PATIENT REGISTRY ANNUAL DATA REPORT 2022

CYSTIC FIBROSIS FOUNDATION®

2022

PATIENT REGISTRY ANNUAL DATA REPORT

CYSTIC FIBROSIS FOUNDATION

MISSION OF THE CYSTIC FIBROSIS FOUNDATION

The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with the disease the opportunity to lead full, productive lives by funding research and drug development, promoting individualized treatment, and ensuring access to high-quality, specialized care.

SOURCE OF DATA

Cystic fibrosis patients under care at CF Foundation-accredited care centers in the United States, who consented to have their data entered.

SUGGESTED CITATION

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

FIGURE PERMISSIONS

To request use of charts and data provided in this report, contact the CF Foundation Patient Registry team by email at **reghelp@cff.org**.

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CYSTIC FIBROSIS FOUNDATION

September 2023

Dear Friends and Colleagues:

We are pleased to share the 2022 Patient Registry Annual Data Report. Many of the positive trends highlighted in last year's report were sustained in 2022. As compared to 2019, median predicted survival increased, pulmonary exacerbations treated with intravenous antibiotics and lung transplants were substantially lower, and reported pregnancies remained high.

While the report demonstrates significantly improved outcomes for people with CF on a population level, we cannot ignore the impact of CFTR modulator therapies. We have for the first time provided an initial characterization of some demographic and clinical features of the following three subgroups: 1) prescribed a highly effective modulator between 2020 and 2022, 2) eligible but NOT prescribed a modulator and 3) NOT eligible for a modulator.

This report also shows that CF care delivery has not returned to the previous baseline. The number of clinical encounters in 2022 remained below that of 2019. There were fewer measures of pulmonary function and fewer respiratory cultures as compared to 2019. Decreased CF health care utilization may relate to an improved health status for many on a CFTR modulator, however this invariably impacts the completeness of the Registry data set and may create bias. We strongly encourage you to carefully read the "About this Report" subsection to gain an understanding of the potential impact of having less data available.

We extend sincere gratitude to each of you who contribute to the Registry's success, most notably the individuals with CF and their families who graciously agree to share their data. We also appreciate the diligent efforts of the Registry coordinators and care team members who collect and enter the data. Thank you all for your hard work throughout the year and your commitment to the CF Foundation and the CF community.

Bruce C. Marshall, MD
Executive Vice President and
Chief Medical Officer
Cystic Fibrosis Foundation

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ABOUT THIS REPORT

The Annual Data Report is based on data entered in the CF Foundation Patient Registry through our online portal, PortCF©. Data are entered by teams of dedicated health professionals in our nationwide network of more than 130 CF Foundation-accredited Care Centers.

Inclusion and Exclusion Criteria

This Annual Data Report contains data from individuals diagnosed with CF who (a) have consented to participate in the Registry and (b) were seen in a CF Care Center during the 2022 calendar year, including those who were born, diagnosed, or died in the year. Data from lung transplant recipients are only included in the chapters on Demographics, Diagnosis, CFTR Gene Mutations, Transplantation, and Survival.

Graphics in gray include data from all individuals with CF.

Graphics in purple show patient-level variation excluding data from lung transplant recipients.

Graphics in blue show center-level variation excluding data from lung transplant recipients.

The included populations represented in the figures vary and are based on the eligibility criteria described in the title and/or footnotes. Figures titled in **gray** reflect patient-level data that include individuals who have received a transplant. Figures titled in **purple** reflect patient-level data, and figures titled in **blue** present data on center-level variation across the CF Care Network. Both the blue and purple-titled figures exclude individuals who have received a lung transplant. To reduce outliers, the majority of the center-level variation figures exclude centers with fewer than 10 individuals for that measure. Some center-level variation figures, such as CF-related diabetes (CFRD), infant, and pulmonary exacerbation measures, include centers with five or more eligible individuals to allow for sufficient comparison.

Data from individuals with a diagnosis of CFSPID/CRMS (CF screen positive, inconclusive diagnosis/CFTR-related metabolic syndrome) or CFTR-related disorder are excluded from all figures except for the one on new diagnoses in the reporting year. Since 2017, data from transplant recipients have been excluded from any chapters not specified in the inclusion criteria, and this is reflected in lower prevalence of some complications (e.g., CF-related diabetes).

New Chapters in This Report

In this year's report, we highlight data on two new categories of the CF population to focus on their diverse and unique care needs: CFTR Modulator Status and Advanced Lung Disease (ALD).

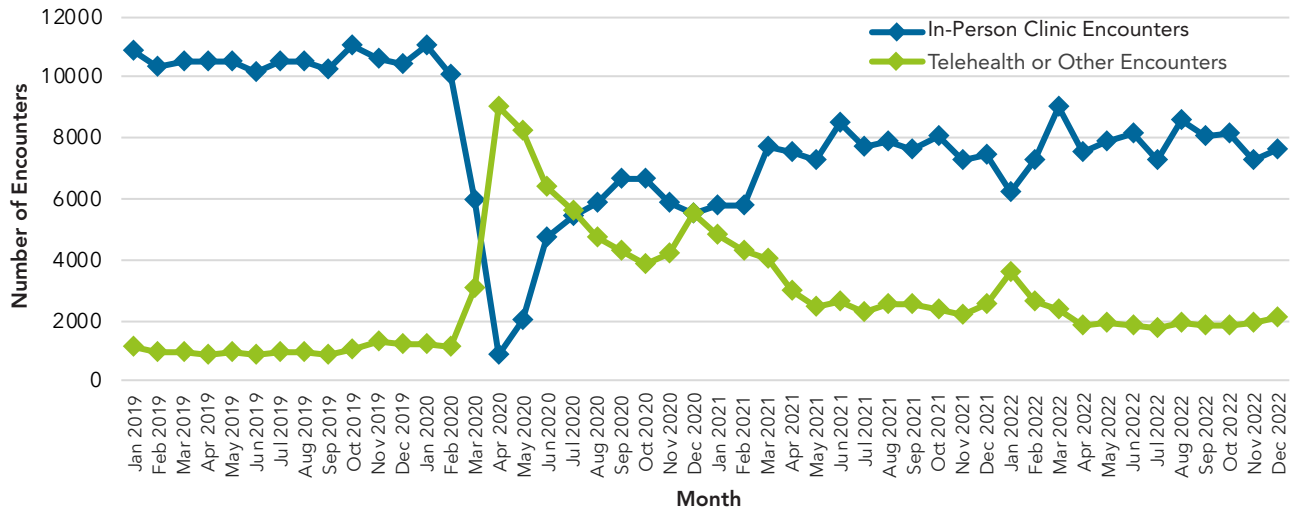
In the CFTR Modulator chapter (page 47), we show lung function, nutrition, pulmonary exacerbations, and CF care utilization among those 12 years and older to illustrate differences among people with CF based on CFTR modulator prescription status. These data are intended to highlight characteristics of those ineligible for CFTR modulator therapy to facilitate the development of novel therapies, support CF care team initiatives, and aid in the planning of research studies.

In the Advanced Lung Disease chapter (page 75), we present characteristics of individuals with advanced CF lung disease collected through the Advanced Lung Disease case report forms (2019–2022). We summarize the proportion receiving advanced CF lung disease guideline-based[1] care. These data highlight the need for continued focus on this population to ensure timely and appropriate discussion of, and referral for, lung transplantation. Recommended testing remains important to ensure all individuals benefit from comprehensive management and close surveillance of advanced CF lung disease.

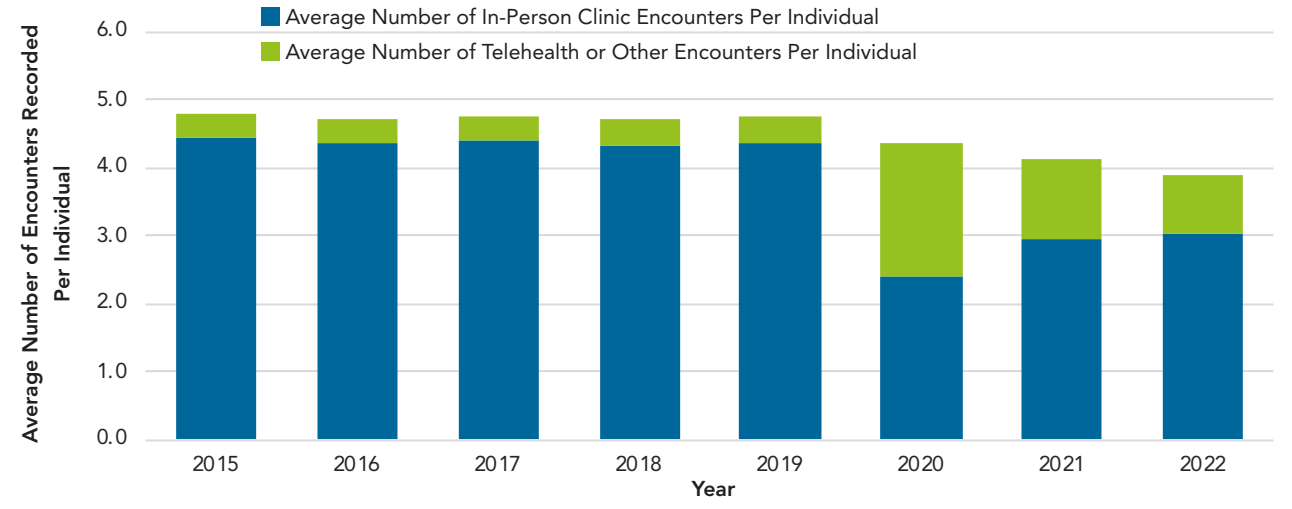
Trends for In-Person Clinic and Telehealth/Other Encounters

The chart below shows the monthly total number of in-person clinic and telehealth or other encounters from January 2019 through December 2022. The average number of clinical encounters and the proportion of in-person clinic encounters in 2022 remains below pre-pandemic values. During this four-year period, most encounters between people with CF and their care teams occurred in-person although telehealth played an important role over time. The total number of encounter records in 2022 (128,990), was lower than the previous two years (3.8 percent and 7.3 percent lower than in 2021 and 2020, respectively). In 2022, there were 25,553 telehealth encounters compared to 57,921 in 2020 and 35,525 in 2021. The number of in-person clinical encounters in 2022 (93,257) was higher than reported in 2020 (70,823) and in 2021 (88,626). Of all encounters in 2022, 16.2 percent and 28.7 percent of visits were reported as telehealth or "other" among pediatric and adult programs, respectively.

Number of Encounters by Location, 2019–2022



Average Number of Encounters Recorded Per Individual, 2015–2022



Reporting of Care in 2022

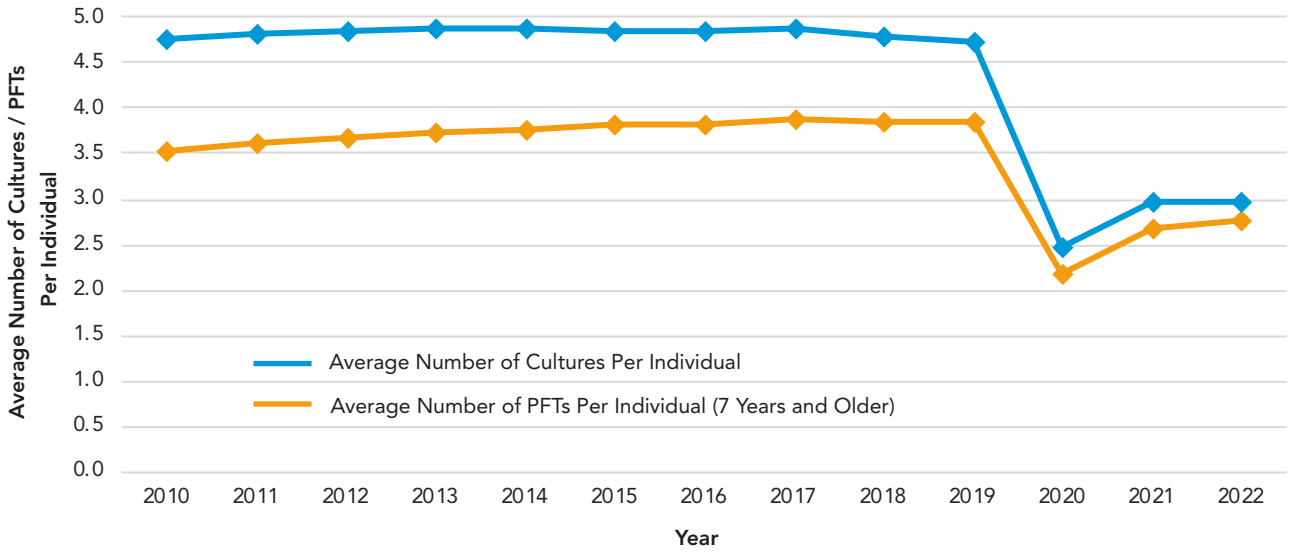
Based on established guidelines for CF care, encounters reported to the CF Foundation Patient Registry (CFFPR) typically include assessments of nutritional status, lung function, infection status, prescribed medications, and CF-related complications. The table below shows the percentage of individuals with these specific data elements provided in 2019 through 2022.

Percentage of Individuals With Specific Data Elements Entered During 2019–2022

Review Year	Individuals With Height/Weight Reported	Individuals 7 and Older With a PFT Reported	Individuals With Microbiology Culture Reported	Individuals With Mycobacterial Culture Reported	Individuals With Medications Reported	Individuals With Complications Reported
2019	98.6%	98.9%	97.3%	52.5%	98.5%	98.2%
2020	97.3%	98.4%	88.1%	34.3%	97.8%	97.5%
2021	97.4%	98.1%	90.7%	32.0%	97.7%	97.1%
2022	98.2%	98.7%	93.1%	32.3%	98.2%	96.9%
Change from 2019 to 2022	*–0.4%*	*–0.2%*	*–4.2%*	*–20.2%*	*–0.3%*	*–1.3%*

The number of measurements per individual for various metrics remained notably lower in 2022 as compared to 2019. This is important because annualized measures of lung function, weight, and height are reported as the mean of the maximum value from each quarter. Through 2019, the average number of pulmonary function test (PFT) measurements (among those age 7 years and older) reported per individual was approximately 4.8 measurements per year, which fell to an average of 2.5 measurements in 2020 with modest recovery to 3.0 in 2021 and 2022. The lower number of PFT measurements may impact the rigor of the FEV_1 results. In addition, prior to 2020, microbiology cultures reported per individual were between 3.5 and 4.0 average cultures per year, which dropped to 2.2 cultures per individual in 2020 with modest recovery to 2.7 in 2021 and 2.8 in 2022. While some of this decrease may be attributable to CFTR modulators, it is important to note that fewer cultures may impact the detection of microorganisms.

Average Number of Cultures and PFTs Entered Per Individual, 2010–2022



Summary

Care delivery and data entry into the CFFPR in 2022 continued to be impacted by a trend of less outpatient visits that began during the COVID-19 pandemic. We encourage readers of this report to interpret the prevalence and incidence data since 2020 in the context of reduced frequency of in-person care, which impacted availability of microbiology cultures, pulmonary function testing, and other clinical measures.

More information about data included in the Annual Data Report and interpretation of the tables and figures can be found in the online Technical Supplement on cff.org.

Summary of the Cystic Fibrosis Foundation Patient Registry, 2007–2022

Demographics[A]	2007	2012	2017	2021	2022
People with CF (n)	24,594	27,725	30,170	32,230	32,621
Newly diagnosed individuals (n)[B]	1,062	1,051	998	888	752
Detected by newborn screening (NBS, %)	31.4	59.7	56.4	62.3	59.8
Median age at diagnosis for all people with CF (months)	6	5	3	3	3
Mean age (years)	18.6	19.8	21.7	23.8	24.4
Median age (years)	16.5	17.7	19.3	21.3	21.9
Adults ≥18 years (%)	45.1	49.2	53.5	58.2	59.4
Race (mutually exclusive)[C]					
White (%)	93.6	92.6	91.8	91.4	91.2
African American (%)	3.4	3.5	3.5	3.5	3.5
Other race (%)	3.0	3.9	4.8	5.2	5.3
Hispanic (any race) (%)	6.5	8.1	9.3	9.9	10.0
Males (%)	51.8	51.6	51.6	51.7	51.7
Mortality[A]					
Total deaths (n)	400	425	388	246	230
Annual mortality rate (per 100) (%)	1.6	1.5	1.3	0.8	0.7
Predicted median survival (five-year increments)	37.5	38.5	43.6	52.7	56.6
95% confidence interval (five-year increments)	36.2–38.6	37.2–39.8	42.2–44.9	51.2–54.3	54.7–58.1
Median age at death (years)	26.1	27.4	30.2	34.3	36.6
GI/Nutrition					
Body mass index (BMI) percentile in individuals 2 to 19 years (median)	48.4	52.6	57.0	62.1	61.3
Weight <10th CDC percentile percentile in individuals 2 to 19 years (%)	17.2	13.6	10.5	8.3	8.8
Height <5th CDC percentile percentile in individuals 2 to 19 years (%)	13.4	11.1	9.8	8.5	8.7
BMI in individuals 20 years and older (median)	21.7	22.1	22.6	23.8	23.8
Pancreatic enzyme replacement therapy (%)	86.8	87.2	85.6	83.1	82.1
Supplemental feeding - tube (%)	10.1	10.7	10.8	7.4	6.6
Supplemental feeding - oral only (%)	37.8	41.3	44.5	36.2	33.8
Pulmonary[D]					
FVC % predicted (mean)	85.7	87.5	88.8	94.4	94.9
FEV_1 % predicted (mean)	74.6	76.1	77.2	84.5	85.0
FEV_1/FVC ratio % predicted (mean)	74.9	74.5	74.1	76.2	76.0
Respiratory Microbiology					
Number of microbiology cultures per patient (mean)	3.3	3.7	3.9	2.7	2.8
Pseudomonas aeruginosa (*P. aeruginosa* or PA) (%)[E]	54.4	49.8	45.7	28.4	26.0
Burkholderia cepacia (*B. cepacia*) complex (%)	2.9	2.6	2.5	1.4	1.3
Staphylococcus aureus (*S. aureus*) (%)[F]	65.7	69.2	70.7	63.8	60.8
Methicillin-sensitive *Staphylococcus aureus* (MSSA) (%)	51.3	52.4	54.9	51.7	50.2
Methicillin-resistant *Staphylococcus aureus* (MRSA) (%)	21.3	26.6	25.9	18.0	15.6
Stenotrophomonas maltophilia (*S. maltophilia*) (%)	12.7	13.5	12.9	5.6	5.0
Mycobacterial species (%)[G]	-	11.9	12.6	9.6	10.3

Table continues on the next page

Summary of the Cystic Fibrosis Foundation Patient Registry, 2007–2022 *continued*

Health Care Utilization and Pulmonary Exacerbations (PEX)[H]	2007	2012	2017	2021	2022
Outpatient visits to CF centers reported per year (mean)	4.2	4.6	4.4	3.0	3.0
Phone, phone w/video, or other visits per year (mean)	0.0	0.0	0.4	1.2	0.8
Treated with IV antibiotics for a PEX (%)	36.3	35.6	34.2	12.1	12.7
Number of PEX per year (mean)	0.7	0.7	0.7	0.2	0.2
Number of days of treatment for all PEX per year (mean)[I]	30.4	28.4	28.9	21.1	19.6
Number of days of home IV treatment for all PEX per year (mean)[I]	13.6	11.1	10.6	6.4	5.8
Number of days of hospitalization for all PEX per year (mean)[I]	16.9	17.2	18.3	14.7	13.9
Pulmonary Therapies[J]					
Dornase alfa (≥6 years) (%)	82.0	87.8	91.7	88.4	85.3
Inhaled tobramycin (PA+ and ≥6 years) (%)[K]	68.7	65.7	70.5	59.6	55.4
Inhaled aztreonam (PA+ and ≥6 years) (%)	-	38.9	43.9	39.0	34.8
Azithromycin (PA+ and ≥6 years) (%)[L]	63.8	70.4	64.9	56.5	53.5
Hypertonic saline (≥6 years) (%)	35.5	60.6	72.2	70.0	66.4
Oxygen (%)[M]	10.0	10.8	11.0	6.7	6.5
Noninvasive ventilation (%)	2.0	2.5	3.1	2.3	2.4
CFTR Modulators					
Individuals <2 years prescribed a modulator (%)	-	0.1	0.9	9.1	20.3
Individuals 2 to 5 years prescribed a modulator (%)	-	0.5	9.2	46.7	46.8
Individuals 6 to 11 years prescribed a modulator (%)	-	3.5	35.7	75.6	80.9
Individuals ≥12 years prescribed a modulator (%)	-	3.7	40.1	85.1	86.0
Transplants[A]					
Lung (all procedures) (n)	174	206	259	56	53
Liver (n)	20	20	17	20	10
Kidney (n)	6	13	10	21	8
Lost to Follow Up[A]					
Lost to follow up (%)[N]	-	3.7	3.3	3.0	3.3

[A] *Includes data from transplant recipients.*

[B] *We anticipate that additional 2022 diagnoses will be entered into the Registry in 2023.*

[C] *Reporting of race in years prior to 2021 included individuals in more than one race category (were not mutually exclusive).*

[D] *Pulmonary function data throughout this report reflect the use of 2012 Global Lung Initiative (GLI) equations.[2] Pulmonary function data are for individuals greater than 7 years of age at the end of the reporting year.*

[E] *Includes PA and multidrug-resistant PA found in any culture during the year.*

[F] *Includes MSSA and MRSA and reflects the prevalence of* S. aureus *among individuals who had a bacterial culture during the year. The percentages for MSSA and MRSA individually are greater than the total* S. aureus *percentage because MSSA and MRSA are not mutually exclusive.*

[G] *Percentage of people with CF with one or more mycobacterial species isolated out of those who had a mycobacterial culture during the year.*

[H] *Defined as a period of treatment with IV antibiotics in the hospital and/or at home.*

[I] *Among those with one or more pulmonary exacerbations in the year.*

[J] *Percentage of people with CF on therapy at any clinical visit in the year. All individuals noted as intolerant or having an allergy to a specific therapy were excluded.*

[K] *Includes Tobramycin solution for inhalation (i.e., TOBI®), TOBI™ Podhaler® (Tobramycin Inhalation Powder), and Bethkis® since 2013. In prior years, only TOBI® was available.*

[L] *Individuals were considered eligible if they met the selection criteria used in the first U.S. azithromycin trial.[3]*

[M] *Includes continuous, nocturnal, or with exertion.*

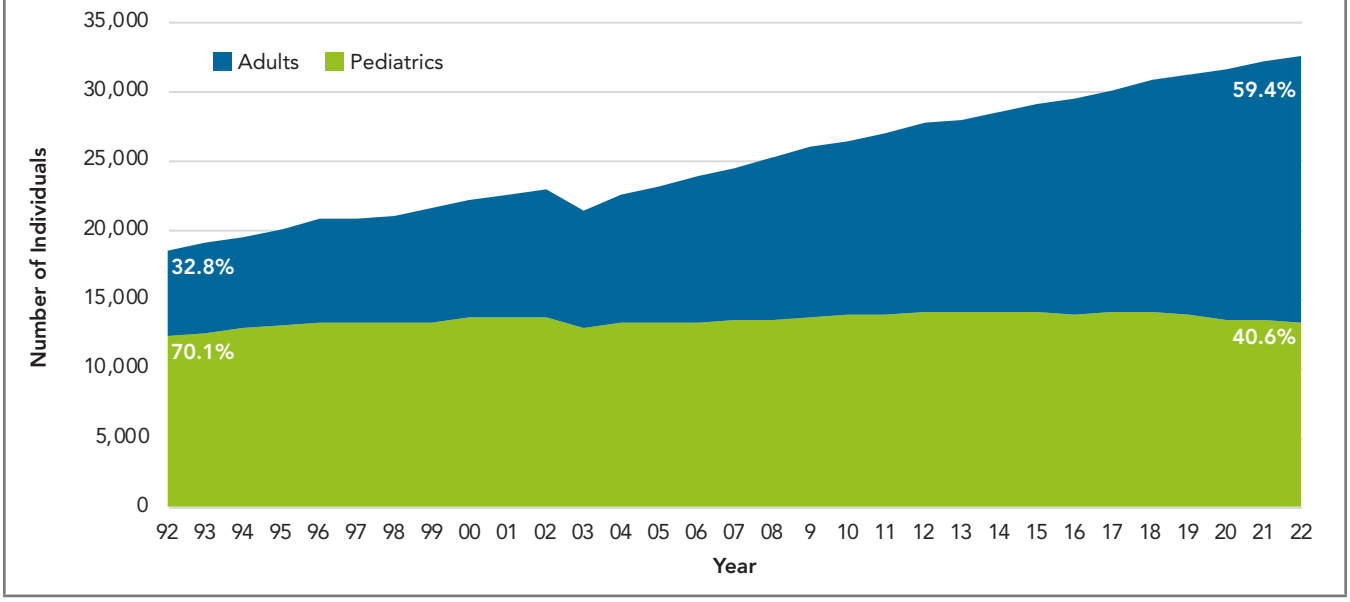
[N] *Defined as patients seen in the previous reporting year (2021) but not the current reporting year (2022), and not known to have died.*

DEMOGRAPHICS

The Registry contains data on people with CF from 1986 to 2022. During that time, substantial changes in specialized CF care and new treatments have led to improved survival. This section shows the current and longitudinal distribution of demographic characteristics of individuals with CF in the Registry.

In 2022, there were 32,621 individuals with CF in the Registry. The number of adults with CF continues to increase, while the number of children remains relatively stable. In 2022, adults were 59.4 percent of the CF population, compared with 32.8 percent in 1992.

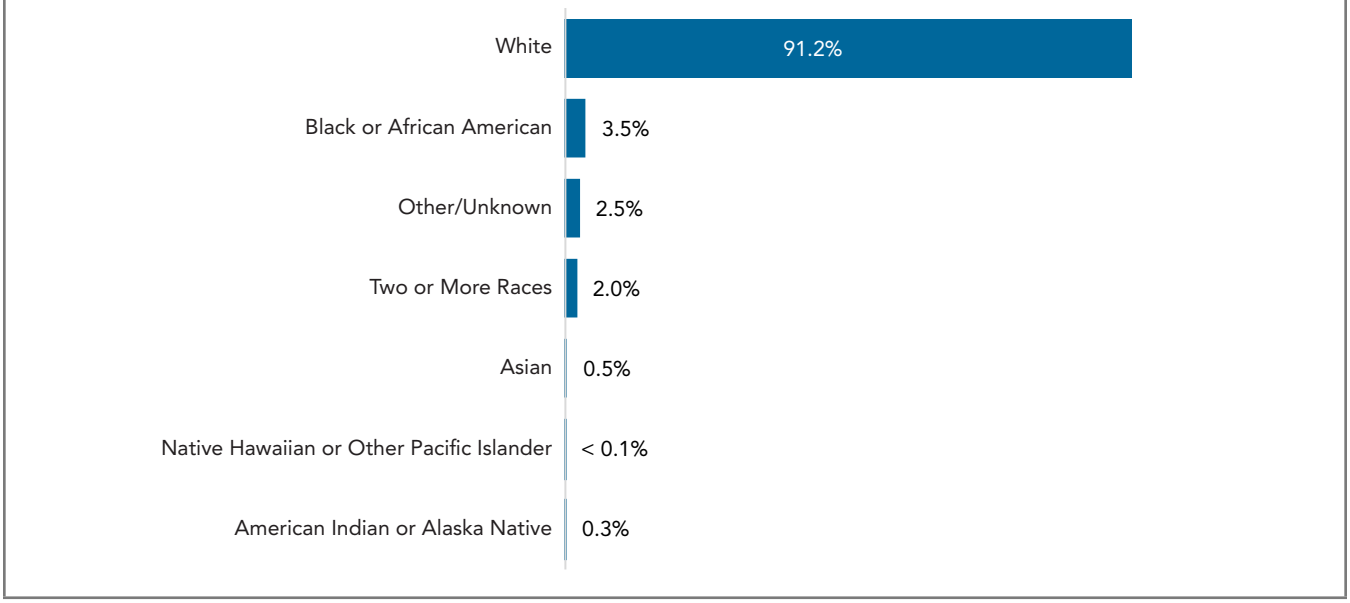
Number of Children and Adults With CF, 1992–2022



The decrease in the number of individuals reported in 2003 is due to a delay in obtaining informed consent forms before the close of the calendar year at some CF Care Centers.

Currently, 10.0 percent of the individuals in the Registry identify as Hispanic. There has been a steady increase over the past 15 years, reflecting national population trends.[4] Hispanic individuals with CF tend to be younger than the overall CF population, with a median age of 15.3 years. In 2022, 3.5 percent of registry participants were identified as Black or African American, and 2.0 percent identified as two or more races.

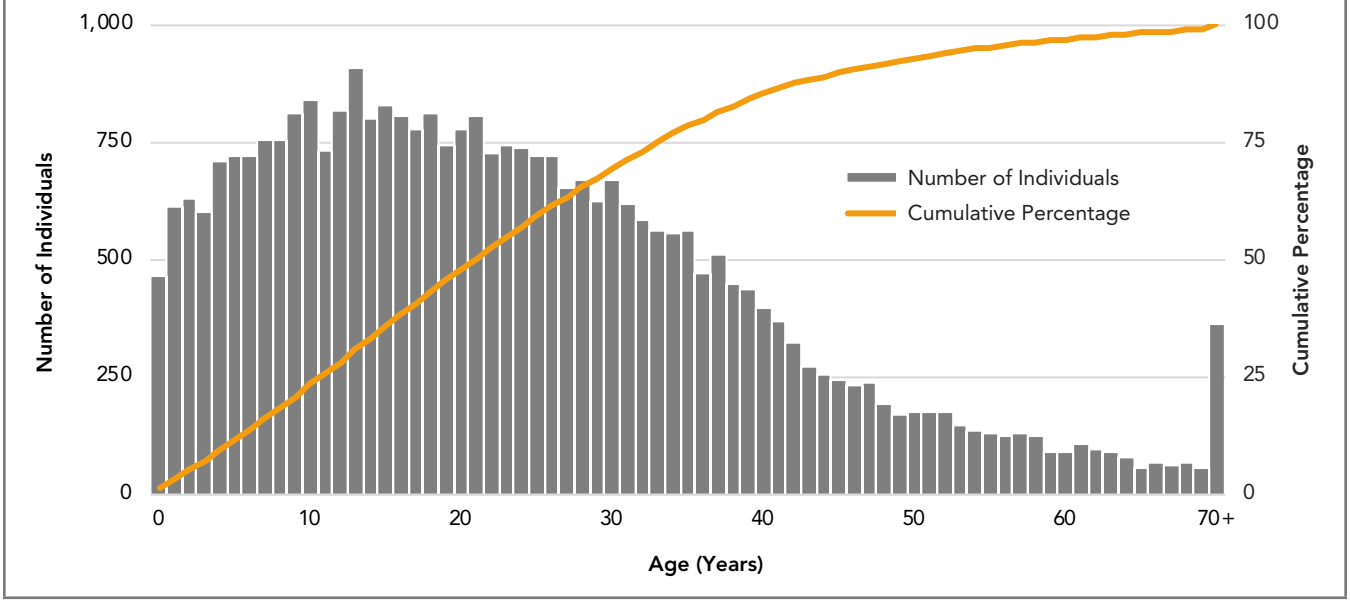
Race Distribution of the CF Population in 2022



The percentages in this chart and the summary table differ from those in prior annual data reports. Data in this chart and summary table include individuals in only one category or race as captured on the CFFPR form

The median age of all people with CF currently in the Registry is 21.9 years. The range is from birth to 91.9 years. The age distribution remains markedly skewed toward younger ages as compared to the general U.S. population.

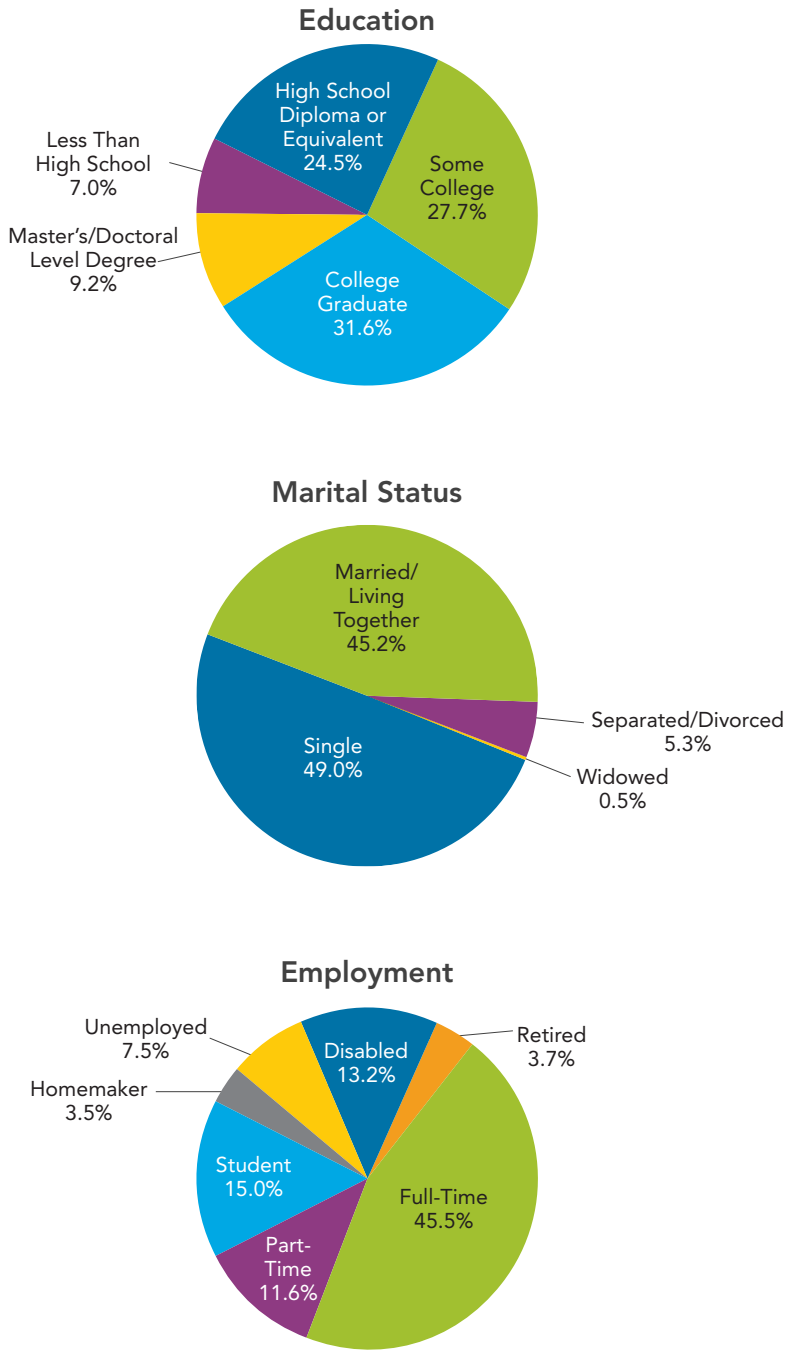
Age Distribution of the CF Population in 2022



Characteristics of Adults With CF

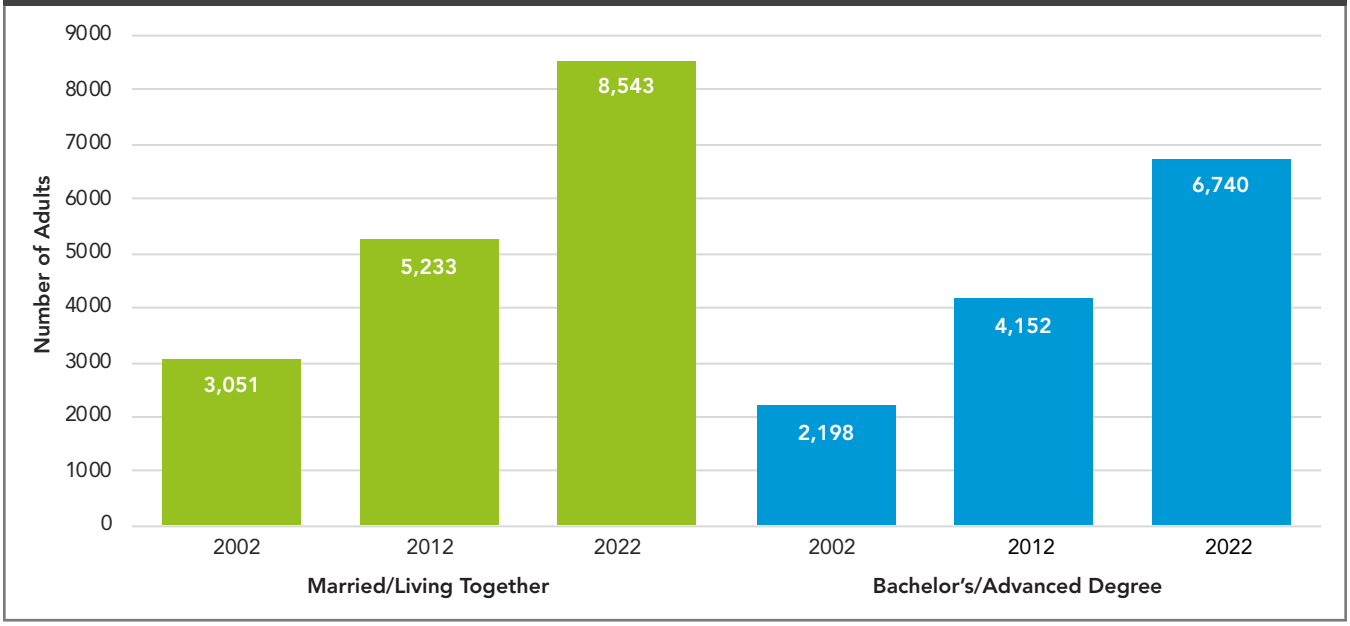
As a growing number of individuals with CF enter adulthood, it is encouraging to note that many are pursuing higher education and employment, are in committed relationships, and are having children of their own. Nearly three-fourths of adults with CF are either studying or working. However, these charts also highlight that approximately 20.0 percent of adults report being disabled or unemployed.

Socioeconomic Characteristics of Adults 18 Years and Older With CF, 2022



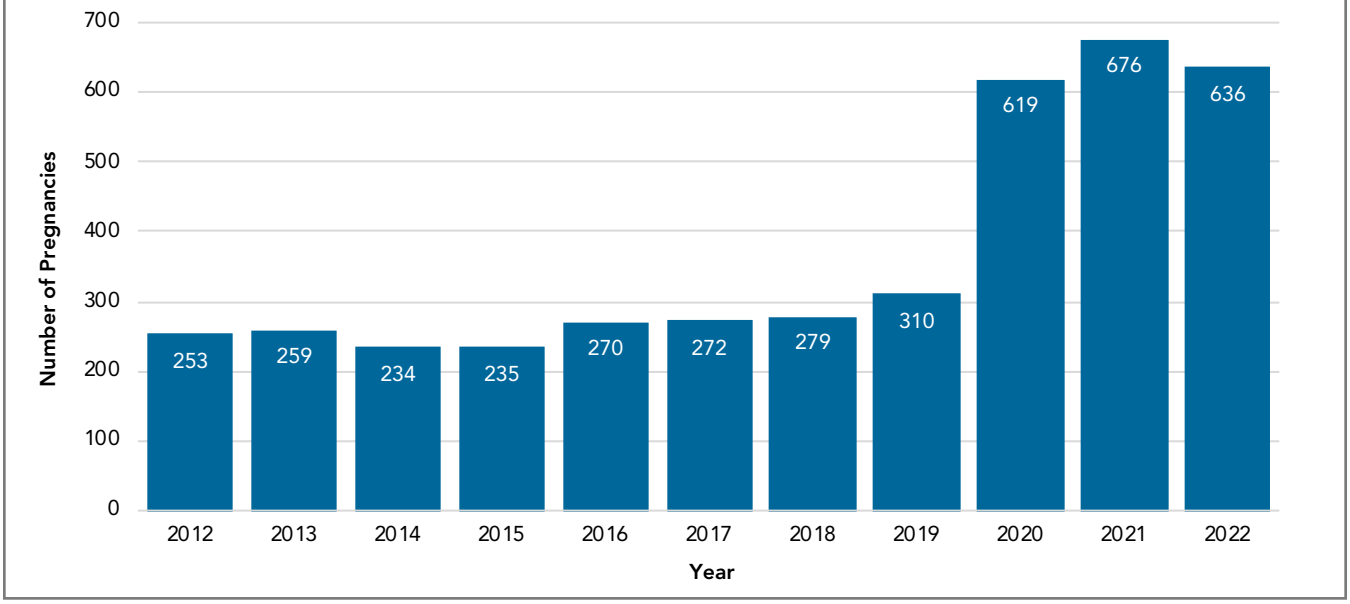
Over the last 20 years, there has been almost a tripling of the number of people who are married or living together as well as the number of people with a college degree.

Characteristics of Adults With CF, 2002, 2012, 2022



The number of pregnancies among women with CF gradually increased through 2019 and then dramatically increased in 2020. Registry data show that 636 women with CF were pregnant in 2022.

Number of Pregnancies in Women 14 to 45 Years With CF, 2012–2022



Health Insurance Information

Barriers to access insurance coverage for specialized care and treatments exist for some individuals with CF. Across all age groups, about half of the individuals in the Registry receive at least some component of their health insurance through federal or state-funded programs. Registry data show that in 2022, many individuals with CF who were age 18 to 25 were covered under their parents' health insurance plan.

Insurance Coverage in 2022

	Age < 18 (%)	Age 18–25 (%)	Age ≥ 26 (%)	All (%)
Number of Individuals (n)	**13,144**	**5,970**	**13,050**	**32,164**
Health insurance (e.g., private insurance)	49.5	61.9	64.6	57.9
Medicare/Indian Health Service	0.8	4.1	24.1	10.9
Medicaid/state programs	56.9	45.3	27.0	42.6
TRICARE or other military health plan	3.1	2.2	1.8	2.4
Other	0.7	1.1	1.2	1.0
No health insurance	0.4	0.7	0.7	0.6

"Insurance coverage" reflects coverage at any point during the year; thus, these categories are not mutually exclusive (except for the "no health insurance" option).

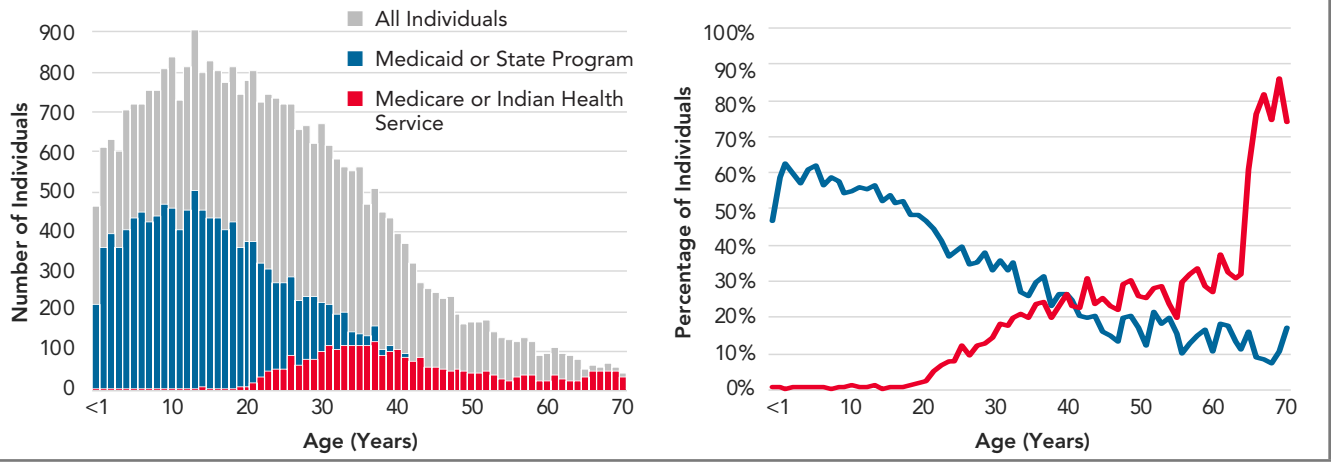
Additional Insurance Information in 2022

Individuals who participated in a patient assistance program (%)	48.4
Individuals 18 to 25 years covered under parents' insurance (%)	50.7

"Patient assistance program" refers to any program that provides free medication or co-pay assistance.

A large proportion of children with CF use Medicaid or state programs, including 58.3 percent of children younger than 10 years of age. Though the overall prevalence of Medicare use is low among the entire population, it increases with age. Among adults aged 30 to 35 years, 18.4 percent reported Medicare coverage. This increased to 27.1 percent among adults aged 40 to 64 years. Individuals aged younger than 65 years who receive Medicare have qualified based on the federal criteria for disability. It is also worth noting that individuals who received insurance from the Indian Health Service are members of a federally recognized American Indian or Alaska Native tribe or their descendants.

