# 2019

# 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
2019 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.

PHOTOGRAPHY BY

John Fedele

SPECIAL ACKNOWLEDGMENTS

Those who contributed to the maintenance of PortCF, analysis of data, and creation of this report:
Bruce Marshall
Albert Faro
Alexander Elbert
Aliza Fink
Josh Cho
Josh Ostrenga
Kristofer Petren
Olga Dorokhina
Runyu Wu
Samar Rizvi
Thomas O'Neil

CYSTIC FIBROSIS FOUNDATION

September 2020

Dear Friends and Colleagues:

We are pleased to share the 2019 Patient Registry Annual Data Report with you during this exciting and yet sobering time. The exciting news is the rapid uptake of the triple-combination (elexacaftor/tezacaftor/ivacaftor) CFTR modulator. We are already seeing what appears to be a significant impact on the number of pulmonary exacerbations. Much more to follow in subsequent reports. While we are excited about the availability of this new therapy, we continue to invest in the Path to a Cure for everyone with cystic fibrosis.

The sobering event that unfolded as we prepared this report is the COVID-19 pandemic. While the CF Foundation has partnered with the CF community to try to keep everyone safe including the provision of portable spirometers to facilitate telehealth visits, the patient registry team has played a pivotal role in a global effort to assess the impact of COVID-19 on people with CF. While people with CF do better than initially feared, it is clearly not a benign infection for those with CF, particularly for those with advanced lung disease and who have undergone transplantation. We continue to collect data on COVID-19 infections in the patient registry and collaborate with international colleagues to gather enough cases for a meaningful assessment of the short and long-term consequences of the infection on people with CF.

**Many thanks to each and every one of you who contribute to the success of the Registry** — most importantly, people with CF and their families who generously agree to share their data and the Registry coordinators and care team members who collect and enter the data. It would not be possible without your vital contributions.

Thank you all for your hard work throughout the year and your commitment to the CF Foundation's mission.

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

# TABLE OF CONTENTS


ABOUT THIS REPORT 5

DEMOGRAPHICS 8

- Characteristics of Adults with CF 10
- Health Insurance Information 12

DIAGNOSIS 13

- Diagnostic Characteristics of Individuals with CF 13
- Diagnostic Tests 16

CFTR GENE MUTATIONS 18

GUIDELINES: CARE, SCREENING, AND PREVENTION 22

- Patient Care Guidelines 22
- Infant Care Guidelines 27

MICROBIOLOGY 30

- *Pseudomonas aeruginosa* 32
- *Staphylococcus aureus* 33
- Nontuberculous Mycobacteria 34

NUTRITION 36

- Infant Feeding 40

PULMONARY AND NUTRITIONAL OUTCOMES 41

PULMONARY FUNCTION 43

- Pulmonary Exacerbations 46

THERAPIES 48

- Gastrointestinal (GI) Therapies 48
- Pulmonary Therapies 50
- CFTR Modulator Therapies 57

COMPLICATIONS 60

- CF Complications by Age, 2019 62
- Cystic Fibrosis-Related Diabetes (CFRD) 64
- Depression and Anxiety 67

TRANSPLANTATION 69

- Lung Transplantation 69

SURVIVAL 72
Median Predicted Survival 72
Median Conditional Predicted Survival 73
Mortality Rate 73
Median Age at Death 74
Causes of Death 74
CF FOUNDATION PATIENT REGISTRY QUESTIONNAIRE 75
REFERENCES 85

# 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 120 CF Foundation-accredited care centers*

## Inclusion 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 2019 calendar year, including those who were born, diagnosed, or died in the year.

Data from individuals who have received a lung transplant are only included in the chapters on Demographics, Diagnosis, CFTR Gene Mutations, Transplantation, and Survival.

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 are have received a transplant. Figures titled in **purple** reflect patient-level data that do NOT include individuals who have received a lung transplant. Figures titled in **blue** present data on center-level variation and include only those centers with 10 or more eligible individuals. Exceptions to this are figures showing center-level variation for infants, people with a G551D mutation, people with cystic fibrosis-related diabetes (CFRD), and people who had a pulmonary exacerbation. For these figures, centers with five or more eligible individuals are included.

**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**

## Exclusion Criteria

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.

Data from individuals who have received a lung transplant are excluded from any chapters not specified above in the inclusion criteria. In the past, data from individuals who received a lung transplant were included in many of the figures. This impacted reporting of prevalent complications in the post-transplant population, such as CFRD and osteoporosis. This year, exclusion of data from individuals who received a lung transplant has resulted in a lower prevalence of these complications as compared to previous years.

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, 2004–2019

| Demographics[A] | 2004 | 2009 | 2014 | 2018 | 2019 |
|---|---|---|---|---|---|
| People with CF (n) | 22,533 | 26,112 | 28,630 | 30,904 | 31,199 |
| Newly diagnosed individuals (n)[B] | 994 | 1,148 | 922 | 979 | 766 |
| Detected by newborn screening (%) | 12.4 | 50.7 | 63.6 | 58.9 | 62.4 |
| Median age at diagnosis for all people with CF (months) | 6 | 5 | 4 | 3 | 3 |
| Mean age (years) | 17.5 | 19.1 | 20.5 | 22.2 | 22.7 |
| Median age (years) | 15.4 | 17.1 | 18.3 | 19.8 | 20.3 |
| Adults ≥18 years (%) | 41.0 | 47.2 | 50.8 | 54.5 | 56.0 |
| Race (not mutually exclusive) | | | | | |
| White (%) | 95.3 | 94.6 | 94.0 | 93.5 | 93.4 |
| African American (%) | 3.9 | 4.3 | 4.6 | 4.8 | 4.7 |
| Other race (%) | 1.9 | 2.6 | 3.1 | 3.7 | 3.8 |
| Hispanic (any race) (%) | 6.1 | 6.9 | 8.3 | 9.4 | 9.4 |
| Males (%) | 52.0 | 51.8 | 51.6 | 51.8 | 51.8 |
| **Mortality[A]** | | | | | |
| Total deaths (n) | 370 | 458 | 473 | 412 | 373 |
| Annual mortality rate (per 100) (%) | 1.6 | 1.8 | 1.7 | 1.3 | 1.2 |
| Predicted median survival (five-year increments) | 34.1 | 37.9 | 40.0 | 44.5 | 46.2 |
| 95% confidence interval (five-year increments) | 33.2 - 35.3 | 36.7 - 38.8 | 38.9 - 41.5 | 43.4 - 45.9 | 45.2 - 47.6 |
| Median age at death (years) | 24.2 | 26.3 | 29.0 | 30.8 | 32.4 |
| **GI/Nutrition** | | | | | |
| Body Mass Index (BMI) percentile in individuals 2 to 19 years (median) | 45.1 | 50.4 | 54.0 | 57.4 | 58.3 |
| Weight <10th CDC percentile (%) | 20.9 | 15.3 | 12.4 | 10.4 | 10.1 |
| Height <5th CDC percentile (%) | 14.6 | 12.4 | 10.5 | 9.5 | 9.5 |
| BMI in individuals 20 to 40 years (median) | 21.2 | 21.6 | 21.9 | 22.3 | 22.5 |
| Pancreatic enzyme replacement therapy (%) | 90.8 | 87.4 | 86.9 | 84.9 | 83.8 |
| Supplemental feeding - tube (%) | 8.8 | 10.5 | 10.8 | 10.7 | 10.3 |
| Supplemental feeding - oral only (%) | 36.7 | 38.3 | 42.9 | 43.7 | 44.4 |
| **Pulmonary[C]** | | | | | |
| FVC % predicted (mean) | 83.8 | 86.7 | 87.7 | 89.3 | 89.9 |
| $FEV_1$ % predicted (mean) | 73.2 | 75.3 | 76.3 | 77.8 | 78.7 |
| $FEV_1$/FVC ratio (mean) | 75.1 | 74.7 | 74.4 | 74.3 | 74.5 |
| **Respiratory Microbiology** | | | | | |
| *Pseudomonas aeruginosa (P. aeruginosa* or *PA) (%)*[D] | 57.5 | 52.0 | 47.6 | 44.4 | 43.2 |
| *Burkholderia cepacia (B. cepacia)* complex *(%)* | 2.9 | 2.7 | 2.5 | 2.6 | 2.6 |
| *Staphylococcus aureus (S. aureus) (%)*[E] | 62.5 | 66.8 | 70.0 | 70.4 | 70.2 |
| Methicillin-sensitive *Staphylococcus aureus* (MSSA) (%) | 52.1 | 51.0 | 53.6 | 55.3 | 55.3 |
| Methicillin-resistant *Staphylococcus aureus* (MRSA) (%) | 14.8 | 24.0 | 26.0 | 25.0 | 24.6 |
| *Stenotrophomonas maltophilia (S. maltophilia) (%)* | 11.8 | 13.0 | 13.5 | 12.3 | 11.9 |
| Mycobacterial species (%)[F] | - | - | 12.2 | 13.7 | 13.9 |

Table continues on the next page

| Summary of the Cystic Fibrosis Foundation Patient Registry, 2004-2019 *continued* | | | | | |
|---|---|---|---|---|---|
| **Health Care Utilization and Pulmonary Exacerbations (PEX)[G]** | **2004** | **2009** | **2014** | **2018** | **2019** |
| Outpatient visits to CF centers reported per year (mean) | 4.1 | 4.3 | 4.5 | 4.3 | 4.3 |
| Treated with IV antibiotics for a pulmonary exacerbation (%) | - | 35.8 | 35.6 | 33.2 | 31.6 |
| Number of pulmonary exacerbations per year (mean) | - | 0.69 | 0.70 | 0.64 | 0.60 |
| Number of days of treatment for all PEX per year (mean)[H] | - | 30.3 | 29.6 | 27.5 | 27.6 |
| Number of days of home IV treatment for all PEX per year (mean)[H] | - | 13.1 | 11.7 | 9.5 | 9.3 |
| Number of days of hospitalization for all PEX per year (mean)[H] | - | 17.2 | 17.9 | 18.0 | 18.3 |
| **Pulmonary Therapies[I]** | | | | | |
| Dornase alfa (≥6 years) (%) | 74.0 | 84.6 | 89.8 | 92.0 | 92.4 |
| Inhaled tobramycin (PA+ and ≥6 years) (%)[J] | 68.8 | 71.4 | 69.8 | 70.2 | 68.2 |
| Inhaled aztreonam (PA+ and ≥6 years) (%) | - | 4.0 | 42.4 | 43.3 | 43.5 |
| Azithromycin (PA+ and ≥6 years) (%)[K] | 49.3 | 67.8 | 68.0 | 64.3 | 64.3 |
| Hypertonic saline (≥6 years) (%) | - | 48.3 | 65.8 | 73.6 | 74.6 |
| Oxygen (%)[L] | 5.9 | 11.0 | 11.3 | 10.8 | 10.9 |
| Non-invasive ventilation (%) | - | 2.2 | 2.9 | 3.2 | 3.1 |
| **CFTR Modulators** | | | | | |
| Ivacaftor (all eligible individuals in that year) (%) | - | - | 62.2 | 66.2 | 58.6 |
| Lumacaftor/ivacaftor (all eligible individuals in that year) (%) | - | - | - | 57.7 | 41.1 |
| Tezacaftor/ivacaftor (all eligible individuals in that year) (%) | - | - | - | 43.8 | 56.6 |
| **Transplants[A]** | | | | | |
| Lung (all procedures) (n) | 178 | 203 | 209 | 257 | 241 |
| Liver (n) | 20 | 17 | 19 | 22 | 17 |
| Kidney (n) | 1 | 6 | 13 | 11 | 12 |
| **Lost to Follow Up[A]** | | | | | |
| Lost to follow up (per 100 people with CF) (%)[M] | - | 3.7 | 3.4 | 2.9 | 2.9 |

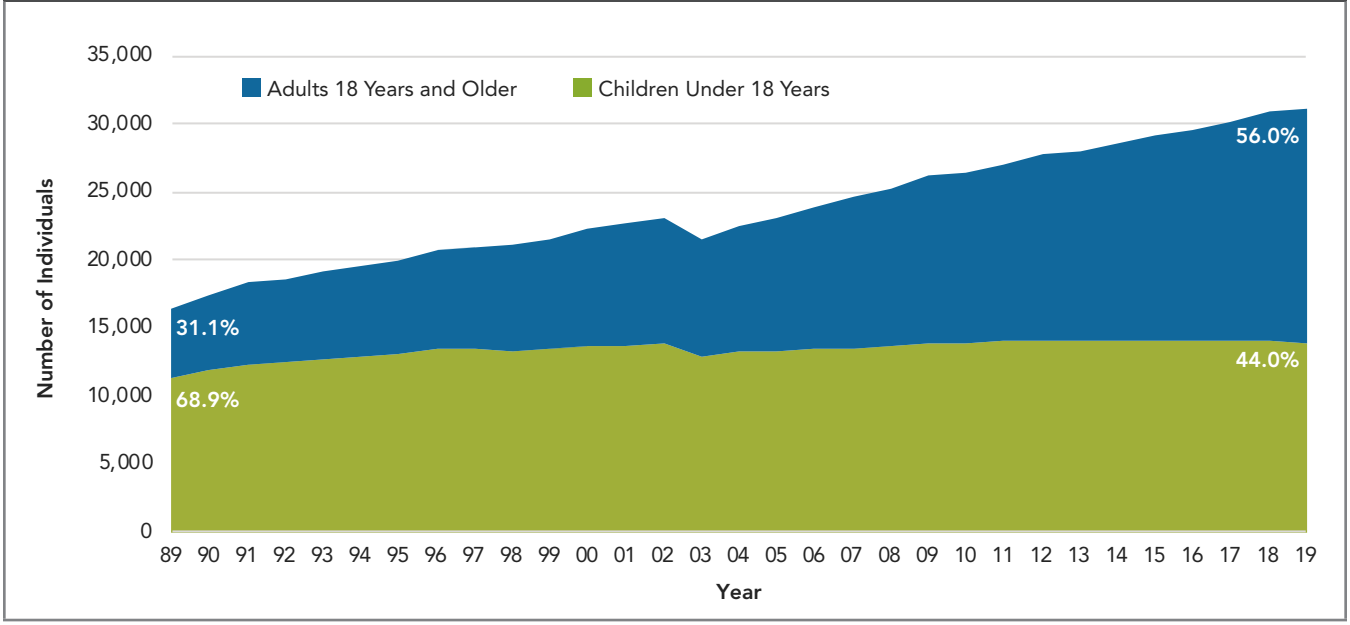
[A] *Includes data from transplant recipients.*
[B] *We anticipate that additional 2019 diagnoses will be entered into the Registry in 2020.*
[C] *Pulmonary function data throughout this report reflect the use of Global Lung Initiative (GLI) equations.*[1]
[D] *Includes PA and multidrug-resistant PA found in any culture during the year.*
[E] *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.*
[F] *Percentage of people with CF with one or more mycobacterial species isolated out of those who had a mycobacterial culture during the year.*
[G] *Defined as a period of treatment with IV antibiotics in the hospital and/or at home.*
[H] *Among those with one or more pulmonary exacerbations in the year.*
[I] *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.*
[J] *Includes TOBI®, TOBI™ Podhaler® and Bethkis® since 2013. In prior years, only TOBI® was available.*
[K] *Individuals were considered eligible if they met the selection criteria used in the first U.S. azithromycin trial.*[2]
[L] *Includes continuous, nocturnal, or with exertion.*
[M] *Defined as patients seen in the previous reporting year (2018) but not the current reporting year (2019), and not known to have died.*

## DEMOGRAPHICS

*The Registry contains data on people with CF from 1986 to 2019. During that time, substantial changes in specialized CF care have led to improved survival. This section shows the current and longitudinal distribution of demographic characteristics of individuals with CF in the Registry.*

In 2019, there were 31,199 individuals with CF in the Registry. The number of adults with CF continues to increase, while the number of children remains relatively stable. In 2019, adults were 56.0 percent of the CF population, compared with 31.1 percent in 1989.

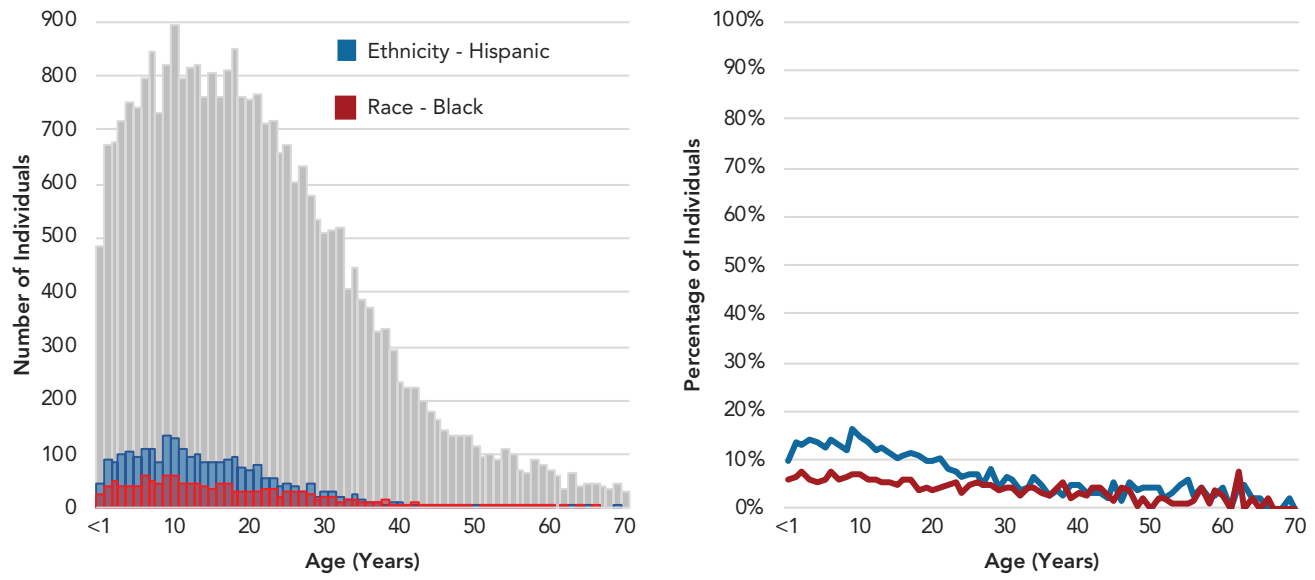
**Number of Children and Adults with CF, 1989–2019**




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

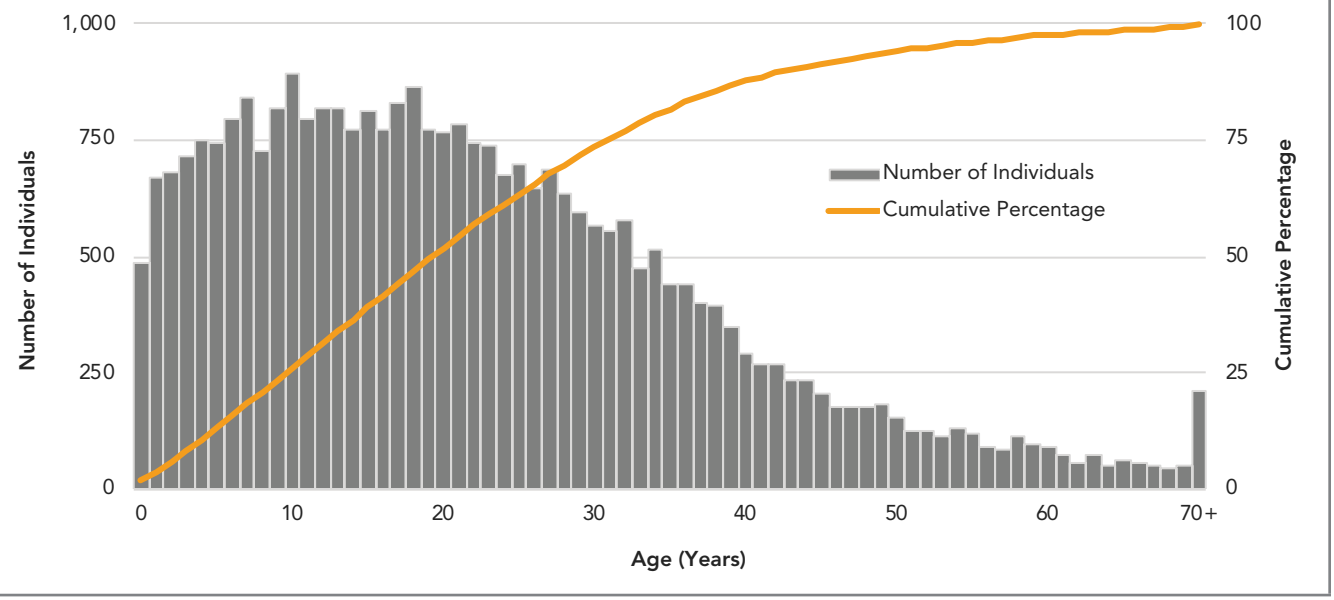
Currently, 9.4 percent of the individuals in the Registry identify as Hispanic. There has been an increase over the past 15 years, reflecting national population trends.[3] Hispanics with CF tend to be younger than the overall CF population, with a median age of 14.0 years.

## Individuals who Identify as Hispanic and/or Black by Age in Years, 2019




The median age of people with CF currently in the Registry is 20.3 years. The range is from birth to 89.7 years. Despite gains in survival, the age distribution remains markedly skewed toward younger ages.

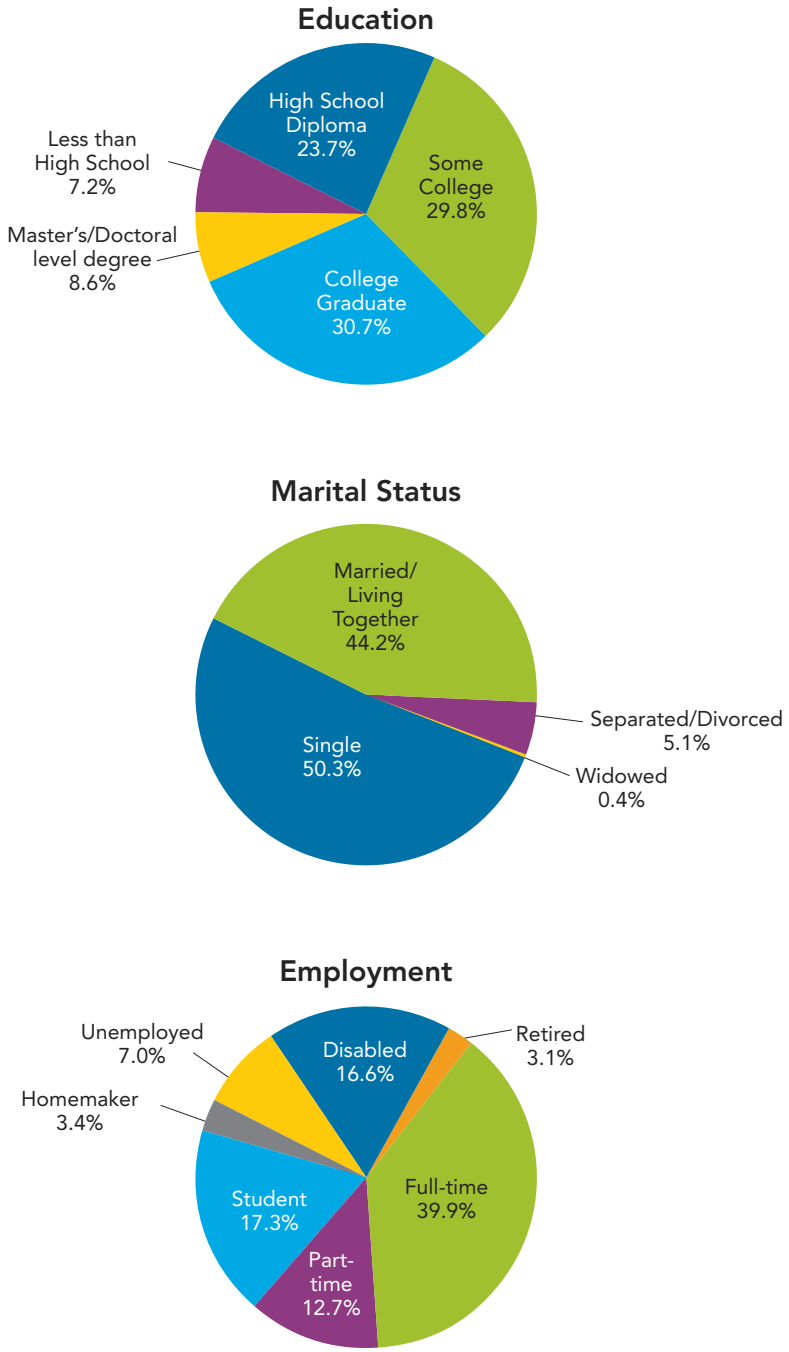
## Age Distribution of the CF Population in 2019



## Characteristics of Adults with CF

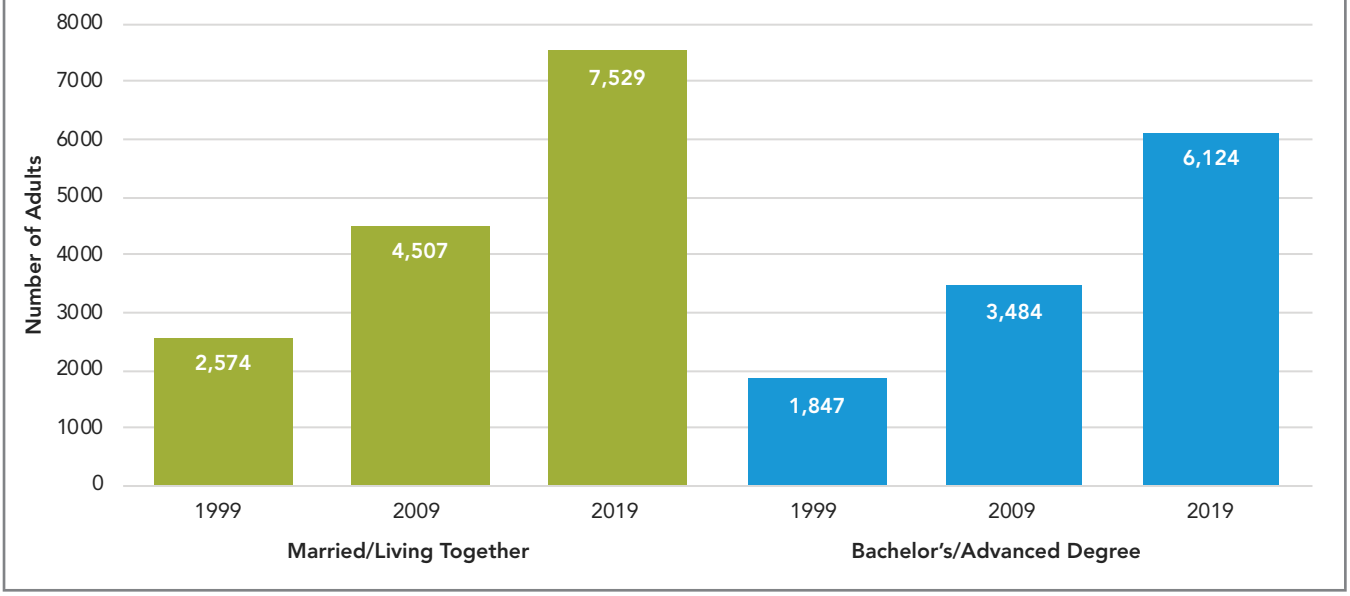
As a growing number of individuals with CF enter adulthood, it is encouraging to note that many are pursuing higher education and employment, are in committed relationships, and are having children of their own. About two-thirds of adults with CF are either studying or working. However, these charts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

### Socioeconomic Characteristics of Adults 18 Years and Older with CF, 2019



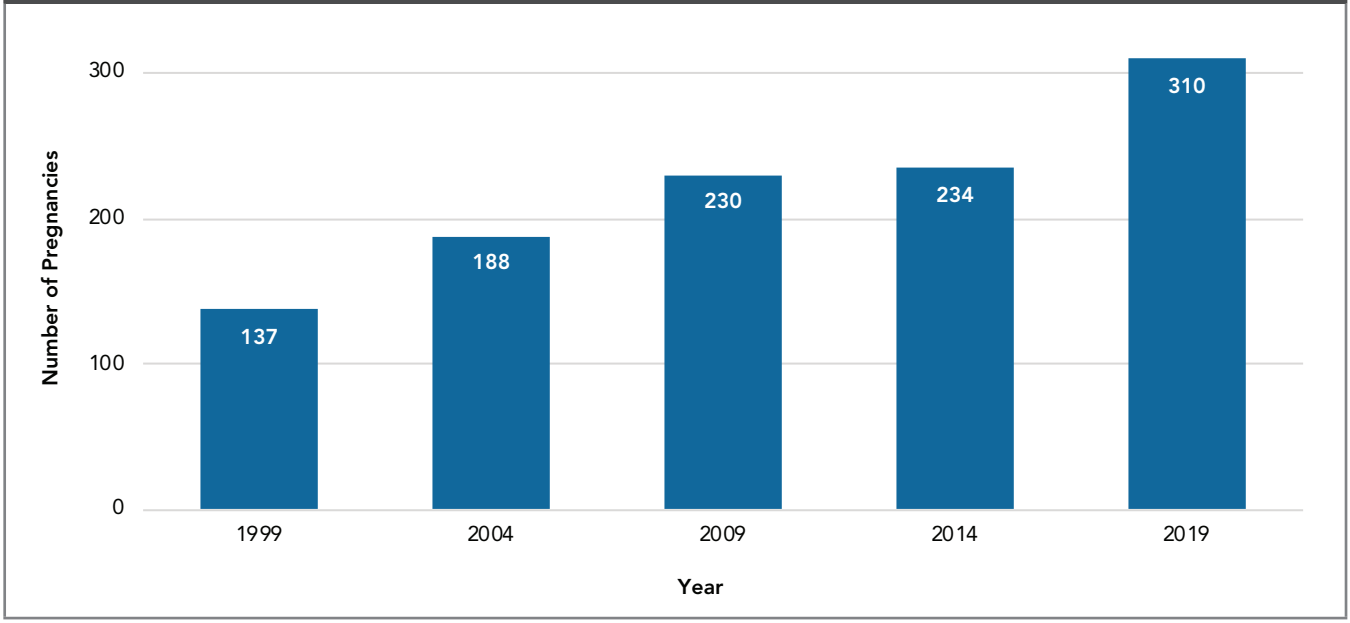
Over the last twenty years, there has been almost a tripling of the number of people who are married or living together and nearly four times the number of people with a college degree.

## Characteristics of Adults with CF, 1999-2019




The number of pregnancies among women with CF has increased steadily since the 1990s. Registry data show that 310 women with CF were pregnant in 2019. The overall pregnancy rate among women with CF has remained relatively constant, in contrast to the pregnancy rate in the general U.S. population, which has declined during this time.[4]

## Number of Pregnancies in Women 14 to 45 Years with CF, 1999–2019



## 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 2019, a majority of individuals with CF who were age 18 to 25 were covered under their parents' health insurance plan.

**Insurance Coverage in 2019**

| | Age < 18 (%) | Age 18 - 25 (%) | Age > 26 (%) | All (%) |
|---|---|---|---|---|
| Number of Individuals (n) | 13,607 | 5,976 | 11,226 | 30,809 |
| Health insurance (e.g., private insurance) | 50.8 | 63.9 | 65.2 | 58.6 |
| Medicare/Indian Health Services | 1.1 | 5.8 | 25.2 | 10.8 |
| Medicaid/state programs | 54.5 | 41.7 | 25.4 | 41.4 |
| TriCare or other military health plan | 3.4 | 2.2 | 1.9 | 2.6 |
| Other | 1.7 | 1.5 | 1.8 | 1.7 |
| No health insurance | 0.6 | 1.3 | 1.1 | 0.9 |

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

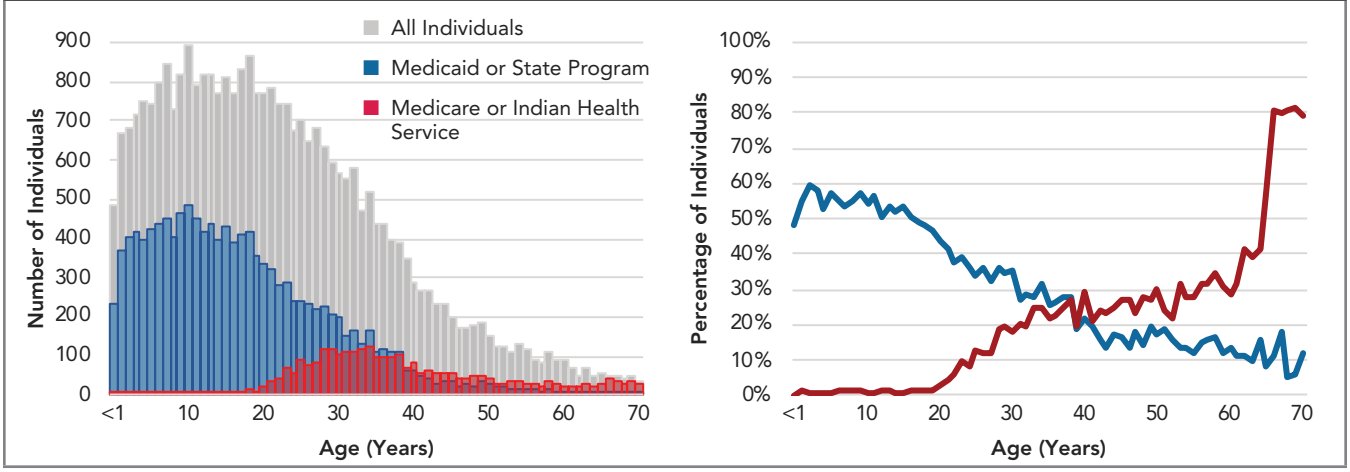
**Additional Insurance Information in 2019**

| | |
|---|---|
| Individuals who participated in a patient assistance program (%) | 47.3 |
| Individuals 18 to 25 years covered under parents' insurance (%) | 53.8 |

*"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 55.3 percent of children younger than 10 years of age. Though the overall prevalence of Medicare use is low, among adults aged 30 to 35 years, 21.8 percent report Medicare coverage. This increases to 27.9 percent among adults aged 40 to 64 years. Individuals aged younger than 65 years who receive Medicare have met the federal criteria for disability.

