI range according to gender.

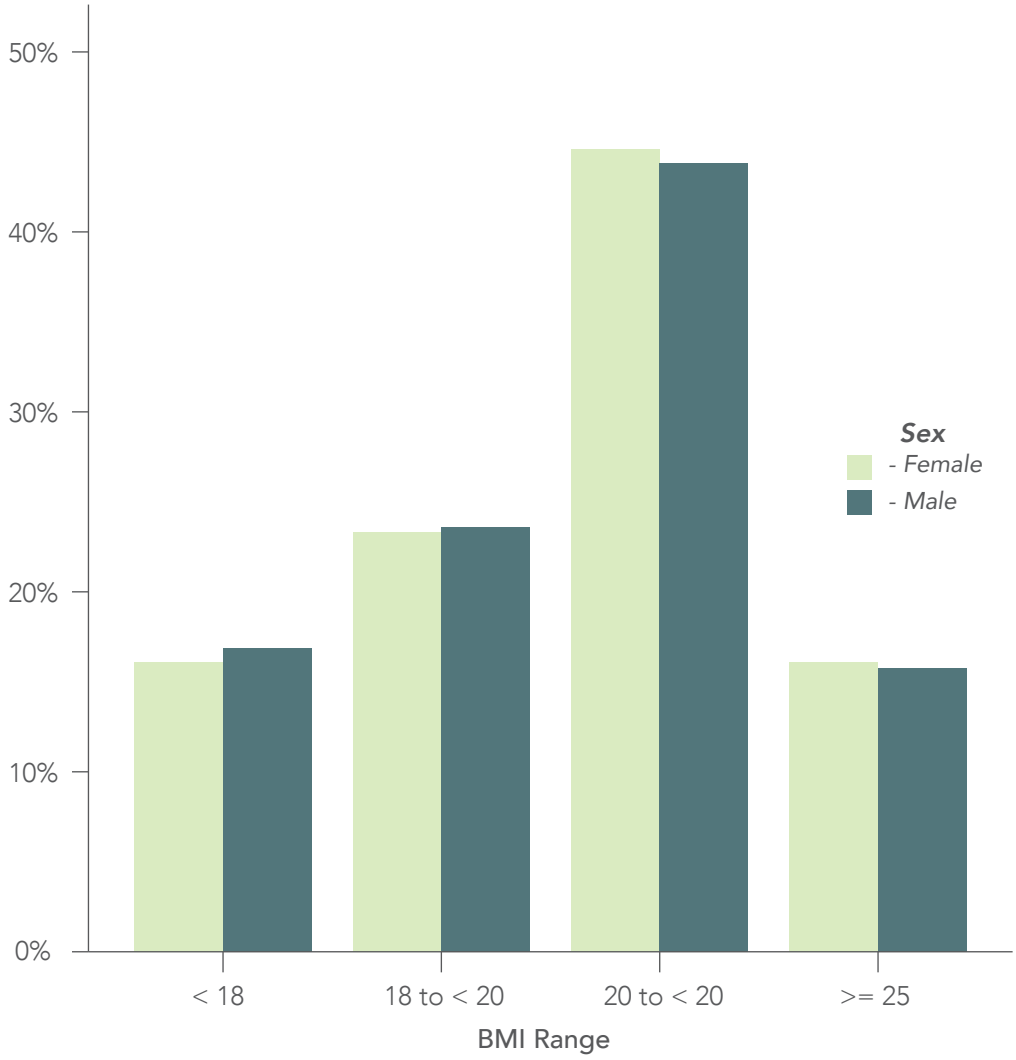


Figure 20

Changes of weight, height, and BMI percentiles according to age – patients 2 to 20 years of age.

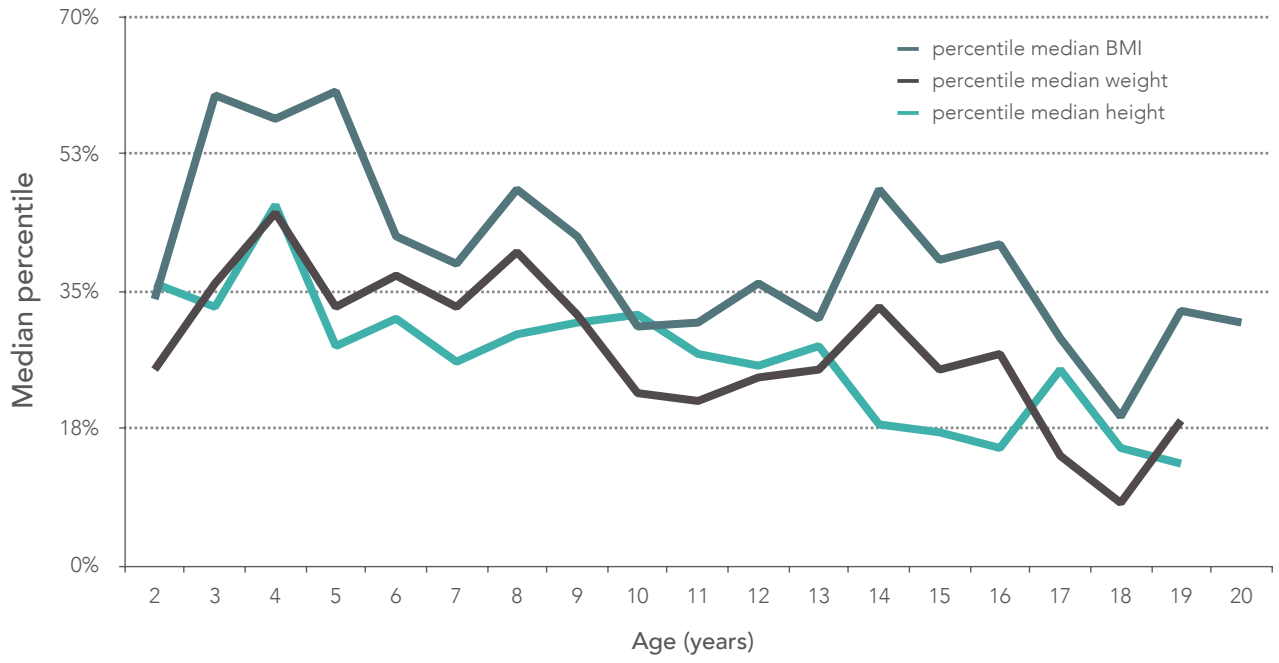
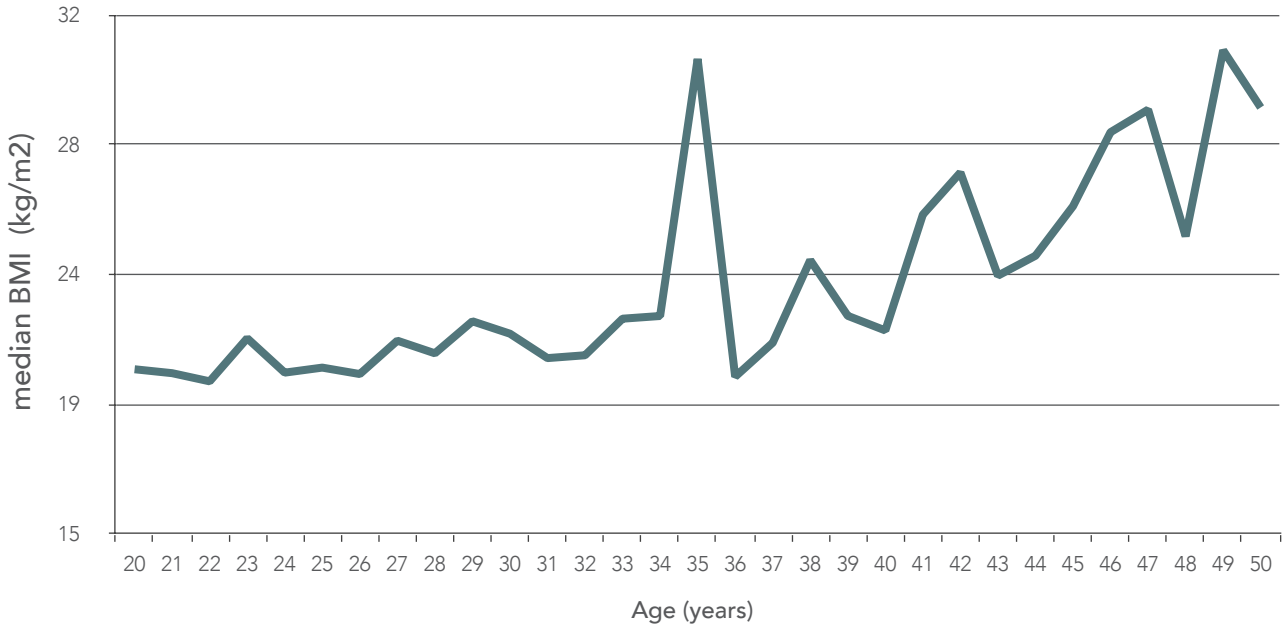


