ORIGINAL ARTICLE
ARTIGO ORIGINAL

Cystic fibrosis demographics and healthcare resource utilization in the Brazilian healthcare system

Demografia da fibrose cística e utilização de recursos de saúde no sistema de saúde brasileiro

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DOI: 10.21115/JBES.v17.p59-70

Keywords:
cystic fibrosis, Datasus, healthcare resource utilization

ABSTRACT

Objective: To describe the demographic characteristics and hospital healthcare resource utilization (HCRU) in people with cystic fibrosis (CF) in Brazil before the introduction of CF Transmembrane Conductance Regulator modulators, using a public health database system. **Methods:** This retrospective, cross-sectional study described demographic characteristics of people with CF using the Outpatient Procedure Information System (SIA) and the Hospital Admission Information System (SIH) databases from 2015 to 2019. Patients were identified in the SIH in each year using the International Classification of Diseases (ICD-10) code E84. For the SIA, in addition to ICD-10, the record of ≥ 1 prescription of dornase alfa, pancreatic enzymes, or inhaled tobramycin in that year was also considered. All analyses were descriptive and stratified by age. **Results:** The number of people with CF in the SIA database increased from 3,737 in 2015 to 4,048 in 2019. Across all years, about half of the population was male (range: 51.4%-52.8%), aged ≥ 12 years, and resided in the southeast region. The number of hospitalizations increased from 1,300 in 2015 to 1,508 in 2019. Annual hospitalization rates per patient were higher among the youngest (<6 years) and oldest (≥18 years) age groups than in the ≥ 6 to < 18-year age group. Most hospitalizations (>80%) required treatment for pulmonary manifestations, and the average length of stay ranged from 11 to 15 days. **Conclusion:** CF poses substantial HCRU burden to the public health system in Brazil. This study showed that people with CF had a high rate of hospitalizations with lengthy stays per hospitalization.

Palavras-chave:
fibrose cística, Datasus, uso de recursos em saúde

RESUMO

Objetivo: Descrever as características demográficas e a utilização de recursos em saúde em pessoas com fibrose cística (FC), antes da introdução dos moduladores de CFTR (do inglês, CF *transmembrane conductance regulator*) no Brasil, utilizando a base de dados do sistema público de saúde brasileiro. **Métodos:** Estudo transversal, retrospectivo, descrevendo as características demográficas e a utilização de recursos em saúde de pessoas com FC. O estudo utilizou a base de dados do Sistema de Informação Hospitalar (SIH) e do Sistema de Informações ambulatoriais de Saúde (SIA) do Departamento de informática do Sistema Único de Saúde do Brasil (Datasus) entre 2015 e 2019. Pacientes foram identificados no SIH em cada ano por meio do código E84 da Classificação Internacional de Doenças (CID-10). Para o SIA, em adição ao CID-10, o registro de ≥ 1 prescrição de dornase alfa, enzimas pancreáticas ou tobramicina inalatória naquele ano também foi considerado. Todas as análises foram descritivas e estratificadas por idade. **Resultados:** O número

Received on: 18/12/2024. **Approved for publication on:** 07/10/2025.
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Institution that conducted the study: IQVIA Brasil.
Financial support: This study was funded by Vertex Pharmaceuticals Incorporated.
Congresses that this study was presented at: VIII Congresso Brasileiro Interdisciplinar de Fibrose Cística (April 2023).
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de pacientes no SIA aumentou de 3.737 em 2015 para 4.048 em 2019. Aproximadamente metade da população com FC era do sexo masculino (intervalo: 51,4%-52,8%), apresentava idade ≥ 12 anos e residia na região Sudeste. O número de hospitalizações na SIH aumentou de 1.300, em 2015, para 1.508, em 2019. Taxas anuais de hospitalização por paciente foram maiores nas faixas etárias de < 6 anos e ≥ 18 anos. A maioria das hospitalizações (>80%) requereu tratamento de manifestações pulmonares, e o tempo médio de hospitalização variou de 11 a 15 dias. **Conclusão:** A FC apresenta uma carga substancial para o paciente e para o sistema de saúde em termos de uso de recursos hospitalares e ambulatoriais. Este estudo evidenciou que pessoas com FC tiveram alta taxa anual de hospitalizações com longa permanência de internação.

Introduction

Cystic fibrosis (CF) is a life-threatening genetic disease that affects > 105,000 people worldwide (Ahern *et al.*, 2022; Guo *et al.*, 2022; Cystic Fibrosis Canada, 2023; Cystic Fibrosis Foundation Patient Registry, 2023; Zolin *et al.*, 2023). In Brazil, the incidence is estimated to be 1 in 7,576 live births (Raskin *et al.*, 2008). According to the Brazilian Registry, the prevalence of CF in the country varies from 44.1% in the Southeast region to 3.4% in the North region (REBRAFC, 2021), and the average (standard deviation [SD]) age of death was 21.5 (9.92) years old in 2021 (REBRAFC, 2021).

Dysfunction of the CF transmembrane conductance regulator (*CFTR*) gene leads to the production of disruptive viscous secretions along epithelial membranes in the lung and other organs, such as the pancreas, liver, and intestine (Dickinson & Collaco, 2021). The progression of CF is not homogeneous and can start anytime from birth to several decades later (Chen *et al.*, 2021). The typical natural history of CF involves intermittent episodes of pulmonary exacerbations, the eventual advancement of lung disease to respiratory failure, and premature death (Turcios, 2020). People with CF experience, on average, a decline in lung function by 1-3 percentage points annually (Liou *et al.*, 2010). Lung disease remains the leading cause of complications and mortality in people with CF (Turcios, 2020). CF is associated with substantial healthcare resource utilization (HCRU) due to its chronic and progressive nature. Studies in the United States, France, and Australia have shown substantial HCRU, which is primarily attributable to hospital stays and medications (Lieu *et al.*, 1999; Ouyang *et al.*, 2009; Briesacher *et al.*, 2011; van Gool *et al.*, 2013; Grosse *et al.*, 2018; Thorat *et al.*, 2021; Durieu *et al.*, 2022).

Significant advances have been made to improve CF treatment and management, including the discovery of the *CFTR* gene, the implementation of widespread screening programs with early diagnosis, a better understanding of the natural course of the disease, improvements in the standard of care, and ultimately, the development of highly effective CFTR modulators (Scotet *et al.*, 2020). These advances have substantially improved overall survival rates (Scotet *et al.*, 2020). In Brazil, newborn screening for CF started in 2001, and by 2021, 61% of all CF diagnoses were through newborn screening (Brazilian Cystic Fibrosis Study Group, 2020). The first CFTR modulator, ivacaftor, was reimbursed by the Brazilian public healthcare system in 2022, and the triple therapy elexacaftor/tezacaftor/ivacaftor was made available more recently, in 2024 (Ministério da Saúde, 2023; Ministério da Saúde, 2024). This study, however, focuses on the period before the introduction of CFTR modulators in Brazil (2015 to 2019).

To better understand the burden of disease in CF, it is important to study the patient population at a country level, including demographic data and healthcare burden. In most countries in Latin America, it is challenging to know the number of people with CF due to the absence of national registries and newborn screening programs. Brazil has a comprehensive registry, the Brazilian Cystic Fibrosis Registry, which includes a total of 6,427 people with CF from 2009 to 2021 and 3,240 people with CF with at least one follow-up visit in 2021 (REBRAFC, 2021).