Medicare/Indian Health Service and Medicaid/State Programs by Age in Years, 2022



DIAGNOSIS

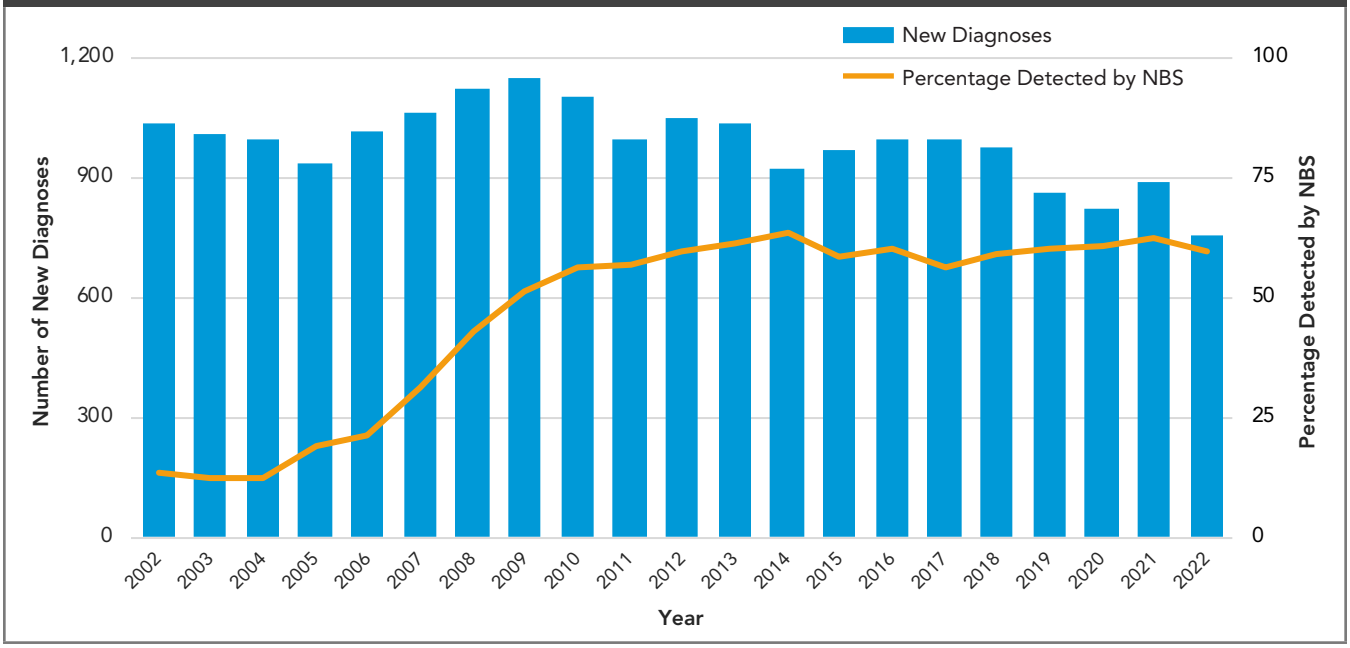
Diagnostic Characteristics of Individuals With CF

This section examines characteristics of individuals diagnosed with CF, as well as trends over time for two key diagnostic tests: genotyping and sweat chloride test.

In 2022, 59.8 percent of all new diagnoses and 91.6 percent of diagnoses among those less than 6 months old were reported as being detected by newborn screening (NBS). Babies diagnosed by NBS were found to have better nutritional outcomes, a more rapid increase in lung function, and longer time to chronic pseudomonal infection than those diagnosed clinically.[5] Diagnosis in the newborn period represents an important opportunity for CF Care Centers to partner with community physicians and families to ensure the best possible care and outcomes for infants with CF.

There is often a lag in reporting of newly diagnosed individuals, particularly infants born late in the year (i.e., late 2022), who were not seen at a CF Care Center before the end of the calendar year. Future reports will be adjusted to include these individuals for the 2022 diagnosis year.

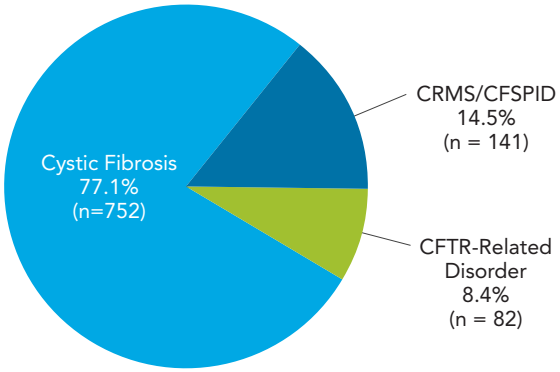
Number of New CF Diagnoses, 2002–2022



With the widespread use of NBS for CF, it was necessary to develop terminology for individuals with a positive NBS who have inconclusive sweat test results and/or fewer than two CF-causing variants. In the United States, this is referred to as CFTR-related metabolic syndrome (CRMS)[6]; other countries use the term CF screen positive, inconclusive diagnosis (CFSPID). Diagnosis guidelines, published in 2017, harmonized the criteria for CRMS/CFSPID.[7] CRMS was added to the Registry as a diagnostic option in 2010. Entry of a diagnosis of CF versus CRMS into the Registry is based on clinical judgment; there is no requirement that individuals meet published diagnostic criteria for CF or CRMS. The percentage of CRMS/CFSPID increased from 14.3 percent of new diagnoses in 2021 to 14.5 percent in 2022.

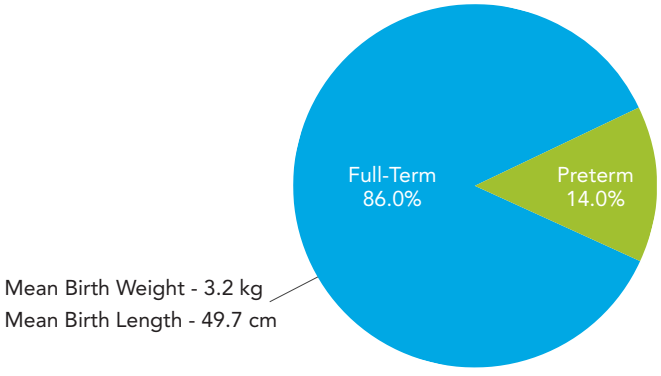
Individuals can also be diagnosed with CFTR-related disorder. This option has been available in the Registry since 2010. Individuals with this diagnosis do not meet diagnostic criteria for CF or CRMS, are affected by CF-related conditions such as congenital bilateral absence of the vas deferens (CBAVD), and often have mutations in the CFTR gene.[8] The percentage of individuals reported to have CFTR-related disorder increased from 7.2 percent of those diagnosed during the year in 2021 to 8.4 percent in 2022. Collection and analysis of data from individuals with CRMS and CFTR-related disorder will provide new and important information for these distinct populations.

CF, CRMS/CFSPID, and CFTR-Related Disorder New Diagnoses, 2022



In 2022, 466 newborn infants were diagnosed with CF. Of the 357 infants with a known gestational age at birth, 86.0 percent were born full-term, comparable with the figure for the general U.S. population.[9] The mean birth weight for full-term infants with CF is also about the same as for the U.S. population,[10] suggesting that babies born with CF do not show nutritional deficiencies at birth.

Gestational Age of Infants Born and Diagnosed With CF in 2022



"Preterm" refers to infants born at a gestational age less than 37 weeks. "Full term" refers to infants born at a gestational age greater than or equal to 37 weeks. Because birth weight and length are greatly influenced by weeks of gestation, mean birth weight and length is not reported for preterm infants in this chart.

The majority of those diagnosed in their first year via NBS are asymptomatic or minimally symptomatic at time of diagnosis. The most prevalent presentation among the population diagnosed before the age of 1 year was meconium ileus, reported in 10.1 percent of infants diagnosed in 2022. Among those diagnosed before age 1 with meconium ileus (or other intestinal obstruction), 37.3 percent had bowel perforation. Since the number of infants with meconium ileus is small, the percentage with bowel perforation may fluctuate year to year. In the past 10 years, the highest prevalence of bowel perforation was 37.3 percent, and the lowest prevalence was 15.9 percent. Among individuals diagnosed after 1 year of age, the most prevalent symptoms reported were acute or persistent respiratory abnormalities.

Symptoms Reported at CF Diagnosis

	All Individuals (%)	Diagnosed in 2022 (%)	Diagnosed in 2022 Age < 1 (%)[A]	Diagnosed in 2022 Age ≥ 1 (%)
Number of Individuals (n)	**32,621**	**752**	**503**	**249**
Asymptomatic				
DNA analysis	14.7	28.5	26.7	32.1
Family history	14.2	11.0	9.7	13.7
Newborn (neonatal) screening	31.2	59.8	86.7	N/A
Prenatal screening (CVS[B], amniocentesis)	2.7	3.3	4.8	N/A
Symptomatic				
Acute or persistent respiratory abnormalities	33.1	15.6	1.2	44.6
CBAVD[C] or infertility/GU[D] abnormalities	0.9	3.7	0.0	11.2
Digital clubbing	0.6	0.7	0.0	2.0
Edema	0.5	0.0	0.0	0.0
Electrolyte imbalance	2.6	0.1	0.0	0.4
Failure to thrive/malnutrition	24.8	3.1	2.6	4.0
Liver problems	1.0	0.7	0.2	1.6
Meconium ileus/other intestinal obstruction	16.3	6.8	10.1	N/A
Nasal polyps/sinus disease	3.7	5.1	0.0	15.3
Rectal prolapse	2.4	0.1	0.0	0.4
Steatorrhea/abnormal stools/malabsorption	19.3	3.3	1.4	7.2
Other	5.3	10.0	3.6	22.9

Data are not mutually exclusive. We anticipate that additional 2022 diagnoses will be entered into the Registry in 2023.

[A]*Those diagnosed in 2022 age <1 include age at diagnosis including some that may have been born in 2021.*

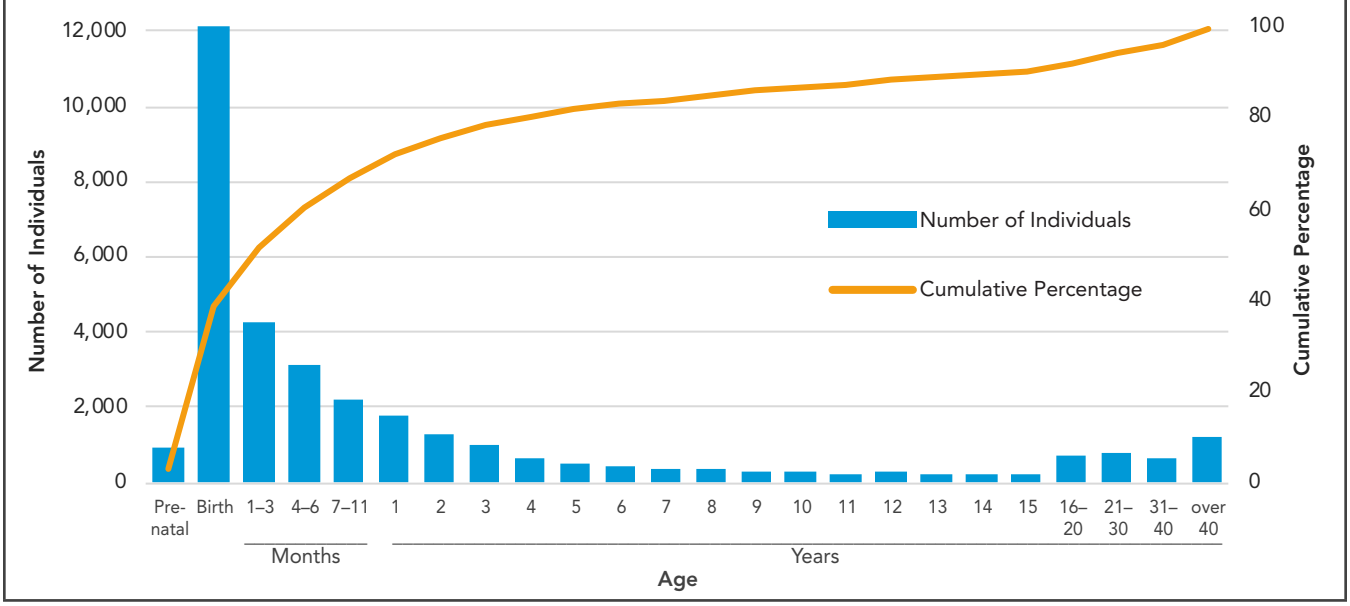
[B]*Chorionic villus sampling.*

[C]*Congenital bilateral absence of the vas deferens.*

[D]*Genitourinary.*

Previous figures in this section refer to infants born or diagnosed in 2022; the following figure includes all individuals followed in the Registry in 2022.

Age at Diagnosis of All Individuals With CF Seen in 2022

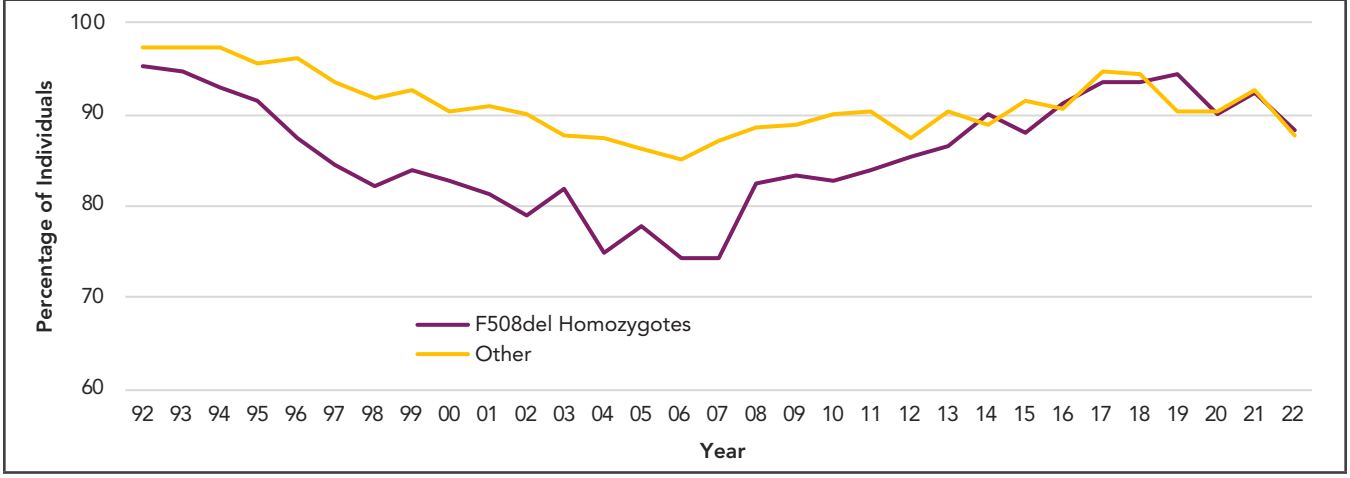


Diagnostic Tests

Sweat Chloride Testing

Sweat chloride testing is an important diagnostic test recommended for all individuals regardless of genotype.[8] In 2022, 90.8 percent of individuals in the Registry had a sweat chloride test result (at any time) recorded. Frequent sweat chloride testing is particularly important when considering the diagnosis of CF in adults who may have rare mutations. Additionally, baseline sweat chloride test values are becoming more important as changes in sweat chloride are now viewed as indicators of the physiological effects of CFTR modulators. In 2022, 13.3 percent of individuals with CF had two or more sweat chloride values reported. Access to sweat chloride testing may have been impacted by the pandemic. As genetic tests to establish a CF diagnosis became more widely available in early 2000s, the proportion of individuals for whom a sweat chloride value was reported to the Registry declined through 2007, with a lower proportion of F508del homozygous individuals reporting compared to those with other CFTR variant combinations. Since 2007, reporting of sweat chloride values has increased and is no longer differentiated by CFTR variant as visualized in the following chart.

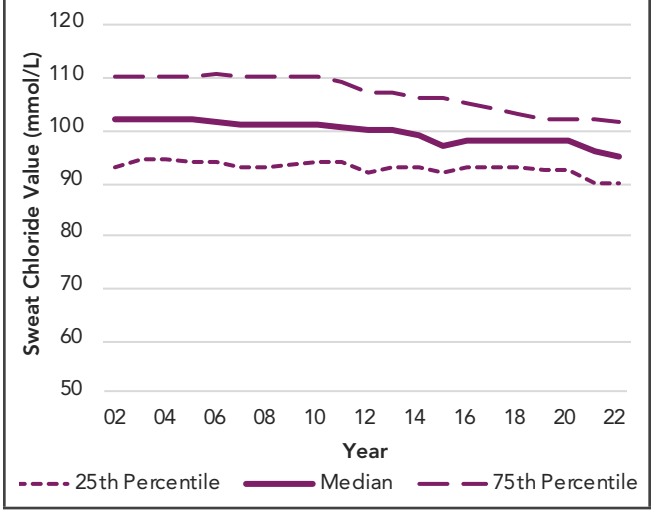
Percentage of Individuals With a Sweat Chloride Test Reported by Year of Diagnosis, 1992–2022



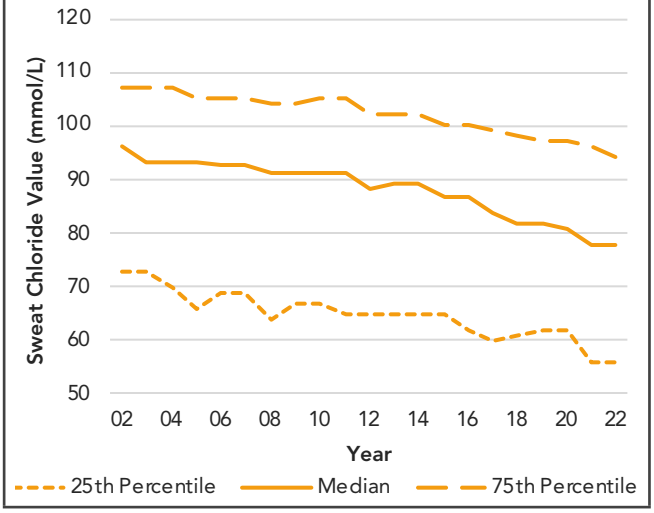
Sweat chloride testing is a critical component of the CF diagnosis regardless of genotype. Some individuals diagnosed in 2022 may not have had a sweat chloride test result entered in the Registry before the close of the reporting year.

Median sweat chloride test results have remained consistent over time for individuals who are F508del homozygous. In contrast, there has been a gradual decline in median sweat chloride values among individuals who are not homozygous for F508del, suggesting that more individuals with these other genotypes are being entered into the Registry.

Sweat Chloride Value of F508del Homozygous Individuals by Year of Diagnosis, 2002–2022



Sweat Chloride Value of Individuals Not Homozygous for F508del by Year of Diagnosis, 2002–2022



Genotyping

The cystic fibrosis transmembrane conductance regulator (CFTR) gene and the most prevalent CF-causing variant (F508del) were both discovered in 1989. Since then, genotyping has become a key component of the diagnostic evaluation. In addition, with the introduction of CFTR modulators, genotyping all people with CF is critical for both research and clinical care. In 2022, 99.4 percent of individuals (n=32,412) in the Registry had been genotyped.

CFTR GENE VARIANTS

To date, more than 2,000 variants have been found in the CFTR gene.[11] Some variants result in virtually no CFTR function and others are associated with some residual function. Various strategies have been used to categorize variants with the goal of grouping individuals with CF with a similar disease course and prognosis. In previous reports, a five-variant class system was used.[12-14] This classification system is helpful for understanding the impact of variants on the biosynthesis and function of the CFTR protein. However, it is increasingly recognized that this classification schema is an oversimplification, given that many variants result in more than one defect in CFTR function. In this era of CFTR modulators, a second approach is being evaluated for variant classification, referred to as theratyping. This system considers whether a variant responds to a specific CFTR modulator.

In this section, we report data on specific variants and the difference in sweat chloride values between disease-causing genotypes with little to no CFTR function versus those with residual CFTR function. The most common CFTR variant is F508del: 85.4 percent of individuals in the Registry who have been genotyped have at least one copy of this variant. There is a substantial drop in prevalence to the next most common variants. No other variant is currently found in more than 5.0 percent of the population with CF in the U.S. CFFPR.

Prevalence of the 25 Most Common CFTR Variants in People With CF Seen in 2022

CFTR Variant			Number of Individuals	Percentage of Individuals
Legacy Name	cDNA Name	Protein Name		
F508del	c.1521_1523delCTT	p.Phe508del	27,699	85.4
G542X	c.1624G>T	p.Gly542X	1,472	4.5
G551D	c.1652G>A	p.Gly551Asp	1,376	4.2
R117H	c.350G>A	p.Arg117His	1,102	3.4
N1303K	c.3909C>G	p.Asn1303Lys	753	2.3
W1282X	c.3846G>A	p.Trp1282X	715	2.2
3849+10kbC->T	c.3718-2477C>T		614	1.9
R553X	c.1657C>T	p.Arg553X	557	1.7
1717-1G->A	c.1585-1G>A		503	1.5
621+1G->T	c.489+1G>T		502	1.5
2789+5G->A	c.2657+5G>A		476	1.5
3120+1G->A	c.2988+1G>A		406	1.3
5T	c.1210-12T[5]		363	1.1
D1152H	c.3454G>C	p.Asp1152His	357	1.1
3272-26A->G	c.3140-26A>G		270	0.8
2184insA	c.2052dupA	p.Gln685ThrfsX4	258	0.8
R1162X	c.3484C>T	p.Arg1162X	248	0.8
L206W	c.617T>G	p.Leu206Trp	247	0.8
I507del	c.1519_1521delATC	p.Ile507del	242	0.7
G85E	c.254G>A	p.Gly85Glu	231	0.7
3659delC	c.3528delC	p.Lys1177SerfsX15	221	0.7
1898+1G->A	c.1766+1G>A		213	0.7
R347P	c.1040G>C	p.Arg347Pro	206	0.6
R334W	c.1000C>T	p.Arg334Trp	198	0.6
A455E	c.1364C>A	p.Ala455Glu	194	0.6

The number and percentage of individuals with a given variant include those with one or two copies of the variant.

F508del Variant Prevalence

F508del Variant	Percentage of Individuals
Homozygous F508del	44.0
Heterozygous F508del	41.4
Neither F508del or Unknown	14.6

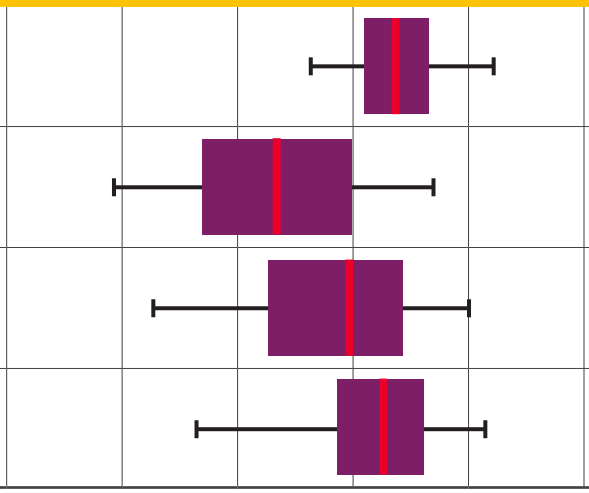
Prevalence is among individuals genotyped.

Among less common variants, the number of individuals with an R117H variant has increased over the years. Among those genotyped in 1993, less than 1.0 percent had an R117H variant, compared with 5.3 percent of those genotyped in 2022. This may be due to the inclusion of R117H in newborn screening algorithms. Of note, 122 (11.1 percent) of the 1,102 individuals with an R117H variant had a sweat chloride value less than 30 mmol/L, which adds to the diagnostic complexity.

The clinical significance of the R117H variant depends in part on the poly-T tract variant on the chromosome. Research indicates that a shorter poly-T tract is associated with a higher likelihood of having CF.[15,16] The Registry has incomplete information on the poly-T tract status for 56.1 percent who are reported as CF with an R117H variant. Of the 482 individuals with R117H and poly-T tract status recorded in the Registry, 163 (33.8 percent) are classified as having 5T.

Individuals with variants typically associated with little or no CFTR function tend to have higher sweat test values and are more likely to be prescribed pancreatic enzyme replacement therapy (PERT) than individuals with a variant typically associated with residual CFTR function (i.e., 96.2 percent vs. 30.5 percent).

Sweat Chloride Value (mmol/L), by Genotypes



	Median	5th Percentile	95th Percentile
Individuals with mutations associated with little or no CFTR function *N=20,043*	101.0	78.0	126.0
Individuals with one or more mutations associated with residual CFTR function *N=4,052*	70.0	28.0	111.0
Individuals with one or more unclassified mutations *N=4,95*	89.0	37.0	120.0
All individuals *N=28,990*	98.0	48.0	124.0

These charts use the highest sweat test value reported to the Registry. For 191 individuals, this value may reflect sweat chloride after initiation of CFTR modulator therapy as baseline value was not reported.

GUIDELINES: CARE, SCREENING, AND PREVENTION

The CF Foundation sponsors the development of clinical practice guidelines to promote high-quality care for both physical and mental health for individuals with CF during infancy, childhood, and adulthood.[17–26] Many CF Care Centers report four clinic visits, two pulmonary function tests, and at least one microbiology culture annually for most of their CF patients. Similarly, among children aged 2 to 5 years, the majority have at least four visits and one or more cultures each year.

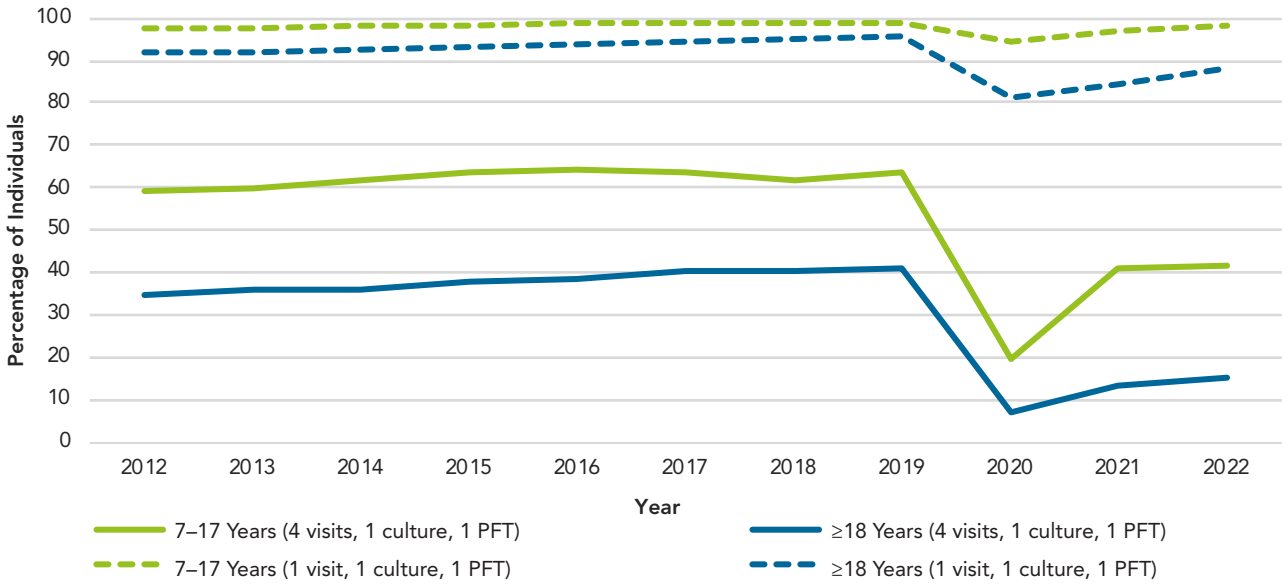
CF Care Centers report that respiratory therapists/physical therapists, dietitians/nutritionists, and social workers evaluate most of their patients at least once per year, as recommended.

The influenza vaccination rate for people with CF age 6 months and older remains high across the CF Care Center network. Smoking and secondhand smoke exposure remain challenges, particularly for infants and young adults.

Patient Care Guidelines

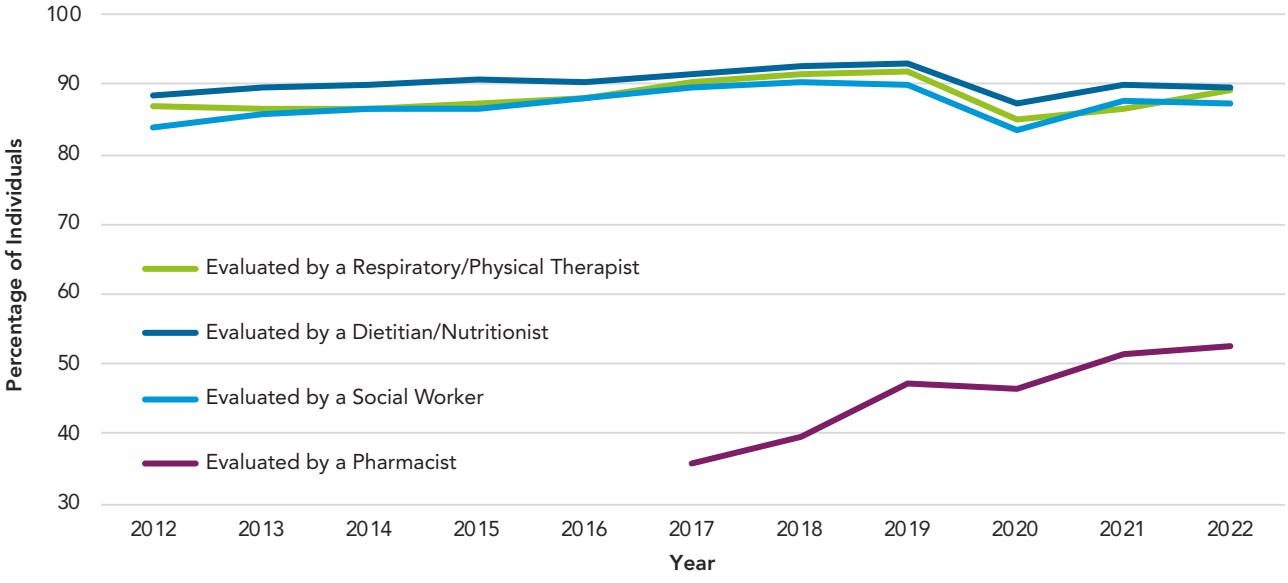
CF care delivery evolved quickly out of necessity during the pandemic. Some of these changes such as the inclusion of telehealth and home spirometry as remote care options have persisted at lower levels. Although in-person clinic attendance and surveillance testing increased as compared to the height of the pandemic, it is still not back to pre-pandemic levels. This likely reflects the improved health status for many people with CF. While many individuals did not have the recommended four clinic visits, four cultures, and two PFTs,[20] annually since 2020, most individuals (88.1 percent) were seen at least once with a culture and PFT in 2022. In 2022, 94.5 percent of individuals had at least one culture (of any kind), and 30.7 percent of individuals had four or more respiratory cultures; 78.0 percent of individuals had at least two PFTs. In addition, there were other touchpoints with the clinical team through telehealth visits and transmission of home spirometry data.

Clinical Encounters, Cultures, and PFTs: 2012–2022



The multidisciplinary care team plays an important role in CF care.[20] In 2022, 75.1 percent of individuals were evaluated by a respiratory/physical therapist, a dietitian/nutritionist, and a social worker. In addition, given the complex treatment regimens in CF including CFTR modulator therapy, the Registry captures whether patients were seen by a pharmacist in clinic. In 2022, 51.7 percent of individuals were seen by a pharmacist at least once during the year.

Percentage of Individuals Evaluated by Multidisciplinary Care Team Members, 2012–2022



The CF Foundation also recommends the inclusion of a mental health professional as part of the CF care team.[18] Information on screening for anxiety and depression is included in the Complications section (page 66).

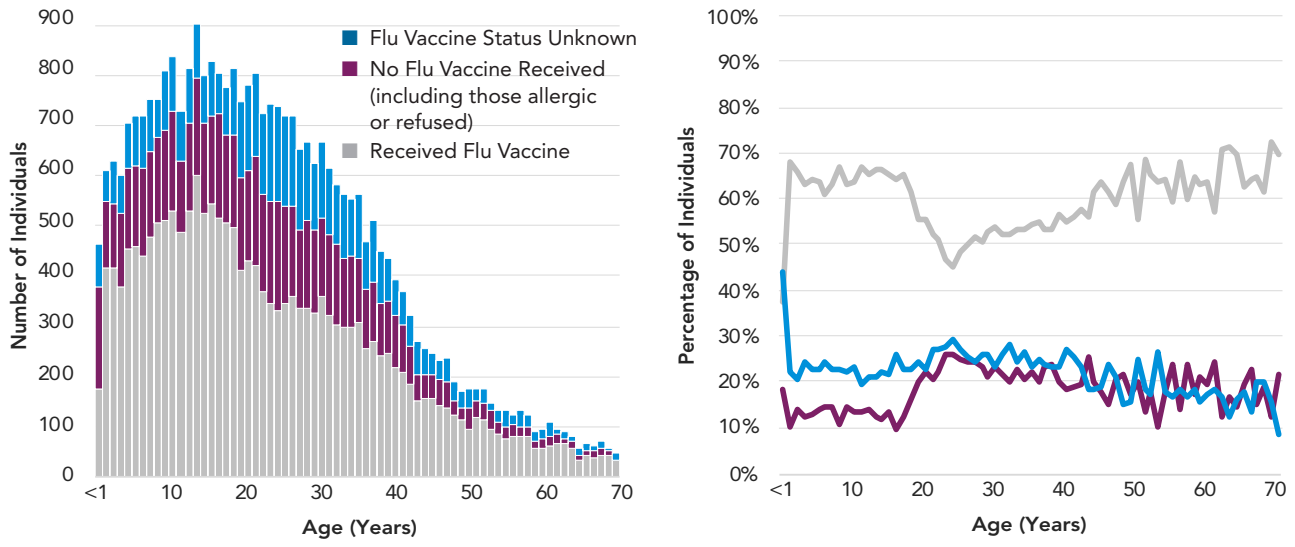
CF Foundation guidelines recommend annual measurement of fat-soluble vitamins to screen for vitamin deficiency.[20,24] Conversely, there have been reports of high vitamin A levels in some patients on CFTR modulators, which may have clinical sequelae.[25] The CF Foundation Hepatobiliary Disease Consensus Group recommends a yearly panel of liver blood tests for all people with CF to screen for possible liver disease.[25] Registry data suggest that these tests are being done for most individuals.

Percentage of Individuals Screened by or Monitored With Annual Labs, by Center

	0 — 50 — 100	Median	Min	Max
Individuals With Fat-Soluble Vitamins Measured		87.9	69.0	100.0
Individuals With Liver Enzymes Measured		89.4	73.1	100.0

Influenza immunization is recommended for individuals with CF age six months and older on an annual basis. In 2022, 71.3 percent of the total population was reported to have received a flu vaccine, compared to 78.1 percent in 2021. Of those with known immunization status, flu immunization was similar among children and adults in 2022, with 74.2 percent of those less than 18 years of age and 69.0 percent of those 18 years or older. The proportion of individuals with an unknown vaccination status was 17.7 percent in 2022, a slight decrease compared to 18.5 percent unknown in 2021. The percent with unknown vaccination status is approximately 5.0 percent higher than pre-pandemic levels.

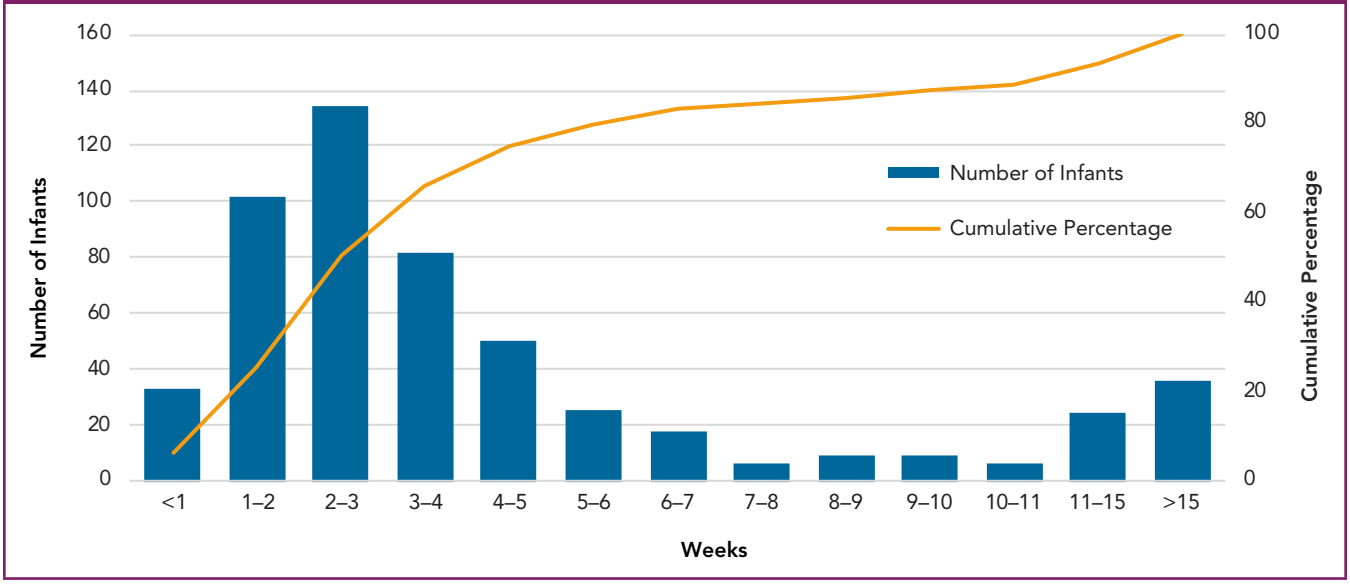
Flu Vaccine Status by Age in Years, 2022 *(Stacked Bar Chart)*



Infant Care Guidelines

The CF Foundation recommends that evaluation and treatment of infants detected by newborn screening be done at a CF Foundation-accredited Care Center, with the goal of an initial visit within 24 to 72 hours of diagnosis. It is important to make a definitive diagnosis as quickly as possible to minimize the stress and uncertainty for families. For those diagnosed with CF, families can be educated about the disease and treatment can be started.[28] Of infants identified by abnormal newborn screening in 2022, 88.7 percent had their first clinic encounter, care episode, or sweat test (first CF event) within 60 days of birth.

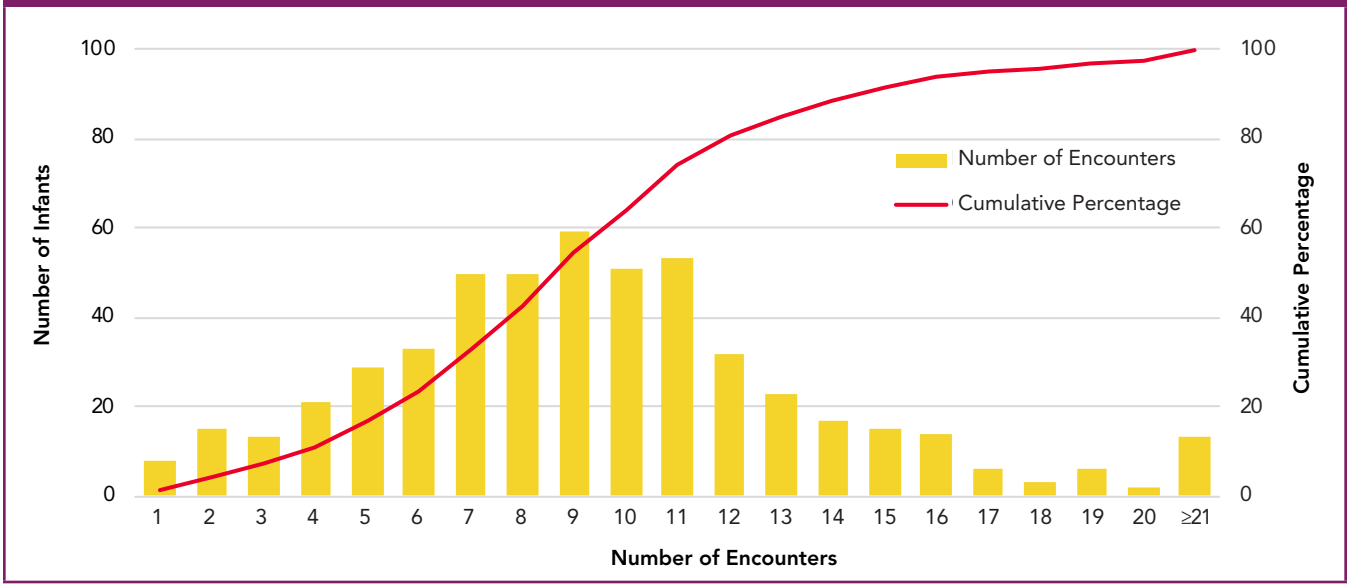
Time to First Clinic Encounter, Care Episode, or Sweat Test for Infants With CF Born in 2021 and Detected by Newborn Screening (n=534)



This chart shows data for children born in 2021 with a full year of follow-up data available. Median time to first CF event for these individuals was 20 days with 85.7 percent within 60 days of birth.

The CF Foundation infant care guidelines recommend monthly CF Care Center visits during the first six months of life and every one to two months in the second six months.[28] Therefore, the expectation is that infants with CF detected by NBS will have 9 to 12 visits in the first year of life. Despite the COVID-19 pandemic, CF Care Centers provided a similar level of care to infants compared to previous years based on median number of clinic visits, number of cultures, and fecal elastase tests performed during the first year of life.

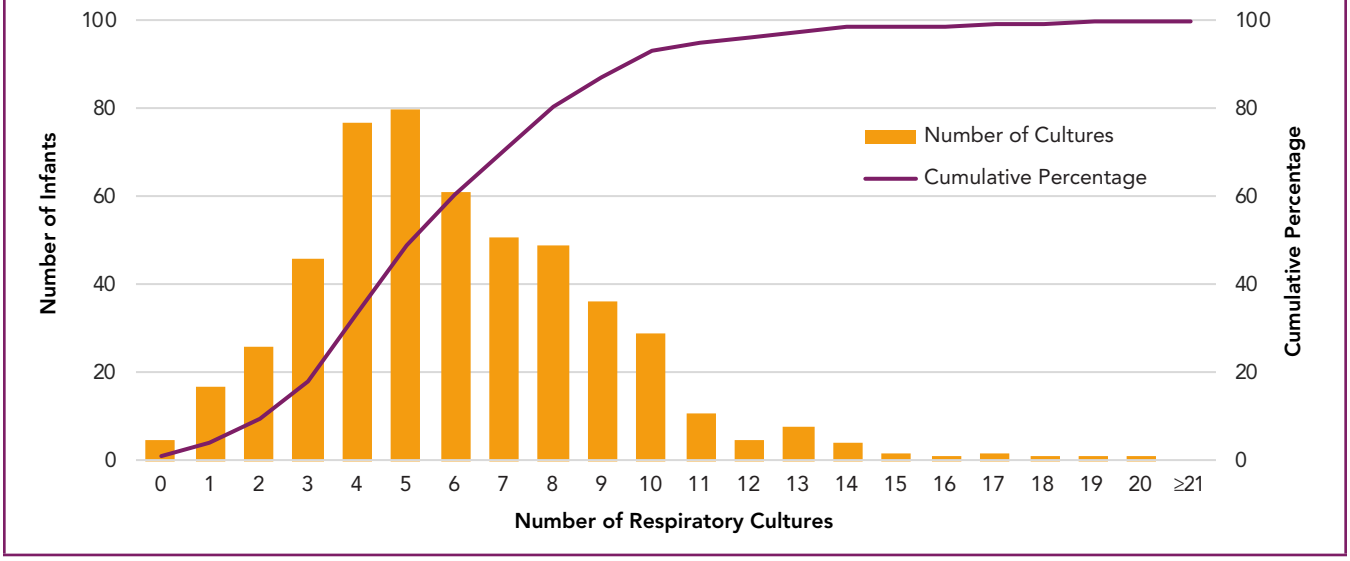
Number of Encounters in the First Year of Life for Infants With CF Born in 2021 and Detected by Newborn Screening (n=513)



The chart shows data for children born in 2021 because a full year of data is available for these individuals. The median number of visits in the first year of life is nine.

Of the 534 infants diagnosed, 513 infants had at least one clinic visit reported in 2022. Infant care guidelines recommend that cultures be performed at least quarterly during the first two years of life.[28] Respiratory cultures are collected at most clinic visits for infants with CF.

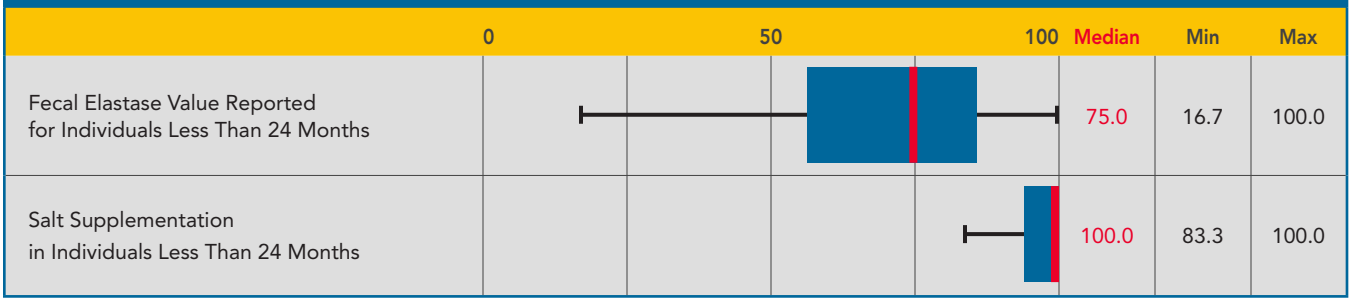
Number of Respiratory Cultures in the First Year of Life for Infants With CF Born in 2021 and Detected by Newborn Screening (n=513)



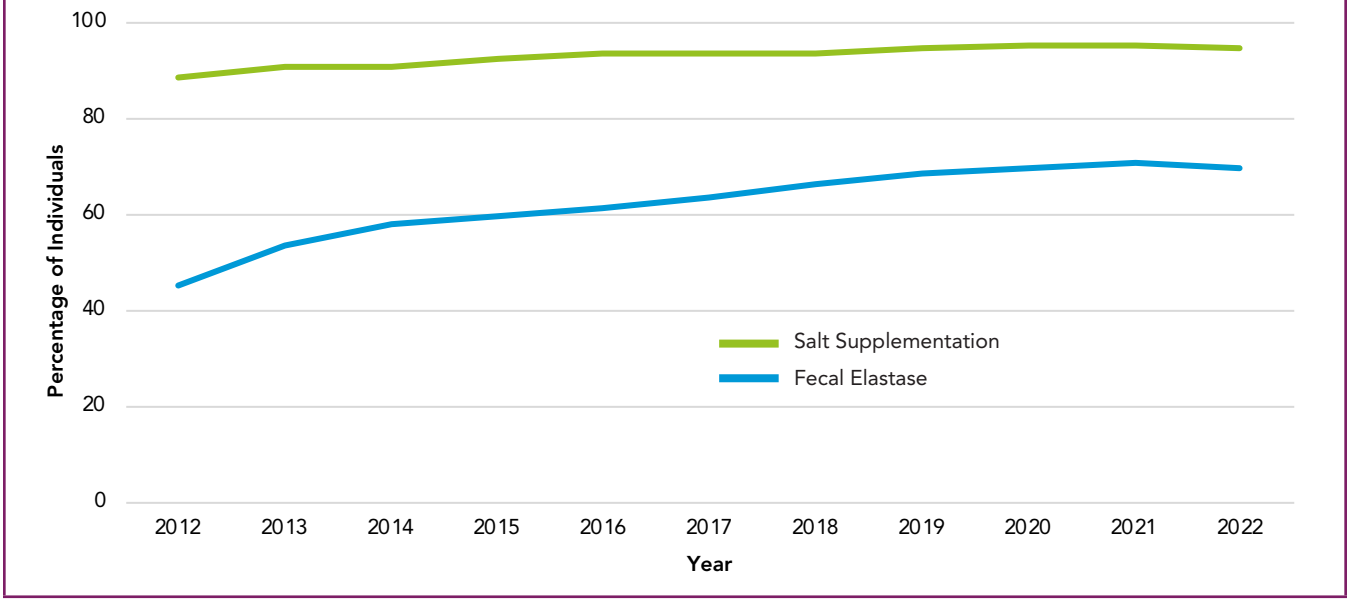
The chart shows data for children born in 2021 because a full year of data is available for these individuals. The median number of cultures in the first year of life is six.