Figure 21

Changes of Z-score average for weight and height according to age – patients 2 to 20 years.

Figure 22

Changes of BMI according to age – patients 20 to 50 years.



6. PULMONARY FUNCTION DATA

Spirometry data were available for 1,101 patients (49.23%). For those with more than one functional test in a given year, data from the best pulmonary function tests were used. Reference expected values for pulmonary function were taken from the work by Stanojevic S 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

Patients according to pulmonary function data.

Percentage of predicted - FVC	
Mean (standard deviation)	81.67 (24.38)
Median (p25;p75)	83.43 (65.00; 98.01)
Minimum; maximum	20.25; 229.35
Total patients	**1,076**

Z Score - FVC	
Mean (standard deviation)	-1.59 (2.10)
Median (p25;p75)	-1.37 (-3.02; -0.17)
Minimum; maximum	-7.52; 10.04
Total patients	**1,076**

Percentage of predicted - FEV1	
Mean (standard deviation)	72.39 (27.30)
Median (p25;p75)	74.73 (50.82; 91.85)
Minimum; maximum	14.99; 203.58
Total patients	**1,076**

Z score - FEV1	
Mean (standard deviation)	-2.22 (2.19)
Median (p25;p75)	-2.08 (-3.98; -0.67)
Minimum; maximum	-6.50; 9.44
Total patients	**1,076**

FEV1/FVC	
Mean (standard deviation)	0.76 (0.14)
Median (p25;p75)	0.78 (0.67-0.86)
Minimum; maximum	0.33-1.00
Total patients	**1,100**

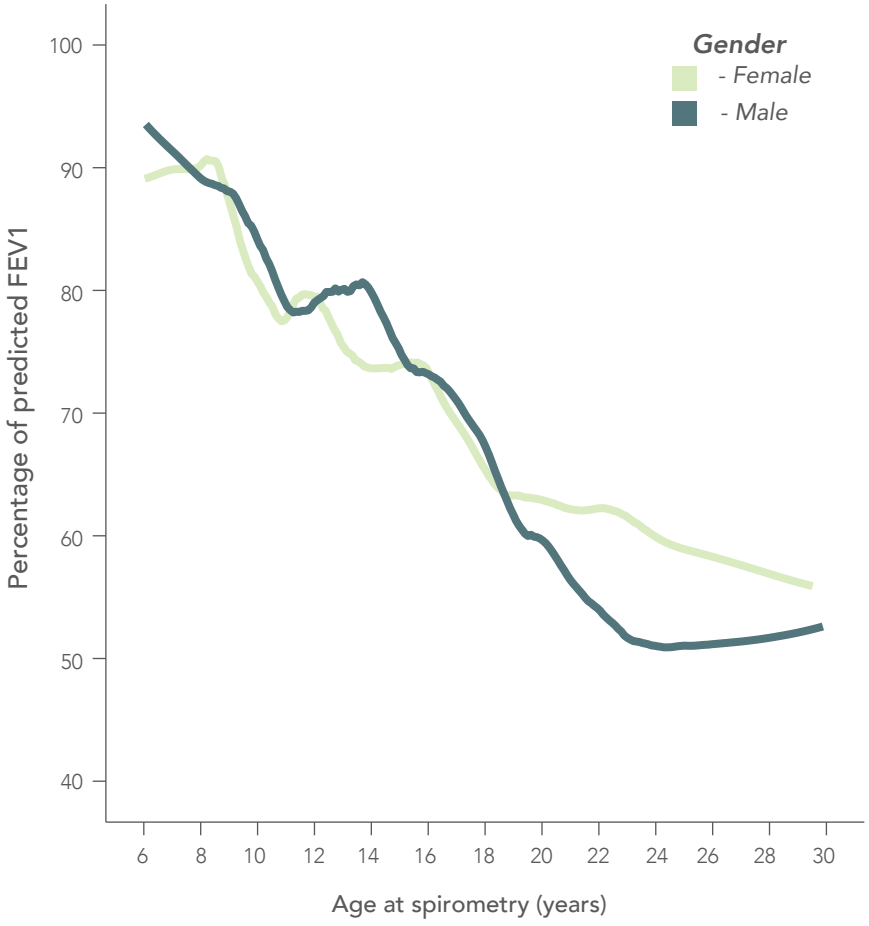
Z Score- FEV1/FVC	
Mean (standard deviation)	-1.44 (1.58)
Median (p25;p75)	-1.47 (-2.68; -0.39)
Minimum; maximum	-5.36; 2.87
Total patients	**1,076**

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

Figure 23

Percentage of forced forced expiratory volume in the first second (FEV1) according to age of patients between 6 and 30 years.

A gradual but sharp fall in the FEV1 values was observed with age, but was less evident after 20 years of age



There is a strong association between the level of obstruction and age group ($p<0.001$) - (Table 18, Figure 24).

A large proportion of young patients with CF already demonstrates significant changes in pulmonary function.