While the Brazilian Cystic Fibrosis Registry is a valuable resource for understanding clinical aspects of CF, it does not report HCRU associated with CF, which is essential for planning healthcare resource allocation. Because of this and to understand the demographic characteristics of people with CF in Brazil, along with assessing the HCRU attributed to the disease, we used data from the public health database system since the majority of people with CF are referred to a public CF center within the national healthcare system (Procianoy *et al.*, 2023). This study uses the public health database system to describe the demographic characteristics and hospital HCRU for people with CF in Brazil.

Methods

Study design

This study was a retrospective, observational, cross-sectional descriptive study of people with CF in Brazil, utilizing public health databases from the Informatics Department of the Brazilian Health System (Datasus) from 2015 to 2019. Annual cross-sectional analyses were conducted over the study period, from January 1, 2015, to December 31, 2019; the study period was intentionally terminated at the end of 2019 to avoid bias due to the COVID-19 pandemic, as well as to avoid bias due to the availability of CFTR modulators in the subsequent years. We used two databases within Datasus to describe the demographic characteristics of people with CF and the HCRU attributed to CF during the specified study period - further described in the "Data Source" section.

Data source

This study was based on outpatient and inpatient administrative data from DATASUS, the Informatics Department of the Brazilian Healthcare System, which is the body responsible for collecting, processing, and disseminating healthcare data in Brazil (Saúde, 2024). Therefore, our study includes data from procedures performed within the Brazilian Health System, which covers over 150 million people in Brazil. Two datasets were considered: the Inpatient Information System (SIH [Sistema de Informações Hospitalares]) and the Outpatient Information System (SIA [Sistema de Informações Ambulatoriais]). SIH and SIA are administrative databases for reimbursement purposes only (Sociais, 2024; Sociais, 2024a), and specific details of the contents in the databases are described elsewhere (Ali *et al*., 2019). Due to its administrative nature, SIH and SIA do not contain clinical data (*e.g*., signs and symptoms). Therefore, the cause of admission according to the International Classification of Diseases, tenth revision code (ICD-10), and the procedures performed during hospitalization were used to identify eligible people with CF. Additionally, data related to patients' age, hospitalization, diagnosis at entry (ICD-10 based), procedures prescribed and performed, and in-hospital length of stay (days) were also extracted.

Study population

To describe the CF population in Brazil, people with CF in the SIA were selected during each cross-sectional year if they had ≥ 1 medical claim with primary or secondary diagnosis of CF and ≥ 1 prescription of one of three medications commonly used for CF treatment (dornase alfa, pancreatic enzymes, or inhaled tobramycin). Diagnosis of CF was based on ICD-10 Clinical Modification codes E84, E84.0, E84.1, E84.8, and E84.9.

For the hospital-related HCRU attributed to CF in Brazil, participants in the SIH were identified by having at least one medical claim with a primary or secondary diagnosis of CF, defined using the same ICD codes listed above. Data between the SIA and SIH could not be linked at the individual level, so it was assumed that the people with CF who were identified in the SIH database were a subset of those identified in the SIA.

Study endpoints and analyses

The baseline demographics and characteristics of people with CF in Brazil were analyzed annually using data from the SIA. Across annual cross-sectional analyses, age was defined as that reported in the SIA database on January 1 of each year.

For hospital-related HCRU in the SIH database, we analyzed hospitalizations (number, length of stay [LOS] in days, and age at hospitalization), intensive care unit (ICU) admissions (number and LOS in days), procedures during hospitalization, occurrence of lung transplants, and deaths in the hospital setting (number and age at death) for each of the annual cross-sectional analyses. Annual rates of hospitalizations were calculated in relation to the total CF population identified in the SIA for each cross-sectional year. Annual rates of hospitalizations were calculated by dividing the total number of hospitalizations from the SIH database by the total number of people with CF from the SIA database for each cross-sectional year. Annual ICU admission rates and the proportion of people with CF undergoing select hospital procedures were reported as a subset of total hospitalizations.

Descriptive statistics were reported for each of the five annual cross-sectional analyses of the study period (2015, 2016, 2017, 2018, and 2019) by four age groups (0 to < 6, 6 to < 12, 12 to < 18, and ≥ 18 years). Count and percentage present categorical variables, and the mean and standard deviation summarize continuous variables. Data were analyzed using Python version 3.6.9.

RESULTS

Descriptive characteristics of the study population

The number of people with CF who met the eligibility criteria in the SIA in 2015 was 3,737, and in 2019, it was 4,048 (Table 1). The overall demographic profile of people with CF remained consistent in each annual cross-sectional analysis during the study period, with a slight majority of the population being male (range 51.4%-52.8%) and the most significant percentage residing in the Southeast region of Brazil (range 48.3%-53.0%). Similarly, the proportion of people with CF across age groups varied marginally from 2015 to 2019, with almost half belonging to the pediatric age groups < 6 years (range 22.0%-23.4%) and 6 to < 12 years (range 25.3%-26.7%). Adults (aged ≥ 18 years) represented about a third of all people with CF (29.7%-33.4%), and adolescents (aged 12 to < 18 years) represented 17.4%-20.8% of the total people with CF in each year (Figure 1A).

Hospital-related healthcare resource utilization

The total number of hospitalizations in people with CF increased from 1,300 in 2015 to 1,508 in 2019 (Figure 1B). Across the annual cross-sectional analyses, children with CF aged < 6 years and 6 to < 12 years accounted for 44% to 52% of hospitalizations, respectively. The annual hospitalization rates were, in general, highest in the youngest (<6 years) and oldest (≥18 years) age groups across the study period (Figure 1B). These ranged from 0.35 to 0.39 in children aged < 6 years and from 0.34 to 0.39 in adults (aged ≥ 18 years) in each of the annual cross-sectional analyses during the study period (Figure 2A). The mean hospital LOS per hospitalization for people with CF was similar across all age groups over the study period and ranged from 11 to 15 days (Figure 2B).

