Patient Registry

Annual Data Report

2014

CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

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
2014 Annual Data Report
Bethesda, Maryland
©2015 Cystic Fibrosis Foundation

PHOTOGRAPHY BY
Cade Martin

SPECIAL ACKNOWLEDGEMENTS
Those who contributed to the maintenance of PortCF, analysis of data and creation of this report:
Bruce Marshall
Alexander Elbert
Kristofer Petren
Samar Rizvi
Aliza Fink
Josh Ostrenga
Ase Sewall

CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

August 2015

Dear Friends and Colleagues:

It is a pleasure to share the 2014 Patient Registry Annual Data Report with you. The impact of the Cystic Fibrosis Foundation Patient Registry continues to grow and inform many important initiatives, including: quality improvement, clinical trial design, retrospective observational studies, prospective "Registry-embedded" observational studies, comparative effectiveness research, and safety and effectiveness studies of newly approved therapies.

Ongoing collaborations with colleagues in the United Kingdom and Canada continue to provide opportunities to compare outcomes and practice patterns across countries and health care systems, and a number of high-quality publications based on Registry data have contributed to our growing knowledge about this disease.

The tremendous success of the Registry would not be possible without the vital contributions of many, most notably the individuals 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. The audit studies conducted to date confirm the high degree of completeness and accuracy of the Registry data. We are deeply grateful to all who have helped make the Registry an indispensable tool in our shared endeavors to help those with CF enjoy the best health and quality of life.

This year's report shows that we have crossed an important threshold in the history of CF, with more than half of individuals with CF in the United States now age 18 or older. This milestone is a tribute to the commitment and leadership of care teams across the country, and also presents a challenge to the CF community as we strive to serve the needs of the growing number of adults living with the disease.

As in previous years, we have included longitudinal analyses and genotype-specific analyses. This year, we have also added histograms showing various attributes by age (e.g., genotype, insurance status, complications). We believe this new graphical display provides fresh insights into the data.

We hope you find this year's report rich and interesting and that you participate in the discussions about what the information means for the CF community. This is a truly exciting time in CF, with advances in health care delivery and new therapeutics that have transformative potential. Together, we will track these and other important developments in the Registry.

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

Bruce C. Marshall, M.D.
Senior Vice President of Clinical Affairs
Cystic Fibrosis Foundation

TABLE OF CONTENTS

ABOUT THIS REPORT

Each year, we strive to improve the Patient Registry Annual Data Report in order to effectively convey the health status of individuals with cystic fibrosis and the care they receive at CF Foundation-accredited care centers. As we did last year, we have created two complementary reports — this comprehensive 2014 Annual Data Report and a shorter Highlights of the 2014 Patient Registry Data Report. Both reports will be available on our website, www.cff.org, to people with CF and their families, clinicians and researchers. If you are interested in data about a specific CF care center, key metrics are available on the Foundation's website (search for "care center data"). You can also ask your care center for information from its center report, which describes the center's patient population, the care they receive and their outcomes.

Graphics in blue show center-level variation

Graphics in purple show patient-level data

As explained below, we continue to use box-and-whisker plots to show variation among individuals in the Registry. Beginning this year, we have focused the center-level box-and-whisker plots on aspects of care that are directly related to care delivered (e.g., percentage of people with CF receiving guideline-recommended therapy) and included more box-and-whisker charts showing population-level variation. We have also added a number of charts displaying cross-sectional data by age to show the pattern of several key attributes or health outcomes from infancy to adulthood.

Report Inclusion and Exclusion Criteria

This report is based on the 2014 data entered into the Registry. Figures are either cross-sectional (2014 data only) or longitudinal (data over several years). When possible, longitudinal graphs include data from 1986 (the first year that we have complete data) through 2014. If a variable was added to the Registry after 1986, or the way in which data was collected for a variable was modified or enhanced, the figure may show a different range of years.

Registry data are updated and processed every year; therefore, we encourage you to compare the 2014 data with the revised results from previous years displayed within this report, rather than referring to previously published reports.

When interpreting longitudinal charts it is important to keep in mind that the Registry reflects a dynamic population of those receiving care at a care center during a specific year. These charts do not necessarily include the same individuals each year. New children and adults with CF are added or return to the Registry, while others are no longer captured in the Registry because they died or were lost to follow-up. These year-to-year changes impact the overall profile of the CF population in the Registry.

