Original Article

DOI: 10.5582/irdr.2017.01043

Nationwide trends of hospitalizations for cystic fibrosis in the United States from 2003 to 2013

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Summary **Cystic fibrosis (CF) is a multisystem autosomal recessive genetic disorder with significant advances in early diagnosis and treatment in the last decade. It is important to provide updated information regarding these changing demographics as they also reflect a considerable improvement in survival. We analyzed the National Inpatient Sample Database (NIS) in the United States for all patients in which CF was the primary discharge diagnosis (ICD-9: 277.0-277.09) from 2003 to 2013 to evaluate the rate of hospitalizations and determine the cost and mortality associated with CF along with other epidemiological findings. The statistical significance of the difference in the number of hospital discharges, lengths of stays and associated hospital costs over the study period was calculated. In 2003, there were 8,328 hospital discharges with the principal discharge diagnosis of CF in the United States, which increased to 12,590 discharges in 2013 ($p < 0.001$). The mean hospital charges increased by 57.64% from US$ 60,051 in 2003 to US$ 94,664 in 2013. The aggregate cost of hospital visits increased by 138.31% from US$ 500,105,727 to US$ 1,191,819,760. In the same time, the mortality decreased by 49.3 %. The number of inpatient discharges related to CF has increased from 2003 to 2013. This is due to increased life expectancy of CF patients, resulting in increased disease prevalence. There has been a significant increase in the mean and aggregate cost associated with CF admissions. Over the last decade, many advances have been made in the diagnosis and treatment of CF, consequentially leading to a significant transformation in the epidemiology and demographics of this chronic disease. Rising hospital costs associated with the care of CF patients necessitates future studies analyzing the diagnostic modalities, algorithms and treatment practices of physician's treating CF patients.**

Keywords: Cystic Fibrosis, epidemiology, length of stay, hospitalizations, mortality, healthcare burden

1. Introduction

Cystic fibrosis (CF) is a multisystem genetic disorder that was first formally described in 1938 by Dr. Dorothy Andersen (*1*). It arises from genetic defects in a single gene on chromosome 7, which encodes the cystic fibrosis transmembrane conductance regulator (CFTR), a chloride channel that is widely distributed in epithelial surfaces (*2*). Defects in CFTR function can lead to recurrent lung infections, sinus disease, pancreatic insufficiency, intestinal obstruction, male infertility and liver diseases in some individuals. Recurrent lung infections can lead to frequent pulmonary exacerbations often requiring inpatient care (*3*).

Around 30,000 individuals with CF currently live in the United States and approximately 70,000 reside worldwide (*4*). Even though a cure for CF has yet to be developed, patients have benefited from a variety of treatments to improve their symptoms. Over the

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last two decades, many advances have been made in the diagnosis and treatment of CF. Implementation of universal screening in 2010 has led to earlier diagnosis of newborn infants (*5*). In the United States Cystic Fibrosis Foundation Patient Registry, the number of newly diagnosed patients detected by newborn screening increased from 8% in 2000 to 72% in 2013 (*6*). This trend towards early diagnosis, specialized CF center care, strategies to avoid cross infection along with the advent of new drugs have contributed to considerable improvement in survival (*7*). The median predicted survival of patients with CF in the US had improved to 40.7 years by 2013 (*6*).

The epidemiology of CF has undergone a significant transformation. Information regarding medical care expenditures for CF is needed to evaluate the cost-effectiveness of new medical technology, therapies, and newborn screening techniques for CF. The aim of this study was to assess recent changes in the frequency and cost of inpatient admissions for a principal diagnosis of CF patients in the US from 2003 to 2013. We also sought to examine shifting demographics, in-hospital mortality, and length of hospitalization related to CF in these patients.

2. Materials and Methods

The National Inpatient Sample (NIS) database was used to obtain a population-based estimate of national trends for CF. The NIS database is a tool developed as a part of the Healthcare Cost and Utilization Project (HCUP), and is sponsored by the Agency for Healthcare Research and Quality. The NIS database is the largest publicly available all-payer inpatient care database in the United States. It is designed to approximate a 20% sample of United States community (nonfederal) hospitals, and is organized according to geographic region, hospital ownership, location, teaching status, and number of beds, among other characteristics. The 2003 NIS database contains a total of approximately 8 million records. The 2013 NIS database contains a total of about 7.1 million records drawn from 44 states and includes information from 4363 hospitals. A comprehensive synopsis on NIS data is available at *http://www.hcup-us.ahrq.gov*. The immense size of the NIS database provides an exceptional sample representation of the general US population. In order to identify cases of CF, the NIS database was queried for hospital data on all discharges with ICD-9-CM primary diagnosis codes of 277.00-277.09 (CF and manifestations associated with CF) from 2003 to 2013. The NIS database provides administrative data for analysis and does not include patient-specific clinical data.