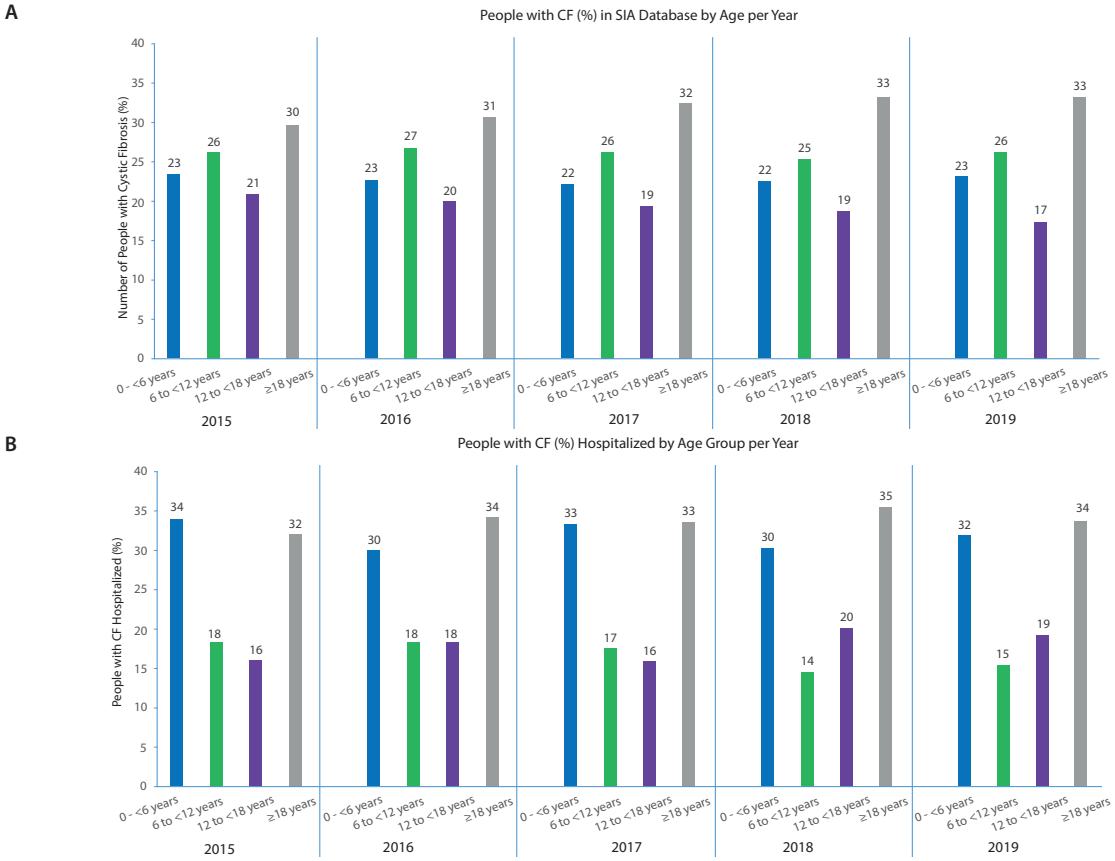
Among all hospitalizations, ICU admissions accounted for 2.3% (85/3,737) in 2015 and 2.9% (119/4,048) in 2019. The overall annual rate of ICU admissions among hospitalized people with CF ranged from 0.07 to 0.08 over the study period. When examined by age groups, the annualized rate of ICU admissions per patient was highest in children aged < 6 years (0.07 to 0.09) and in adults aged ≥ 18 years (0.06 to 0.1) during the study period (Figure 2C). The mean ICU LOS across the study period was greatest (7 to 12 days) in the children aged < 6 years (Figure 2D).

Table 1. Demographics of people with CF in Brazil using the SIA database, 2015 to 2019

	2015				2016			
Age group (years)	**0 to <6**	**6 to <12**	**12 to <18**	**≥18 years**	**0 to <6**	**6 to <12**	**12 to <18**	**≥18 years**
Patients – N (%)	873 (23.4)	975 (26.1)	779 (20.8)	1,110 (29.7)	861 (22.7)	1,013 (26.7)	758 (20.0)	1,161 (30.6)
Age*, years								
Mean (SD)	3.9 (1.6)	9.5 (1.7)	15.3 (1.7)	34.5 (16.0)	3.8 (1.6)	9.4 (1.7)	15.4 (1.7)	33.9 (15.9)
Median (IQI)	4 (3)	10 (3)	15 (3)	28 (19)	4 (2)	9 (3)	15 (3)	28 (18)
Minimum	1	7	13	19	1	7	13	19
Maximum	6	12	18	93	6	12	18	90
Gender – N (%)								
Male	448 (51.3)	524 (53.7)	434 (55.7)	564 (50.8)	457 (53.1)	520 (51.3)	421 (55.5)	583 (50.2)
Female	425 (48.7)	451 (46.3)	345 (44.3)	546 (49.2)	404 (46.9)	493 (48.7)	337 (44.5)	578 (49.8)
Race/ethnicity – N (%)								
White	157 (18.0)	142 (14.6)	142 (18.2)	214 (19.3)	154 (17.9)	175 (17.3)	154 (20.3)	228 (19.6)
Black and other	112 (12.8)	134 (13.7)	95 (12.2)	119 (10.7)	111 (12.9)	159 (15.7)	106 (14.0)	136 (11.7)
Missing	604 (69.2)	699 (71.7)	542 (69.6)	777 (70.0)	596 (69.2)	679 (67.0)	498 (65.7)	797 (68.6)
Geographic location – N (%)								
Southeast	484 (55.4)	450 (46.2)	368 (47.2)	546 (49.2)	475 (55.2)	470 (46.4)	342 (45.1)	544 (46.9)
South	143 (16.4)	202 (20.7)	166 (21.3)	243 (21.9)	141 (16.4)	197 (19.4)	182 (24.0)	271 (23.3)
Midwest	70 (8.0)	70 (7.2)	58 (7.4)	47 (4.2)	69 (8.0)	84 (8.3)	57 (7.5)	56 (4.8)
Northeast	146 (16.7)	214 (21.9)	162 (20.8)	236 (21.3)	154 (17.9)	213 (21.0)	151 (19.9)	239 (20.6)
North	30 (3.4)	39 (4.0)	25 (3.2)	38 (3.4)	22 (2.6)	49 (4.8)	26 (3.4)	51 (4.4)
Unknown/missing	0	0	0	0	0	0	0	0
	2017				**2018**			
Age group (years)	**0 to <6**	**6 to <12**	**12 to <18**	**≥18 years**	**0 to <6**	**6 to <12**	**12 to <18**	**≥18 years**
Patients – N (%)	889 (22.0)	1,056 (26.2)	779 (19.3)	1,310 (32.5)	940 (22.5)	1,059 (25.3)	784 (18.8)	1,396 (33.4)
Age*, years								
Mean (SD)	3.8 (1.5)	9.3 (1.7)	15.4 (1.7)	34.5 (16.3)	3.9 (1.5)	9.4 (1.6)	15.6 (1.7)	34.2 (15.8)
Median (IQI)	4 (2)	9 (3)	15 (3)	28 (20)	4 (2)	9 (3)	16 (3)	28 (20)
Minimum	1	7	13	19	1	7	13	19
Maximum	6	12	18	91	6	12	18	90
Gender – N (%)								
Male	459 (51.6)	560 (53.0)	439 (56.4)	665 (50.8)	471 (50.1)	567 (53.5)	422 (53.8)	685 (49.1)
Female	430 (48.4)	496 (47.0)	340 (43.6)	645 (49.2)	469 (49.9)	492 (46.5)	362 (46.2)	711 (50.9)
Race/ethnicity – N (%)								
White	167 (18.8)	197 (18.7)	145 (18.6)	270 (20.6)	240 (25.5)	291 (27.5)	195 (24.9)	460 (33.0)
Black and other	109 (12.3)	168 (15.9)	123 (15.8)	153 (11.7)	147 (15.6)	179 (16.9)	136 (17.3)	184 (13.2)
Missing	613 (69.0)	691 (65.4)	511 (65.6)	887 (67.7)	550 (58.5)	592 (55.9)	373 (47.6)	701 (50.2)
Geographic location – N (%)								
Southeast	475 (53.4)	519 (49.1)	358 (46.0)	639 (48.8)	489 (52.0)	528 (49.9)	362 (46.2)	704 (50.4)
South	149 (16.8)	206 (19.5)	178 (22.8)	283 (21.6)	155 (16.5)	209 (19.7)	182 (23.2)	297 (21.3)
Midwest	72 (8.1)	75 (7.1)	58 (7.4)	64 (4.9)	70 (7.4)	68 (6.4)	49 (6.3)	73 (5.2)
Northeast	181 (20.4)	195 (18.5)	147 (18.9)	269 (20.5)	208 (22.1)	210 (19.8)	159 (20.3)	278 (19.9)
North	12 (1.3)	61 (5.8)	38 (4.9)	55 (4.2)	18 (1.9)	44 (4.2)	32 (4.1)	44 (3.2)
Unknown/missing	0	0	0	0	0	0	0	0