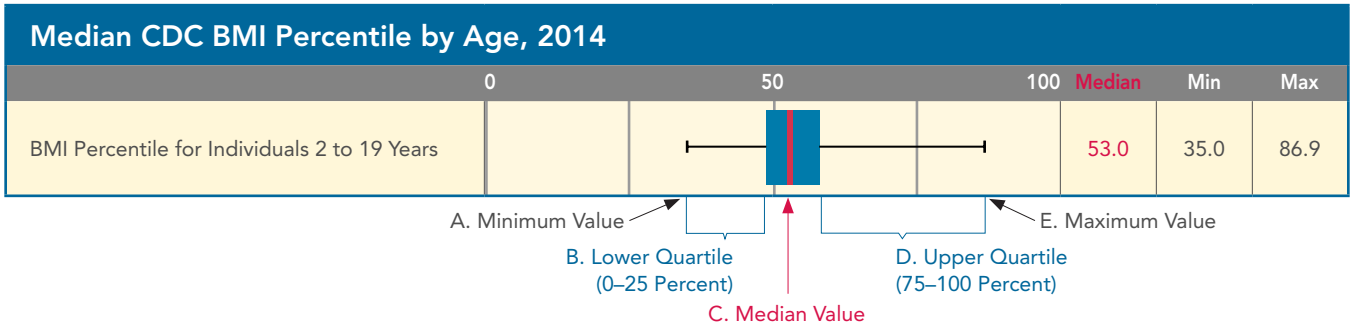
The report contains data from individuals diagnosed with CF who have consented to participate in the Registry and were seen in a CF center in 2014, or who were born, diagnosed or died in 2014. Data from individuals with a diagnosis of CFTR-related metabolic syndrome (CRMS) or CFTR-related disorders were excluded from all figures except the figure specifically related to new diagnoses in 2014. Data from individuals who have received a lung transplant were excluded from the analyses of pulmonary function, pulmonary therapies, pulmonary complications, respiratory cultures and airway clearance data.

The individuals represented in the figures vary and are based on the eligibility criteria described in the title and/or footnotes for the specific figure.

Figures presenting data on center-level variation include only those centers reporting at least 10 eligible individuals. Exceptions to this rule are figures showing center-level variation among infants or among individuals with a G551D mutation, Cystic fibrosis-related diabetes or pulmonary exacerbations. For these figures, centers reporting five or more eligible individuals are included.

Box-and-Whisker Charts to Show Center-Level and Population-Level Variation

Throughout the report, box-and-whisker plots are used in two ways: to show center-level and population-level variation. For example, the box-and-whisker plot below shows the median body mass index (BMI) percentile among individuals ages 2 to 19 years, across all centers:



The box-and-whisker plots showing center-level variation are constructed by first determining the median value for individuals at each center. We then create the box-and-whisker plots using the summary numbers from each center.

Box-and-whisker plots provide the following information as noted in the figure above:

A. Minimum: The lowest median BMI percentile at any center (left "whisker").

B. 0-25th percentile: the lowest 25 percent of all centers' medians fall in this range.

C. Median: 50 percent of observations fall below and 50 percent fall above. Median values, shown by a red line, are preferable to mean values because they are not skewed by extreme values.

D. "Box": The 25th to 75th percentile values.

E. 75th – 100th percentile: the highest 25 percent of all centers' medians fall in this range.

F. Maximum: The highest median BMI percentile of all the centers (right "whisker").

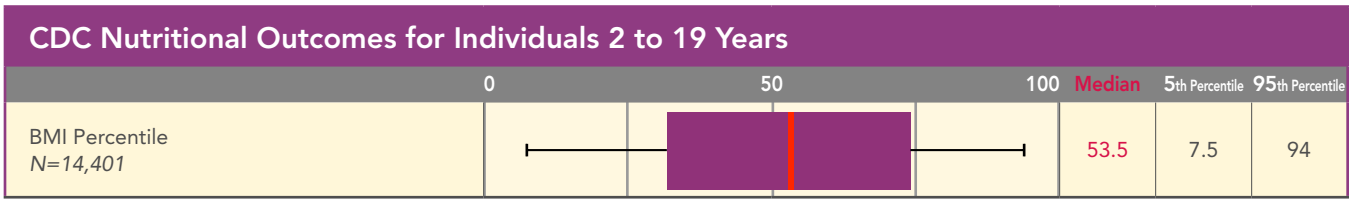
Plots with no shading show data for all individuals

Plots with gray shading show data for infants

Plots with yellow shading show data for children

Plots with blue shading show data for adults

In addition, box-and-whisker plots are used to show the distribution of population-level variations for outcomes and process measures. An example is the figure below, which also displays the variation in BMI percentile among individuals ages 2 to 19 in the 2014 reporting year. In this case, each individual's data is included in the box-and-whisker plot. As a result, the median value is nearly identical but there is much wider variation in the population-level plot as compared to the center-level.