2.1. *Variables recorded*

Patient demographics included age and gender. Hospital characteristics included the location (metropolitan *vs.* non-metropolitan), bed size (small, medium, and large) and region (Northeast, Midwest, South and West). Per HCUP net definitions, metropolitan areas are those with a population of at least 50,000 people. Areas with less than 50,000 people are non-metropolitan areas. Hospital bed size varies depending on the hospital's location and teaching status. Small hospitals range from 1 to 299 beds, medium hospitals range from 50 to 499 beds, and large hospitals range from 100 to 500 or more beds. The payer status for all admissions was also considered and divided into categories of Medicare, Medicaid, private insurance, uninsured, and other. "Hospital Charges" are defined as the amount the hospital charged for the patient's entire hospital stay, not including professional (physician) fees. NIS defines "aggregate charges" or the "national bill" as the sum of all charges for all hospital stays in the United States. "Length of stay" is the number of nights the patient remained in the hospital per stay.

2.2. *Statistical methods*

The trends for average length of stay, mean total charges, and total number of discharges specifically for the diagnosis of CF were plotted and analyzed from 2003 to 2013. The frequency of discharges with CF was calculated by dividing the annual number of discharges with a primary discharge diagnosis of CF by the total number of all discharges listed in the NIS for each year.

The temporal trend in the frequency of discharges, length of stay and mortality was assessed by linear and polynomial regression. The most appropriate functional form for the trend was assessed by examination of regression diagnostic plots. Linear shape was determined for frequency of discharges and mortality. P value < 0.05 was considered statistically significant. All analyses were performed using SAS (version 9.4, The SAS Institute, Cary, NC).

In addition, the frequency per 10,000 admissions was also calculated for each variable. The numbers represent the density of patients admitted and discharged with the primary diagnosis of CF compared with the total number of hospital discharges per category in that year. Each frequency was calculated by dividing the number of patients discharged with primary diagnosis of CF by the total discharges in the specific categorical variable for the same year and multiplying that number by 10,000. We viewed the counts as arising from a Poisson distribution, yielding Poisson rates that were compared over time using Poisson regression and yielded relative rates (RRs) and 95% confidence intervals (95% CI) that expressed the ratio of rate per 10,000 in 2013 to that of 2003.

3. Results

3.1. *Number and cost of cystic fibrosis discharges*

From 2003 to 2013, the total number of hospital discharges with the principal diagnosis of CF increased by 51.2% from 8,328 to 12,590 ($p < 0.001$) (Table 1). The majority of these patients were admitted due to a pulmonary exacerbation (approximately 72% in 2003 *vs*. 89% in 2013). The number of patients admitted by specific CF related ICD 9 codes are listed in Table 2. The frequency of hospital discharges from CF as the principal diagnosis increased from 2.24 per 10,000 discharges to 3.53 per 10,000 discharges (RR = 1.57, 95% CI: 1.53-1.62; $p < 0.001$). The linear trend of CF discharges also showed a statistically significant increase from 2003 to 2013 ($R^2 = 0.19666$; $p < 0.01$) (Figure 1).

The average length of stay of a CF patient showed a marginal increase from 10.1 days in 2003 to 10.3 days in 2013 (Figure 2). The mean hospital charges per patient increased 57.64% from US$ 60,051 in 2003 to US$ 94,664 in 2013 (Adjusted for inflation). The aggregate cost of hospital visits of patients with the principal diagnosis of CF increased 138.31% from US$ 500,105,727 in 2003 to US$ 1,191,819,760 in 2013.

The percent mortality of patients admitted with a principal diagnosis of CF decreased from 1.44% in 2003 to 0.71% in 2013 with a statistically significant decrease in the linear trend ($R^2 = 0.59914$; $p < 0.01$) (Figure 3).