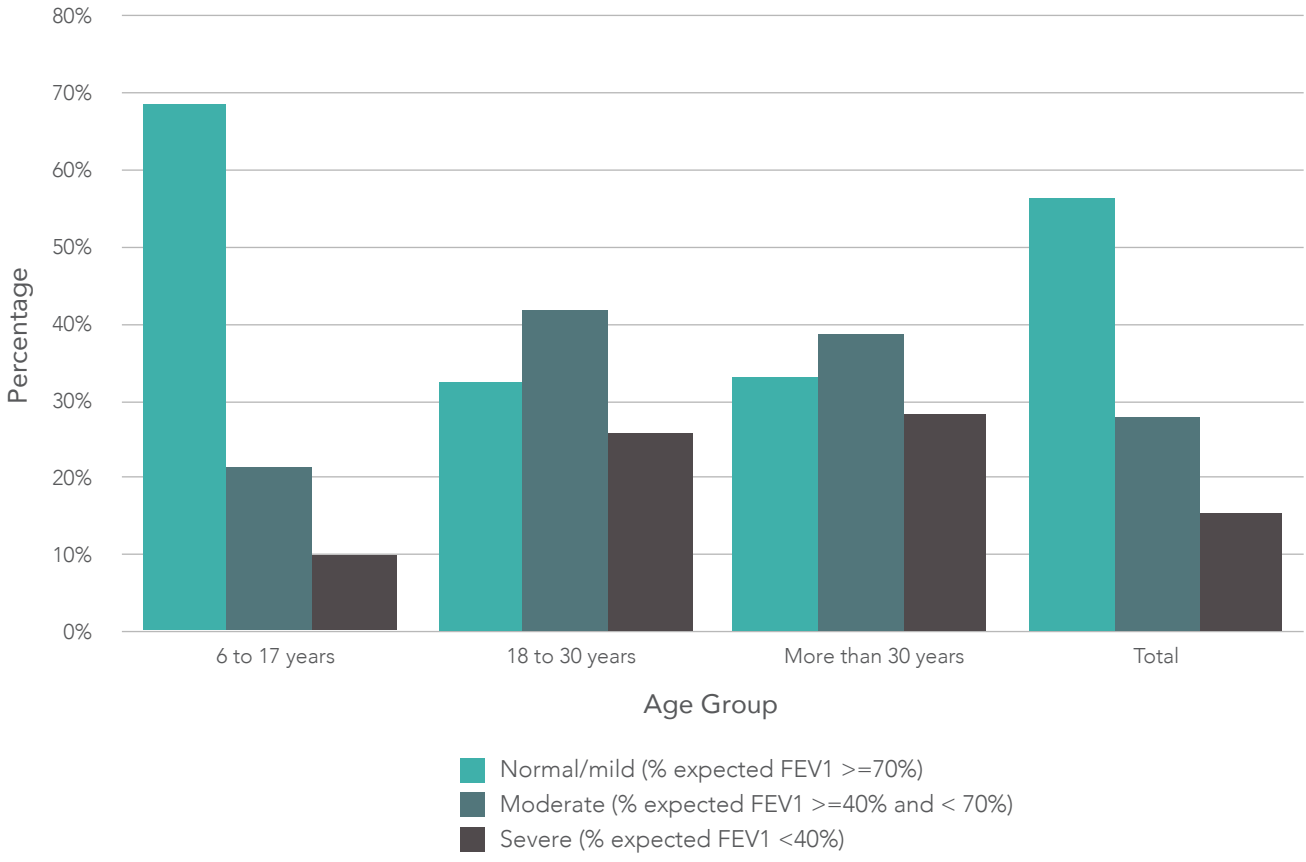
Table 18

Spirometry results distributed by level of obstruction, according to age group.

	Age group			
Obstruction level (% expected FEV1)	6 to 17 years	18 to 30 years	More than 30 years	Total
Normal/mild (>=70%)	486 (68.6%)	84 (32.4%)	36 (33.0%)	606 (56.3%)
Moderate (>=40% e < 70%)	152 (21.5%)	108 (41.7%)	42 (38.5%)	302 (28.1%)
Severe (<40%)	70 (9.9%)	67 (25.9%)	31 (28.4%)	168 (15.6%)
Total patients	**708 (100%)**	**259 (100%)**	**109 (100%)**	**1,076 (100%)**

Figure 24

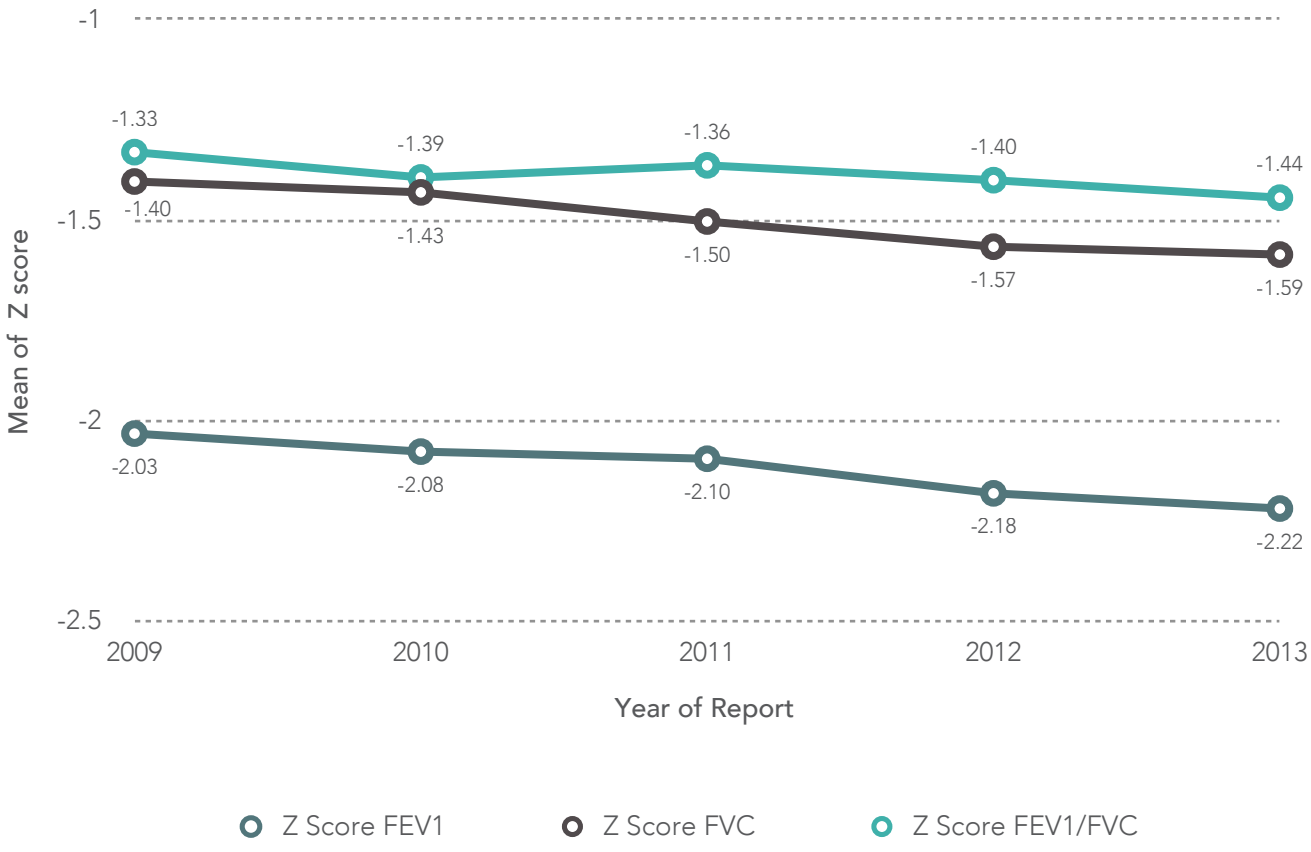
Distribution of patients according to level of obstruction by age group.