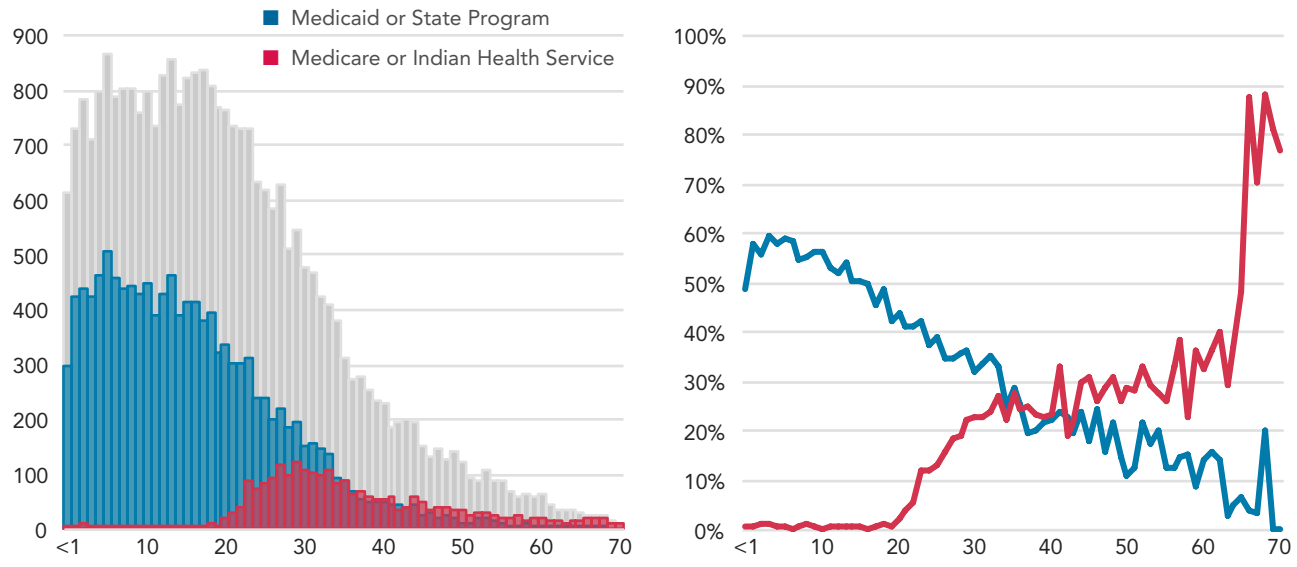


Using Combined Data Charts to Display Selected Attributes, by Age

Throughout this report, combined data charts are used to display selected attributes or health outcomes for people with CF by age; histograms for raw patient counts and line charts for percentage of total individuals per age. Within these charts, the figure on the left shows the total number of people with CF at each age, as well as the number with the attribute displayed. The figure on the right shows the percentage of people with CF at each age with the attribute. We removed the age cohorts over age 70 for this display because there were less than 10 individuals at any age above this age range. The light gray bars in the background represent the total number of people with CF, at each age, in the 2014 Registry data. For consistency across the report and to allow comparisons across different attributes, these gray bars always represent the total number of people with CF in that age cohort and remain consistent throughout the report. Bars of other colors are used to show the number of people with a selected attribute (e.g., a complication).

Below, the histogram on the left shows the number of people who reported Medicaid as a form of insurance, in blue, and the number of people who reported Medicare as a form of insurance, in red. The line graph on the right shows the percentage of people who selected each insurance type with the percentage lines using the same color scheme as the bar chart. These charts provide insight into how attributes change across the ages in the 2014 Registry data.

Medicare/Indian Health Service vs. Medicaid/State Programs by Age, 2014



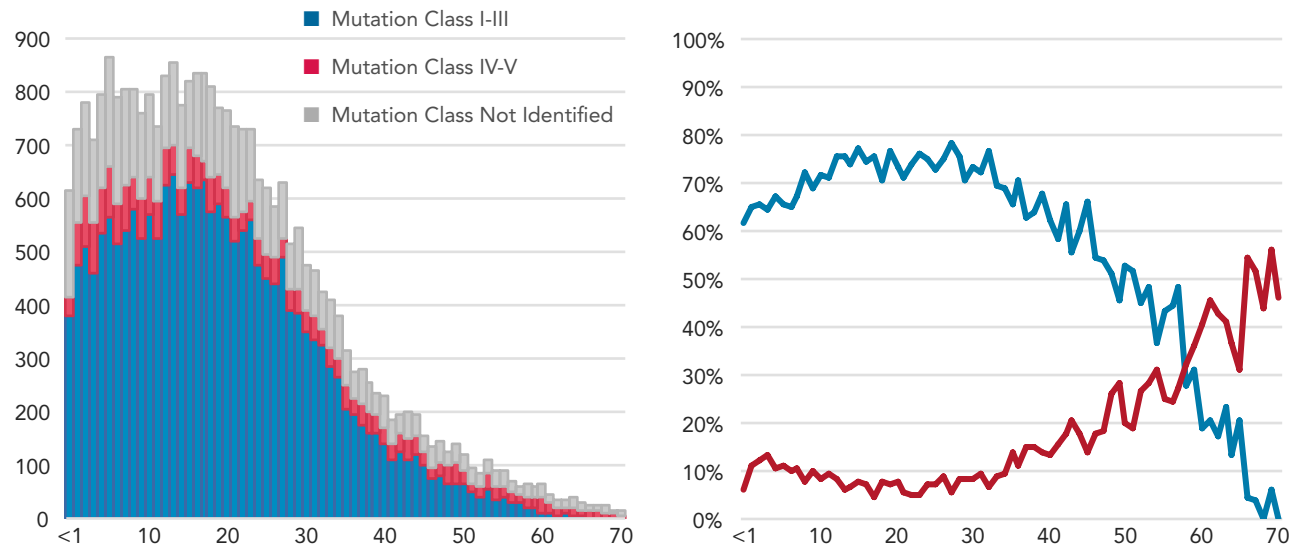
In most cases where this type of display is used, the categories are not mutually exclusive, so an individual can be counted in more than one of the categories. In cases where the attributes are mutually exclusive, such as mutation class or lung function cohorts, a stacked bar is shown.