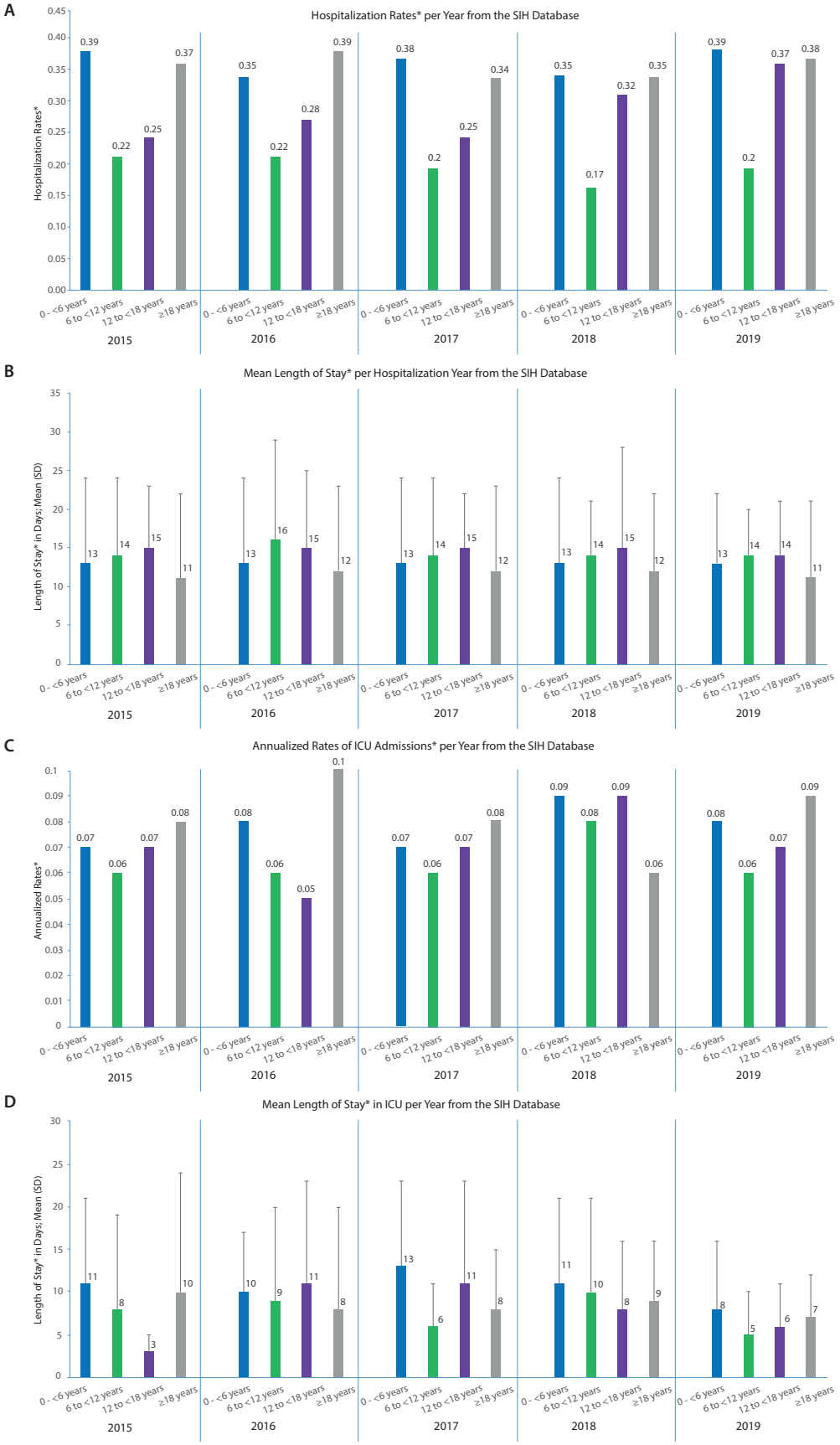
	2019			
Age group (years)	**0 to <6**	**6 to <12**	**12 to <18**	**≥18**
Patients – n (%)	937 (23.1)	1,062 (26.2)	704 (17.4)	1,345 (33.2)
Age*, years				
Mean (SD)	3.9 (1.5)	9.4 (1.6)	15.6 (1.7)	32.8 (15.0)
Median (IQI)	4 (2)	9 (3)	16 (3)	28 (17)
Minimum	1	7	13	19
Maximum	6	12	18	92
Gender – n (%)				
Male	447 (47.7)	562 (52.9)	387 (55.0)	683 (50.8)
Female	490 (52.3)	500 (47.1)	317 (45.0)	662 (49.2)
Race/ethnicity – n (%)				
White	240 (25.6)	291 (27.4)	195 (27.7)	460 (34.2)
Black and other	147 (15.7)	179 (16.9)	136 (19.3)	184 (13.7)
Missing	550 (58.7)	592 (55.7)	373 (53.0)	701 (52.1)
Geographic location – n (%)				
Southeast	517 (55.2)	558 (52.5)	348 (49.4)	720 (53.5)
South	157 (16.8)	223 (21.0)	164 (23.3)	321 (23.9)
Midwest	71 (7.6)	76 (7.2)	49 (7.0)	80 (5.9)
Northeast	174 (18.6)	171 (16.1)	108 (15.3)	184 (13.7)
North	18 (1.9)	34 (3.2)	35 (5.0)	40 (3.0)
Unknown/missing	0	0	0	0

*Age at index date: considered the age calculated between the date of birth and the first ICD-10 claim in database in the respective year.
ICU: intensive care unit; IQI: interquartile interval; people with CF: people with cystic fibrosis; SD: standard deviation; SIA: outpatient procedure information system.



CF: cystic fibrosis; SIA: outpatient procedure information system; SIH: hospital admission information system.

Figure 1. Proportion of people with CF by age groups (**A**) as reported in the SIA database and (**B**) hospitalized as reported in the SIH database



* Annualized rate of duration: total number of days at hospital or ICU summed across all CF patients from the SIH database, divided by the number of people with CF from the SIA database for each respective year and age group.

* Length of stay: difference between the start date of hospital admission and the end date of hospital admission in days.

*Annualized rate of ICU admissions: total number of ICU admissions from the SIH divided by the total number of hospitalizations from the SIH database for each respective year and age group.

* Difference between the start date of ICU admission and the end date of ICU admission in days.

CF: cystic fibrosis; ICU: intensive care unit; SD: standard deviation; SIA: outpatient procedure information system; SIH: hospital admission information system.

Figure 2. Annual rates of (**A**) hospitalizations, **(B**) length of stay (days), (**C**) ICU admissions, and (**D**) ICU length of stay of people with CF by age group in the SIH database. The annual rate of hospitalization and ICU admissions was calculated by dividing the total number of hospitalizations from the SIH database by the total number of patients with CF, according to age groups from the SIA database, for each respective year

Across the annual cross-sectional years, most procedures performed in the hospital were related to pulmonary manifestations of CF (>80%; Supplementary Table 1). In addition to procedures, most people with CF required CF treatments for pulmonary manifestations (over 75% across the study period). More than 60% of people with CF who were hospitalized with respiratory disorders and systemic complications required physical therapy. Across all the age groups, approximately 14%-25% of CF hospitalizations required inhalation or nebulization, bacterial culture, and chest X-ray during the study period. Notably, children aged < 6 years, 6 to < 12 years, and 12 to < 18 years required a higher number of procedures (except chest x-rays) than the oldest age groups (≥18 years).