Analysis of changes in pulmonary function over time (2009 to 2013), showed that the Z score values for FEV1, FVC, and Tiffeneau index did not show improvements over the period under study (Figure 25).

Figure 25

Variations in the Z scores for FVC, FEV1, and Tiffeneau index from 2009 to 2013.



Analysis of the relationship between pulmonary function and nutritional status, showed that there was an association between the percentage of predicted FEV1 and percentage of BMI (pediatric population) or absolute value of BMI (adult population) - Figures 26 and 27.

Figure 26

Percentage of predicted FEV1 according to BMI percentile in patients aged 6 to 19 years.

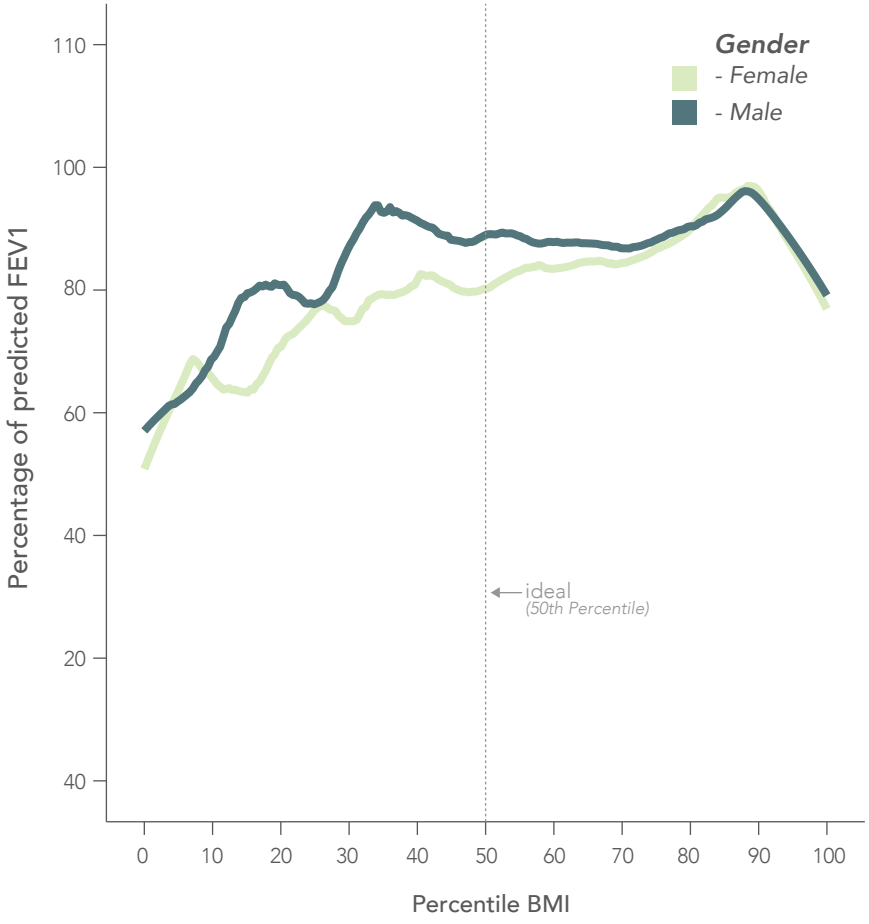
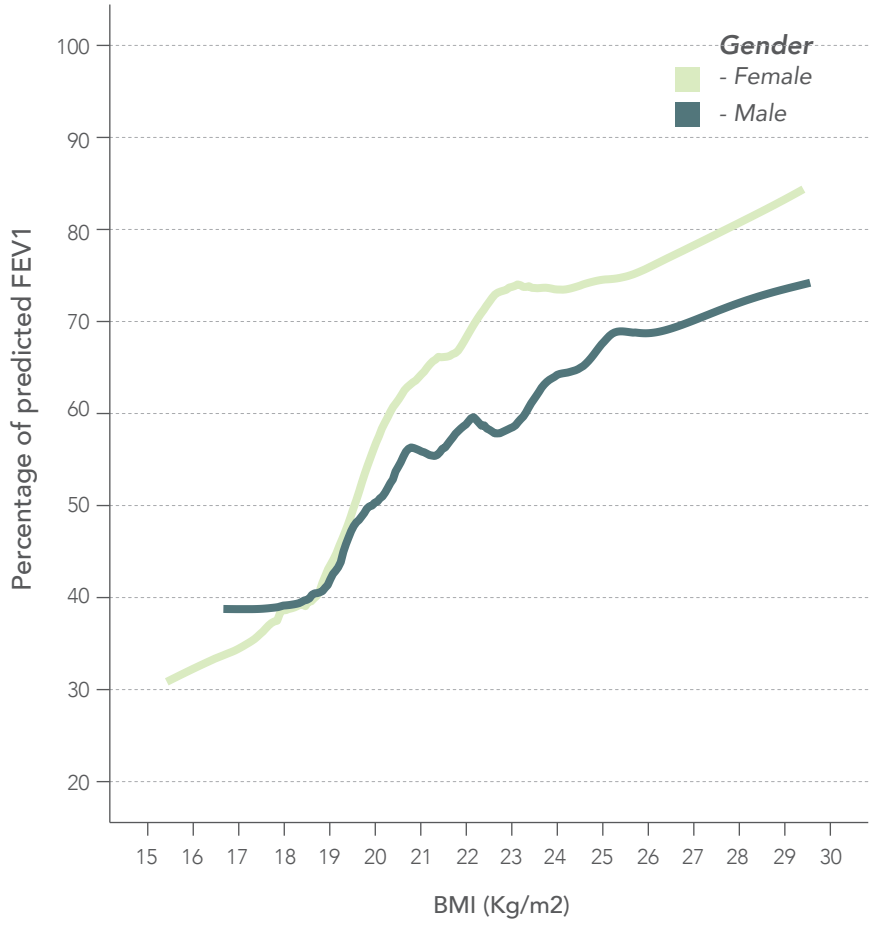


Figure 27

Percentage of predicted FEV1 according to BMI in patients aged 20 to 40 years.



7. MICROBIOLOGICAL DATA

Microbiological data refers to identification of pathogens at least once a year; since there is no standardization with regard to the processing techniques and culture sampling from the respiratory tract of patients with cystic fibrosis in Brazil, data should be analyzed with caution.

Table 19

Identified microorganisms.