**Medicare/Indian Health Service and Medicaid/State Programs by Age in Years, 2019**



# DIAGNOSIS

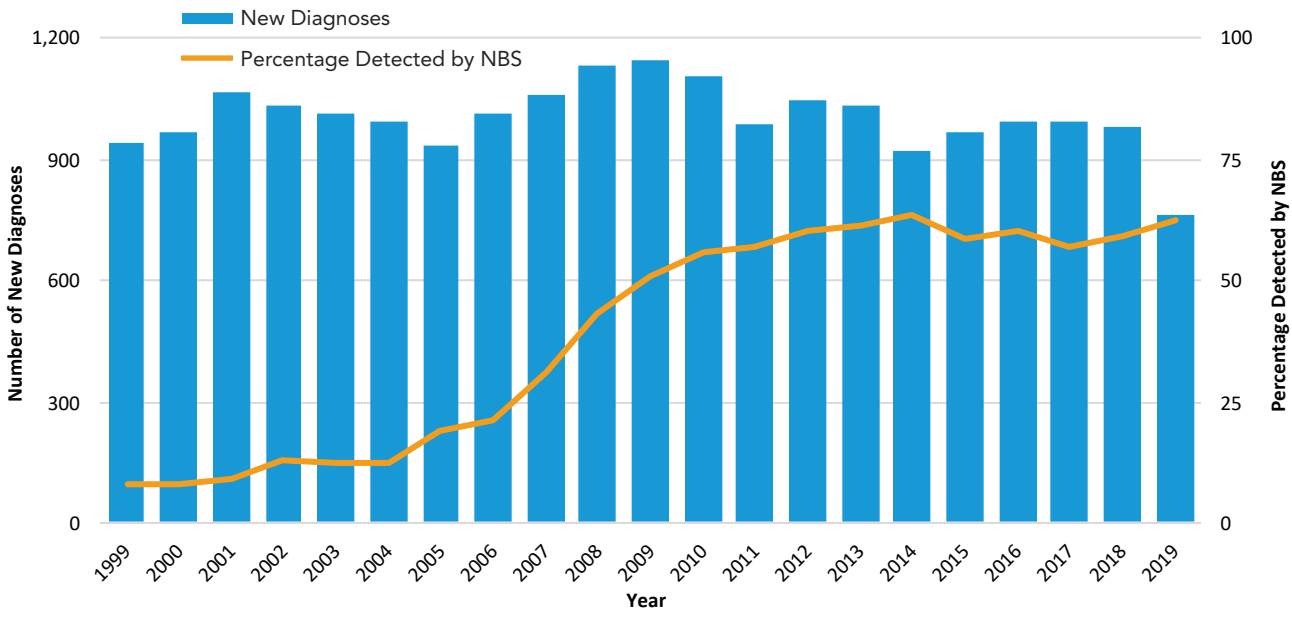
## Diagnostic Characteristics of Individuals with CF

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

In 2019, 62.5 percent of total new diagnoses and 92.3 percent of diagnoses among those less than 6 months old were reported as being detected by newborn screening (NBS). There is evidence that individuals diagnosed prior to the onset of symptoms have better lung function and nutritional outcomes later in life.[5] Diagnosis in the newborn period also 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.

Some of the decrease in newly diagnosed individuals observed in the most recent reporting year is due to infants born late in the year (i.e., late 2019) who were not seen at a CF care center before the end of the year. Therefore, their data were not included in the Registry. Future reports will be adjusted to include these individuals for the 2019 diagnosis year.

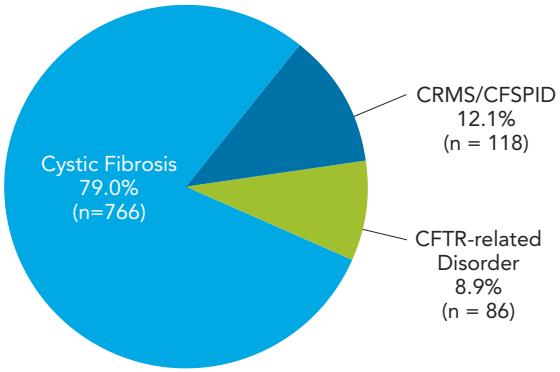
**Number of New CF Diagnoses, 1999–2019**




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 genetic mutations. 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 a clinical decision; there is no requirement that individuals meet published diagnostic criteria for CF or CRMS. The percentage of CRMS/CFSPID decreased from 13.1 percent of those diagnosed during the year in 2018 to 12.2 percent in 2019.

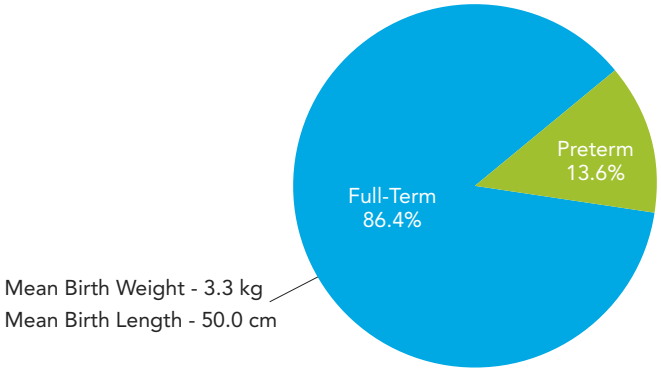
Individuals can also be diagnosed with CFTR-related disorder. This option has been available in the Registry since 2010. Individuals with this diagnosis do not meet diagnostic criteria for CF or CRMS, are affected by CF-related conditions such as congenital bilateral absence of the vas deferens (CBAVD), and often have mutations in the CFTR gene.[8] The percentage of individuals reported to have CFTR-related disorder slightly increased from 8.4 percent of those diagnosed during the year in 2018 to 8.9 percent in 2019. 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 Diagnoses, 2019




In 2019, 486 newborn infants were diagnosed with CF. Of the 390 infants with a known gestational age at birth, 86.4 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 initially show nutritional deficiencies.

## Gestational Age of Infants Born and Diagnosed with CF in 2019




*"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.*

The majority of those diagnosed in their first year are asymptomatic or minimally symptomatic at time of diagnosis. Among the 9.9 percent of infants diagnosed in 2019 before age one with meconium ileus (or other intestinal obstruction), 26.9 percent had bowel perforation. Since the number of infants with meconium ileus is small, the percentage with bowel perforation may fluctuate year to year, ranging from 15.9 percent to 34.1 percent over the last several years. Those diagnosed after age one often present with acute or persistent respiratory abnormalities.

## Symptoms Reported at CF Diagnosis

| | All Individuals (%) | Diagnosed in 2019 (%) | Diagnosed in 2019 Age < 1 (%) | Diagnosed in 2019 Age ≥ 1 (%) |
|---|---|---|---|---|
| **Number of Individuals (n)** | **31,199** | **766** | **541** | **225** |
| **Asymptomatic** | | | | |
| DNA analysis | 13.5 | 28.1 | 25.1 | 34.4 |
| Family history | 14.6 | 9.8 | 8.4 | 12.9 |
| Newborn (neonatal) screening | 27.9 | 62.4 | 87.6 | N/A |
| Prenatal screening (CVS[A], amniocentesis) | 2.5 | 2.4 | 3.4 | N/A |
| **Symptomatic** | | | | |
| Acute or persistent respiratory abnormalities | 35.5 | 15.0 | 1.7 | 44.0 |
| CBAVD[B] or infertility/GU[C] abnormalities | 0.6 | 2.2 | 0.0 | 7.1 |
| Digital clubbing | 0.5 | 0.8 | 0.0 | 2.5 |
| Edema | 0.5 | 0.0 | 0.0 | 0.0 |
| Electrolyte imbalance | 3.0 | 0.1 | 0.2 | 0.0 |
| Failure to thrive/malnutrition | 27.3 | 5.9 | 4.6 | 8.7 |
| Liver problems | 1.1 | 0.5 | 0.2 | 1.2 |
| Meconium ileus/other intestinal obstruction | 17.0 | 6.9 | 9.9 | N/A |
| Nasal polyps/sinus disease | 3.7 | 4.4 | 0.0 | 14.1 |
| Rectal prolapse | 2.6 | 0.4 | 0.2 | 0.8 |
| Steatorrhea/abnormal stools/malabsorption | 21.2 | 5.2 | 5.0 | 5.8 |
| Other | 5.0 | 5.2 | 1.3 | 13.7 |

*Data are not mutually exclusive. We anticipate that additional 2019 diagnoses will be entered into the Registry in 2020.*

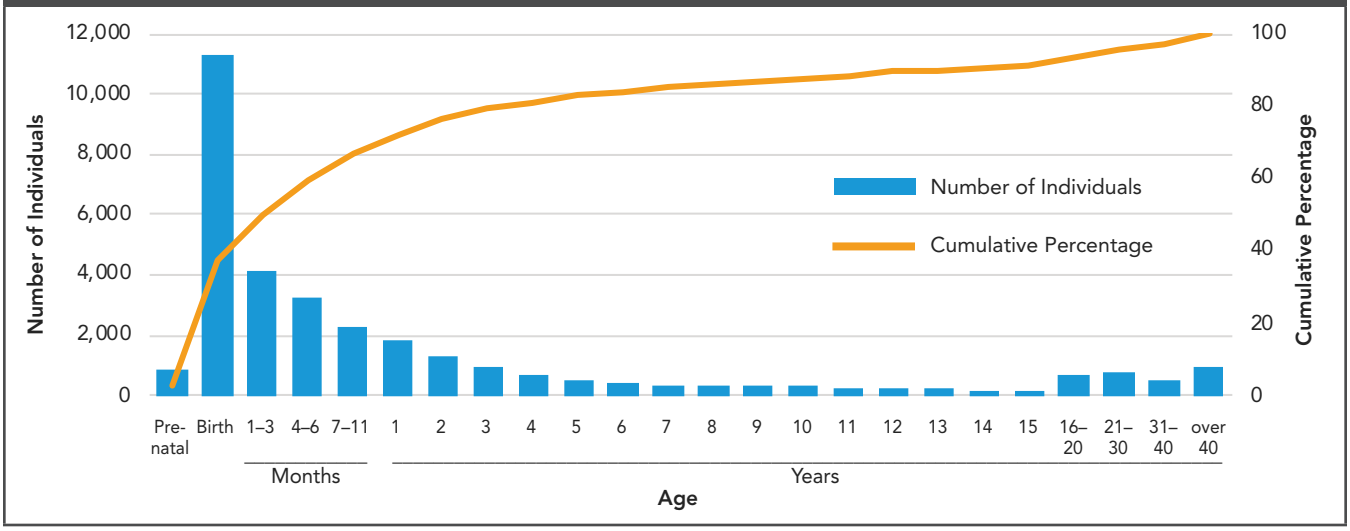
[A] *Chorionic villus sampling*

[B] *Congenital bilateral absence of the vas deferens*

[C] *Genitourinary*

**Previous figures in this section refer to infants born or diagnosed in 2019; the following figure includes all individuals followed in the Registry in 2019.**

## Age at Diagnosis of All Individuals with CF Seen in 2019

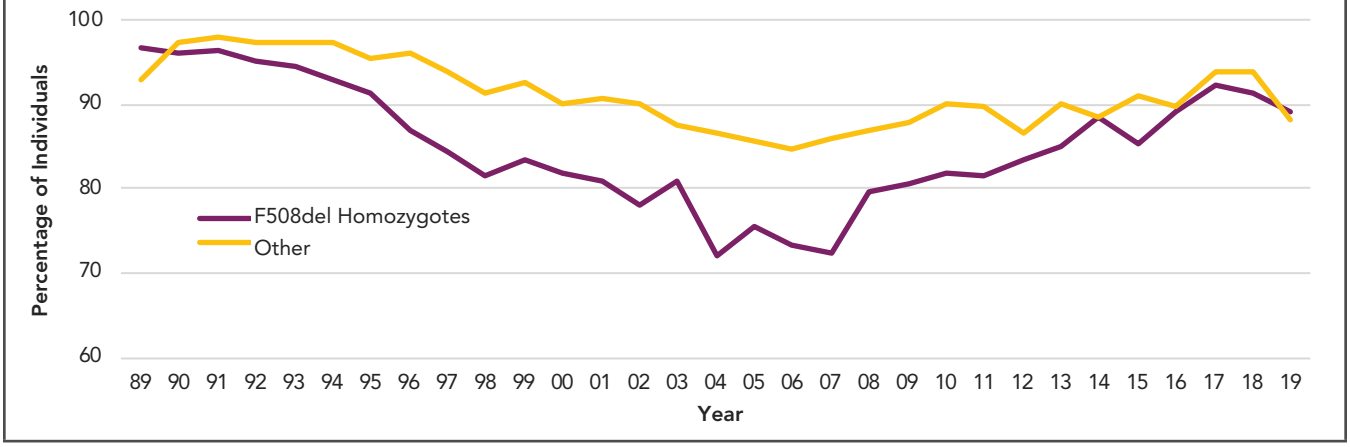



## Diagnostic Tests

### *Sweat Chloride Testing*

Sweat chloride testing is an important diagnostic test recommended for all individuals regardless of genotype.[8] In 2019, 90.3 percent of individuals in the Registry had a sweat chloride test result recorded. Baseline sweat chloride tests are becoming more important, as changes in sweat chloride are now viewed as indicators of the physiological effects of CFTR modulators.

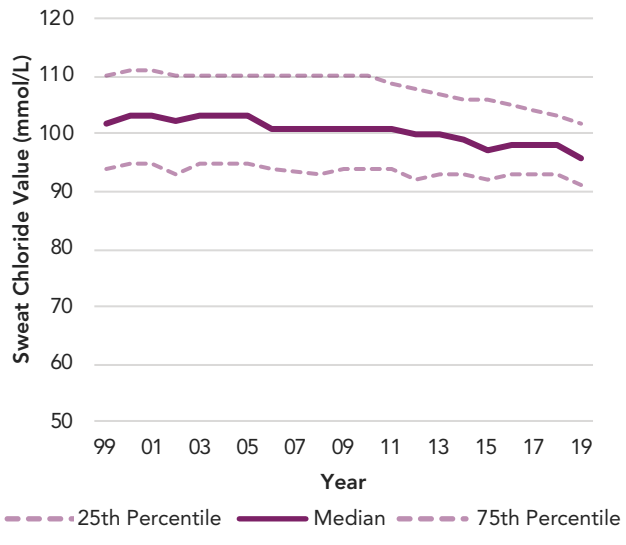
## Percentage of Individuals with a Sweat Chloride Test Reported by Year of Diagnosis, 1989-2019



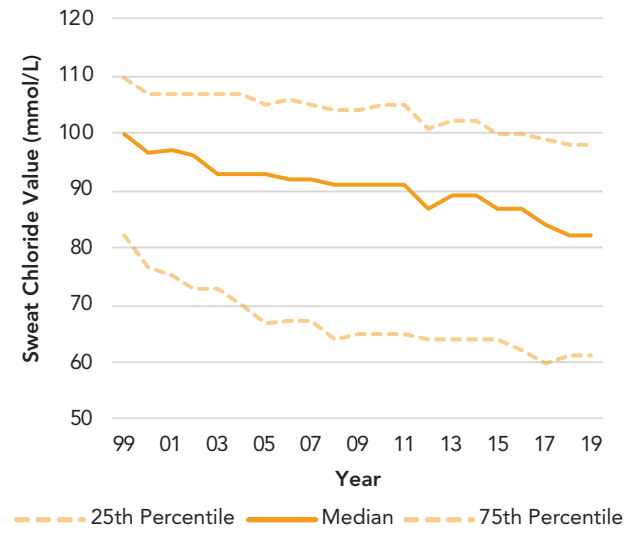

*Some individuals diagnosed in 2019 may not have had a sweat chloride test result entered in the Registry before the close of the reporting year.*

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

**Sweat Chloride Value of F508del Homozygous Individuals by Year of Diagnosis, 1999-2019**




**Sweat Chloride Value of Individuals Not Homozygous for F508del by Year of Diagnosis, 1999-2019**




## *Genotyping*

The cystic fibrosis transmembrane conductance regulator (CFTR) gene and the most prevalent CF-causing mutation (F508del) were discovered in 1989. Since then, genotyping has become a key component of the diagnostic work-up. In addition, with the introduction of CFTR modulators, genotyping all people with CF is important for research and clinical care. In 2019, 99.4 percent of individuals (n=30,998) in the Registry had been genotyped.

## CFTR GENE MUTATIONS

*To date, more than 2,000 mutations have been found in the CFTR gene.[11] Some mutations result in virtually no CFTR function and others are associated with some residual function. Various strategies have been used to categorize mutations with the goal of grouping individuals with CF with a similar prognosis. In previous reports, a five-mutation class system was used.[12-14] This classification system is helpful for understanding the impact of mutations on the biosynthesis and function of the CFTR protein. However, it is increasingly recognized that this classification schema is an oversimplification, given that many mutations lead to more than one defect in CFTR function.*

In this era of CFTR modulators, a second approach is being evaluated for mutation classification, referred to as theratyping. This system considers whether a mutation responds to a specific CFTR modulator. However, theratyping is still in progress and there is not yet a standard way to report this information. In this section, we report data on specific mutations and the difference in sweat chloride values between genotypes with little to no CFTR function versus those with residual CFTR function.

The most common CFTR mutation is F508del: 85.3 percent of individuals in the Registry who have been genotyped have at least one copy of this mutation. There is a substantial drop in prevalence from F508del to the next most common mutations. No other mutation is currently found in more than 5 percent of the population with CF.

## Prevalence of the 25 Most Common CFTR Mutations in People with CF Seen in 2019

| CFTR Mutation | | | Number of Individuals | Percent of Individuals |
|---|---|---|---|---|
| Legacy Name | cDNA Name | Protein Name | | |
| F508del | c.1521_1523delCTT | p.Phe508del | 26,626 | 85.3 |
| G542X | c.1624G>T | p.Gly542X | 1,418 | 4.5 |
| G551D | c.1652G>A | p.Gly551Asp | 1,365 | 4.4 |
| R117H | c.350G>A | p.Arg117His | 983 | 3.2 |
| N1303K | c.3909C>G | p.Asn1303Lys | 736 | 2.4 |
| W1282X | c.3846G>A | p.Trp1282X | 701 | 2.2 |
| 3849+10kbC->T | c.3718-2477C>T | | 573 | 1.8 |
| R553X | c.1657C>T | p.Arg553X | 548 | 1.8 |
| 1717-1G->A | c.1585-1G>A | | 498 | 1.6 |
| 621+1G->T | c.489+1G>T | | 493 | 1.6 |
| 2789+5G->A | c.2657+5G>A | | 456 | 1.5 |
| 3120+1G->A | c.2988+1G>A | | 377 | 1.2 |
| D1152H | c.3454G>C | p.Asp1152His | 321 | 1.0 |
| 5T | c.1210-12T[5] | | 307 | 1.0 |
| 2184insA | c.2052dupA | p.Gln685ThrfsX4 | 244 | 0.8 |
| 3272-26A->G | c.3140-26A>G | | 243 | 0.8 |
| R1162X | c.3484C>T | p.Arg1162X | 242 | 0.8 |
| I507del | c.1519_1521delATC | p.Ile507del | 237 | 0.8 |
| 3659delC | c.3528delC | p.Lys1177SerfsX15 | 221 | 0.7 |
| 1898+1G->A | c.1766+1G>A | | 214 | 0.7 |
| G85E | c.254G>A | p.Gly85Glu | 212 | 0.7 |
| L206W | c.617T>G | p.Leu206Trp | 205 | 0.7 |
| R334W | c.1000C>T | p.Arg334Trp | 187 | 0.6 |
| R347P | c.1040G>C | p.Arg347Pro | 186 | 0.6 |
| A455E | c.1364C>A | p.Ala455Glu | 177 | 0.6 |

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

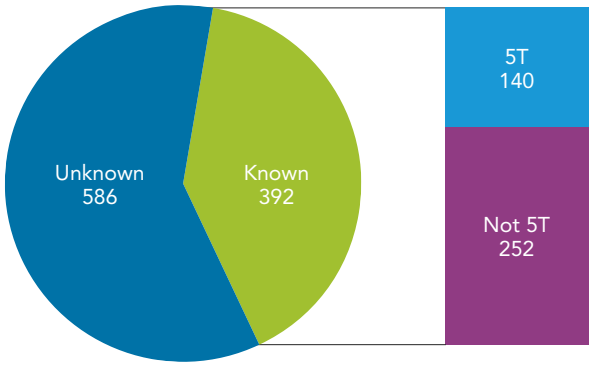
## F508del Mutation Prevalence

| F508del Mutation | Percent of Individuals |
|---|---|
| Homozygous F508del | 44.4 |
| Heterozygous F508del | 40.9 |
| Neither F508del or Unknown | 14.7 |

Among less common mutations, the number of individuals with an R117H mutation has increased over the years. Among those genotyped in 1993, less than 1 percent had an R117H mutation, compared with 4.7 percent of those genotyped in 2019. This may be due to the inclusion of R117H in newborn screening algorithms. Of note, 107 (10.9 percent) of the 978 patients with an R117H mutation had a sweat chloride value less than 30 mmol/L.

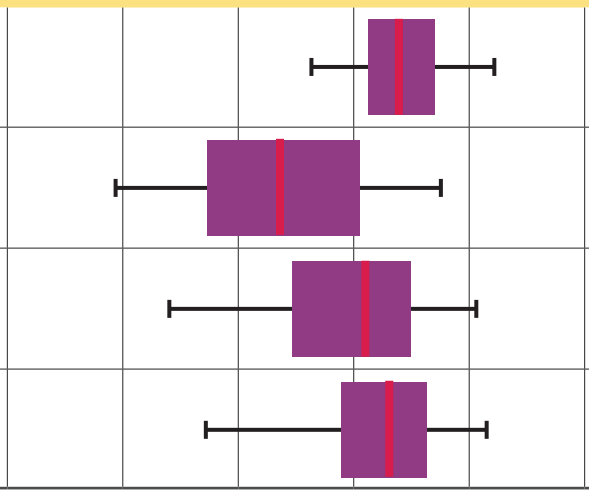
The clinical significance of the R117H mutation depends in part on the poly-T tract variant on the chromosome. Research indicates that a shorter poly-T tract is associated with a higher likelihood of having CF.[15,16] Unfortunately, the Registry has incomplete information on the poly-T tract status for the majority of individuals (59.9 percent) who are reported as having a diagnosis of CF and an R117H mutation. Of the 392 individuals with poly-T tract status recorded in the Registry, 140 (35.7 percent) are classified as having 5T.

**Poly-T Tract Status of Individuals with an R117H Mutation, 2019**



Individuals with mutations typically associated with little or no CFTR function tend to be younger, to have higher sweat test values, and to be more likely to be prescribed pancreatic enzyme replacement therapies (PERT) than individuals with a mutation typically associated with residual CFTR function (e.g., 96.7 percent of individuals with the former as compared to 33.7 percent of the latter are taking PERT).

## Sweat Chloride Value (mmol/L), by Genotypes




| | Median | 5th Percentile | 95th Percentile |
|---|---|---|---|
| Individuals with mutations associated with little or no CFTR function *N=19,281* | 102.0 | 79.0 | 126.0 |
| Individuals with one or more mutations associated with residual CFTR function *N=3,620* | 71.0 | 28.0 | 113.0 |
| Individuals with one or more unclassified mutations *N=3,883* | 94.0 | 41.0 | 122.0 |
| All individuals *N=27,677* | 99.0 | 51.0 | 125.0 |

*These charts use the highest sweat test value reported to the Registry. For 132 individuals, this value may reflect sweat chloride values after initiation of CFTR modulator therapy.*

## GUIDELINES: CARE, SCREENING, AND PREVENTION

*The CF Foundation sponsors the development of clinical practice guidelines to promote high-quality physical and mental health care for individuals with CF during infancy, childhood, and adulthood.[17-26] Many CF care centers report four office visits, two pulmonary function tests, and at least one microbiology culture annually for the majority of their CF patients. Similarly, among children age 2 to 5, the majority have at least four visits and at least one culture 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.[21]*

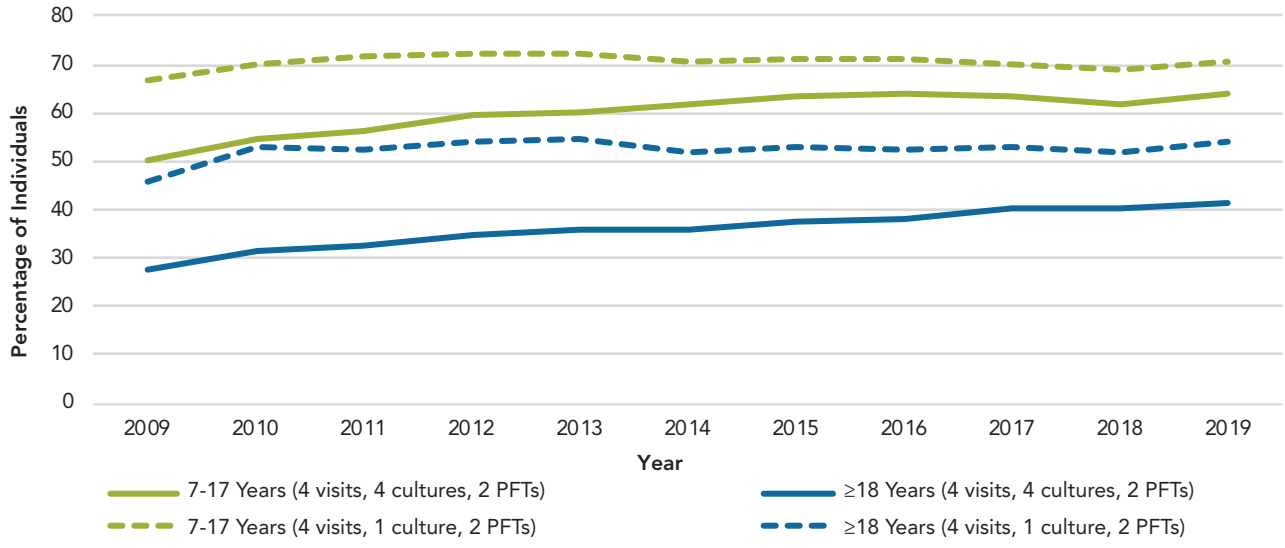
*There is significant variation by CF care center in several key screening measures, including dual-energy X-ray absorptiometry (DXA) scans for osteopenia/osteoporosis. The influenza vaccination rate for people with CF age six months and older remains high across the CF care center network. Smoking and secondhand smoke exposure remain challenges, particularly for infants and young adults.*

### Patient Care Guidelines

The percentage of individuals who receive care that meets CF Foundation care guidelines has gradually increased. Because individuals should be able to perform reliable pulmonary function tests (PFTs) at age six and older, we use guidelines criteria for those age seven and older to ensure that individuals were eligible to perform a reliable PFT for the entire year.

Over the past decade, the number of children and adults receiving, at a minimum, the annual recommended four office visits, four respiratory cultures, and two PFTs[20,21] has steadily increased. The percentage of adults who receive care that meets guidelines criteria remains lower than that observed in children. However, the percentage of those meeting guidelines continues to rise. Currently, more than half of adults are being seen at least four times, complete two or more PFTs, and are cultured at least once during the year. Many factors may impact metrics, such as the fact that some stable individuals may not need face-to-face encounters in the clinic setting.

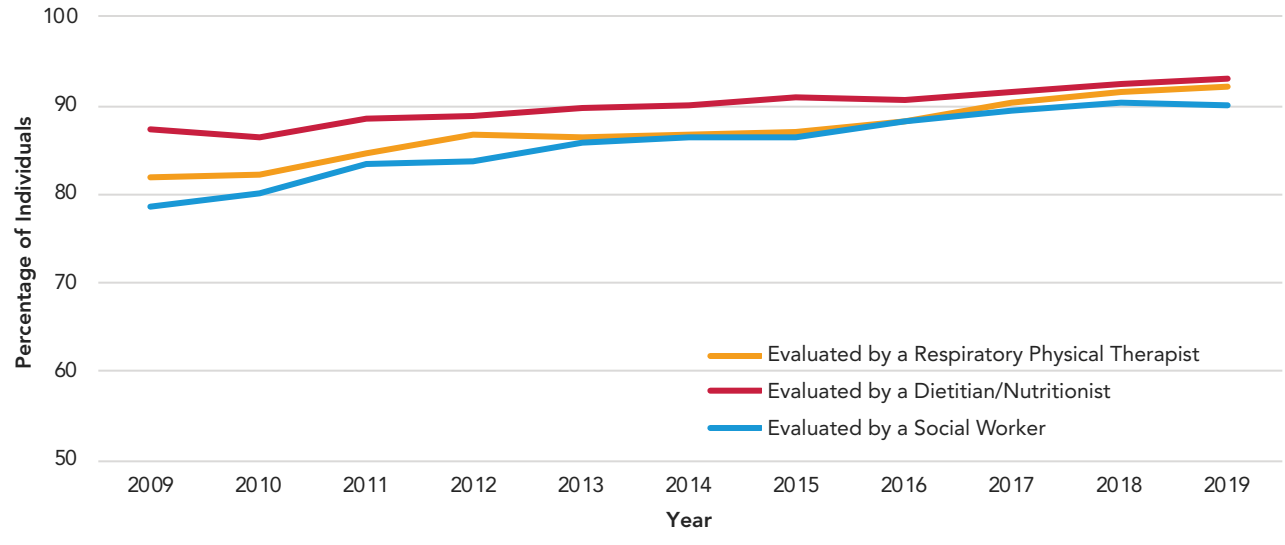
## Percentage of Individuals Meeting Guidelines for Visits, Cultures and PFTs, 2009–2019




The guidelines on infection prevention and control recommend that individuals with CF have quarterly respiratory cultures.[20-22] In 2019, 98.6 percent of individuals received at least one culture, and 55.5 percent of individuals had four or more respiratory cultures. Those aged younger than 18 were more likely to meet the recommendation for four cultures.

The multidisciplinary care team plays an important role in CF care.[20] Over time, there has been an increase in the number of individuals with CF who receive an annual evaluation from a respiratory/physical therapist, dietitian/nutritionist, and social worker. In 2019, 80.5 percent of individuals were evaluated by all three specialists. In addition, to support individuals' complex treatment regimens, the Registry now reports whether patients are seen by a pharmacist in clinic. In 2019, 46.7 percent of individuals were seen by a pharmacist at least once, an increase from 39.0 percent in 2018.

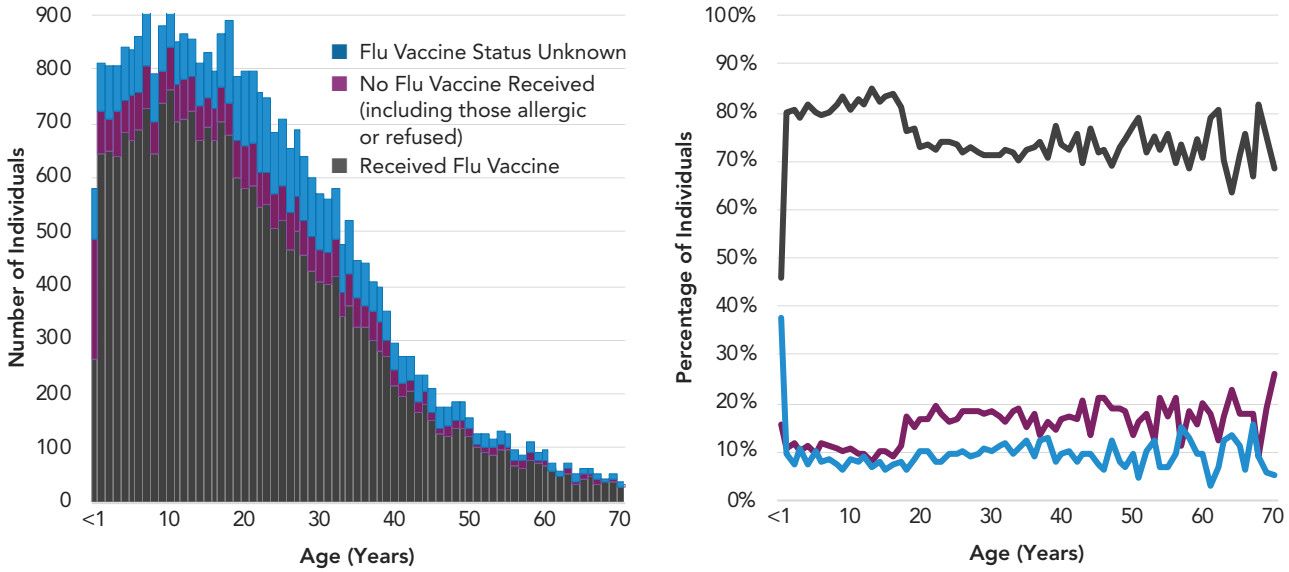
## Percentage of Individuals Evaluated by Multidisciplinary Care Team Members, 2009–2019



The CF Foundation 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 67).

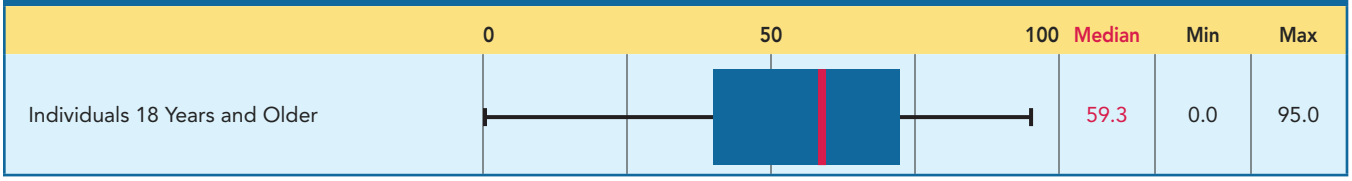
The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices recommends influenza vaccination for all individuals with CF age six months and older.[23] The influenza vaccination rate of people with CF age six months and older is 78.3 percent of the total population and 89.9 percent of those with a known vaccination status (excluding 13.0 percent with unknown status).