Caution must be used when interpreting the data in these charts because there have been changes in the diagnosis, treatment and survival of people with CF over time. Specifically, universal newborn screening for CF has been in place in the United States since 2010 and was implemented even earlier in many states. Therefore, the diagnostic and clinical

characteristics of very young individuals included in the Registry in recent years are different than those of similarly aged individuals included in the Registry previously. Prior to newborn screening, most infants were diagnosed because of clinical symptoms. Now, asymptomatic and potentially healthier infants are being diagnosed with CF and included in the Registry earlier than they previously would have been. Within older ages, we see an effect referred to as survival bias, which is particularly evident in cross-sectional data. Older individuals currently in the Registry have survived and are likely healthier, and are therefore not representative of other people with CF who were included in the same birth cohort for analysis done at younger ages. We must keep these and other potential biases in mind when interpreting the data.

These two specific biases can be seen in the chart below. Individuals with a genotype with two mutations within classes I to III are typically associated with a severe phenotype and are assigned to the mutation class I-III group, whereas individuals with one or more mutations within classes IV or V are typically associated with a milder phenotype and are assigned to the mutation class IV-V group. We see a modest increase in number and percentage of individuals with class IV and V mutations among those ages 5 and younger, i.e., children born in the era of universal newborn screening for CF. At older ages, the greater proportion of individuals observed with a genotype consisting of one or more mutations from classes IV or V is the result of survivor bias.

Mutation Class Status by Age, 2014 *(Stacked Bar Chart)*



Data Audit Summary

The CF Foundation continued to conduct independent audits of the PortCF data to confirm data completeness and data accuracy using medical records. In 2014, the 2013 Registry data of 20 programs were compared to medical records. The audit reviewed 979 individuals, 4,284 encounters and 678 care episodes. Similar to an audit conducted in 2013, we found a high degree of completeness and accuracy of the data in the Registry.

Summary of the Cystic Fibrosis Foundation Patient Registry, 1999-2014

Demographics	1999	2004	2009	2013	2014
People with CF (n)	21,561	22,590	26,283	28,134	28,676
Newly diagnosed individuals (n)[A]	931	999	1,160	1,039	859
Detected by newborn screening (%)	7.9	11. 6	49.8	60.7	63.4
Mean age at diagnosis (years)	3.0	3.2	3.5	3.7	3.7
Median age at diagnosis (months)	6	6	5	4	4
Mean age (years)	16.6	17.5	19.1	20.2	20.6
Median age (years)	14.5	15.5	17.2	17.9	18.3
Adults ≥ 18 years (%)	37.9	41.0	47.2	49.7	50.7
Race (not mutually exclusive)					
White (%)	95.5	95.2	94.5	93.9	93.9
African American (%)	3.8	3.9	4.3	4.6	4.6
Other race (%)	1.4	1.9	2.6	3.2	3.1
Hispanic (any race) (%)	5.0	6.0	6.7	8.0	8.2
Males (%)	52.9	52.0	51.8	51.5	51.6
Mortality					
Total deaths (n)	460	372	455	418	461
Annual mortality rate (per 100)	2.1	1.6	1.7	1.5	1.6
Predicted median survival (years)	28.9	34.4	34.7	40.4	39.3
95% confidence interval (years)	27.4-31.3	32.3-37.1	33.0-37.4	37.4-43.8	37.3-41.4
Median age at death (years)	26.0	26.1	27.0	28.2	29.1
GI/Nutrition					
BMI percentile, individuals 2 to 19 years (median)	39.4	44.3	49.7	52.8	53.5
Percent weight < 10th CDC percentile	26.0	21.5	15.8	13.6	13.1
Percent height < 5th CDC percentile	16.5	14.4	11.9	10.6	10.5
BMI, individuals 20 to 40 years (median)	20.8	21.5	22.1	22.2	22.3
Pancreatic enzyme replacement therapy (%)	96.2	94.6	90.2	87.4	87.3
Supplemental feeding - tube (%)	-	9.2	11.5	11.2	11.4
Supplemental feeding - oral only (%)	-	37.1	40.5	42.7	44.5
Pulmonary					
FVC % predicted (mean)[B]	81.7	83.7	86.5	87.4	87.7
FEV_1 % predicted (mean)[B]	70.6	73.2	75.2	76.1	76.2
Respiratory Microbiology					
P. aeruginosa (PA) (%)[C]	59.1	57.3	51.9	48.7	47.5
Multidrug-resistant PA (%)[D]	-	8.9	8.6	8.6	8.6
B. cepacia complex (%)	3.3	2.9	2.7	2.6	2.5
S. aureus (SA) (%)[E]	47.4	62.3	66.6	69.3	70.0
Methicillin-sensitive *S. aureus* (MSSA) (%)	44.3	51.9	50.8	51.7	53.6
Methicillin-resistant *S. aureus* (MRSA) (%)	4.2	14.8	23.9	25.7	25.9
S. maltophilia (%)	6.6	11.9	13.1	13.8	13.5
Mycobacterial species (%)[F]	-	-	-	12.1	12.2