Identified microorganisms	n	%
Oxacillin-sensitive S. aureus	1,217	54.4%
Pseudomonas aeruginosa	984	44.0%
Non-mucoid Pseudomonas aeruginosa	689	30.8%
Mucoid Pseudomonas aeruginosa	480	21.4%
Burkholderia cepacia complex	231	10.3%
Haemophilus influenzae	194	8.7%
Oxacillin-resistant S. aureus	181	8.1%
Stenotrophomonas maltophilia	110	4.9%
Klebsiella pneumoniae	101	4.5%
Serratia sp.	73	3.3%
Candida sp	70	3.1%
Achromobacter sp.	62	2.8%
Aspergillus fumigatus	42	1.9%
Escherichia coli	37	1.7%
Other Pseudomonas	33	1.5%
Nontuberculous Mycobacteria	8	0.4%
Mycobacterium tuberculosis	6	0.3%
Total patients	**2,238**	**100%**

A high proportion of patients with *P. aeruginosa* positive cultures was observed in the first years of life (Table 20 and Figure 28), but analysis of data from 2009 to 2013 showed a tendency of decreasing proportion of mucoid *P. aeruginosa* over the years (Figure 29).

Table 20

Microorganisms according to age group.

	Microorganisms identified						
Age group	*Oxacillin-sensitive S. aureus*	*Pseudomonas aeruginosa*	Burkholderia cepacia complex	*Oxacillin-resistant S. aureus*	*Haemophilus influenzae*	*Stenotrophomonas maltophilia*	n°
Until 5 years	50.50%	37.62%	8.32%	7.33%	12.87%	4.36%	505
> 5 to 10	67.53%	36.56%	10.54%	7.74%	10.97%	5.16%	465
>10 to 15	61.71%	43.99%	11.81%	8.55%	8.76%	7.33%	491
>15 to 20	54.12%	49.71%	11.18%	8.24%	6.18%	5.00%	340
>20 to 25	38.55%	52.51%	9.50%	7.82%	4.47%	1.12%	179
>25 to 30	41.11%	63.33%	18.89%	14.44%	3.33%	2.22%	90
>30 to 35	40.00%	63.33%	8.33%	11.67%	3.33%	3.33%	60
>35 years	27.37%	46.32%	4.21%	4.21%	1.05%	4.21%	95

** total: 2,225 patients (13 patients without information about age)*

Figure 28

Prevalence of pathogens by age group.

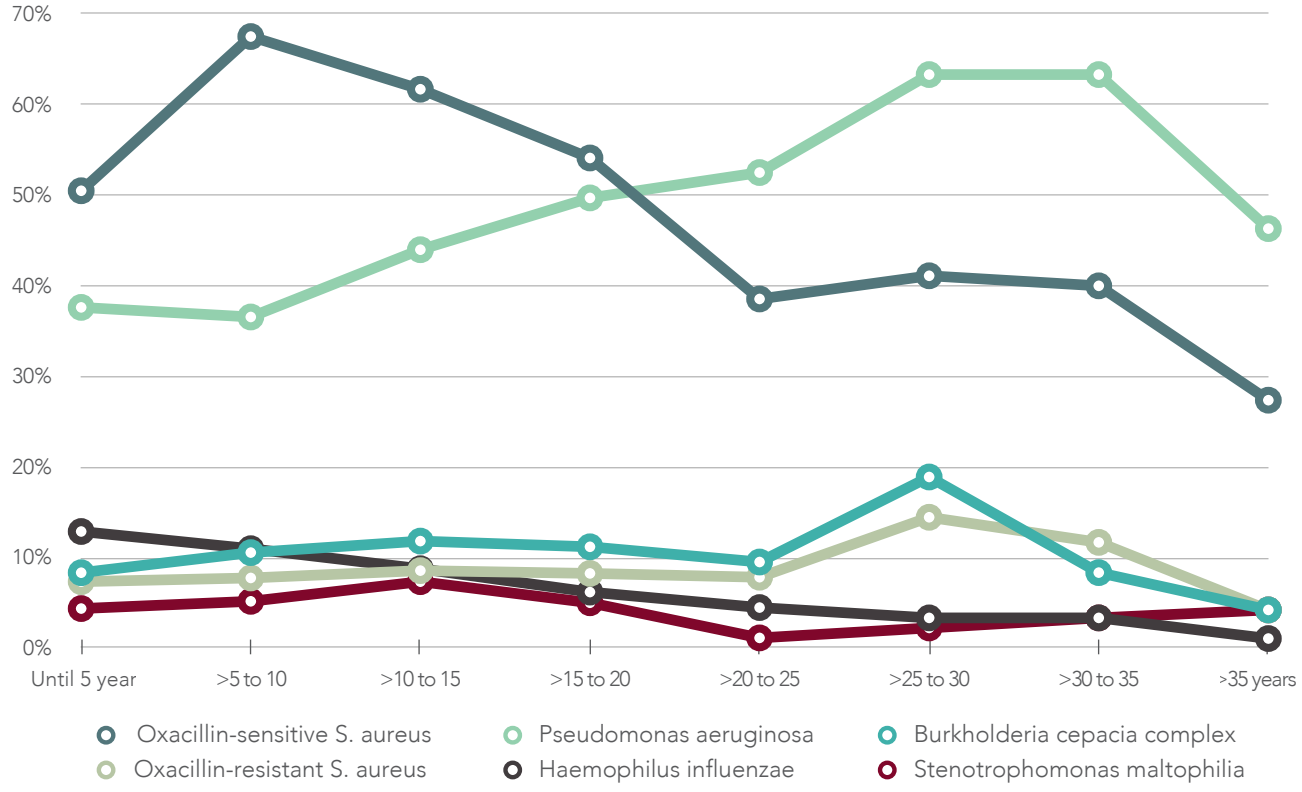
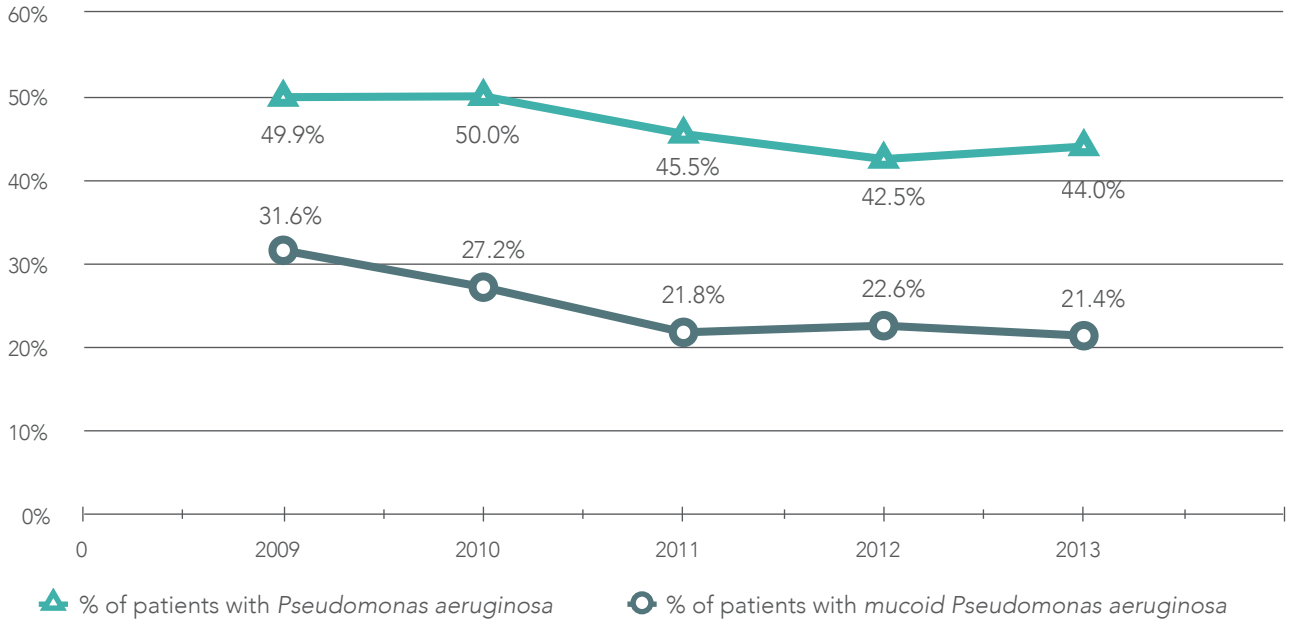


Figure 29

Percentage of patients with Pseudomonas aeruginosa from 2009 to 2013.