**Flu Vaccine Status by Age in Years, 2019** *(Stacked Bar Chart)*



The CF Foundation consensus statement on bone health and disease recommends screening all adults with CF with a DXA scan and subsequent follow-up based on the findings of the baseline scan.[24] Annual screenings are recommended only for individuals with DXA z-scores that are lower than two standard deviations below the mean, with less frequent screening recommended for those with higher values. Therefore, in the figure below, we group five years of data.

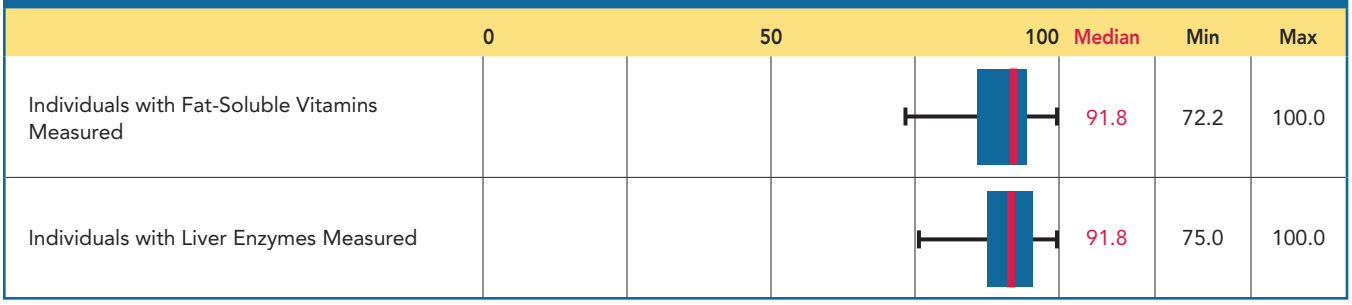
## Percentage of Individuals with a DXA Scan in the Past Five Years, by Center



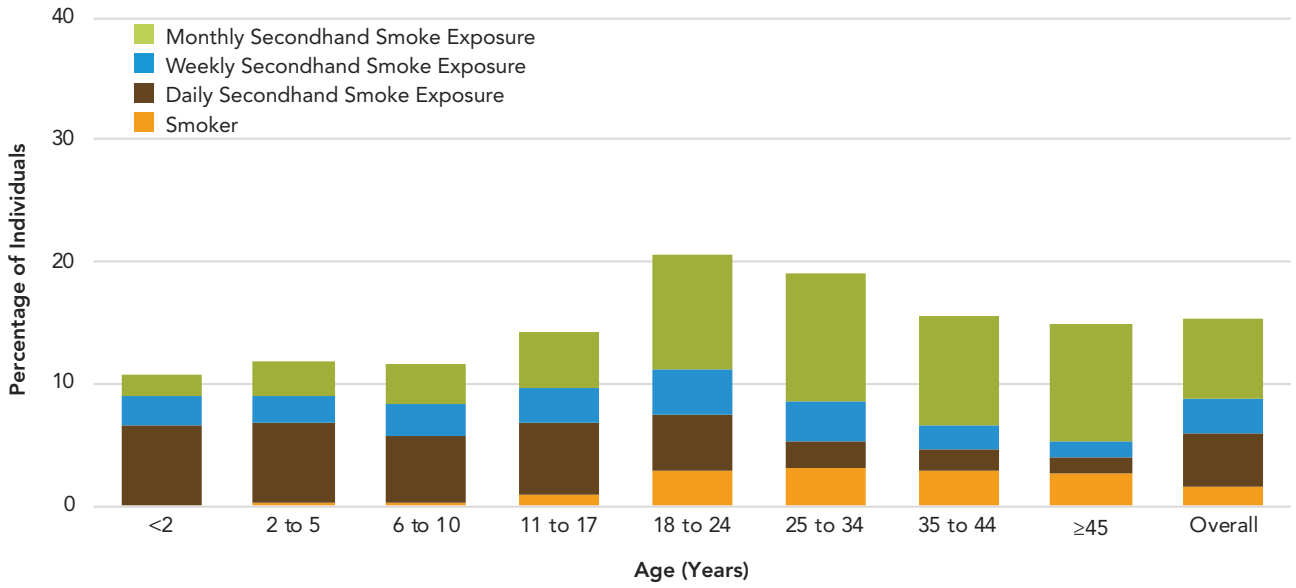

*Includes any DXA scans performed during 2015–2019.*

CF Foundation guidelines recommend annual measurement of fat-soluble vitamins to screen for vitamin deficiency.[20,25] 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.[26] Registry data suggest that these tests are being done on the majority of individuals.

## Percentage of Individuals Screened by or Monitored with Annual Labs, by Center



## Tobacco Smoke Exposure by Age in 2019

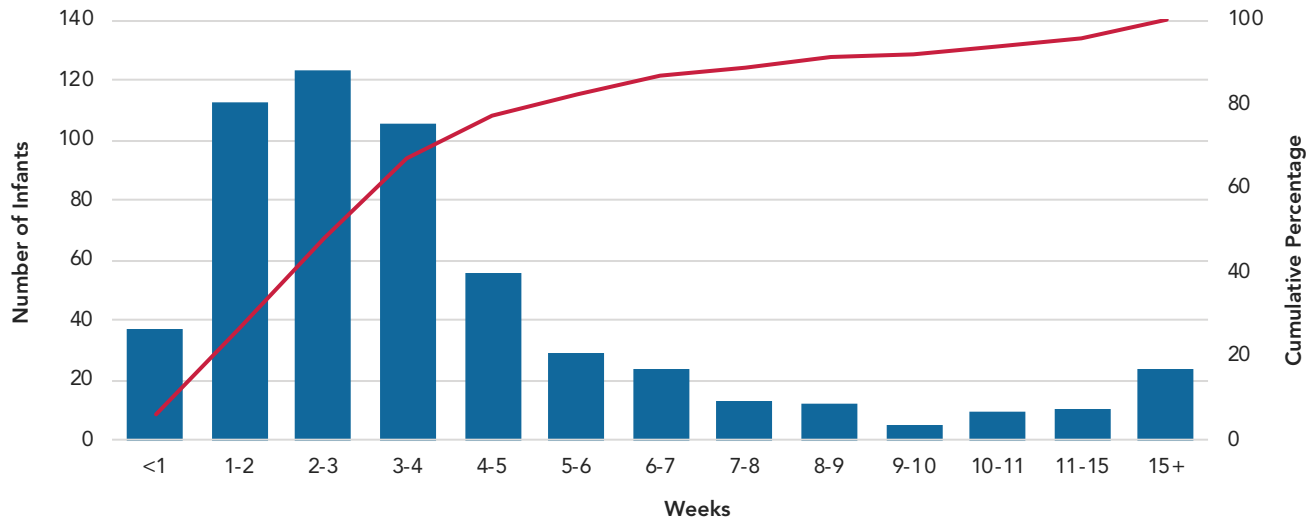



Tobacco smoke and secondhand smoke exposure remain significant concerns, especially for infants and young adults.[27] In 2019, 15.3 percent of individuals with CF reported monthly or more frequent exposure to tobacco smoke, either secondhand or as a smoker. Cigarette smoking prevalence is lower in the CF population than in the general U.S. population; 1.9 percent of adults with CF are smokers, compared with 16.0 percent in the general population in 2019.[28] Smoke exposure was unknown for 34.6 percent of individuals with CF, who were excluded from the analyses.

## Infant Care Guidelines

The CF Foundation recommends that evaluation and treatment of infants detected by newborn screening should 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.[5] Of infants detected by newborn screening in 2018, 89.3 percent had their first clinic encounter, care episode, or sweat test (first CF event) within 60 days of birth.

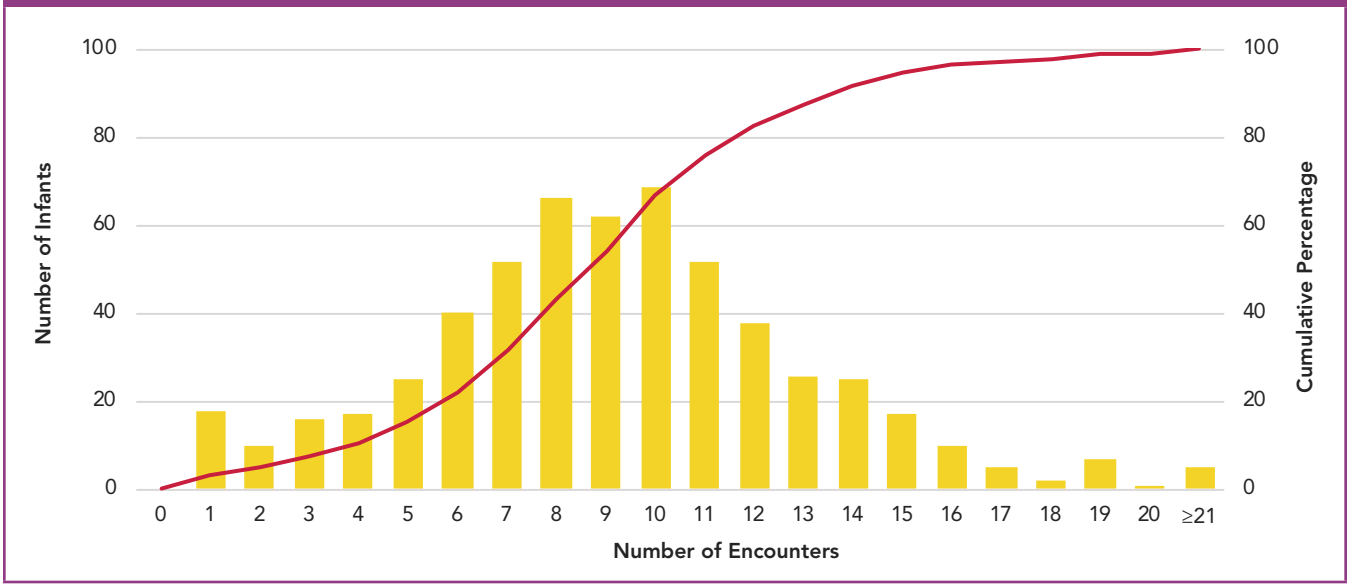
**Time from Birth to First Recorded Sweat Test for Infants with CF Born in 2018 and Detected by Newborn Screening** (n=563)




*This chart shows data for children born in 2018 because a full year of data is available for these individuals. Median time to first CF event for these individuals is 21 days.*

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.[5] Therefore, we expect infants with CF detected by NBS to have 9 to 12 visits in the first year of life. There is marked variation in the number of encounters for individuals in the first year of life across the CF care center network.

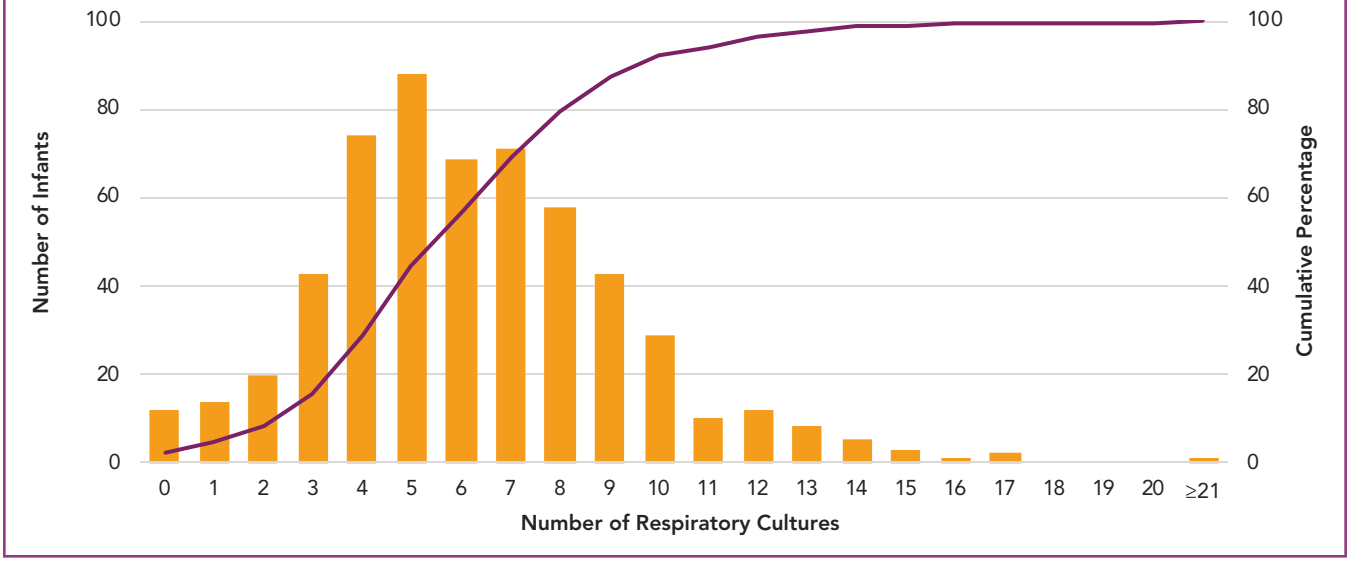
## Number of Encounters in the First Year of Life for Infants with CF Born in 2018 and Detected by Newborn Screening (n=563)




*The chart shows data for children born in 2018 because a full year of data is available for these individuals. The median number of visits in the first year of life is nine.*

Respiratory cultures are being collected at the majority of clinic visits for infants with CF. Infant care guidelines recommend that cultures be performed at least quarterly during the first two years of life.[5]

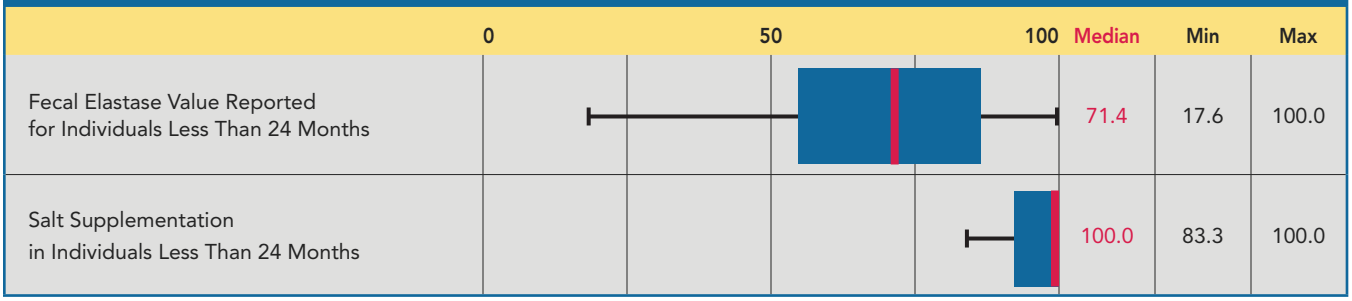
## Number of Respiratory Cultures in the First Year of Life for Infants with CF Born in 2018 and Detected by Newborn Screening (n=563)



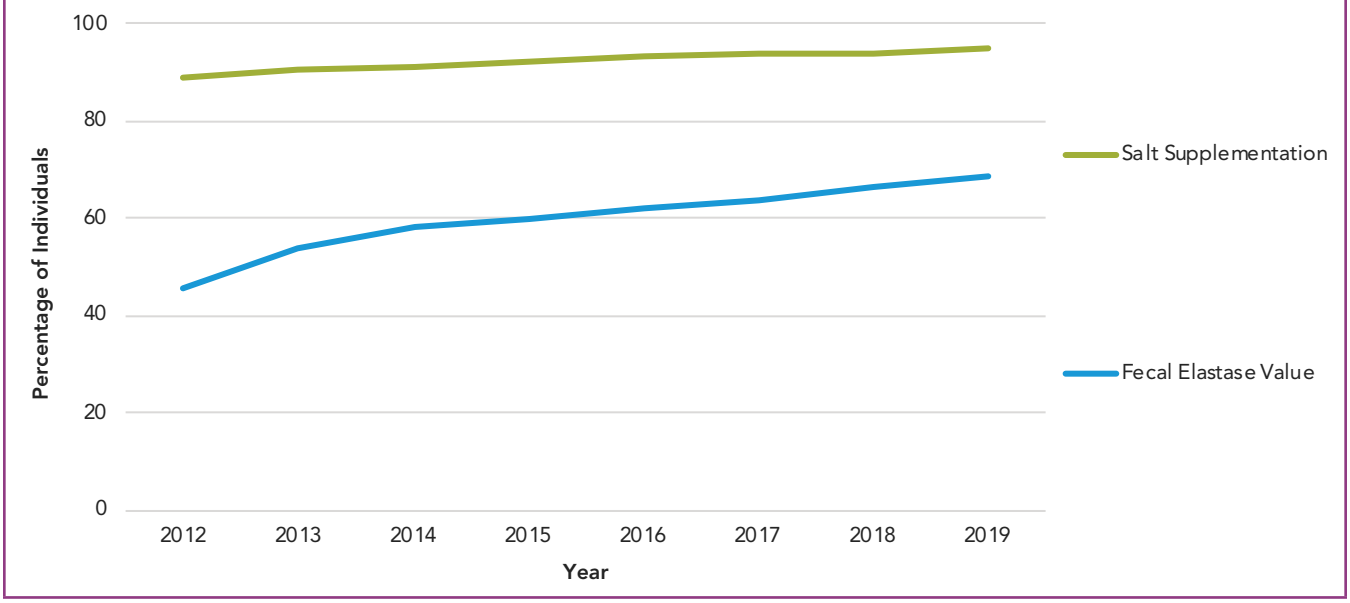

*The chart shows data for children born in 2018 because a full year of data is available for these individuals. The median number of cultures in the first year of life is six.*

Fecal elastase testing, which provides an objective measure of pancreatic function, is recommended in the infant care guidelines.[5] 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 widely followed across the CF care center network.

## Infant Care Guidelines, by Center




## Testing and Therapies for Individuals Under 24 Months of Age, 2012-2019



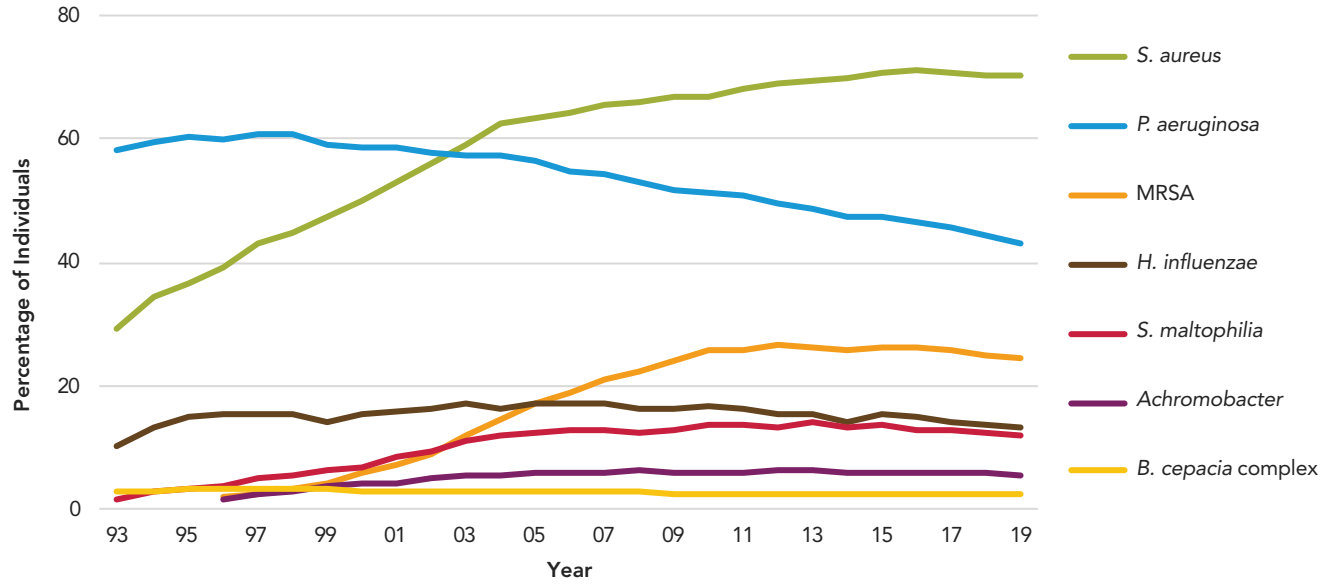
## MICROBIOLOGY

*This section provides information on trends in CF airway pathogens over time and by age group for individuals who never received a lung 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.*[29]

The prevalence of *Pseudomonas aeruginosa* (*P. aeruginosa* or PA) continues to decrease. This may relate in part to widespread implementation of therapy to eradicate initial acquisition.[22,29] Despite this, the prevalence of infection with multidrug-resistant *P. aeruginosa* (MDR-PA) has remained constant.

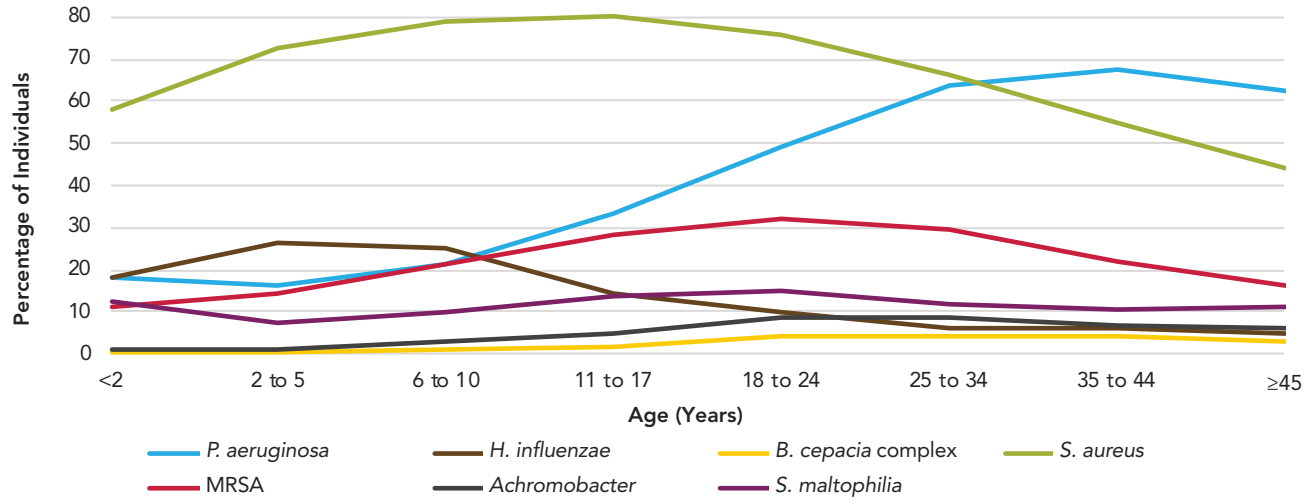
Some of the increase in *Staphylococcus aureus* (*S. aureus*) may be due to improved microbiologic practices for detection and reporting of Gram-positive organisms. From 2000 to 2010, there was a significant increase in the number of individuals with CF with a positive culture for methicillin-resistant *S. aureus* (MRSA). Since 2010, prevalence appears to have plateaued. The stabilization of prevalence is potentially due to increased awareness and infection prevention and control strategies.

**Prevalence of Respiratory Microorganisms, 1993–2019**



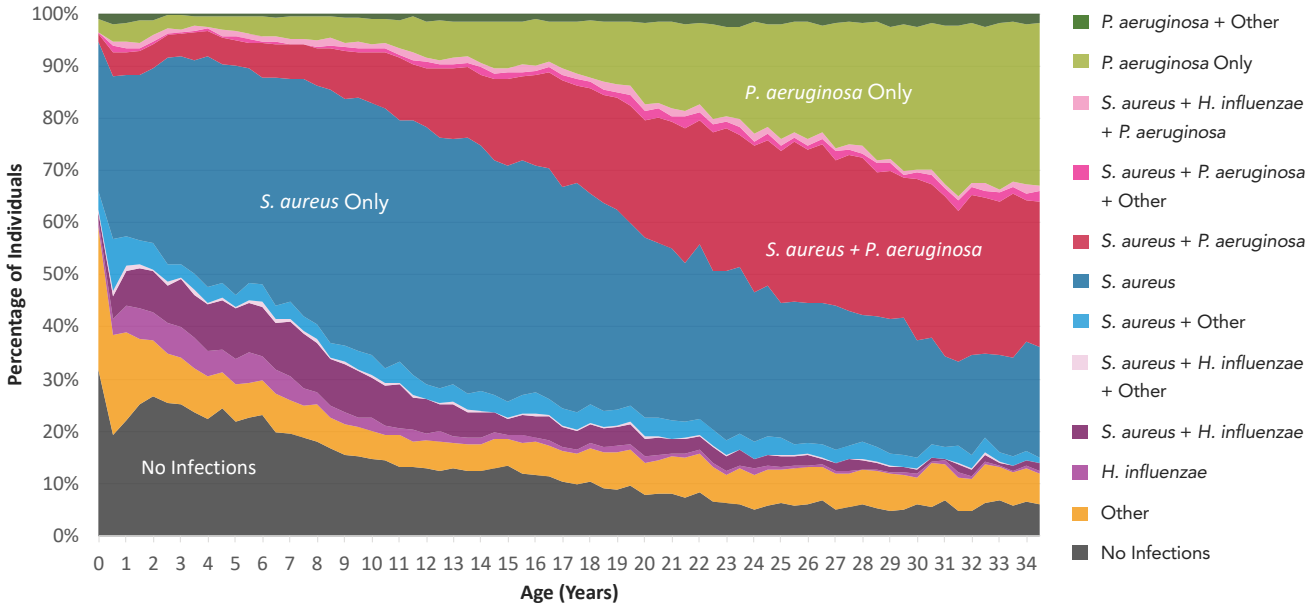
The graph shows the proportion of individuals in various age groups who cultured positive for the bacterial species indicated during 2019.

## Prevalence of Respiratory Microorganisms by Age Cohort, 2019




The microorganisms observed in bacterial cultures change as individuals age. Even at very young ages, more than 60 percent of individuals have at least one microorganism, and this increases to more than 80 percent in older ages. *S. aureus* is the most common microorganism overall and, as individuals age, it is commonly observed in concert with *P. aeruginosa*.

## Microbial Diversity by Age, Birth to 34 Years

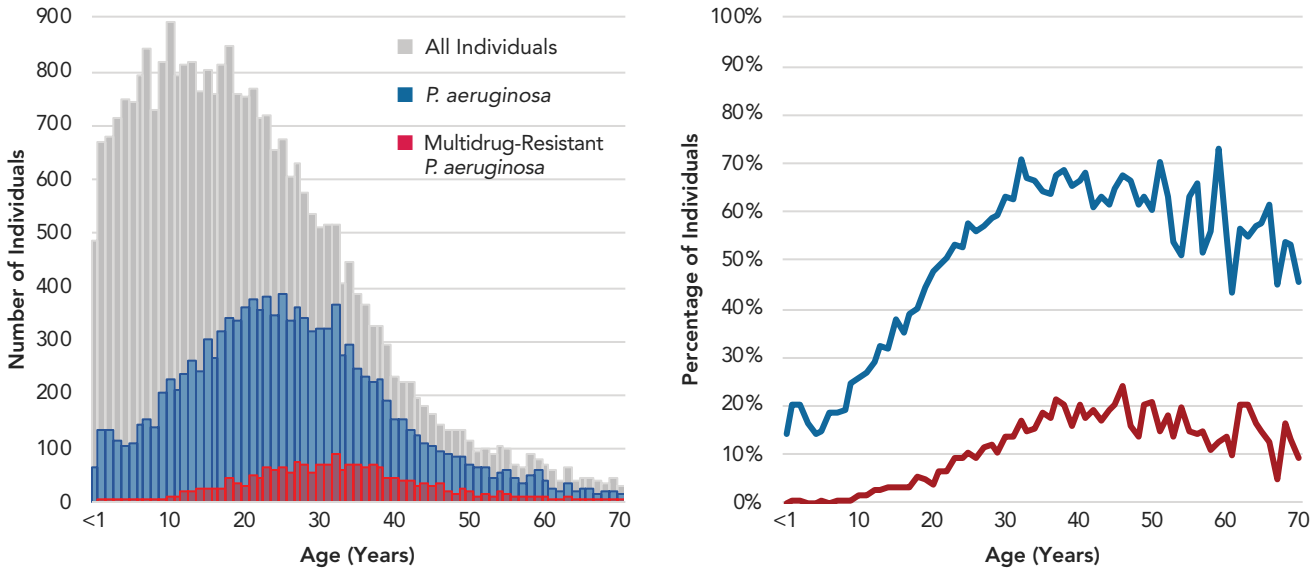


## *Pseudomonas aeruginosa*

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 (44.8 percent had a positive culture in 1999 compared with 25.1 percent in 2019). Many individuals with CF now transition to adult care without *P. aeruginosa* in their respiratory tract.

Rates of MDR-PA infection are greatest in older adolescents and adults with CF. This finding likely reflects cumulative exposure to antibiotics. The clinical significance of this drug resistance is unclear. Among the individuals with CF who had at least one bacterial culture in 2019, 7.3 percent were reported to have MDR-PA. Among the individuals with CF with a *P. aeruginosa* infection in 2019, 16.9 percent were reported to have MDR-PA.

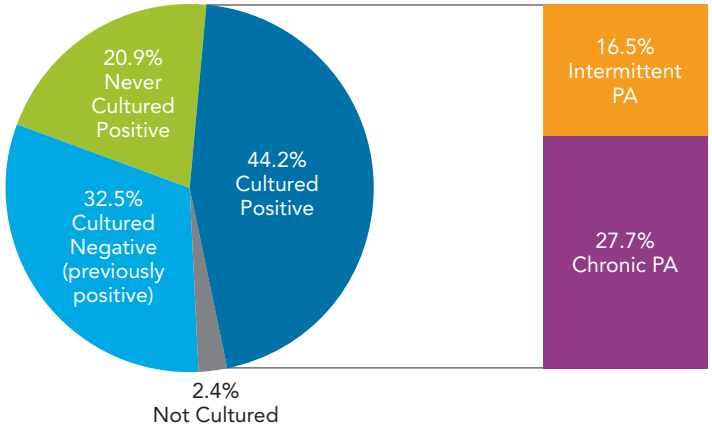
### *P. aeruginosa* and Multidrug-Resistant *P. aeruginosa* by Age in Years, 2019




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

The Leeds criteria are used to categorize individuals on the basis of *P. aeruginosa* infection status.[30] The Leeds criteria categories are "never having a positive *P. aeruginosa* culture," "free of a positive *P. aeruginosa* culture in the past 12 months," "intermittent infection" (less than 50 percent of their cultures in the past year were positive for *P. aeruginosa*), and "chronic infection" (more than 50 percent of their cultures in the past year were positive for *P. aeruginosa*).

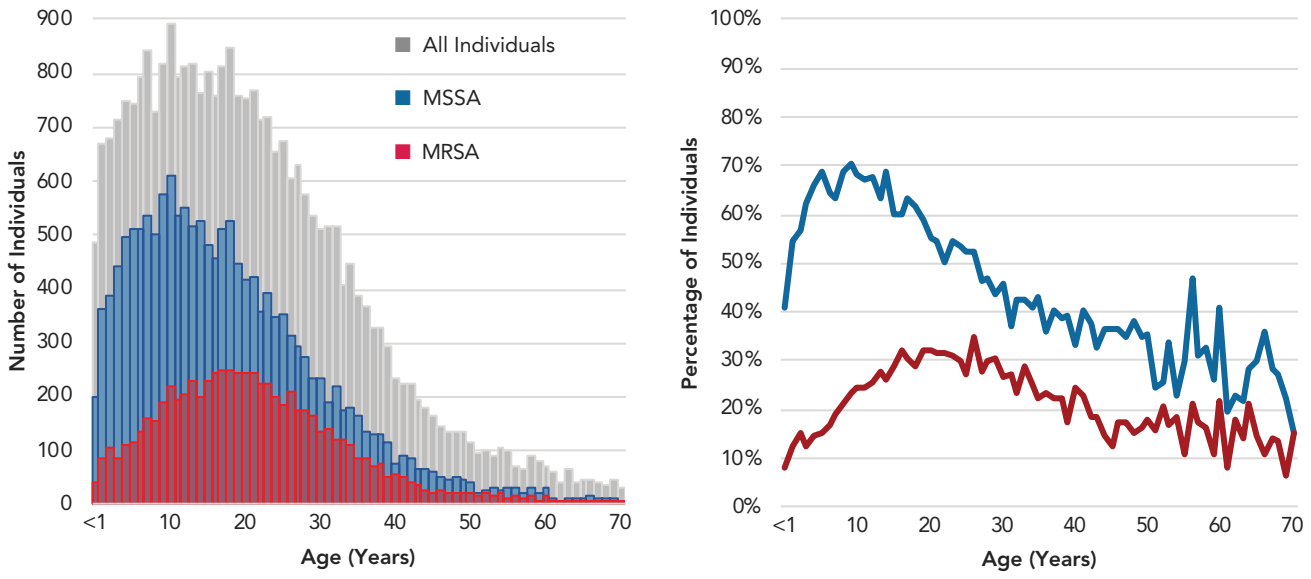
### *P. aeruginosa* Status Using Leeds Criteria, 2019




## *Staphylococcus aureus*

Overall, more than half of individuals had at least one culture positive for methicillin-sensitive *S. aureus* (MSSA) in 2019. This chart shows that the highest prevalence of MRSA occurs in individuals between the ages of 10 and 30, whereas MSSA peaks among those younger than 15.