3.2. *Patient characteristic by age*

The highest number of patient discharges in both 2003 and 2013 was noted in the 18-44 age group (Table 1). The frequency of discharges was noted to be higher in the 1-17 age group with the rates being 19.3 per 10,000 in 2003 and 32.8 per 10,000 in 2013, respectively (RR = 1.69, 95% CI: 1.62-1.77; $p < 0.001$). The increase in the frequency of discharge rates was most remarkable in age groups 1-17, 18-44, and 45-64. A drop in the rate of discharges was noted in the age group < 1 (RR = 0.81, 95% CI: 0.70-0.95; $p < 0.05$).

3.3. *Patient characteristics by sex*

The absolute number of CF admissions and discharges was noted to be greatest in females both in 2003 and 2013, with the frequency increasing from 2.03 per 10,000 discharges in 2003 to 3.36 per 10,000 discharges in 2013. (RR = 1.65, 95% CI: 1.59-1.72; $p < 0.001$). The increase for males went from 2.5 per 10,000 discharges in 2003 to 3.77 per 10,000 discharges in 2013 (RR = 1.51, 95% CI: 1.45-1.58; $p < 0.001$).

3.4. *Patient characteristics by payer group*

The relative frequency of CF discharges increased for all types of payer groups over this 10-year period. The highest absolute number of CF discharges was in the Medicaid group in both 2003 and 2013, which increased from 3.54 per 10,000 discharges in 2003 to 5.54 per 10,000 discharges in 2013 (RR = 1.56, 95% CI: 1.49-1.64; $p < 0.001$). While the rate of discharge in patients with private insurance was overall second, a higher increase was seen in this group (84.75%) as compared to patients with Medicaid (56.5%). While there was also an increase in discharges in the Medicare group (RR = 1.66, 95% CI: 1.54-1.80; $p < 0.001$), a drop in the number of discharges was noted in the Uninsured/Other group (RR = 0.05, 95% CI: 0.78-0.94; $p = 0.001$).

3.5. *Cystic Fibrosis discharges by hospital location, hospital characteristics and region*

Southern United States had the highest number of both CF discharges in 2003 as well as 2013. On the contrary, the West had the highest frequency of CF discharges in 2003 with 2.6 per 10,000 discharges and 2013 with 4.0 per 10,000 discharges. The Northeast carried the second highest frequency of discharges (2.4 per 10,000 discharges) in 2003. The frequency of CF discharges doubled in the Midwest from 2003 (1.9 per 10,000 discharges) to 2013 (3.9 per 10,000 discharges) (RR = 1.98, 95% CI: 1.87-2.10; $p < 0.001$). The frequency of discharges in the Northeast (RR = 1.38, 95% CI: 1.36-1.47; $p < 0.001$), South (RR = 1.49, 95% CI: 1.42-1.56, $p < 0.001$) and West (RR = 1.52, 95% CI: 1.43-1.61; $p < 0.001$) also showed a statistically significant increase in 2013 compared to 2003.

In 2003, CF patients were more likely to be admitted to a hospital with a small number of beds (3.05 per 10,000 discharges), whereas by 2013, they were more likely to be admitted to a hospital with a large number of beds (4.1 per 10,000 discharges). It was also noted that in both 2003 and 2013, greater than 95% of CF patients were admitted to a hospital located in a metropolitan area rather than a non-metropolitan area.

4. Discussion

The primary finding of this manuscript is that in a large multi-institutional observational cohort within the United States, there was a consistent increase in CF admissions from 2003 to 2013. The majority of these admissions were due to pulmonary exacerbations. There has been an increase in life expectancy of CF patients over the last 2 decades, which has led to an increase in disease prevalence (*8*). An increased prevalence leads to an increased number of patients with pulmonary or non-pulmonary exacerbations of CF requiring hospitalizations. According to the CF registry, there were 28,103 patients in the registry in 2013 compared to approximately 15,000 in 1986. In today's era, the number of adults living with CF continues to increase, while the number of children has

Table 1. Trends in characteristics of CF related hospitalizations from 2003 to 2013