Fecal elastase testing, which provides an objective measure of pancreatic function, is recommended in the infant care guidelines.[28] There is marked variation in the use of this test across the CF Care Center network. The guidelines also recommend that infants begin salt supplementation after diagnosis, and this is highly followed across the CF Care Center network.

Infant Care Guidelines, by Center



Testing and Therapies for Individuals Under 24 Months of Age, 2012–2022



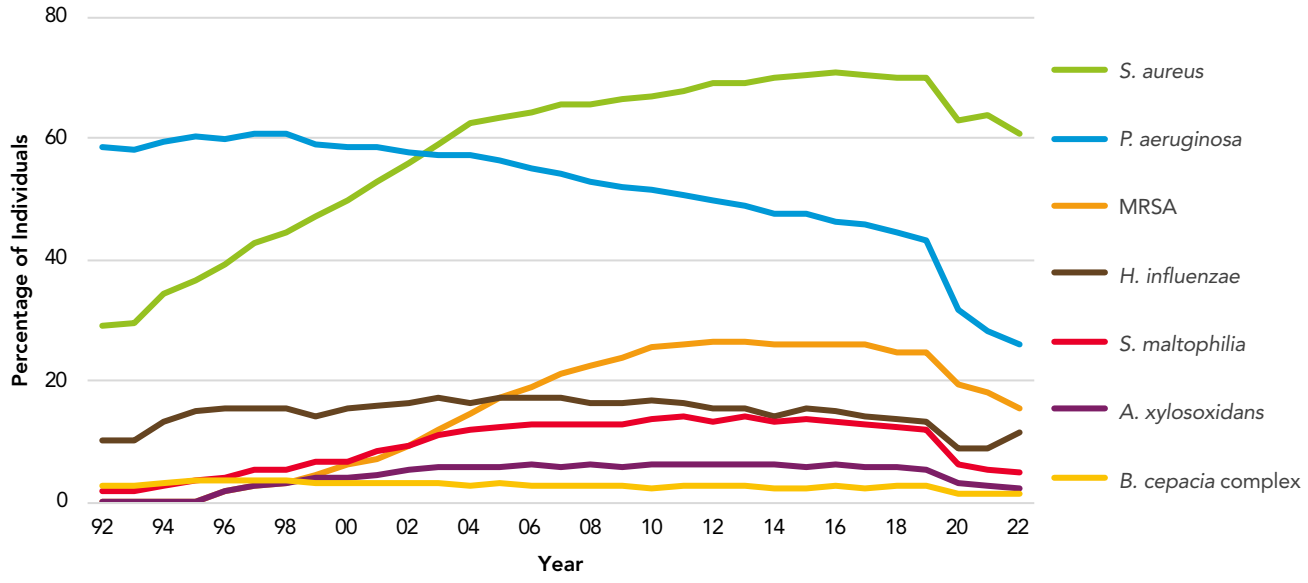
MICROBIOLOGY

This section provides information on trends in airway pathogens over time and by age group for individuals with CF. It also includes historical data on lung transplant recipients prior to the year of their transplant. Infection prevention and control guidelines provide current best practices for reducing exposure to CF pathogens in the health care setting and in everyday life.[21]

As noted in the About this Report section, the decreased number of cultures collected in 2022 is likely a contributing factor to the lower prevalence of bacterial and mycobacterial pathogens. Less frequent culture surveillance during the COVID-19 pandemic and increased use of highly effective modulator therapy (HEMT), as well as more stringent infection prevention and control strategies, may have impacted detection of microorganisms.

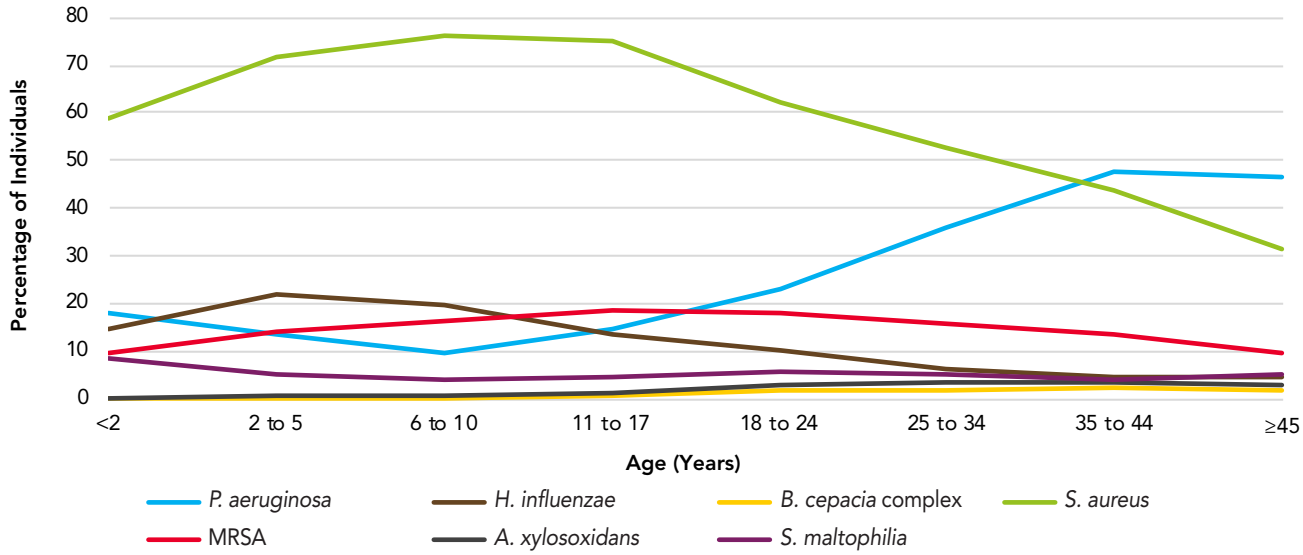
The graph shows the prevalence of *Pseudomonas aeruginosa* (*P. aeruginosa* or PA) continues to decrease over time. This may relate in part to widespread implementation of eradication strategies at the time of initial acquisition.[21,25] The prevalence of multidrug-resistant *P. aeruginosa* (MDR-PA) dropped from 3.5 percent in 2021 to 3.3 percent in 2022.

Prevalence of Respiratory Microorganisms, 1992–2022



The graph shows the proportion of individuals in various age groups who cultured positive for the bacterial species indicated during 2022.

Prevalence of Respiratory Microorganisms by Age Cohort, 2022

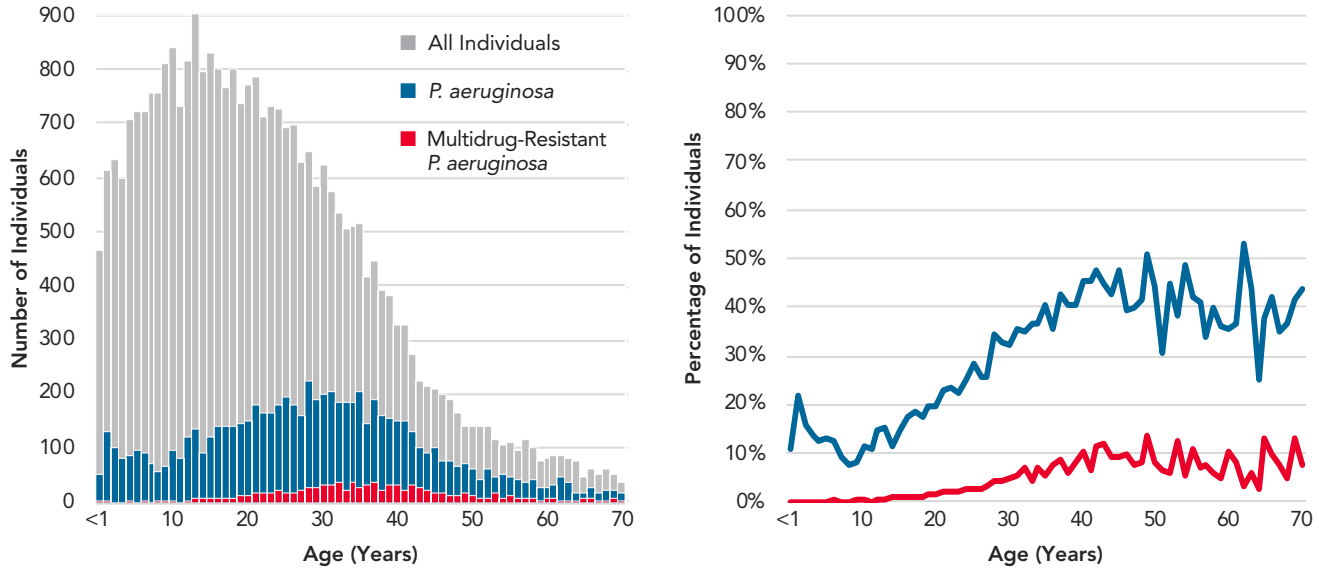


Pseudomonas aeruginosa

The percentage of individuals with a positive culture for *P. aeruginosa* has continued to decline over time, with the largest decrease observed among individuals younger than 18 years (43.8 percent had a positive culture in 2002 compared with 13.5 percent in 2022).

Rates of multi-drug resistant *Pseudomonas aeruginosa* (MDR-PA) infection are greatest in older adolescents and adults with CF. This finding likely reflects cumulative exposure to antibiotics. Among the individuals with CF who had at least one bacterial culture in 2022, 3.3 percent were reported to have MDR-PA. Among the individuals with CF and a culture that grew *P. aeruginosa* in 2022, 12.7 percent were reported to have MDR-PA.

P. aeruginosa and Multidrug-Resistant *P. aeruginosa* by Age in Years, 2022

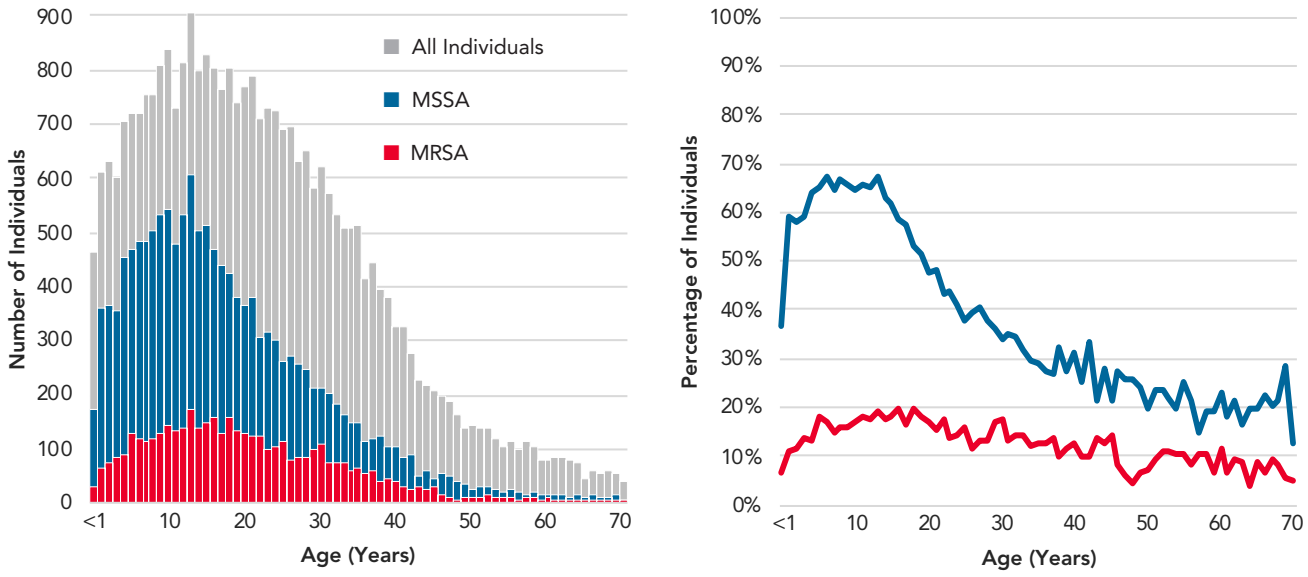


Multidrug resistance is defined as resistance to all antibiotics tested in two or more antibiotic classes in a single culture.

Staphylococcus aureus

Approximately half (50.2 percent) of individuals who provided a respiratory sample had at least one culture positive for methicillin-sensitive *S. aureus* (MSSA) in 2022. This chart shows that MSSA peaks among those younger than 15 whereas the highest prevalence of MRSA occurs in individuals between the ages of 10 and 20.

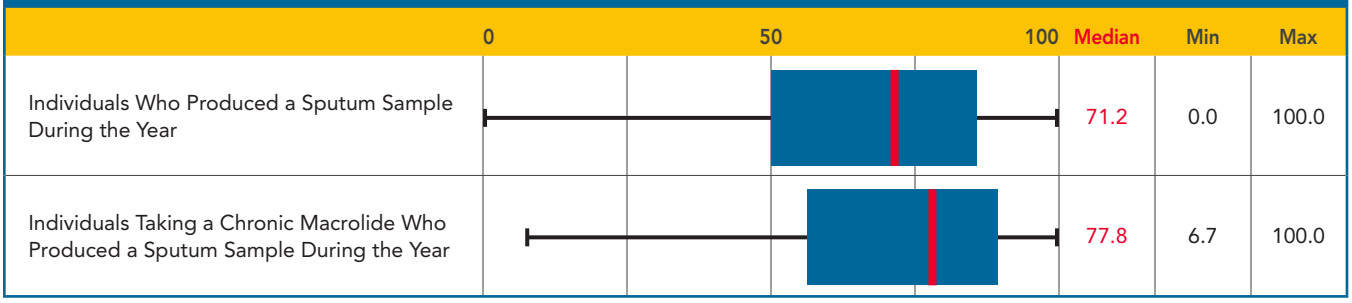
MSSA and MRSA by Age in Years, 2022



Nontuberculous Mycobacteria

Since a throat swab is insufficient for a mycobacterial culture, the CF Foundation/European Cystic Fibrosis Society Guidelines Committee recommends that individuals with CF who can expectorate sputum should be cultured for NTM infections annually.[29] Individuals should also be screened before and six months after beginning chronic azithromycin therapy and annually thereafter.[3] The data show improvement in screening rates over time, but wide variation by CF Care Center persists. Additionally, the median percentage of individuals (by Center) who produced a sputum sample in 2022 remained stable as compared to 2021, 71.2 percent and 71.4 percent, respectively, but lower than 2019 and earlier.

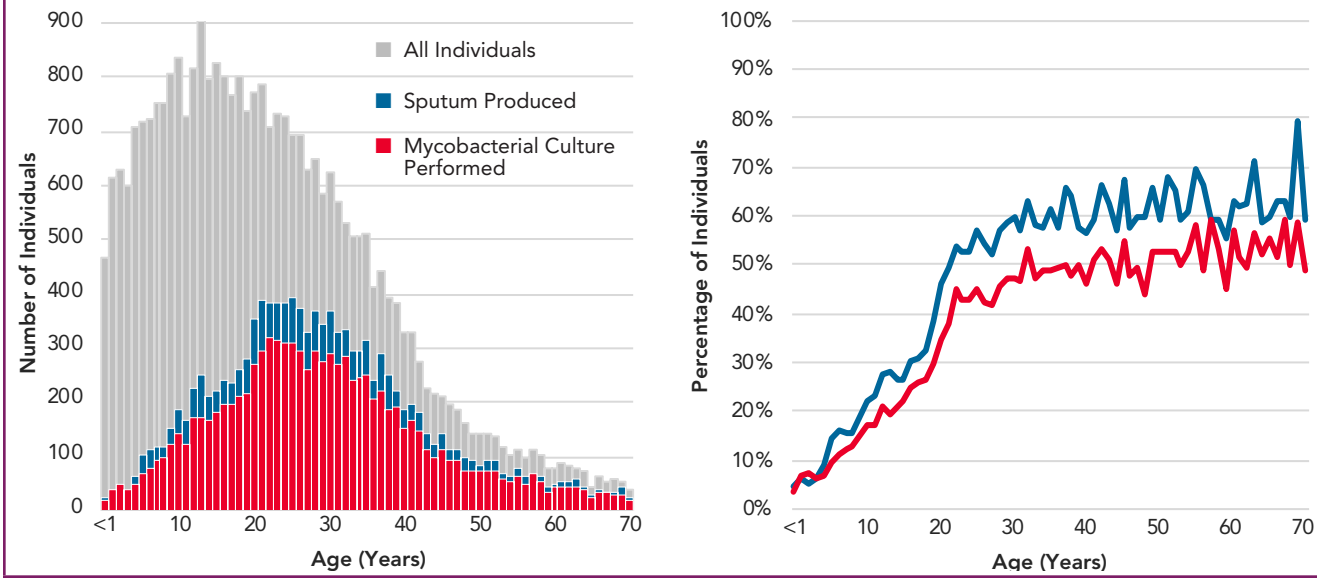
Percentage of Individuals With a Mycobacterial Culture, by Center



Chronic macrolide includes options for oral azithromycin and oral clarithromycin.

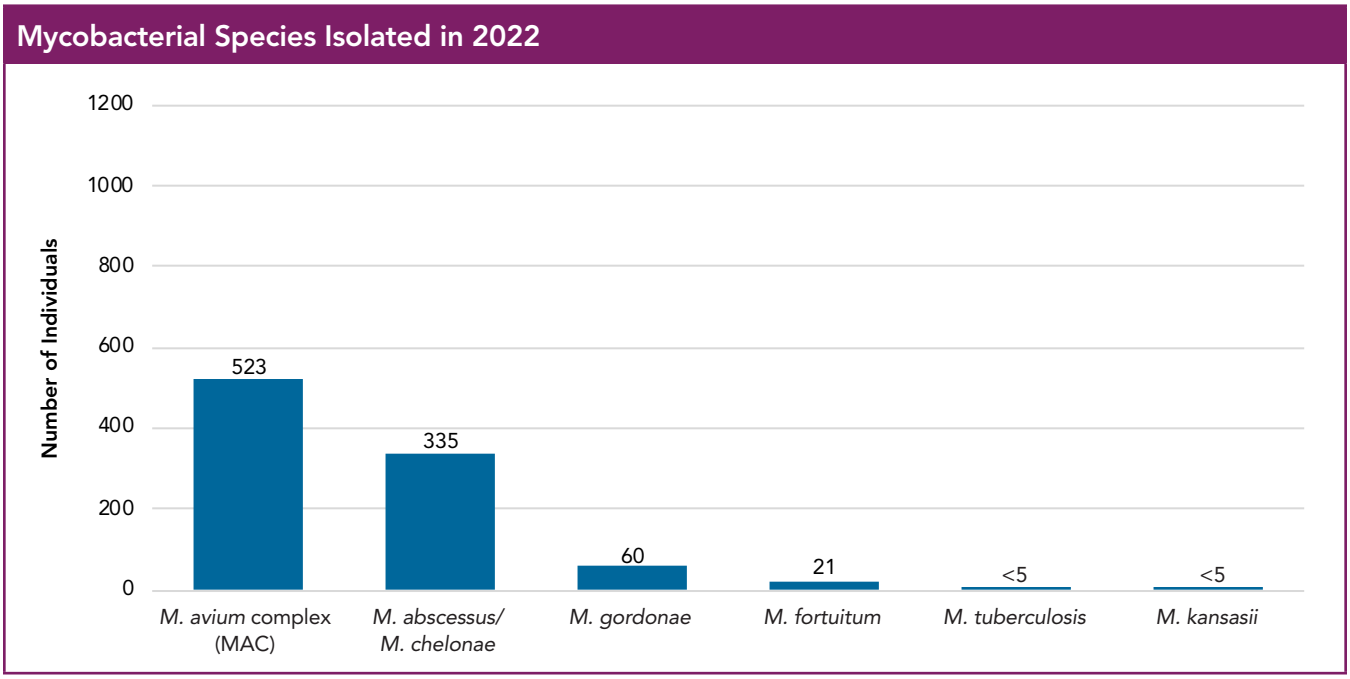
The graph below shows the proportion of individuals providing a sputum sample for mycobacterial culture surveillance across the age range.

Sputum Produced and Mycobacterial Cultures by Age in Years, 2022



Of the 10,053 individuals who had a mycobacterial culture performed in 2022, 1,038 (10.3 percent) had a mycobacterial species isolated one or more times, a slight increase from 10.0 percent in 2021. The prevalence of positive NTM cultures remains below that found in 2019 (13.9 percent) and earlier.

Mycobacterial Species Isolated in 2022



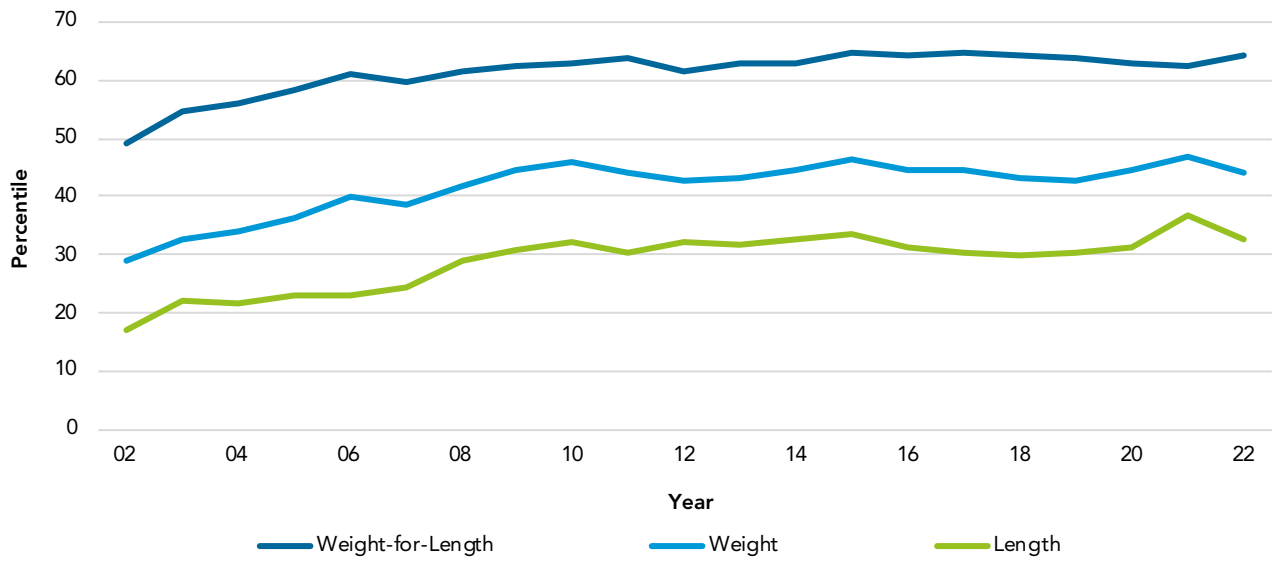
Data are not mutually exclusive. Some individuals had more than one species isolated in 2022.

NUTRITION

Nutritional outcomes are a key measure of health in people with CF. This section is divided into three age groups to report nutrition metrics: infants younger than 2 years, children 2 to 19 years, and adults 20 years and older for individuals who never received a lung transplant or prior to the year of lung transplant, if applicable. Overall improvements in nutritional metrics are observed for all ages. CF Foundation evidence-informed guidelines recommend enteral tube feeding to improve age-dependent anthropometrics and nutrition in individuals with CF who are unable to consume adequate nutrition to meet goals.[30]

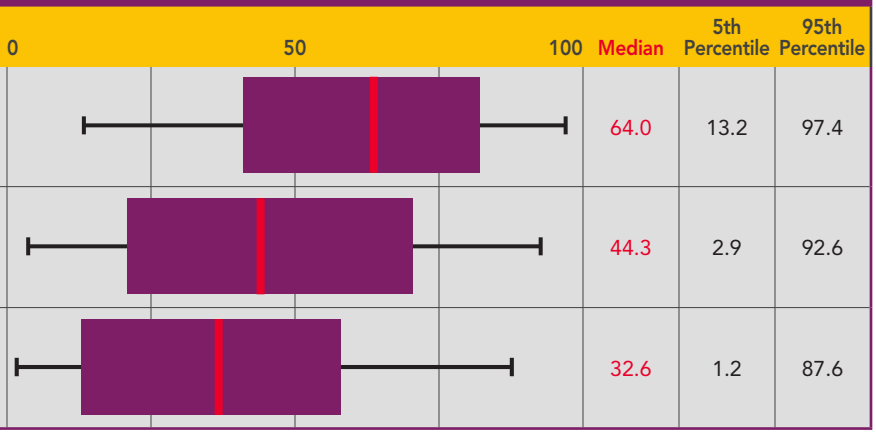
Goals for weight-for-length and body mass index (BMI) percentile in children are based on Centers for Disease Control and Prevention (CDC) growth curves. However, the CDC and the American Academy of Pediatrics recommend the use of World Health Organization (WHO) growth curves for children younger than 24 months of age.[31] WHO growth curves are used to report the data below.

Median WHO Nutritional Outcome Percentiles for Infants Under 24 Months, 2002–2022



The following charts show the population-level variation first for infants <24 months using WHO weight-for-length, weight, and length percentiles by age and then for children aged 2 to 19 years using height, weight, and BMI percentiles calculated from CDC growth standards. As would be expected for a large population, there is substantial variation observed for all three metrics in both age groups. Among infants under 24 months of age, the median values for weight-for-length are above the recommendation of 50th percentile.

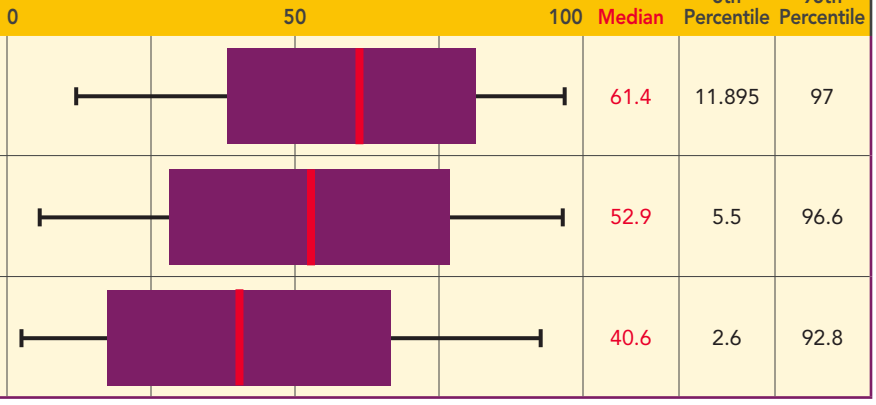
WHO Nutritional Outcomes for Infants Under 24 Months



	Median	5th Percentile	95th Percentile
Weight-for-Length *N=1,527*	64.0	13.2	97.4
Weight Percentile *N=1,537*	44.3	2.9	92.6
Length Percentile *N=1,528*	32.6	1.2	87.6

The target BMI percentile established by the CF Foundation nutrition guidelines for children aged 2 to 19 years is at or above the 50th percentile using CDC growth curves.[24] In 2022, the median weight and BMI percentiles were above the 50th percentile. The median height percentile remains well below the 50th percentile.

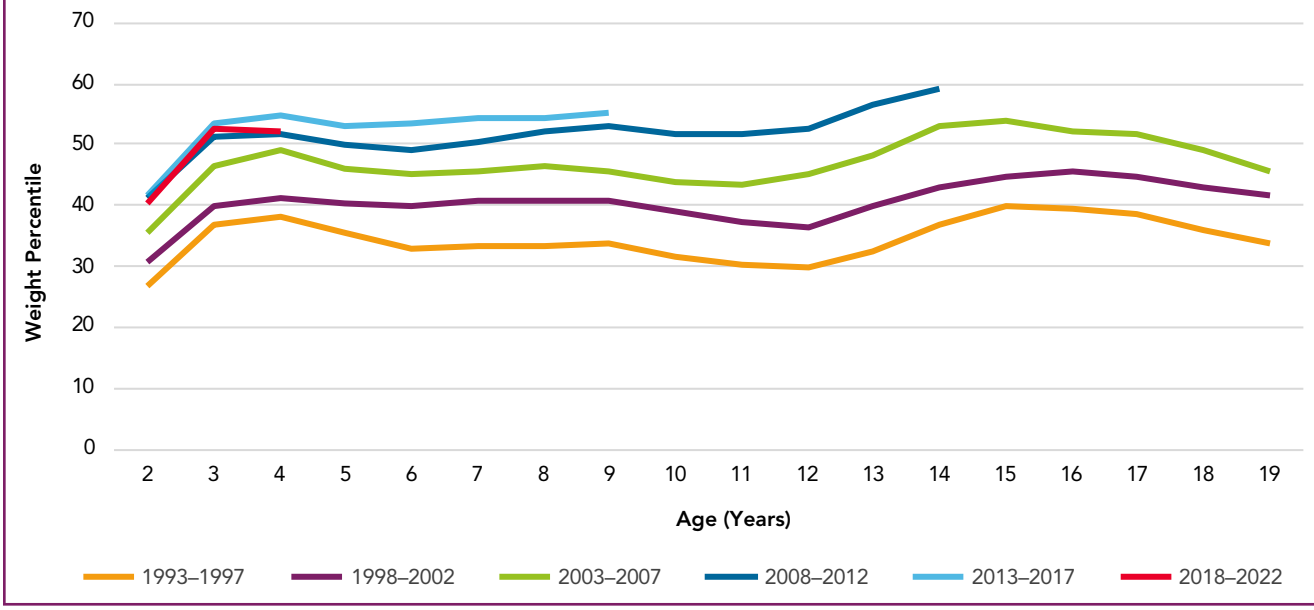
CDC Nutritional Outcomes for Individuals 2 to 19 Years



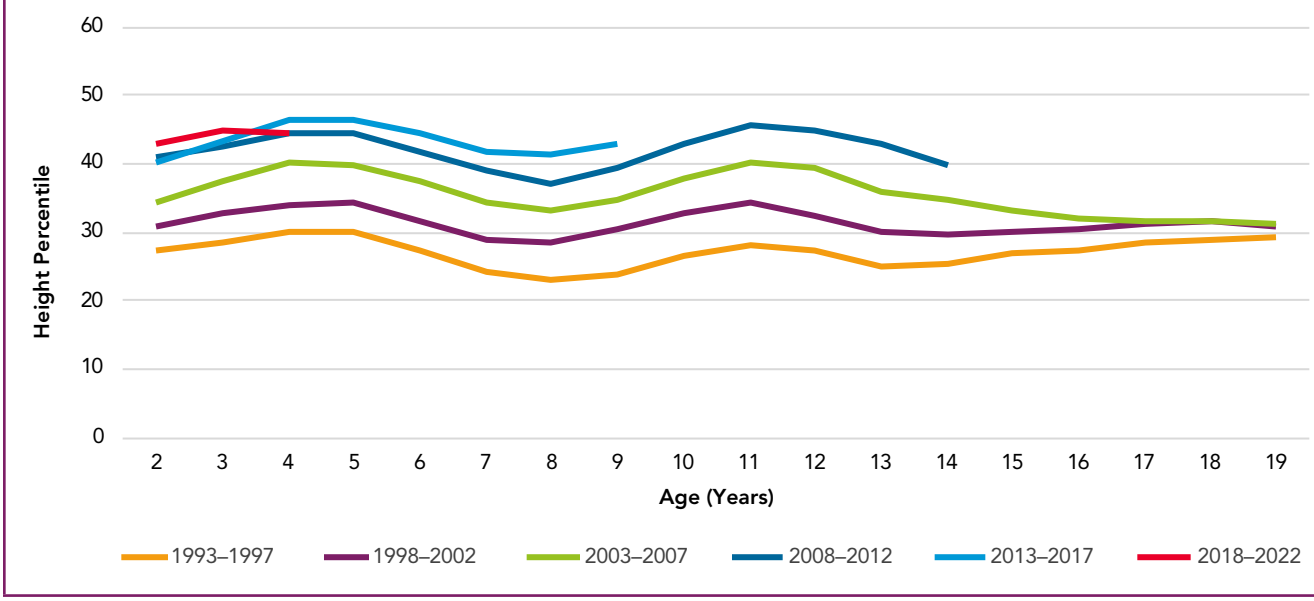
	Median	5th Percentile	95th Percentile
BMI Percentile *N=13,460*	61.4	11.895	97
Weight Percentile *N=13,595*	52.9	5.5	96.6
Height Percentile *N=13,584*	40.6	2.6	92.8

The median height percentiles reported among children 2–19 years of age do not exceed 50th percentile for any birth cohorts from 1993–1997 to 2018–2022. In contrast, median weight percentiles for those born after 2008 are at or above the 50th percentile from age 3 onward.[32] All percentile values are calculated in reference to the CDC growth standards.

Median CDC Weight Percentile, by Age and Birth Cohort in 2022

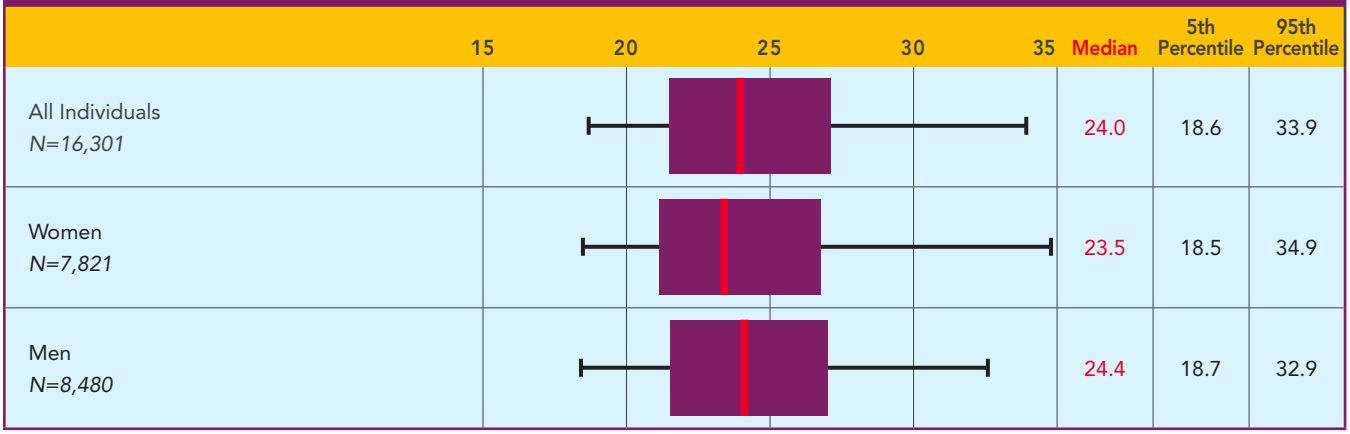


Median CDC Height Percentile, by Age and Birth Cohort in 2022



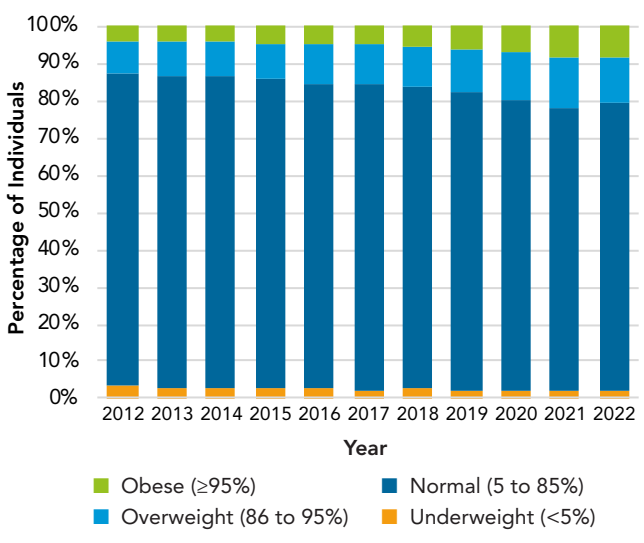
For individuals aged 20 years and older, the goal BMI established by the CF Foundation nutrition guidelines is at or above 22 for women and 23 for men.[24] This chart shows that more than half of individuals in this age range achieved this goal in 2022.

BMI Value for Adults 20 Years and Older

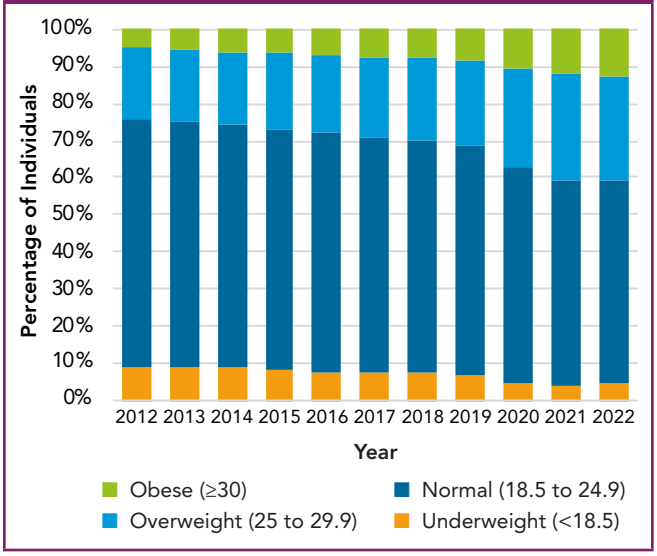


Improvements in nutrition and dietary interventions have substantially decreased the percentage of adults that are significantly underweight, defined as a BMI less than 18.5 (only 4.4 percent in 2022 compared to 15.7 percent in 2002). Conversely, 40.9 percent of adults have a BMI in the range categorized by CDC as overweight (28.1 percent) or obese (12.8 percent), with a higher prevalence in men (44.6 percent) than women (36.9 percent). The percentage of adults who are overweight or obese has more than doubled in the past 20 years (15.8 percent in 2002). Much of this increase is likely attributable to CFTR modulator therapy.[33] Avoiding extremes of nutritional outcomes for all age ranges is important for long-term health.

BMI Percentile Category Distribution for Individuals 2-19 Years, 2012–2022

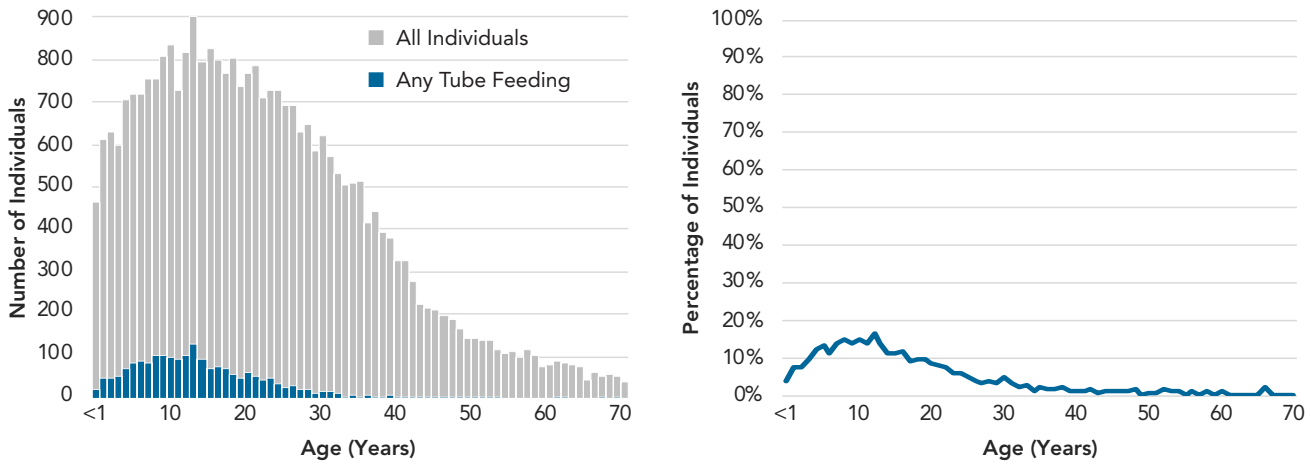


BMI Category Distribution for Individuals 20 Years and Older, 2012–2022



Despite these gains, tube feeding is still used to improve nutritional outcomes primarily for children, adolescents, and young adults with CF.

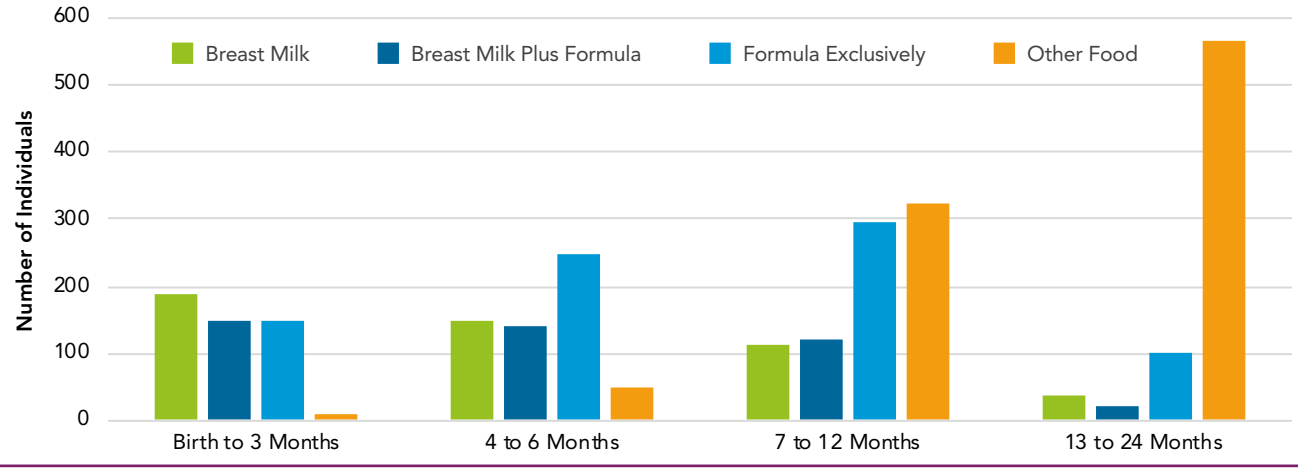
Tube Feeding by Age in Years, 2022



Infant Feeding

Most infants with CF receive formula as the primary form of feeding or as a supplement to breastfeeding. Cow's milk-based formula with the standard caloric density of 20 calories per ounce is the most common formula used from birth to age 3 months. More calorie-dense formulas are used after 3 months of age. CF Foundation infant care guidelines recommend human breast milk or standard infant formula as the initial form of feeding. Fortified human breast milk, calorie-dense formulas, or complementary foods are recommended if the infant is failing to gain weight adequately.[28]

Form of Feeding by Age in 2022*



**Infants may be included in more than one age category. They may also be counted more than once within an age category if different forms of feeding were recorded during separate clinic visits while within the same age category.*

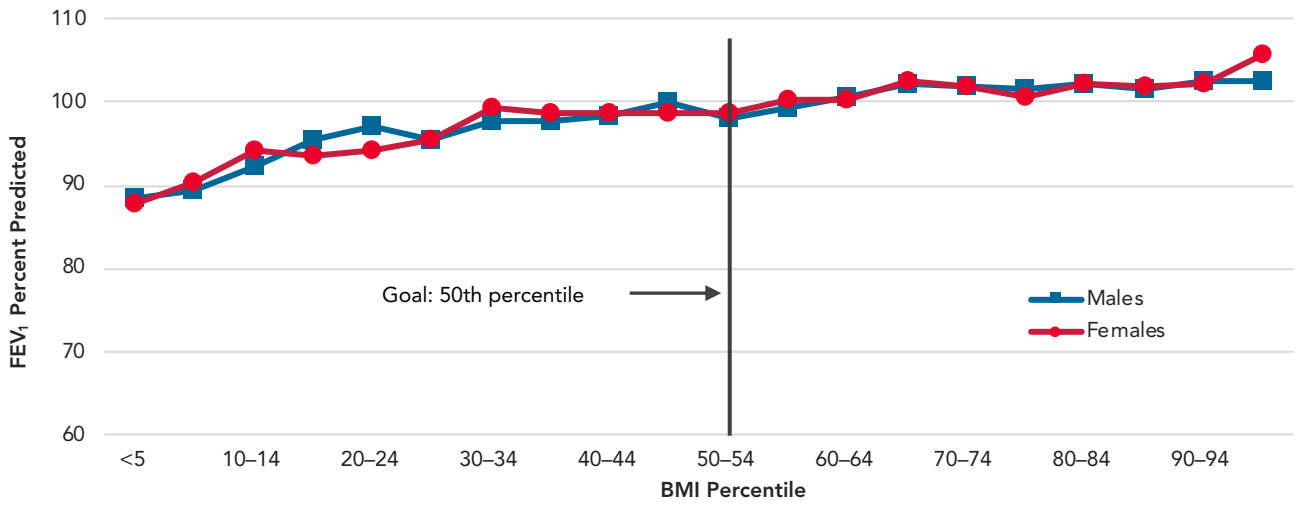
PULMONARY AND NUTRITIONAL OUTCOMES

Pulmonary and nutritional outcomes are two key measures of CF health. The data show that for all people with CF, better pulmonary function and optimal BMI percentile are associated. However, with the increase in BMI noted over time, particularly with CFTR modulator therapy, emphasis on a healthy diet is necessary to prevent obesity and associated comorbidities.