### MSSA and MRSA by Age in Years, 2019

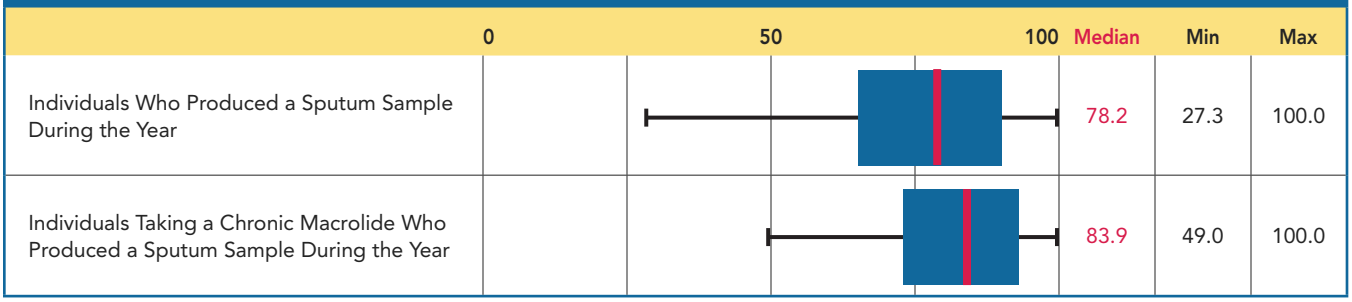


## Nontuberculous Mycobacteria

Prevalence of nontuberculous mycobacteria (NTM) infections is increasing in the general population.[31] Since 2010, the Registry has collected more robust information on mycobacterial cultures and NTM infections.

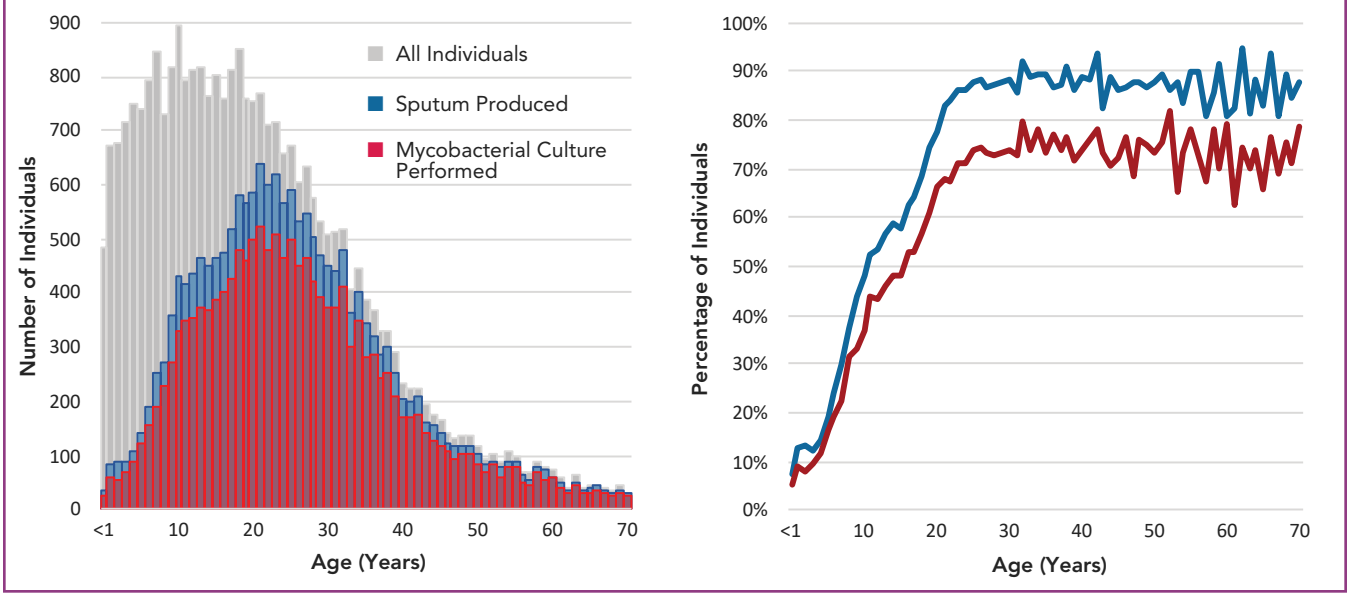
The CF Foundation/European Cystic Fibrosis Society Guidelines Committee recommends that individuals with CF who are able to expectorate be cultured for NTM infections annually.[32] Individuals should also be screened before and six months after beginning azithromycin and annually thereafter.[2] The data show improvement in screening rates over time, but wide variation by CF care center persists in these measures.

### Percentage of Individuals with a Mycobacterial Culture, by Center



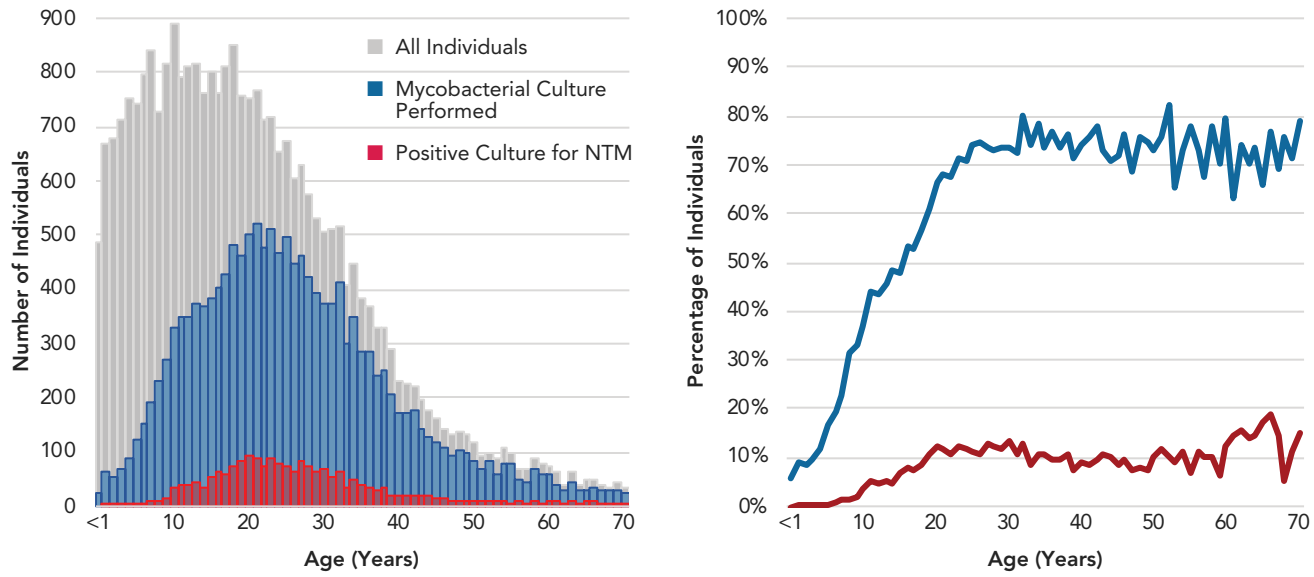

A throat swab is insufficient for a mycobacterial culture, so a patient must be able to produce sputum for this culture to be performed. A majority (79.5 percent) of the individuals who produced a sputum culture for a bacterial culture also had a mycobacterial culture performed during the year.

### Sputum Produced and Mycobacterial Cultures by Age in Years, 2019



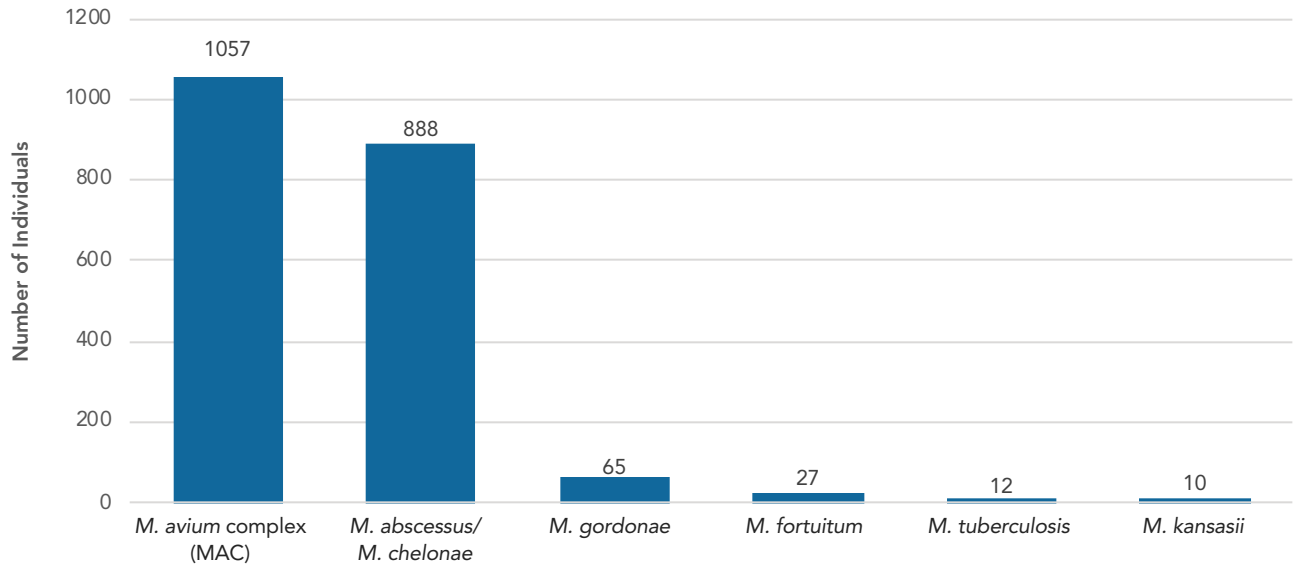
Among those cultured, the percentage of positive cultures increases until age 20, after which the percentage with a positive culture plateaus and remains relatively constant until age 60.

## Positive Cultures for NTM by Age in Years, 2019




Of the 15,497 individuals who had a mycobacterial culture performed in 2019, 2,149 (13.9 percent) had a mycobacterial species isolated one or more times. The relative proportion of *M. abscessus* isolated in 2019 is higher than reported more than a decade ago in a CF Foundation-supported multicenter prevalence study.[33]

## Mycobacterial Species Isolated in 2019



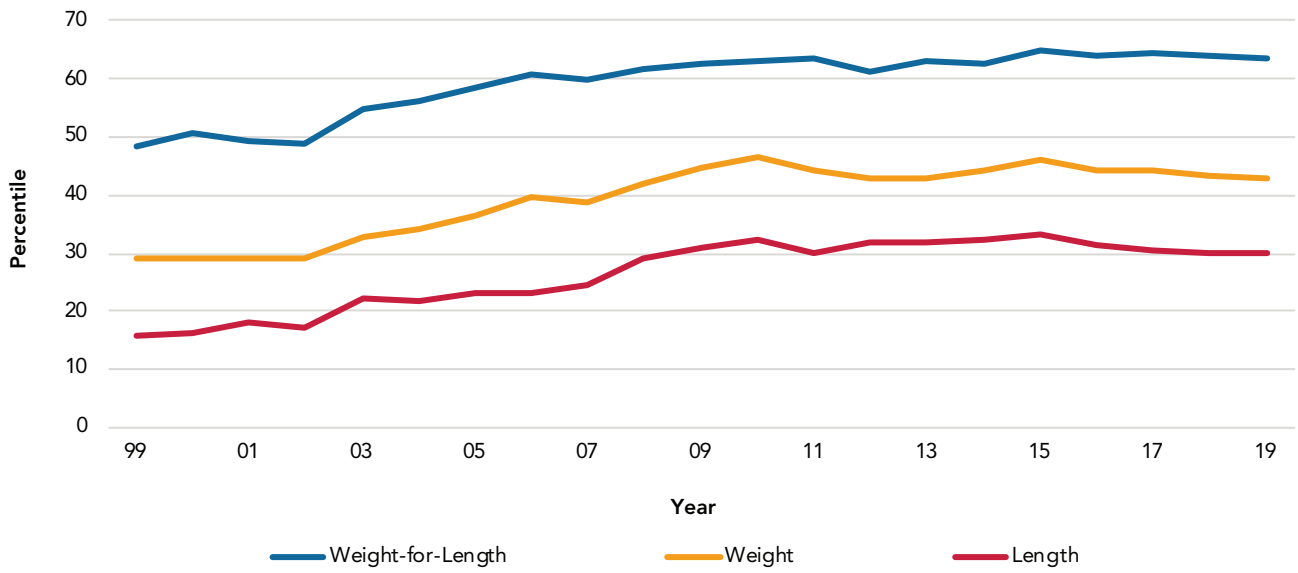

*Data are not mutually exclusive. Some individuals had more than one species isolated in 2019.*

## 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. Overall improvements in nutritional metrics are observed for all ages. Recent CF Foundation evidence-informed guidelines recommend enteral tube feeding as a means to improve age-dependent anthropometrics and nutrition in individuals with CF who are unable to consume adequate nutrition to meet goals.*[34]

Goals for CF Foundation weight-for-length and 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 less than 24 months of age.[35] WHO growth curves are used to report the data below.

**Median WHO Nutritional Outcome Percentiles for Infants Under 24 Months, 1999–2019**



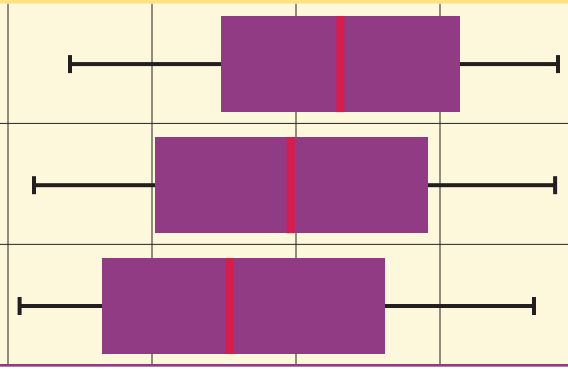
The following charts show the population-level variation in infants for WHO weight-for-length, weight, and length percentiles by age. As would be expected for a large population, there is substantial variation observed for all three metrics. The median values for weight-for-length and BMI percentile are above the recommendation of 50th percentile. However, we still see evidence that infants' and children's growth is below what is expected for the U.S. population.

## All Individuals, WHO Nutritional Outcomes for Infants Under 24 Months


| | Median | 5th Percentile | 95th Percentile |
|---|---|---|---|
| Weight-for-Length *N=1,682* | 63.7 | 14.7 | 96.2 |
| Weight Percentile *N=1,685* | 42.8 | 4.1 | 91.8 |
| Length Percentile *N=1,685* | 30.2 | 1.1 | 85.8 |

The goal established by the CF Foundation nutrition guidelines for children age 2 to 19 years is a BMI percentile at or above 50 using CDC growth curves.[25] The median BMI percentile is above the 50th percentile; however, length percentile remains well below that of the general population.

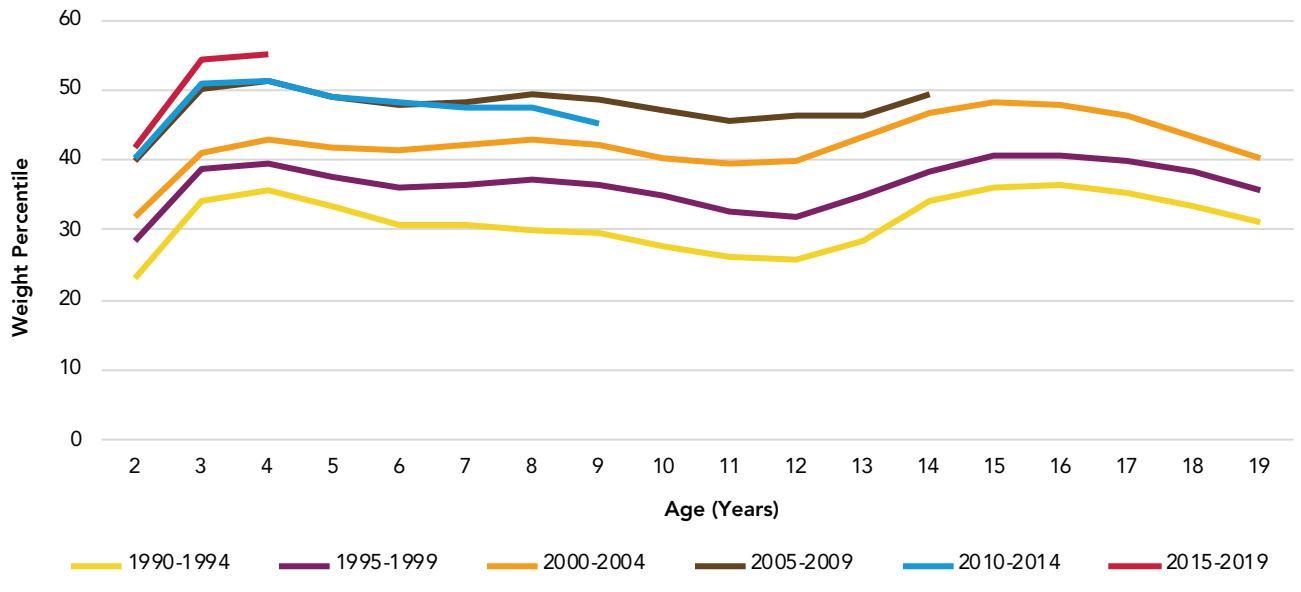
## All Individuals, CDC Nutritional Outcomes for Individuals 2 to 19 Years



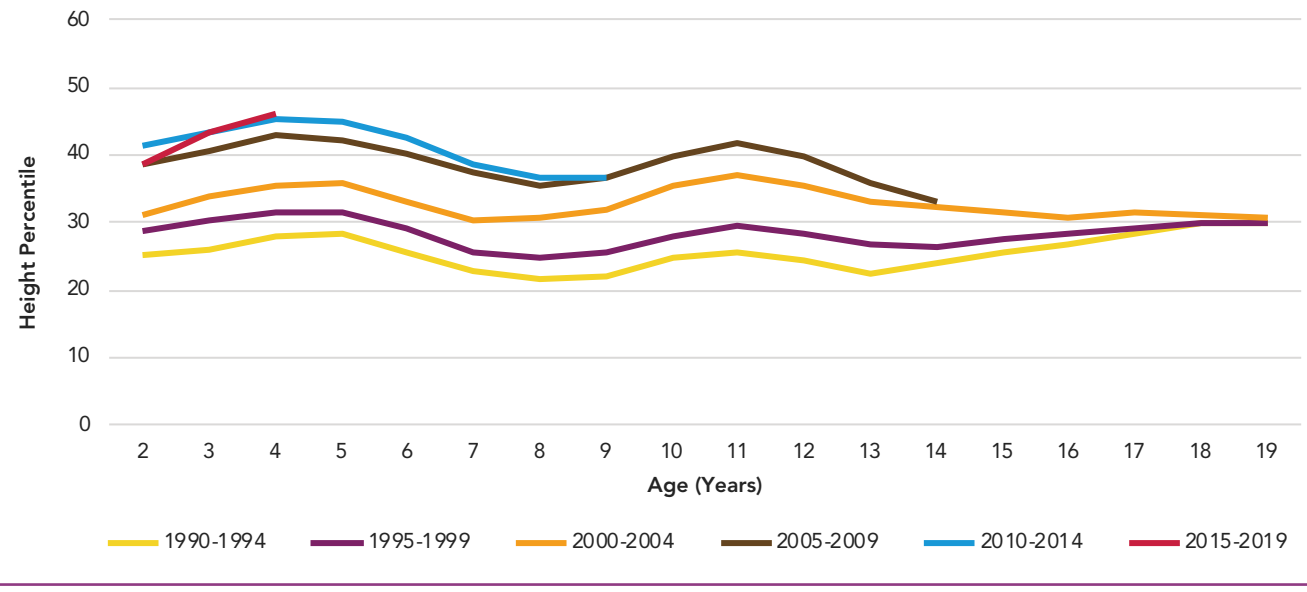

| | Median | 5th Percentile | 95th Percentile |
|---|---|---|---|
| BMI Percentile *N=13,947* | 58.4 | 10.5 | 95.7 |
| Weight Percentile *N=14,060* | 49.3 | 4.4 | 94.9 |
| Height Percentile *N=14,057* | 38.4 | 2.2 | 91.7 |

For individuals born between 1990 and 2004, we observed improved weight and height percentiles with successive birth cohorts. Beginning with birth cohorts in 2005, there have been fewer observed increases with subsequent birth cohorts. For height, the most notable improvements were seen in the youngest cohorts. More recently, there is less change between cohorts. This is potentially a result of the stabilization of improvements observed from early intervention due to newborn screening.[36,37]

## Median CDC Weight Percentile, by Age and Birth Cohort in 2019

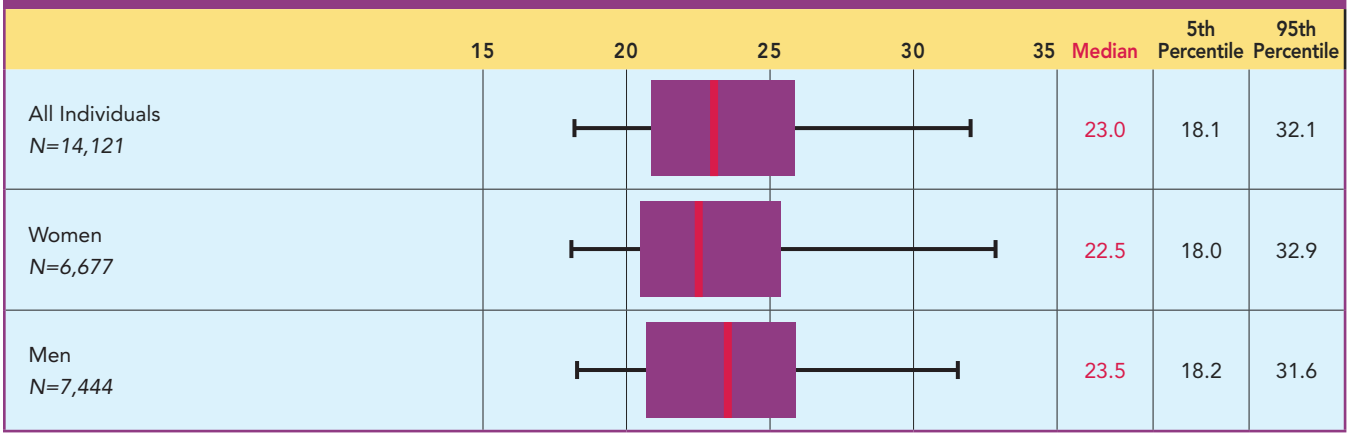



## Median CDC Height Percentile, by Age and Birth Cohort in 2019



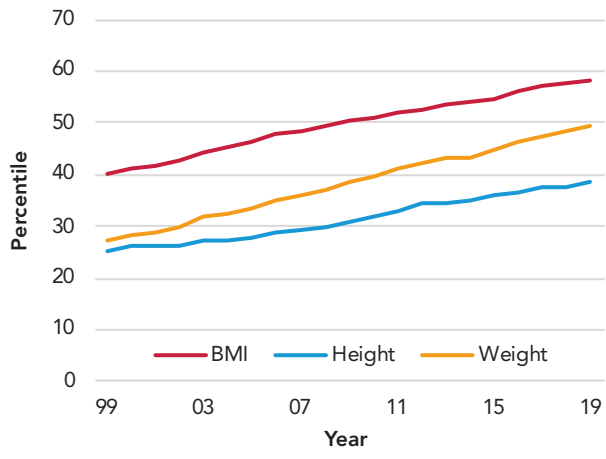
The BMI goal established by the CF Foundation nutrition guidelines is at or above 22 for women and 23 for men age 20 years and older.[25] Improvements in nutrition and dietary interventions have substantially decreased the percentage of adults that are currently malnourished, defined as a BMI less than 18.5 (6.6 percent in 2019 compared to 18.2 percent in 1999). However, currently, 31.4 percent of adults have a BMI in the range categorized by CDC as overweight (23.1 percent) or obese (8.3 percent), with a higher prevalence in men (35.5 percent) than women (27.1 percent). The percentage of adults who are overweight or obese has more than doubled in the past 20 years (12.8 percent in 1999).

## BMI Value for Adults 20 Years and Older

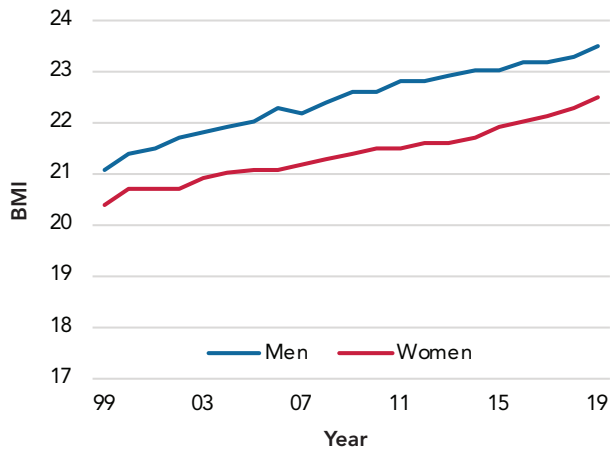



Significant progress in nutritional outcomes continues for all people with CF. Aging of the CF population and a greater number of late diagnoses with genotypes associated with milder disease may be contributing to the trend in adult nutritional outcomes shown below.

## Median Nutritional Outcomes Percentiles for Individuals 2 to 19 Years, 1999–2019

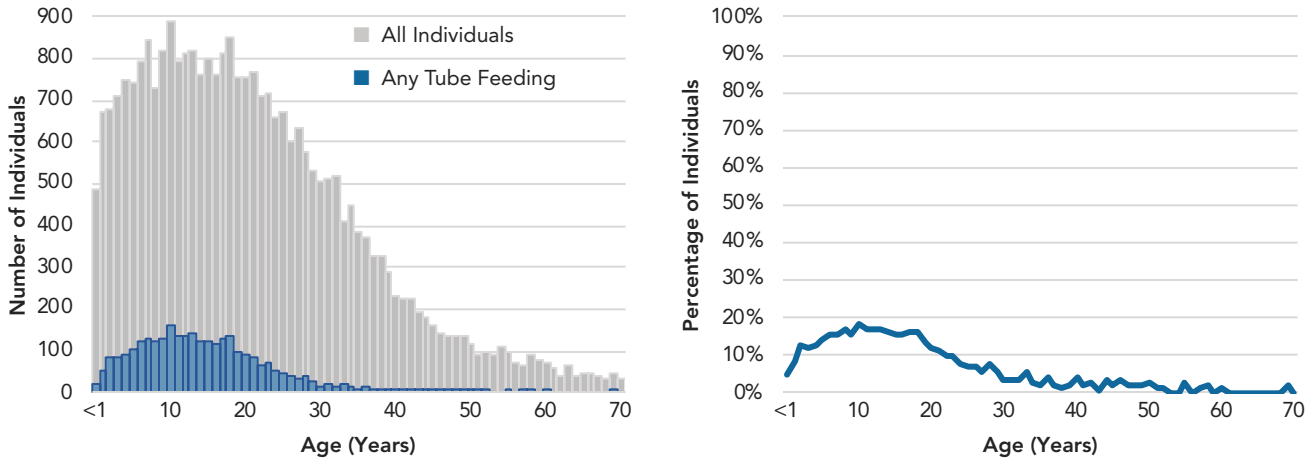



## Median BMI Values for Adults 20 Years and Older, 1999–2019



For some individuals with CF, tube feeding is a tool to improve nutritional outcomes. Use of tube feeding is most common in children and adolescents with up to 20 percent reporting tube feedings. Among individuals who use tube feeding, the two most commonly recommended strategies for using pancreatic enzymes were administering the enzymes by mouth before and after the feeding and infusing the tube feeding through an immobilized lipase cartridge.

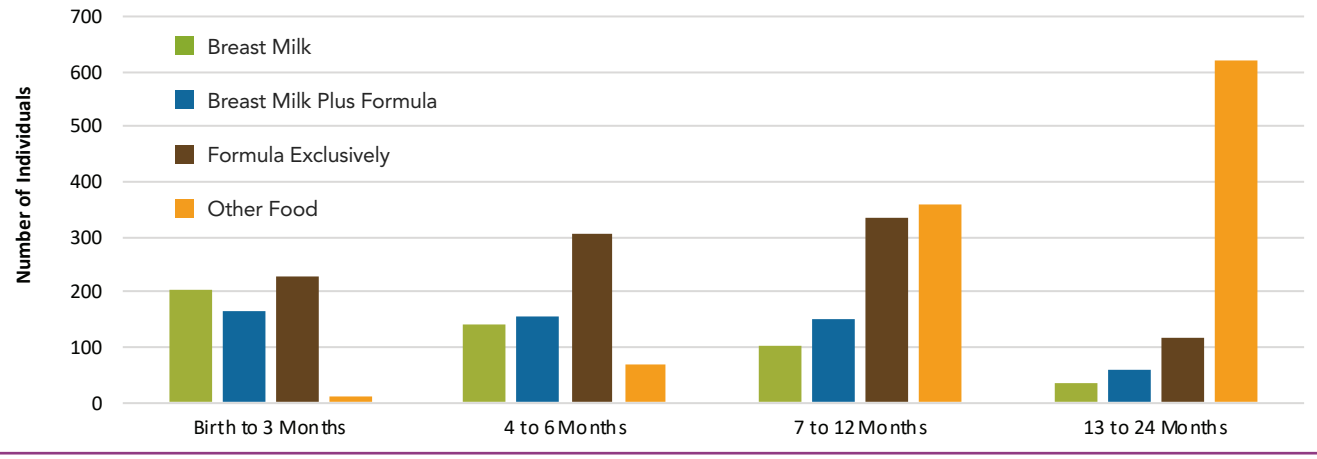
## Tube Feeding by Age in Years, 2019




## Infant Feeding

The majority of infants with CF receive formula feeding 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 feeding 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.[5]

## Form of Feeding by Age in 2019*




**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.*

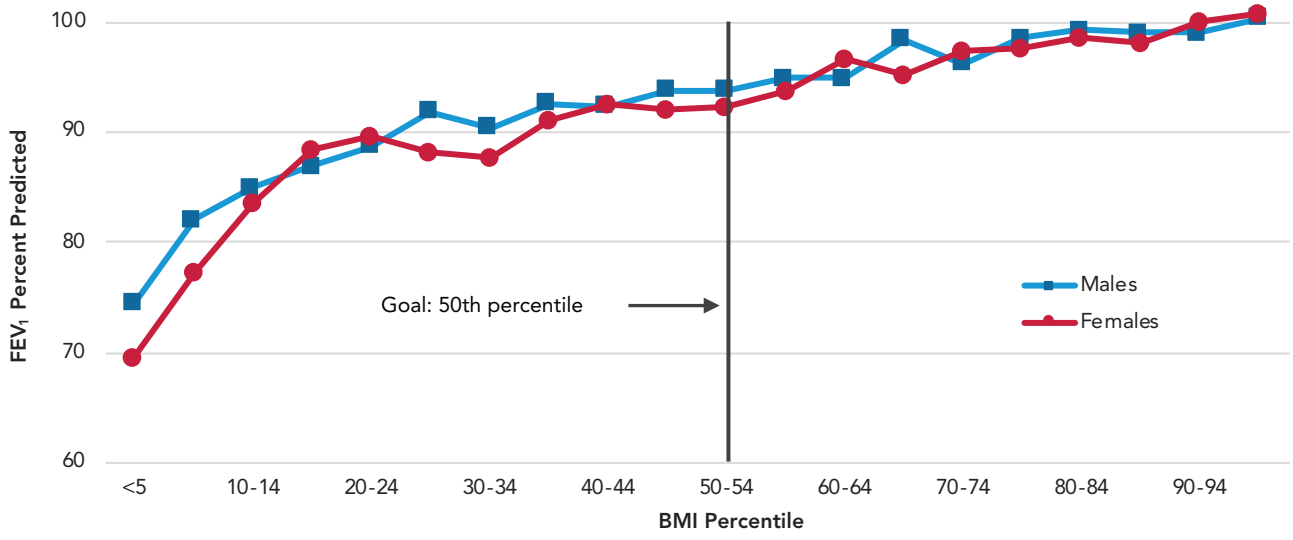
# PULMONARY AND NUTRITIONAL OUTCOMES

*Pulmonary and nutritional outcomes are two key measures of CF health. These metrics are the primary focus of quality improvement work within the CF care center network. The data show that for all people with CF, better pulmonary function, and higher BMI percentile are associated.*

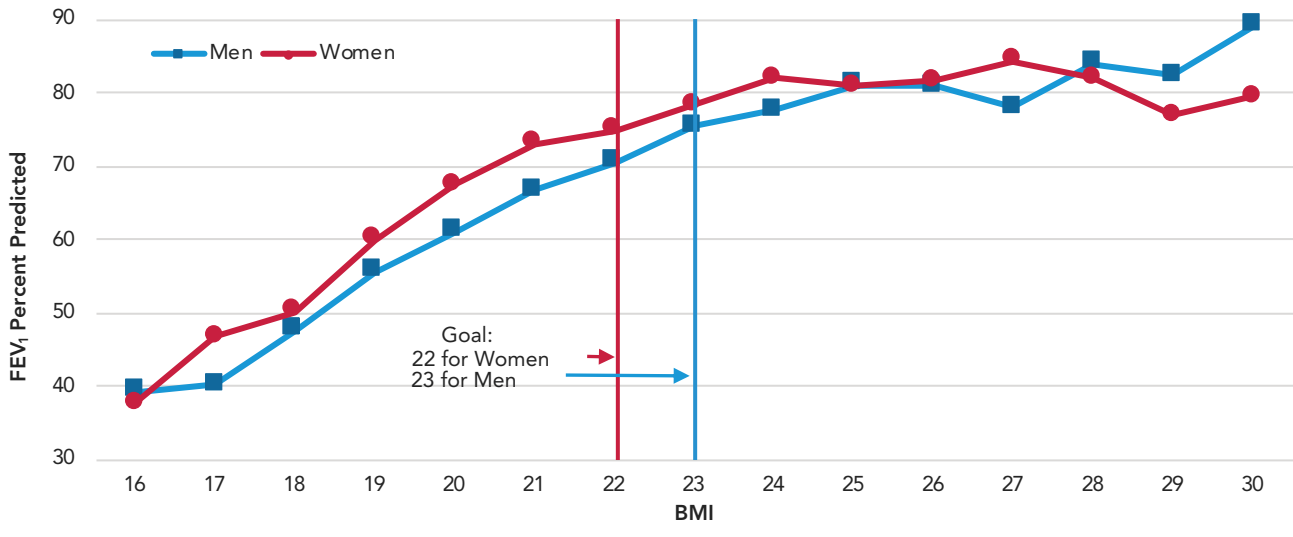
*Pulmonary and nutritional goals[25] are as follows:*

- *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 2019

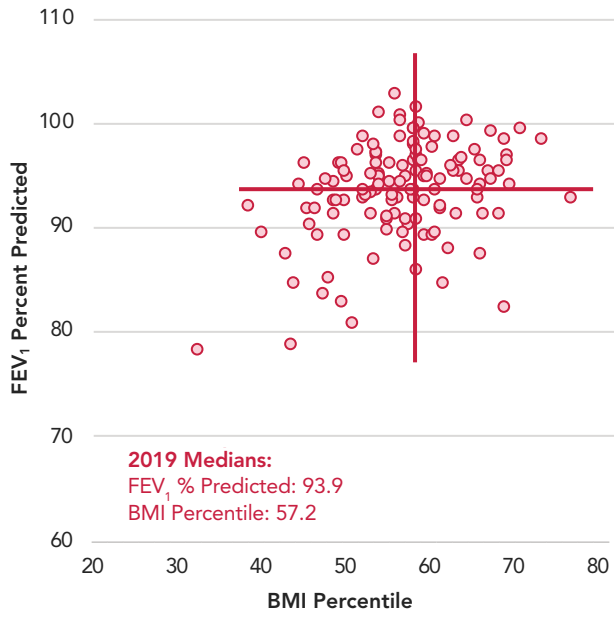



## $FEV_1$ Percent Predicted vs. BMI Value for Adults 20 to 40 Years in 2019

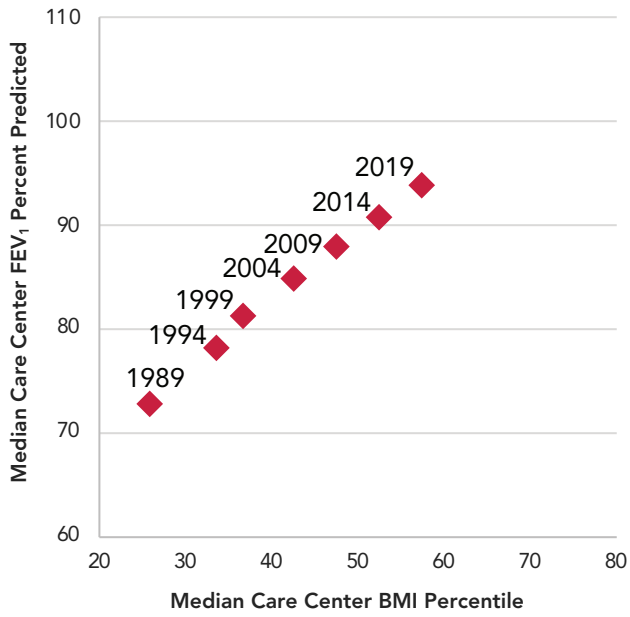


The figures below on the left show median BMI percentile and $FEV_1$ percent predicted values for each center in 2019. The figures on the right show how median values for all centers have improved over the last 30 years.