Table continues on the next page

Summary of the Cystic Fibrosis Foundation Patient Registry, 1999-2014 *continued*					
Health Care Utilization and Pulmonary Exacerbations[G]	**1999**	**2004**	**2009**	**2013**	**2014**
Outpatient visits to CF centers reported per year (mean)	5.3	4.1	4.3	4.7	4.5
Treated with IV antibiotics for a pulmonary exacerbation (%)	-	34.9	35.8	35.0	35.2
Number of pulmonary exacerbations per year (mean)	-	0.6	0.7	0.7	0.7
Number of days of treatment for pulmonary exacerbation per year (mean)[H]	-	29.8	32.0	30.7	31.8
Number of days of home IV treatment for exacerbations per year (mean)[H]	-	13.1	13.3	11.8	11.8
Number of days of hospitalization for pulmonary exacerbation per year (mean)[H]	-	16.7	18.7	18.9	20.0
Pulmonary Therapies[I]					
Dornase alfa (≥ 6 years) (%)	58.1	70.6	81.0	85.1	86.0
Inhaled tobramycin (PA+ and ≥ 6 years) (%)[J]	62.0	68.8	71.5	66.4	69.8
Inhaled aztreonam (PA+ and ≥ 6 years) (%)	-	-	4.0	41.5	42.5
Azithromycin (PA+ and ≥ 6 years) (%)[K]	-	-	67.0	67.3	67.5
Hypertonic saline (≥ 6 years) (%)	-	-	48.3	63.3	65.7
Ibuprofen (6-12 years with FEV_1 ≥60 percent) (%)	-	-	3.6	3.0	2.7
Ivacaftor (≥ 6 years with G551D mutation) (%)	-	-	-	86.8	89.5
Oxygen (%)[L]	-	-	10.8	11.5	11.3
Non-invasive ventilation (%)	-	-	2.2	2.8	2.9
Transplants					
Lung (all procedures) (n)	142	178	210	239	202
Liver (n)	13	19	17	13	13
Kidney (n)	1	1	6	11	8

[A] *We anticipate that additional 2014 diagnoses will be entered into the Registry in 2015.*

[B] *Pulmonary function data throughout this report reflect the use of GLI equations[1] for both children and adults.*

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

[D] *Defined as resistant to all antibiotics tested in two or more classes.*

[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] *Percent of individuals with one or more mycobacterial species isolated out of those patients who had a mycobacterial culture during the year. This includes* M. tuberculosis *as well as nontuberculous mycobacteria (NTM) species.*

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

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

[I] *Percent of individuals on therapy at any encounter in the year. All patients noted as intolerant or having an allergy to a specific therapy were excluded.*

[J] *Includes TOBI®, TOBI® Podhaler™ and Bethkis® in 2013 — in prior years, only TOBI® was available.*

[K] *Individuals were considered eligible if they met the selection criteria used in the U.S. azithromycin trial.[2]*

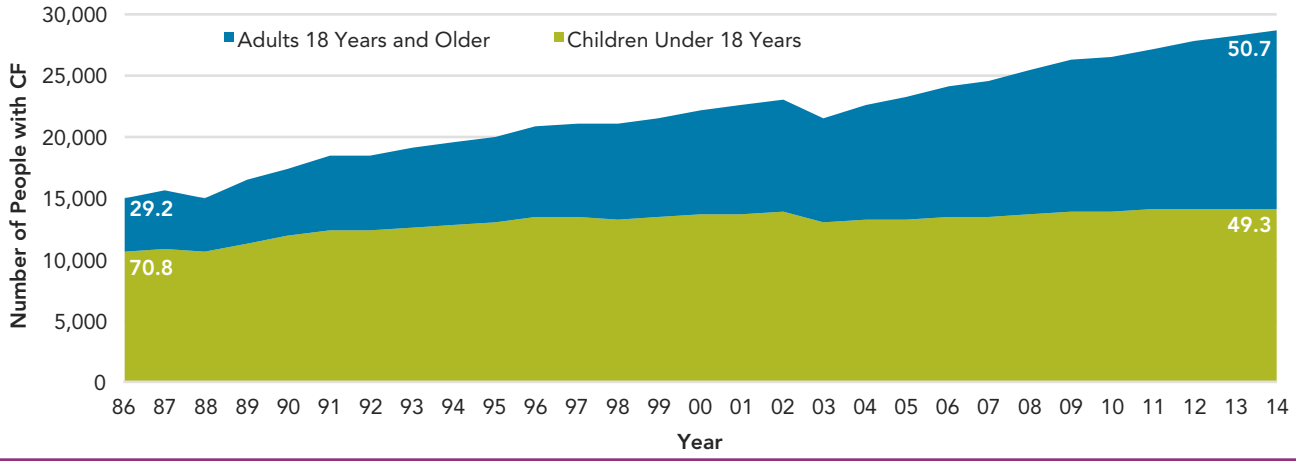
[L] *Includes continuous, nocturnal or with exertion.*

DEMOGRAPHICS

The Registry contains data on people with CF from 1986 to 2014. During that time, substantial changes in the care people with CF receive have led to improved survival. This section shows the current and longitudinal distribution of demographic characteristics of individuals with CF in the Registry.

In 2014, there were 28,676 individuals with CF in the Registry. For the first time, the Registry has more adults (ages 18 and older) than children. The number of adults with CF continues to increase, while the number of children has remained relatively stable. In 2014, adults comprised 50.7 percent of the CF population, compared with 29.2 percent in 1986.