There were no records of lung transplantation from 2015 to 2017. Seven (0.17%) and eleven (0.27%) lung transplants were reported in 2018 and 2019, respectively (Table 2). The inpatient death rate among people with CF was approximately 2% each year.

Discussion

The current study provides a real-world annual cross-sectional descriptive assessment of demographic characteristics and hospital HCRU for people with CF in the Brazilian public healthcare system between 2015 and 2019. The study identified 3,737 people with CF in 2015 and 4,048 in 2019. Most people with CF identified in this study resided in the Southeast region, were primarily male, and aged ≥ 12 years. This study also assessed hospital HCRU in people with CF between 2015 and 2019; the hospitalization rates were highest in children aged < 6 years and adults aged ≥ 18 years, with extended hospital LOS across all age groups but especially among children. As expected, most hospitalizations were associated with pulmonary manifestations. The study also reported a minimal number of lung transplants between 2015 and 2019. The findings from this study highlight the considerable burden of HCRU attributed to CF in the Brazilian healthcare system.

The number of people with CF in the SIA database was overall higher than that reported by the REBRAFC from 2015 to 2019 (Brazilian Cystic Fibrosis Study Group). The organization of the Brazilian public health system might partially explain this difference. Many specialized CF reference centers providing data to the REBRAFC are part of highly complex hospitals. Due to the healthcare system's principles of responsibility, these centers are primarily located in state capitals, potentially limiting access for patients residing in more remote areas. As a result, a certain proportion of people with CF may receive treatment outside these reference centers (*i.e.*, in their municipalities of residence) (da Mota Almeida Peroni *et al.*, 2019; Zuppo Laper *et al.*, 2024). Another factor is that some people with CF did not agree to participate in the registry data collection. Finally, it is also possible that the greater number of people with CF in the SIA reflects the increasing number of diagnoses due to expanded newborn screening for CF in Brazil (Athanazio *et al.*, 2017; Ministério da Saúde, 2021), which may not be captured by specialized CF centers. However, despite the difference in the total number of people with CF, the proportion of pediatric patients in the total CF population observed in our study is consistent with that reported in REBRAFC (Brazilian Cystic Fibrosis Study Group, 2021). Our results on geography are consistent with those reported in REBRAFC, which noted that most people with CF resided in the Southeast region of Brazil (Brazilian Cystic Fibrosis Study Group, 2021), likely due to better access to healthcare in this area.

In terms of hospital HCRU among people with CF, the number of hospitalizations due to CF in the SIH ranged from 1,300 in 2015 to 1,508 in 2019, representing an annual rate of hospitalizations from 40.4 to 37.3 per 100 patients and a hospital LOS per hospitalization ranging from 11 to 15 days. Many of the hospitalizations in this study required treatment and/or procedures for pulmonary manifestations of CF, which is consistent with the natural course of the disease. Our results are also in agreement with an HCRU study conducted in Canada, which reported an annual rate of 39.8 hospitalizations per 100 patients with CF (Skolnik *et al.*, 2021). It is important to note that the CF annual rate of hospitalizations and LOS per hospitalization was higher than that of other respiratory diseases in Brazil, such as asthma, which has a hospitalization rate ranging from 1.1 to 13.9 per 100 patients and a mean hospital LOS of 3 days, and pneumonia with a hospitalization rate of up to 15 per 100 patient-years in children aged ≤ 4 years (Cardoso *et al.*, 2017; Zhao *et al.*, 2020; Fonseca *et al.*, 2021; Magalhães *et al.*, 2021). The same trend could be seen in other countries such as the USA and Ethiopia, where the average LOS per CF hospitalization is considerably longer than that reported for

Table 2. Number of inpatient deaths and lung transplantations among people with CF in the SIH database

Outcome variable	2015	2016	2017	2018	2019
People with CF in the outpatient procedure information system database – n	3,737	3,793	4,034	4,179	4,048
Death in the hospital setting in the SIH database – n (%)[a]	65 (1.7)	71 (1.9)	73 (1.8)	66 (1.6)	67 (1.7)
Lung transplant in the SIH database – n (%)[b]	0	0	0	7 (<1)	11 (<1)

[a] Death at hospital: total number of in-hospital deaths divided by the number of patients with CF from the SIA database for each respective year.
[b] Number of lung transplantations – N (%): total number of lung transplantations divided by the total number of patients with CF from the SIH database for each respective year.
CF: cystic fibrosis; SIH: hospital admission information system.

patients with other respiratory conditions (Kaur *et al.*, 2015; Williams *et al.*, 2018; Amare *et al.*, 2022). Importantly, the hospital burden attributed to CF-related hospital LOS in Brazil (from 11 to 15 days) is substantially larger than other conditions, such as non-communicable diseases (*e.g.*, cardiovascular diseases, communicable diseases, and maternal, perinatal, and nutritional conditions), which have a mean LOS of 5 days, regardless of the patients' age (Zhao *et al.*, 2020).

Regarding the HCRU by age group, our study identified that over 50% of all hospitalizations were in children aged < 12 years across all study years, with the age group of < 6 years contributing up to 34% of all hospitalizations despite comprising around 23% of the study population. The literature has shown that children and older adults with CF have substantial HCRU due to early onset and the progressive nature of the disease, resulting in high rates of hospitalization from early ages to adult life (Perkins *et al.*, 2021; Thorat *et al.*, 2021), differing from trends observed in other respiratory diseases, such as asthma, in which hospitalizations have a declining trend by age (Fonseca *et al.*, 2021). Our study reported that the high hospitalization rate in pediatric patients is consistent with findings from other real-world studies. A single-center study in the USA identified that the proportion of people with CF with at least one inpatient admission was 33.3% in children aged ≤ 11 years, which is lower than the rate observed in our study (Perkins *et al.*, 2021). Specifically, regarding younger children, our study reported that over one-third of all hospitalizations occurred in children aged < 6 years, with extended hospital LOS observed in this age group. Other published literature reports that up to 30% of people with CF have at least one pulmonary exacerbation-related hospitalization during their first years of life, some require repeated admissions, and no change in the proportion of young patients hospitalized over time (Martiniano *et al.*, 2021; Huang *et al.*, 2022). A study evaluating the burden of CF in children aged < 12 years in the USA identified that the hospitalization rate among children aged ≤ 6 years was higher than that in children aged > 6 years (Bresnick *et al.*, 2021). A Brazilian study also identified that 25% of all deaths among people with CF were reported in children aged ≤ 4 years (Santo & Silva-Filho, 2021). It is possible that factors such as high prevalence of malnutrition, high prevalence of early *Pseudomonas* colonization, late diagnosis, as well as other clinical and socioeconomic factors, also contribute to increased burden of CF at early ages in Brazil, as observed in other Latin American countries (Martins *et al.*, 2018; Bustamante *et al.*, 2021; Godoy *et al.*, 2023).

Although our study did not evaluate costs, some published evidence suggests that hospital costs are responsible for the majority of HCRU costs in CF. An Australian study reported that the most significant proportion of costs in CF management is incurred in the hospital sector, accounting for 50%-77% of costs, followed by pharmaceuticals, which range from 13% to 33% (van Gool *et al.*, 2013). Our study reported the HCRU burden attributed to CF, including hospital stays, procedures, and medications, suggesting that the cost burden associated with CF to the Brazilian healthcare system is likely substantial.