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

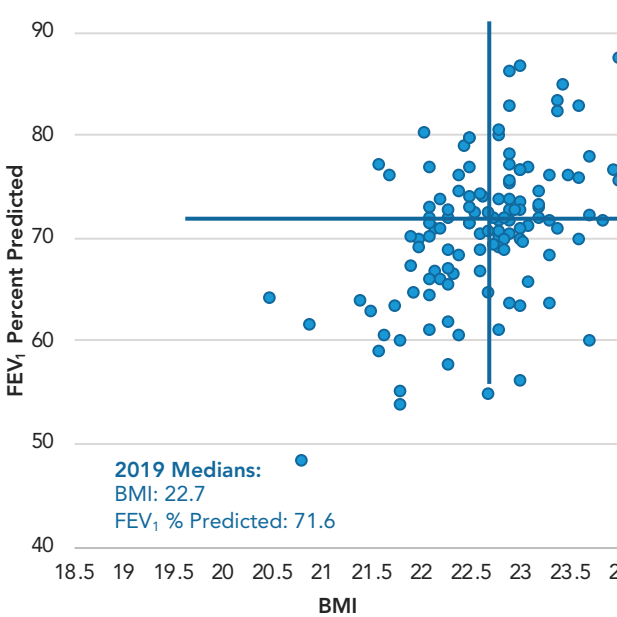



## Median Care Center Value for Individuals 6 to 19 Years, 1989-2019

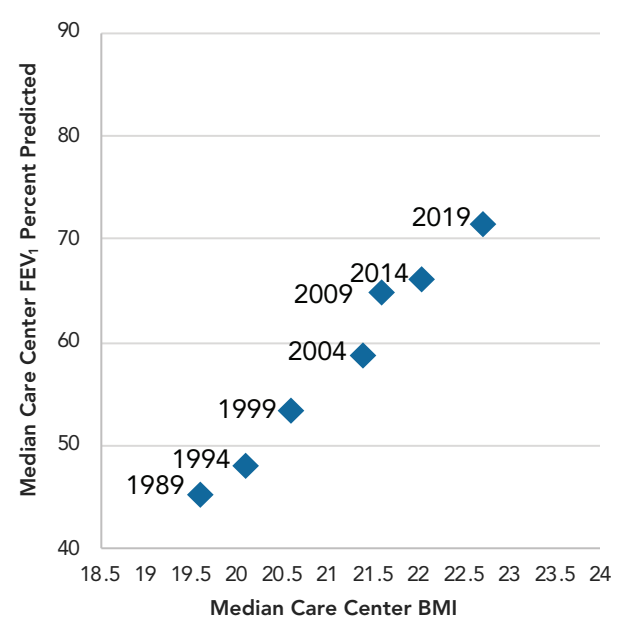



*In prior years, this chart reported data on individuals aged 6 to 17 years. As a result, it appears that the median $FEV_1$ percent predicted has decreased between 2018 and 2019.*

## 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, 1989-2019



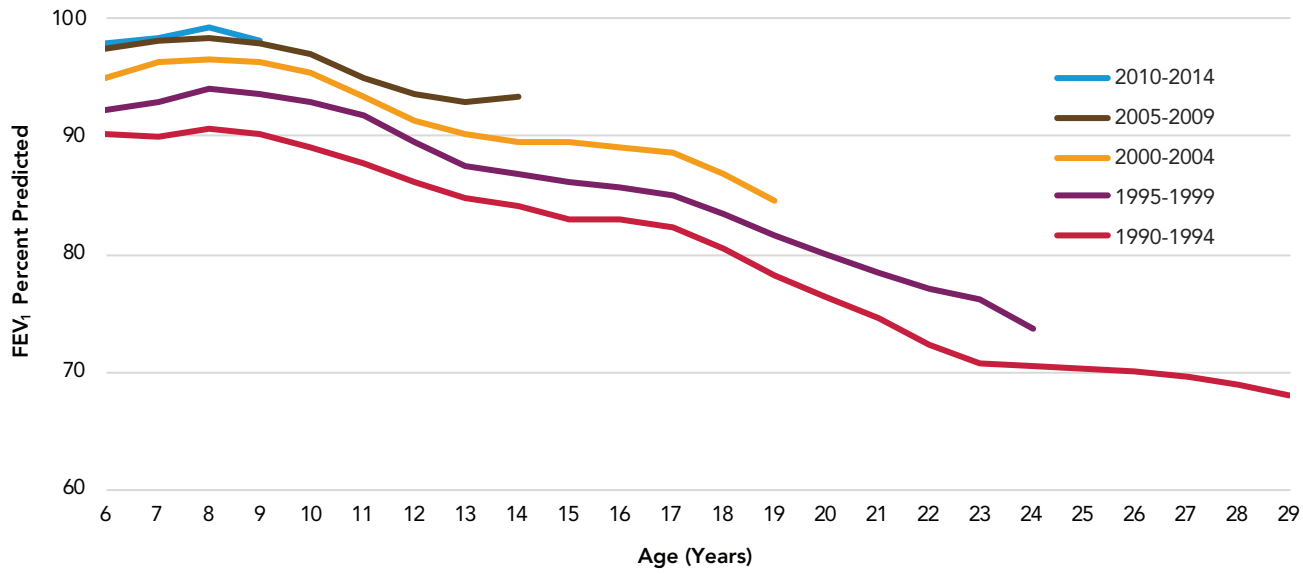
# PULMONARY FUNCTION

*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 never had a lung transplant, as well as variations in pulmonary function across CF care centers. Pulmonary function is measured using the $FEV_1$ percent predicted and calculated using the Global Lung Initiative (GLI) reference equations.[1]*

*Successive birth cohorts show improved pulmonary function across all ages for individuals who are old enough to perform reliable pulmonary function testing. The majority of those aged 18 years now have an $FEV_1$ percent predicted greater than or equal to 70.*

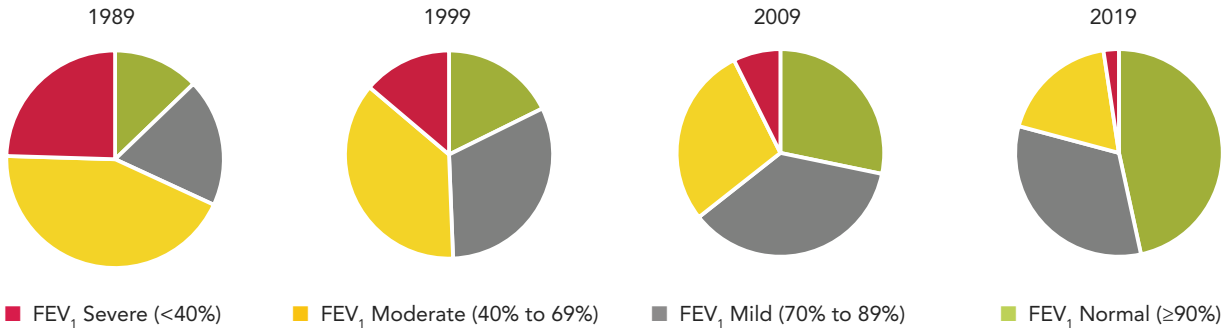
$FEV_1$ percent predicted is steadily improving and currently is greater than 90 percent predicted into early adolescence.

**Median $FEV_1$ Percent Predicted, by Age and Birth Cohort**



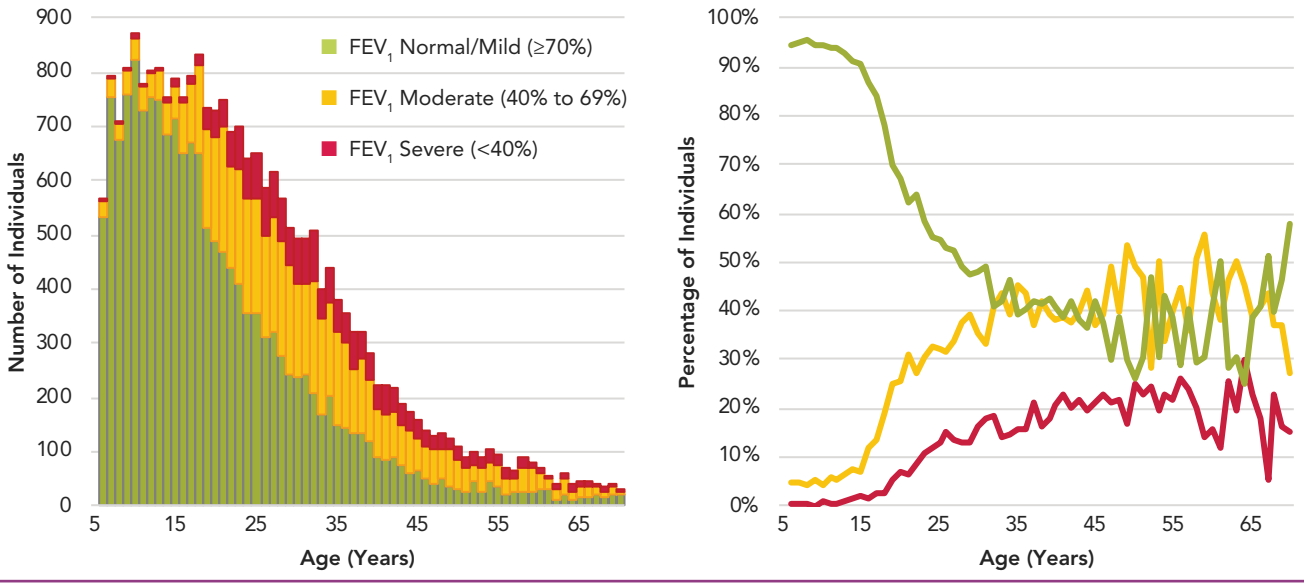
The proportion of people with CF aged 18 years who are in the normal/mild lung disease category ($FEV_1$ ≥70 percent predicted) has increased from 33.8 percent in 1989 to 78.3 percent in 2019. The proportion in the severe lung disease category ($FEV_1$ <40 percent predicted) has decreased from 24.0 percent in 1988 to 2.6 percent in 2019.

## Median $FEV_1$ Percent Predicted in 18-Year-Olds, 1989–2019



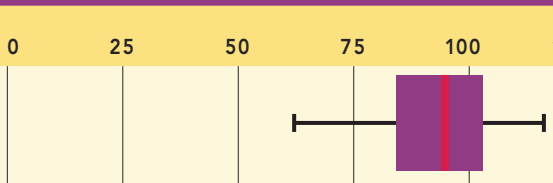

It is important to point out that spirometry is not a sensitive measure of early lung disease in CF. With that caveat in mind, the vast majority of children have normal or "mild" impairment in pulmonary function. This proportion decreases until age 35, when the population has nearly equal proportions of individuals with normal/mild or moderate lung disease.

## Pulmonary Function Impairment by Age in Years, 2019 (Stacked Bar Chart)



The median $FEV_1$ percent predicted among individuals aged 6 to 17 is 95.2 percent. About half of the adults have an $FEV_1$ percent predicted that is greater than 70.0 percent, representing mild disease. However, a wide variation in lung function is observed among adults with a quarter having a $FEV_1$ percent predicted less than 50.0 percent.

## $FEV_1$ Percent Predicted



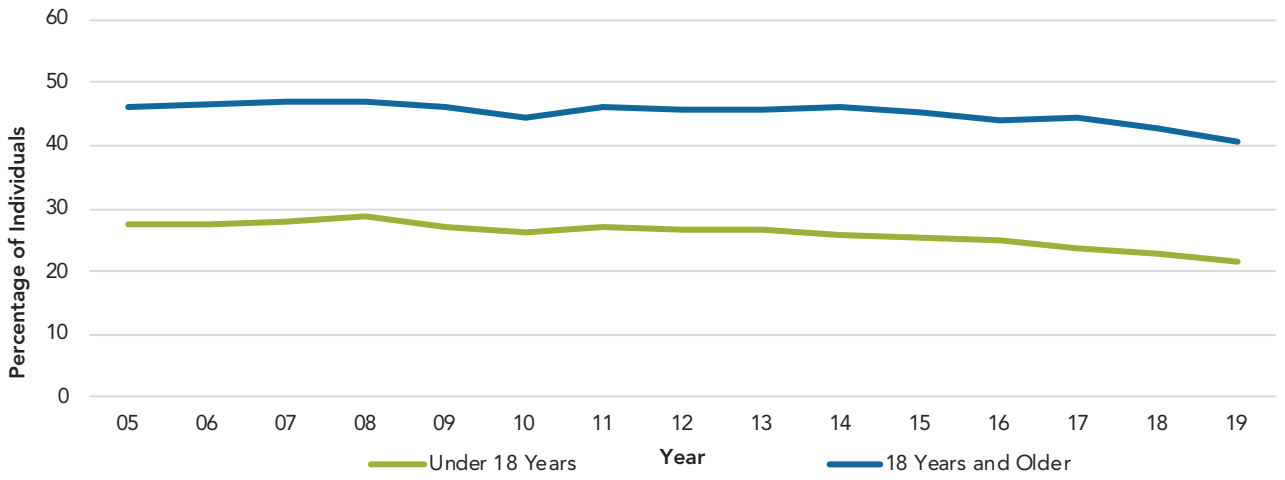

| | Median | 5th Percentile | 95th Percentile |
|---|---|---|---|
| All Individuals 6 to 17 Years *N=9,343* | 95.2 | 61.8 | 117.5 |
| All Individuals 18 Years and Older *N=15,307* | 71.1 | 29.8 | 106.5 |

## 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 among individuals who never had a lung transplant, as well as variation in exacerbation rates and treatment characteristics by CF care center.

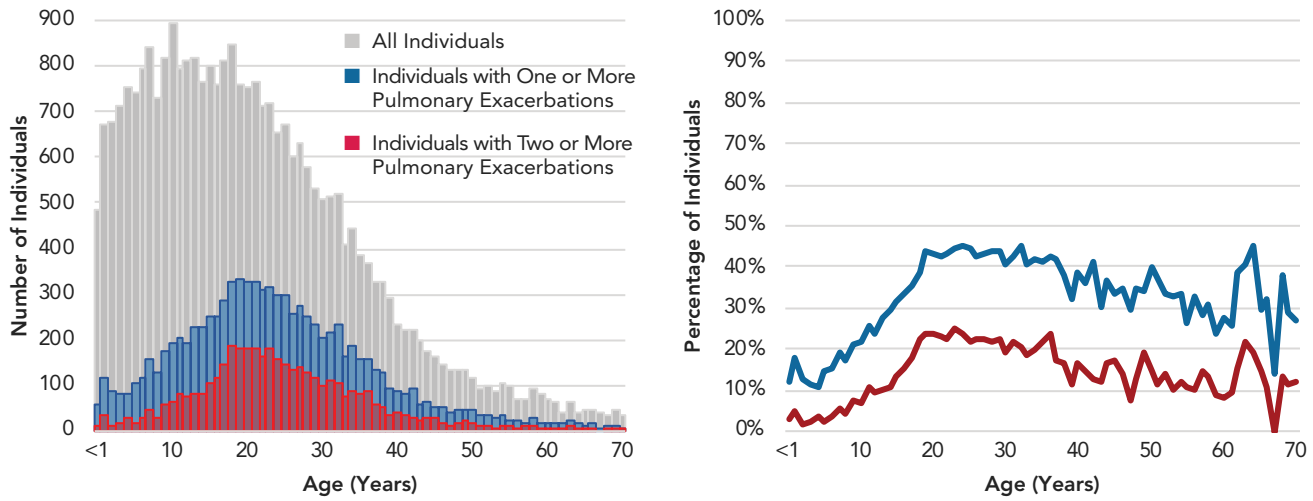
Despite notable improvements in pulmonary function and nutritional status over the years, there has not been a marked change in the proportion of individuals with CF who are treated with IV antibiotics for pulmonary exacerbations; however, in recent years it appears that the percentage is beginning to decrease in both children and adults.

### Individuals Treated with IV Antibiotics for a Pulmonary Exacerbation, 2005–2019



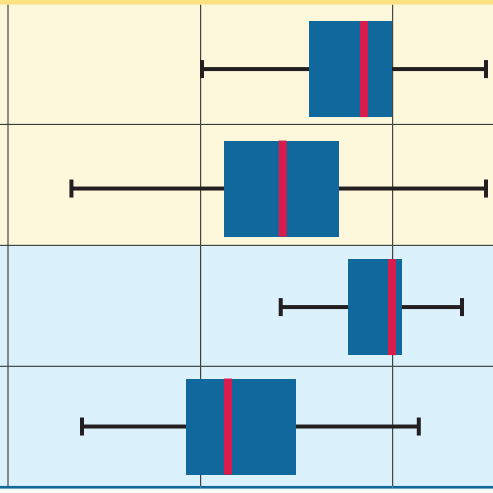

Individuals with CF who are between ages 15 and 40 are more likely than those in other age groups to have a pulmonary exacerbation that is treated by IV antibiotics during the year.

### Pulmonary Exacerbations by Age in Years, 2019



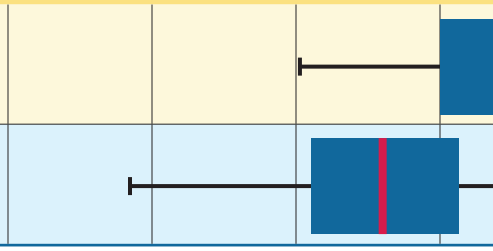
When the CF Foundation developed guidelines for the treatment of pulmonary exacerbations in 2009, little published literature or data were available upon which to base recommendations.[38] Current practice within the CF Foundation care center network indicates a median treatment duration of about two weeks, with adults more likely to complete some of their treatment at home. Further research is underway to develop evidence for best practices in the treatment of pulmonary exacerbations.[39]

## 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 | 13.0 | 7.0 | 17.5 |
| Median Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Individuals Less than 18 Years | 10.0 | 2.2 | 17.5 |
| Median Total Duration of IV Antibiotic Treatment for a Pulmonary Exacerbation in Individuals 18 Years and Older | 14.0 | 9.8 | 16.5 |
| Median Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Individuals 18 Years and Older | 8.0 | 2.8 | 15.0 |

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




| | Median | Min | Max |
|---|---|---|---|
| Individuals Less than 18 Years | 88.1 | 50.1 | 100.0 |
| Individuals 18 Years and Older | 65.3 | 20.6 | 100.0 |

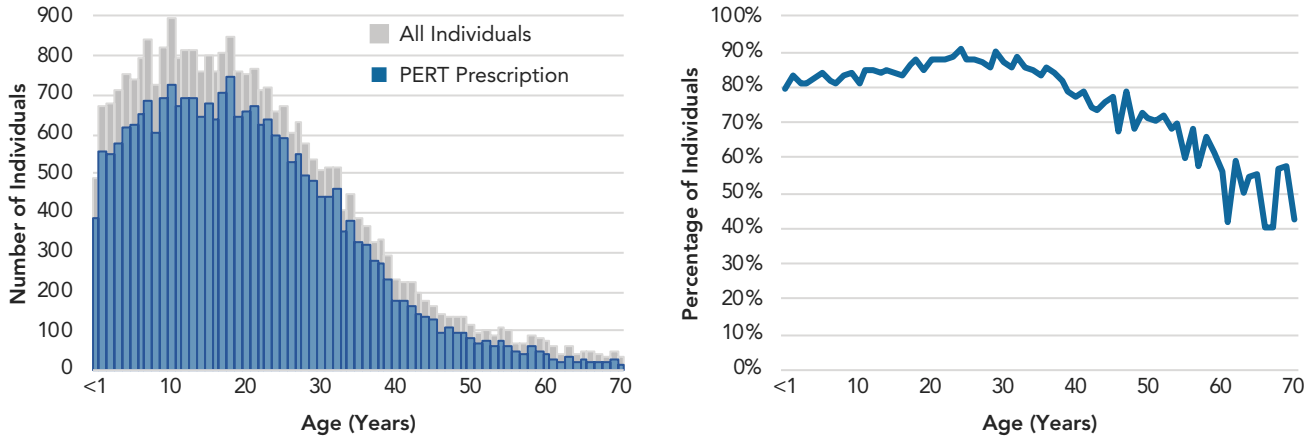
# THERAPIES

## Gastrointestinal (GI) Therapies

*The CF Foundation infant clinical care guidelines recommend that pancreatic enzyme replacement therapies (PERT) be started for all infants with two CFTR mutations associated with pancreatic insufficiency, a fecal elastase value below 200 µg/g of stool, and/or signs of malabsorption.*[5]

A large proportion of individuals of all ages are prescribed PERT. The decrease in the proportion of older individuals with CF prescribed PERT is most likely due to individuals with "milder" genotypes surviving longer.

**Pancreatic Enzyme Replacement Therapy (PERT) Prescription by Age in Years, 2019**




For individuals age two 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.[25] The mean dose of lipase units/kg/meal for individuals 2 to 19 years is 1,985 and for individuals 20 years and older, the mean dose is 1,833, suggesting that children and adults on average are receiving a sufficient dosage of PERT.

Infants with evidence of pancreatic insufficiency are recommended to receive 2,000 to 5,000 lipase units per feeding (total lipase dose), with adjustments as the infant grows.[7] Registry data show that the mean highest dose of lipase among children younger than two years is 1,699 units/kg/meal suggesting that infants may not be receiving an adequate dosage of PERT, or that there is some residual pancreatic function in younger individuals.

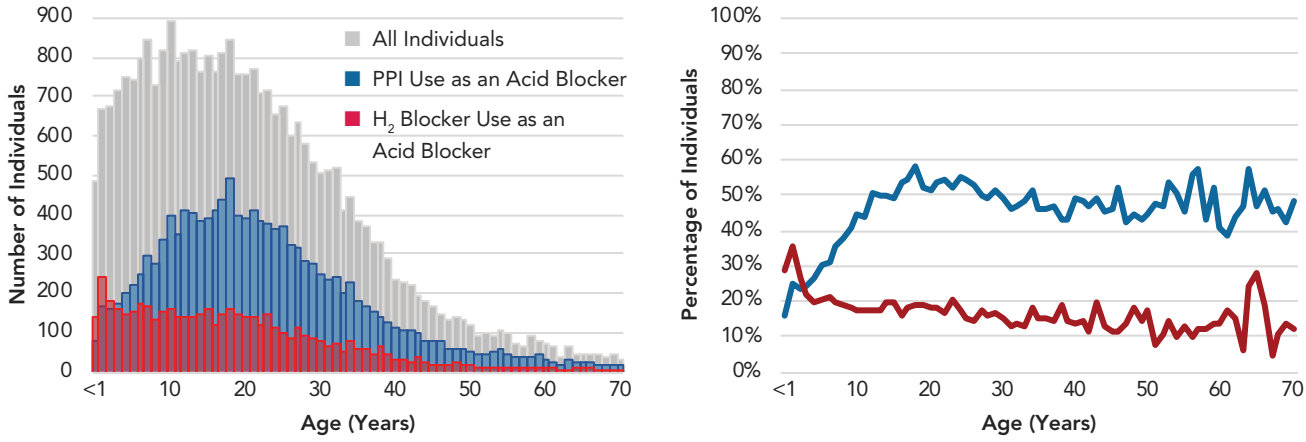
For infants with CF younger than two years, the infant clinical care guidelines recommend assessment of pancreatic functional status by measurement of fecal elastase.[5] Data on fecal elastase test results have been collected in the Registry since 2010, with an increased number of individuals undergoing fecal elastase testing. About 72.0 percent of infants born in 2019 were tested and have a fecal elastase value. Among individuals with a clinic visit, aged younger than two years in 2019, 30.1 percent did not have a fecal elastase value reported. Of those not tested, 88.6 percent were prescribed PERT. Almost all individuals with a known fecal elastase value of less than 200 µg/g of stool were prescribed PERT. Approximately 23.2 percent of individuals with fecal elastase values greater than or equal to 200 µg/g of stool were also prescribed PERT.

## Pancreatic Enzyme Use by Fecal Elastase Value in Infants Under 24 Months, 2019

| Pancreatic Enzyme Replacement Therapy | Fecal Elastase Value <200 | Fecal Elastase Value ≥ 200 |
|---|---|---|
| On PERT | 909 | 61 |
| Not on PERT | 12 | 202 |

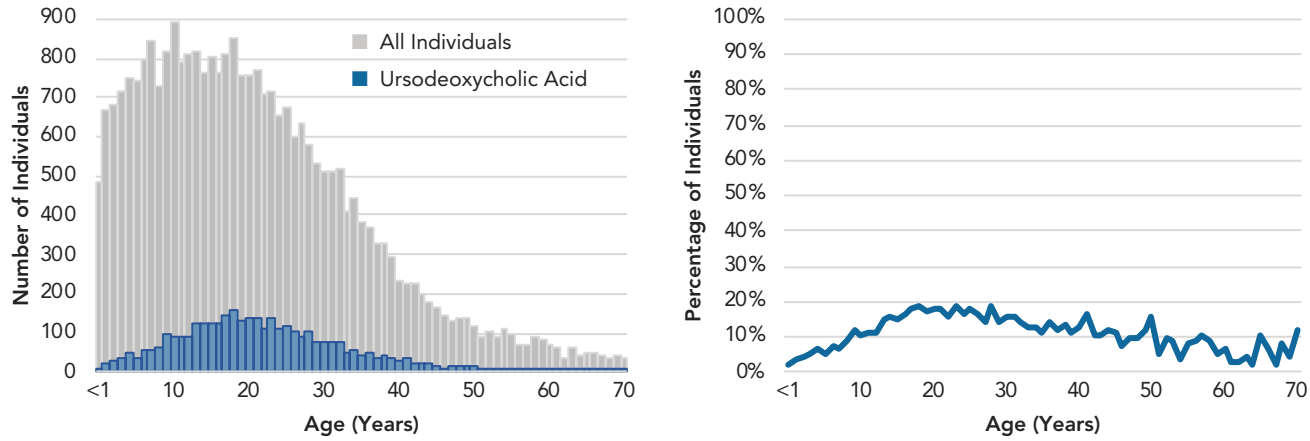
Acid blockers are commonly prescribed for people with CF to treat gastroesophageal reflux disease (GERD) and/or to decrease the acidity of the stomach to increase the effectiveness of PERT. Overall, proton pump inhibitors (PPIs) are prescribed more often (44.9 percent of individuals) than H2 blockers (18.0 percent of individuals). H2 blockers are used more frequently in younger individuals and their use tapers among older individuals. Use of PPIs increases with age until age 20 and then is prescribed to 50.1 percent of individuals age 20 and older.

## PPI and $H_2$ Blocker Use by Age in Years, 2019




In 2019, 89.8 percent of individuals age 2 to 19 and 82.3 percent of individuals age 20 and older were prescribed CF-specific vitamins, including vitamins A, D, E, and K. Additionally, 12.6 percent of individuals were prescribed ursodeoxycholic acid, which is most commonly prescribed to those with abnormal liver function tests or suspected CF liver disease.

## Ursodeoxycholic Acid Prescription by Age in Years, 2019

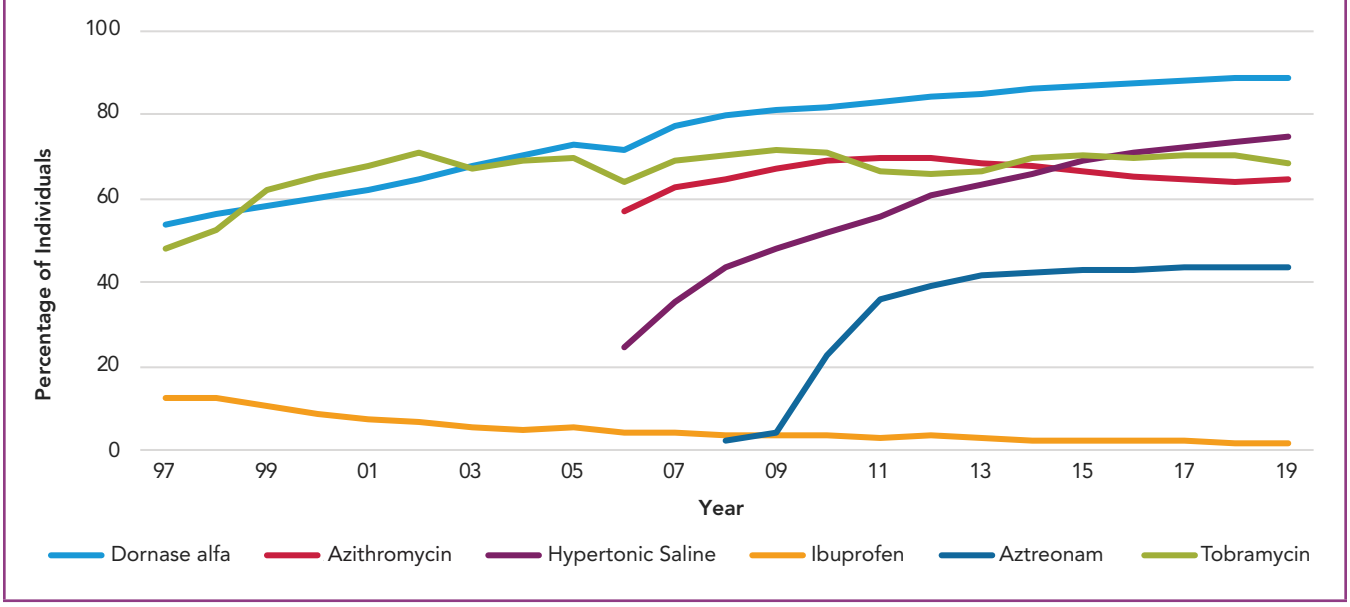


## Pulmonary Therapies

*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.*[40]

Many of the CF therapies are used by between 60 and 80 percent of the eligible population. The use of most therapies has increased over time. In recent years, additional formulations of inhaled tobramycin have become available, and they are included in the chart below. Dornase alfa, which is recommended for individuals aged 6 and older, is used by the vast majority of people and its use continues to rise. Use of chronic inhaled antibiotics seems to have plateaued. The availability of multiple pulmonary therapies for CF is beneficial; however, this also contributes to treatment complexity and overall burden on individuals with CF and their caregivers.