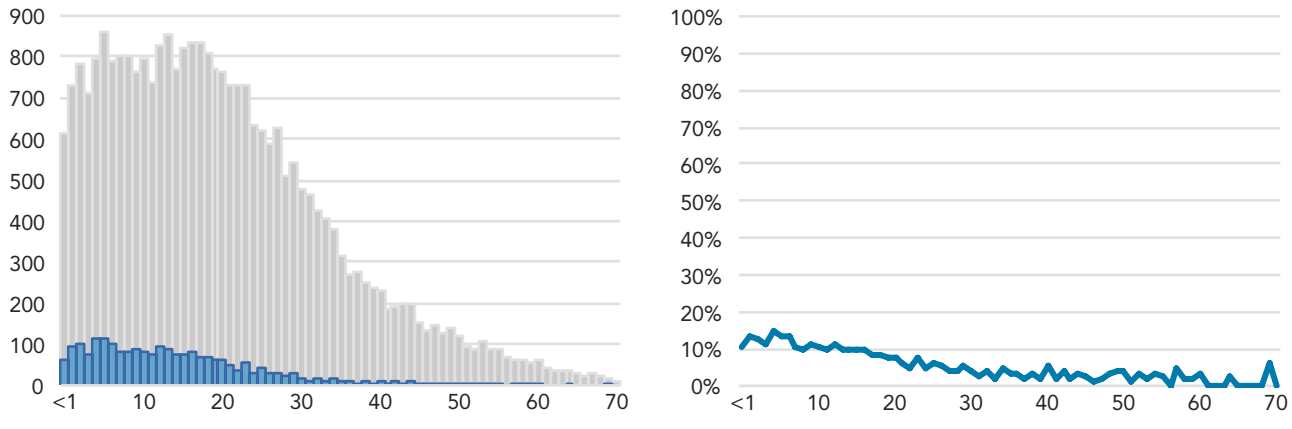
Number of Children and Adults with CF, 1986–2014



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 care centers.

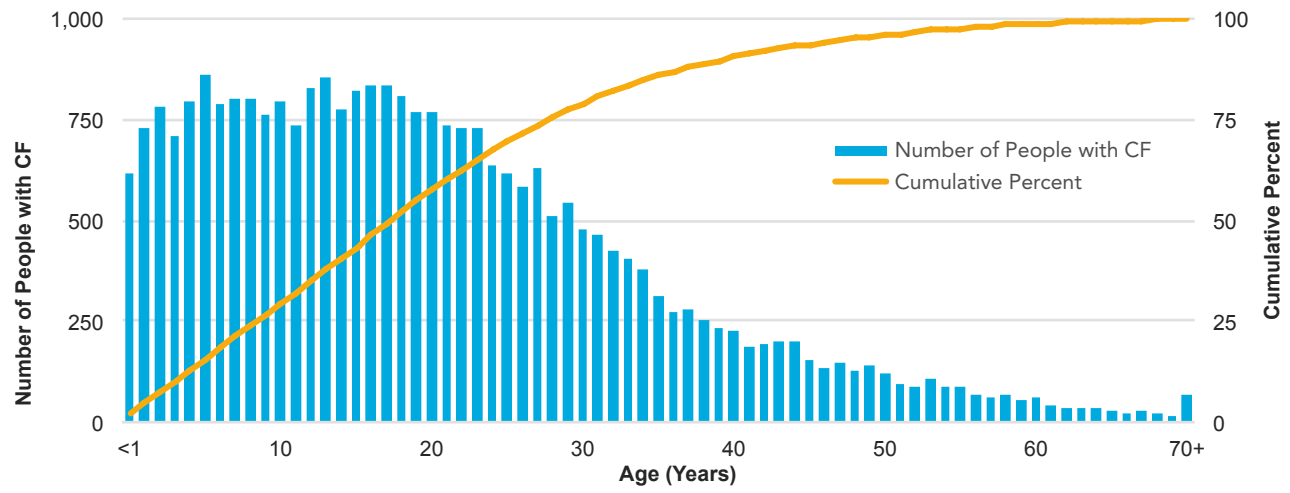
Currently, 8.2 percent of individuals in the Registry are reported as Hispanic. Hispanics with CF tend to be younger than the overall CF population, which reflects national population trends.[3]

Hispanic Ethnicity by Age, 2014



The median age of people with CF currently in the Registry is 18.3 years. The range is from birth to 86.7 years. Despite gains in survival, the age distribution remains markedly skewed toward younger ages.