Given the observational nature of the study, it is subject to inherent limitations associated with observational real-world research, *e.g.*, inconsistent and incomplete data collection or misreported ICD-10 codes (Santo & Silva-Filho, 2021). To minimize this misclassification, individuals identified in the SIA were required to have at least one prescription for a CF medication alongside an ICD-10 diagnosis code for CF. Data for specific demographic characteristics, such as race/ethnicity, were not well captured in the SIA database. Given that only ICD-10 codes were used to identify patients in the SIH database, misclassification in ICD-10 codes may have led to underestimation if CF was reported as a consequence or clinical manifestation of the disease, without the ICD-10 code for CF.

The REBRAFC encompasses hospitals and centers in both the private and public sectors, whereas the SIA and SIH only capture data from the public sector. Despite 75.8% of the Brazilian population relying solely on the Public Health System for their healthcare in 2020 (Agência Nacional de Saúde, 2023), not all hospitals have the necessary infrastructure to provide adequate treatment for patients with CF (Procianoy *et al.*, 2023). In these cases, the Brazilian government outsources the services to its supplementary system (Castro *et al.*, 2019). For this reason, it is possible that some CF cases may have been diagnosed or treated outside of the public healthcare system and were not captured in our analysis. An example of this is the fewer lung transplants reported among people with CF in this study than in those reported in the REBRAFC. In our study, a total of 18 lung transplants were reported between 2015 and 2019, while during the same time period, the REBRAFC reported a total of 62 lung transplants (Brazilian Cystic Fibrosis Study Group, 2020, Brazilian Cystic Fibrosis Study Group, 2021). The discrepancy between the two data points is unclear but could reflect inconsistency in coding or patients requiring transplants being treated outside of the public healthcare system, and thus not captured in the SIH database.

The cross-sectional nature of the study design did not provide longitudinal trends for outcomes, and no formal statistical comparison was applied; so, the interpretation of the results is only descriptive. Moreover, because the two databases were not linked through patient identification numbers, the number of people with CF in the SIA database was used as a proxy for calculating the hospitalization rate, given the unknown actual number of people with CF in the SIH database. Finally, outcomes related to medication use and comorbidities had missing/sparse data, which limited our ability to quantify this information.

Conclusion

This cross-sectional study highlights the considerable hospital HCRU burden of CF to the public healthcare system in Brazil from 2015 through 2019. People with CF experience a significant burden of hospitalizations, with lengthy stays per hospitalization contributing to substantial use of healthcare resources from the public healthcare system. These findings support the planning of resource allocation and health policy guidelines in Brazil.

Acknowledgements

The authors want to thank Paula Cristina Pungartnik, Suelen Silva, and Alessandro Bigoni of IQVIA Brazil for their work on the data analysis and writing/review of early drafts of the manuscript. We would also like to acknowledge the support provided by Krishan Mistry in the execution of the study. Vasilis Nikolaou provided biostatistics support, and Tracy Bunting-Early, PhD, of Vertex Pharmaceuticals Incorporated, provided writing support under the guidance of the authors. Shivali Arora, an employee of Vertex Pharmaceuticals Incorporated, provided additional editorial and project management support.

References

Agência Nacional de Saúde. Dados e Indicadores do Setor — Agência Nacional de Saúde Suplementar. 2023. Available from: https://www.gov.br/ans/pt-br/acesso-a-informacao/perfil-do-setor/dados-e-indicadores-do-setor. Accessed on: Jun 16, 2023.

Ahern S, Salimi F, Caruso M, Ruseckaite R, Wark P, Schultz A, et al. The Australian Cystic Fibrosis Data Registry (ACFDR) Annual Report, Monash University, Department of Epidemiology and Preventive Medicine. Report No 23. 2022.

Ali MS, Ichihara MY, Lopes LC, Barbosa GCG, Pita R, Carreiro RP, et al. Administrative Data Linkage in Brazil: Potentials for Health Technology Assessment. Front Pharmacol. 2019;10:984.

Amare RA, Fisseha G, Berhe A, Tirore LL. Incidence of recovery from severe pneumonia and its predictors among children 2-59 months admitted to pediatric ward of Ayder Comprehensive Specialized Hospital, Tigray, Ethiopia: A retrospective Cohort study. J Family Med Prim Care. 2022;11(9):5285-92.

Athanazio RA, Silva Filho LVRF, Vergara AA, Ribeiro AF, Riedi CA, Procianoy EDFA, et al.; Grupo de Trabalho das Diretrizes Brasileiras de Diagnóstico e Tratamento da Fibrose Cística. Brazilian guidelines for the diagnosis and treatment of cystic fibrosis. J Bras Pneumol. 2017;43(3):219-45.

Brasil. Ministério da Saúde. DATASUS. Informatics Department of SUS. 2024. Available from: http://www2.datasus.gov.br/DATASUS/index.php.

Brazilian Cystic Fibrosis Study Group (GBEFC). Brazilian Cystic Fibrosis Registry (REBRAFC) Annual Report 2018. 2018.

Brazilian Cystic Fibrosis Study Group (GBEFC). Brazilian Cystic Fibrosis Registry (REBRAFC) Annual Report 2019. 2019.

Brazilian Cystic Fibrosis Study Group (GBEFC). Brazilian Cystic Fibrosis Registry (REBRAFC) Annual Report 2020. 2020.

Brazilian Cystic Fibrosis Study Group (GBEFC). Brazilian Cystic Fibrosis Registry (REBRAFC) Annual Report 2021. 2021.

Bresnick K, Arteaga-Solis E, Millar SJ, Laird G, LeCamus C. Burden of cystic fibrosis in children <12 years of age prior to the introduction of CFTR modulator therapies. BMJ Open Respir Res. 2021;8(1):e000998.

Briesacher BA, Quittner AL, Fouayzi H, Zhang J, Swensen A. Nationwide trends in the medical care costs of privately insured patients with cystic fibrosis (CF), 2001-2007. Pediatr Pulmonol. 2011;46(8):770-6.

Bustamante AE, Fernández LT, Rivas LC, Mercado-Longoria R. Disparities in cystic fibrosis survival in Mexico: Impact of socioeconomic status. Pediatr Pulmonol. 2021;56(6):1566-72.

Cardoso TA, Roncada C, Silva ERD, Pinto LA, Jones MH, Stein RT, et al. The impact of asthma in Brazil: a longitudinal analysis of data from a Brazilian national database system. J Bras Pneumol. 2017;43(3):163-8.

Castro MC, Massuda A, Almeida G, Menezes-Filho NA, Andrade MV, de Souza Noronha KVM, et al. Brazil's unified health system: the first 30 years and prospects for the future. Lancet. 2019;394(10195):345-56.

Chen Q, Shen Y, Zheng J. A review of cystic fibrosis: Basic and clinical aspects. Animal Model Exp Med. 2021;4(3):220-32.

Cystic Fibrosis Canada. The Canadian Cystic Fibrosis Registry 2021 Annual Data Report. Toronto, Canada. 2023.

Cystic Fibrosis Foundation Patient Registry. 2022 Annual Data Report. Bethesda, Maryland. 2023.

da Mota Almeida Peroni F, Lindelow M, Oliveira De Souza D, Sjoblom M. Realizing the right to health in Brazil's Unified Health System through the lens of breast and cervical cancer. Int J Equity Health. 2019;18(1):39.