Category	Categorical Variable	2003 Cystic Fibrosis (N,) C	2013 Cystic Fibrosis (N,) A	2003 Total (N,) D	2013 Total (N,) B	Cystic Fibrosis per 10,000 admissions in 2003	Cystic Fibrosis per 10,000 admissions in 2013	RR (95% CI)	*p* value
All discharges		8,328 (100.00)	12,590 (100.00)	37,074,605 (100)	35,597,792 (100)	2.24	3.53	1.57 (1.53-1.62)	< 0.001
Age group (years)	< 1	379 (4.55)	285 (2.26)	4,581,417 (12.36)	4,232,808 (11.9)	0.82	0.67	0.81 (0.70-0.95)	0.008
	1-17	3,415 (41.01)	4,570 (36.30)	1,762,383 (4.75)	1,393,028 (3.9)	19.3	32.8	1.69 (1.62-1.77)	< 0.001
	18-44	4,261 (51.17)	7,165 (56.91)	9,772,014 (26.36)	8,727,809 (24.5)	4.36	8.2	1.88 (1.81-1.95)	< 0.001
	45-64	207 (2.48)	520 (4.13)	8,086,876 (21.81)	8,753,270 (24.6)	0.25	0.6	2.32 (1.98-2.73)	< 0.001
	65-84	*	*	10,150,753 (27.38)	9,581,434 (26.9)	*	*		
Sex	Male	3,757 (45.11)	5,720 (45.43)	15,064,915 (40.63)	15,154,195 (42.6)	2.5	3.77	1.51 (1.45-1.58)	< 0.001
	Female	4,442 (53.34)	6,870 (54.57)	21,861,583 (58.97)	20,436,357 (57.4)	2.03	3.36	1.65 (1.59-1.72)	< 0.001
Payer	Medicare	1,015 (12.18)	1,715 (13.62)	13,761,829 (37.12)	13,986,550 (39.4)	0.95	1.22	1.66 (1.54-1.80)	< 0.001
	Medicaid	2,420 (29.06)	4,110 (32.64))	6,828,282 (18.42)	7,417,129 (20.9)	3.54	5.54	1.56 (1.49-1.64)	< 0.001
	Private Insurance	4,008 (48.12)	5,915 (46.98	13,555,962 (36.56)	10,851,650 (30.5)	2.95	5.45	1.84 (1.77-1.92)	< 0.001
	Uninsured/Other	865 (10.4)	850 (6.75)	2854601 (7.7)	3,287,333 (9.2)	3.03	2.5	0.85 (0.78-0.94)	0.001
Median income for zip code	Low ($0-35,999)	2,124 (25.50)	2,870 (22.80)	10,061,048 (27.14)	10,199,933 (28.65)	2.1	2.8	1.33 (1.26-1.41)	< 0.001
	Not low ($36,000+)	6,029 (72.39)	9,560 (75.93)	26,173,832 (70.60)	24,599,165 (69.10)	2.3	3.8	1.69 (1.63-1.74)	< 0.001
Owner	Government	1,137 (13.65)	2,660 (21.13)	5,172,217 (13.95)	4,291,755 (12.06)	2.2	6.2	2.82 (2.63-3.02)	< 0.001
	Private, not-for-profit	6,600 (79.25)	9,640 (76.57)	26,964,496 (72.73)	26,111,822 (73.35)	2.4	3.7	1.51 (1.46-1.56)	< 0.001
	Private, for-profit	592 (7.11)	290 (2.30)	4,937,891 (13.32)	5,194,215 (14.59)	1.2	0.55	0.47 (0.40-0.54)	< 0.001
Location	Non-metropolitan	387 (4.65)	155 (1.23)	5,583,485 (15.06)	3,954,149 (11.1)	0.7	0.4	0.57 (0.47-0.68)	< 0.001
	Metropolitan	7,941 (95.35)	12,435 (98.7)	31,471,911 (84.89)	31,643,643 (88.9)	2.5	3.9	1.56 (1.51-1.60)	< 0.001
Bed Size	Small	1,321 (15.87)	985 (7.82)	4,327,304 (11.67)	4,884,892 (13.7)	3.05	2.0	0.66 (0.61-0.72)	< 0.001
	Medium	1,907 (22.90)	2,780 (22.08)	9,613,451 (25.93)	9,512,936 (26.7)	1.98	2.9	1.47 (1.39-1.56)	< 0.001
	Large	5,099 (61.23)	8,825 (70.10)	23,114,641 (62.35)	21,199,964 (59.6)	2.2	4.1	1.89 (1.82-1.95)	< 0.001
Region	Northeast	1,765 (21.19	2,265 (17.99)	7,264,150 (19.59)	6,730,965 (18.9)	2.4	3.3	1.38 (1.36-1.47)	< 0.001
	Midwest	1,675 (20.11)	3,120 (24.78)	8,520,023 (22.98)	8,004,912 (22.5)	1.9	3.9	1.98 (1.87-2.10)	< 0.001
	South	3,017 (36.22)	4,375 (34.75)	14,205,434 (38.32)	13,818,031 (38.8)	2.1	3.1	1.49 (1.42-1.56)	< 0.001
	West	1,871 (22.47)	2,830 (22.48)	7,084,998 (19.11)	7,043,884 (19.8)	2.6	4.0	1.52 (1.43-1.61)	< 0.001