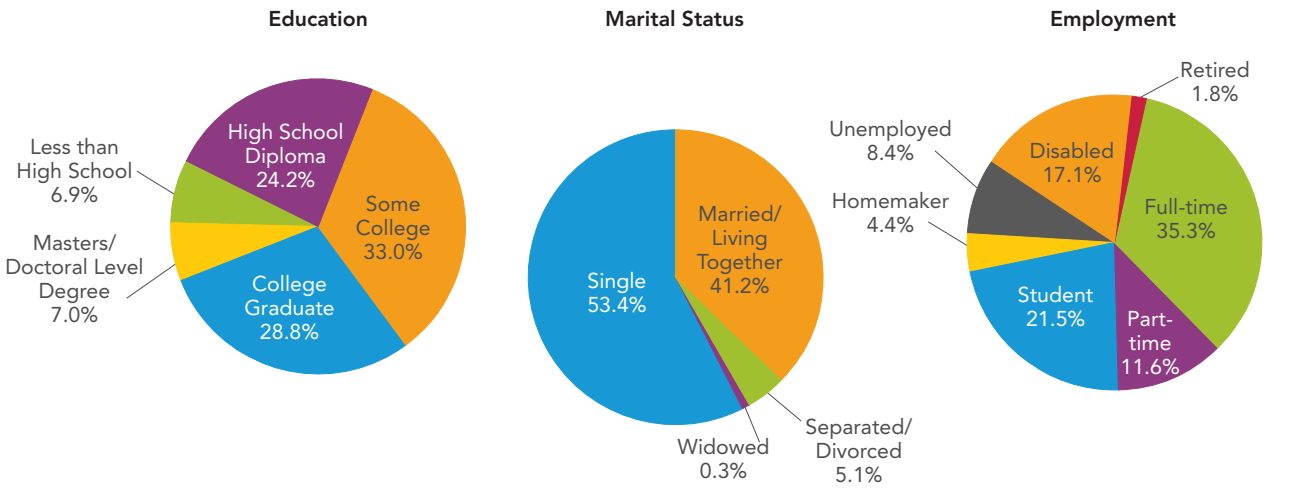
Age Distribution of the CF Population in 2014



Characteristics of Adults with CF 18 Years and Older

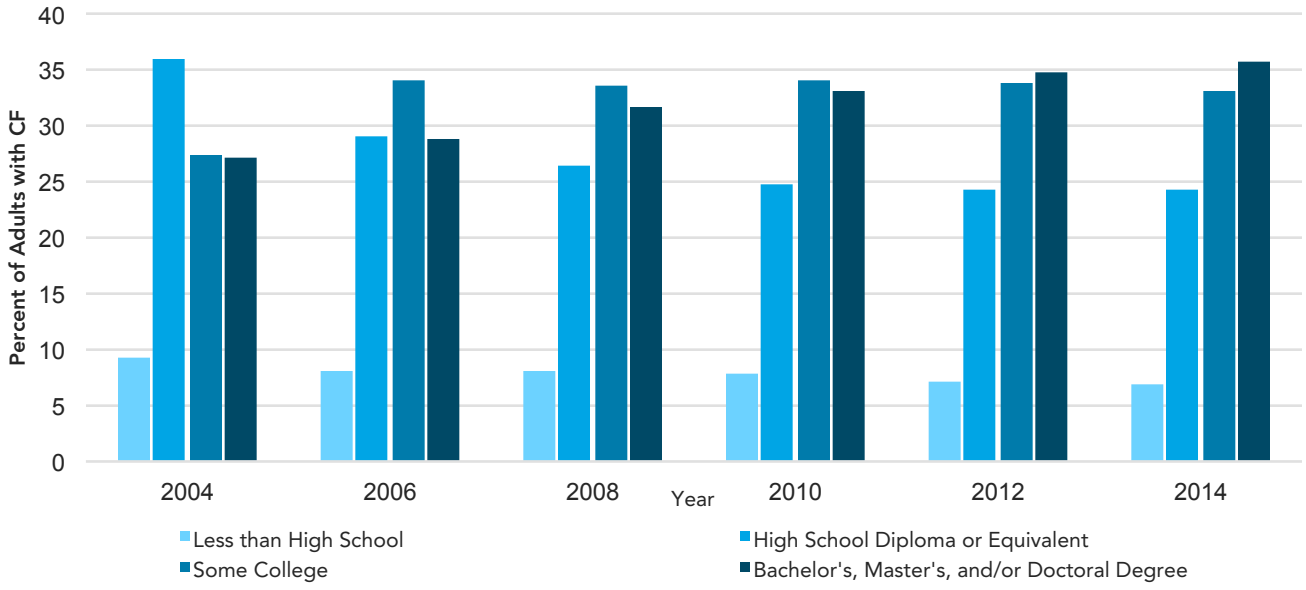
As a growing number of individuals with CF enter adulthood, it is encouraging to note that many of them are pursuing higher education and employment, and are in committed relationships and having children of their own. About two-thirds of adults are either students or working.