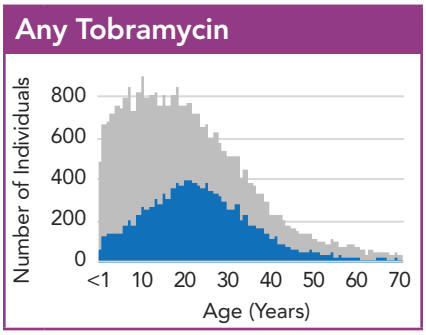
**Medication Prescription in Eligible Individuals, 1997-2019**

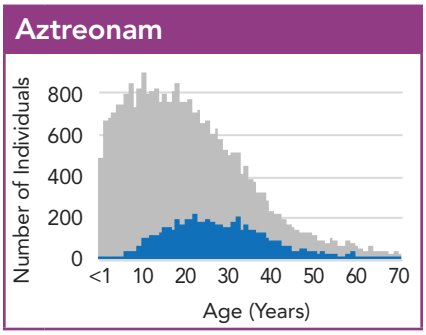


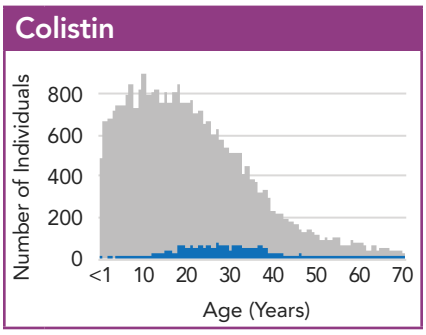

*Tobramycin includes all available formulations of inhaled tobramycin. Dornase alfa, tobramycin solution for inhalation, and inhaled aztreonam were approved by the Food and Drug Administration in 1993, 1997, and 2010, respectively.*

## *Pulmonary Medication Prescriptions by Age*

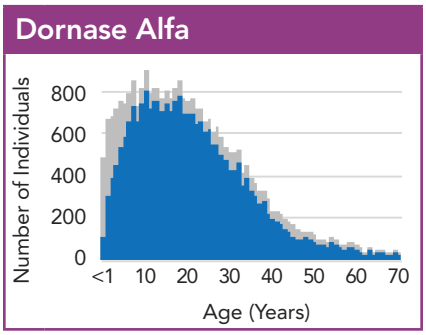
There are three classes of inhaled antibiotics for treatment of *P. aeruginosa* infections. Tobramycin is used most frequently, followed by aztreonam, and then colistin. For all medications, peak use occurs during adolescence and young adulthood.

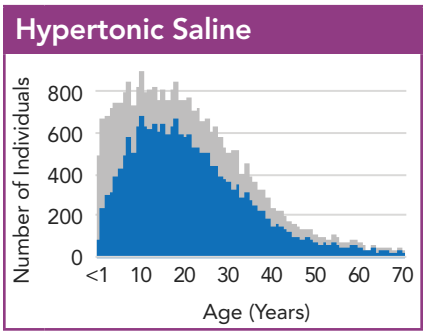


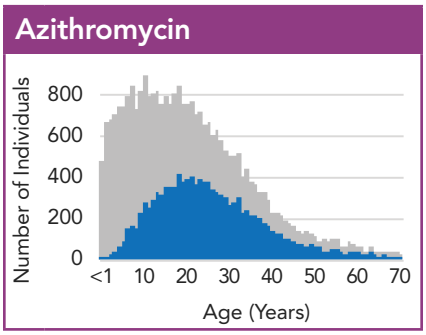



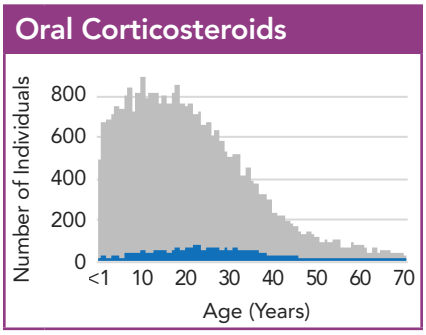

Dornase alfa and hypertonic saline are each prescribed for the majority of individuals with CF. Azithromycin is also widely used in individuals with *P. aeruginosa*, with peak use occurring at slightly older ages than for use of dornase alfa and hypertonic saline.

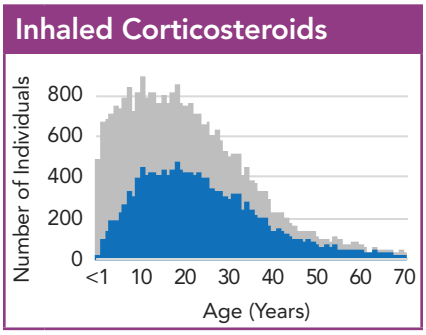


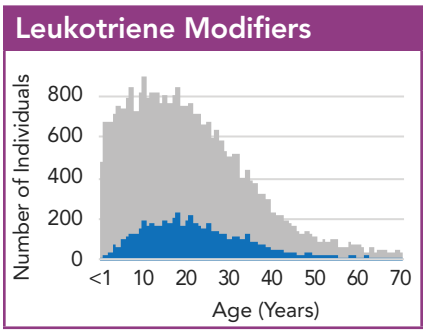




A substantial proportion of individuals with CF are prescribed inhaled corticosteroids and, to a lesser degree, leukotriene modifiers. Oral corticosteroids are used infrequently.

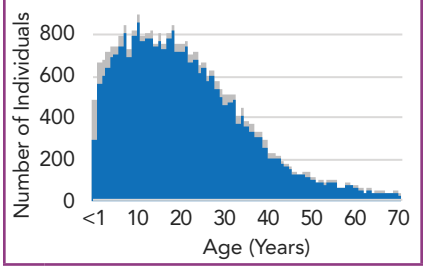


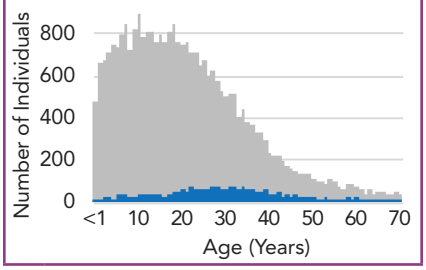



Bronchodilators are used extensively among individuals with CF. Almost all people with CF are prescribed beta agonists, except for a very small percentage who are prescribed anticholinergics. The vast majority of those prescribed beta agonists are on short-acting formulations.

## Inhaled Beta Agonists

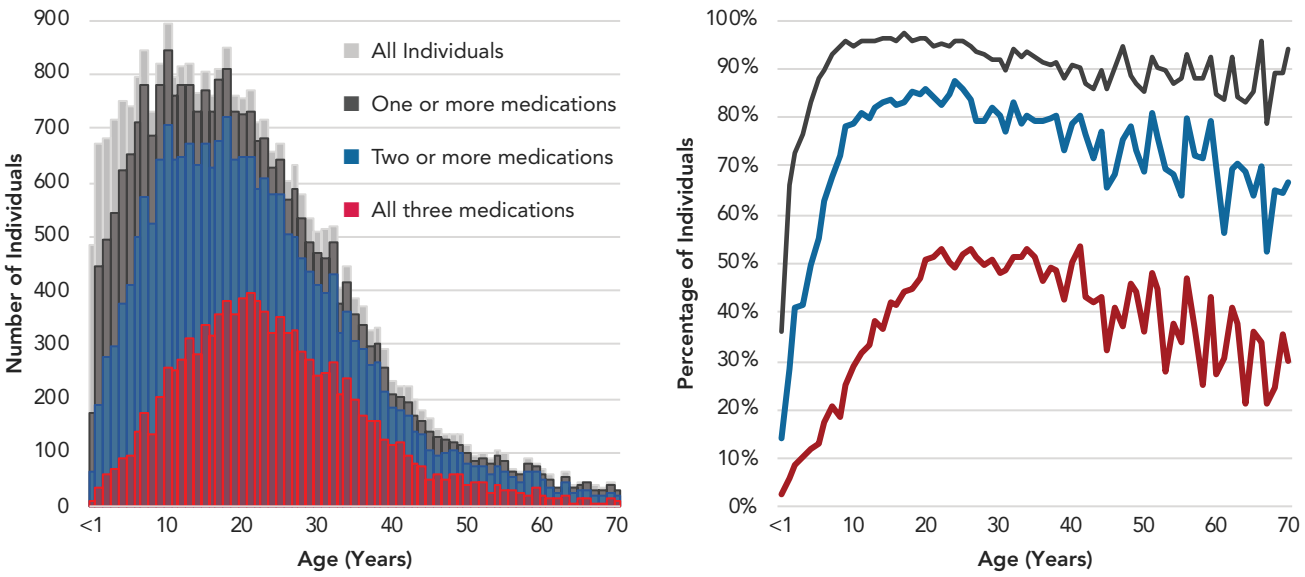



## Inhaled Anticholinergics




Multiple pulmonary therapies are available for individuals with CF. Inhaled medications are effective treatments for pulmonary disease, and they require time to prepare, administer, and clean equipment after treatment. Those with *P. aeruginosa* infection or colonization are typically prescribed inhaled antibiotics. Almost all individuals are prescribed at least one inhaled medication, and about 80 percent of individuals aged 15 to 40 are prescribed two or more of these therapies.

## Inhaled Medication Prescription by Age in Years, 2019

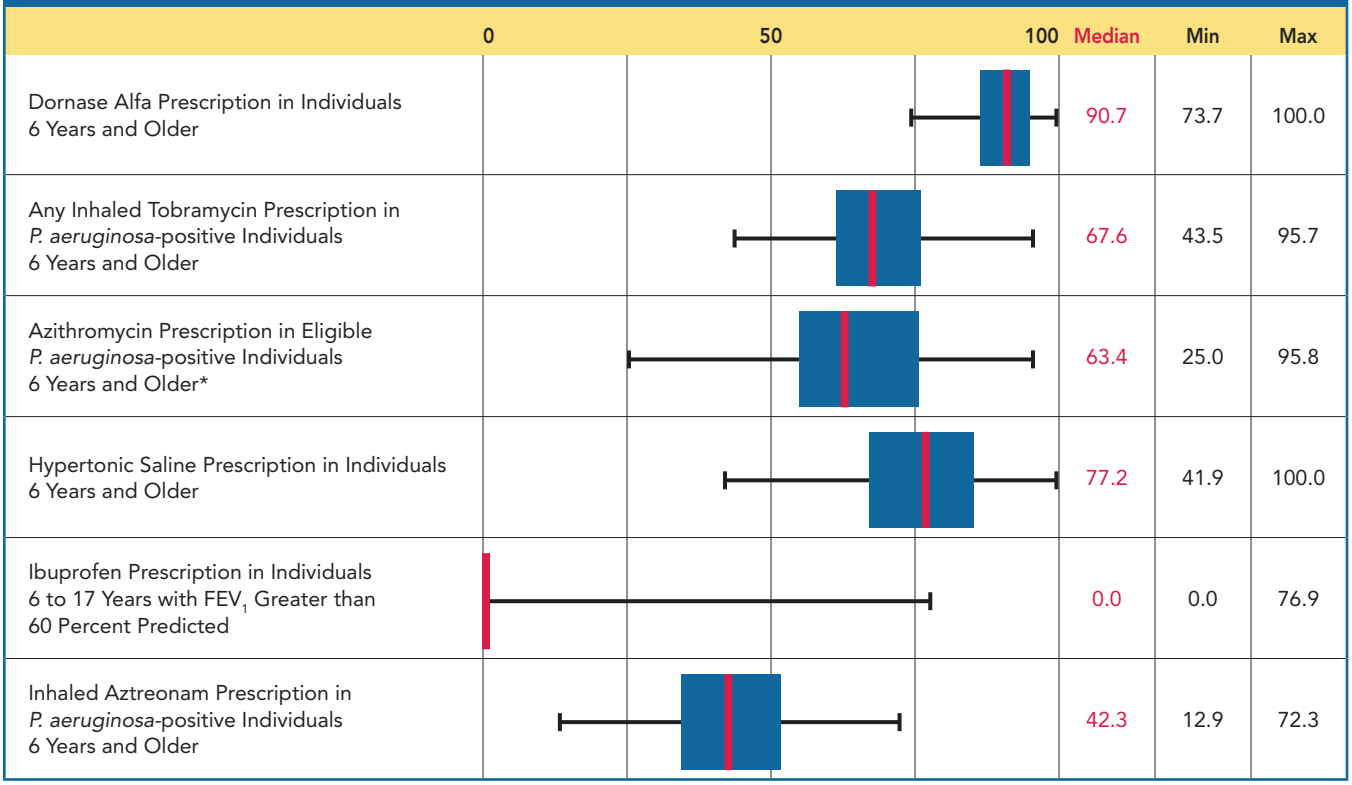



*Inhaled medication includes dornase alfa, hypertonic saline, and inhaled antibiotics. Inhaled antibiotics includes the use of tobramycin (or other aminoglycosides), aztreonam, or colistin.*

## *Medications Recommended for Chronic Use*

Recommended therapies are widely prescribed, with the exception of ibuprofen; however, there is considerable variation across the CF Foundation care center network. Increasingly, individuals with CF are using multiple inhaled antibiotics for the treatment of *P. aeruginosa* infections. CFTR modulators are discussed in a separate chapter (p. 57).

### Pulmonary Therapies Recommended for Chronic Use, by Center

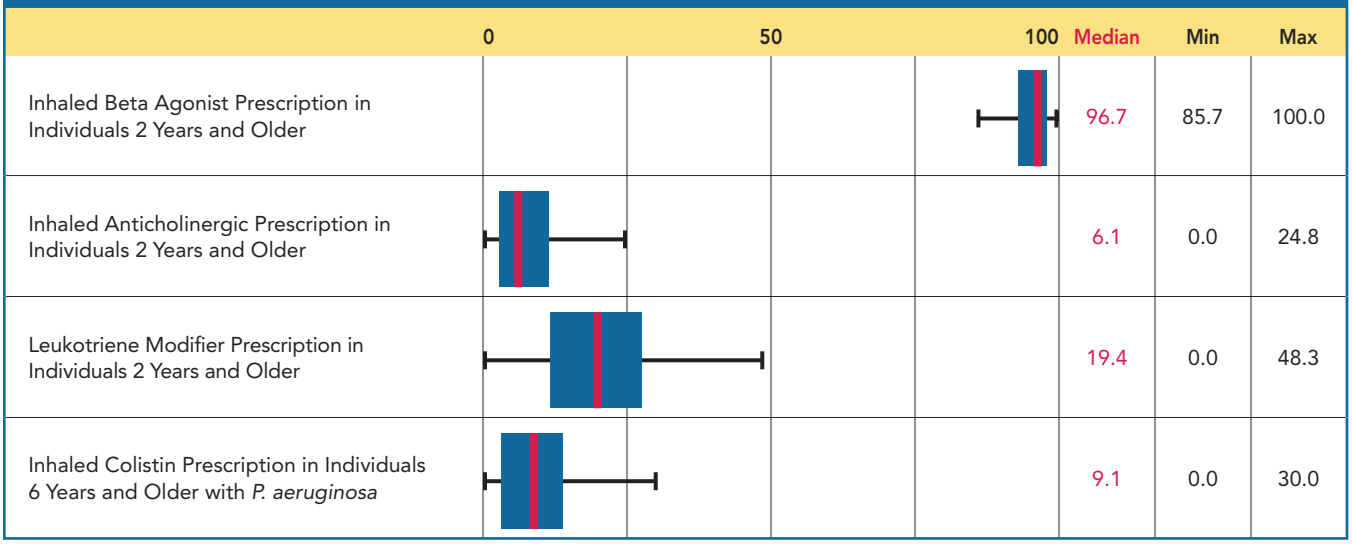



**Individuals were considered eligible if they met the selection criteria used in the U.S. trial of azithromycin in individuals chronically infected with* Pseudomonas aeruginosa.[2]

### *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.[40] Use of colistin has decreased in recent years. Inhaled beta agonists are used extensively, but the other medications are used infrequently. Adult use of ibuprofen is less than two percent.

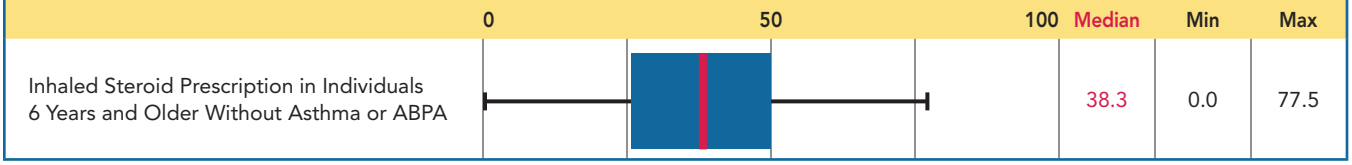
**Pulmonary Therapies with Insufficient Evidence to Recommend For or Against Chronic Use, by Center**




### *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).[41]

**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 from ages two to five.[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 selectively offered to these individuals on the basis of individual circumstances. The chart below shows the use of medications among children younger than age six.

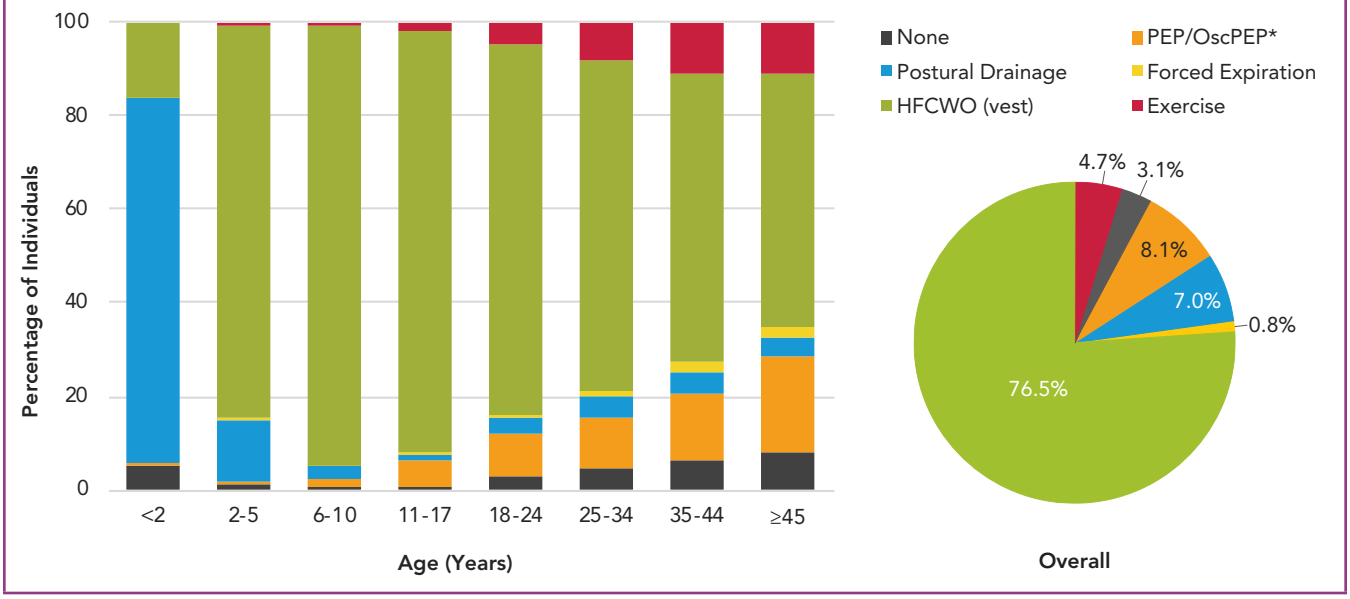
**Medication Use in Individuals Under 6 Years, 2019**

| | Age < 3 Years (%) | Age 3 to 5 Years (%) |
|---|---|---|
| **Number of Individuals (n)** | **1,791** | **2,197** |
| Dornase Alfa | 44.9 | 70.9 |
| Hypertonic Saline | 34.7 | 51.6 |
| Inhaled Bronchodilators | 81.5 | 92.6 |
| Inhaled Corticosteroids | 14.9 | 27.5 |
| Inhaled Tobramycin | 18.0 | 19.2 |
| Azithromycin | 3.4 | 9.4 |
| Inhaled Aztreonam | 0.9 | 3.0 |

### *Airway Clearance Techniques*

The CF Foundation pulmonary guidelines recommend airway clearance for all individuals with CF.[41] A high-frequency chest wall oscillation (HFCWO) vest is the most widely used airway clearance technique in persons with CF after infancy.

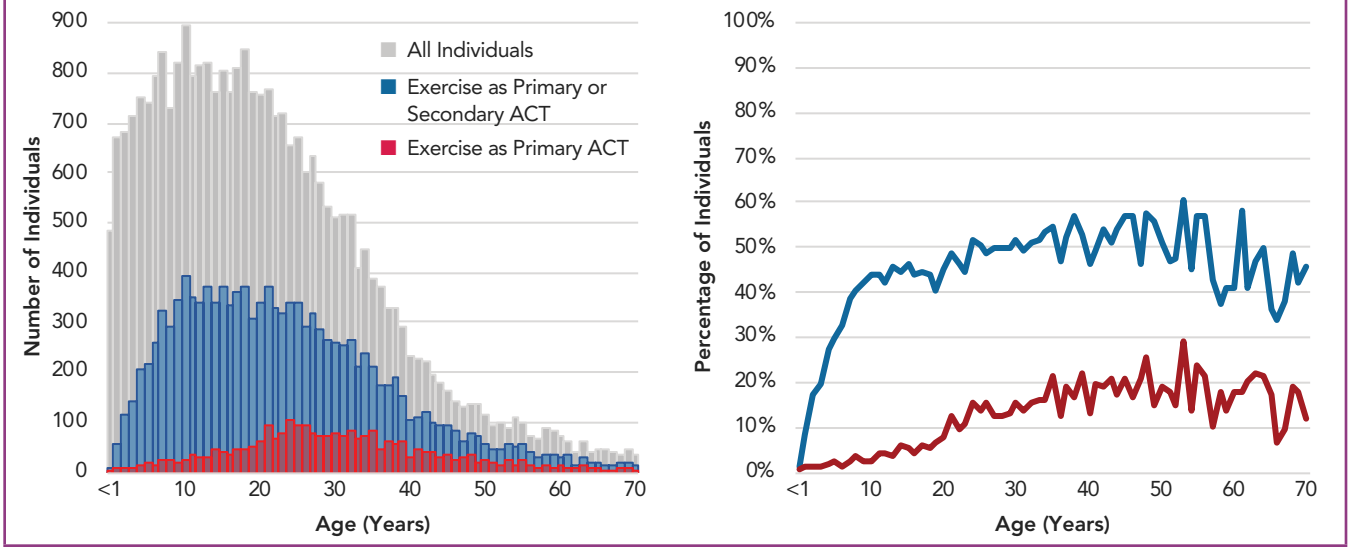
## Primary Airway Clearance Techniques by Age and Overall, 2019




**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.[41] Many individuals with CF report exercising in addition to their primary method of airway clearance, with 35.4 percent of children and 49.0 percent of adults identifying exercise as one of their methods of airway clearance.

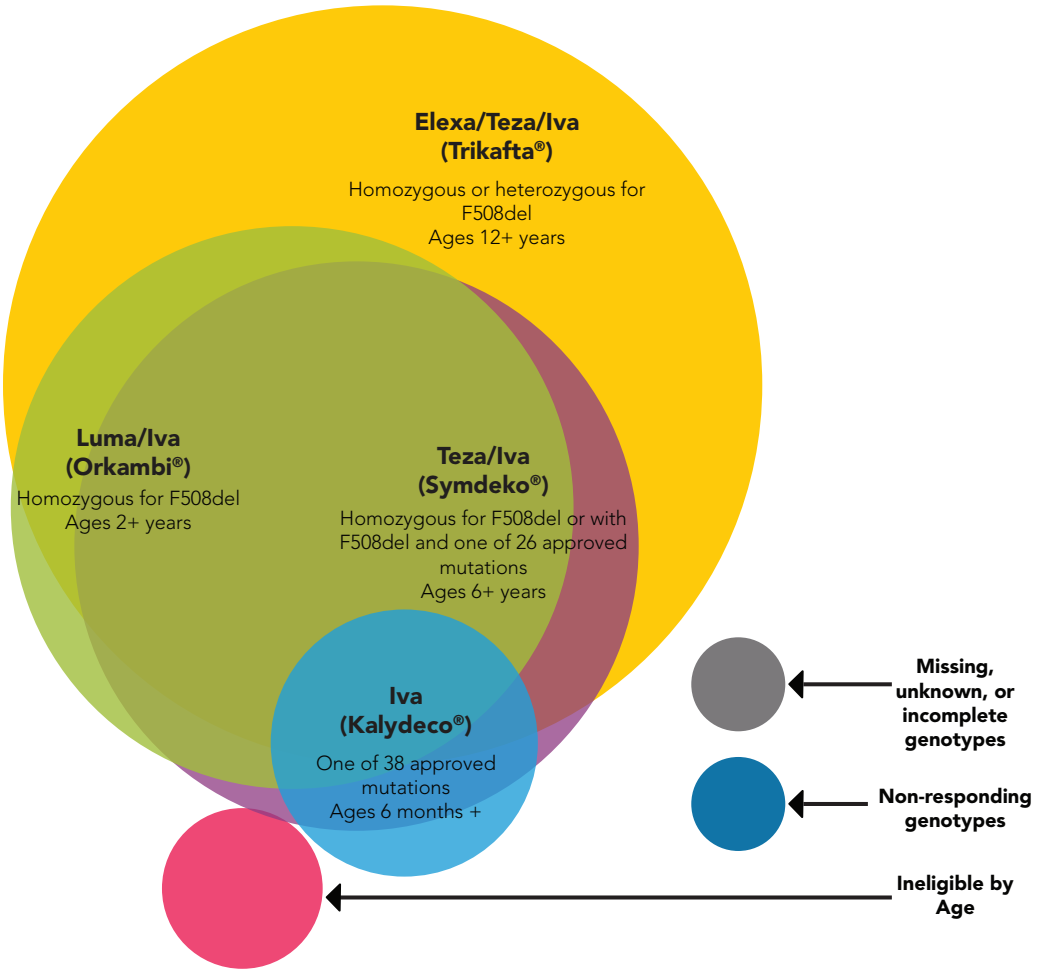
## Exercise as an Airway Clearance Technique (ACT) by Age in Years, 2019



## CFTR Modulator Therapies

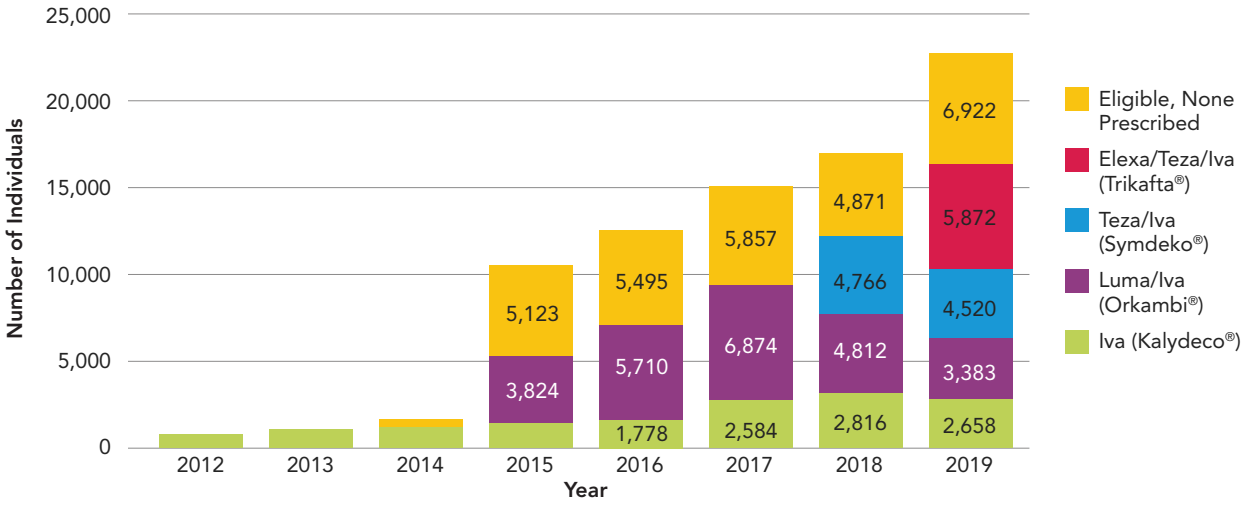
On October 21, 2019, the US Food and Drug Administration (FDA) approved a new triple-combination therapy (elexacaftor/tezacaftor/ivacaftor) for individuals with CF who are aged 12 years and older and have at least one allele with the F508del mutation. This significantly expanded eligibility of people with CF to approximately 80.5 percent of the registry population based on their age and genotype.

The overlapping circles in the figure below show that many people are now eligible for more than one CFTR modulator. Approximately 10 percent of children with CF are too young and therefore not eligible at this time. The remaining approximately 9.5 percent of the registry population is comprised of individuals with a variety of minimal function mutations (including rare missense, nonsense, splicing, deletions, insertions, etc.) not currently known to be responsive to CFTR modulators (dark blue circle) AND individuals who have missing, unknown, or incomplete genotypes (gray circle). We estimate approximately 2.5 percent may have mutations that prove to be responsive to a CFTR modulator via theratyping or by a more extensive genotype analysis. The remaining approximately 7 percent of the patient population may require genetic-based therapy, including 3 percent who could benefit from a nonsense-specific therapy or genetic-based therapy.



Approval of elexacaftor/tezacaftor/ivacaftor increased both the number of people who were eligible for CFTR modulators (23,355) and the number of people who were prescribed such therapies (16,433). In addition to the new CFTR modulator, age limits for previously approved modulators were lowered over the last several years. Of those currently eligible, 70.0 percent of individuals were prescribed a CFTR modulator in 2019. For ivacaftor, prescription rates differ by mutation — 93.2 percent of individuals with G551D or other gating mutation compared to 63.2 percent of individuals with an R117H mutation. Lumacaftor/ivacaftor was prescribed for 41.1 percent of eligible individuals (21.0 percent of those younger than 6, 57.7 percent of those age 6 to 17, and 25.9 percent of those age 18 and older); a decrease from 2018, in part due to 663 individuals switching to tezacaftor/ivacaftor. Tezacaftor/ivacaftor was prescribed for 4,520 individuals. Elexacaftor/tezacaftor/ivacaftor was prescribed for 5,872 individuals with CF despite the FDA approval coming late in 2019. Thirty-eight percent of those were prescribed a CFTR modulator for the first time.

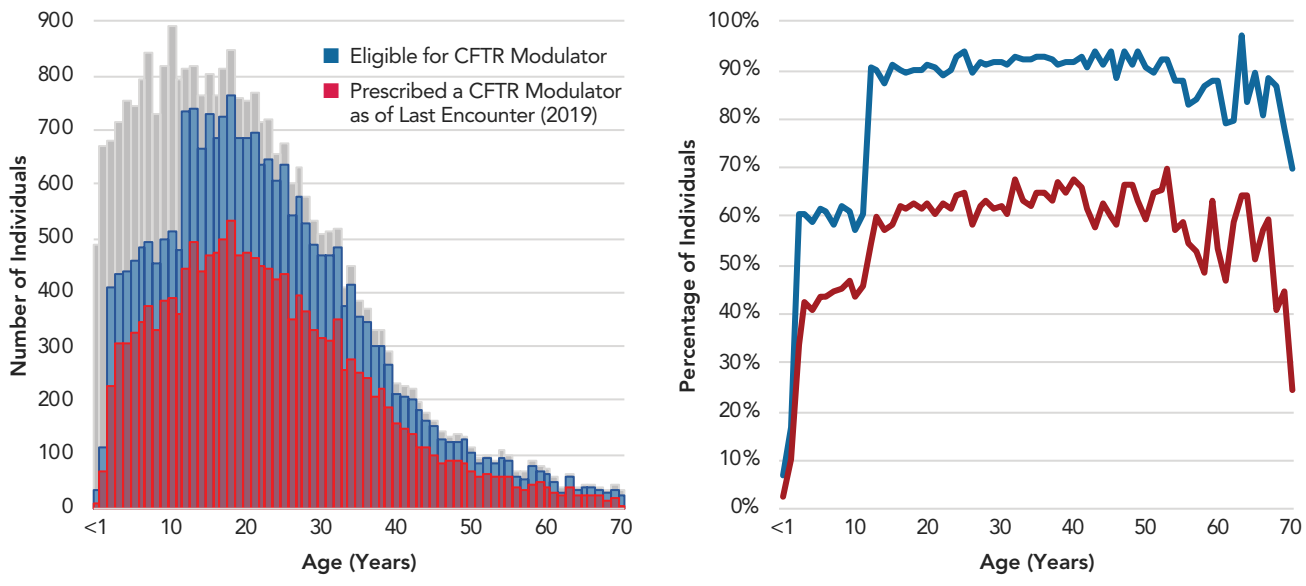
## CFTR Modulators by Year




| | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|---|---|
| Total Eligible | 954 | 992 | 1,801 | 10,591 | 12,983 | 15,435 | 17,265 | 23,355 |
| Pct Eligible on CFTRm | 83% | 98% | 68% | 52% | 58% | 62% | 72% | 70% |
| Total on Modulators | 796 | 977 | 1,231 | 5,468 | 7,488 | 9,578 | 12,394 | 16,433 |

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

## CFTR Modulator Use by Age, 2019




Variability across centers exists with prescription rates ranging from a minimum of 42.4 percent to a maximum of 91.6 percent. No significant differences in prescription rates are seen between pediatric and adult programs. With continued uptake of elexacaftor/tezacaftor/ivacaftor in 2020, we anticipate a continued increase in the prescription of CFTR modulators to the eligible patient population.