CF, cystic fibrosis.

Table 2. Admission by specific ICD- 9 codes for CF

ICD – 9 Code	2003 (%)	2013 (%)
277.0 (CF, not otherwise specified)	1,820 (21.85)	710 (5.64)
277.01 (CF with Meconium Ileus)	40 (0.5)	80 (0.6)
277.02 (CF with Pulmonary Manifestations)	5,989 (71.91)	11,235 (89.24)
277.03 (CF with Gastrointestinal Manifestations)	335 (4.02)	380 (3.01)
277.09 (CF with Other Manifestations)	144 (1.73)	185 (1.47)

CF, cystic fibrosis.

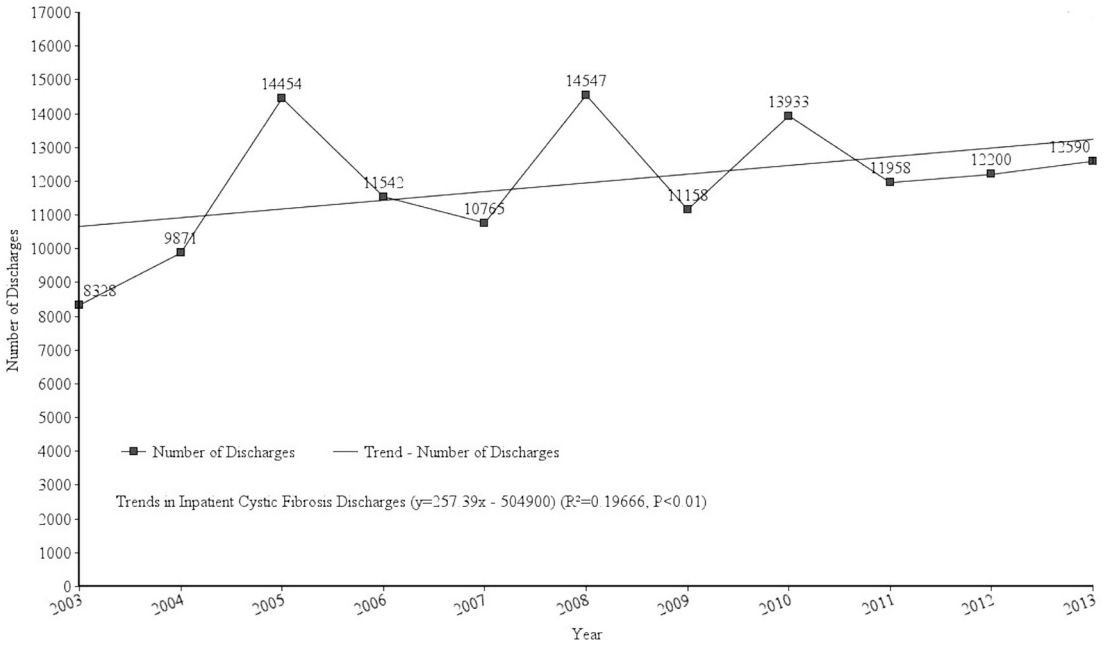

Figure 1. Trends of inpatient CF discharges. CF, cystic fibrosis.