8. CLINICAL TREATMENT DATA

Figure 30

Distribution of patients by number of visits in 2013.

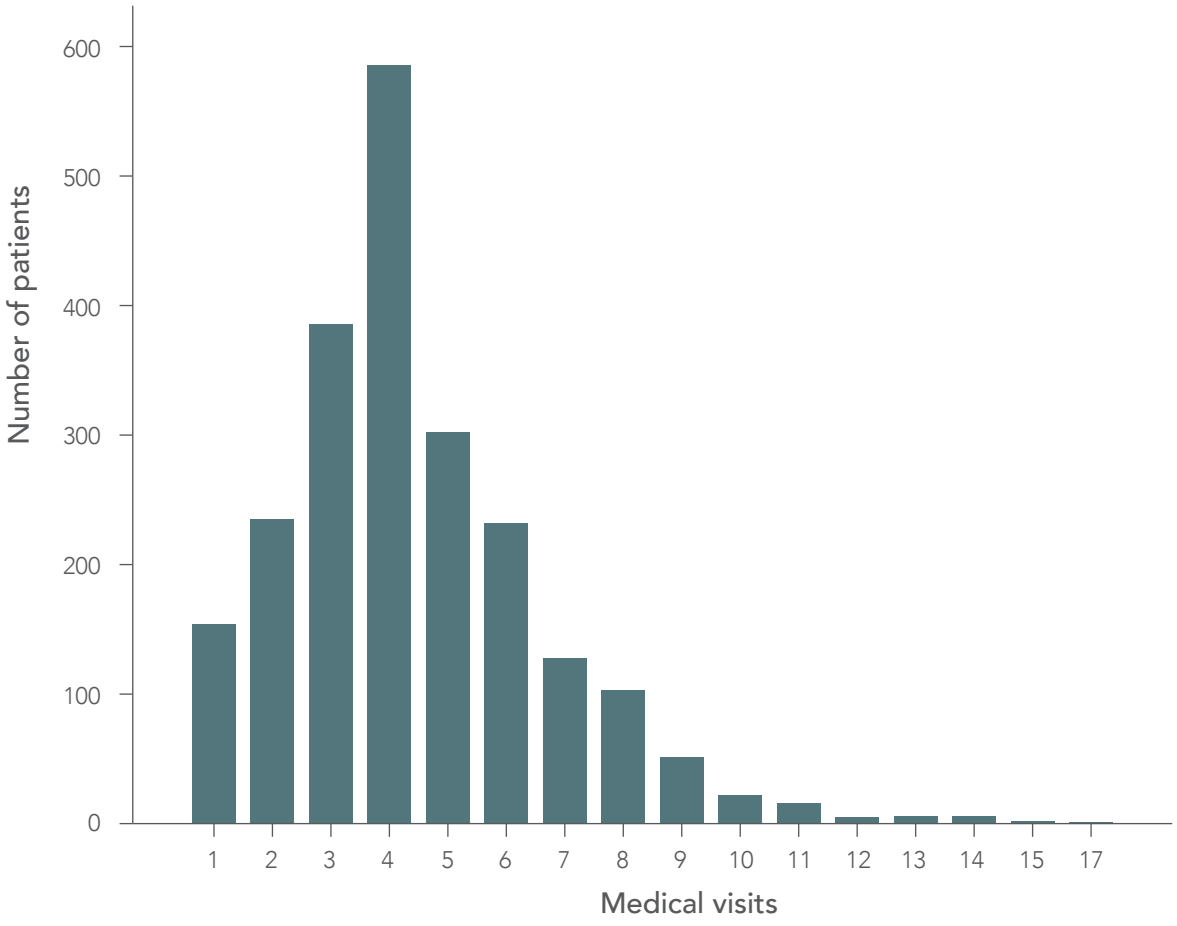


Table 21

Deaths

Deaths	n (%)
No	2,208 (98.7%)
Yes	30 (1.3%)
Cause of Death	
Respiratory causes	26
Accidental	1
Pancreatic insufficiency	1
Kidney failure	1
Multiple organ and system failure	1
Total of patients	**2,238 (100%)**

Age at death (years)	
mean (standard deviation)	19.10 (11.31)
median (p25-p75)	20.64 (12.69-26.44)
minimum-maximum	0.41-41.73

Table 22

Distribution of patients according to the Shwachman-Kulczycki score

Escore total	n (%)
mean (standard deviation)	77.17 (17.27)
median (p25-p75)	80 (65-90)
minimum-maximum	10-100
CLASSIFICATION	
Severe (≤ 40)	73 (4.0%)
Moderate (41 to 55)	184 (10.0%)
Average (56 to 70)	365 (19.9%)
Good (71 to 85)	616 (33.6%)
Excellent (86-100)	594 (32.4%)
Total of patients	**1,832 (100%)**
Patients without data	406

Table 23

Shwachman-Kulczycki Score: Total score by age group.

	Faixa etária					
Total score	Up to 5 years	> 5 to 10	>10 to 15	>15 to 20	>20 years	Total
Severe (≤ 40)	8 (1.9%)	4 (1.0%)	12 (2.9%)	16 (5.7%)	32 (9.9%)	72 (3.9%)
Moderate (41 to 55)	14 (3.2%)	18 (4.7%)	50 (12.3%)	45 (16.1%)	56 (17.4%)	183 (10.0%)
Average (56 to 70)	51 (11.8%)	57 (14.8%)	95 (23.3%)	69 (24.6%)	93 (28.9%)	365 (20.0%)
Good (71 to 85)	131 (30.3%)	147 (38.1%)	149 (36.5%)	94 (33.6%)	95 (29.5%)	616 (33.7%)
Excellent (86-100)	228 (52.8%)	160 (41.5%)	102 (25.0%)	56 (20.0%)	46 (14.3%)	592 (32.4%)
Total of patients	**432 (100%)**	**386 (100%)**	**408 (100%)**	**280 (100%)**	**322 (100%)**	**1,828*(100%)**

** 410 patients without age or score data*

Figure 31

Confidence interval (95%) for the median Shwachman-Kulczycki scores according to age group.