## Modulator Prescription in Eligible Individuals, by Center

| | 0 — 50 — 100 | Median | Min | Max |
|---|---|---|---|---|
| Eligible Individuals Prescribed a Modulator | | 70.0 | 42.4 | 91.6 |
| Eligible Individuals Less than 18 Years Prescribed a Modulator | | 74.2 | 37.3 | 100.0 |
| Eligible Individuals 18 Years and Older Prescribed a Modulator | | 70.0 | 40.0 | 95.2 |

# COMPLICATIONS

*Management of complications secondary to CF is important for maintaining an individual's health and quality of life. Complications of CF can affect many different organ systems; 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 more is higher among individuals who received a lung transplant than among individuals who have never had a lung transplant. As a result of removing individuals who had a transplant from the analyses, rates of some complications (e.g., CF-related diabetes (CFRD) and osteoporosis) are lower in 2019 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 recent publication and implementation of mental health screening guidelines,[18] an increase in the reporting of anxiety and depression has been observed.*

**Complications of CF, 2019**

| | Age < 18 (%) | Age ≥ 18 (%) | All (%) |
|---|---|---|---|
| **Number of Individuals (n)** | **13,684** | **15,729** | **29,413** |
| Percent with no complications | 26.5 | 4.6 | 14.8 |
| Percent with complications not reported[A] | 1.1 | 1.6 | 1.4 |
| **Cystic Fibrosis-Related Diabetes** | | | |
| Cystic fibrosis-related diabetes (CFRD)[B] | 5.3 | 30.8 | 19.0 |
| **Hepatobiliary** | | | |
| Gall stones[C] | 0.1 | 0.4 | 0.2 |
| Gall stones, requiring surgery/procedure[C] | 0.1 | 0.3 | 0.2 |
| Liver disease, cirrhosis[D] | 2.3 | 4.2 | 3.3 |
| Liver disease, non-cirrhosis[C] | 3.8 | 4.2 | 4.0 |
| Acute hepatitis[C] | 0.0 | 0.1 | 0.1 |
| Hepatic steatosis | 0.5 | 0.7 | 0.6 |
| Liver disease, other[C] | 2.0 | 1.7 | 1.8 |
| **Bone/Joints** | | | |
| Arthritis/arthropathy | 0.4 | 5.7 | 3.2 |
| Bone fracture[C] | 0.2 | 0.2 | 0.2 |
| Osteopenia | 1.1 | 17.9 | 10.0 |
| Osteoporosis | 0.3 | 7.0 | 3.9 |
| **Pulmonary** | | | |
| Allergic bronchopulmonary aspergillosis (ABPA) | 2.4 | 8.0 | 5.4 |
| Asthma | 27.9 | 34.6 | 31.5 |
| Hemoptysis | 0.8 | 5.8 | 3.4 |
| *Hemoptysis, massive[C]* | *<0.1* | *0.7* | *0.4* |
| Pneumothorax requiring chest tube[C] | <0.1 | 0.4 | 0.2 |

Table continues on the next page

| Complications of CF, 2019 *continued* | | | |
|---|---|---|---|
| **GI** | **Age < 18 (%)** | **Age ≥ 18 (%)** | **All (%)** |
| Distal intestinal obstruction syndrome (DIOS)[C] | 1.7 | 2.4 | 2.1 |
| Fibrosing colonopathy/colonic stricture[C] | <0.1 | <0.1 | <0.1 |
| Gastroesophageal reflux disease (GERD) | 31.8 | 41.2 | 36.8 |
| GI bleed requiring hospitalization (non-variceal)[C] | <0.1 | <0.1 | <0.1 |
| History of intestinal or colon surgery | 4.3 | 2.2 | 3.2 |
| Pancreatitis[C] | 0.3 | 1.3 | 0.8 |
| Peptic ulcer disease[C] | <0.1 | 0.1 | <0.1 |
| Rectal prolapse[C] | 0.3 | 0.1 | 0.2 |
| **Mental Health** | | | |
| Anxiety disorder | 5.0 | 23.8 | 15.0 |
| Depression | 3.5 | 28.3 | 16.7 |
| **Other Complications** | | | |
| Cancer confirmed by histology[C] | 0.0 | 0.4 | 0.2 |
| Hearing loss | 1.3 | 3.6 | 2.5 |
| Hypertension | 0.4 | 6.4 | 3.6 |
| Kidney stones[C] | 0.1 | 1.3 | 0.7 |
| Nasal polyps requiring surgery[C] | 1.3 | 1.2 | 1.3 |
| Renal failure requiring dialysis[E] | <0.1 | 0.2 | 0.1 |
| Sinus disease | 21.1 | 55.7 | 39.5 |

[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 66 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 is the reason for the decrease in the observed number of reported acute complications, most notably DIOS.*
[D] *See table below for secondary complications.*
[E] *Cause other than CFRD.*

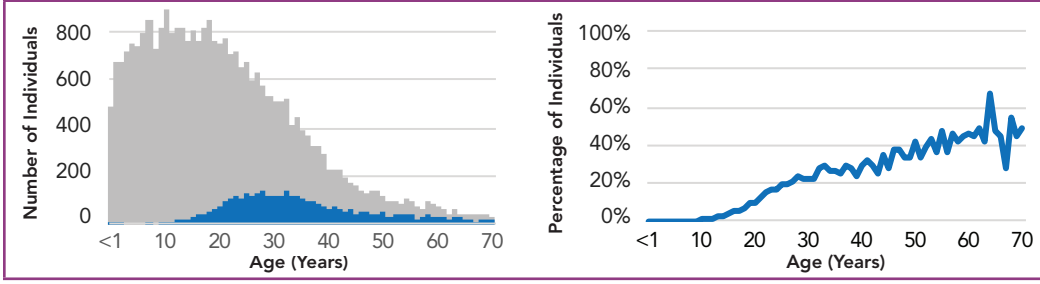
The table below highlights the prevalence of clinical manifestations of portal hypertension among individuals with cirrhosis.

| Complications of Cirrhosis, 2019 (n=965) | | | |
|---|---|---|---|
| | **All (%)** | **Age < 18 (%)** | **Age ≥ 18 (%)** |
| **Number of Individuals (n)** | **965** | **317** | **648** |
| Esophageal varices | 21.2 | 17.4 | 23.1 |
| Gastric varices | 5.1 | 4.7 | 5.2 |
| GI bleed related to varices | 2.0 | 1.9 | 2.0 |
| Splenomegaly | 34.9 | 41.3 | 31.8 |
| Hypersplenism | 10.9 | 11.7 | 10.5 |
| Encephalopathy | 1.0 | 0.3 | 1.4 |
| Ascites | 5.2 | 1.6 | 6.9 |

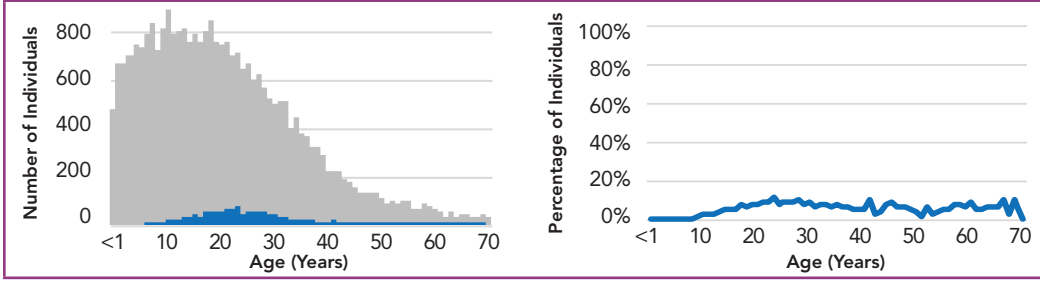
## CF Complications by Age, 2019

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

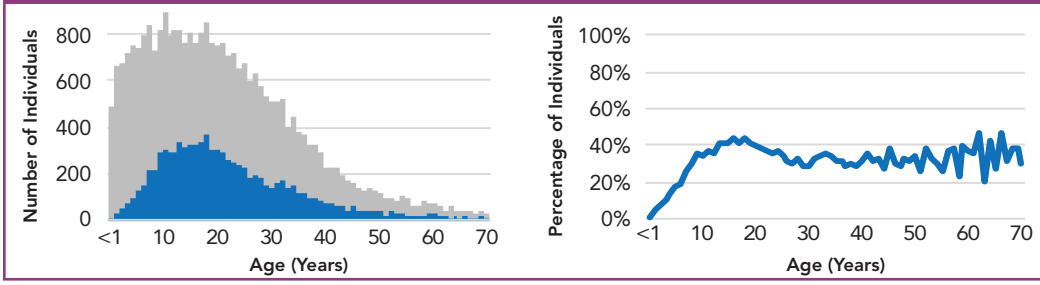
### Bone Disease (Osteopenia, Osteoporosis, or Bone Fracture)



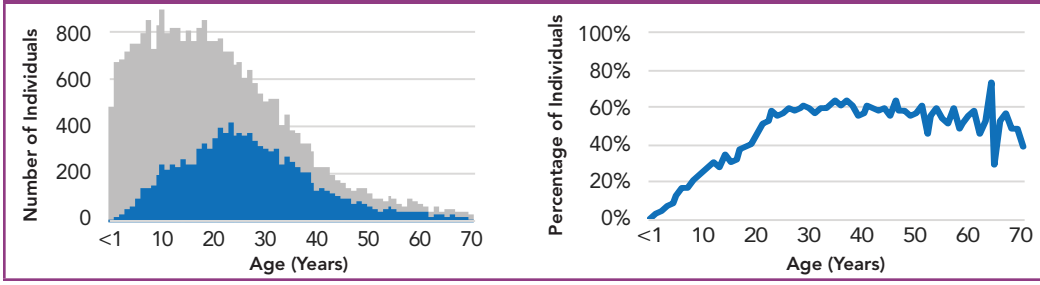

### Allergic Bronchopulmonary Aspergillosis (ABPA)



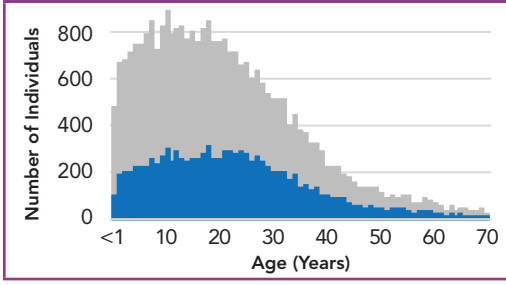

### Asthma

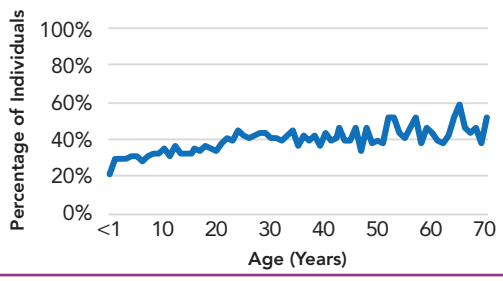



### Sinus Disease

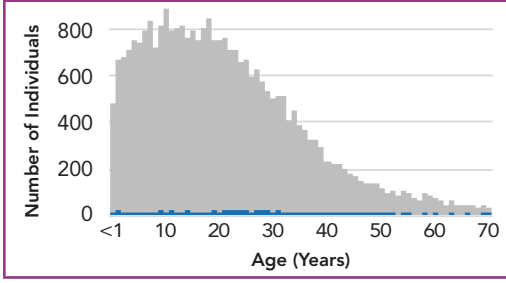


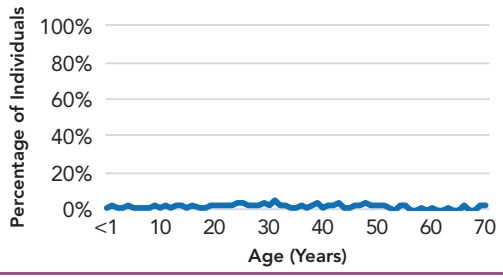
## Gastroesophageal Reflux Disease (GERD)



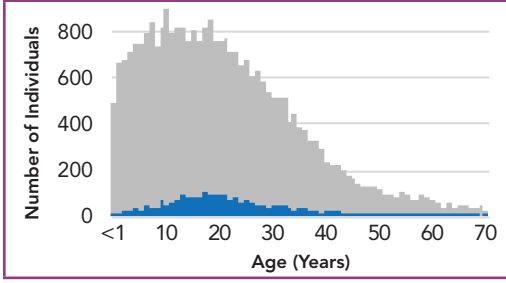



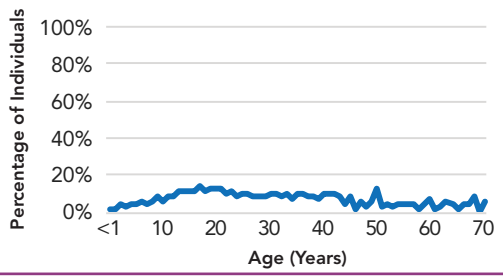

## Distal Intestinal Obstruction Syndrome (DIOS)



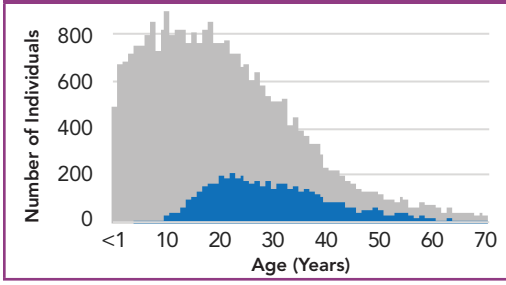



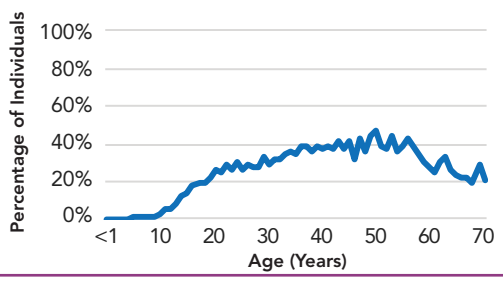

## Liver Disease (All Types)



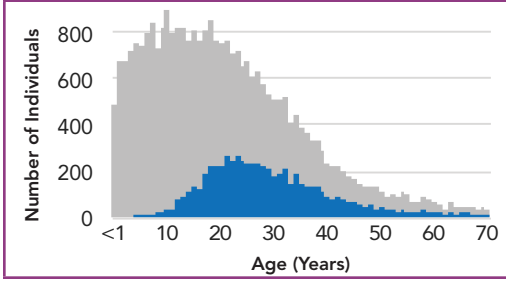



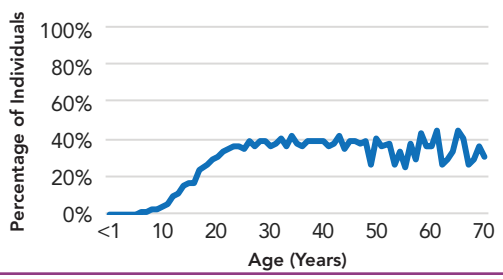

## Cystic Fibrosis Related-Diabetes (CFRD)




## Depression or Anxiety



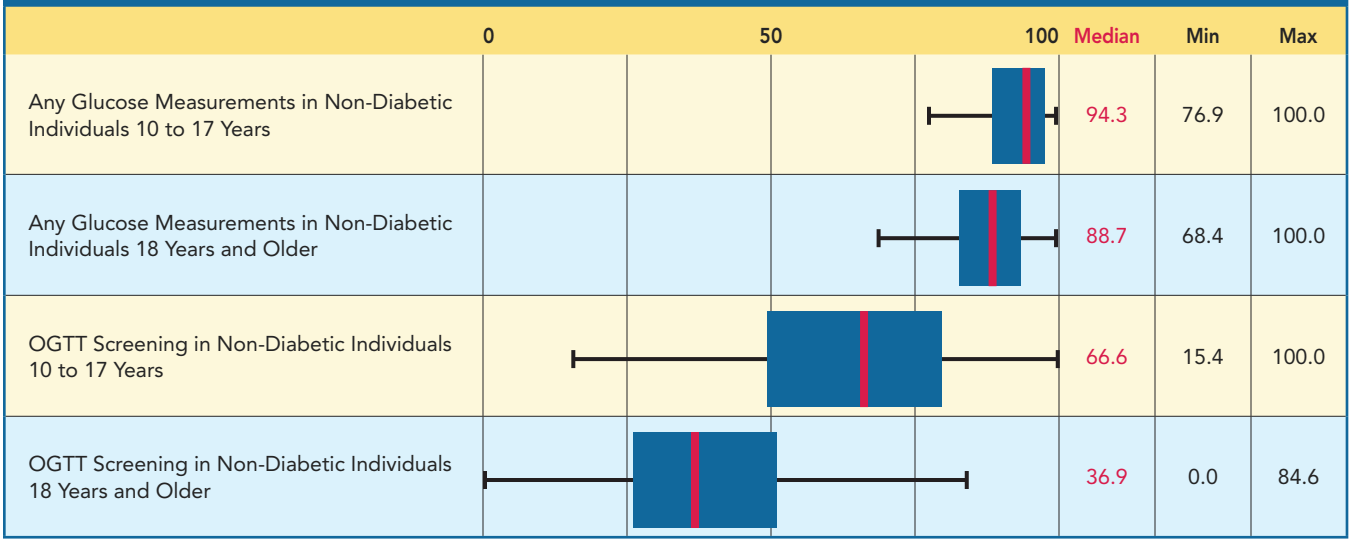



## Cystic Fibrosis-Related Diabetes (CFRD)

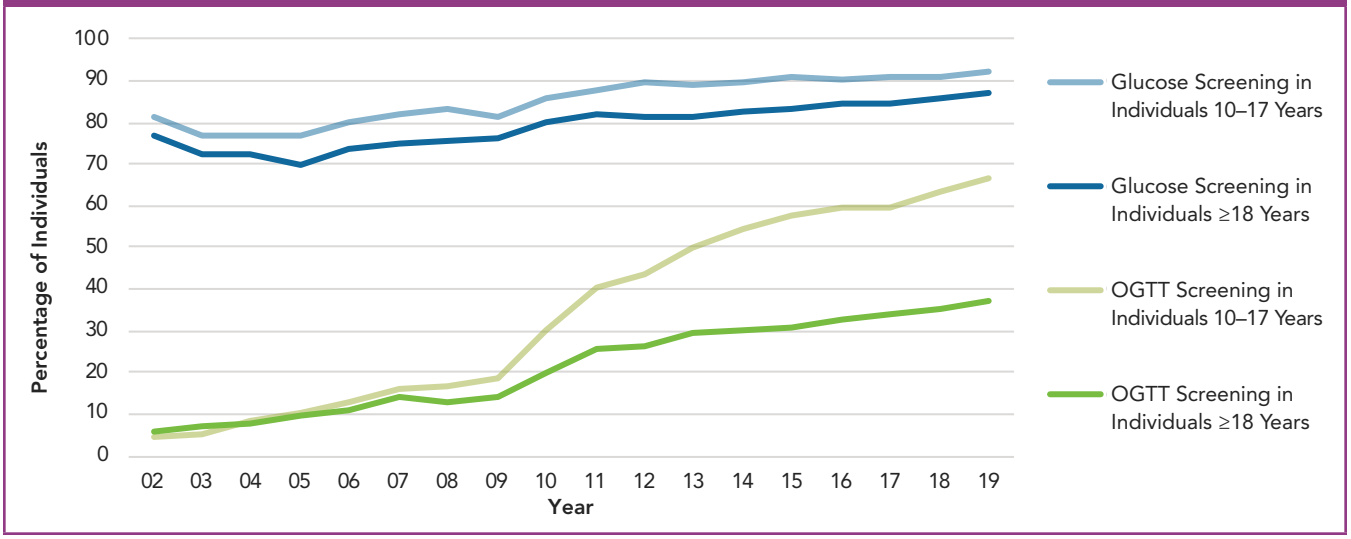
CFRD is associated with weight loss, lung function decline, and increased mortality.[42] Early diagnosis and treatment may minimize the impact of CFRD. The CF Foundation/American Diabetes Association clinical practice guidelines for CFRD recommend screening all individuals annually, starting at age 10, with an oral glucose tolerance test (OGTT).[42]

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. It is encouraging to note that rates of screening adolescents for CFRD using the OGTT continues to increase since the CF Foundation clinical care guidelines for CFRD were published in 2010,[42] while use in adults lags behind.

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

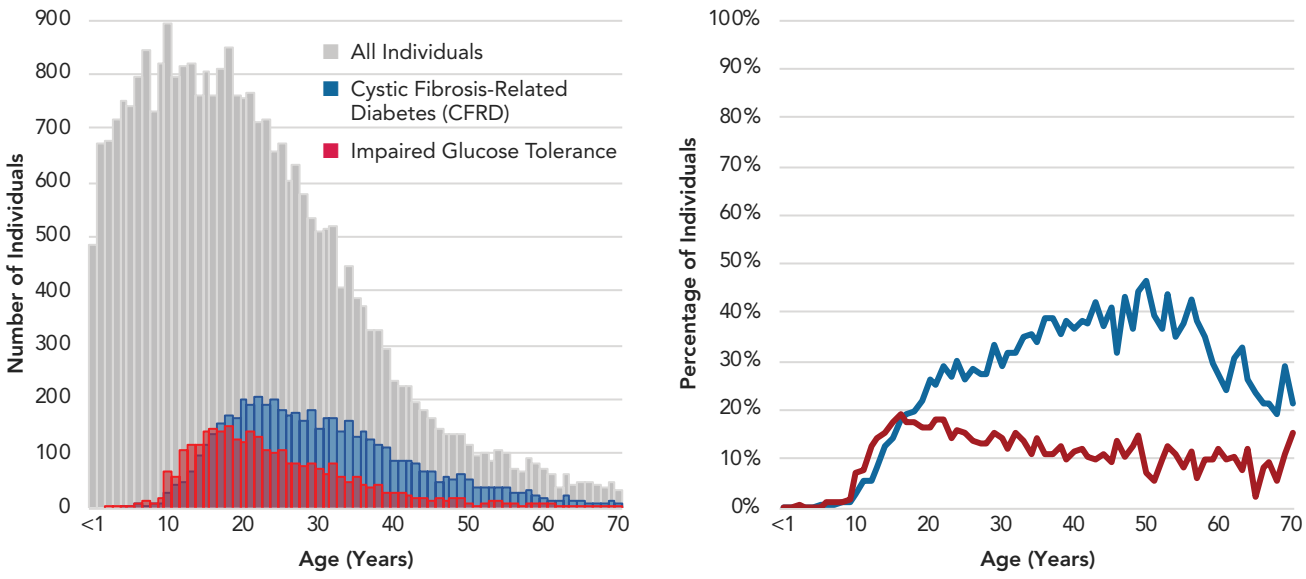



### Blood Glucose and OGTT Screening for Individuals without CFRD, 2002–2019



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, 2019




The vast majority of 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.[42]

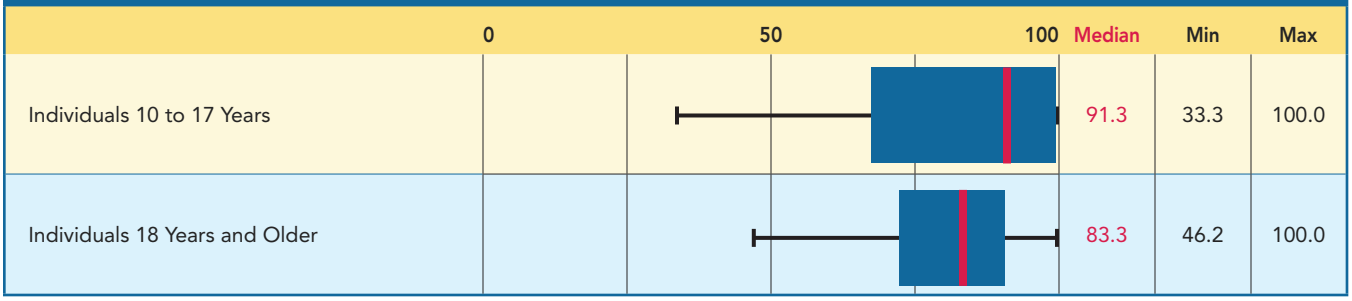
## CFRD Treatment in 2019

| | Percent of People with CFRD on Treatment |
|---|---|
| Dietary change | 19.4 |
| Oral hypoglycemic agents | 3.7 |
| Intermittent insulin (with illness, steroids, etc.) | 4.5 |
| Chronic insulin | 74.0 |
| No treatment noted in reporting year | 13.3 |

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

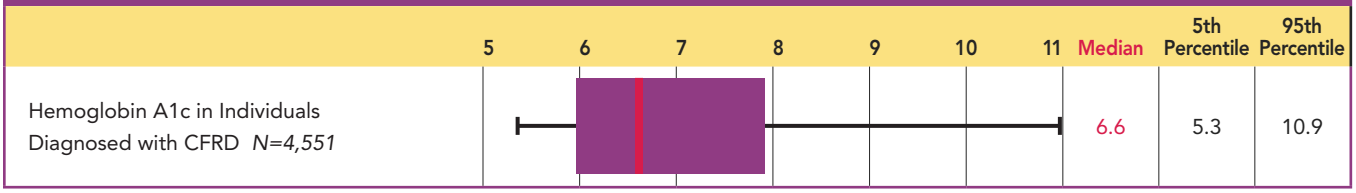
The clinical practice guidelines recommend regular hemoglobin A1c (HbA1c) measurements for individuals with CFRD.[42] Variation by CF care centers in the percentage of individuals with CFRD with one or more HbA1c measurements during the year shows that a majority of centers test most of their patients at least annually.

## Percent 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.[42] More than half of individuals with CFRD are meeting this guideline.

## Hemoglobin A1c Lab Values Reported, 2019




Rates of secondary complications of CFRD, including retinopathy, microalbuminuria, kidney disease, and neuropathy remain low. 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.[42]

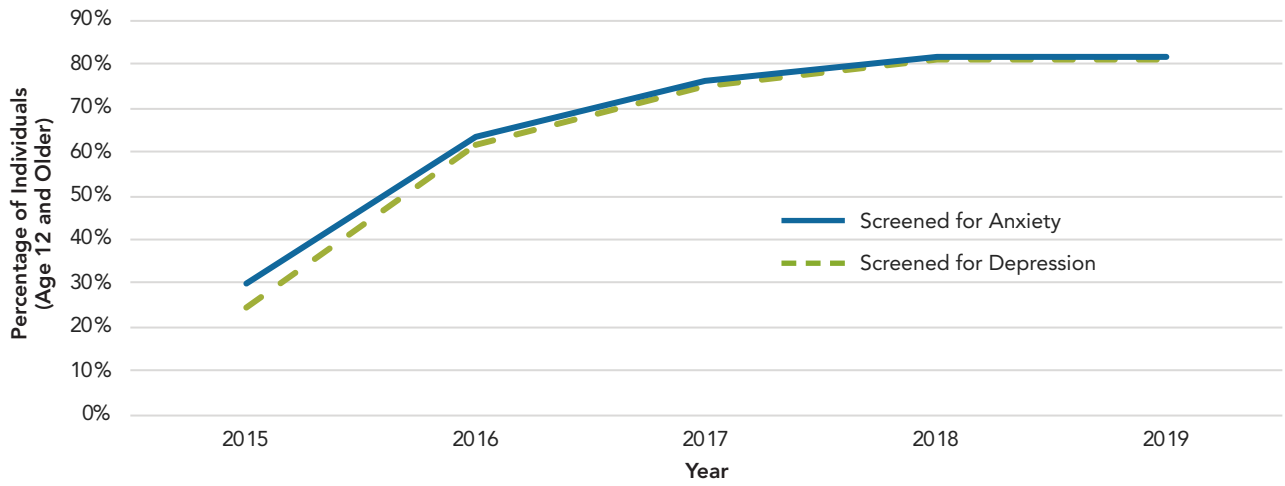
## Complications of CFRD in 2019

| | All (%) | Age < 18 (%) | Age ≥ 18 (%) |
|---|---|---|---|
| **Number of Individuals (n)** | **5,574** | **725** | **4,849** |
| Retinopathy | 0.8 | 0.0 | 0.9 |
| Microalbuminuria | 1.2 | 0.4 | 1.3 |
| Chronic renal insufficiency | 1.5 | <0.1 | 1.8 |
| Chronic renal failure requiring dialysis | 0.1 | <0.1 | 0.2 |
| Peripheral neuropathy | 1.0 | 0.0 | 1.1 |
| Any episodes of severe hypoglycemia | 5.1 | 4.9 | 5.2 |

## 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 and older, as well as caregivers of children with CF.

### Depression and Anxiety Screening for Individuals 12 Years Old and Older, 2015 to 2019



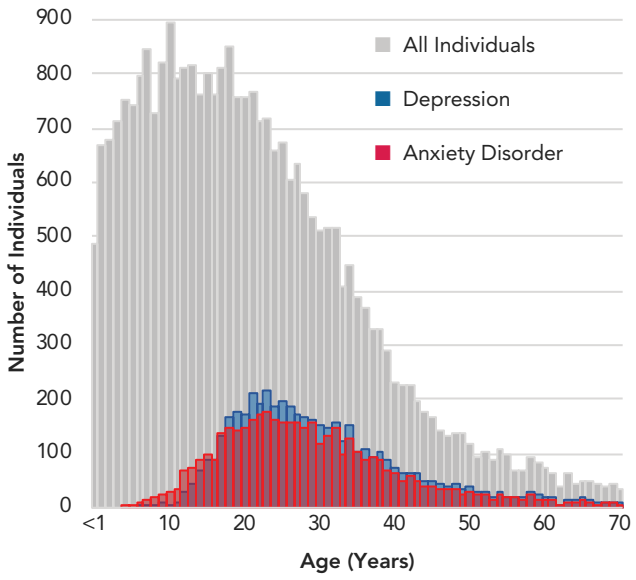

No differences are observed between screening rates for adolescents and adults. Of note, wide variation in screening across the CF care center network remains even as overall screening rates increase. Data on caregiver screening are not included in the Registry at this time.

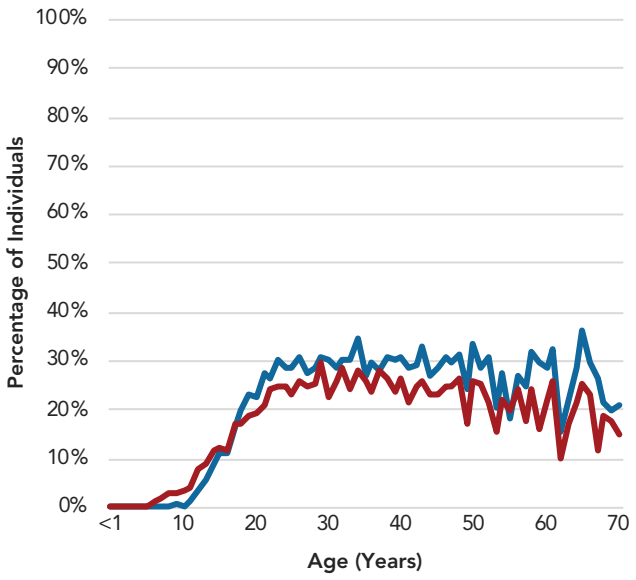
### Percentage of Individuals with Mental Health Screening, by Center

| | 0 — 50 — 100 | Median | Min | Max |
|---|---|---|---|---|
| Depression Screening Performed in Individuals 12 to 17 Years | | 83.9 | 35.7 | 100.0 |
| Depression Screening Performed in Individuals 18 Years and Older | | 89.9 | 56.8 | 100.0 |
| Anxiety Screening Performed in Individuals 12 to 17 Years | | 83.3 | 35.7 | 100.0 |
| Anxiety Screening Performed in Individuals 18 Years and Older | | 89.5 | 56.8 | 100.0 |

Prevalence of both anxiety and depression increase through adolescence and early adulthood, then remain high at older ages. There is substantial overlap in individuals who report both anxiety and depression; among individuals who report anxiety or depression, 43.7 percent report both conditions.

## Depression and Anxiety by Age in Years, 2019



# TRANSPLANTATION

*Lung transplantation remains an option for some individuals with severe lung disease. The number of lung transplant procedures for individuals with CF fluctuates yearly, with an overall upward trend.*

In 2019, there were 1,957 individuals in the Registry who were reported to have ever received a lung, kidney, heart, or liver transplant.