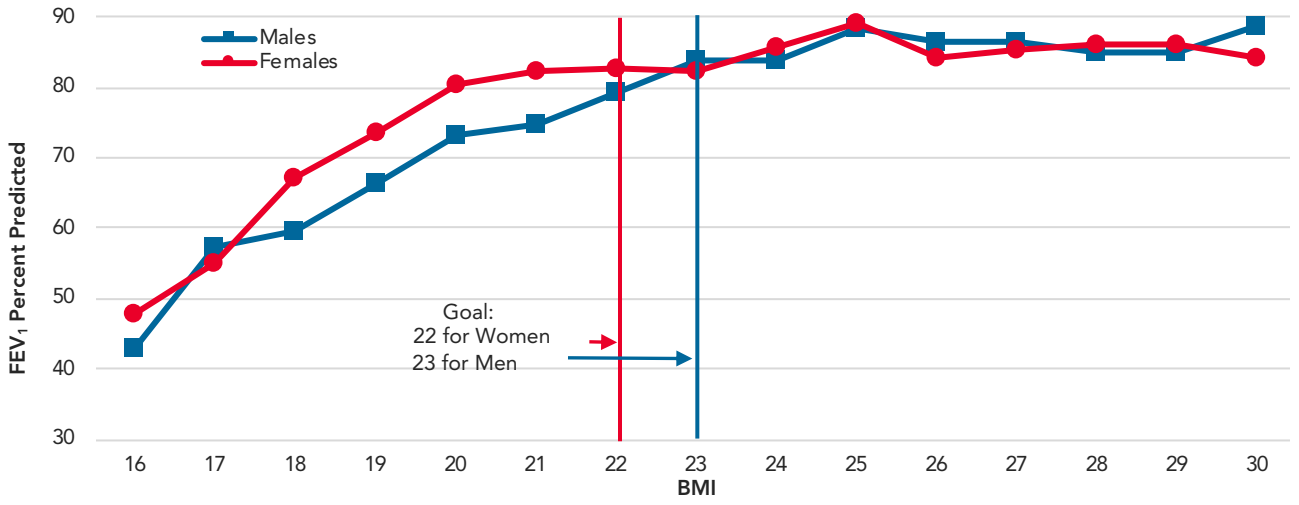
Pulmonary and nutritional goals[24] are as follows:

- *For children, FEV_1 percent predicted greater than or equal to 100, and BMI percentile meeting or exceeding the 50th percentile.*
- *For adults, FEV_1 percent predicted greater than or equal to 75, and BMI value greater than or equal to 22 for women and 23 for men.*

FEV_1 Percent Predicted vs. BMI Percentile for Children 6 to 19 Years in 2022

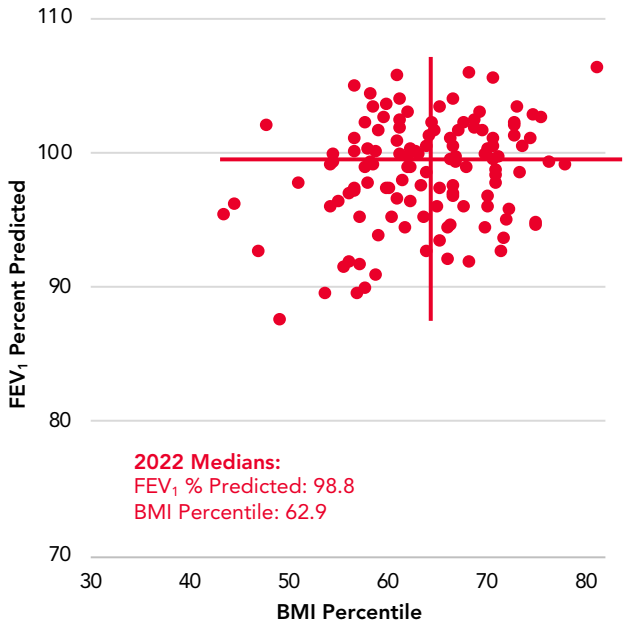


FEV_1 Percent Predicted vs. BMI Value for Adults 20 to 40 Years in 2022

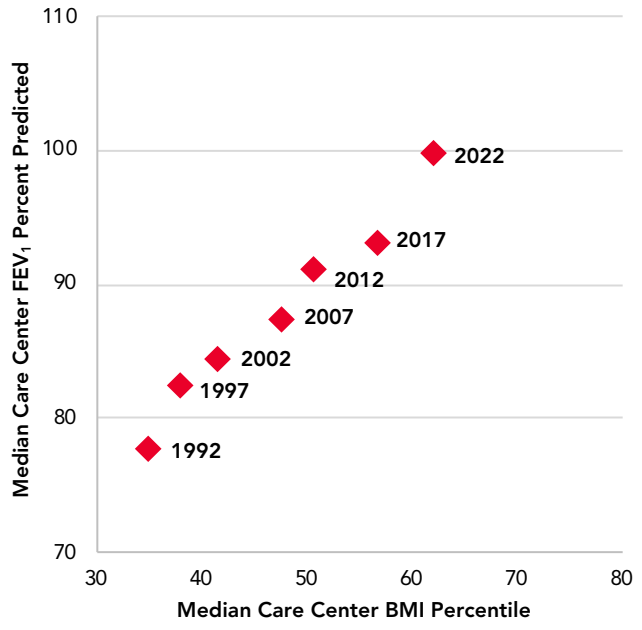


The figures below on the left show median BMI percentile and FEV_1 percent predicted values for each center in 2022. The figures on the right show how median values for all centers have improved over the last 30 years.

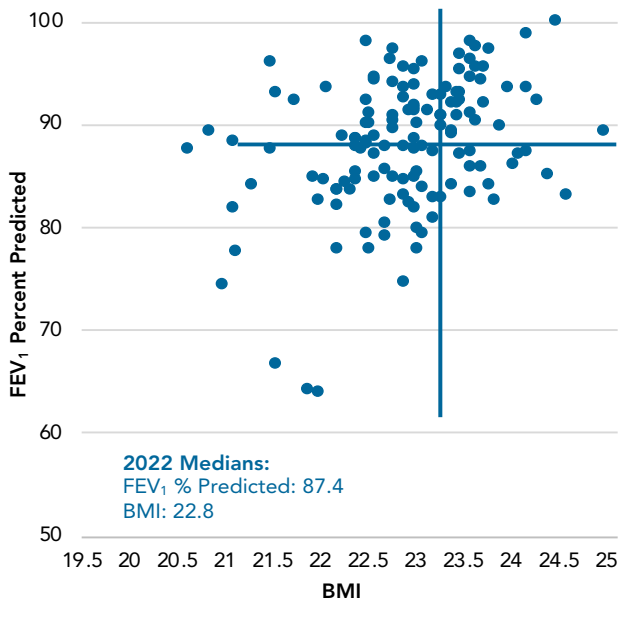
Median FEV_1 Percent Predicted vs. Median BMI Percentile for Individuals 6 to 19 Years, by Center



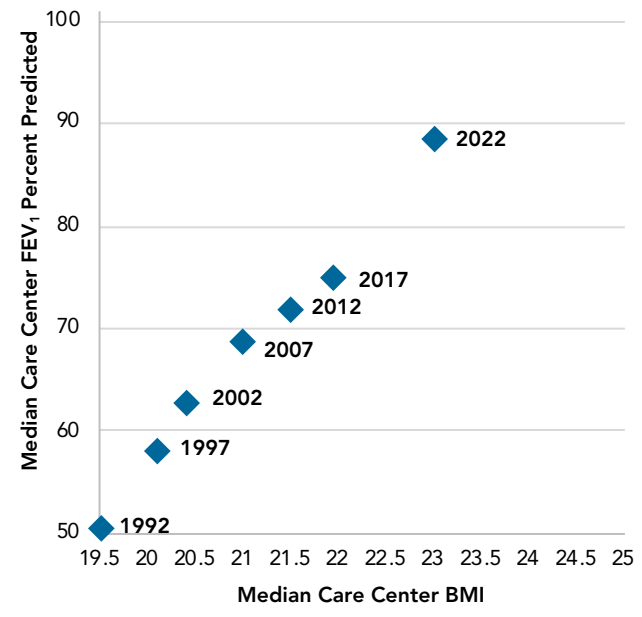
Median Care Center Value for Individuals 6 to 19 Years, 1992–2022



Median FEV_1 Percent Predicted vs. Median BMI Value for Individuals 20 to 40 Years, by Center



Median Care Center Value for Individuals 20 to 40 Years, 1992–2022



PULMONARY FUNCTION

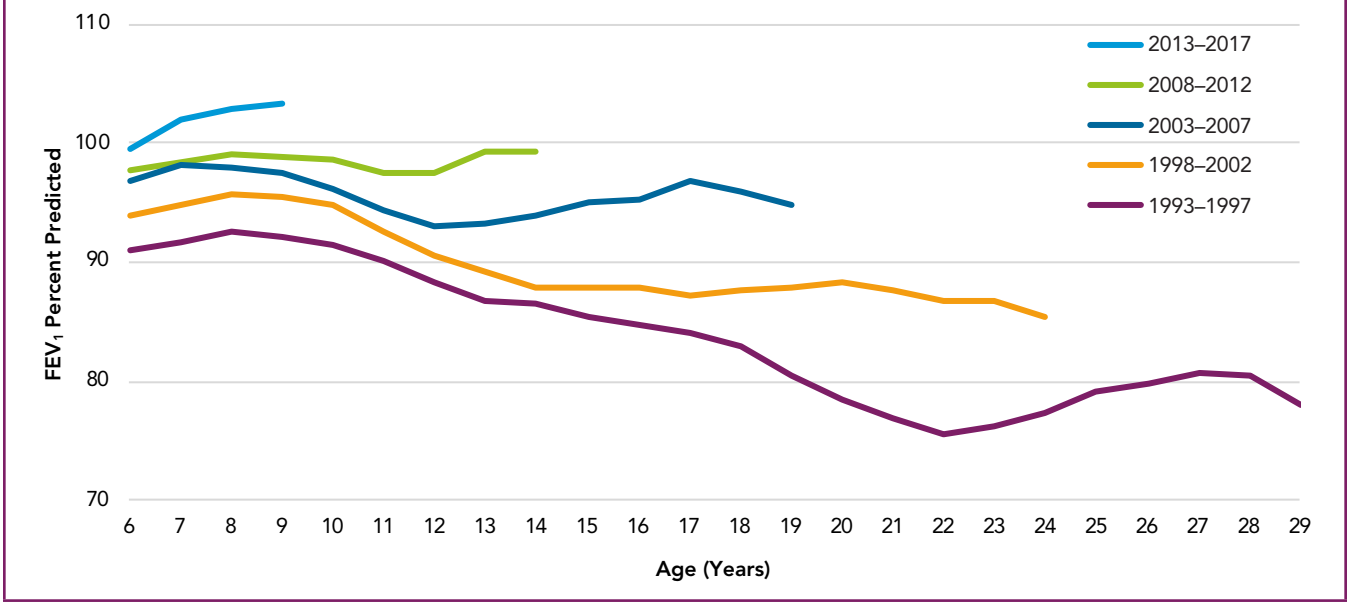
Pulmonary function is an important clinical indicator of the health of individuals with CF. This section provides information on trends in pulmonary function by age for individuals who have not had a lung transplant or prior to the year of lung transplantation, if applicable. Variations in pulmonary function across CF Care Centers is also shown. Pulmonary function is assessed by FEV_1 percent predicted as calculated using the 2012 Global Lung Initiative (GLI) reference equations.[2]

Successive birth cohorts show improved pulmonary function across all ages for individuals who are old enough to reliably perform pulmonary function testing.

As noted in the About this Report section, we captured approximately 60.0 percent of the usual number of spirometry measurements per individual in 2022 as compared to 2019, and some of that data was obtained from home spirometers. Also of note, there were fewer height measurements reported for growing children less than 18 years of age. Less frequent measures or missing data may have impacted the accuracy of the population, center, and individual-level annualized FEV_1 percent predicted values.

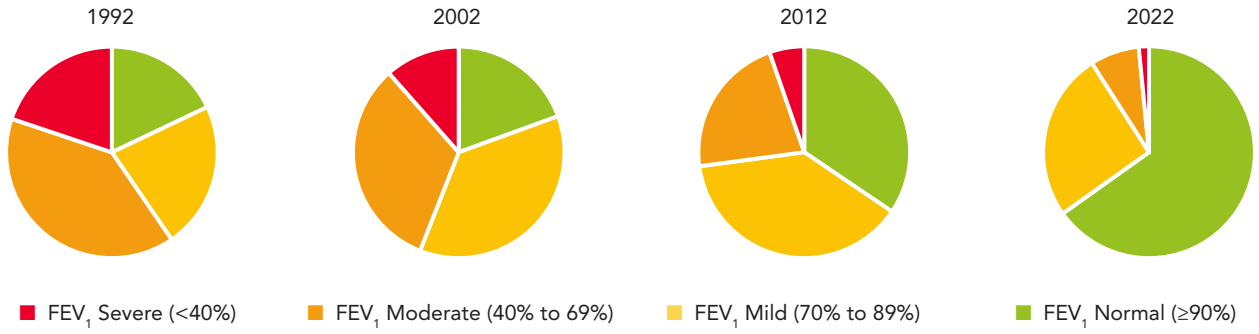
The figure below shows the median FEV_1 percent predicted by birth cohort. The birth cohorts diverge unlike similar graphs in annual registry reports from 2019 and earlier. Among individuals born between 2013 and 2017, median FEV_1 percent predicted increased to 100.0 percent predicted among those who attained 8 to 9 years of age in 2022. For the older cohorts (1993–1997, 1998–2002), median FEV_1 percent predicted has decreased or stabilized among the older age groups reported.

Median FEV_1 Percent Predicted, by Age and Birth Cohort



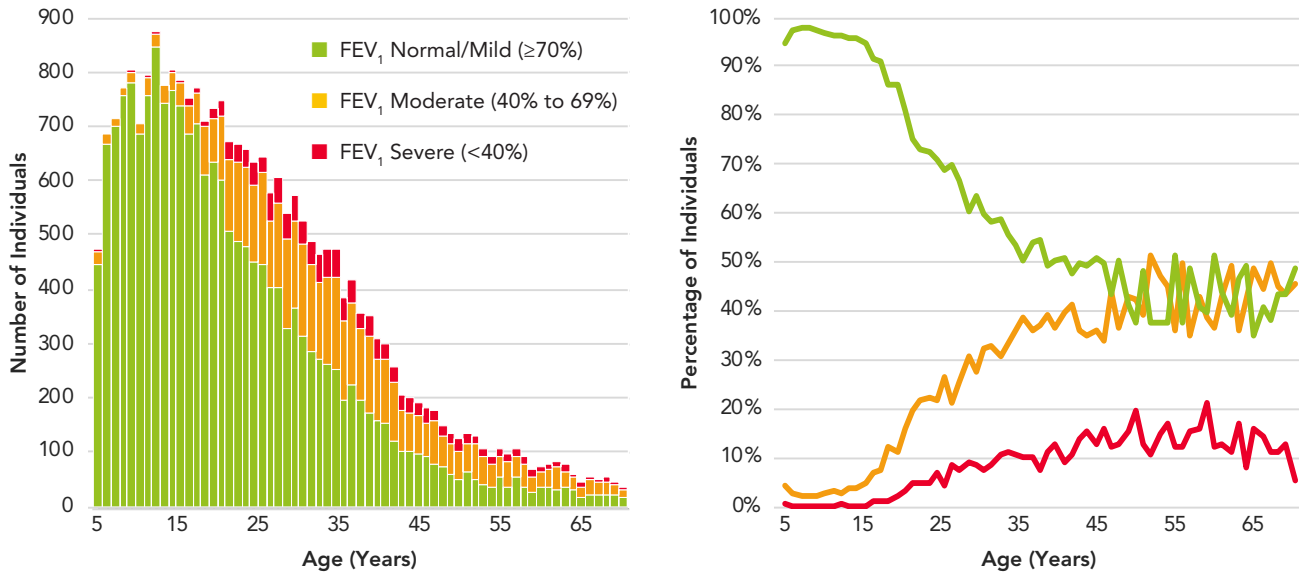
The proportion of people with CF aged 18 years who are in the normal or mild lung disease categories (FEV_1 ≥70 percent predicted) more than doubled from 41.2 percent in 1992 to 91.2 percent in 2022. The proportion with severely reduced lung function aged 18 years (FEV_1 <40 percent predicted) decreased from 19.2 percent in 1992 to 1.3 percent in 2022.

Median FEV_1 Percent Predicted in 18-Year-Olds, 1992–2022



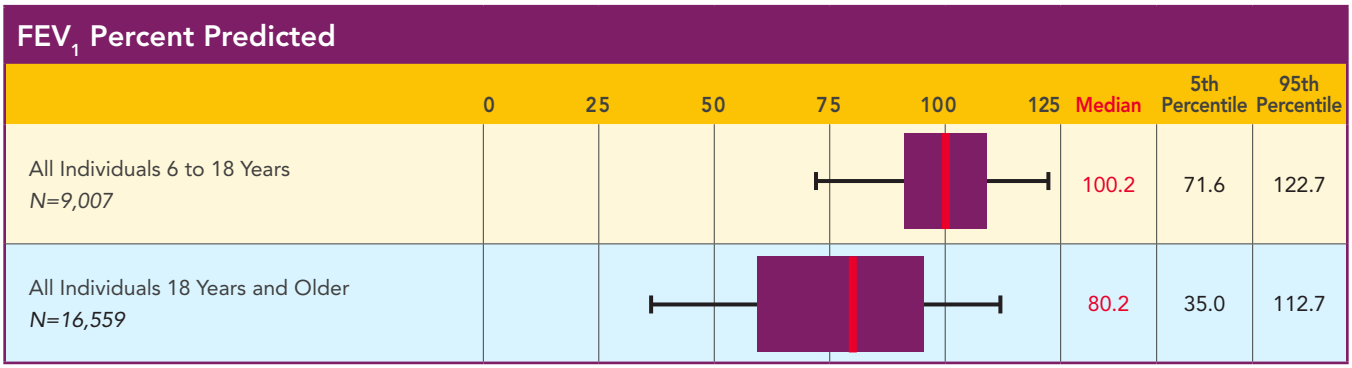
Although much focus is placed on spirometry, it is not a sensitive measure of early lung disease in CF and may underrepresent the extent of early structural lung disease. With that caveat in mind, most children have normal or "mild" impairment in pulmonary function as defined by FEV_1 percent predicted. Moderate and severe impairment in pulmonary function becomes apparent in adolescence and early adulthood.

Pulmonary Function Impairment by Age in Years, 2022 (Stacked Bar Chart)



The median FEV_1 percent predicted among individuals aged 6 to 18 is 100.2 percent, and for individuals aged 18 years or older it is 80.2 percent. A wide spectrum of lung function is observed among adults where half have only mildly reduced lung function (FEV_1 percent predicted greater than 70.0 percent), and a quarter have an FEV_1 percent predicted less than 50.0 percent.

FEV_1 Percent Predicted

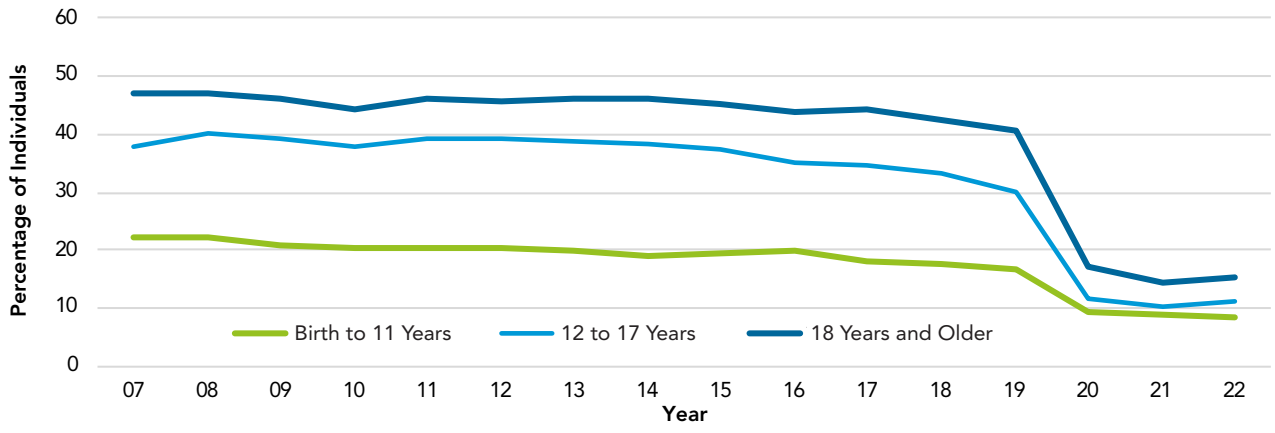


Pulmonary Exacerbations

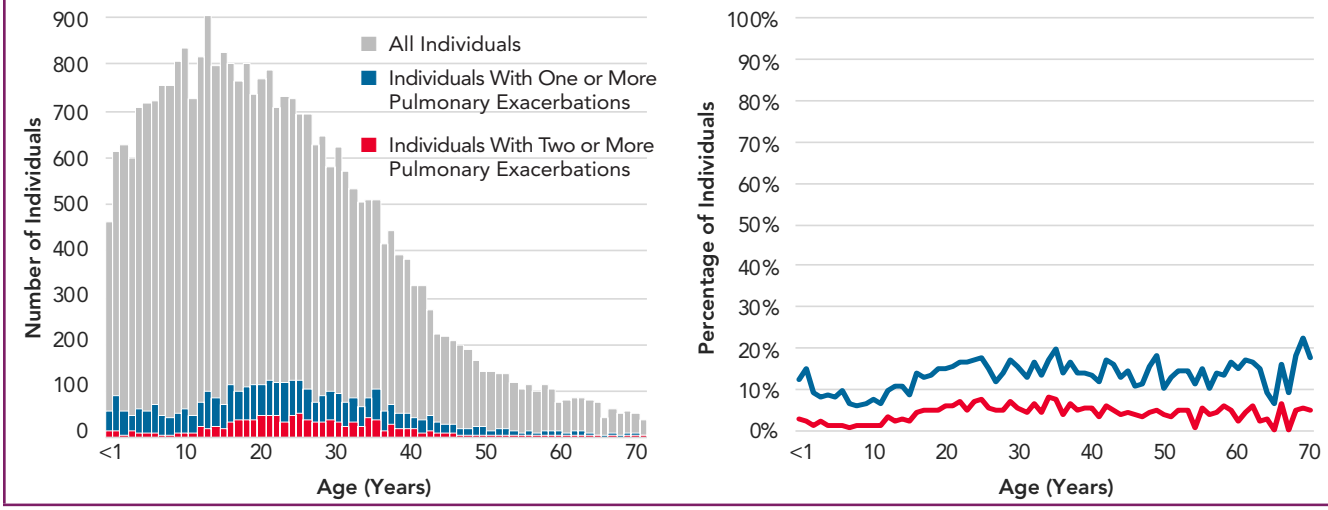
Pulmonary exacerbations, characterized by intravenous (IV) antibiotic treatment in the hospital or at home, are associated with morbidity, mortality, and decreased quality of life. They are also a major driver of health care costs. This section displays trends in the rate of pulmonary exacerbations over time and by age group for individuals who have not received a lung transplant and up until the year prior to the lung transplant for those who have. Additionally, variation in exacerbation rates and treatment characteristics by CF Care Center is shown.

Despite notable improvements in pulmonary function and nutritional status over the years, until recently the proportion of individuals with CF who were treated with IV antibiotics for pulmonary exacerbations remained stable. In 2020, a substantial decrease in number of reported exacerbations was observed, particularly in adolescents and adults. The marked decrease in 2020 was sustained through 2022. The robust uptake of elexacaftor/tezacaftor/ivacaftor and decreased exposure to viruses during the pandemic are likely contributing factors.

Individuals Treated With IV Antibiotics for a Pulmonary Exacerbation, 2007–2022

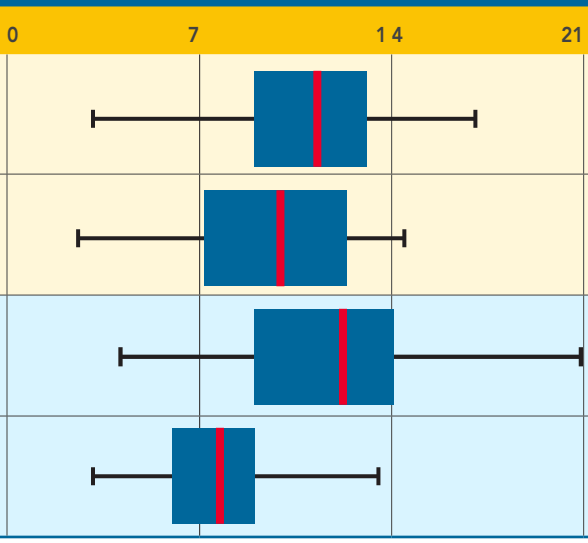


Pulmonary Exacerbations by Age in Years, 2022



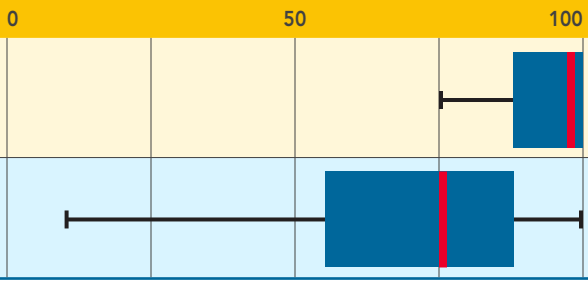
When the CF Foundation developed guidelines for the treatment of pulmonary exacerbations in 2009, little published literature or data were available upon which to base recommendations.[34] More recently published research suggested that 10 to 14 days of treatment with intravenous antibiotics (duration based on whether there is an early response to treatment) is appropriate.[35] Current practice within the CF Foundation Care Center network indicates a median treatment duration of 11–12 days, with adults much more likely to complete the treatment course at home.

Duration of Pulmonary Exacerbation Treatment in Days, by Center



	Median	Min	Max
Median Total Duration of IV Antibiotic Treatment for a Pulmonary Exacerbation in Individuals Less Than 18 Years Old	11.3	3.0	17.0
Median Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Individuals Less Than 18 Years Old	10.0	2.5	14.5
Median Total Duration of IV Antibiotic Treatment for a Pulmonary Exacerbation in Individuals 18 Years and Older	12.2	4.0	21.0
Median Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Individuals 18 Years and Older	7.8	3.0	13.5

Percentage of Total Pulmonary Exacerbation Treatment Duration in Hospital, by Center



	Median	Min	Max
Individuals Birth to 17 Years	97.9	75.1	100.0
Individuals 18 Years and Older	75.8	10.4	100.0

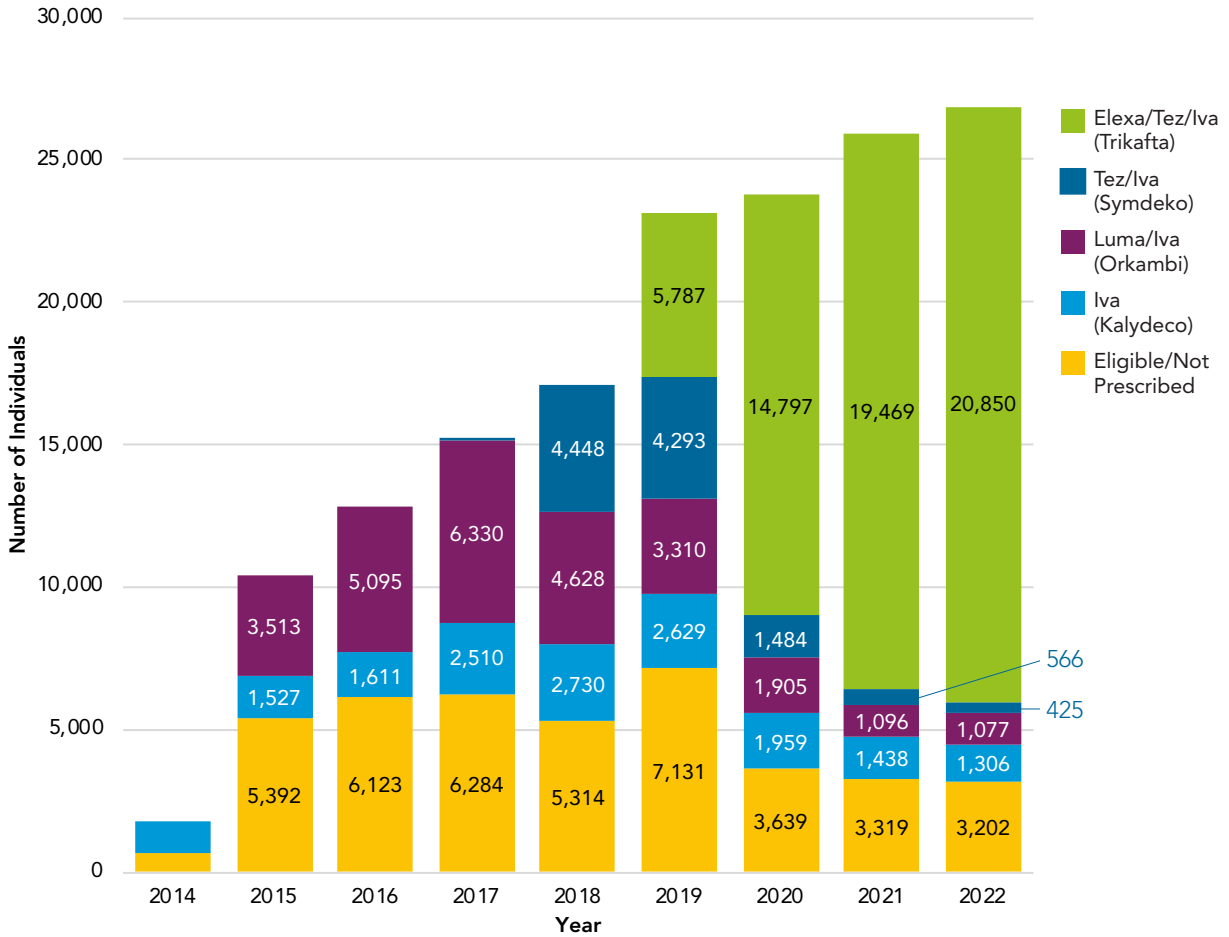
THERAPIES

CFTR Modulator Therapies

On September 2, 2022, the U.S. Food and Drug Administration (FDA) expanded the availability of Orkambi® (lumacaftor/ivacaftor) to children with cystic fibrosis aged 1 through 2 who have two copies of the F508del variant. The label extension made 350 children eligible and 132 (37.7 percent) were prescribed CFTR modulator therapy in 2022.

By the end of 2022, 23,658 of the 28,860 (82.0 percent) people eligible based on age and genotype for a CFTR modulator had at least one prescription reported in the Registry. As shown in the chart below, most individuals prescribed a CFTR modulator were prescribed elexacaftor/tezacaftor/ivacaftor (ETI). The number of eligible individuals who were not prescribed a CFTR modulator fell from 3,319 (12.8 percent) in 2021 to 3,202 (11.9 percent) in 2022.

CFTR Modulators by Year, 2014–2022*

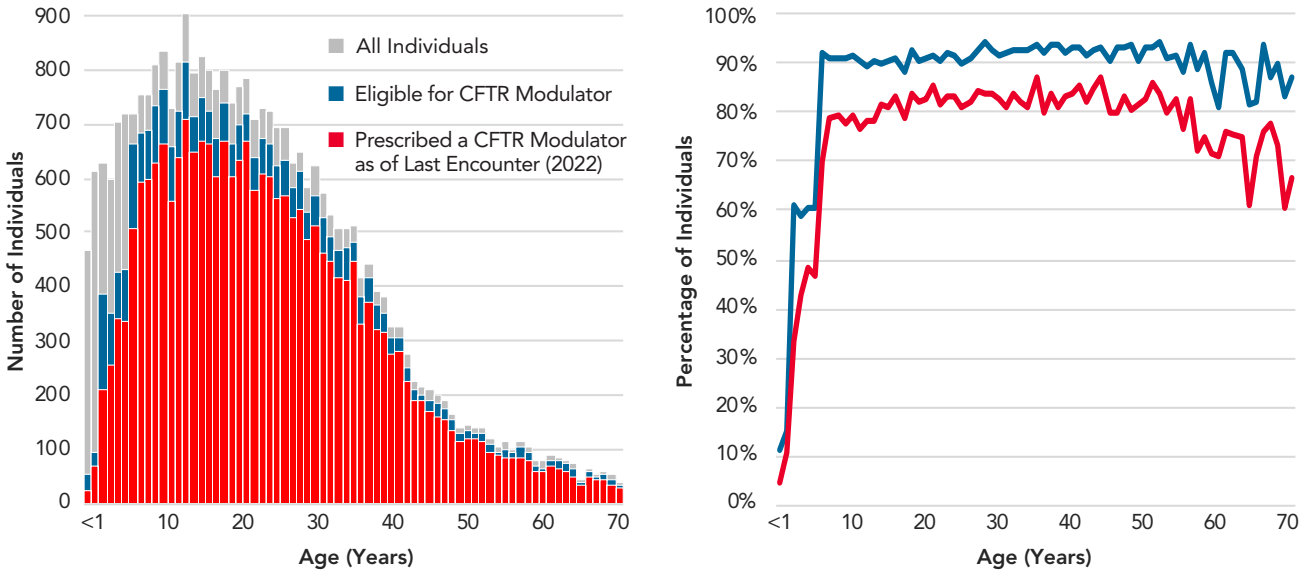


	2014	2015	2016	2017	2018	2019	2020	2021	2022
Total Eligible	1,765	10,432	12,829	15,230	17,120	23,150	23,784	25,888	28,860
% Eligible on Modulators	60.6%	48.3%	52.3%	58.7%	69.0%	69.2%	84.7%	87.2%	82.0%
Total on Modulators	1,070	5,040	6,706	8,946	11,806	16,019	20,145	22,569	23,658

**The numbers in this chart include individuals based only on their most recent medications form entered in the reporting year, and do not include individuals on modulator therapy but not eligible.*

The graph below shows eligibility and prescription of a CFTR modulator by age.

CFTR Modulator Use by Age, 2022



The proportion of eligible people with CF prescribed a modulator varied across care centers, ranging from a minimum of 75.0 percent to a maximum of 100.0 percent. There is more variation among the pediatric CF centers.

Modulator Prescription in Eligible Individuals, by Center

	0 — 50 — 100	Median	Min	Max
Eligible Individuals Prescribed a Modulator		90.7	75.0	100.0
Eligible Individuals Less Than 18 Years Prescribed a Modulator		88.0	65.8	100.0
Eligible Individuals 18 Years and Older Prescribed a Modulator		93.1	81.4	100.0

Eligible but Not Prescribed a CFTR Modulator in 2018–2022

The reasons for which an eligible individual might not be prescribed a CFTR modulator (CFTRm) are complex, ranging from fear of side effects, to individual preference including perceived clinical stability, to limited access and affordability. As CFTR modulator therapy becomes available to increasingly younger ages, it will be important to characterize the population with no reported prescription despite being eligible given their smaller population size.

We present descriptive statistics and clinical characteristics on the group of people who were not prescribed any CFTRm (excluding individuals who had a lung transplant). Based on review of medication data contributed, only 607 individuals aged 12 years and older who were eligible for a CFTRm in 2020 did not have a reported prescription in any year from 2018–2022. To highlight possible differences among those eligible for modulator therapy but not prescribed, we compared these individuals to 14,403 individuals aged 12 years or older as of 2020 who had a prescription for either ivacaftor or elexacaftor/tezacaftor/ivacaftor, referred to as highly effective modulator therapy (HEMT), in all years 2020–2022. We focused on those aged 12 years or older as of 2020 to avoid conflating changes in these indicators over time with the FDA label expansion of CFTRm access when elexacaftor/tezacaftor/ivacaftor was approved for those aged 6–11 years in 2021. We also restricted to those prescribed HEMT in all calendar years to avoid inclusion of individuals who may interrupt CFTRm therapy or change the type of modulator prescribed over time.

Demographic characteristics, sweat chloride values, and insurance status of the two cohorts are shown in the table below. Those with no CFTRm prescription were slightly older than those with a HEMT prescription (median age 28.5 years compared to 27.6 years). The distribution of race among those eligible for CFTRm therapy but not prescribed is similar to the overall CF population.

Demographics for HEMT Prescribed and Eligible but Not Prescribed Individuals

	HEMT Prescribed	Eligible but Not Prescribed
Number of Individuals (n)	**14,403**	**607**
Male (%)	51.9	52.4
Race (%)		
White	94.8	91.9
Black or African American	1.9	4.5
Other	3.2	3.6
Hispanic (any race) (%)	6.1	10.9
Mean Age (as of 12/31/2022)	30.3	32.4
Median Age (as of 12/31/2022)	27.6	28.5

Data in this table include individuals in only one category of race as captured on the CFFPR form.

As shown in the table below, individuals eligible but not prescribed a CFTRm had a lower median sweat chloride compared to those with a HEMT prescription 2020–2022.

Sweat Test Data for HEMT Prescribed and Eligible but Not Prescribed Individuals

	HEMT Prescribed	Eligible but Not Prescribed
Number of Individuals (n)	**12,735**	**540**
Median of Highest Sweat Value in Registry, mmol/L	101.0	86.0

Some individuals in either cohort may not have had a sweat chloride test result entered in the Registry.

In the following table, the distribution of insurance coverage is presented for 2022. Individuals eligible but not prescribed a CFTRm had a lower prevalence of private insurance (60.4 percent), but similar Medicare and Medicaid coverage as those prescribed HEMT. The proportion with no insurance is higher among those with no prescription reported (1.0 percent) compared to 0.4 percent among those prescribed HEMT.

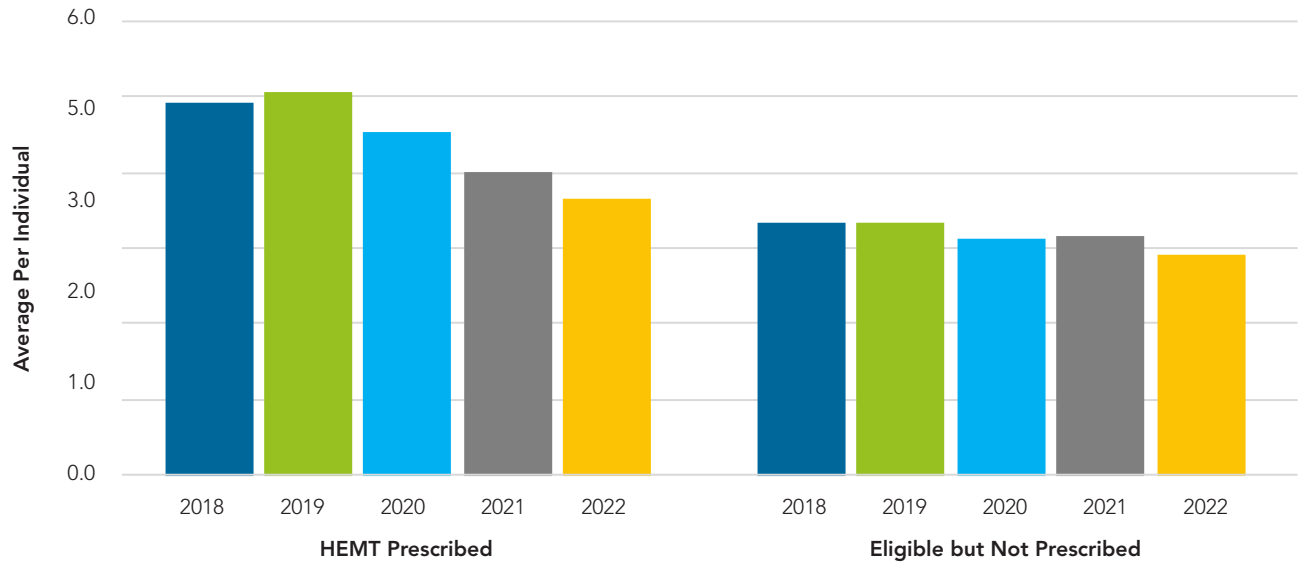
Insurance Coverage for HEMT Prescribed and Eligible but Not Prescribed Individuals

Insurance Coverage in 2022	HEMT Prescribed	Eligible but Not Prescribed
Number of Individuals (n)	**14,288**	**598**
Health Insurance (e.g., Private Insurance) (%)	64.2	60.4
Medicare/Indian Health Services (%)	13.8	12.4
Medicaid/State Programs (%)	36.1	37.4
TRICARE or Other Military Health Plan (%)	2.1	1.2
Other (%)	1.0	1.2
No Health Insurance (%)	0.4	1.0

"Insurance coverage" reflects coverage at any point during the year; thus, these categories are not mutually exclusive (except for the "no health insurance" option).

In the figure below, CF care utilization is lower in all years among those eligible but not prescribed CFTRm compared to those prescribed HEMT. While the number of CF care visits per person has decreased among those prescribed a CFTRm, the decline in average number of visits per year is less pronounced among individuals not prescribed although that number was lower to begin with. There are likely complex factors driving utilization of CF care and CFTRm treatment decisions.

Average Clinic or Telehealth/Other Visits Per Individual by Modulator Status, 2018–2022



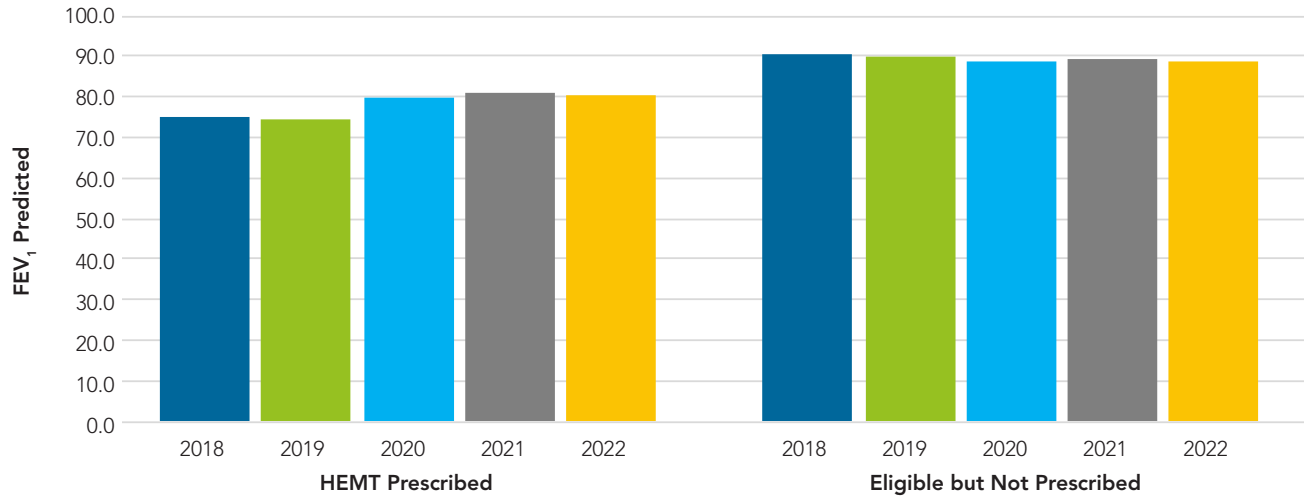
In the table below, the annual mean BMI percentile (aged 12–19 years) and BMI value (aged 20 years and older) between 2018 and 2022 are presented. BMI percentiles and values among HEMT prescribed group have increased over the five-year period, compared to those not prescribed (where BMI percentiles and values have remained stable). Among the group with no CFTRm prescription 2018–2022, the average BMI values for each year were higher than the population prescribed HEMT.