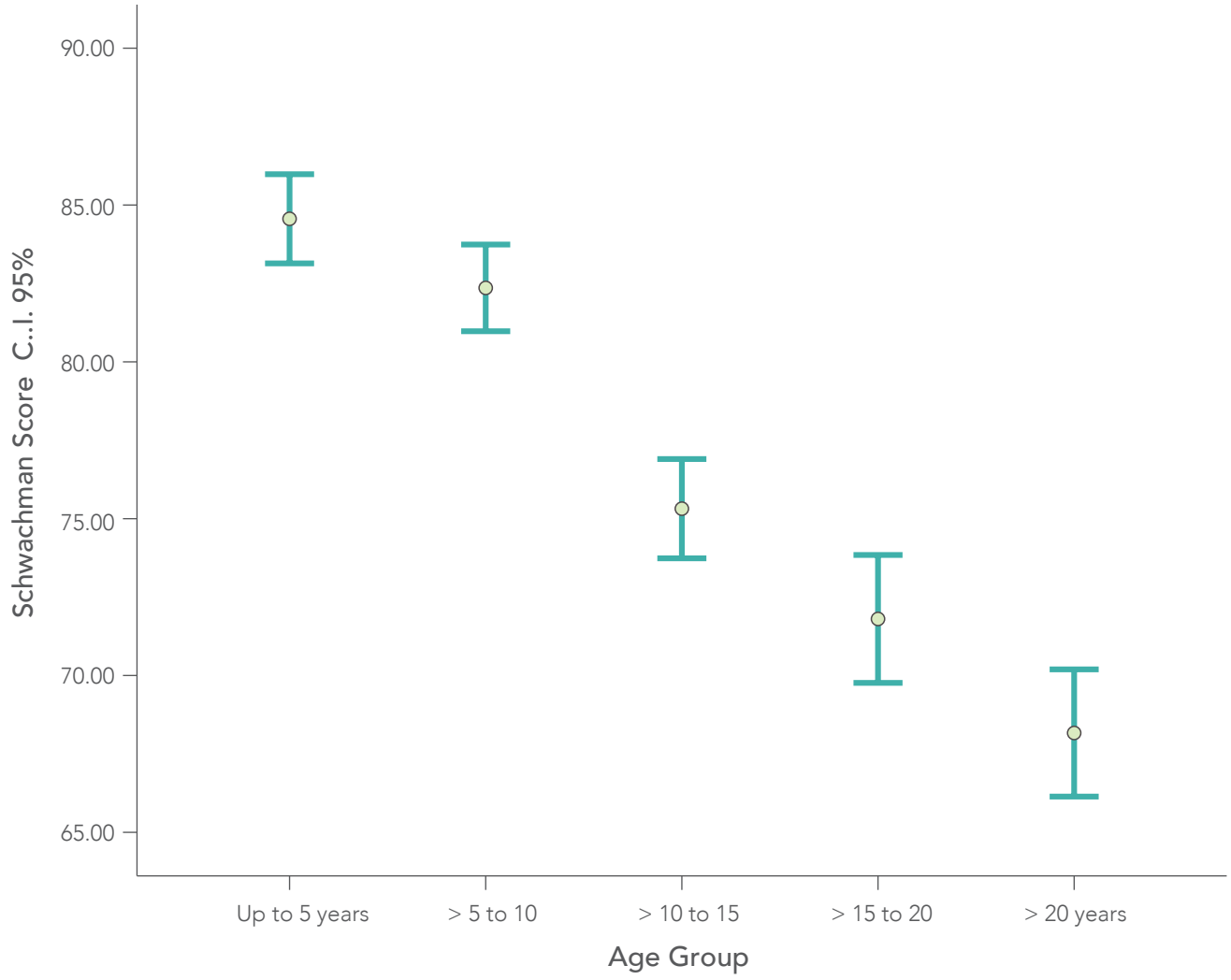


Table 24

Complications in the last year.

Complications in the last year	n (%)
Asthma	307 (13.7%)
Evidence of hepatic disease	173 (7.7%)
Gastroesophageal reflux disease	157 (7.0%)
Diabetes	83 (3.7%)
Nasal polyposis	75 (3.4%)
Hemoptysis	65 (2.9%)
Osteopenia / Osteoporosis	63 (2.8%)
Chronic atelectasis	39 (1.7%)
Cholelithiasis	33 (1.5%)
Pulmonary hypertension	23 (1.0%)
Cirrhosis with portal hypertension	22 (1.0%)
Allergic bronchopulmonary aspergillosis	15 (0.7%)
Distal intestinal obstruction syndrome	14 (0.6%)
Pancreatitis	7 (0.3%)
Pneumothorax	3 (0.1%)
Hematemesis	2 (0.1%)
Colon stenosis	1 (0.045%)
Total patients	**2,238 (100%)**

n = number of patients

Table 25

Transplants.

Transplants	n (%)
Pulmonary transplant - *cadaver donor*	17 (0.8%)
Hepatic transplant	1 (0.045%)
Total patients	**2,238 (100%)**

Table 26

Oxygen therapy.

Oxygen therapy	n (%)
No	2,137 (95.5%)
Yes	101 (4.5%)
Continuous	63 (2.8%)
Night-time	38 (1.7%)
Total patients	**2,238 (100%)**

Table 27

Insulin.

Insulin use	n (%)
No	2,141 (95.7%)
Yes	97 (4.3%)
Total patients	**2,238 (100%)**

Table 28

Inhaled medications.

Bronchodilators	n (%)
Short acting Beta 2 agonist	773 (34.5%)
Long acting Beta 2 agonist	478 (21.4%)
Anticholinergic	96 (4.3%)

Antibiotics	n (%)
Inhalation tobramycin 300mg	857 (38.3%)
Colomycin	475 (21.2%)
Other	53 (2.4%)
Amikacin	15 (0.7%)
Gentamicin	12 (0.5%)
Injectable tobramycin	10 (0.4%)
Vancomycin	7 (0.3%)

Mucolytics	n (%)
Dornase alfa	1,656 (74.0%)
N acetylcysteine	78 (3.5%)

Saline solution	n (%)
Saline solution 0.9%	325 (14.5%)
Hypertonic saline 3%	122 (5.5%)
Hypertonic saline 5%	95 (4.2%)
Hypertonic saline 7%	386 (17.2%)
Total patients	**2,238 (100%)**

n = number of patients

Table 31

Oral medications.

	n (%)
Pancreatic Enzymes	1,817 (81.2%)
Less than 5,000 U/kg/day	555 (24.8%)
5,000 - 10,000 U/kg/day	1029 (46.0%)
More than 10,000 U/kg/day	211 (9.4%)
Unknown	22 (1.0%)
Nutritional Supplements	1,421 (63.5%)
Oral	1,240 (55.4%)
Gastric tubes	57 (2.5%)
Probe	10 (0.4%)
Unknown	114 (5.1%)

	n (%)
Azithromycin	860 (38.4%)
Proton pump inhibitors	513 (22.9%)
Ursodeoxycholic acid	459 (20.5%)
H2 Blockers	151 (6.7%)
Corticosteroids	146 (6.5%)
Ibuprofen (Pulmonary Disease)	17 (0.8%)
Ibuprofen or Other NSAID (Arthropathy)	7 (0.3%)
Total patients	**2,238 (100%)**

n = number of patients

Table 29

P. aeruginosa eradication treatment.

Treatment of *P. aeruginosa*	n (%)
Yes	467 (20.9%)
No	1,034 (46.2%)
Unknown	737 (32.9%)
Total of patients	**2,238 (100%)**

Table 30

Intravenous treatments – admissions.