Dickinson KM, Collaco JM. Cystic Fibrosis. Pediatr Rev. 2021;42(2):55-67.

Durieu I, Dalon F, Reynaud Q, Lemonnier L, Dehillotte C, Bérard M, et al. Temporal trends in healthcare resource use and associated costs of patients with cystic fibrosis. J Cyst Fibros. 2022;21(1):88-95.

Fonseca LGA, Florêncio RB, Lima INDF, Peroni Gualdi L. Time trend of Brazilian hospital admissions and deaths due to asthma among children and teenagers, 1998-2019. PLoS One. 2021;16(3):e0248472.

Godoy C, Paixão DC, Boa-Sorte NCA, Amorim T, da Silva Filho LVRF, Souza EL. Five-year performance analysis of a cystic fibrosis newborn screening program in northeastern Brazil. J Pediatr (Rio J). 2023;99(1):23-30.

Grosse SD, Do TQN, Vu M, Feng LB, Berry JG, Sawicki GS. Healthcare expenditures for privately insured US patients with cystic fibrosis, 2010-2016. Pediatr Pulmonol. 2018;53(12):1611-8.

Guo J, Garratt A, Hill A. Worldwide rates of diagnosis and effective treatment for cystic fibrosis. J Cyst Fibros. 2022;21(3):456-62.

Huang L, Lai HJ, Antos N, Rock MJ, Asfour F, Howenstine M, et al. Defining and identifying early-onset lung disease in cystic fibrosis with cumulative clinical characteristics. Pediatr Pulmonol. 2022;57(10):2363-73.

Kaur BP, Lahewala S, Arora S, Agnihotri K, Panaich SS, Secord E, et al. Asthma: Hospitalization Trends and Predictors of In-Hospital Mortality and Hospitalization Costs in the USA (2001-2010). Int Arch Allergy Immunol. 2015;168(2):71-8.

Lieu TA, Ray GT, Farmer G, Shay GF. The cost of medical care for patients with cystic fibrosis in a health maintenance organization. Pediatrics. 1999;103(6):e72.

Liou TG, Elkin EP, Pasta DJ, Jacobs JR, Konstan MW, Morgan WJ, et al. Year-to-year changes in lung function in individuals with cystic fibrosis. J Cyst Fibros. 2010;9(4):250-6.

Magalhães LS, Policena GM, Carneiro VSM, Costa LDC, Costa MSND, Vieira MADS. Analysis of the trend of hospitalizations for asthma in children and adolescents in Brazil. J Pediatr (Rio J). 2021;97(3):309-14.

Martiniano SL, Elbert AA, Farrell PM, Ren CL, Sontag MK, Wu R, et al. Outcomes of infants born during the first 9 years of CF newborn screening in the United States: A retrospective Cystic Fibrosis Foundation Patient Registry cohort study. Pediatr Pulmonol. 2021;56(12):3758-67.

Martins JP, Forte GC, Simon MISDS, Epifanio M, Pinto LA, Marostica PJC. The role of neonatal screening in nutritional evolution in the first 12 months after diagnosis of cystic fibrosis. Rev Assoc Med Bras (1992). 2018;64(11):1032-7.

Ministério da Saúde. Indicadores da Triagem Neonatal no Brasil. 2021. Available from: https://www.gov.br/saude/pt-br/composicao/saes/sangue/pntn/indicadores-da-triagem-neonatal. Accessed on: Feb 20, 2024.

Ministério da Saúde, S. d. C., Tecnologia, Inovação e Complexo da Saúde - SECTICS. Relatório de Recomendação nº 844 - MEDICAMENTO. Elexacaftor/Tezacaftor/Ivacaftor para o tratamento de pacientes com fibrose cística com 6 anos de idade ou mais com ao menos uma mutação F508del no gene regulador de condução transmembrana de fibrose cística. Brasília (DF); 2023.

Ministério da Saúde. Secretaria de Ciência, T., Inovação e Complexo da Saúde - SECTICS. Relatório de Recomendação nº 892 - PROTOCOLOS & DIRETRIZES. Protocolo Clínico e Diretrizes Terapêuticas Fibrose Cística. Brasília (DF); 2024.

Ouyang L, Grosse SD, Amendah DD, Schechter MS. Healthcare expenditures for privately insured people with cystic fibrosis. Pediatr Pulmonol. 2009;44(10):989-96.

Perkins RC, Shah M, Sawicki GS. An evaluation of healthcare utilization and clinical charges in children and adults with cystic fibrosis. Pediatr Pulmonol. 2021;56(5):928-38.

Procianoy EDFA, Ludwig Neto N, Ribeiro AF. Patient care in cystic fibrosis centers: a real-world analysis in Brazil. J Bras Pneumol. 2023;49(1):e20220306.

Raskin S, Pereira-Ferrari L, Reis FC, Abreu F, Marostica P, Rozov T, et al. Incidence of cystic fibrosis in five different states of Brazil as determined by screening of p.F508del, mutation at the CFTR gene in newborns and patients. J Cyst Fibros. 2008;7(1):15-22.

Santo AH, Silva-Filho LVRFD. Cystic fibrosis-related mortality trends in Brazil for the 1999-2017 period: a multiple-cause-of-death study. J Bras Pneumol. 2021;47(2):e20200166.

Scotet V, L'Hostis C, Férec C. The Changing Epidemiology of Cystic Fibrosis: Incidence, Survival and Impact of the CFTR Gene Discovery. Genes (Basel). 2020;11(6):589.

Skolnik K, Ronksley P, Pendharkar SR, Wick JP, Quon BS, Williamson T. Hospital costs of Canadian cystic fibrosis patients. Can J Respir Crit Care Sleep Med. 2021;6:145-52.

Sociais, I. C. d. E. Sistema de Informacões Ambulatoriais do SUS-SIA/SUS. 2024.

Sociais, I. C. d. E. Sistema de Informacões Hospitalares do SUS-SIH/SUS. 2024a.

Thorat T, McGarry LJ, Bonafede MM, Limone BL, Rubin JL, Jariwala-Parikh K, et al. Healthcare resource utilization and costs among children with cystic fibrosis in the United States. Pediatr Pulmonol. 2021;56(9):2833-44.

Turcios NL. Cystic Fibrosis Lung Disease: An Overview. Respir Care. 2020;65(2):233-51.

van Gool K, Norman R, Delatycki MB, Hall J, Massie J. Understanding the costs of care for cystic fibrosis: an analysis by age and health state. Value Health. 2013;16(2):345-55.

Williams S, Gousen S, DeFrances C. National Hospital Care Survey Demonstration Projects: Pneumonia Inpatient Hospitalizations and Emergency Department Visits. Natl Health Stat Report. 2018;(116):1-11.

Zhao Q, Coelho MSZS, Li S, Saldiva PHN, Abramson MJ, Huxley RR, et al. Trends in Hospital Admission Rates and Associated Direct Healthcare Costs in Brazil: A Nationwide Retrospective Study between 2000 and 2015. Innovation (Camb). 2020;1(1):100013.

Zolin A, Orenti A, Jung A, van Rens J. The European Cystic Fibrosis Society Patient Registry (ECFSPR) Annual Report 2021. 2023

Zuppo Laper I, Camacho-Hubner C, Vansan Ferreira R, Leite Bertoli de Souza C, Simões MV, Fernandes F, et al. Assessment of potential transthyretin amyloid cardiomyopathy cases in the Brazilian public health system using a machine learning model. PLoS One. 2024;19(2):e0278738.