Nutritional Outcomes of HEMT Prescribed and Eligible but Not Prescribed Individuals in 2018–2022

BMI Percentile in Individuals Age 12–19 Years (Mean)	2018	2019	2020	2021	2022
HEMT Prescribed	53.0	52.9	57.3	58.6	57.8
Eligible but Not Prescribed	65.7	65.7	63.8	65.0	63.2
BMI in Individuals 20 Years and Older (Mean)					
HEMT Prescribed	23.5	23.6	24.3	24.7	24.6
Eligible but Not Prescribed	25.8	26.0	26.3	26.0	26.2

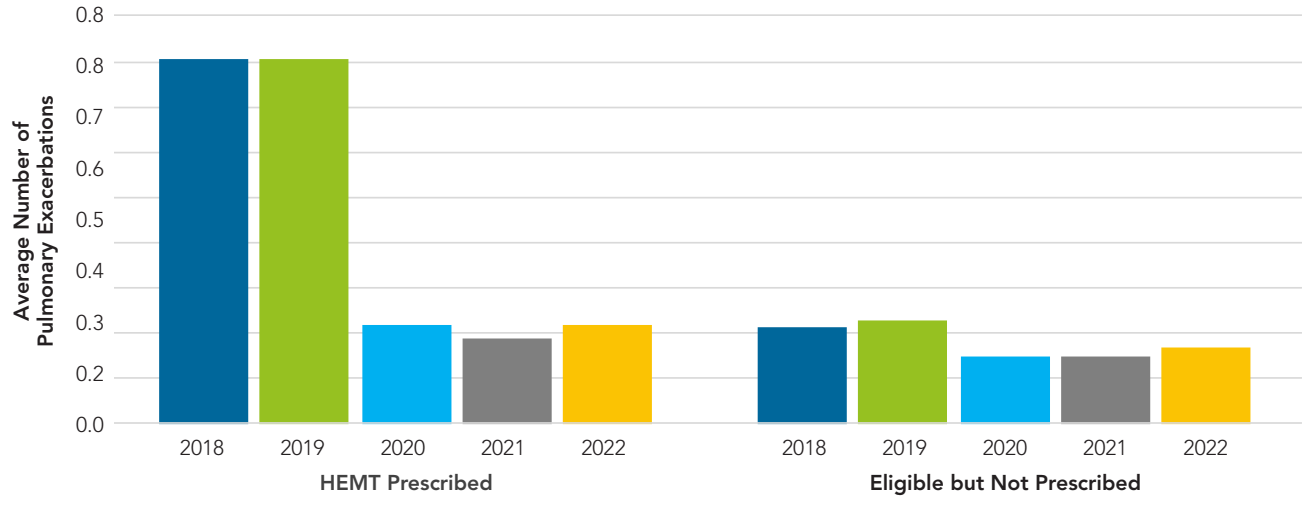
Average annualized FEV_1 percent predicted from 2018–2022 is presented in the tables below. For those prescribed HEMT from 2020–2022, the average annual lung function increased from 2019 to 2020 and then remained stable in 2021 and 2022. Among the group with no CFTRm prescription from 2018–2022, the average annualized lung function for each year was higher than the population prescribed HEMT and remained relatively stable over the five-year period.

Average FEV_1 Percent Predicted by Modulator Status, 2018–2022



In the figure below, the average number of pulmonary exacerbations per year are summarized. In both groups, the average number of exacerbations decreased from 2019 to 2020, although individuals with a HEMT modulator prescription had a much higher average exacerbation rate in 2018–2019 (approximately 0.8 per person) than those with no reported CFTRm prescription (approximately 0.2 per person). The average rate of pulmonary exacerbations in both groups are similar and relatively stable in 2020–2022.

Average Number of Pulmonary Exacerbations Per Individual by Modulator Status, 2018–2022



Characteristics of Individuals Ineligible for Any CFTR Modulator

Improvements in health outcomes of the overall CF population have been reported over the past three years, primarily evidenced by increased FEV_1 percent predicted values and reduced pulmonary exacerbation rates. Nevertheless, Registry data presented for the entire CF population in aggregate may not reflect the health status of those ineligible for CFTRm therapy as they are a much smaller population. The purpose of this chapter is to characterize the people with CF who are not currently eligible for a CFTRm based on CFTR genotype. The tables and figures in this chapter are restricted to individuals aged 12 years and older with no history of lung transplant to avoid conflating changes with the expansion of CFTRm access with the approval of elexacaftor/tezacaftor/ivacaftor to individuals aged 6–11 years in 2021.

There were a total of 1,514 individuals ineligible for a CFTRm aged 12 years or older contributing data to the Registry in 2022. Demographic characteristics and insurance status are presented in the tables below. The modulator ineligible population has a much larger proportion of non-white individuals with 14.1 percent Black or African American race reported compared to the overall CF population. A larger proportion of the modulator ineligible population were identified as Hispanic ethnicity (21.9 percent) compared to the overall CF population (see page 8).

Demographics of CFTRm Ineligible Indviduals Aged 12 Years and Older

	CFTRm Ineligible
Number of Individuals (n)	**1,514**
Male (%)	52.2
Race (%)	
White	75.8
Black or African American	14.1
Other	11.1
Hispanic (any race) (%)	21.9
Mean Age (as of 12/31/2022)	29.4
Median Age (as of 12/31/2022)	25.2

Data in this table include individuals in only one category of race as captured on the CFFPR form.

A total of 1,410 people who were CFTRm ineligible contributed sweat chloride data to the CFFPR. The median highest value reported is 96.0 mmol/L.

Sweat Test Data of CFTRm Ineligible Individuals Aged 12 Years and Older

	CFTRm Ineligible
Number of Individuals (n)	**1,410**
Median of Highest Sweat Value in Registry, mmol/L	96.0

Some individuals in the cohort may not have had a sweat chloride test result entered in the Registry.

As shown in the table below, the modulator ineligible population has a higher percentage of people on Medicaid (47.7 percent) and the lower percentage of people with private insurance (50.4 percent) in 2022 compared to the CF population as a whole. The percentage of people on Medicaid among the ineligible population is higher than in the CF Population aged 12 years or older as a whole (37.6 percent).

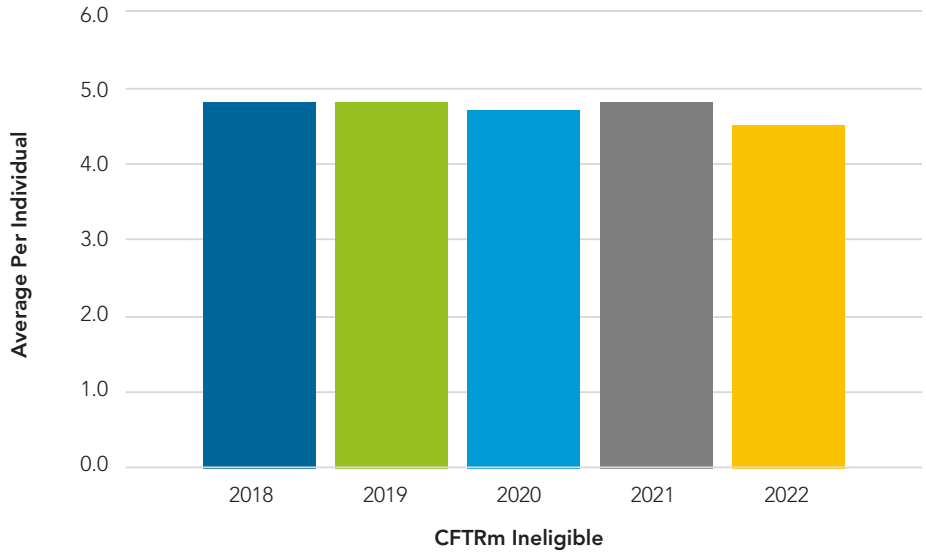
Insurance Coverage of CFTRm Ineligible Individuals Aged 12 Years and Older

Insurance Coverage in 2022	CFTRm Ineligible
Number of Individuals (n)	**1,483**
Health Insurance (e.g., Private Insurance) (%)	50.4
Medicare/Indian Health Services (%)	13.1
Medicaid/State Programs (%)	47.7
TRICARE or Other Military Health Plan (%)	1.7
Other (%)	1.4
No Health Insurance (%)	0.7

"Insurance coverage" reflects coverage at any point during the year; thus, these categories are not mutually exclusive (except for the "no health insurance" option).

The chart below depicts the average number of clinic or telehealth/other visits per individual, by year among the individuals that were CFTRm ineligible aged 12 years or older from 2018–2022. From 2018 to 2022, the average number of visits remained relatively stable, even during the COVID-19 pandemic. CF care utilization was the lowest in 2022 at 4.5 visits per person.

Average Clinic or Telehealth/Other Visits Per Individual, 2018–2022



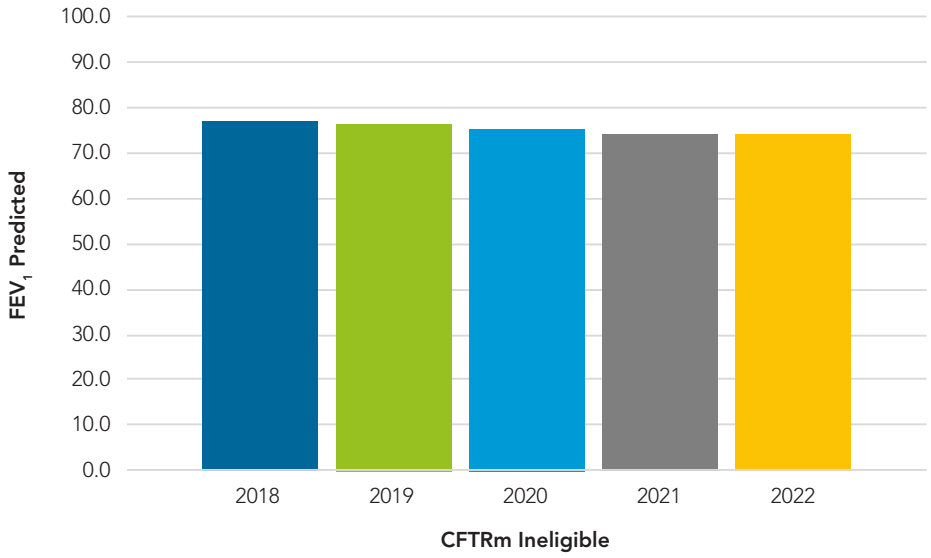
The table below presents cross-sectional nutritional indices for BMI percentiles (aged 12–19 years) and BMI value (aged 20 years and older) for those ineligible for a CFTRm. BMI percentiles and values are relatively stable when comparing annualized average measures from 2018–2022.

Nutritional Outcomes of CFTRm Ineligible Individuals in 2018–2022

	2018	2019	2020	2021	2022
BMI Percentile in Individuals Age 12–19 Years (Mean)	51.1	50.9	50.7	52.2	51.2
BMI in Individuals 20 Years and Older (Mean)	23.8	23.9	23.9	23.8	23.9

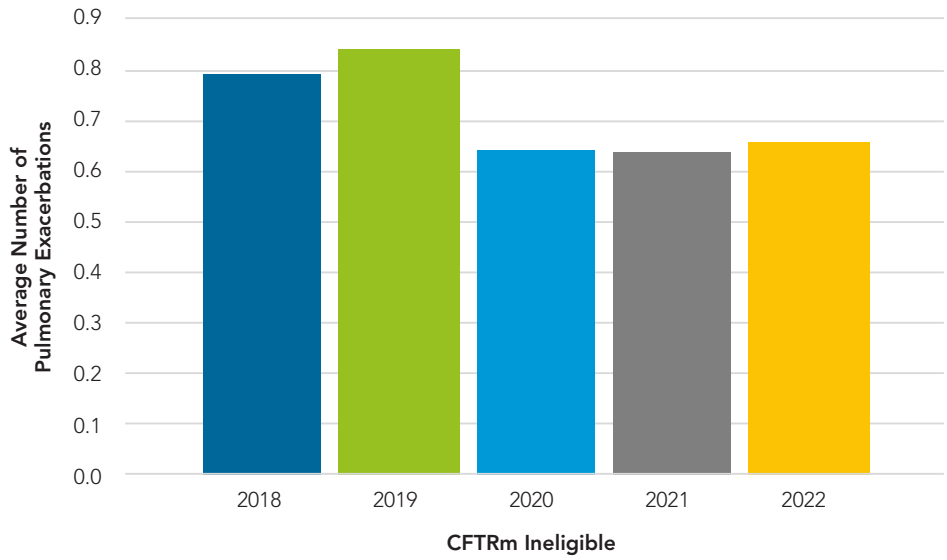
In the figures below, cross-sectional summary data on lung function and pulmonary exacerbations are presented. Overall, the average FEV_1 percent predicted is declining each year among individuals that were CFTRm ineligible aged 12 years and older from 2018 to 2022.

Average FEV_1 Percent Predicted, 2018–2022



In the figure below, the average number of pulmonary exacerbations per person for individuals that were CFTRm ineligible aged 12 years and older were presented by year. The average number of pulmonary exacerbations per person in this group was the lowest in 2020. In 2022, the average number of exacerbations per person (0.6) was higher than the average number of pulmonary exacerbation per person among the CF population as a whole (0.2 exacerbations per person).

Average Number of Pulmonary Exacerbations Per Individual, 2018–2022

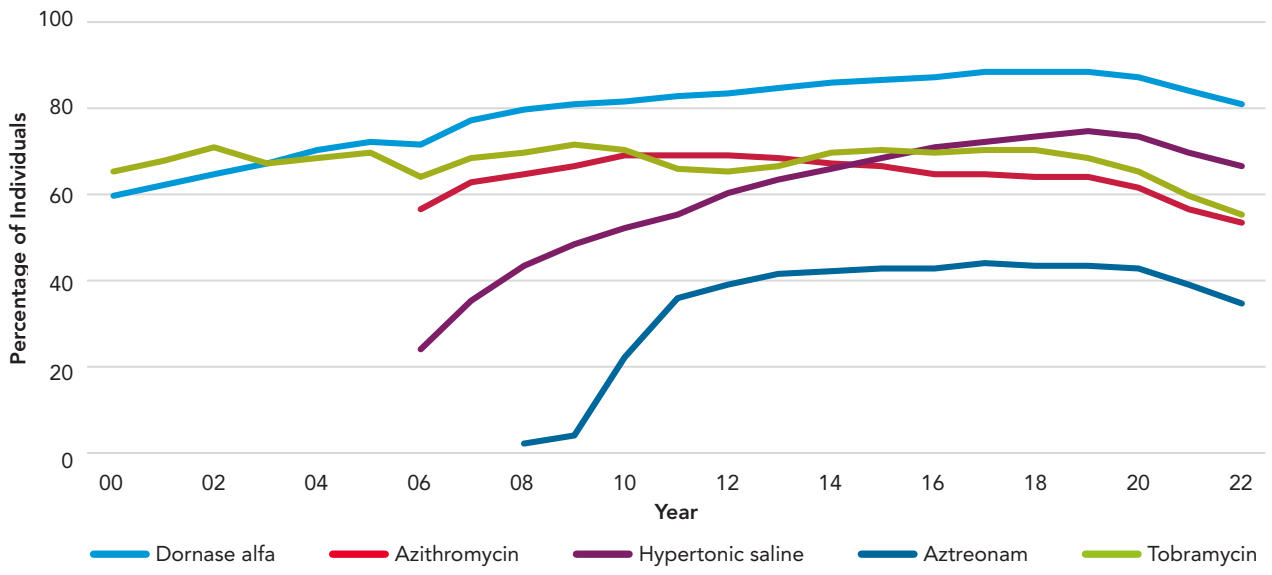


Pulmonary Therapies

Chronic pulmonary therapies are a major component of the treatment regimen for individuals with CF. This section provides data on uptake and trends in the prescription of pulmonary medications recommended for chronic use by the CF Foundation pulmonary guidelines committee for individuals never transplanted. Data are also provided on medications that are not recommended and on those for which the committee did not find sufficient evidence to recommend for or against chronic use.[36]

The 2022 data indicate a modest decrease in the prescription of many recommended therapies. It will be important to monitor this trend over time. The availability of multiple pulmonary therapies for CF is beneficial; however, it contributes to treatment complexity and overall burden for individuals with CF and their caregivers. Some people with CF who are benefiting from a CFTR modulator have discontinued one or more chronic therapies. The SIMPLIFY study showed no significant decrease in FEV_1 after stopping dornase alfa or hypertonic saline for six weeks.[37] Studies are underway to assess the longer-term impact of discontinuing therapies.

Medication Prescription in Eligible Individuals, 1999–2022

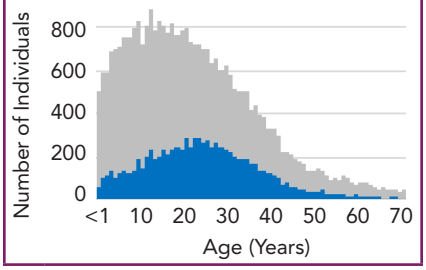


Medications reported among eligible individuals aged 6 or older according to Cystic Fibrosis Foundation guidelines. Tobramycin includes all available formulations of inhaled tobramycin. Dornase alfa, tobramycin solution for inhalation, and inhaled aztreonam were approved by the Food and Drug Administration in 1993, 1997, and 2010, respectively.

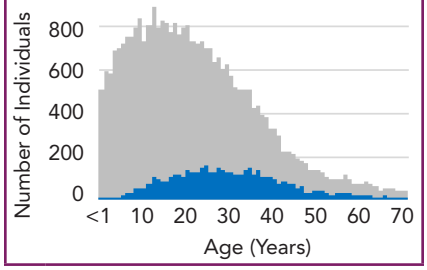
Pulmonary Medication Prescriptions by Age

There are three primary inhaled antibiotics used for treatment of *P. aeruginosa* infections. Tobramycin is used most frequently, followed by aztreonam, and then colistin.

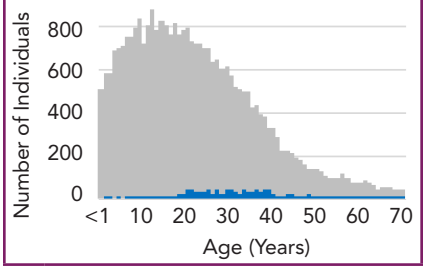
Any Tobramycin



Aztreonam

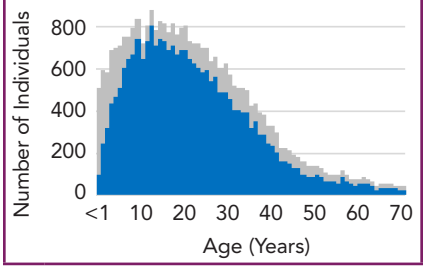


Colistin

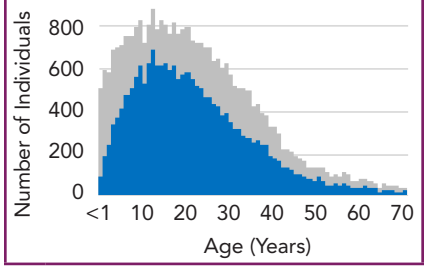


Dornase alfa and hypertonic saline are each prescribed for most individuals with CF. Azithromycin is also widely used in individuals with *P. aeruginosa*, with peak use occurring at slightly older ages than for use of dornase alfa and hypertonic saline.

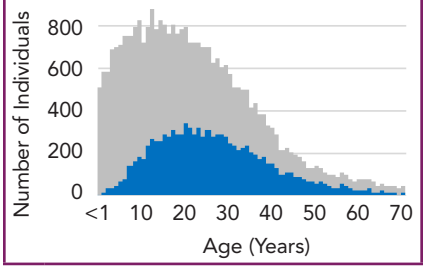
Dornase Alfa



Hypertonic Saline

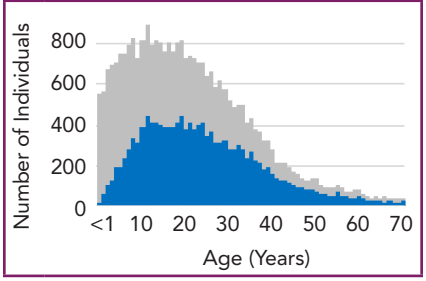


Azithromycin

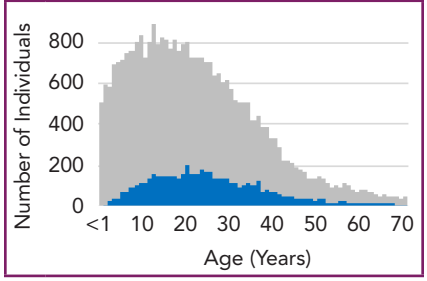


A substantial proportion of individuals with CF are prescribed inhaled corticosteroids and, to a lesser extent, leukotriene modifiers. Oral corticosteroids are used very infrequently.

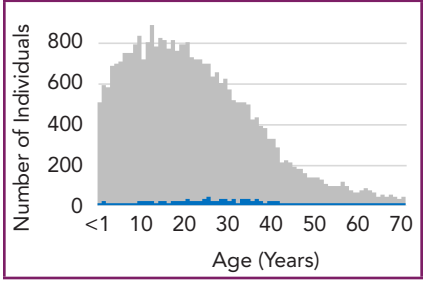
Inhaled Corticosteroids



Leukotriene Modifiers

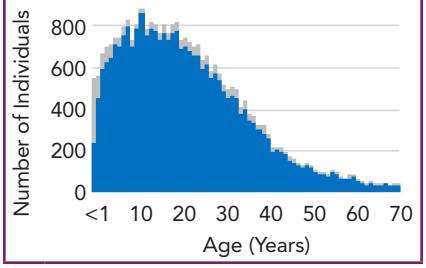


Oral Corticosteroids

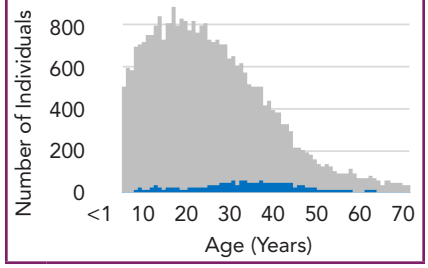


Bronchodilators are used extensively among individuals with CF. Almost all people with CF are prescribed beta agonists and a very small percentage are prescribed anticholinergics. The vast majority of those prescribed beta agonists are on short-acting formulations.

Inhaled Beta Agonists

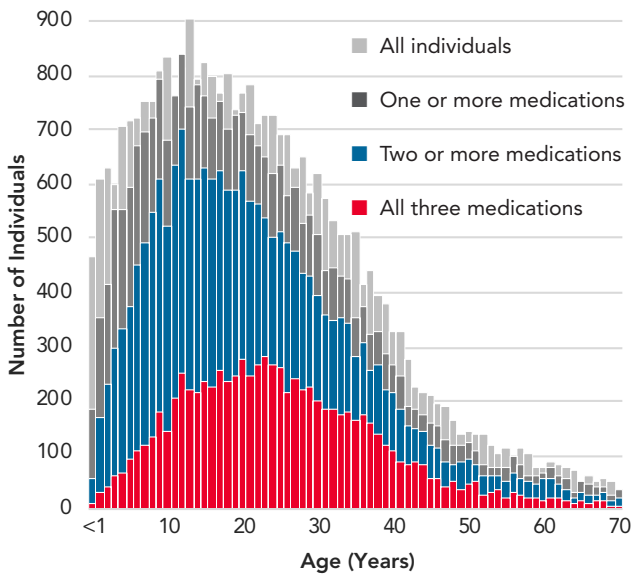


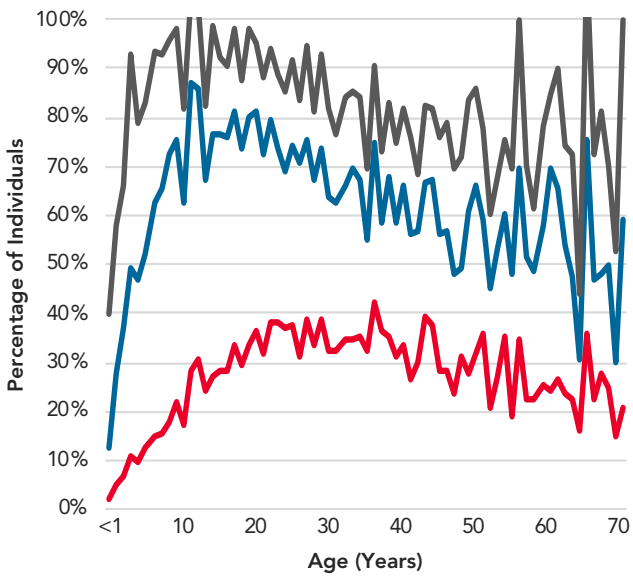
Inhaled Anticholinergics



Inhaled medications are effective treatments for pulmonary disease, and some individuals with CF are using multiple inhaled antibiotics for the treatment of *P. aeruginosa* infections.

Inhaled Medication Prescription by Age in Years, 2022



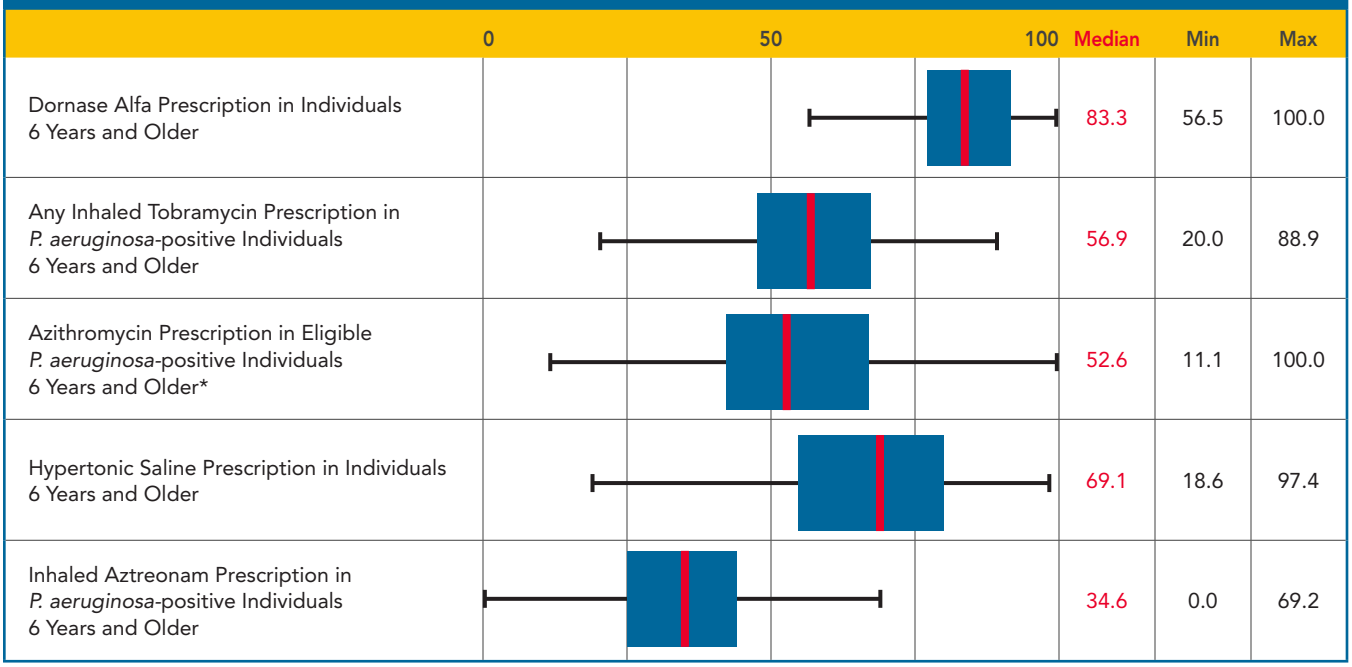


Inhaled medication use in the figure above includes dornase alfa, hypertonic saline, and an inhaled antibiotic. Note that the prescription of an inhaled antibiotic is primarily limited to individuals with P. aeruginosa.

Medications Recommended for Chronic Use

Recommended therapies are widely prescribed. However, there is considerable variation in prescription patterns across the CF Foundation Care Center network, particularly for any inhaled tobramycin, azithromycin, and aztreonam among *P. aeruginosa*-positive individuals aged 6 years and older. There is additional variation in the center-level hypertonic saline prescriptions, with a range of 18.6 percent to 97.4 percent.

Pulmonary Therapies Recommended for Chronic Use, by Center

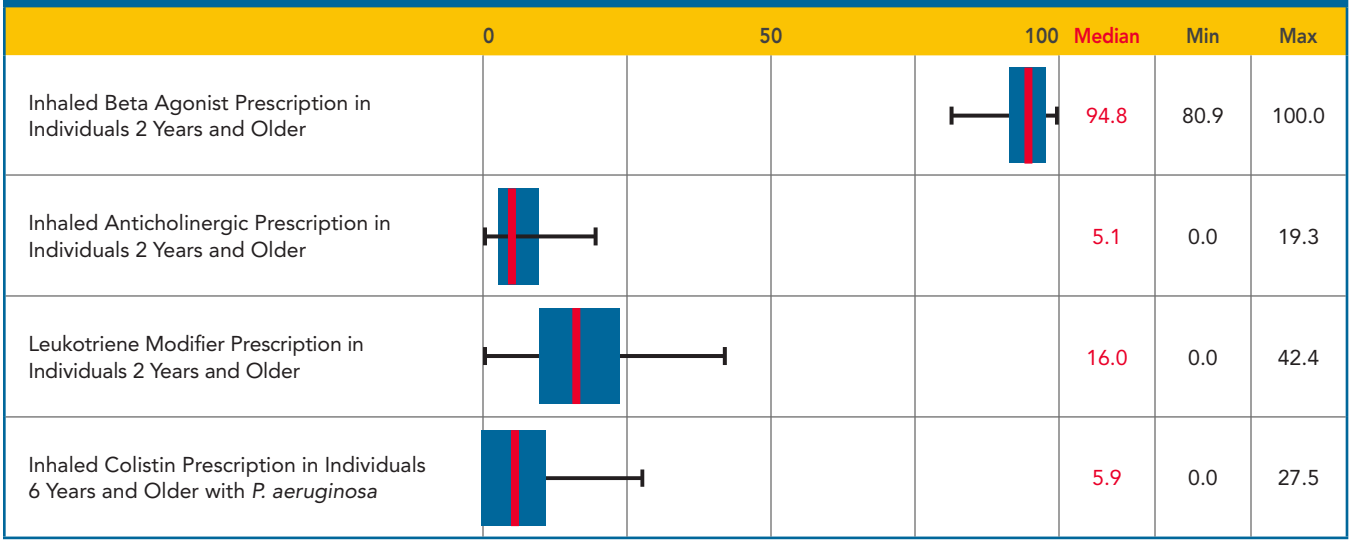


**Individuals were considered eligible if they met the selection criteria used in the U.S. trial of azithromycin in individuals chronically infected with* Pseudomonas aeruginosa.[3]

Medications With Insufficient Evidence to Recommend for or Against Chronic Use

In 2013, the CF Foundation pulmonary guidelines committee determined that there was insufficient evidence to recommend for or against the chronic use of inhaled beta agonists, inhaled anticholinergics, inhaled colistin, leukotriene modifiers, and ibuprofen for adults to improve lung function, reduce exacerbations, or improve quality of life.[36] Inhaled beta agonists are used extensively, but the other medications are used infrequently. Use of colistin has decreased in recent years. Adult use of ibuprofen is less than 2.0 percent (not shown).

Pulmonary Therapies With Insufficient Evidence to Recommend for or Against Chronic Use, by Center



Medications Not Recommended for Chronic Use

Inhaled steroids continue to be commonly prescribed, despite the recommendation against their chronic use in the absence of asthma or allergic bronchopulmonary aspergillosis (ABPA).[35]

Pulmonary Therapies Not Recommended for Chronic Use, by Center

Medication Use in Young Children

In 2016, the CF Foundation released the first set of guidelines focusing on the preschool timeframe for children aged 2 to 5.[17] Although the results of rigorous efficacy trials are not available for this age group, the guidelines recommend that dornase alfa and hypertonic saline be considered depending on individual circumstances. The chart below shows the use of medications among children aged 5 years and younger.

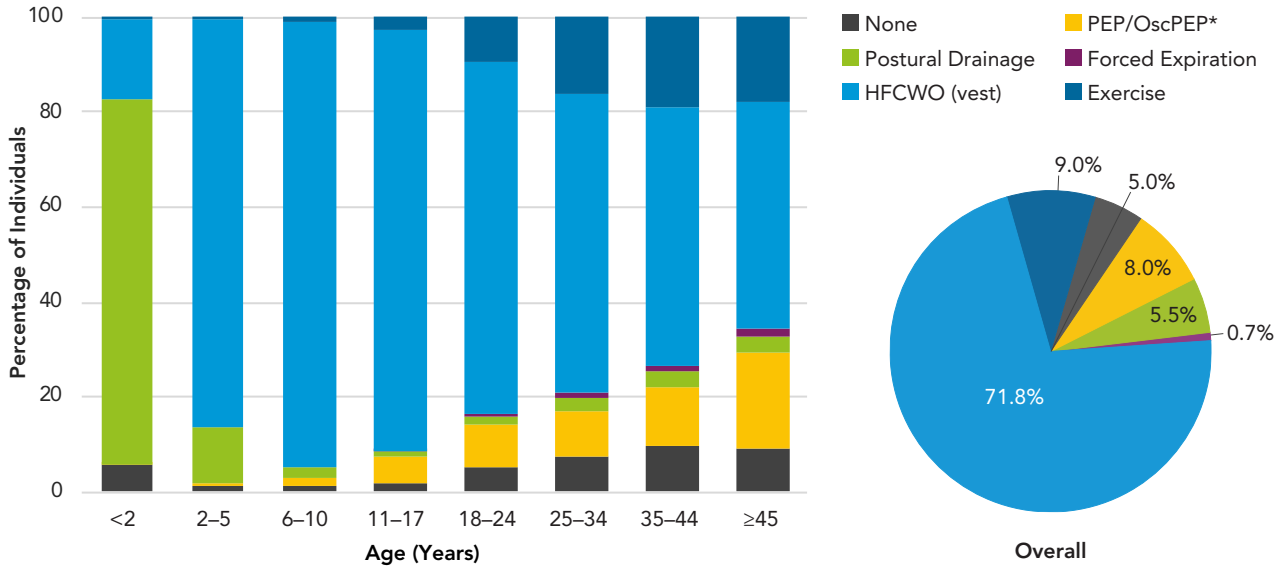
Medication Use in Individuals Under 6 Years, 2022

	Age < 3 Years (%)	Age 3 to 5 Years (%)
Number of Individuals (n)	**1,645**	**2,015**
Dornase Alfa	44.2	68.1
Hypertonic Saline	34.9	54.4
Inhaled Bronchodilators	81.9	91.8
Inhaled Corticosteroids	14.7	24.2
Inhaled Tobramycin	16.8	17.5
Azithromycin	3.6	9.6
Inhaled Aztreonam	1.0	2.6

Airway Clearance Techniques

The CF Foundation pulmonary guidelines recommend airway clearance for all individuals with CF.[38] A high-frequency chest wall oscillation (HFCWO) vest is the most widely used airway clearance technique in persons with CF after infancy. The percentage of individuals using no airway clearance or substituting exercise for airway clearance has grown in the last couple years.

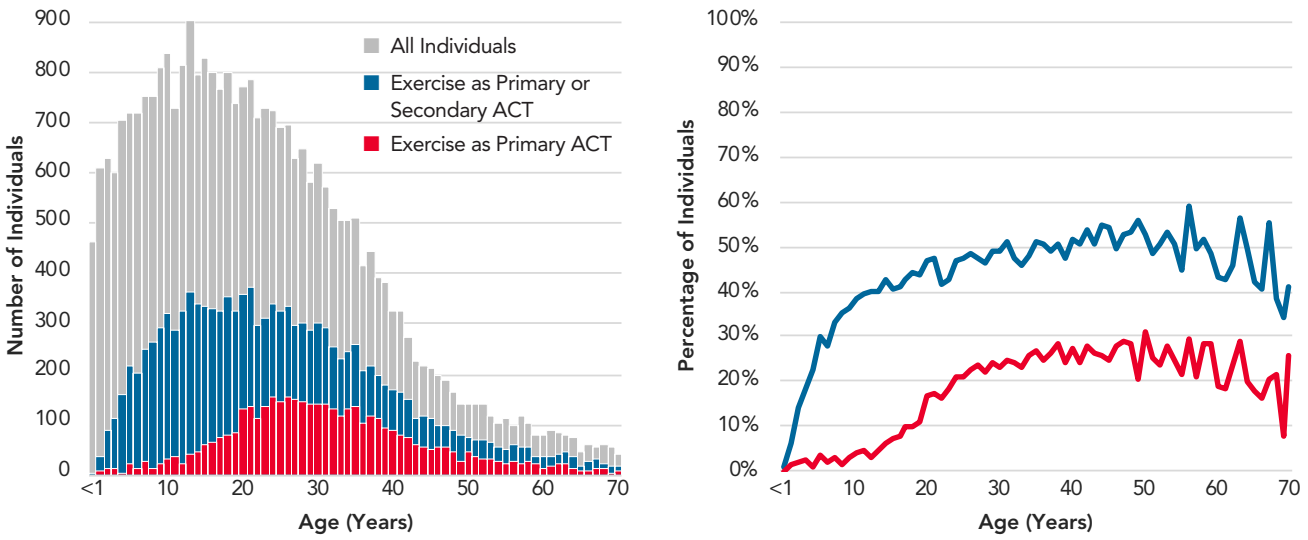
Primary Airway Clearance Techniques by Age and Overall, 2022



**Positive Expiratory Pressure (PEP)/Oscillating Positive Expiratory Pressure (OscPEP)*

The CF Foundation pulmonary guidelines recommend aerobic exercise as an adjunct therapy for airway clearance and for its additional benefits to overall health.[38] Many individuals with CF report exercising in addition to their primary method of airway clearance, with 32.2 percent of children and 47.8 percent of adults using exercise as one of their methods of airway clearance.

Exercise as an Airway Clearance Technique (ACT) by Age in Years, 2022

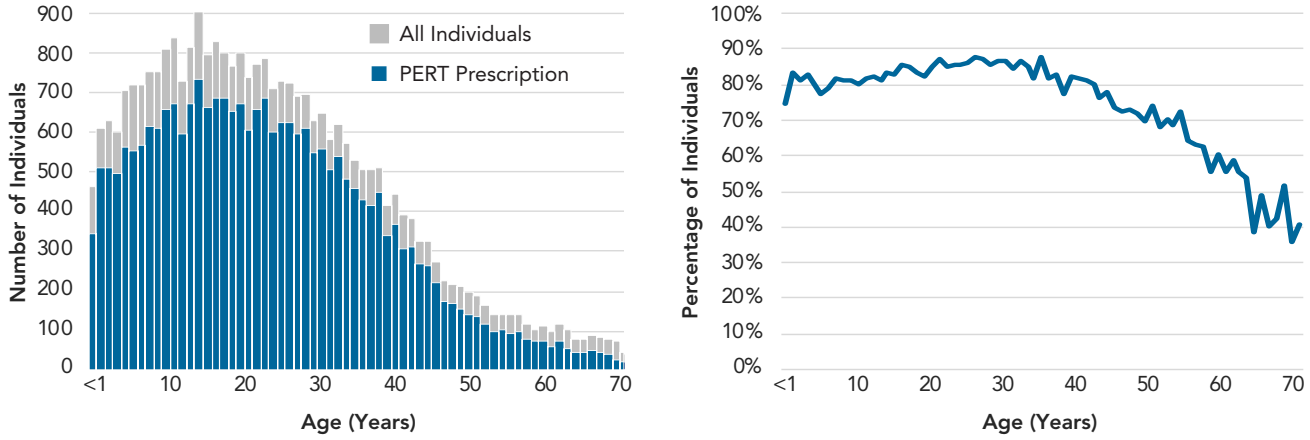


Gastrointestinal (GI) Therapies

The CF Foundation infant clinical care guidelines recommend that pancreatic enzyme replacement therapy (PERT) be started for all infants with two CFTR variants associated with pancreatic insufficiency, a fecal elastase value below 200 µg/g of stool, and/or signs of malabsorption.[28] In addition to pancreatic insufficiency, there is increasing attention on other GI manifestations of CF including gastroesophageal reflux disease (GERD) and CF liver disease.

Overall, a large proportion of individuals of all ages are prescribed PERT. The decrease in the proportion of older individuals with CF prescribed PERT is likely due to survival bias. Individuals with pancreatic sufficiency may have milder CF lung disease and fewer complications.

Pancreatic Enzyme Replacement Therapy (PERT) Prescription by Age in Years, 2022



For individuals aged 2 years and older, the recommended upper limit for enzyme dosing is 2,500 lipase units/kg/meal and a total of 10,000 lipase units/kg/day.[24] The mean dose of lipase units/kg/meal for individuals 2 to 19 years is 1,935 and for individuals 20 years and older, the mean dose is 1,789, suggesting that children and adults on average are not exceeding the maximum recommended dose of PERT.

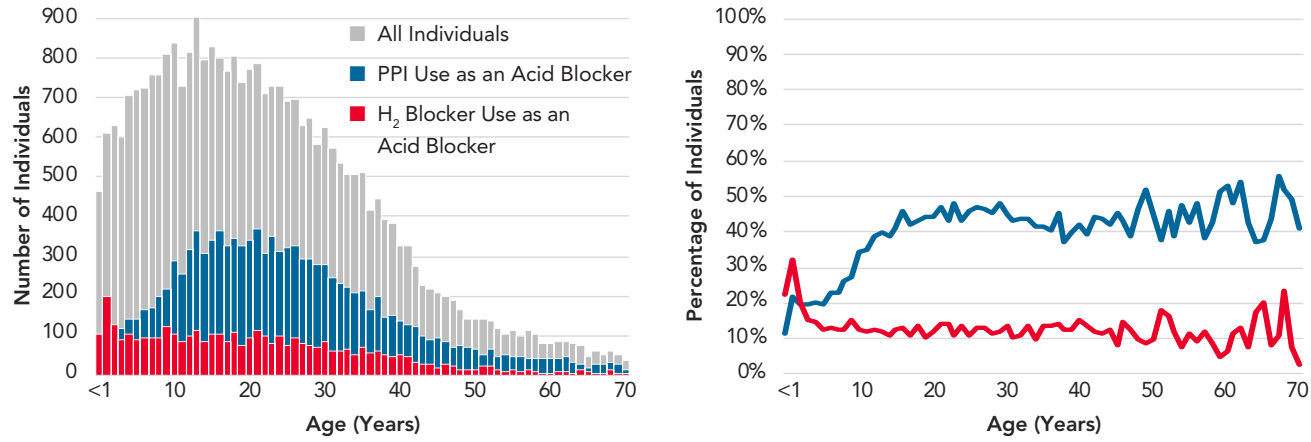
Infants with evidence of pancreatic insufficiency are recommended to receive 2,000 to 5,000 units of lipase total per feeding with adjustments as the infant grows.[7] Registry data show that the mean highest weight-based dose of lipase among children younger than 2 years is 1,745 units/kg/feeding or meal.

For infants with CF younger than 2 years, the infant clinical care guidelines recommend assessment of pancreatic functional status by measurement of fecal elastase.[28] Data on fecal elastase test results have been collected in the Registry since 2010, with an increasing number of individuals undergoing fecal elastase testing overall. However, 69.3 percent of infants born in 2022 had a fecal elastase value, this is a decrease from 80.0 percent reported for infants born in 2021. Nearly all individuals with a known fecal elastase value of less than 200 µg/g of stool were prescribed PERT. Approximately 26.6 percent of individuals with fecal elastase values greater than or equal to 200 µg/g of stool were also prescribed PERT based on clinical assessment.

Pancreatic Enzyme Use by Fecal Elastase Value in Infants Under 24 Months, 2022		
Pancreatic Enzyme Replacement Therapy	**Fecal Elastase Value <200**	**Fecal Elastase Value ≥ 200**
On PERT	852	67
Not on PERT	9	185

Acid blockers are commonly prescribed for people with CF to treat GERD and/or to decrease the acidity of the stomach to increase the effectiveness of PERT. Overall, proton pump inhibitors (PPIs) are prescribed more often (38.3 percent of individuals) than H_2 blockers (13.2 percent of individuals). H_2 blockers are used more frequently in younger individuals. Use of PPIs increases with age until age 20 and overall is prescribed to 43.4 percent of individuals 20 years and older.

PPI and H_2 Blocker Use by Age in Years, 2022



In 2022, 87.2 percent of individuals aged 2 to 19 and 74.5 percent of individuals age 20 and older were prescribed CF-specific vitamins targeting supplementation of vitamins A, D, E, and K. In terms of liver manifestations of CF, 11.7 percent of individuals were prescribed ursodeoxycholic acid, primarily for those with abnormal liver function tests or suspected CF liver disease.

COMPLICATIONS

Recognition and management of the multi-organ system health issues associated with CF is important for maintaining an individual's health and quality of life. Complications of CF can affect many different aspects of health; they can be the direct result of the malfunction or deficiency of the CFTR protein or a downstream effect of the disease or its treatment. The prevalence of some non-pulmonary CF complications is higher among individuals who received a lung transplant than among individuals who have never had a lung transplant. Since 2017, we have censored individuals at the year of transplant when calculating the prevalence of complications. As a result, some complications (e.g., CF-related diabetes and osteoporosis) are lower in 2022 than reported previously.

CFRD remains an important and highly prevalent complication that greatly impacts quality of life and is associated with increased morbidity and mortality. As the population ages, a larger proportion of individuals are reporting complications typically seen in older adults, including bone and joint disease and sinus disease.

Furthermore, along with the publication and implementation of mental health screening guidelines,[18] of the prevalence of anxiety and depression that has been reported, in 2022, anxiety disorder and depression were reported in 13.7 percent and 9.5 percent in individuals with CF less than 18 years of age as compared to 13.4 percent and 10.2 percent in 2021.