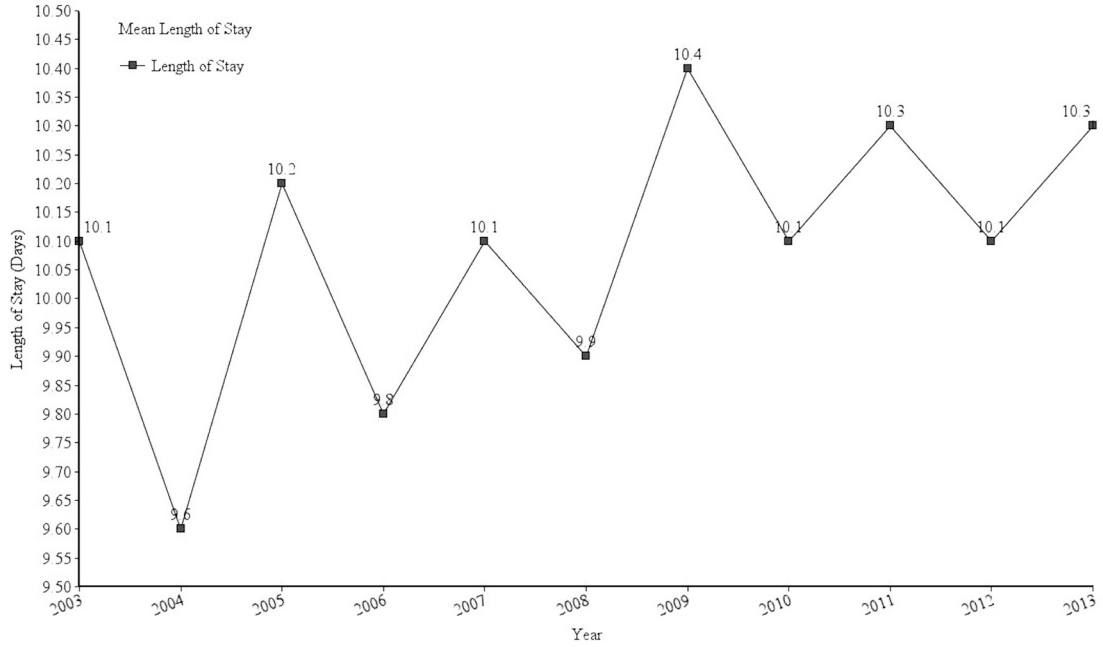

Figure 2. Trends of mean length of stay of CF patients. CF, cystic fibrosis.

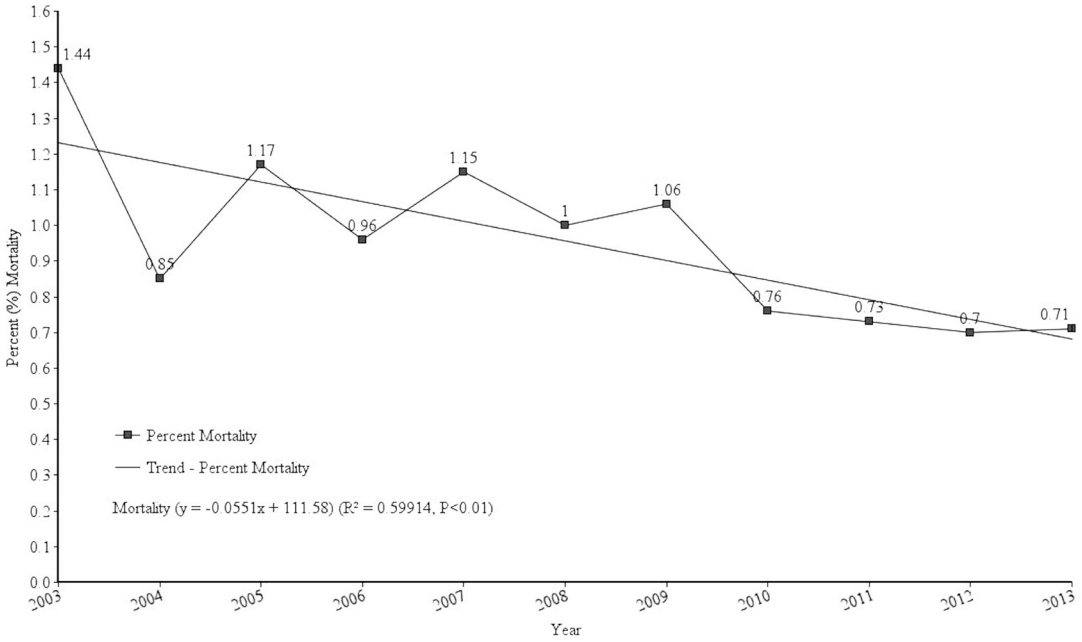

Figure 3. Trends in inpatient mortality of CF patients. CF, cystic fibrosis.