Supplementary information:

Supplementary Table 1. Procedures performed during hospitalization in the SIH database

	2015				2016				2017			
	0 to <6 N=440	6 to <12 N=238	12 to <18 N=208	≥18 N=414	0 to <6 N=396	6 to <12 N=243	12 to <18 N=232	≥18 N=451	0 - <6 N=447	6 to <12 N=235	12 to <18 N=213	≥18 N=450
Procedures performed – N (%)												
Inhalation or nebulization	95 (21.6)	63 (26.5)	49 (23.6)	74 (17.9)	75 (18.9)	48 (19.8)	39 (16.8)	83 (18.4)	65 (14.5)	37 (15.7)	44 (20.7)	85 (18.9)
Physical therapy for a patient with a respiratory disorder with systemic complications	199 (45.2)	102 (42.9)	113 (54.3)	132 (31.9)	177 (44.7)	130 (53.5)	117 (50.4)	156 (34.6)	211 (47.2)	109 (46.4)	126 (59.2)	145 (32.2)
Physical therapy for a patient with a respiratory disorder without systemic complications	53 (12.1)	41 (17.2)	38 (18.3)	47 (11.4)	53 (13.4)	49 (20.2)	37 (16.0)	75 (16.6)	68 (15.2)	47 (20)	49 (23)	81 (18)
CF treatment with pulmonary manifestation	377 (85.7)	212 (89.1)	185 (88.9)	340 (82.1)	314 (79.3)	216 (88.9)	207 (89.2)	363 (80.5)	362 (81.0)	205 (87.2)	199 (93.4)	385 (85.6)
Complete blood measurement	203 (46.1)	106 (44.5)	122 (58.7)	295 (71.3)	182 (46.0)	111 (45.7)	113 (48.7)	309 (68.5)	207 (46.3)	99 (42.1)	104 (48.8)	308 (68.4)
Potassium measurement	179 (40.7)	73 (30.7)	111 (53.4)	243 (58.7)	163 (41.2)	82 (33.7)	117 (50.4)	276 (61.2)	204 (45.6)	76 (32.3)	108 (50.7)	290 (64.4)
Glucose measurement	77 (17.5)	31 (13.0)	61 (29.3)	127 (30.7)	75 (18.9)	47 (19.3)	66 (28.5)	130 (28.8)	88 (19.7)	41 (17.5)	53 (24.9)	110 (24.4)
Sodium measurement	167 (38.0)	67 (28.2)	101 (48.6)	217 (52.4)	161 (40.7)	78 (32.1)	113 (48.7)	272 (60.3)	196 (43.9)	74 (31.5)	105 (49.3)	281 (62.4)
Creatinine measurement	140 (31.8)	80 (33.6)	107 (51.4)	275 (66.4)	143 (36.1)	89 (36.6)	121 (52.2)	300 (66.5)	168 (37.6)	84 (35.7)	122 (57.3)	305 (67.8)
Urea measurement	139 (31.6)	75 (31.5)	103 (49.5)	251 (60.6)	123 (31.1)	78 (32.1)	114 (49.1)	280 (62.1)	161 (36.0)	81 (34.5)	114 (53.5)	286 (63.6)
Oxygen therapy	3 (0.7)	1 (0.4)	2 (1.0)	7 (1.7)	3 (0.8)	5 (2.1)	6 (2.6)	9 (2)	5 (1.1)	7 (3.0)	6 (2.8)	18 (4)
Bacteria culture for identification	125 (28.4)	62 (26.1)	68 (32.7)	102 (24.6)	112 (28.3)	77 (31.7)	85 (36.6)	114 (25.3)	161 (36.0)	66 (28.1)	95 (44.6)	131 (29.1)
Chest X-ray	90 (20.5)	55 (23.1)	45 (21.6)	132 (31.9)	88 (22.2)	64 (26.3)	63 (27.2)	177 (39.3)	112 (25.1)	72 (30.6)	68 (31.9)	170 (37.8)
Pediatric enteral nutrition	29 (6.6)	25 (10.5)	0	0	24 (6.1)	30 (12.4)	0	0	43 (9.6)	20 (8.51)	0	0

Supplementary Table 1. Procedures performed during hospitalization in the SIH database **(continued)**

	2018				2019			
	0 to <6 N=414	**6 to <12 N= 199**	**12 to <18 N= 275**	**≥18 N=486**	**0 to <6 N=480**	**6 to <12 N= 232**	**12 to <18 N=289**	**≥18 N=507**
Procedures performed – N (%)								
Inhalation or nebulization	86 (20.1)	38 (19.1)	41 (14.9)	98 (20.2)	94 (19.6)	46 (19.8)	45 (15.6)	89 (17.6)
Physical therapy for a patient with a respiratory disorder with systemic complications	203 (49.0)	114 (57.3)	159 (57.8)	175 (36.0)	230 (47.9)	125 (53.9)	159 (55.0)	194 (38.3)
Physical therapy for a patient with a respiratory disorder without systemic complications	69 (16.7)	39 (19.6)	62 (22.6)	52 (10.7)	121 (25.2)	48 (20.7)	81 (28.0)	74 (14.6)
CF treatment with pulmonary manifestation	317 (76.6)	159 (79.9)	238 (86.6)	409 (84.2)	395 (82.3)	189 (81.5)	263 (91)	420 (82.8)
Complete blood measurement	202 (48.8)	101 (50.8)	145 (52.7)	324 (66. 7)	230 (47.9)	121 (52.2)	178 (61.6)	333 (65.7)
Potassium measurement	199 (48.1)	78 (39.2)	153 (55.6)	292 (60.1)	189 (39.4)	93 (40.1)	159 (55.0)	303 (59.8)
Glucose measurement	59 (14.3)	39 (19.6)	70 (25.5)	114 (23.5)	61 (12.7)	40 (17.2)	46 (15.9)	132 (26.0)
Sodium measurement	190 (45.9)	78 (39.2)	150 (54.6)	284 (58.4)	181 (37.7)	91 (39.2)	158 (54.7)	300 (59.2)
Creatinine measurement	181 (43.7)	82 (41.2)	158 (57.5)	305 (62.8)	167 (34.8)	103 (44.4)	159 (55.0)	328 (64.7)
Urea measurement	169 (40.8)	82 (41.2)	147 (53.5)	293 (60.3)	151 (31.5)	98 (42.2)	145 (50.2)	313 (61.7)
Oxygen therapy	7 (1.7)	13 (6.5)	6 (2.2)	21 (4.3)	2 (0.4)	3 (1.3)	5 (1.7)	23 (4.5)
Bacteria culture for identification	146 (35.3)	76 (38.2)	129 (46.9)	110 (22.6)	164 (34.2)	95 (41.0)	139 (48.1)	135 (26.6)
Chest X-ray	126 (30.4)	64 (32.2)	86 (31.3)	174 (35.8)	122 (25.4)	62 (26.7)	87 (30.1)	188 (37.1)
Pediatric enteral nutrition	40 (9.7)	24 (12.1)	0	0	22 (4.6)	28 (12.1)	0	0

The denominator for the percentage was the number of hospitalization events from the SIH database for each respective year and age group.
CF: cystic fibrosis; SIH: hospital admission information system.