Complications of CF, 2022

	Age < 18 (%)	Age ≥ 18 (%)	All (%)
Number of Individuals (n)	**13,243**	**17,840**	**31,083**
Percentage with no complications	25.7	4.1	13.3
Percentage with complications not reported[A]	1.7	3.2	2.6
Cystic Fibrosis-Related Diabetes			
Cystic fibrosis-related diabetes (CFRD)[B]	4.5	29.7	19.0
Hepatobiliary			
Gallstones[C]	0.2	0.4	0.3
Liver disease, cirrhosis[D]	1.7	4.0	3.0
Liver disease, non-cirrhosis[C]	3.2	3.1	3.1
Acute hepatitis[C]	0.1	0.1	0.1
Hepatic steatosis	0.4	1.2	0.9
Liver disease, other[C]	1.6	1.5	1.6
Bone/Joints			
Arthritis/arthropathy	0.2	5.8	3.4
Bone fracture[C]	0.3	0.2	0.2
Osteopenia	0.9	18.5	11.0
Osteoporosis	0.3	7.8	4.6
Pulmonary			
Allergic bronchopulmonary aspergillosis (ABPA)	1.4	6.5	4.3
Asthma	24.4	34.6	30.3
Hemoptysis	0.3	2.4	1.5
Hemoptysis, massive[C]	<0.1	0.2	0.1
Pneumothorax requiring chest tube[C]	<0.1	0.1	0.1

Table continues on the next page

Complications of CF, 2022 *continued*			
GI	**Age < 18 (%)**	**Age ≥ 18 (%)**	**All (%)**
Distal intestinal obstruction syndrome (DIOS)[C]	1.5	1.4	1.4
Fibrosing colonopathy/colonic stricture[C]	<0.1	<0.1	<0.1
Gastroesophageal reflux disease (GERD)	27.6	41.9	35.8
GI bleed requiring hospitalization (non-variceal)[C]	<0.1	<0.1	<0.1
History of intestinal or colon surgery	5.4	2.9	3.9
Pancreatitis[C]	0.4	1.5	1.0
Rectal prolapse[C]	0.3	0.1	0.2
C. diff. colitis	0.1	0.2	0.1
Mental Health[E]			
Anxiety disorder	13.7	29.4	26.0
Depression	9.5	29.6	25.3
Other Complications			
Cancer confirmed by histology[C]	0.0	0.3	0.2
Hearing loss	1.2	3.8	2.7
Hypertension	0.6	7.6	4.6
Kidney stones[C]	0.1	1.4	0.8
Nasal polyps requiring surgery[C]	2.1	1.6	1.8
Renal failure requiring dialysis[F]	<0.1	0.1	<0.1
Sinus disease	17.2	51.0	36.6

[A] *Individuals for whom the complications case report form was not completed were considered to not have any complications, as in previous years.*

[B] *See table on page 72 for secondary complications.*

[C] *At the end of 2015, the data entry for complications was revised such that acute complications would no longer carry forward from one encounter to the next. We hypothesize that this impacted the number of reported acute complications in subsequent years.*

[D] *See table below for secondary complications.*

[E] *Percentages for mental health disorders include individuals age 12 years and older at the end of the reporting year. In years prior to 2021, reporting included all individuals. The number of individuals between the ages of 12 and 17 is 4,909.*

[F] *Cause other than CFRD.*

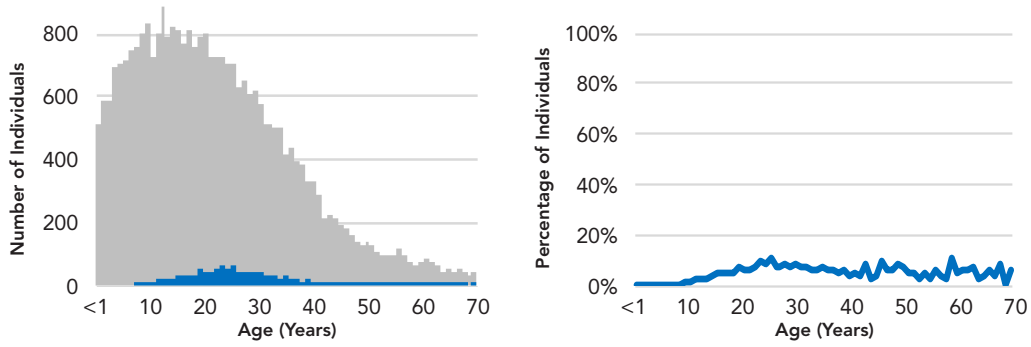
The table below highlights the prevalence of clinical manifestations of portal hypertension among individuals with cirrhosis.

Complications of Cirrhosis, 2022 (n=913)			
	Age < 18 (%)	**Age ≥ 18 (%)**	**All (%)**
Number of Individuals (n)	**218**	**695**	**913**
Esophageal varices	18.8	23.7	22.6
Gastric varices	6.4	4.6	5.0
GI bleed related to varices	1.8	2.7	2.5
Splenomegaly	40.8	36.1	37.2
Hypersplenism	11.5	12.2	12.0
Encephalopathy	1.4	2.9	2.5
Ascites	4.1	8.1	7.1

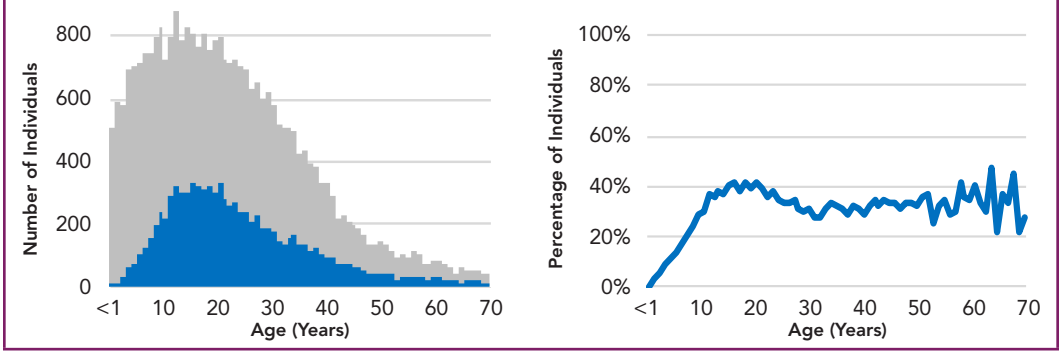
CF Complications by Age

Reported complications differ in their distribution by age. Some are relatively stable over time while others increase with age. The prevalence of bone disease and GERD is higher in the older age groups. The prevalence of asthma peaks during adolescence and then decreases among adults, while the prevalence of sinus disease increases in adolescence and in young adults and remains high through the older ages. The prevalence of CFRD is higher in adolescence and adulthood. ABPA and DIOS are less common overall but occur in all age groups. Liver disease is more prevalent in adolescents and young adults.

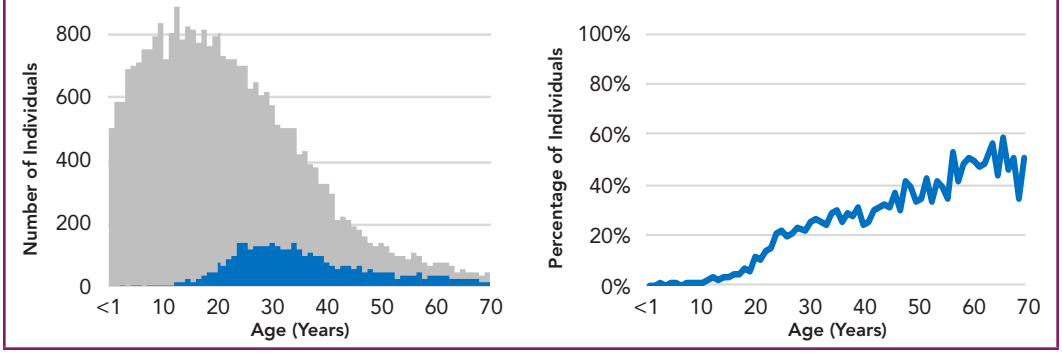
Allergic Bronchopulmonary Aspergillosis (ABPA)



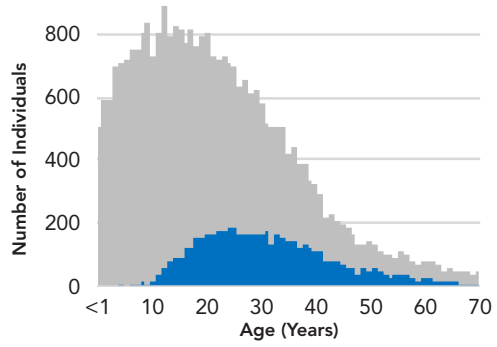
Asthma

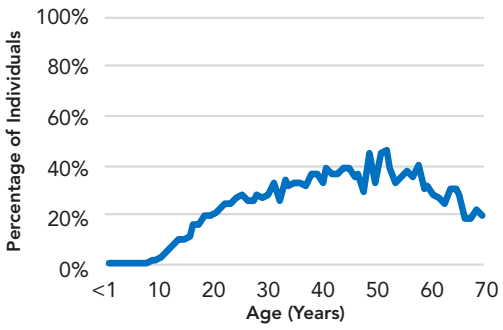


Bone Disease (Osteopenia, Osteoporosis, or Bone Fracture)

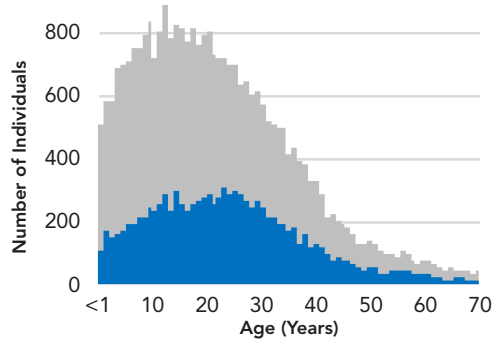


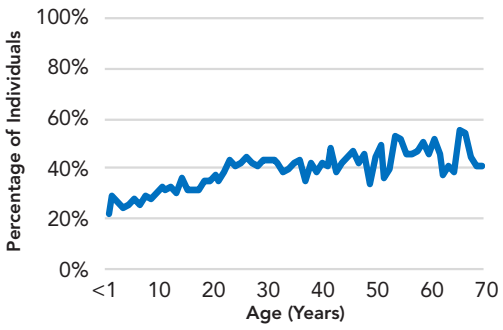
Cystic Fibrosis-Related Diabetes (CFRD)



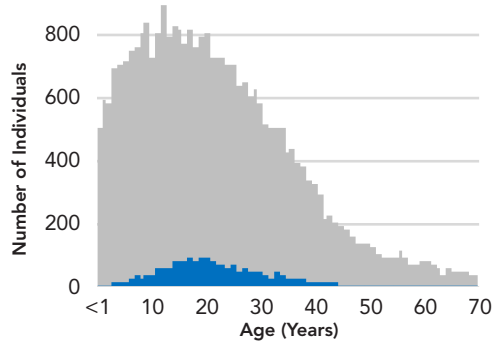


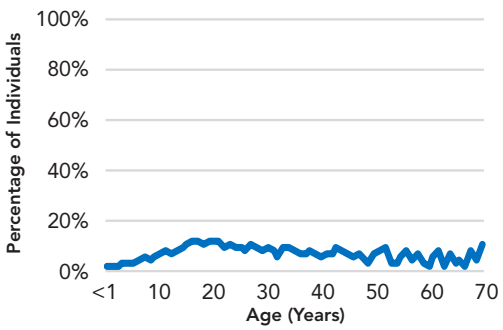
Gastroesophageal Reflux Disease (GERD)



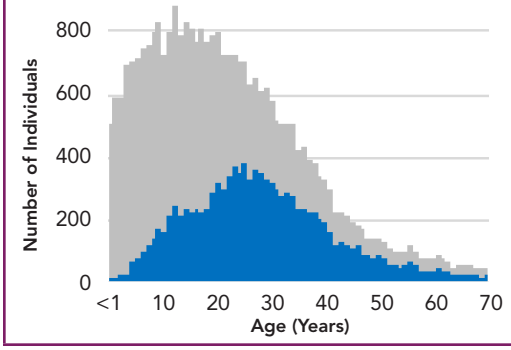


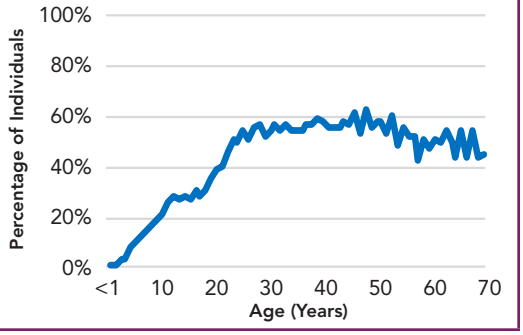
Liver Disease (All Types)





Sinus Disease



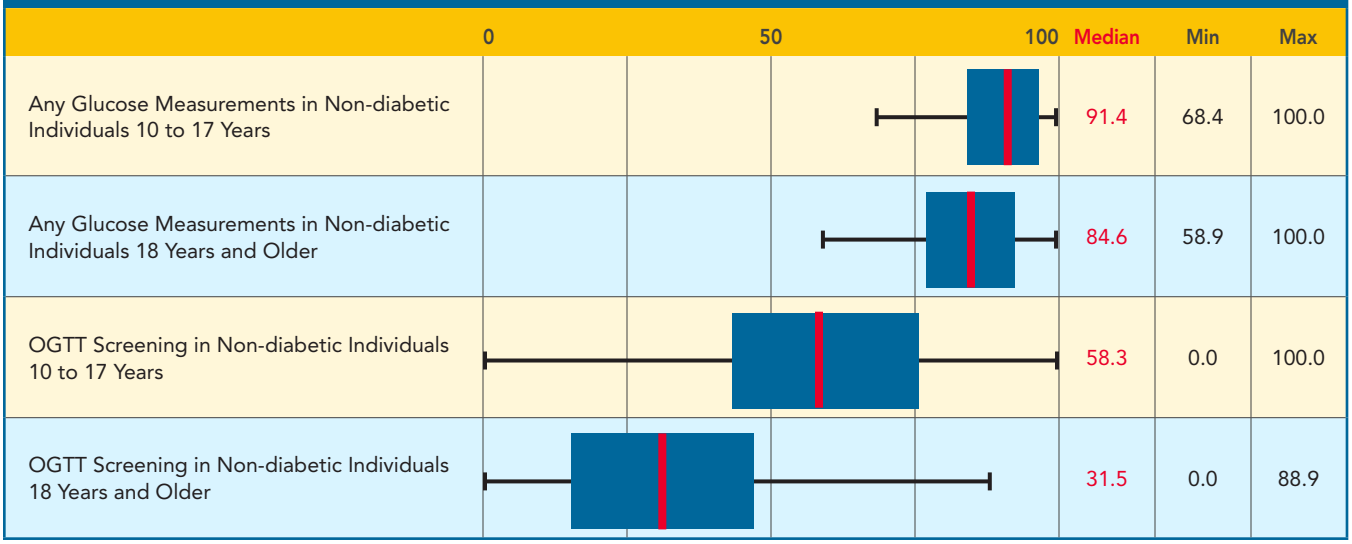


Cystic Fibrosis-Related Diabetes (CFRD)

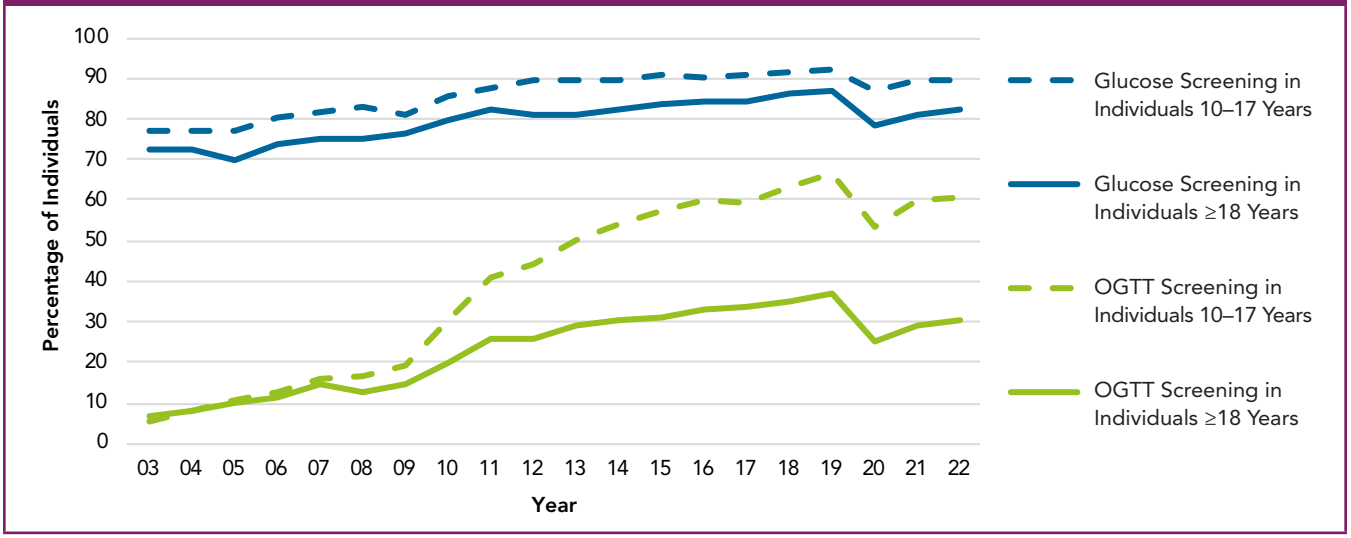
CFRD is an important complication of CF associated with weight loss, lung function decline, and increased mortality.[39] Early diagnosis and treatment may minimize the impact of CFRD. The CF Foundation/American Diabetes Association clinical practice guidelines for CFRD recommend screening all individuals annually, starting at age 10, with an oral glucose tolerance test (OGTT).[39]

Blood glucose testing is routinely performed at most CF Care Centers. The recommended OGTT is used less frequently, and substantial variation exists across CF Care Centers. CF rates of screening for CFRD using the OGTT have not returned to their highest proportion since 2019, with a much higher proportion of adolescents screened compared to adults.

Percentage of Non-Diabetic Individuals Receiving Glucose Testing, by Center

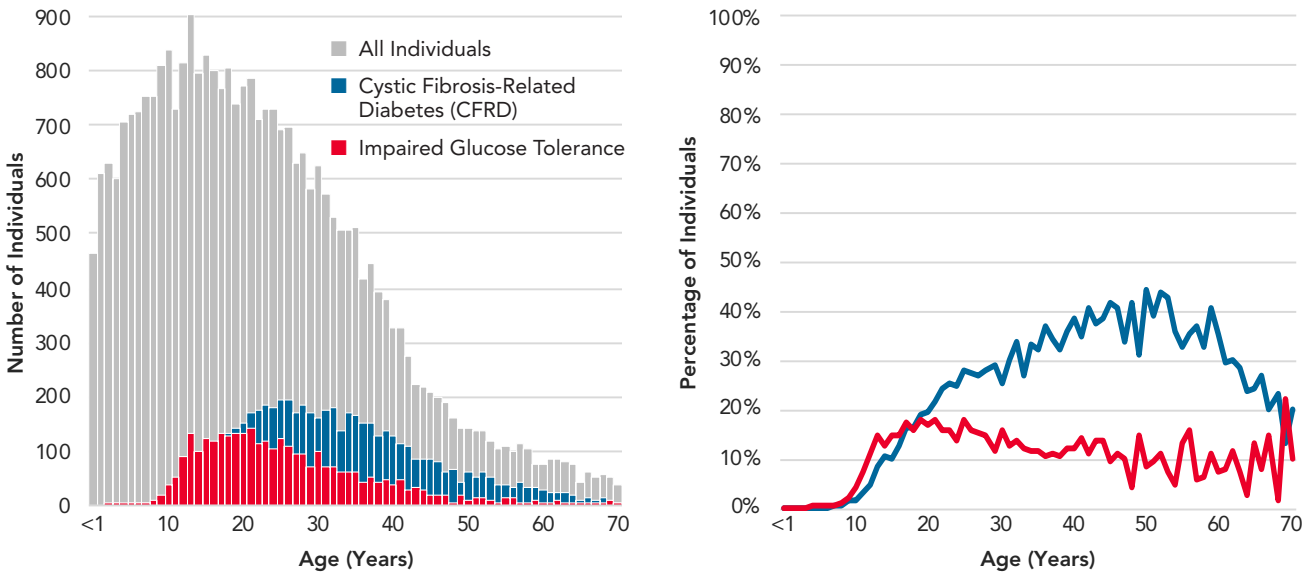


Blood Glucose and OGTT Screening for Individuals Without CFRD, 2003–2022



Prevalence of CFRD is higher among adults as compared to children with CF. Impaired glucose tolerance is most prevalent in adolescence; these individuals are at increased risk for developing CFRD and may benefit from increased monitoring.

CFRD and Impaired Glucose Tolerance by Age in Years, 2022



Most individuals who were diagnosed with CFRD are noted in the Registry as being treated with insulin, as recommended in the CF Foundation CFRD clinical care guidelines.[39]

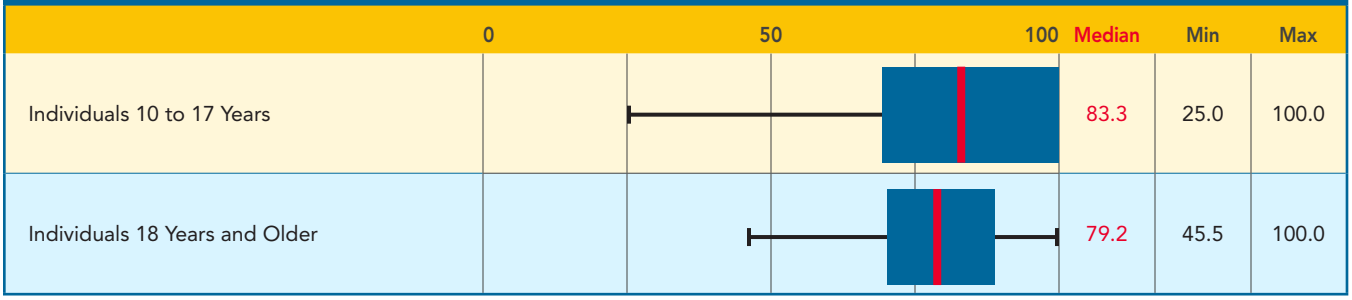
CFRD Treatment in 2022

	Percentage of People With CFRD on Treatment
Dietary change	24.8
Oral hypoglycemic agents	4.3
Intermittent insulin (with illness, steroids, etc.)	3.6
Chronic insulin	68.0
Other diabetes treatments	2.2
No treatment noted in reporting year	14.9

The data are not mutually exclusive and represent CFRD treatment at any point during the year.

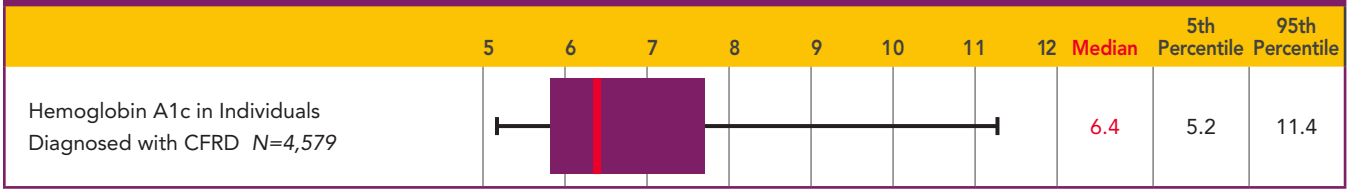
The clinical practice guidelines recommend regular hemoglobin A1c (HbA1c) measurements for individuals with CFRD.[39] Although there is variation by CF Care Centers in the percentage of individuals with CFRD with one or more HbA1c measurements reported during the year the majority of centers test most of their patients at least annually.

Percentage of Individuals With CFRD With One or More Hemoglobin A1c Measurement, by Center



The goal established by the CF Foundation guidelines for CFRD is an HbA1c less than 7.0 percent for individuals with CFRD.[39] More than half of individuals with CFRD are meeting this guideline.

Hemoglobin A1c Lab Values Reported, 2022



Rates of secondary complications of CFRD, including retinopathy, microalbuminuria, kidney disease, and neuropathy remain low. Episodes of severe hypoglycemia can be dangerous in individuals with CFRD. As the CF population continues to age, adult CF care providers should continue to screen individuals for these complications, as recommended by the CF Foundation clinical care guidelines for CFRD.[39]

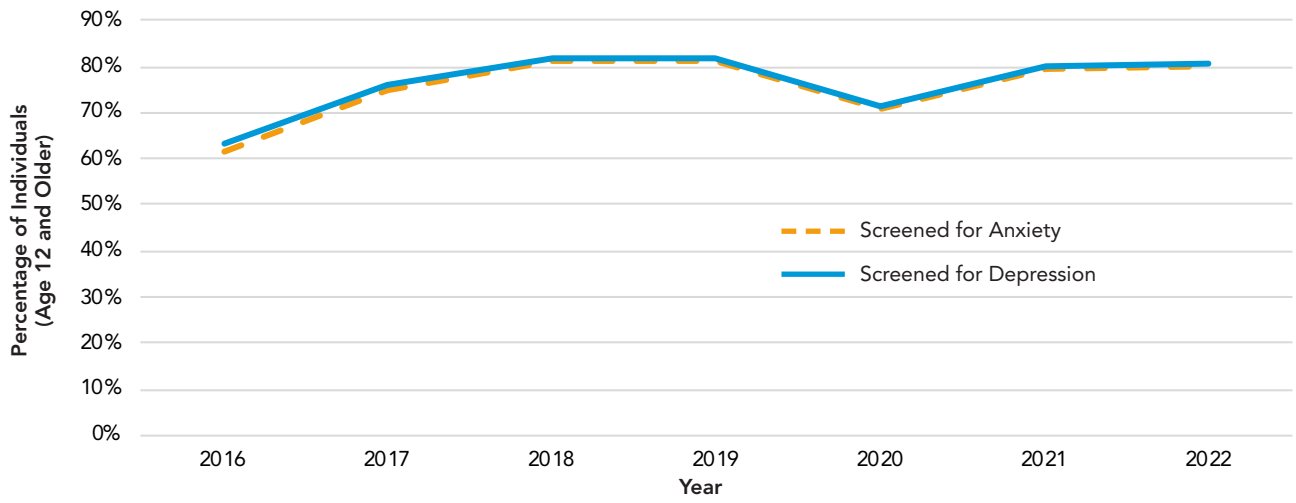
Complications of CFRD in 2022

	Age < 18 (%)	Age ≥ 18 (%)	All (%)
Number of Individuals (n)	**599**	**5,292**	**5,891**
Retinopathy	0.0	1.1	1.0
Microalbuminuria	0.2	1.4	1.2
Chronic renal insufficiency	0.2	1.8	1.6
Chronic renal failure requiring dialysis	0.0	0.2	0.2
Peripheral neuropathy	0.2	1.5	1.4
Any episodes of severe hypoglycemia	3.9	3.6	3.7

Depression and Anxiety

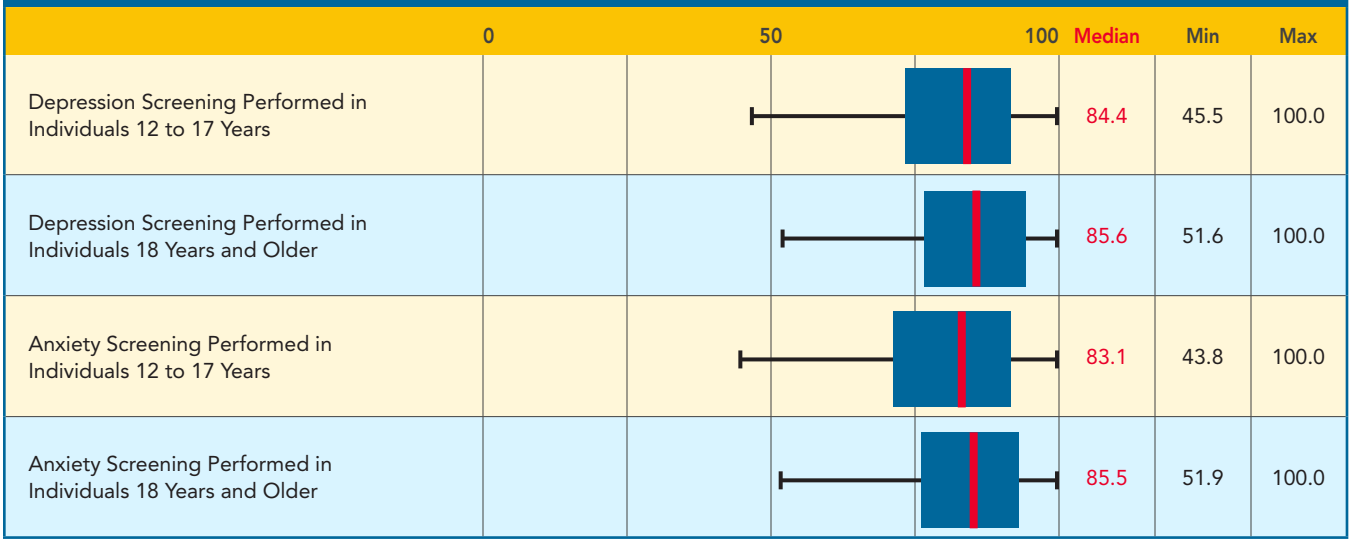
Addressing the mental health of all individuals with CF is critical to maintaining their overall health and quality of life. In 2015, the CF Foundation and the European CF Society published guidelines on screening and treatment for depression and anxiety among individuals with CF and caregivers of children with CF.[18] These guidelines recommend annual screenings for all individuals with CF who are age 12 years and older, as well as caregivers of children with CF. The graph below shows recovery of screening rates for anxiety and depression in 2022 to pre-pandemic levels.

Depression and Anxiety Screening for Individuals 12 Years Old and Older, 2016–2022



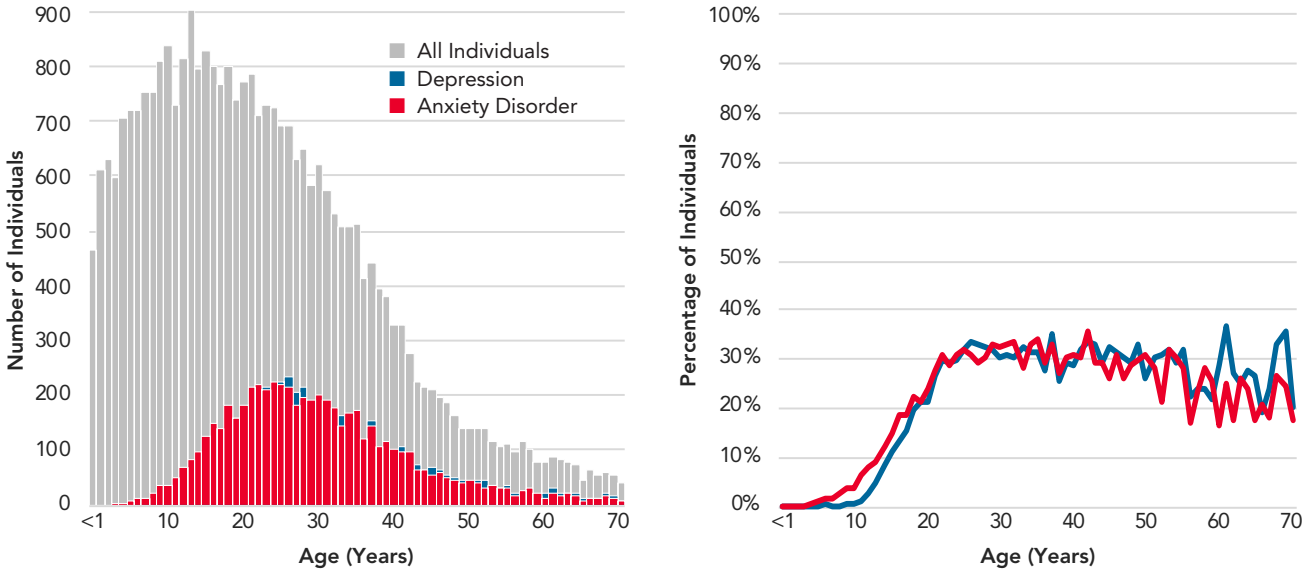
No significant differences are observed between screening rates for adolescents and adults. Of note, wide variation in screening across the CF Care Center network remains.

Percentage of Individuals With Mental Health Screening, by Center



Prevalence of both anxiety and depression increased through adolescence and early adulthood, then remained high at older ages. There is substantial overlap, and many individuals experience both anxiety and depression. Among individuals who reported anxiety or depression, 47.5 percent reported both conditions.

Depression and Anxiety by Age in Years, 2022



Advanced Lung Disease (ALD)

Recognizing a need to monitor uptake of the recent guidelines[40] for management of advanced CF lung disease and collect more detailed clinical information to support research, ALD-specific case report forms were added to the Registry in 2019.

ALD reporting was only completed for individuals with CF that met specific criteria including an FEV_1 less than 40 percent predicted, use of supplemental oxygen, or other clinical signs of advanced lung disease. In 2019, a total of 1,787 people contributed data on ALD indicators. This group includes people with advanced lung disease prior to 2019 as well as incident cases in that year. From 2020 onward, new cases of advanced lung disease were reported using the ALD Initiation form. In 2019, more than 90.0 percent of those reported had an annualized FEV_1 percent predicted value less than 40. In 2020–2022, that proportion dropped to 20.0 percent of newly identified ALD cases, indicating that other criteria are driving identification of ALD among the CF population. There were 236 and 133 incident cases in 2021 and 2022, respectively.

Of note, once an individual met criteria for ALD, they continued to be monitored (unless lung transplant or death occurred) even if their lung function improved such that they would not meet criteria for an incident ALD case. This case definition allowed for longitudinal follow-up for this group to monitor clinical trends. The approval of elexacaftor/tezacaftor/ivacaftor in 2019 and its rapid uptake has changed the disease trajectory of many individuals with CF, including those with ALD.

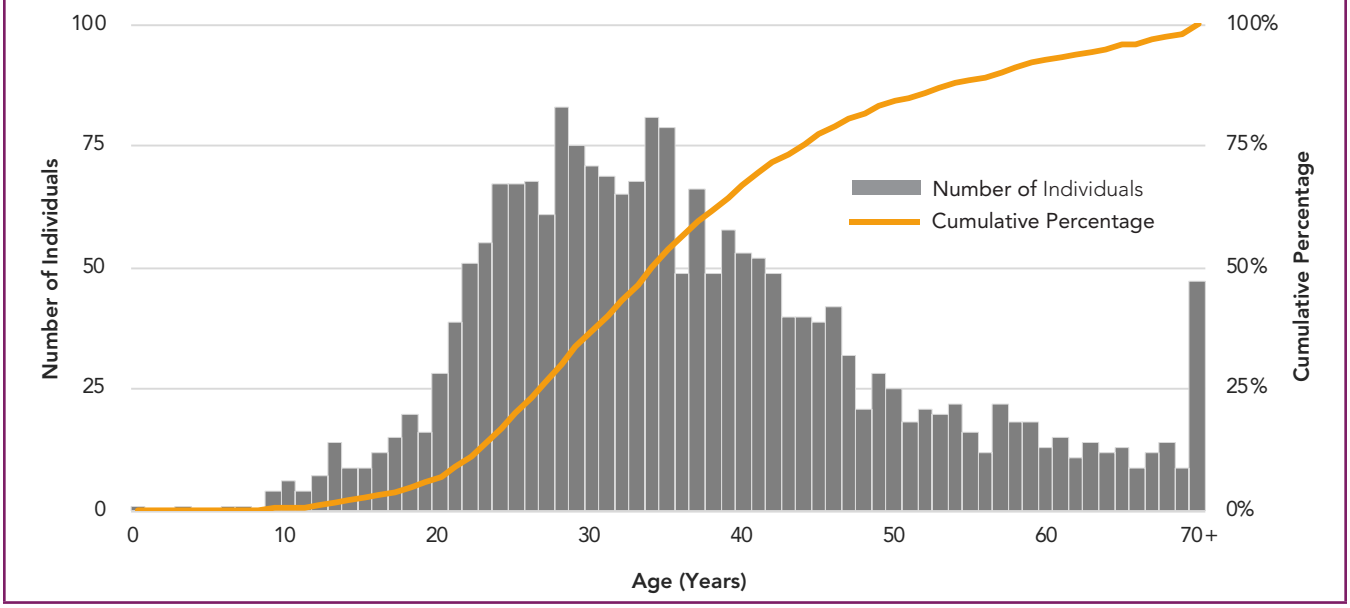
Summary of the Cystic Fibrosis Foundation Patient Registry ALD Individuals, 2019–2022				
Demographics	**2019**	**2020**	**2021**	**2022**
Individuals with ALD (n)[A]	1,787	1,950	2,087	2,126
Newly enrolled individuals with ALD (n)[B]	847	263	236	133
Mean age (years)	34.5	35.6	36.5	37.4
Median age (years)	32.1	33.1	34.0	34.8
Adults ≥18 years (%)	93.7	94.8	95.4	96.0
Race (mutually exclusive)[C]				
White (%)	91.2	91.1	90.5	90.8
African American (%)	4.5	4.6	5.1	5.0
Other race (%)	4.3	4.3	4.4	4.2
Hispanic (any race) (%)	8.8	8.8	8.7	9.1
Males (%)	54.9	54.7	54.6	54.3
Pulmonary[D]				
FVC % predicted (mean)	57.1	62.2	63.7	64.3
FEV_1 % predicted (mean)	35.6	40.1	40.8	41.1
FEV_1/FVC ratio % predicted (mean)	54.3	55.2	54.5	54.1
Respiratory Microbiology				
Number of microbiology cultures per patient (mean)	4.7	2.2	2.6	2.6
Pseudomonas aeruginosa (*P. aeruginosa* or *PA*) (%)[E]	75.2	63.1	62.0	59.5
Burkholderia cepacia (*B. cepacia*) complex (%)	5.1	3.4	3.3	3.2
Staphylococcus aureus (*S. aureus*) (%)[F]	58.3	48.5	46.4	44.2
Methicillin-sensitive *Staphylococcus aureus* (MSSA) (%)	36.7	27.7	30.8	29.1
Methicillin-resistant *Staphylococcus aureus* (MRSA) (%)	32.0	25.5	21.4	19.6
Stenotrophomonas maltophilia (*S. maltophilia*) (%)	16.4	7.4	6.6	7.6
Mycobacterial species (%)[G]	11.6	9.3	8.5	10.0
Health Care Utilization and Pulmonary Exacerbations (PEX)[H]				
Outpatient visits to CF Care Centers reported per year (mean)	5.6	2.5	2.9	3.0
Treated with IV antibiotics for a pulmonary exacerbation (%)	75.9	36.7	34.0	34.9
Number of pulmonary exacerbations per year (mean)	2.1	0.8	0.7	0.7
Number of days of treatment for all PEX per year (mean)[I]	45.3	32.0	30.8	28.8
Number of days of home IV treatment for all PEX per year (mean)[I]	16.5	11.8	11.2	10.1
Number of days of hospitalization for all PEX per year (mean)[I]	28.8	20.2	19.6	18.8
Pulmonary Therapies[J]				
Dornase alfa (≥6 years) (%)	95.0	94.7	91.2	90.2
Inhaled tobramycin (PA+ and ≥6 years) (%)[K]	72.5	70.5	63.3	60.7
Inhaled aztreonam (PA+ and ≥6 years) (%)	59.7	57.9	49.7	49.1
Azithromycin (PA+ and ≥6 years) (%)[L]	73.9	71.3	66.7	65.9
Hypertonic saline (≥6 years) (%)	81.5	78.1	73.6	71.2
Oxygen (%)[M]	57.9	45.1	41.1	38.6
Non-invasive ventilation (%)	16.6	13.2	11.8	10.9
CFTR Modulators				
Individuals prescribed a modulator (≥6 years) (%)	72.3	86.9	88.9	89.3

[A] *Includes all CF patients enrolled in the ALD cohort by the year specified.*
[B] *For 2019, new incident cases of ALD include individuals who may have met ALD criteria in prior years.*
[C] *Reporting of race in years prior to 2021 included individuals in more than one race category (not mutually exclusive).*
[D] *Pulmonary function data throughout this report reflect the use of Global Lung Initiative (GLI) equations.[2] Pulmonary function data are for individuals greater than 7 years of age at the end of the reporting year.*
[E] *Includes PA and multidrug-resistant PA found in any culture during the year.*
[F] *Includes MSSA and MRSA and reflects the prevalence of S. aureus among individuals who had a bacterial culture during the year. The percentages for MSSA and MRSA individually are greater than the total S. aureus percentage because MSSA and MRSA are not mutually exclusive.*
[G] *Percentage of people with CF with one or more mycobacterial species isolated out of those who had a mycobacterial culture during the year.*
[H] *Defined as a period of treatment with IV antibiotics in the hospital and/or at home.*
[I] *Among those with one or more pulmonary exacerbations in the year.*
[J] *Percentage of people with CF on therapy at any clinical visit in the year. All individuals noted as intolerant or having an allergy to a specific therapy were excluded.*
[K] *Includes Tobramycin solution for inhalation (i.e., TOBI®), TOBI™ Podhaler® (Tobramycin Inhalation Powder), and Bethkis® since 2013. In prior years, only TOBI® was available.*
[L] *Individuals were considered eligible if they met the selection criteria used in the first U.S. azithromycin trial.[3]*
[M] *Includes continuous, nocturnal, or with exertion.*

More than 90.0 percent of individuals with CF identified as having ALD were adults, with a median age in the mid-30s across all four years. Age distribution in the ALD group is skewed toward the older population with a median age of 34.8 years in 2022. In 2022, only 4.0 percent of those reported as having ALD were younger than 18 years. The racial composition of individuals with ALD was similar to that of the entire Registry population. In comparison to the general CF population, individuals with ALD had significantly lower lung function, higher prevalence of *P. aeruginosa* and *B. cepacia* complex, and similar NTM prevalence, but noticeably lower prevalence of methicillin-sensitive *S. aureus*. The rate of pulmonary exacerbations for individuals with ALD was three times greater than the overall CF population (0.7 versus 0.2 pulmonary exacerbations per individual in 2022), and their recorded use of pulmonary therapies was higher than in the general CF population. Nearly 90.0 percent of people with ALD were prescribed a CFTR modulator in 2022.

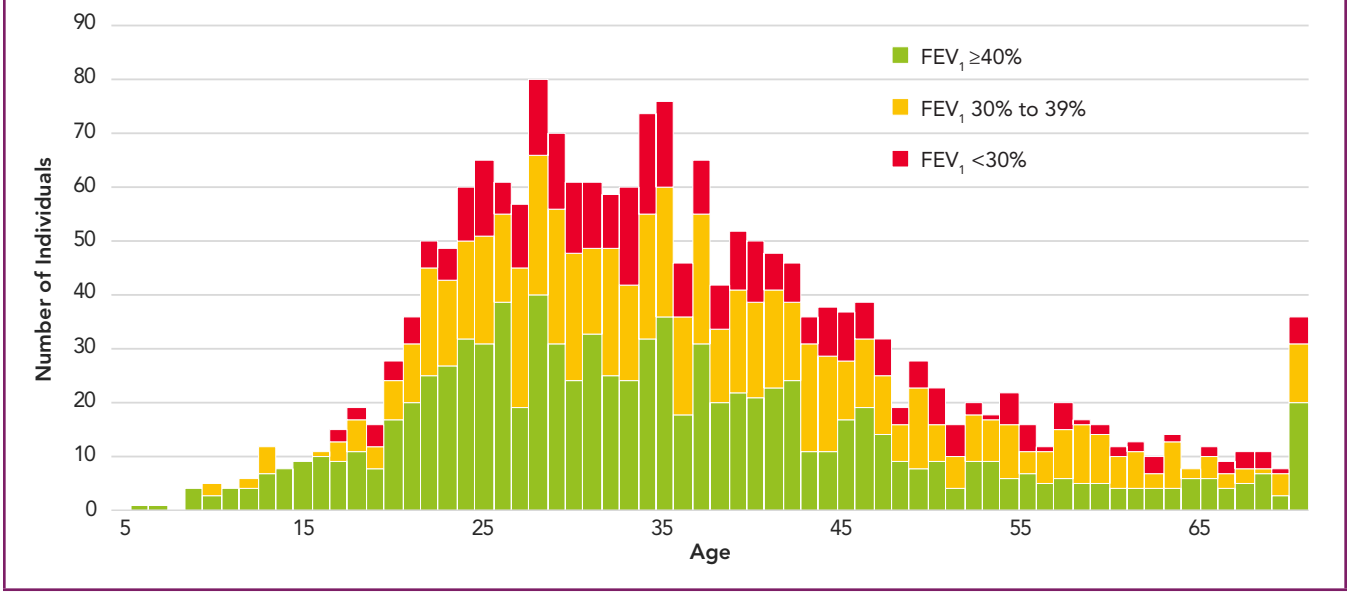
Age distribution in the ALD group is skewed toward the older population with a median age of 34.8 years.

Age Distribution of the Advanced CF Lung Disease Population in 2022



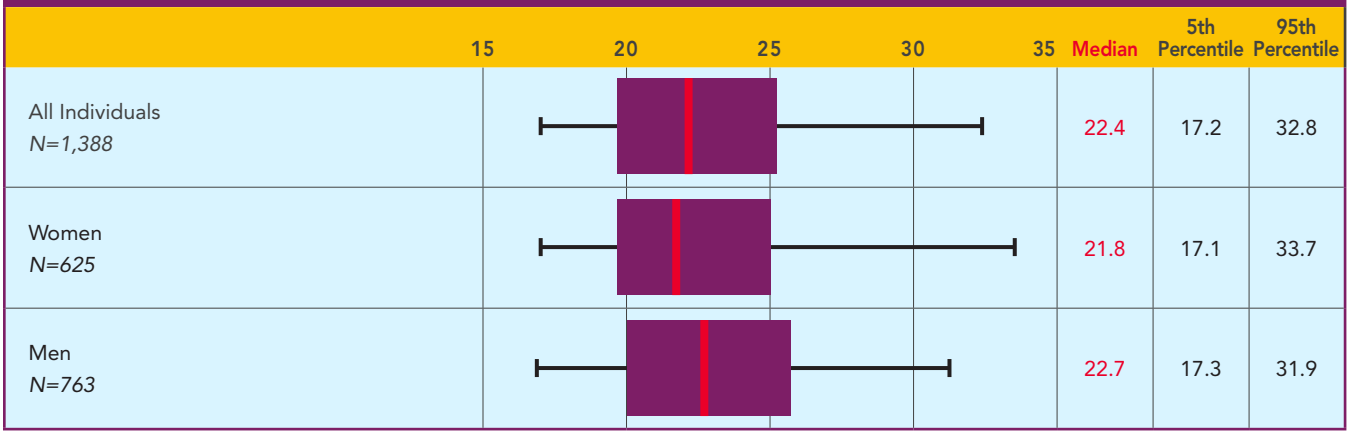
In 2022, a relatively high percentage of those in the ALD group had an FEV_1 percent predicted greater than or equal to 40.0 percent, especially in people younger than 25 years of age.