remained relatively stable; adults comprise 51.6 percent of the CF population, compared with 29.2 percent in 1986 (*4*). Mortality from CF is primarily related to respiratory deterioration, however, newer therapies in chronic inhaled antibiotics, mucociliary clearance, and CFTR modulators are improving treatment for CF. These therapies have reduced the number of pulmonary exacerbations and have led to an improved FEV1 and quality of life. This has translated over the years to a longer life span in the CF patient. The median predicted survival of patients with CF has increased to 40.7 years in the year 2013, compared to only 16 years of age in 1970 (*9*). Unsurprisingly, as the CF population grows older, there remains a higher chance of recurrent CF exacerbations during one's lifetime, ultimately leading to increasing health-care needs, including hospitalization.

The average length of stay of a CF admission showed a marginal increase from 2003 to 2013. Despite this minimal change in length of stay in the hospital, the aggregate costs of hospital visits for a patient with CF increased by 138% to approximately 1.1 billion USD from 2003 to 2013. Mean hospital costs for each patient also increased by 57.64% (from $ 60,051 per admission in 2003 to $ 94,664 per admission in 2013; adjusted for inflation). In the same time, the mortality decreased by 49.3 %. This increase in cost and decrease in mortality is a result of substantial changes in CF care between 2003 and 2013.

Implementation of universal screening in 2010 has led to earlier diagnosis of newborn infants (*5*). Of the persons diagnosed in 2013, 72.4% were diagnosed by newborn screening compared with only 8.0% of those diagnosed in 2000 (*10*). Daily regimens in CF patients include airway clearance therapy, inhaled mucolytic agents, antibiotics and a high calorie, high fat diet (*11,12*). Based on the CF registry, successive birth cohorts have shown improved pulmonary function. The majority of 18-year-olds now have normal lung function or mild obstruction, and an improved nutritional status with improved weight and height percentiles. Recommended therapies are more widely prescribed in 2013 compared to 2003. For example, the use of hypertonic saline has increased from 24.4 % in 2006 to 63.2 % in 2013 (*10*). Dornase alfa (also known as Pulmozyme®) was approved by the U.S. Food and Drug Administration (FDA) in 1993; its use increased from 67.6% of patients in 2003 to 85% of patients in 2013 (*10*). Inhaled aztreonam (also known as Cayston®) was FDA-approved in 2010 and its use increased from 2.5% of patients in 2008 to 41.5% of patients in 2013 (*10*). Over the past 4 years, the CF community has been introduced to the CFTR modulators, ivacaftor (Kalydeco®) and lumacaftor/ivacaftor (Orkambi®), which address the underlying cause of CF in certain mutations by improving chloride transport at the cellular level.

Improved patient outcomes are attributed to not only new treatment modalities, but also to the practice of the care center model recommended by the Cystic Fibrosis Foundation (CFF). There are more than 120 CF Centers nationwide, accredited by the CFF to deliver comprehensive multidisciplinary specialized care while adhering to clinical practice guidelines. For instance, due to widespread adoption of eradication strategies, prevalence of P. aeruginosa infection has decreased (*10*). Cystic fibrosis-related Diabetes (CFRD) is a highly prevalent complication of CF that increases

morbidity and mortality. Since the publication of the CF Foundation CFRD guidelines in 2010, rates of Oral Glucose Tolerance Test (OGTT) screening have also increased, allowing for closer monitoring and management (*13*). The CF care team is multi-disciplinary and at minimum includes a physician, nurse, dietitian, respiratory therapist, and social worker. Today, the complexity of CF care continues to evolve as the CF patient grows older: pharmaceutical, mental health, cancer screening, and palliative care disciplines are recognized as important issues that must be addressed. Lung transplant remains an option for patients with advanced lung disease despite conventional therapies. The total number of patients receiving lung transplantation has increased from 152 in 2003 to 246 in 2013 (*10*). All of these care measures are contributing to decreased mortality while inevitably leading to significantly increased costs associated with CF-related hospitalization.