Treatment	n (%)
Without treatment or data	1,714 (76.6%)
With treatment	524 (23.4%)
Home treatment*	87 (16.6%)
Hospital treatment*	423 (80.7%)
Home and Hospital treatment*	14 (2.7%)
Total of patients	**2,238 (100%)**

** Percentage of total of patients in treatment*

Cycles	
mean (standard deviation)	1,65 (1.01)
median (p25-p75)	1 (1-2)
minimum-maximum	1-8
Total of patients	**494**

Days	
mean (standard deviation)	26.62 (29.78)
median (p25-p75)	15 (14-30)
minimum-maximum	2-365
Total of patients	**498**

Implanted catheter	n (%)
No	2,199 (98.3%)
Yes	39 (1.7%)
Total of patients	**2.238(100%)**

n = número de pacientes.

Table 31

Intravenous antibiotics: Days of treatment according to age group.

	Age group					
Days	**Up to 5 years**	**> 5 to 10**	**>10 to 15**	**>15 to 20**	**>20 years**	**Total**
Mean (sd)	21.6 (30.4)	25.0 (29.4)	25.5 (18.1)	27.7 (22.1)	32.7 (41.6)	26.6 (29.8)
median (p25-p75)	14 (14-21)	15 (14-26)	18 (14-35)	20 (14-35)	21 (14-35)	15 (14-30)
minimum-maximum	3-284	2-195	14-30	5-114	5-365	2-365
Total patients	**101**	**73**	**129**	**77**	**116**	**496**

Table 32

Intravenous antibiotics: - Drugs utilized.

Used Drugs	**n**	**(%)**
Ceftazidime	311	13.9%
Amikacin	290	13.0%
Oxacillin	168	7.5%
Ciprofloxacin	115	5.1%
Imipenem or Meropenem	102	4.6%
Sulfa trimethoprim	86	3.8%
Injectable tobramycin	71	3.2%
Vancomycin	70	3.1%
Piperacillin /Tazobactam	60	2.7%
Cefepime	48	2.1%
Gentamicin	36	1.6%
Linezolid	14	0.6%
Ticarcillin /Piperacillin	12	0.5%
Colimycin	9	0.4%
Cefuroxime	5	0.2%
Aztreonam	1	0.04%
Chloramphenicol	-	-
Others	53	2.4%
Total patients	**2,238**	**100%**

n = number of patients.

Table 33

Specific Data for Adult Population.

	Sex		
	Male	**Female**	**Total**
Azoospermia or Hypospermia	35 (12.7%)	-	35
Pregnancy	-	2 (0.8%)	2
Oral or injectable contraceptives	-	45 (17.2%)	45
Common-law marriage	44 (16.0%)	73 (27.9%)	117 (21.8%)
Employment	107 (38.9%)	90 (34.4%)	197 (36.7%)
Total patients age ≥ 18 years	**275**	**262**	**537**

Centers that contributed to this report with follow-up data for patients in 2013 (alphabetical order of state).

Name	City	State	Person in charge
Hospital Universitário Prof. Alberto Antunes – UFAL	Maceió	AL	Katharina Vidal de Medeiros Moura
Hospital Especializado Otavio Mangabeira	Salvador	BA	Maria Angélica Santana
Hospital Universitário Prof. Edgar Santos	Salvador	BA	Edna Lúcia Santos de Souza
Hospital Infantil Albert Sabin	Fortaleza	CE	Cláudia de Castro e Silva
Hospital da Criança de Brasília José Alencar	Brasília	DF	Luciana de Freitas Velloso Monte
Hospital Infantil Nossa Senhora da Glória	Vitória	ES	Roberta de Cássia Melotti
Hospital Dr Dório Silva	Vitória	ES	Daniele Menezes Torres
Hospital das Clínicas da UFGO	Goiânia	GO	Lusmaia Damaceno Camargo Costa
APAE Anápolis	Anápolis	GO	Eliane Pereira dos Santos
Hospital Infantil João Paulo II	Belo Horizonte	MG	Alberto Andrade Vergara
Consultorio Francisco Reis	Belo Horizonte	MG	Francisco José Caldeira Reis
Hospital Julia Kubitschek	Belo Horizonte	MG	Marcelo de Fuccio
Hospital Universitário da UFJF	Juiz de Fora	MG	Marta Cristina Duarte
Hospital Universitário Maria Aparecida Pedrossian	Campo Grande	MS	Valéria Cristina de Ruchkys
Instituto Materno Infantil de Pernambuco	Recife	PE	Murilo Carlos Amorim de Britto
Hospital Pequeno Príncipe	Curitiba	PR	Paulo Kussek
Hospital das Clínicas da UFPR	Curitiba	PR	Carlos Antônio Riedi
Hospital das Clínicas da UFPR - Adultos	Curitiba	PR	Mariane Martynychen
Instituto Fernandes Figueira	Rio de Janeiro	RJ	Laurinda Yoko Shinzato Higa
Hospital Universitário Pedro Ernesto - UERJ	Rio de Janeiro	RJ	Agnaldo J. Lopes

Name	City	State	Person in charge
Hospital de Pediatria da Universidadedo Rio Grande do Norte	Natal	RN	Vera Maria Dantas
Hospital de Clínicas de Porto Alegre - UFRGS	Porto Alegre	RS	Fernando Abreu e Silva
Hospital de Clínicas de Porto Alegre - Adultos	Porto Alegre	RS	Paulo de Tarso Roth Dalcin
Hospital São Lucas - PUCRS	Porto Alegre	RS	Paulo Cauduro Maróstica
Santa Casa de Porto Alegre	Porto Alegre	RS	Gilberto Bueno Fischer
Hospital Infantil Joana de Gusmão	Florianópolis	SC	Norberto Ludwig Neto
Hospital Infantil Jeser Amarante Faria	Joinville	SC	Tiago Neves Veras e Rafaela C. Benvenutti da Costa
Hospital das Clínicas da UNESP	Botucatu	SP	Giesela Fleischer Ferrari
Hospital das Clínicas da UNICAMP (pediatria)	Campinas	SP	Antonio Fernando Ribeiro
Hospital das Clínicas da USP Ribeirão Preto	Ribeirão Preto	SP	Lidia Alice Gomes M. M. Torres
Hospital de Base Fac Med de SJ Rio Preto	São José do Rio Preto	SP	Katia Izabel de Oliveira
Irmandade da Santa Casa de Misericórdia de São Paulo	São Paulo	SP	Neiva Damaceno
Instituto da Criança do Hospital das Clínicas da FMUSP	São Paulo	SP	Joaquim Carlos Rodrigues
Hospital da UNIFESP	São Paulo	SP	Sonia Mayumi Chiba
Hospital das Clínicas da FMUSP	São Paulo	SP	Rafael Stelmach
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