Pulmonary Function Impairment in ALD Individuals by Age in Years, 2022 *(Stacked Bar Chart)*



The median BMI values of adults 20 years of age or older in the ALD group in 2022 were lower than in the CF Registry population with the same age, (22.4 versus 24.0). However, there are overweight and obese individuals with CF in the ALD group.

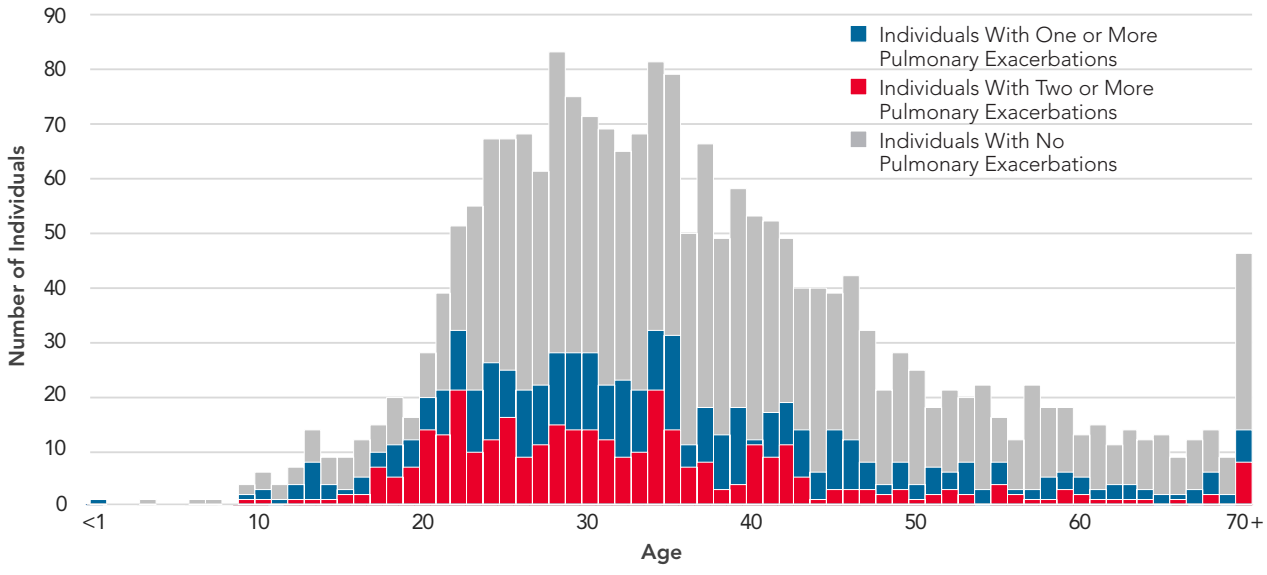
BMI Value for Adults With ALD 20 Years and Older



	Median	5th Percentile	95th Percentile
All Individuals *N=1,388*	22.4	17.2	32.8
Women *N=625*	21.8	17.1	33.7
Men *N=763*	22.7	17.3	31.9

Individuals with ALD suffer from pulmonary exacerbations more often than other individuals with CF (34.8 percent versus 12.7 percent). Adults aged 20 to 35 have more frequent pulmonary exacerbations than other age categories in the ALD group. In 2022, the average number of days spent treating pulmonary exacerbations in the ALD group was higher than the average for other individuals with CF treated for pulmonary exacerbations (28.8 days versus 17.5 days).

Pulmonary Exacerbations in Advanced Lung Disease Individuals by Age in Years, 2022



Since the ALD guidelines were adopted, the Registry data show that recommended testing is not being performed in all eligible Registry participants. In 2022, 16.9 percent of individuals received at least one blood gas analysis, 19.9 percent received at least one six-minute walk test, and 19.2 percent received an echocardiogram. Nearly 65.0 percent of individuals with ALD did not receive any of these recommended annual tests in 2022.

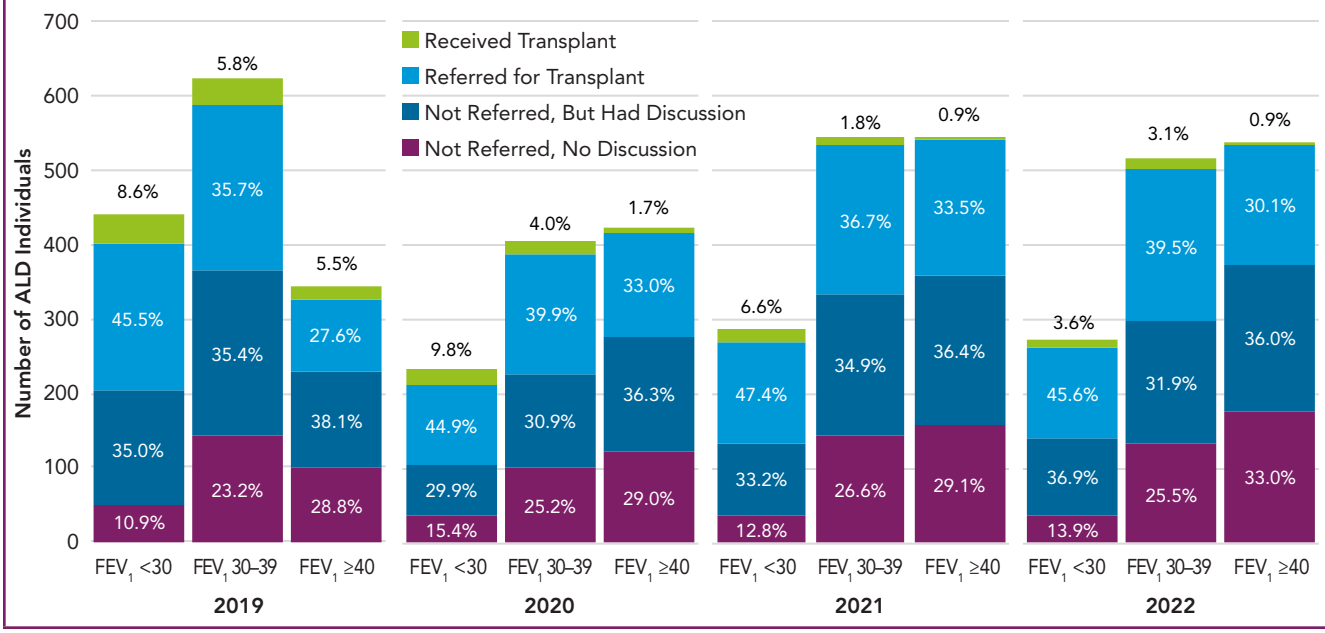
Advanced Lung Disease Interventions and Tests

	2019	2020	2021	2022
Number of Individuals (n)[A]	**1,388**	**1,218**	**1,556**	**1,455**
At Least One Intensive Care Unit (ICU) Admission (%)	9.9	5.3	4.2	4.7
At Least One Echocardiogram Performed (%)	27.9	16.1	18.4	19.2
At Least One Blood Gas Analysis Performed (%)	29.0	15.6	14.3	16.9
At Least One Bronchial Artery Embolization Performed (%)	2.7	1.4	1.1	0.3
At Least One Six Minute Walk Performed (%)	29.5	15.3	16.8	19.9
AAt Least One Echocardiogram, Blood Gas Analysis, or Six Minute Walk Performed (%)	48.3	29.1	31.2	35.4

[A]*Includes all CF patients enrolled in the ALD cohort and contributing ALD annual data for the year specified.*

Based on 2019 to 2022 data, about half of all individuals in the ALD group with an FEV_1 less than 30.0 percent predicted were referred for a lung transplant, despite the guideline recommendation to refer all individuals that fall in this FEV_1 percent predicted category.[40] Across all years, approximately 10.0 to 30.0 percent of individuals with ALD were reported as having had no discussion with their care teams about lung transplantation. In 2022, of the individuals with ALD who were not referred for a lung transplant evaluation, "patient stable" was the most selected reason at 58.0 percent. Other reasons for not referring individuals with ALD were patient declined to pursue (18.3 percent), adherence issues (6.6 percent), no social support (5.1 percent), substance misuse (3.9 percent), poor nutritional status (3.3 percent), and mental health (2.9 percent).

Referral Status by FEV_1 Category for Advanced Lung Disease Individuals, 2019–2022



TRANSPLANTATION

Historically, the majority of transplants among people with CF have been lung transplants. The procedure remains a viable option for some individuals with CF and advanced lung disease. The number of lung transplant procedures for individuals with CF fluctuates yearly with an overall upward trend through 2019. In 2020, there was a marked decrease in the number of individuals on the waitlist and receiving lung transplants in the context of the COVID-19 pandemic and the availability of elexacaftor/tezacaftor/ivacaftor for those aged 12 and older. The small number of lung transplants among people with CF continued through 2021 and 2022. Interestingly, there was also a decrease in the number of liver (20.0 in 2021 versus 10.0 in 2022) and kidney (21.0 in 2021 versus 8.0 in 2022) transplants as well.

In 2022, there were 1,758 individuals in the Registry who were reported to have ever received a lung, kidney, heart, or liver transplant.

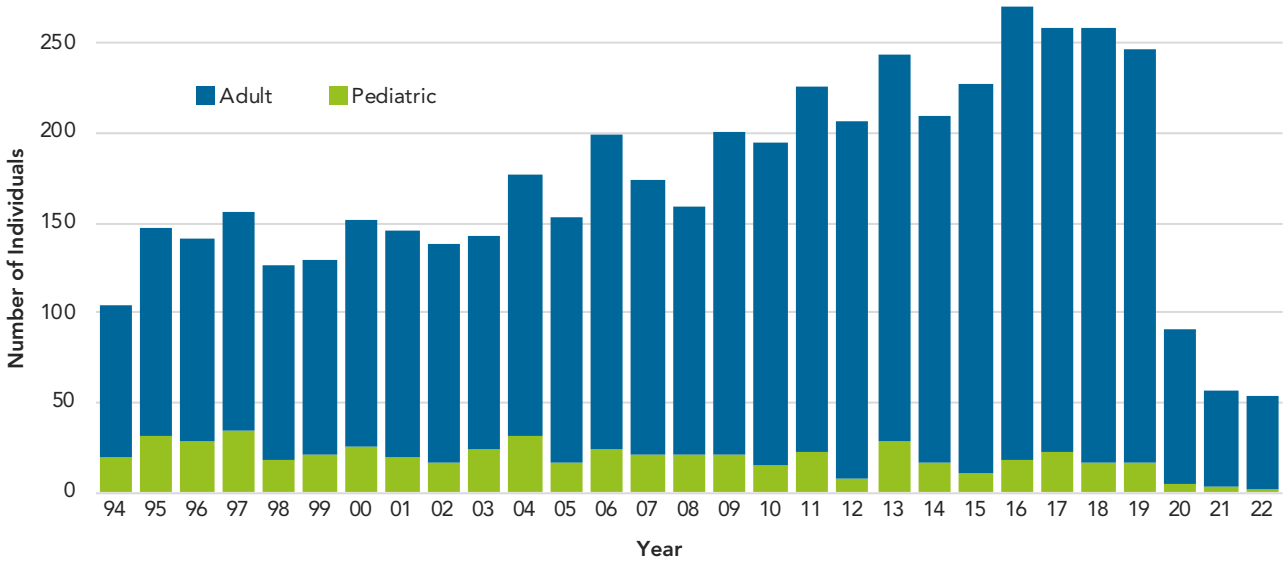
Transplant Status of People with CF in 2022 (All Organs)

	Number of Individuals
Accepted, on waiting list	48
Evaluated, rejected	112
Received transplant this year	69
Received transplant in a prior year	1,689

Lung Transplantation

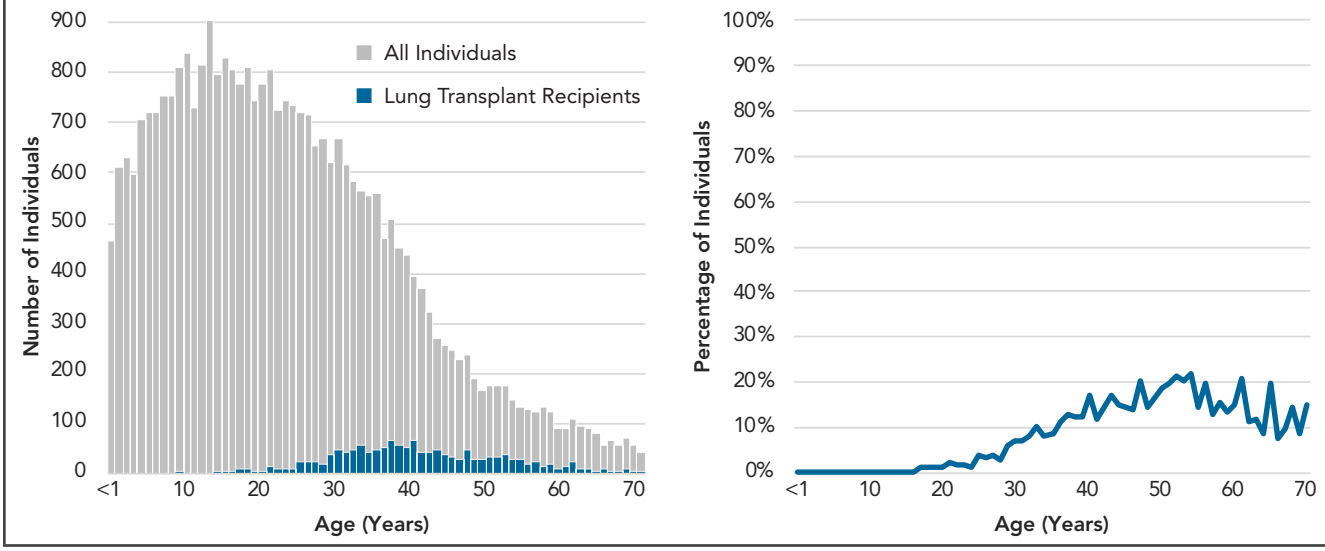
Of the 1,758 individuals reported as transplant recipients in the 2022 Registry data, 1,538 had a lung transplant. A total of 53 Registry participants were reported as receiving a lung transplant in 2022, as compared to 2,692 total lung transplants (for any underlying cause) reported by the United Network for Organ Sharing (UNOS).[41] The number of lung transplants among individuals with CF reported to the Registry in 2022 was far lower than reported in 2019 in contrast to an overall increase in the number of lung transplants in the United States.[42] The number of those with CF on the wait list was also much lower in 2022 as compared to 2019 and prior years.

Number of Individuals Receiving a Lung Transplant, 1994–2022



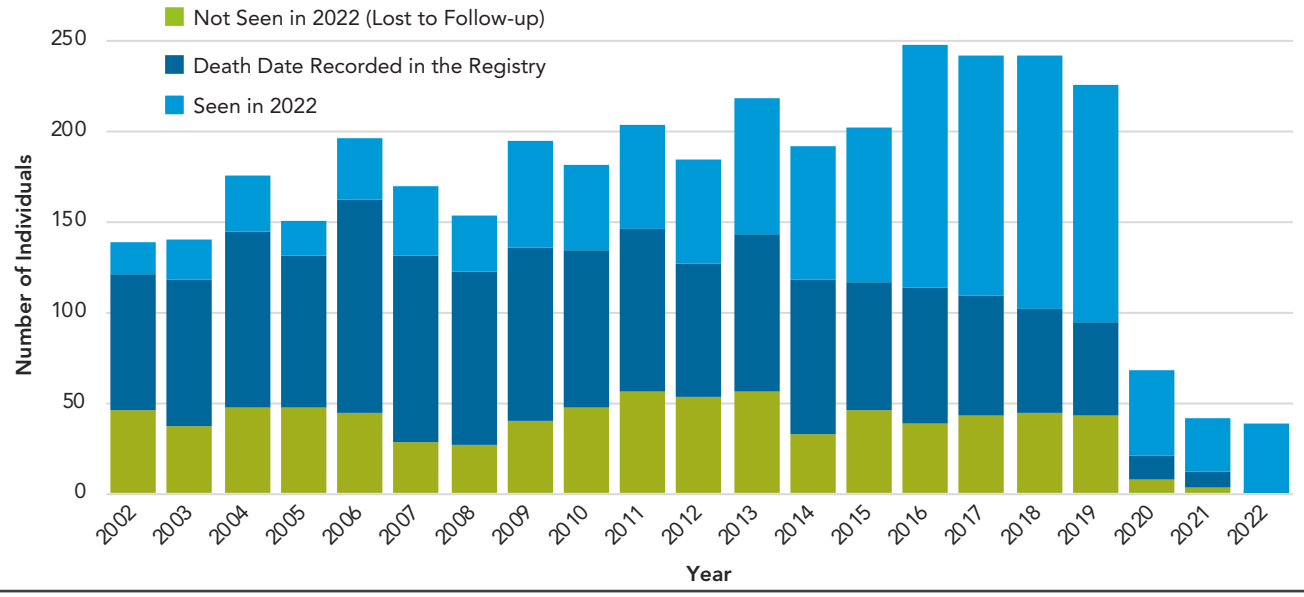
The decreased number of lung transplants reported in the Registry in 2020 through 2022 coincides with the availability of elexacaftor/tezacaftor/ivacaftor. Overall, lung transplant recipients were 4.7 percent of all individuals with CF included in the Registry; the majority are age 30 years and older.

Lung Transplant Distribution in People With CF Seen in 2022



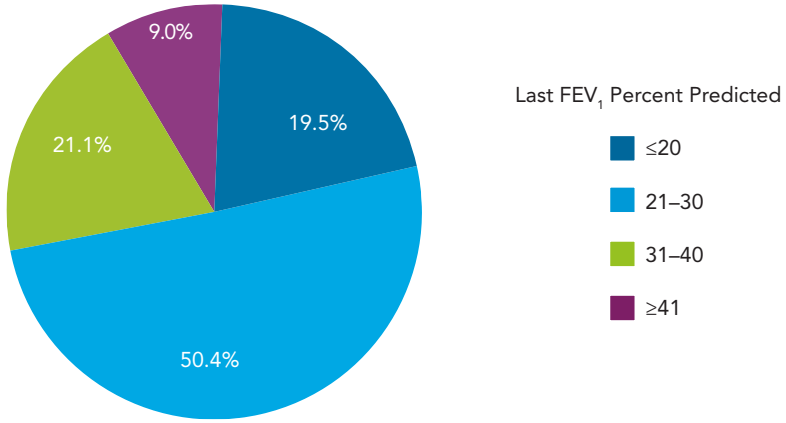
While most CF care occurs within CF Foundation-accredited Care Centers, much of the transplant and post-transplant care occurs at transplant centers. Therefore, some of these individuals are lost to follow-up in the Registry. A recent CF Foundation-supported position paper highlights the need for continued specialized CF care following transplant and proposes two models by which this can be achieved.[43] Optimal care for CF transplant recipients must include the expertise of knowledgeable CF multidisciplinary care teams as well as transplant teams.

Status of Lung Transplant Recipients by Year of Transplant, 2001–2022



The last documented FEV_1 percent predicted prior to lung transplant demonstrates that most individuals have FEV_1 percent predicted values less than 30.0 percent with 19.5 percent having FEV_1 percent predicted values less than 20.0 percent. The data underscore the severity of disease at the time of transplant and the potential benefit of earlier conversations about lung transplantation.[44]

Last FEV_1 Percent Predicted Prior to Lung Transplant, 2019–2022 (N=136)



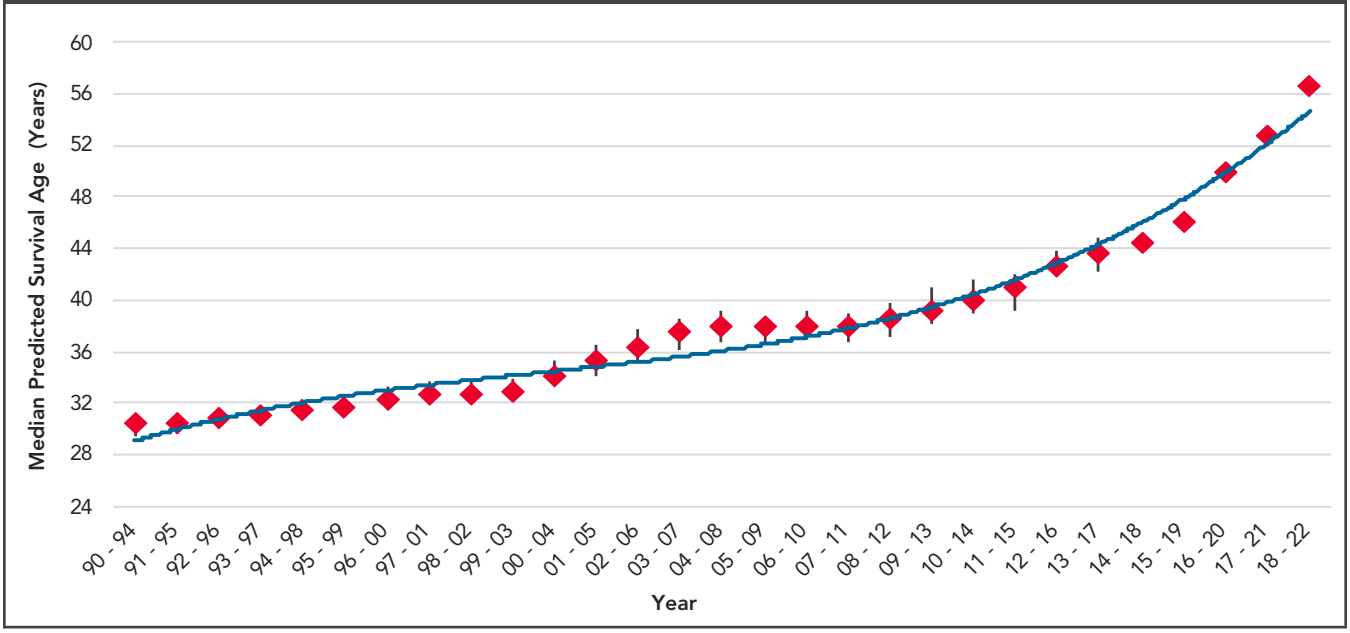
SURVIVAL

There have been substantial improvements in the survival of people with CF over the last few decades. There are several different metrics to describe the survival of people living with CF in the United States. Definitions for these metrics are provided in the Technical Supplement, available on cff.org.

Median Predicted Survival

The median predicted survival age of an individual born with CF in 2022 was 68.2 years (95.0 percent confidence interval: 63.0–76.2 years). Given the instability of annual survival estimates with the relatively low number of deaths in any given year, the estimate is more accurate when grouped into five-year increments. The following graph shows gains in median predicted survival from 1990 to 2022 in five-year increments.* For individuals born between 2018 and 2022, the median predicted survival age was 56.6 years (95.0 percent confidence interval: 54.7–58.1 years). This means that half of individuals born during 2018 to 2022 are predicted to live beyond 56.6 years of age. This prediction assumes no further improvement in mortality rate and, thus, does not consider the potential impact of CFTR modulators on younger individuals with CF or additional future improvements in clinical care.

Median Predicted Survival Age, 1990–2022 In Five-Year Increments

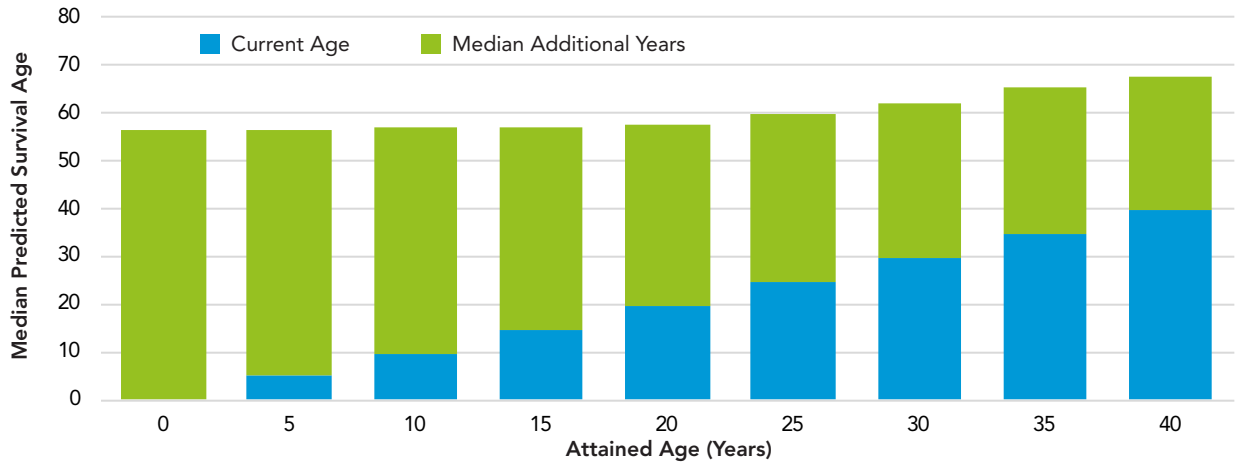


**Using the currently recommended method for calculating median predicted survival. For more information about the methodology, please see the Technical Supplement available at cff.org.*

Median Conditional Predicted Survival

Median conditional predicted survival at specific ages is another metric to help understand changes in survival over time. This metric reflects the population-based median for all individuals of a specific attained age and does not take individual characteristics into consideration. The predictions do not account for the potential impact of CFTR modulators and other improvements in clinical care. The figure ends at age 40 because the number of individuals beyond that age are currently too small to accurately predict survival.

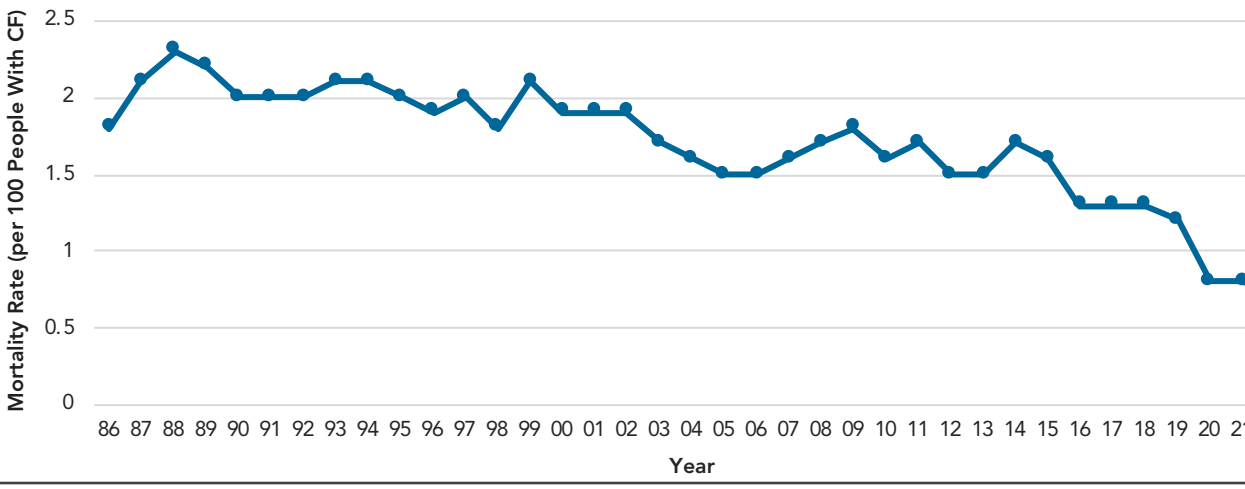
Median Conditional Predicted Survival Age Based on Attained Age, 2018– 2022



Mortality Rate

The mortality rate in 2022 was 0.7 deaths per 100 individuals with CF in the Registry. There has been a steady decrease in the mortality rate over the last 30 years. This is encouraging and has resulted in an aging population with an increase in the median age of individuals in the Registry from 12.6 years in 1992 to 21.9 years in 2022.

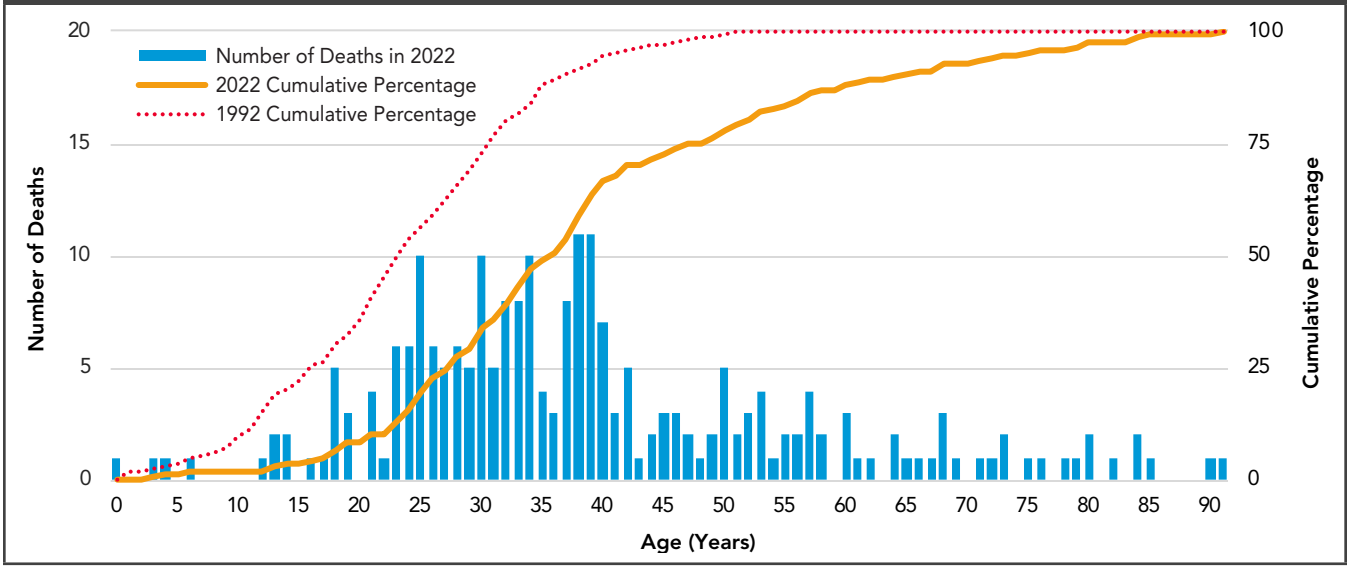
Annual Mortality Rate (per 100 People With CF), 1986–2022



Median Age at Death

The median age was 36.6 years for the 230 reported deaths in 2022. About 8.3 percent of deaths occurred before 20 years of age. A comparison of the cumulative percentage for age at death between 1990 and 2020 shows a substantial shift of the curve toward the right with a larger proportion of deaths occurring at older ages. The median age at death reflects the age distribution of deaths in 2022 and cannot be used to predict survival of the entire population.

Age at Death in 2022 (With 1992 Cumulative Percentage for Comparison)



Causes of Death

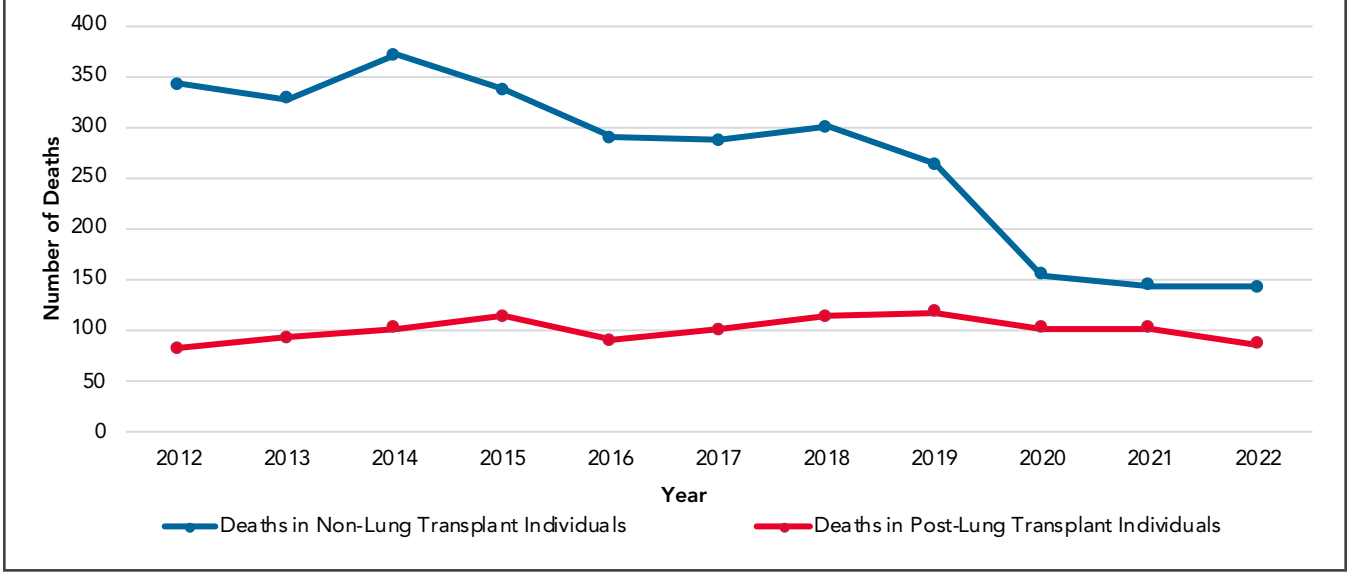
Among the 230 deaths in 2022, the primary causes were respiratory/cardiorespiratory and transplant-related, like previous years. Of these, 47.8 percent of deaths occurred in people who were F508del homozygotes, reflecting their distribution in the Registry. Although 4.7 percent of people in the Registry are post-transplant, 93 of the 230 deaths (40.4 percent) occurred in transplant recipients. Note that the primary cause of death for these individuals was not always reported as transplant related. COVID-19 was a contributing factor in 13 deaths.

Primary Cause of Death in 2022

Cause	Number of Individuals	Percentage
Respiratory/cardiorespiratory	88	38.3
Transplant-Related	36	15.7
Other	59	25.7
Unknown	26	11.3
Liver Disease/Liver Failure	10	4.3
Suicide or Drug Overdose	11	4.8

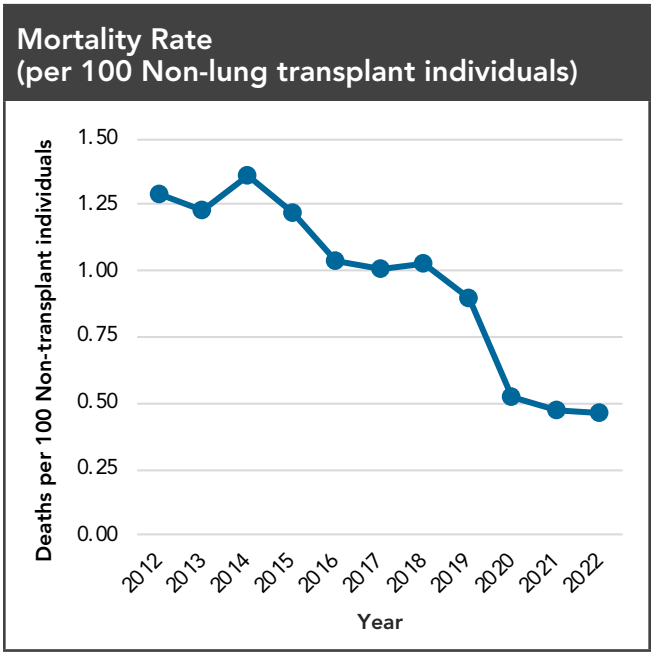
This graph shows that the number of deaths in lung transplant recipients has remained relatively stable from 2012 to 2022 whereas the number of deaths among individuals who have not had a lung transplant has decreased, particularly over the last few years.

Number of Deaths by Lung Transplant Status, 2012–2022

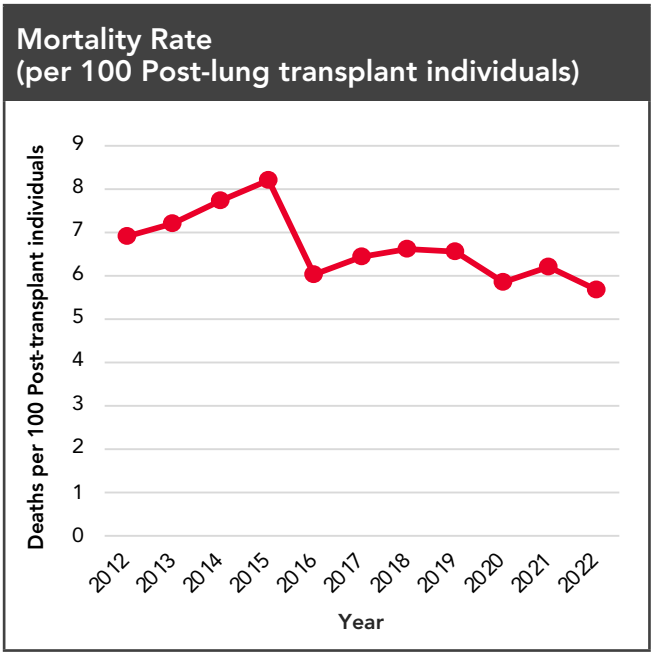


Despite the stable number of deaths in transplant recipients, the increasing number of transplant recipients in the Registry leads to a decrease in mortality rate for both groups of individuals. It is important to note that not all individuals who have undergone a lung transplant procedure return to a CF Foundation accredited Care Center and so missing data may impact these findings.

Mortality Rate (per 100 Non-lung transplant individuals)



Mortality Rate (per 100 Post-lung transplant individuals)



CF FOUNDATION PATIENT REGISTRY QUESTIONNAIRE

2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

DEMOGRAPHIC DATA

Demographics

CFF Patient Number: _____
Last Name: _____
First Name: _____
Middle Name: _____
Last Name at Birth (if different): _____
Last 4 digits of SSN: _____
Date of Birth: (MM/DD/YYYY)
State of Birth: _____
Gender: ○ Male ○ Female
Current Zip: _____
Emergency Phone: _____
Is patient residing in the US permanently?
○ Yes ○ No
Email: _____

Race/Ethnicity Information

Race:
○ White
○ Black or African American
○ American Indian or Alaska Native
○ Asian
○ Native Hawaiian or Other Pacific Islander
○ Some other race
○ Two or more races
If two or more races, specify Mixed Race components:
☐ White
☐ Black or African American
☐ American Indian or Alaska Native
☐ Asian
☐ Native Hawaiian or Other Pacific Islander

Is the Patient of Hispanic Origin?
○ Yes ○ No ○ Unknown

Death Information

Date of Death: (MM/DD/YYYY)

Check if date of death is approximate: ☐

Primary Cause of death:
○ Respiratory/cardiorespiratory
○ Liver Disease/Liver Failure
○ Trauma
○ Suicide
○ Transplant related: Bronchiolitis obliterans
○ Transplant related: Other
○ Drug Overdose
○ Other
○ Unknown

Additional Information

Additional Information: _____

CF DIAGNOSIS

History of patient diagnosis*

Date of Diagnosis: (MM/DD/YYYY)
Date is an approximation: ☐

Diagnosis:
○ Cystic Fibrosis
○ CFTR-related metabolic syndrome
○ CFTR-related disorder
○ CF, CRMS and CFTR-related disorder all ruled out

Patient was diagnosed with CF after false negative result by newborn screening:
○ Yes ○ No ○ Unknown

Diagnosis Suggested by the following:
☐ Acute or persistent respiratory abnormalities
☐ CBAVD (absent vas deferens) or related abnormalities
☐ Digital clubbing
☐ DNA Analysis
☐ Edema
☐ Electrolyte imbalance
☐ Elevated immunoreactive trypsinogen (IRT) at CF newborn screening
☐ Failure to thrive/malnutrition
☐ Family history
☐ Infertility/GU abnormalities
☐ Less than 2 identified disease causing mutations
☐ Liver problems
☐ Meconium ileus/other intestinal obstruction (provide details below)
○ meconium ileus with perforation
○ meconium ileus without perforation
Other neonatal bowel obstruction: _____
☐ Nasal polyps/sinus disease
☐ Newborn (neonatal) screening
☐ Non-diagnostic sweat chloride value(<60 mmol/L)
☐ Pancreatitis (not explained by other etiologies)
☐ Persistent respiratory colonization/infection with a typical CF pathogen(s) (e.g., Pseudomonas aeruginosa)
☐ Prenatal screening (CVS, amnio)
☐ Pulmonary mycobacterial infection
☐ Rectal prolapsed
☐ Repeat Normal Sweat Testing
☐ Steatorrhea/abnormal stools/malabsorption
☐ Transepithelial potential differences
☐ Other, specify: _____
☐ Unknown

Date & value of documented positive quantitative pilocarpine iontophoresis sweat test (Chloride)*

Date of Test: MM/DD/YY
Value (mmol/L): _____
Quantity Not Sufficient: ☐

If sweat test value <=60, CF diagnosis was suggested by:
☐ DNA Analysis/genotyping
☐ Transepithelial potential differences
☐ Clinical presentation (pancreatic fxn tests, Microbiology, etc.)
☐ Unknown

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

*repeated entries can be recorded
[ ] indicates values calculated by the registry

2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

Parents' Information

Please note that values of height and weight can be entered in any units, but will be saved in metrics!

Not available: ☐

Mother height: _____ ○ cm ○ inches

Father height: _____ ○ cm ○ inches

(Information not required for patients 21 years of age and older)

Birth Measurements

Baby delivered:

○ Full term (>= 37 weeks gestational age)

○ Premature (< 37 weeks gestational age)

○ Unknown

Specify gestational age(only if premature):_____

Birth length: _____ ○ cm ○ inches

Birth weight:_____ ○ kg ○ lb

Genotype Information

For a list of mutation options, please contact reghelp@cff.org

Has this patient been genotyped? ___ Yes ___ No

Date: (MM/DD/YYYY) Date is an approximation: ☐

Select Mutation 1: _____ Other genotype: _____

Poly T tract: ○ 5T ○ 7T ○ 9T ○ not 5T ○ Unknown

Poly TG repeats: ○ 9 ○ 10 ○11 ○12 ○13

○ Other/unknown/not done

Select Mutation 2: _____ Other genotype: _____

Poly T tract: ○ 5T ○ 7T ○ 9T ○ not 5T ○ Unknown

Poly TG repeats: ○ 9 ○ 10 ○11 ○12 ○13

○ Other/unknown/not done

Select Mutation 3: _____ Other genotype: _____

Additional information about genotype not captured above:_____

ENCOUNTER DATA

Vital Signs/Encounter Start

Encounter date: (MM/DD/YYYY)

Location: ○ Clinic ○ Hospital ○ Home IV ○ Other

Height : _____ ○ cm ○ inches

[Height Percentile _____]

Weight : _____ ○ kg ○ lb

[Weight Percentile _____]

[BMI value: _____]

[BMI Percentile: _____]

[Weight for Length percentile: _____]

Exacerbation Assessment

Were there crackles (rales) on physical exam at this visit?

○ Yes ○ No ○ Physical exam data not available

What was your assessment regarding pulmonary exacerbation at this visit?

○ Absent

○ Mild exacerbation

○ Moderate exacerbation

○ Severe exacerbation

○ Don't know/unable to answer

Was a follow up visit scheduled?

○ Yes ○ No ○ Unknown

If Yes, indicate when:*

○ In less than 2 weeks

○ 2-4 weeks

○ 5-6 weeks

○ 7 weeks or later

If you determined that an exacerbation was present, please select the treatment course prescribed to treat the exacerbation:

☐ Increased airway clearance, exercise, and/or bronchodilators

☐ Oral NON-quinolone antibiotic (e.g. azithromycin, Bactrim, Augmentin, etc.)

☐ Oral quinolone antibiotic (e.g. ciprofloxacin (Cipro), levofloxacin)

☐ Inhaled antibiotic

☐ Inhaled antibiotic PLUS Oral NON-quinolone antibiotic

☐ Inhaled antibiotic PLUS an oral quinolone antibiotic

☐ None of the above

If none of the above, the specify:_____

(Note: if you elected to treat with hospital or home IV antibiotics, please start a care episode and enter the requested data.)