We also analyzed data on the basis of patient characteristics by age, sex and payer status. The frequency of discharges increased for age groups above 1. The highest frequency of hospital discharges was seen in ages 18-44 in both 2003 and 2013, likely because more complications requiring hospitalizations occur in CF patients as they age. Adult CF patients (> 18 years) have higher rates of exacerbations requiring IV antibiotic therapy (*14*). The median age of CF patients in 2013 was 17.9 years. Prior to initiation of universal newborn screening in 2010, most infants were diagnosed based on clinical symptoms. Following newborn screening implementation, asymptomatic, healthier infants are being diagnosed with CF earlier, which may explain the decreased rate of hospital admissions and discharges in infants. Despite a slightly higher male population among CF patients, more females were hospitalized with CF. This finding is consistent with previous studies, which have demonstrated poorer outcomes among female patients with CF thus leading to more frequent exacerbations and hospitalizations (*15,16*).

In terms of payer status, the highest number of hospital discharges was seen in the Medicaid group in both 2003 and 2013. This was observed in spite of the fact that in 2013, more patients had private health insurance as compared to any other insurance (*10*). Medicaid patients may be less likely to seek care at onset of an exacerbation secondary to concerns of limited access to healthcare (*17*). Delayed care increases risk for worsening exacerbation and need for hospital admission. The difference in socioeconomic factors among patients with insurance can impact care for CF as Medicaid patients have a 3.7-fold higher death risk than CF patients without Medicaid (*18*). In previous studies, CF patients with Medicaid were found to have worse lung function and need for more IV antibiotics for pulmonary exacerbations which could explain the increased need for inpatient hospitalizations (*19-21*). It is also important to remember that Medicare uses a prospective payment system where re-imbursement is based on a predetermined amount instead of the traditional fee for service model (*https://www.cms.gov/*). Hospitals can be placed at financial risk for increased length of stay in these scenarios. Early discharges in these patients can occasionally lead to an early recurrence of the exacerbation and thus lead to an overall increased number of admissions and discharges. A drop in the number of uninsured patients is encouraging because CF patients without health insurance have been shown to have a higher mortality rate (*22*).

We also analyzed the data with respect to hospital characteristics such as hospital region (Northeast, Midwest, South and West) and bed size. The South had the highest number of CF discharges in both 2003 and 2013. This may be because the South had the highest number of total hospital discharges in the same time frame. We also found that the Western U.S. had the highest frequency of CF hospital discharges in both 2003 and 2013. Midwest had the highest increase. The frequency of hospital discharges more than doubled in the Midwest from 2003 to 2013. In terms of hospital size, patients with CF were more likely to be admitted to hospitals with large bed size in 2013 compared to hospitals with small bed size in 2003, and to hospitals within a metropolitan area. This is consistent with the CFF accreditation criteria for CF care centers to have the supportive infrastructure necessary to support a multidisciplinary model of care, which is more often available in larger hospitals and in metropolitan areas.

The design of this study and the nature of the NIS database set leads to some important limitations. As this is an administrative data set, it reflects the coding practices of each institution. Thus it is likely that these results underestimate the actual number of patients admitted and discharged with the diagnosis of CF. Discharges may have been coded with an alternative diagnosis such as viral or bacterial pneumonia, hypoxemia and sepsis. This data set also does not control for errors during the entry of the data. Additionally, the NIS data set does not provide details regarding the patient or the hospital, which could help explain the trends in hospital discharges and associated costs. Patient- specific clinical information was not obtainable thereby limiting the demographic data presented in the research. Further studies analyzing hospital coding practices may clarify these concerns.

5. Conclusion

Over the last decade, many advances have been made in the diagnosis and treatment of CF, consequentially leading to a significant transformation in the epidemiology and demographics of this chronic disease.

It is important to provide updated information regarding these changing demographics as they also reflect a considerable improvement in survival. Rising hospital costs associated with the care of CF patients necessitates future studies analyzing the diagnostic modalities, algorithms and treatment practices of physician's treating CF patients.

Acknowledgements

We would like to acknowledge the Division of Pulmonary, Critical Care & Sleep Medicine at Northwell Health, the Cystic Fibrosis Center at Northwell Health and the Cystic Fibrosis Center at Monmouth Medical Center. This study was not funded by any sources.

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(Received July 25, 2017; Revised August 22, 2017; Accepted 26, 2017)