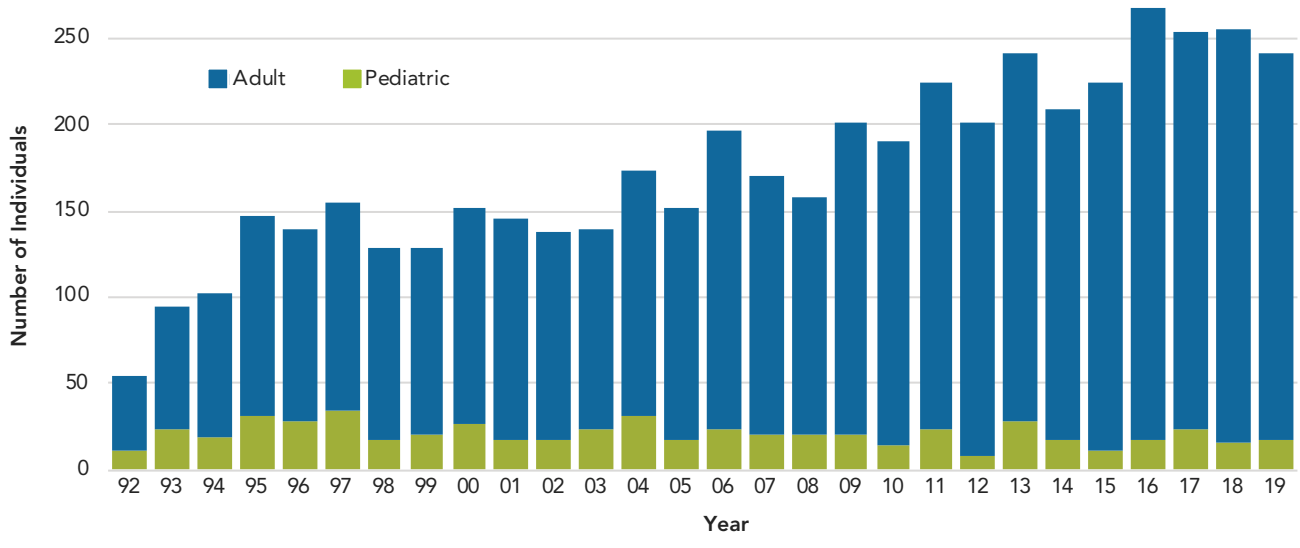
**Transplant Status of People with CF in 2019** (All Organs)

| | Number of Individuals |
|---|---|
| Accepted, on waiting list | 113 |
| Evaluated, rejected | 179 |
| Received transplant this year | 261 |
| Received transplant in a prior year | 1,696 |

## Lung Transplantation

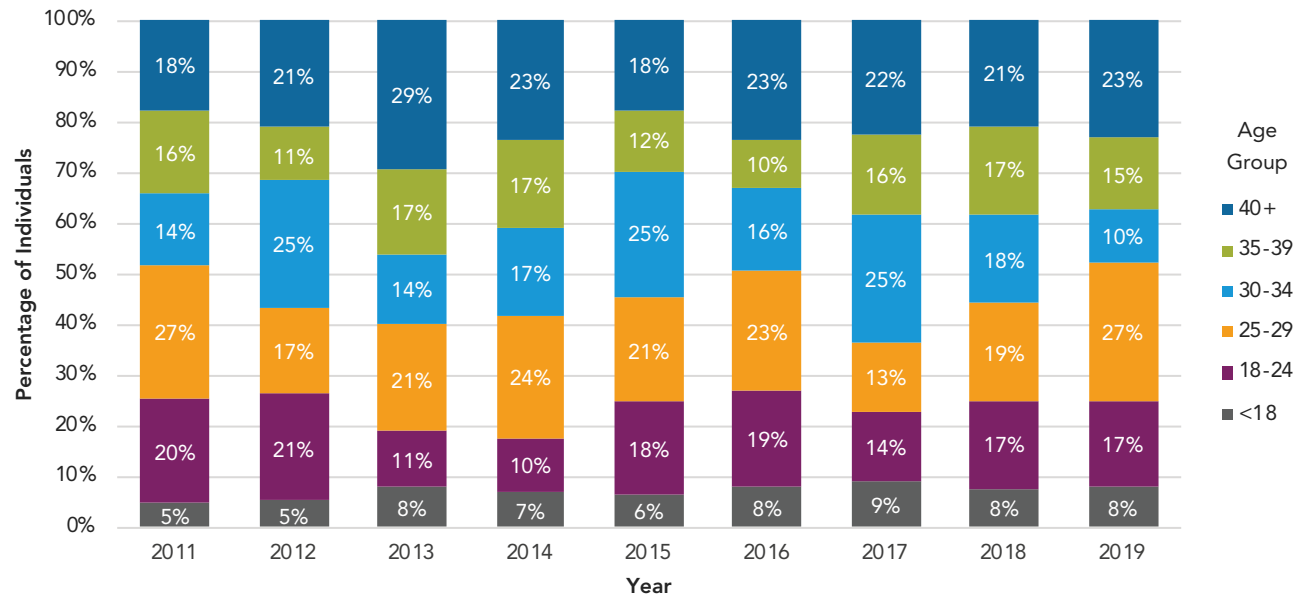
There were 1,786 post-lung transplant individuals in the Registry in 2019, including 241 individuals who were reported to have received a lung transplant in 2019. The number of CF lung transplants reported to the Registry is similar to the previous year, despite an overall modest increase in lung transplants in 2019 (2,714) compared to 2018 (2,530) as reported by the United Network for Organ Sharing.[43] Overall, 7.1 percent of CF transplants performed in 2019 were among individuals younger than age 18.

**Number of Individuals Receiving a Lung Transplant, 1992-2019**



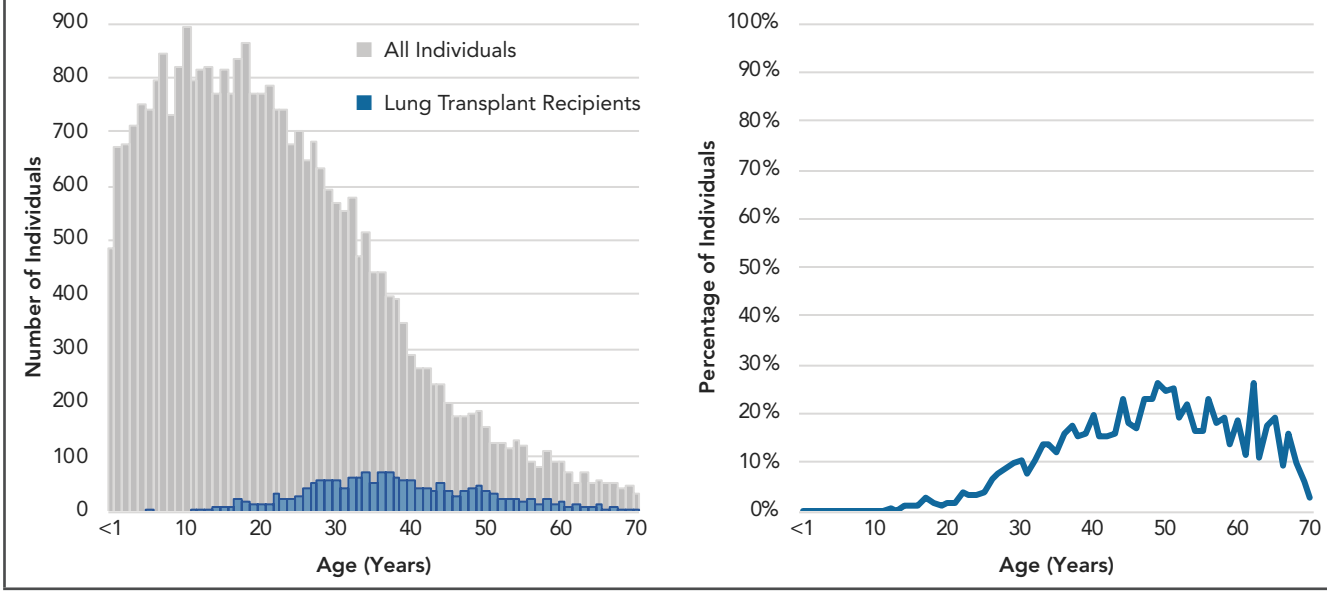
Since 1992, there has been a steady increase in the number of lung transplants observed among individuals with CF. With improvements in survival, lung function, and BMI in the CF patient population, there was a sense that the age of transplant recipients would increase and there would be fewer pediatric transplants. Based on the data, that has not occurred to date. Specifically, between 2011 and 2019, the percentage of transplant recipients younger than age 18 has remained stable, ranging from 5.0 percent to 9.0 percent. In 2019, 44.0 percent of lung transplants occurred among individuals aged 18 to less than 30 years.

## Age of First Lung Transplant by Year of Transplant, 2011-2019



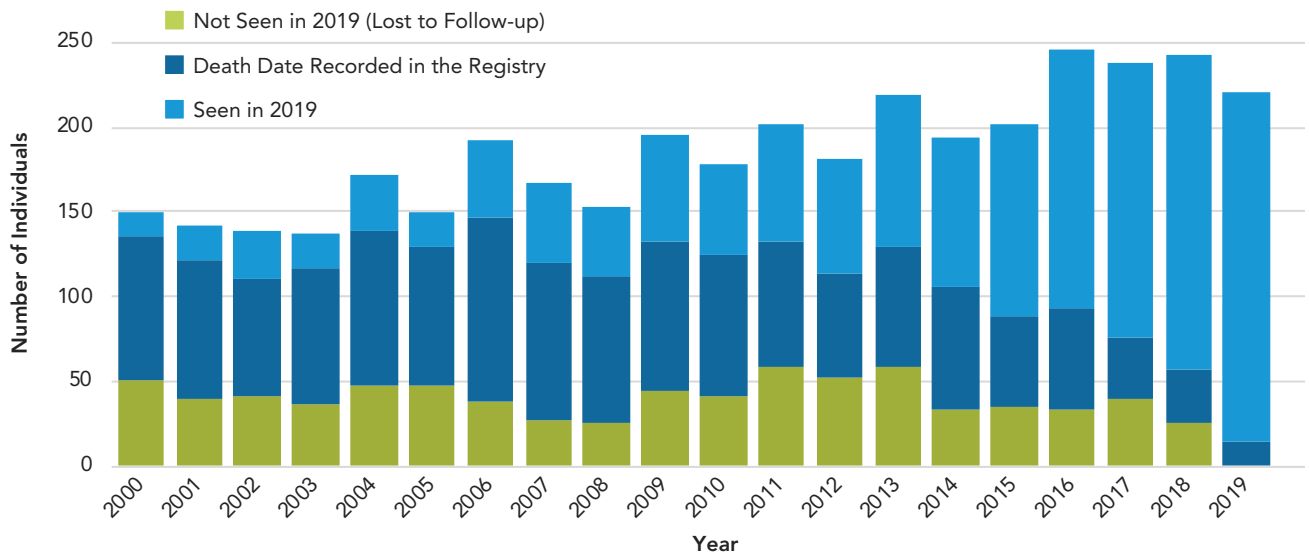

Overall, lung transplant recipients are a relatively small proportion of individuals included in the Registry; the majority are age 30 years and older.

## Lung Transplant Distribution in People with CF Seen in 2019



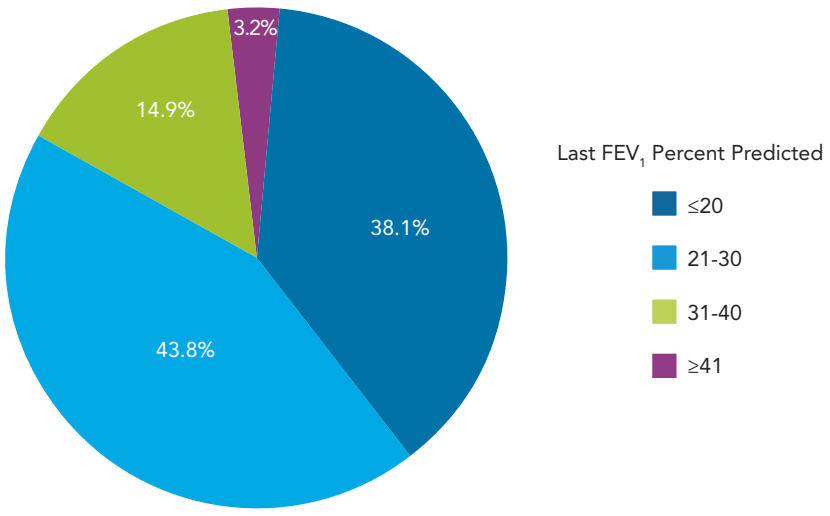
While most CF care occurs within CF Foundation-accredited care centers, transplant and post-transplant care typically occurs at transplant centers. Therefore, some of these individuals are lost to follow-up in the Registry. Optimal care for CF transplant recipients should include periodic follow-up at a CF Foundation-accredited care center.

## 2019 Status of Lung Transplant Recipients by Year of Transplant, 2000-2019




The last documented $FEV_1$ percent predicted prior to lung transplant demonstrates that the vast majority of individuals have $FEV_1$ percent predicted values less than 30 percent with almost half having $FEV_1$ percent predicted values less than 20 percent. The data underscores 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, 2017-2019



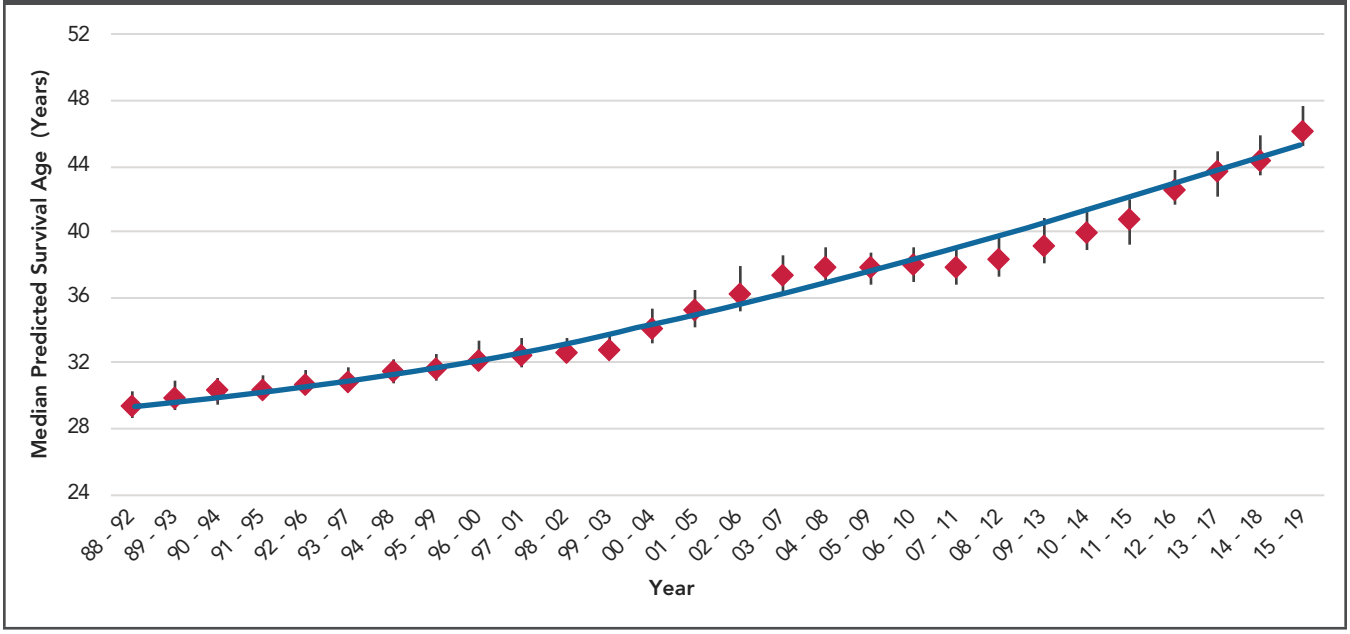
## SURVIVAL

*Over time, there have been substantial improvements in the survival of people with CF. We used a number of metrics to describe the survival of people living with CF in the United States. Definitions for these metrics are provided in the Technical Supplement that can be found on cff.org.*

### Median Predicted Survival

In 2019, the median predicted survival age of those born in 2019 was 48.4 years (95 percent confidence interval: 45.9 - 51.5 years). Given the instability of annual survival estimates due to the relatively low number of deaths in a given year, we group the data into five-year increments. The following graph shows gains in median predicted survival from 1987 to 2019 in five-year increments.* Between 2015 and 2019, the median predicted survival age was 46.2 years (95 percent confidence interval: 45.2 - 47.6 years). This means that half of individuals born from 2015 to 2019 are predicted to live beyond 46.2 years of age. This prediction assumes no further improvement in mortality rate and thus does not take into account the potential impact of CFTR modulators and other improvements in clinical care.

**Median Predicted Survival Age, 1988–2019** In Five Year Increments

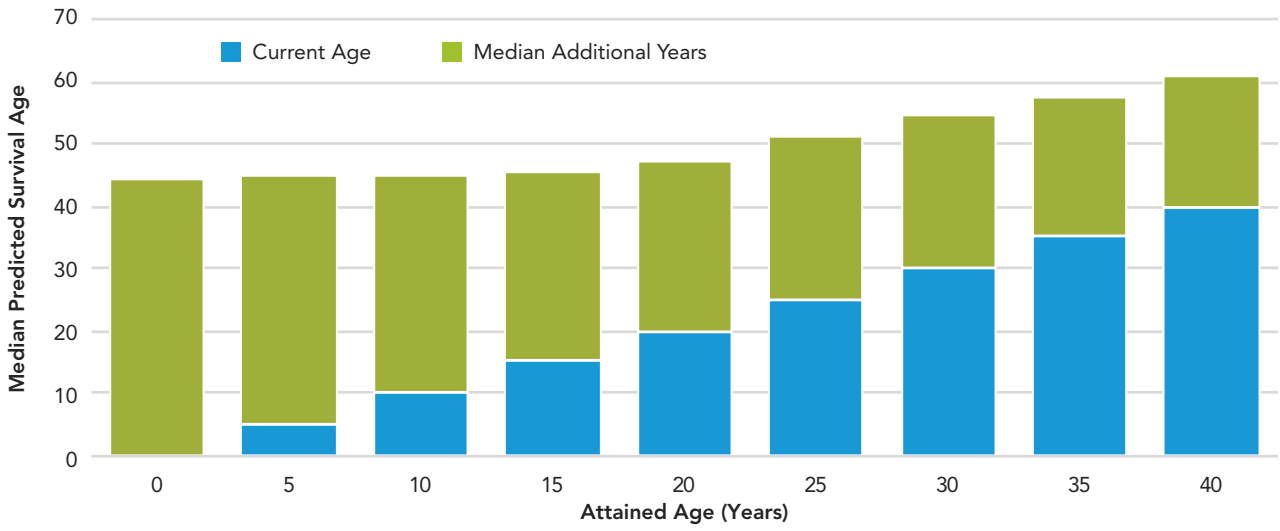



**Using the currently recommended method for calculating median predicted survival. For more information about the methodology, please see the Technical Supplement available at cff.org.*

## Median Conditional Predicted Survival

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

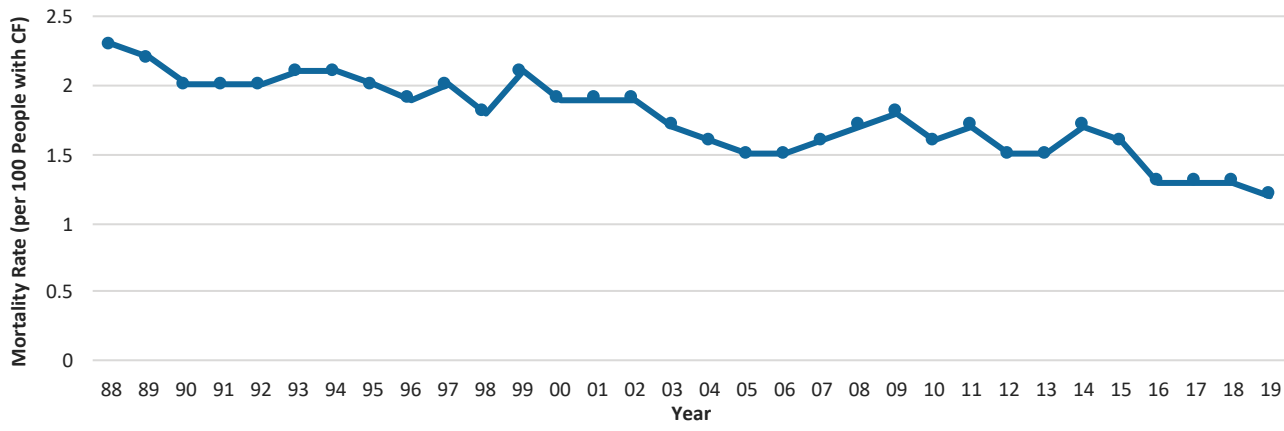
**Median Conditional Predicted Survival Based on Attained Age, 2015-2019**




## Mortality Rate

The mortality rate in 2019 was 1.2 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, given that the median age of individuals in the Registry has increased from 12.0 years in 1989 to 20.3 years in 2019.

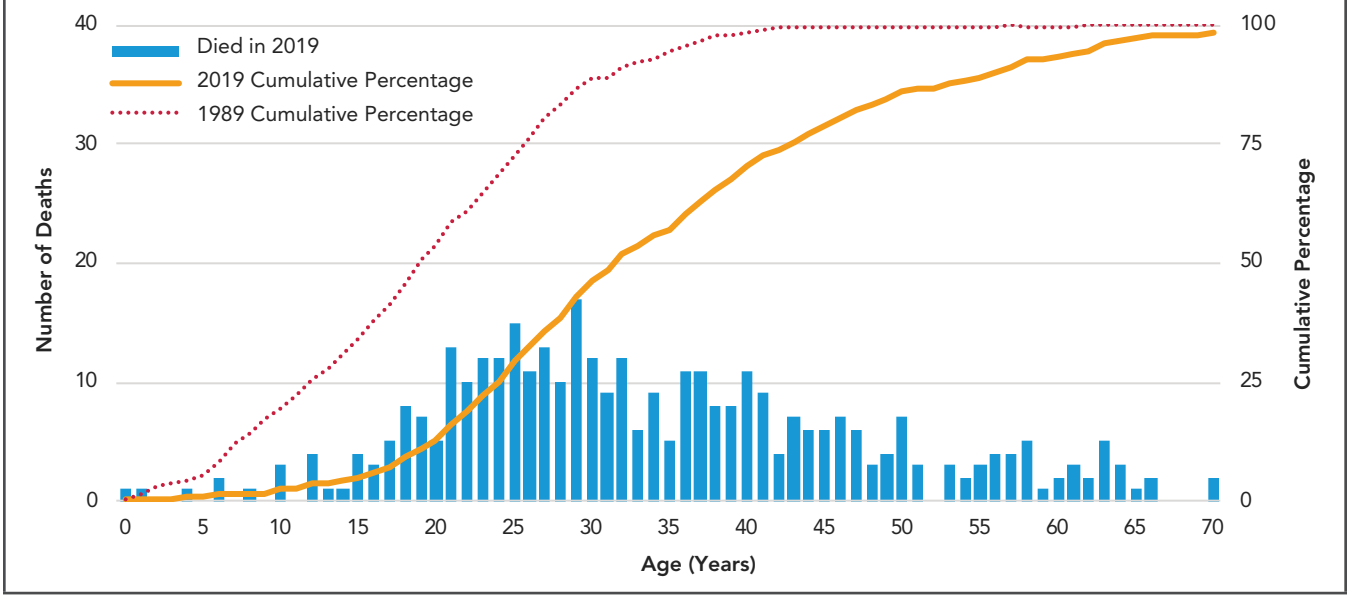
**Annual Mortality Rate (per 100 people with CF), 1988-2019**



## Median Age at Death

The median age at death was 32.4 years for the 373 people with CF who were reported to have died in 2019. About 11.3 percent of deaths occurred before 20 years of age. Comparing the cumulative percentage for age at death between 1988 and 2019 shows a substantial shift of the curve toward the right and a less steep curve, indicating that deaths are occurring at older ages and are spread across a wider age range. The median age at death reflects the reality of deaths in 2019 and cannot be used to predict survival of the entire population.

**Age at Death in 2019 (with 1989 Cumulative Percentage for Comparison)**




## Causes of Death

Among the 373 deaths in 2019, the primary causes were respiratory/cardiorespiratory and transplant-related, similar to previous years. Of these, 44.5 percent of deaths occurred in people who were F508del homozygotes, reflecting their distribution in the Registry. While 5.7 percent of people in the Registry are post-transplant, 123 deaths (33.0 percent) occurred in transplant recipients. Note that the primary cause of death for these individuals was not always categorized as transplant-related.

**Primary Cause of Death in 2019**

| Cause | Number of Individuals | Percent |
|---|---|---|
| Respiratory/cardiorespiratory | 232 | 62.2 |
| Transplant-related | 61 | 16.4 |
| Other | 40 | 10.7 |
| Unknown | 22 | 5.9 |
| Liver Disease/Liver Failure | 12 | 3.2 |
| Suicide or Drug Overdose | 6 | 1.6 |

## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

### DEMOGRAPHIC DATA

**Demographics**

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

## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

**Parents' Information** *(information not required for patients 21 years of age and older)*
Not available: ☐
Mother height: _____ ○ cm ○ inches
Father height: _____ ○ cm ○ inches

**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

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)
○ MSSA (methicillin sensitive Staph aureus)

Haemophilius influenzae (any species): ☐

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

# 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

**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
☐ Streptococcus milleri

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

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

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
Tobi Podhaler (Tobramycin Inhalation Powder): ☐
Frequency: ○ Four 28mg capsules BID alternate month
○ Other regimen (different dose or freq)
○ Eradication
Bethkis: ☐
Frequency: ○ 300 mg BID alternate month
○ Other regimen (different dose or freq)
○ Eradication

Other inhaled aminoglycoside (e.g. gentamcin, amikacin, or tobramycin preparation): ☐
Frequency: ○ Alternate Month

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

## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

○ Continuous
○ Other regimen (different dose or freq)
○ Eradication

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

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

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)
Acetylcysteine or Mucomist: ☐
High-dose ibuprofen (e.g. 25-30 mg/kg): ☐
Key:
**FORM NAME**
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

Total (mg/dose): _____
Hypertonic saline: ☐
Concentration (%):○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10
Frequency: ○ QD ○ BID ○ Other

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

**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: ☐

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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: ____

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

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

*GI other*
Ursodeoxycholic acid: ☐

## Pulmonary

**Pulmonary Function Tests (PFTs)**
Unable to Perform test: ☐
Reason why PFTs have not been done: _____

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:_____ ]

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## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

[% 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

*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:

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

☐ 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

**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**
☐ 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

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## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

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

**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: _____

**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

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

○ None
○ Other
Specify if other technique:_____

**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

**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
☐ 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
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
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: [ ]

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## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

[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 ○ Unknown

*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

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

**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: ☐

**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

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

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

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## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

○ 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

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: ☐

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

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

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## 2019 Cystic Fibrosis Foundation Patient Registry Questionnaire

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

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

**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
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: _____

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

# REFERENCES


1. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J*. 2012;40(6):1324–1343.
2. Saiman L, Marshall BC, Mayer-Hamblett N, et al. Azithromycin in patients with cystic fibrosis chronically infected with *Pseudomonas aeruginosa*: a randomized controlled trial. *JAMA*. 2003;290(13):1749–1756.
3. U.S. Census Bureau Population Division. The Hispanic Population in the United States: 2018 Population Estimates. Available at: https://www.census.gov/quickfacts/fact/table/US/RHI725218#RHI725218. Accessed July 13, 2020.
4. Curtin SC, Abma JC, Ventura SJ, Henshaw SK. Pregnancy rates for U.S. women continue to drop. National Center for Health Statistics Data Brief. 2013 Dec:1–8.
5. Cystic Fibrosis Foundation, Borowitz D, Robinson KA, et al. Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis. *J Pediatr*. 2009 Dec;155(6 Suppl):S73–S93.
6. Cystic Fibrosis Foundation, Borowitz D, Parad RB, et al. Cystic Fibrosis Foundation practice guidelines for the management of infants with cystic fibrosis transmembrane conductance regulator-related metabolic syndrome during the first two years of life and beyond. *J Pediatr*. 2009 Dec;155(6 Suppl):S106–S116.
7. Farrell PM, White TB, Ren CL, et al. Diagnosis of Cystic Fibrosis: Consensus Guidelines from the Cystic Fibrosis Foundation. *J Pediatr*. 2017 Feb;181:S4–S15 e1.
8. Bombieri C, Claustres M, De Boeck K, et al. Recommendations for the classification of diseases as CFTR-related disorders. *J Cyst Fibros*. 2011;10(Suppl 2):S86–S102.
9. Martin JA, Hamilton BE, Osterman MJK. Births in the United States, 2018. NCHS Data Brief, no 346. Hyattsville, MD: National Center for Health Statistics. 2019.
10. United States Department of Health and Human Services (US DHHS), Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS), Division of Vital Statistics. Natality public-use data 2007-2018, on CDC WONDER Online Database. September 2019. Available at: http://wonder.cdc.gov/natality-current.html. Accessed July 13, 2020.
11. US CF Foundation, Johns Hopkins University, The Hospital for Sick Children. The Clinical and Functional Translation of CFTR (CFTR2). Available at: https://cftr2.org. Accessed July 13, 2020.
12. De Boeck K, Zolin A, Cuppens H, Olesen HV, Viviani L. The relative frequency of CFTR mutation classes in European patients with cystic fibrosis. *J Cyst Fibros*. 2014;13(4):403–409.
13. Green DM, McDougal KE, Blackman SM, et al. Mutations that permit residual CFTR function delay acquisition of multiple respiratory pathogens in CF patients. *Respir Res*. 2010;11(1):140.
14. Welsh MJ, Smith AE. Molecular mechanisms of CFTR chloride channel dysfunction in cystic fibrosis. *Cell*. 1993 Jul 2;73(7):1251–1254.
15. Kiesewetter S, Macek M Jr, Davis C, et al. A mutation in CFTR produces different phenotypes depending on chromosomal background. *Nat Genet*. 1993;5(3):274–278.
16. Thauvin-Robinet C, Munck A, Huet F, et al. The very low penetrance of cystic fibrosis for the R117H mutation: a reappraisal for genetic counselling and newborn screening. *J Med Genet*. 2009;46(11):752–758.
17. Lahiri T, Hempstead SE, Brady C, et al. Clinical Practice Guidelines from the Cystic Fibrosis Foundation for Preschoolers with Cystic Fibrosis. *Pediatrics*. 2016;137(4).
18. Quittner AL, Abbott J, Georgiopoulos AM, et al. International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety. *Thorax*. 2016;71(1):26–34.
19. Yankaskas JR, Marshall BC, Sufian B, Simon RH, Rodman D. Cystic fibrosis adult care: consensus conference report. *Chest*. 2004;125(1 Suppl):1S–39S.
20. Cystic Fibrosis Foundation. Clinical care practice guidelines for cystic fibrosis. Available at: https://www.cff.org/Care/Clinical-Care-Guidelines. Accessed July 13, 2020.
21. Saiman L, Siegel J, Cystic Fibrosis Foundation Consensus Conference on Infection Control Participants. Infection control recommendations for patients with cystic fibrosis: microbiology, important pathogens, and infection control practices to prevent patient-to-patient transmission. *Am J Infect Control*. 2003;31(3 Suppl):S1–S62.
22. Saiman L, Siegel JD, LiPuma JJ, et al. Infection prevention and control guideline for cystic fibrosis: 2013 update. *Infect Control Hosp Epidemiol*. 2014 Aug;35(Suppl 1):S1–S67.

23. Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines. *MMWR Recomm Rep*. 2016;65(5):1–54.

24. Aris RM, Merkel PA, Bachrach LK, et al. Guide to bone health and disease in cystic fibrosis. *J Clin Endocrinol Metab*. 2005 Mar;90(3):1888–1896.

25. Stallings VA, Stark LJ, Robinson KA, et al. Evidence-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review. *J Am Diet Assoc*. 2008 May;108(5):832–839.

26. Sokol RJ, Durie PR. Recommendations for management of liver and biliary tract disease in cystic fibrosis. Cystic Fibrosis Foundation Hepatobiliary Disease Consensus Group. *J Pediatr Gastroenterol Nutr*. 1999;28(Suppl 1):S1–S13.

27. United States Public Health Service, Office of the Surgeon General. The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. Rockville, MD: U.S. Dept. of Health and Human Services, Public Health Service, Office of the Surgeon General; 2006. Available at: https://www.ncbi.nlm.nih.gov/books/NBK44324. Accessed July 20, 2020.

28. Centers for Disease Control and Prevention (CDC). Behavioral Risk Factor Surveillance System Survey Data Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2019. Available at: https://www.cdc.gov/brfss/brfssprevalence/index.html. Accessed July 15, 2020.

29. Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al. Cystic Fibrosis Foundation pulmonary guideline. Pharmacologic approaches to prevention and eradication of initial Pseudomonas aeruginosa infection. *Ann Am Thorac Soc*. 2014;11(10):1640–1650.

30. Lee TW, Brownlee KG, Conway SP, Denton M, Littlewood JM. Evaluation of a new definition for chronic *Pseudomonas aeruginosa* infection in cystic fibrosis patients. *J Cyst Fibros*. 2003 Mar;2(1):29–34.

31. Billinger ME, Olivier KN, Viboud C, et al. Nontuberculous mycobacteria-associated lung disease in hospitalized persons, United States, 1998-2005. *Emerg Infect Dis*. 2009;15(10):1562–1569.

32. Floto RA, Olivier KN, Saiman L, et al. US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis: executive summary. *Thorax*. 2016;71(1):88–90.

33. Olivier KN, Weber DJ, Wallace RJ Jr, et al. Nontuberculous mycobacteria. I: multicenter prevalence study in cystic fibrosis. *Am J Respir Crit Care Med*. 2003 Mar;167(6):828–834.

34. Schwarzenberg SJ, Hempstead SE, McDonald CM, et al. Enteral tube feeding for individuals with cystic fibrosis: Cystic Fibrosis Foundation evidence-informed guidelines. *J Cyst Fibros*. 2016;15(6):724–735.

35. Grummer-Strawn LM, Reinold C, Krebs NF, Centers for Disease Control and Prevention. Use of World Health Organization and CDC growth charts for children aged 0-59 months in the United States. *MMWR Recomm Rep*. 2010;59(RR-9):1–15.

36. Leung DH, Heltshe SL, Borowitz D, et al. Effects of diagnosis by newborn screening for cystic fibrosis on weight and length in the first year of life. *JAMA Pediatr*. 2017;171(6):546–554.

37. Yen EH, Quinton H, Borowitz D. Better nutritional status in early childhood is associated with improved clinical outcomes and survival in patients with cystic fibrosis. *J Pediatr.* 2013;162(3):530–535 e1.

38. Flume PA, Mogayzel PJ Jr, Robinson KA, et al. Cystic fibrosis pulmonary guidelines: treatment of pulmonary exacerbations. *Am J Respir Crit Care Med*. 2009 Nov;180(9):802–808.

39. ClinicalTrials.gov. Standardized Treatment of Pulmonary Exacerbations II. 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT02781610?term=stop+cystic+fibrosis&rank=2. Accessed July 15, 2020.

40. Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013 Apr;187(7):680–689.

41. Flume PA, Robinson KA, O'Sullivan BP, et al. Cystic fibrosis pulmonary guidelines: airway clearance therapies. *Respir Care*. 2009 Apr;54(4):522–537.

42. Moran A, Brunzell C, Cohen RC, et al. Clinical care guidelines for cystic fibrosis-related diabetes: a position statement of the American Diabetes Association and a clinical practice guideline of the Cystic Fibrosis Foundation, endorsed by the Pediatric Endocrine Society. *Diabetes Care*. 2010 Dec;33(12):2697–2708.

43. U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. Transplants by organ type. 2019. Available at: https://unos.org/data/transplant-trends. Accessed June 15, 2020.

44. Ramos KJ, Smith PJ, McKone EF, et al. Lung transplant referral for individuals with cystic fibrosis: Cystic Fibrosis Foundation consensus guidelines. *J Cyst Fibros*. 2019 May;18(3):321-333.

## NOTES

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4550 Montgomery Ave., Suite 1100N
Bethesda, MD 20814
1.800.FIGHT.CF
cff.org
info@cff.org