Consultations with Care Team Members

☐ Patient consulted with a Social Worker at this visit

☐ Patient was seen by a Dietitian/Nutritionist at this visit

☐ Patient was seen by a Physical therapist at this visit

☐ Patient was seen by a Respiratory therapist at this visit

☐ Patient consulted with a Pharmacist at this visit

☐ Patient was seen by a Mental Health Coordinator at this visit

Other

Record any additional information about this encounter:

Custom field 1:_____

Custom field 2:_____

Custom field 3: _____

Microbiology

Bacterial Culture

Bacterial culture done? ☐

Date of Culture: (MM/DD/YYYY)

Type of Specimen:

○ sputum ○ induced sputum

○ throat/nasal ○ bronchoscopy

Culture Results:

○ Microorganisms ○ Normal flora

○ No growth/sterile culture

Staphylococcus aureus: ☐

○ MRSA (methicillin resistant Staph aureus)

Key:

FORM NAME

○ radio buttons (select one option only)

☐ check box (multiple selections allowed)

*repeated entries can be recorded

[ ] indicates values calculated by the registry

○ MSSA (methicillin sensitive Staph aureus)

Haemophilius influenzae (any species): ☐

Pseudomonas aeruginosa: ☐
☐ mucoid ☐ non mucoid ☐ mucoid status unknown

Susceptibility Testing *(Please use the most resistant PA strain. If multiple PA strains are resistant to the same number of classes of antibiotics then use the following schema: Beta lactams> Quinolones>Aminoglycosides).*

Resistant to All Aminoglycosides Tested (e.g., tobramycin, gentamicin, amikacin):
○ Yes ○ No ○Testing not done

Resistant to All Quinolones Tested (e.g., ciprofloxacin, levofloxacin, moxifloxacin):
○ Yes ○ No ○ Testing not done

Resistant to All Beta Lactams Tested (e.g., ceftazidime, imipenem, meropenem, piperacillin/tazobactam (Zosyn), ticarcillin/clavulanic acid (Timentin), aztreonam):
○Yes ○ No ○ Testing not done

Burkholderia species: ☐
☐ B. gladioli
☐ B. cenocepacia
☐ B. multivorans
☐ Burkholderia – other
☐ B. cepacia ☐ B. stabilis ☐ B. vietnamiensis
☐ B. dolosa ☐ B. anthina ☐ B. ambifaria
☐ B. pyrrocinia ☐ B. ubonensis ☐ B. arboris
☐ B. latens ☐ B. lata ☐ B. metallica
☐ B. seminalis ☐ B. contaminans
☐ B. diffusa ☐ B. pseudomallei

Was the identification of the Burkholderia species confirmed at the CFF reference lab? ○ Yes ○ No ○ Unknown

Other microorganisms:
☐ Alcaligenes (Achromobacter) xylosoxidans
☐ Stenotrophomonas (Xanthomonas)/Maltophilia
☐ Other types:
☐ Acinetobacter baumannii ☐ Acinetobacter species -other*
☐ Agrobacterium species ☐ Bordetella species
☐ Brevundimonas species ☐ Chryseobacterium species
☐ Cupriadidus metallidurans ☐ Cupriavidus pauculus
☐ Cupriavidus respiraculi ☐ Delftia acidivordans
☐ Delftia species - other* ☐ Enterobacter species
☐ Exophilia dermatitidis ☐ Herbaspirillum frisingense
☐ Herbaspirillum seropedicae ☐ Inquilinus limosus
☐ Klebsiella pneumoniae ☐ Klebsiella species - other*
☐ Ochrobacterum species ☐ Pandoraea apista
☐ Pandoraea norimbergensis ☐ Pandoraea pulmonicola
☐ Pandoraea sputorum ☐ Pandoraea species - other*
☐ Pseudomonas mendocina
☐ Pseudomonas pseudoalcaligenes
☐ Pseudomonas putida ☐ Pseudomonas stutzeri
☐ Pseudomonas species - other*
☐ Ralstonia insidiosa ☐ Ralstonia pickettii
☐ Ralstonia species - other* ☐ Serratia marcescens

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

☐ Streptococcus milleri

Fungal/Yeast:
☐ Aspergillus (any species) ☐ Candida (any species)
☐ Scedosporium species

Other bacterial or fungal species: ☐
Specify: _____

Mycobacterial culture
Was Mycobacterial culture done? ☐
Date of Culture: (MM/DD/YYYY)

Type of Specimen:
○ sputum ○ induced sputum ○ bronchoscopy

AFB Smear:
○ Positive ○ Negative ○ Not done

Culture Results:
○ Microorganisms
○ Normal flora
○ No growth/sterile culture

Mycobacterial Species:
☐ Mycobacterial tuberculosis
☐ Mycobacterium abscessus/chelonae
☐ Mycobacterium avium complex (MAC)
☐ Mycobacterium fortuitum group
☐ Mycobacterium gordonae
☐ Mycobacterium kansasii
☐ Mycobacterium marinum
☐ Mycobacterium terrae
☐ Other
Specify: _____

Please note: The option Mycobacterium avium complex (MAC) includes M. avium subsp. Avium, M. avium subsp. Hominissuis, M. avium subsp paratuberculosis, and M. intracellulare.

Medications

Not on Medications
This patient is not on any of the pulmonary medications below: ☐

Pulmonary Medications
Antibiotics – inhaled and/or oral
Tobramycin Based Medications
Tobramycin solution for inhalation (i.e. TOBI): ☐
Frequency: ○ 300 mg BID alternate month schedule
○ 300 mg BID continuous
○ Other regimen (different dose or freq)
○ Eradication
○ PRN/As needed
Tobi Podhaler (Tobramycin Inhalation Powder): ☐
Frequency: ○ Four 28mg capsules BID alternate month
○ Other regimen (different dose or freq)
○ Eradication
○ PRN/As needed
Bethkis: ☐

*repeated entries can be recorded
[ ] indicates values calculated by the registry

2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

Frequency: ○ 300 mg BID alternate month
○ Other regimen (different dose or freq)
○ Eradication
○ PRN/As needed

Other inhaled aminoglycoside (e.g. gentamcin, amikacin, or tobramycin preparation): ☐
Frequency: ○ Alternate Month
○ Continuous
○ Other regimen (different dose or freq)
○ Eradication
○ PRN/As needed

Colistin: ☐
Frequency: ○ Alternate Month
○ Continuous
○ Other regimen (different dose or freq)
○ Eradication
○ PRN/As needed

Aztreonam – Inhaled: ☐
Frequency: ○ 75 mg TID Alternate Month Schedule
○ 75 mg TID Continuous
○ Other Regimen
○ Eradication
○ PRN/As needed

Other inhaled antibiotics: ☐
Comments:_____

Oral macrolide antibiotic: ☐
☐ azithromycin (Zithromax)
☐ clarithromycin (Biaxin)

Other oral antibiotic: ☐
☐ Quinolone (Cipro, Levaquin, gatifloxacin, etc.)
☐ Cephalosporin (cephalexin, Keflex, cefixime, etc.)
☐ Sulfa (Bactrim, Septra, etc.)
☐ Amoxicillin (Augmentin, etc.)
☐ Tetracycline (doxycycline, Vibramycin, minocycline, etc.)
☐ Other

CFTR Modulators
Ivacaftor Monotherapy (i.e. Kalydeco): ☐
Frequency: ○ 50 mg BID
○ 75 mg BID
○ 150mg BID
○ Other Regimen (different dose or freq)
Ivacaftor/Lumacaftor Combination Therapy (i.e. Orkambi): ☐
Frequency: ○ Full dose BID
○ Half dose BID
○ Other Regimen (different dose or freq)
Tezacaftor/Ivacaftor Combination Therapy): ☐
Frequency: ○ Full dose BID
○ Half dose BID
○ Other Regimen (different dose or freq)
Elexacaftor/Tezacaftor/Ivacaftor Triple Combination Therapy: ☐
Frequency: ○ Full dose BID
○ Half dose BID
○ Other Regimen (different dose or freq)

Other Medications
Dornase alfa (i.e. Pulmozyme): ☐
Frequency: ○ 2.5 mg QD
○ 2.5 mg BID
○ Other regimen (different dose or frequency)
○ PRN/As needed

Bronchitol (Mannitol): ☐
Frequency: ○ 400 mg BID
○ Other regimen (different dose or frequency)

Acetylcysteine or Mucomist: ☐
High-dose ibuprofen (e.g. 25-30 mg/kg): ☐
Total (mg/dose): _____
Hypertonic saline: ☐
Concentration (%):○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10
Frequency: ○ QD ○ BID ○ Other ○ PRN/As needed

Bronchodilators (oral):
☐ Beta agonist (e.g. Proventil Repetabs, Volmax, etc.)
☐ Theophylline product (e.g. Theodur, Slo-bid, Uniphyl)

Bronchodilators (inhaled)
☐ Short acting beta agonist (e.g. albuterol, Proventil, Ventolin, Xopenex, etc.)
☐ Long acting beta agonist (e.g. salmeterol, Serevent, Foradil, Brovana, etc.)
☐ Short acting anticholinergic (e.g. ipratroprium, Atrovent)
☐ Long acting anticholinergic (e.g. tiotroprium, Spiriva, etc.)
☐ Combination beta agonist and anticholinergic (e.g. Combivent, DuoNeb, etc.)

Corticosteriods:
☐ Oral (e.g. Prednisone, Methylprednisolone [Medrol], Dexamethasone, other)
Total (mg/dose):_____
Frequency: ○ Short Term (Less Than Two Weeks)
○ Chronic, Low Dose
○ Chronic, High Dose
○ Other
☐ Inhaled (e.g. fluticasone, Flovent, budesonide, Pulmicort, etc.)
☐ Inhaled in combination with a bronchodilator (e.g. Advair, Symbicort)

Other:
☐ Leukotriene modifiers (e.g. montelukast, Singulair, zafirlukast, Accolate, zileuton, Zyflo, etc.)
☐ Mast cell stabilizers (e.g. cromolyn, Intal, nedocromil, Tilade, etc.)
☐ Antifungals (e.g. itraconazole, Sporanox) Note: exclude topical agents for skin conditions and agents used for oral thrush)

Drug Intolerance/Allergies:
☐ Dornase alfa (i.e. Pulmozyme)
☐ TOBI or other aminoglycoside

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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☐ Aztreonam
☐ Colistin
☐ Macrolide antibiotics
☐ High-dose ibuprofen
☐ Hypertonic saline
☐ Ivacaftor (i.e. Kalydeco)
☐ Ivacaftor Lumacaftor (i.e. Orkambi)
☐ Tezacaftor/Ivacaftor (i.e. Symdeko)
☐ Elexacaftor/Tezacaftor/Ivacaftor (i.e. Trikafta)

GI/Nutrition/Endrocrine Medications

This Patient is on enzyme medications: ○ Yes ○ No

For all enzymes, "capsules per largest meal" options are:
○ .5 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 ○ 10+
"Total capsules per day" is a numeric free text field.

Enzymes

Creon

Creon 1203: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Creon 1206: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Creon 1212: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Creon 1224: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Creon 1236: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Pancreaze

Pancreaze MT4: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Pancreaze MT10: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Pancreaze MT16: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Pancreaze MT20: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____

Ultresa

Ultresa 14: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Ultresa 20: ☐
Number of capsules per largest meal of the day:____
Total capsules per day:____
Ultresa 23: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Pertzye (Pancrecarb)

Pertzye 4000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Pertzye 8000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Pertzye 16000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Pertzye 24000: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Zenpep

Zenpep 3: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Zenpep 5: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Zenpep 10: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Zenpep 15: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Zenpep 20: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Zenpep 25: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Zenpep 40: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

Viokace

Viokace 10: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Viokace 20: ☐
Number of capsules per largest meal of the day:____
Total capsules per day: ____

Other Enzymes

Please specify if other enzymes: _____

Acid Blocker

Acid Blocker (Daily use. Check all that apply since last visit):
☐ H2 Blocker (e.g. Zantac, Pepcid, etc.)
☐ Proton Pump Inhibitor (e.g. Prilosec, Nexium, etc.)
☐ Unknown

Key:

FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

GI other
Ursodeoxycholic acid: ☐

Pulmonary

Pulmonary Function Tests (PFTs)
Unable to Perform test: ☐
Reason why PFTs have not been done: _____
Was pulmonary function testing done in a hospital/clinic setting with hospital equipment?
○ Yes ○ No ○Unknown

FVC measure (L): _____
[Predicted value:_____]
[Reference equation:_____]
[% Predicted:_____]
[Relative change since previous measurement:_____]
[Days since last measured:____]
FEV1 measure (L): _____
[Predicted value:_____]
[Reference equation:_____]
[% Predicted:_____]
[Relative change since previous measurement:_____]
[Days since last measured:____]
FEF25-75 measure (L/sec): _____
[Predicted value:_____]
[Reference equation:_____]
[% Predicted:_____]
[CF Specific FEV 1 percentile (ages 6-21):]

GI/Nutrition

Assessment of oral intake: ○ Done ○ Not done
Is patient currently receiving supplemental feeding?
○ Yes ○ No ○Unknown
Feeding:
☐ oral supplementation (Scandishakes, Pediasure, Instant Breakfast, etc.)
☐ nasogastric tube (NG)
☐ gastrostomy tube/button (G-Tube)
☐ jejunal tube (J-tube)
☐ total parenteral nutrition (TPN)

If using a tube (NG, G-tube or J-tube), was the patient recommended to use pancreatic enzymes with supplemental feedings?
☐ No enzymes recommended with tube feeding
☐ Yes enzymes mixed into the formula
☐ Yes, enzymes administered directly through the tube (i.e. not into the formula)
☐ Yes, enzymes taken by mouth prior to, during and/or after the feeding
☐ Yes, formula infused through Relizorb (enzyme cartridge)
☐ Other

CF specific vitamins (i.e. with additional vitamins A, D, E, and K): ○ Yes ○ No

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

Infants under 2 years of age
Salt supplementation: ○ Yes ○ No

Select type of feeding:
○ Breast milk ○ Breast milk plus formula
○ Formula exclusively ○ Other food
○ Unknown

If receiving any formula feeding, select type of formula and caloric density:
○ Cow's milk ○ Soy milk
○ Predigested ○ Other

Caloric Density:
○ 20 cal/oz ○ 22 cal/oz
○ 24 cal/oz ○ 27 cal/oz
○ 30 cal/oz ○ Other, specify:_____

Complications

Patient does not have any complications: ☐

Diabetes Status
○ Impaired Glucose Tolerance (FBG < 126, 2-h PG 140-199)
○ CFRD with or without fasting hyperglycemia
○ Type 1 Diabetes
○ Type 2 Diabetes
CFRD secondary complications:
☐ Retinopathy
☐ Microalbuminuria
☐ Chronic renal insufficiency
☐ Chronic renal failure requiring dialysis
☐ Peripheral neuropathy

Hepatobiliary
☐ Gall stones
☐ Gall stones, requiring surgery/procedure
☐ Liver disease, cirrhosis
Please specify complications related to cirrhosis:
☐ Esophageal varices
☐ Gastric varices
☐ GI bleed related to varices
☐ Splenomegaly
☐ Hypersplenism (i.e., WBC <3.0 or platelets <100,000)
☐ Ascites
☐ Encephalopathy
☐ Liver disease, non- cirrhosis
☐ Acute Liver Failure (No underlying liver disease, ALT>3X ULN, INR>2, not responsive to vitamin K)
☐ Hepatic Steatosis
☐ Liver disease, other: _____

Acute Hepatitis (ALT > 5X ULN and duration of illness < 6 months) ☐
☐ Infectious (Hepatitis A,B,C,EBV,CMV or other known infectious cause)
☐ Non-infectious (Autoimmune, Drug Induced, Alcohol or other known cause)
☐ Unknown

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

Bone/Joints
☐ Arthritis/Arthropathy
☐ Bone fracture
☐ Osteopenia
☐ Osteoporosis

Pulmonary
☐ Allergic Bronchial Pulmonary Aspergillosis (ABPA)
☐ Asthma
☐ Hemoptysis
Please specify selection of hemoptysis:
☐ Hemoptysis, massive
☐ Hemoptysis, other
☐ Pneumothorax requiring chest tube

GI
☐ Chronic constipation
☐ Distal intestinal obstruction syndrome (DIOS, Meconium ileus equiv.)
☐ Fibrosing colonopathy/colonic stricture (report incidence only)
☐ GERD (Gastro-Esophageal Reflux Disease)
☐ GI Bleed req hosp non variceal
☐ History of intestinal or colon surgery
☐ Pancreatitis
☐ Peptic ulcer disease
☐ Rectal prolapse
☐ C. diff. colitis

Other Complications
☐ Absence of Vas Deferens
☐ Anxiety Disorder
☐ Cancer confirmed by histology
☐ Depression
☐ Hearing loss
☐ Hypertension
☐ Kidney Stones
☐ Nasal polyps
☐ Renal failure requiring dialysis (cause other than CFRD)
☐ Sinus Disease (symptomatic)
☐ Urinary incontinence

Complications not listed above
Enter additional complications: _____

Lab

Blood counts
WBC count x1,000/microL(typical clinical value: 3.0 to 30.0): _____
Platelet Count x1,000/microL(typical clinical value: 100 to 500):_____
Hemoglobin (grams per deciliter):_____

Serum Creatinine
Serum Creatinine Level (mg/dL): _____

Liver Function Tests (LFTs)
Alanine Aminotransferase (ALT or SGPT), IU/L: _____
GGTP (gamma glutamyl transpeptidase), IU/L: _____
Aspartate Aminotransferase (AST), IU/L: _____
Alkaline phosphatase (ALP), IU/L: _____
Total Bilirubin, mg/dL: _____
Albumin, g/dL: _____

Glucose Test
Random blood glucose (mg/dL):_____
Fasting blood glucose (mg/dL):_____

If OGTT performed:
OGTT Fasting glucose level (mg/dL):_____
1 hour (mg/dL)(not required):_____
2 hour (mg/dL):_____

Hemoglobin A1C (Hgb A1C)
Hgb A1C value, %:_____

Fecal Elastase
Fecal Elastase Value (microg/g of stool):_____

Act/Exercise

Primary Airway Clearance Technique (ACT)
○ Positive Expiratory Pressure (PEP)
○ Postural drainage with clapping (CPT)
○ Forced expiratory techniques (e.g. autogenic drainage, huff cough, active cycle breathing)
○ Oscillating PEP (e.g. Flutter, acapella, IPV)
○ High frequency chest wall oscillation (e.g. Vest)
○ Exercise
○ None
○ Other
Specify if other technique:_____
☐ Please check if patient is using this technique PRN or As needed

Secondary Airway Clearance Technique (ACT)
☐ Positive Expiratory Pressure (PEP)
☐ Postural drainage with clapping (CPT)
☐ Forced expiratory techniques (e.g. autogenic drainage, huff cough, active cycle breathing)
☐ Oscillating PEP (e.g. Flutter, acapella, IPV)
☐ High frequency chest wall oscillation (e.g. Vest)
☐ Exercise
☐ PRN/As Needed

CARE EPISODE

Care Episode Segment*

Start date: (MM/DD/YYYY)
End date: (MM/DD/YYYY)
Location: ○ Hospital ○ Home IV
Reasons:
☐ Pulmonary Exacerbation
☐ Pulmonary Complication Other than exacerbation
☐ GI Complications
☐ Transplant related
☐ Sinus infection

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

☐ Non-transplant surgery
☐ NTM Pulmonary Infection
☐ Other
Please specify reason: _____

Care Episode Measurements

At the beginning of Care Episode:
FVC (L):_____
FEV1 (L):_____
FEF25-75 (L):_____
Height: _____ ○ cm ○ inches
Weight: _____ ○ kg ○ lb
Please note that values of height and weight can be entered in any units, but will be saved in metrics!
Date recorded: (MM/DD/YYYY)
Check if data were impossible to measure: ☐

At the end of Care Episode:
FVC (L):_____
FEV1 (L):_____
FEF25-75 (L):_____
Height: _____ ○ cm ○ inches
Weight: _____ ○ kg ○ lb
Please note that values of height and weight can be entered in any units, but will be saved in metrics!
Date recorded: (MM/DD/YYYY)
Check if data were impossible to measure: ☐

Comments:_____

ANNUAL REVIEW

Annual Review Year: (YYYY)

Patient Statistics
Number of Encounters recorded by Center: [ ]
Number of Encounters recorded by other Care Centers: [ ]
[Number of Care Episodes recorded by Care Center: [ ]
Number of Care Episodes recorded by Other Care Centers: [ ]

Demographics Update
Current Zip: _____
Patient is: [alive or dead]

Pulmonary
Did this patient use oxygen therapy during the reporting year?
○ Yes, Continuously
○ Yes, Nocturnal and/or with exertion
○ Yes, During exacerbation
○ Yes, prn
○ No
○ Unknown

Did this patient use non-invasive ventilation during the reporting year (i.e., assisted breathing, BiPap, CPAP, etc)
○ Yes ○ No ○ Unknown

Was a Chest X Ray performed during the reporting year?
○ Yes ○ No ○ Unknown

Did the patient receive an influenza vaccination this season (Sept through Jan)?
○ Yes ○ No ○ Allergic/Refused ○ Unknown

Covid-19 Vaccination
Did the patient receive a Covid-19 vaccination this year?
○ Yes (Please complete Covid-19 Vaccination form)
○ No
○ Unknown
Specify why vaccination wasn't done:
○ Ineligible by Age
○ Allergic
○ Patient refused vaccination
○ Other
Specify other reasons why vaccination wasn't done: _____

Mycobacterial Culture
[According to the encounters a Mycobacterial culture has been performed during this reporting year: ○ Yes ○ No]
Please check to confirm the above is correct: ☐
Was treatment INITIATED for a pulmonary mycobacterial infection during this reporting year?
○ Yes ○ No ○ Unknown

Was an IgE screening for ABPA performed in this reporting year? ○ Yes ○ No ○ Unknown

Did this patient smoke cigarettes during the reporting year?
○ No
○ Occasionally
○ Yes, Regularly, less than 1 ppd
○ Yes, Regularly, 1 ppd or more
○ Declined to answer
○ Not Known
○ Not Applicable

Does anyone in the patient's household smoke cigarettes?
○ Yes ○ No ○ Unknown

During the reporting year, how often was this patient exposed to secondhand smoke?
○ Daily
○ Several Times Per Week
○ Several Times Per Month or less
○ Never
○ Declined to answer
○ Not Known

CFTR Modulators
Was Elexacaftor/Tezacaftor/Ivacaftor Triple Combination Therapy initiated during the reporting year?
○ Yes ○ No ○ Unknown
Approximate date patient started taking this drug: (MM/DD/YYYY)

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

Liver

[According to the encounters data liver function tests were done in this reporting year ○ Yes ○ No]

Please check to confirm that information about liver function tests above is correct. If it is incorrect, please return to the encounter forms and enter correct information into the lab section of the encounter form: ☐

Eye

Was any eye exam performed to check for cataracts in this reporting year?

○ Yes ○ No ○ Unknown

Growth and Nutrition

Fat soluble vitamin levels measured?

○ Yes ○ No ○ Unknown

Has this patient been on growth hormone in the reporting year? ○ Yes ○ No ○ Unknown

Was a DEXA scan for bone density performed in the reporting year? Please enter findings of osteoporosis or osteopenia into the complications section of last patient encounter. ○ Yes ○ No ○ Unknown

Results of DEXA Scan:

○ Normal ○ Osteopenia
○ Osteoporosis ○ Other
○ Unknown

Diabetes Status

Status from recent encounter [does or does not] indicate CFRD.

○ Normal Glucose Metabolism (includes normal, random, fasting, or OGTT)
○ Impaired Glucose Tolerance (FBG < 126, 2-h PG 140-199)
○ CFRD with or without fasting hyperglycemia (2-h PG >= 200)
○ Type 1 Diabetes
○ Type 2 Diabetes

Was a retinal eye exam performed by an opthalmologist in this reporting year? ○ Yes ○ No ○ Unknown

Was a spot urine sent for albumin/creatinine ratio in this reporting year? ○ Yes ○ No ○ Unknown

If positive findings, please update CFRD secondary complications in the most recent encounter of the patient.

Was the patient prescribed treatment for CFRD?

○ Yes ○ No

Select all that apply:

☐ Dietary change
☐ Oral hypoglycemic agents
☐ Intermittent insulin (with illness, steroids, etc.)
☐ Chronic insulin
☐ Other diabetes drugs

Specify other diabetes drugs:_____

Key:

FORM NAME

○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

Did the patient experience any episodes of severe hypoglycemia (became unconscious or required help to resolve) during the reporting year?

○ Yes ○ No ○ Unknown

Sinus Surgery (SS)

Has the patient had sinus surgery in the reporting year?

○ Yes ○ No ○ Unknown

Is this the first sinus surgery?

○ Yes ○ No ○ Unknown

Transplantation

What is the transplantation status of the patient currently? If the patient had transplantation in previous years please select or keep "Had transplantation" option.

○ Not pertinent
○ Accepted, on waiting list
○ Evaluated, final decision pending
○ Evaluated, rejected
○ Had transplantation

Transplant

☐ Lung: Bilateral
Number this year:__ Date of last transplant: (MM/DD/YYYY)
☐ Heart/lung
Number this year:__ Date of last transplant: (MM/DD/YYYY)
☐ Lung: Lobar/Cadaveric
Number this year:__ Date of last transplant: (MM/DD/YYYY)
☐ Lung: Lobar/living donor
Number this year:__ Date of last transplant: (MM/DD/YYYY)
☐ Liver
Number this year:__ Date of last transplant: (MM/DD/YYYY)
☐ Kidney
Number this year:__ Date of last transplant: (MM/DD/YYYY)
☐ Other
Number this year:__ Date of last transplant: (MM/DD/YYYY)
Specify transplant type: _____

Were there post transplant complications? ☐

Select those that apply:

☐ Bronchiolitis obliterans syndrome
☐ Lympho-proliferative disorder
☐ Other
Specify other complication: _____

Colorectal Cancer Screening/Surveillance

Did the patient undergo a colonoscopy (screening or surveillance during the reporting year?

○ Yes ○ No ○ Unknown

What were the results of the colonoscopy?

○ Normal
○ Colorectal Cancer
○ Adenomatous polyps
○ Indeterminate results (e.g. inadequate preparation)

Clinical Trials

Has this patient participated in any interventional (drug) studies?

○ Yes ○ No ○ Unknown

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

Has this patient participated in any observational studies?
○ Yes ○ No ○ Unknown

Health Insurance Coverage

It is important for us to have accurate numbers of patients who have specific types of coverage:

☐ Health Insurance Policy (e.g. Private Insurance)
☐ Medicare
☐ Medicaid
☐ State special needs program, e.g., BCMH, CCS, CRS, GHPP, etc.
☐ TriCare or other military health plan
☐ Indian Health Service
☐ Other
Specify if other insurance:_____

Patient has no health insurance: ☐

Was patient covered under parent's health insurance plan?
○ Yes ○ No ○ Unknown

Did patient receive free medicine or co-pay/deductible assistance from a Patient Assistance Program?
○ Yes ○ No ○ Unknown

Socio-economic Status

Education of Patient:
○ Less than High School
○ High School diploma or equivalent
○ Some College
○ College Graduate
○ Masters/Doctoral level degree
○ Unknown/Not applicable

Education of father of patient:
○ Less than High School
○ High School diploma or equivalent
○ Some College
○ College Graduate
○ Masters/Doctoral level degree
○ Unknown/Not applicable

Education of mother of patient:
○ Less than High School
○ High School diploma or equivalent
○ Some College
○ College Graduate
○ Masters/Doctoral level degree
○ Unknown/Not applicable

Education of spouse of patient:
○ Less than High School
○ High School diploma or equivalent
○ Some College
○ College Graduate
○ Masters/Doctoral level degree
○ Unknown/Not applicable

What was the total combined income of the household before taxes where the patient resided for the majority of the reporting year?
○ <$10,000 ○ $10,000 to $19,999
○ $20,000 to $29,999 ○ $30,000 to $39,999
○ $40,000 to $49,999 ○ $50,000 to $59,999
○ $60,000 to $69,999 ○ $70,000 to $79,999
○ $80,000 to $89,999 ○ >$90,000
○ Unknown or Prefer not to Answer

How many people currently live in the patient's household (including the patient)?
○ 1 ○ 2 ○ 3 ○ 4
○ 5 ○ 6 ○ 7 ○ 8
○ 9 ○ 10 ○ 11 ○ 12 or more
○ Unknown

Mental Health

Was the patient screened for symptoms of classic depression using Patient Health Questionnaire (PHQ-9) or other valid depression screening tools?
○ Yes ○ No ○ Unknown

Was the patient screened for the anxiety disorder using Generalized Anxiety Disorder Tool (GAD-7 or similar)?
○ Yes ○ No ○ Unknown

Age 18 and Older

Marital Status:
○ Single (never married)
○ Living Together
○ Married
○ Separated
○ Divorced
○ Widowed
○ Unknown

Employment:
☐ Part Time
☐ Full time homemaker
☐ Full time employment
☐ Unemployed
☐ Student
☐ Disabled
☐ Retired
☐ Unknown

Pregnancy

Was patient pregnant during the reporting year?
○ Yes ○ No ○ Unknown

Date of menstrual period BEFORE pregnancy (if known): (MM/DD/YYYY)

If Yes, indicate outcome: ○ Live Birth
○ Still Birth
○ Spontaneous Abortion
○ Therapeutic Abortion
○ Undelivered
○ Unknown

Date of outcome (if known): (MM/DD/YYYY)

Age 2 and Younger

Did the patient attend day care during this reporting year?
○ Yes ○ No ○ Unknown

Did the family receive genetic counseling this reporting year?
○ Yes ○ No ○ Unknown

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

Was the patient given palivizumab (Synagis) this season (Sept through January)?
○ Yes ○ No ○ Unknown

Other
Please use this field to record any additional information about this patient: _____

ALD INITIATION

Date patient flagged for ALD: (MM/DD/YYYY)
Select all reasons for flagging ALD:
☐ FEV1pp<40% when stable
☐ Referred for lung transplantation evaluation
☐ Respiratory failure (requiring ICU admission)
☐ Hypercarbia
☐ Daytime supplemental oxygen at rest
☐ Pulmonary Hypertension
☐ Six-minute walk distance <400m
☐ Rapid rate of FEV1 decline
☐ Supplemental oxygen requirement with exercise or sleep
☐ Pneumothorax (recurrent and/or persistent)
☐ Massive Hemoptysis (>240 ml)
☐ Other
Specify other reasons for including patient: _____

ALD ANNUAL

Interventions

Review Year:

Thoracic Procedure(s)
Did patient have a thoracic procedure during the reporting year?
○ Yes ○ No ○ Unknown

Thoracic procedure type(s):
☐ Lung resection
☐ Thoracotomy
☐ Video thoracotomy
☐ Tube thoracotomy
☐ Pleurodesis

Pleurodesis side:
○ Unilateral ○ Bilateral ○ Unknown

Other Interventions
Was patient enrolled in pulmonary rehabilitation during the reporting year?
○ Yes ○ No ○ Unknown
Was the patient seen by a palliative care specialist during the reporting year?
○ Yes ○ No ○ Unknown

Specify type(s) of palliative care services:
☐ Documented advance care planning conversation
☐ Documentation of an advance directive
☐ Referral to palliative care specialist
☐ Referral to hospice
☐ Referral to outpatient/community palliative care

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

Embolization For Hemoptysis
Embolization Date (if performed): (MM/DD/YYYY)

ICU Admissions
Was patient admitted to ICU this year?
○ Yes ○ No ○ Unknown
Date of admission to ICU: (MM/DD/YYYY)
Date of discharge from ICU: (MM/DD/YYYY)
Primary reason for admission:
○ Post-surgical procedure with observation
○ Respiratory failure
○ Hemoptysis
○ Pneumothorax
○ Shock
○ Densensitization for antibiotics
○ Other
○ Unknown

Intubation
Was patient intubated?
○ Yes ○ No ○ Unknown
Date of intubation: (MM/DD/YYYY)
Date of extubation: (MM/DD/YYYY)
Was a tracheostomy performed?
○ Yes ○ No ○ Unknown

ECMO/Novalung
Was patient placed on ECMO/Novalung?
○ Yes ○ No ○ Unknown
Date ECMO/Novalung started: (MM/DD/YYYY)
Date ECMO/Novalung ended: (MM/DD/YYYY)
Cannulation strategy used:
○ VV-Single Cannula
○ Code 2VV-Double Cannula
○ Veno-Arterial
○ Veno-Arterial-Venous
○ Unknown
Was ECMO/Novalung used in combination with ventilator?
○ Yes ○ No ○ Unknown

Labs/Tests

Echocardiogram
Was ECHO performed during the reporting year?
○ Yes ○ No ○ Unknown
Date of last echocardiogram: (MM/DD/YYYY)
Could PA pressure be estimated?
○ Yes ○ No ○ Unknown
Estimated RVSP or PASP, mmHg: _____
Tricuspid annular plane systolic excursion, mm: _____

Right Heart Catheterization (RHC)
Was Right Heart Catheterization (RHC) done during the reporting year?
○ Yes ○ No ○ Unknown
Date of last RHC: (MM/DD/YYYY)

*repeated entries can be recorded
[ ] indicates values calculated by the registry

Mean PA pressure from RHC, mmHg: _____
Systemic systolic pressure, mmHg: _____
Systemic diastolic pressure, mmHg: _____
Heart Rate: _____
PA systolic pressure, mmH: _____
PA diastolic pressure, mmHg: _____
Pulmonary capillary wedge pressure (PCW), mmHg: _____
Cardiac Index (L/min/m2): _____

Six Minute Walk
Date of six-minute walk test: (MM/DD/YYYY)
Six minute walk distance, m: _____
Was supplemental oxygen titrated?
○ Yes ○ No ○ Unknown

Blood Gas Analysis
Date of blood gas analysis: (MM/DD/YYYY)
Blood source:
○ Venous ○ Arterial
Type of blood gas analysis:
○ Stable blood gas
○ Worst blood gas in a year
○ Last blood gas prior to discharge
Blood pH: _____
PaO2, mm Hg: _____
PaCO2, mm Hg: _____

Transplant Consideration and Referral

Transplant Consideration
Was transplant discussed with patient at the care program?
○ Yes ○ No ○ Unknown

Transplant Referral And Evaluation
Was patient referred to a transplant program?
○ Yes ○ No ○ Unknown
If patient was not referred for transplant, select reasons:
☐ Patient stable
☐ Patient declined to pursue
☐ Substance misuse (alcohol, marijuana, illicit drugs etc.)
☐ Chronic opioid use
☐ Smoking tobacco
☐ Inadequate medical insurance
☐ Limited social support
☐ Adherence issues
☐ Poor nutritional status
☐ Microbiological reasons
☐ Mental health
☐ Uncontrolled diabetes
☐ Physical inactivity/deconditioning
☐ Other
Specify other reasons for not referring: _____
Date patient referred for transplant: (MM/DD/YYYY)
State of primary referral program:
Primary referral program:
○ AL
  ○ University of Alabama Hospital
○ AZ
  ○ Banner University Medical Center – Tucson
  ○ Mayo Clinic Hospital
  ○ St Joseph's Hospital and Medical Center
○ CA
  ○ Cedars-Sinai Medical Center
  ○ Childrens Hospital Los Angeles
  ○ Keck Hospital of USC
  ○ Lucile Salter Packard Children's Hospital at Stanford
  ○ Stanford Health Care
  ○ University of California San Diego Medical Center
  ○ University of California San Francisco Medical Center
  ○ University of California at Los Angeles Medical Center
○ CO
  ○ University of Colorado Hospital/Health Science Center
○ FL
  ○ Florida Hospital Medical Center
  ○ Jackson Memorial Hospital University of Miami School of Medicine
  ○ Mayo Clinic Florida
  ○ Tampa General Hospital
  ○ UF Health Shands Hospital
○ GA
  ○ Emory University Hospital
○ IA
  ○ University of Iowa Hospitals and Clinics Transplant Programs
○ IL
  ○ Advocate Christ Medical Center
  ○ Loyola University Medical Center
  ○ Northwestern Memorial Hospital
  ○ University of Chicago Medical Center
○ IN
  ○ Indiana University Health
○ KY
  ○ Jewish Hospital
  ○ University of Kentucky Medical Center
○ LA
  ○ Ochsner Foundation Hospital
○ MA
  ○ Boston Children's Hospital
  ○ Brigham and Women's Hospital
  ○ Massachusetts General Hospital
○ MD
  ○ Johns Hopkins Hospital
  ○ University of Maryland Medical System
○ MI
  ○ Henry Ford Hospital
  ○ Spectrum Health
  ○ University of Michigan Medical Center
○ MN
  ○ Saint Marys Hospital (Mayo Clinic)
  ○ University of Minnesota Medical Center, Fairview
○ MO
  ○ Barnes-Jewish Hospital
  ○ St Louis Children's Hospital at Washington University Medical Center
○ NC
  ○ Duke University Hospital
  ○ University of North Carolina Hospitals
○ NE
  ○ The Nebraska Medical Center

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

○ NJ
- ○ Newark Beth Israel Medical Center

○ NY
- ○ Mount Sinai Medical Center
- ○ NY Presbyterian Hospital/Columbia Univ Medical Center

○ OH
- ○ Children's Hospital Medical Center
- ○ Nationwide Children's Hospital
- ○ Ohio State University Medical Center
- ○ The Cleveland Clinic Foundation
- ○ University Hospitals of Cleveland

○ OK
- ○ Integris Baptist Medical Center

○ PA
- ○ Allegheny General Hospital
- ○ Children's Hospital of Pennsylvania
- ○ Children's Hospital of Pittsburgh of UPMC
- ○ Hospital of the University of Pennsylvania
- ○ Temple University Hospital
- ○ University of Pittsburgh Medical Center

○ SC
- ○ Medical University of South Carolina

○ TN
- ○ Baptist Memorial Hospital
- ○ Vanderbilt University Medical Center and Nashville VA Medical Center

○ TX
- ○ Baylor University Medical Center
- ○ CHI St. Luke's Health Baylor College of Medicine Medical Center
- ○ Houston Methodist Hospital
- ○ Memorial Hermann Hospital, University of Texas at Houston
- ○ Scott and White Memorial Hospital
- ○ Texas Children's Hospital
- ○ UT Southwestern Medical Center/William P Clements Jr University Hospital
- ○ University Hospital, University of Texas Health Science Center
- ○ University of Texas Medical Branch at Galveston

○ UT
- ○ University of Utah Medical Center

○ VA
- ○ Inova Fairfax Hospital
- ○ University of Virginia Health Sciences Center

○ WA
- ○ University of Washington Medical Center

○ WI
- ○ Aurora St. Luke's Medical Center
- ○ Froedtert Memoria Lutheran Hospital
- ○ University of Wisconsin Hospital and Clinics

Was patient evaluated for transplant at primary referral program?
○ Yes ○ No ○ Unknown

If patient evaluated for transplant at primary referral program, specify outcome:
○ Listed
○ Delisted
○ Denied
○ Pt declined to pursue
○ Unknown

Date listed for transplant: (MM/DD/YYYY)

Key:

FORM NAME

○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

Was the patient removed from the transplant waitlist in the reporting year?
○ Yes ○ No ○ Unknown

Select all reasons for delisting:
☐ Condition improved
☐ Patient declined transplant
☐ Too sick to transplant
☐ Died
☐ Other

Other reasons for delisting: _____

If transplant deferred, specify reason:
☐ Patient stable
☐ Additional testing necessary
☐ Poor nutritional status
☐ Limited social support
☐ Financial hardship
☐ Substance misuse
☐ Other

Other reason(s) for transplant deferral:_____

If patient was denied for transplant, specify reason:
☐ Too sick
☐ Microbiological reasons
☐ Limited social support
☐ Substance misuse
☐ Malignancy
☐ Poor nutritional status
☐ Renal disease
☐ Liver disease
☐ Financial hardship
☐ Other, specify

Other reasons patient denied for transplant: _____

Was pt referred to another program for second opinion?
○ Yes ○ No ○ Unknown

State of second referral program:

Second referral program:

○ AL
- ○ University of Alabama Hospital

○ AZ
- ○ Banner University Medical Center – Tucson
- ○ Mayo Clinic Hospital
- ○ St Joseph's Hospital and Medical Center

○ CA
- ○ Cedars-Sinai Medical Center
- ○ Childrens Hospital Los Angeles
- ○ Keck Hospital of USC
- ○ Lucile Salter Packard Children's Hospital at Stanford
- ○ Stanford Health Care
- ○ University of California San Diego Medical Center
- ○ University of California San Francisco Medical Center
- ○ University of California at Los Angeles Medical Center

○ CO
- ○ University of Colorado Hospital/Health Science Center

○ FL

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○ Florida Hospital Medical Center
○ Jackson Memorial Hospital University of Miami School of Medicine
○ Mayo Clinic Florida
○ Tampa General Hospital
○ UF Health Shands Hospital

○ GA
○ Emory University Hospital

○ IA
○ University of Iowa Hospitals and Clinics Transplant Programs

○ IL
○ Advocate Christ Medical Center
○ Loyola University Medical Center
○ Northwestern Memorial Hospital
○ University of Chicago Medical Center

○ IN
○ Indiana University Health

○ KY
○ Jewish Hospital
○ University of Kentucky Medical Center

○ LA
○ Ochsner Foundation Hospital

○ MA
○ Boston Children's Hospital
○ Brigham and Women's Hospital
○ Massachusetts General Hospital

○ MD
○ Johns Hopkins Hospital
○ University of Maryland Medical System

○ MI
○ Henry Ford Hospital
○ Spectrum Health
○ University of Michigan Medical Center

○ MN
○ Saint Marys Hospital (Mayo Clinic)
○ University of Minnesota Medical Center, Fairview

○ MO
○ Barnes-Jewish Hospital
○ St Louis Children's Hospital at Washington University Medical Center

○ NC
○ Duke University Hospital
○ University of North Carolina Hospitals

○ NE
○ The Nebraska Medical Center

○ NJ
○ Newark Beth Israel Medical Center

○ NY
○ Mount Sinai Medical Center
○ NY Presbyterian Hospital/Columbia Univ Medical Center

○ OH
○ Children's Hospital Medical Center
○ Nationwide Children's Hospital
○ Ohio State University Medical Center
○ The Cleveland Clinic Foundation
○ University Hospitals of Cleveland

○ OK
○ Integris Baptist Medical Center

○ PA
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○ Children's Hospital of Pennsylvania
○ Children's Hospital of Pittsburgh of UPMC
○ Hospital of the University of Pennsylvania
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○ Baylor University Medical Center
○ CHI St. Luke's Health Baylor College of Medicine Medical Center
○ Houston Methodist Hospital
○ Memorial Hermann Hospital, University of Texas at Houston
○ Scott and White Memorial Hospital
○ Texas Children's Hospital
○ UT Southwestern Medical Center/William P Clements Jr University Hospital
○ University Hospital, University of Texas Health Science Center
○ University of Texas Medical Branch at Galveston

○ UT
○ University of Utah Medical Center

○ VA
○ Inova Fairfax Hospital
○ University of Virginia Health Sciences Center

○ WA
○ University of Washington Medical Center

○ WI
○ Aurora St. Luke's Medical Center
○ Froedtert Memoria Lutheran Hospital
○ University of Wisconsin Hospital and Clinics

If patient evaluated for transplant at second program, specify outcome:
○ Listed
○ Delisted
○ Denied
○ Pt declined to pursue
○ Unknown

COVID

Covid-19 Event

Was patient tested for Covid-19?
○ Yes, testing was done
○ No testing was done, but there were strong reasons to suspect Covid-19

Non-Testing Reasons for Suspecting/Treating COVID-19:
☐ Known contact with Sars-cov-2 carrier
☐ X-Ray or CT scan imaging
☐ Patient has symptomatology consistent with COVID-19
☐ Other

Other reasons to suspect Covid-19: _____

Testing

Select all applicable reasons for testing:
☐ Pre-admission/procedure
☐ Known contact with Sars-cov-2 carrier
☐ Patient has symptomatology consistent with COVID-19
☐ Other reasons for testing

Other reasons for testing: _____

Testing date: (MM/DD/YYYY)

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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2022 Cystic Fibrosis Foundation Patient Registry Questionnaire

Type of specimen:
○ Nasopharyngeal swab (PCR test)
○ Saliva (PCR test)
○ Serology (antibody test)
○ Nasopharyngeal swab (antigen test)
Testing Result:
○ Positive ○ Negative ○ Inconclusive
Test Comments: _____

Please describe confirmed or suspected event:
Did patient have any symptoms related to COVID-19 at presentation?
○ Yes, symptomatic
○ No, patient was asymptomatic
Date of first symptoms: (MM/DD/YYYY)
Signs and Symptoms at manifestation:
☐ Cough, different from CF
☐ New shortness of breath or difficulty breathing
☐ Chills
☐ Fever (>=38C)
☐ Headache
☐ Muscle pain
☐ New loss of taste or smell
☐ Repeated shaking with chills
☐ Other
Other symptoms, not included above: _____

Treatment
Where was the patient treated for Covid-19 symptoms?
☐ Self-quarantine at home
☐ Admitted to hospital
☐ Other
Specify other treatment location: _____
Date admitted to hospital: (MM/DD/YYYY)
Make sure to create a care episode if a patient was hospitalized.

Was patient admitted to ICU?
○ Yes ○ No
Was patient on supplemental oxygen?
○ Yes ○ No
Did the patient require non-invasive respiratory support (CPAP, biPAP; High-flow)?
○ Yes ○ No
Did the patient require mechanical ventilation?
○ Yes ○ No
Did the patient require ECMO support?
○ Yes ○ No
Did the patient require treatment therapies?
○ Yes ○ No ○ Unknown
Specify if the following therapies were used to treat the patient:
☐ Antiviral therapy
☐ Antibiotics
☐ Systemic steroids
☐ Immune modulators
☐ Other
Other Therapies: _____

Complications/Co-morbidities
COVID-19 associated complications/comorbidities (e.g. stroke, secondary infection): _____

Please be sure to enter or update patient data in the appropriate tabs of an encounter form (e.g. complications, labs). For any data entry questions, contact reghelp@cff.org.

Follow-up
Has patient recovered?
○ Yes
○ Currently Hospitalized
○ Currently in ICU
○ Currently in domestic quarantine
○ Deceased
○ Unknown

Date of recovery (i.e. end of symptoms OR negative COVID-19 test): (MM/DD/YYYY)

COVID-19 Vaccination

Covid-19 Vaccination
Please enter the date of first vaccination shot, even if it is approx.: (MM/DD/YYYY)
Please enter the date of second vaccination shot, if known and required: (MM/DD/YYYY)
The patient received a vaccine developed by:
○ Pfizer
○ Moderna
○ AstraZeneca
○ Novavax
○ Johnson&Johnson
○ Other or Unknown
Specify other vaccine manufacturer, if known: _____

Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)
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