Socioeconomic Characteristics of Adults 18 Years and Older with CF in 2014



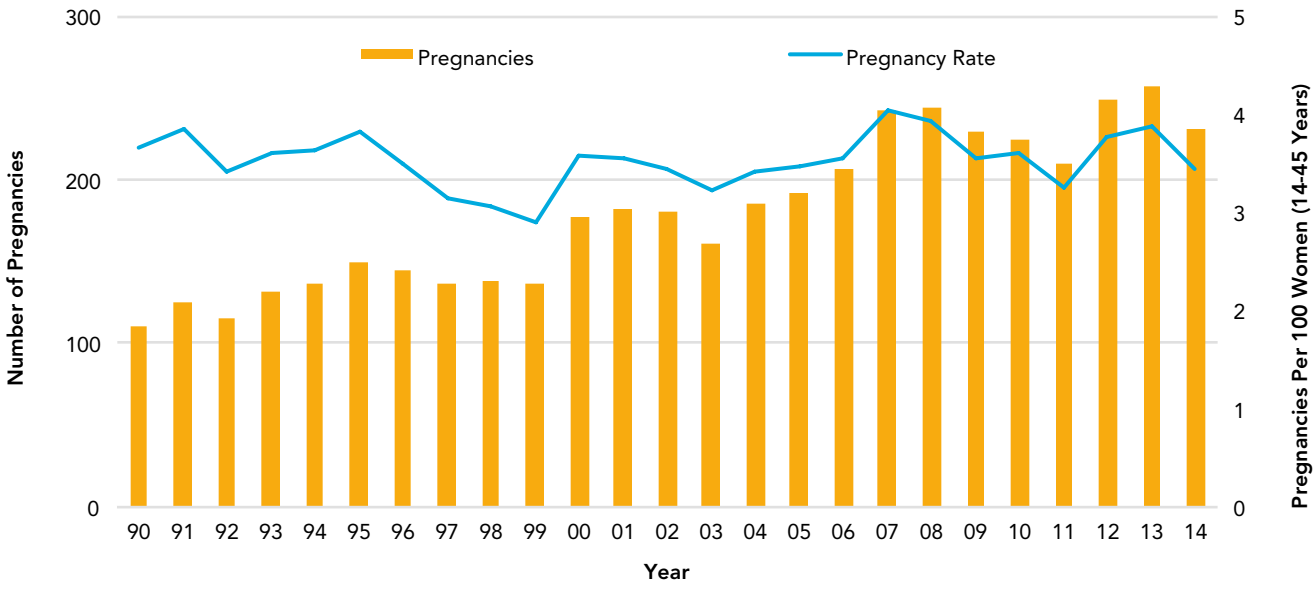
Since 1994, the percentage of adults with CF who report being married or living with a partner increased almost 10 percentage points. In addition, the chart below indicates that about 36 percent of adults in the Registry are college graduates, representing an increase of almost 10 percentage points over the past decade.

Educational Attainment of Adults with CF 18 Years and Older, 2004–2014



The number of pregnancies among women with CF has increased steadily since the 1990s. Registry data show that, in 2014, 232 women with CF were pregnant. 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]

Pregnancies and Pregnancy Rate in Women Ages 14 to 45 Years with CF, 1990–2014



Insurance Information

Access to CF specialized care and treatments is a challenge for some individuals with CF. In all age groups, about half of the individuals in the Registry are receiving at least some component of their health insurance through federal or state-funded programs. Registry data show that a majority of people with CF ages 18 to 25 received health insurance through their parent's plan in 2014.

Insurance Coverage in 2014

	Under 18 Years	18 to 25 Years	26 Years and Older	All
Number of individuals (n)	13,890	5,655	8,503	28,048
Health insurance policy (e.g. private insurance) (%)	53.9	64.8	66.4	59.9
Medicare/Indian Health Services (%)	0.8	6.3	25.9	9.5
Medicaid/state programs (%)	55.2	43.3	27.4	44.4
TriCare or other military health plan (%)	3.0	2.6	1.6	2.5
Other (%)	4.0	4.1	3.2	3.8
No health insurance (%)	0.4	1.4	1.2	0.8

Insurance coverage reflects a patient's coverage at any point during the year, thus, the data are not mutually exclusive (except for the "no health insurance" option).

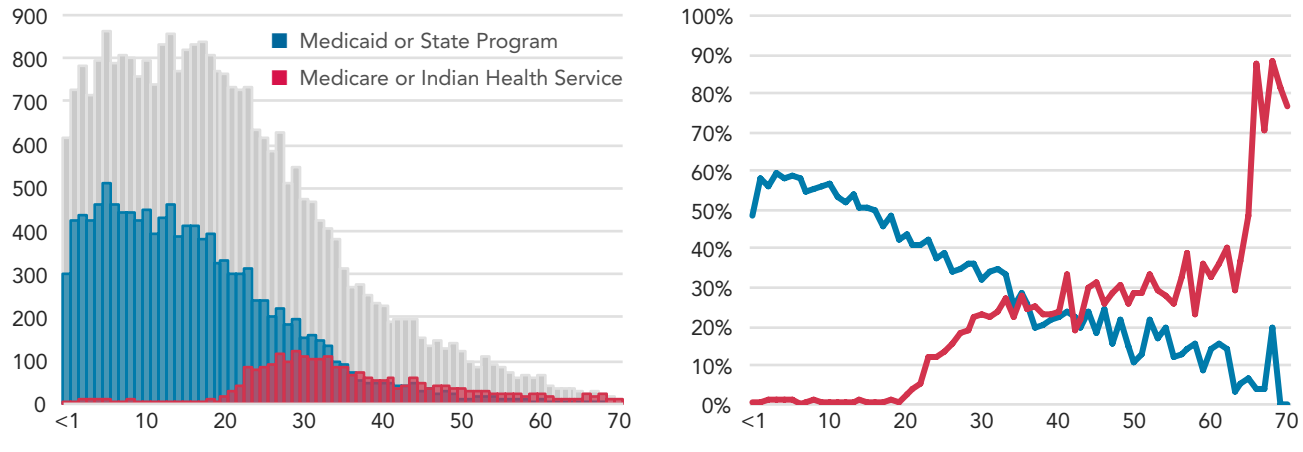
Additional Insurance Information in 2014

Individuals who participated in a patient assistance program (%)	26.7
Individuals 18 to 25 years covered under parent's insurance (%)	56.7

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

A large portion of children with CF use Medicaid or state programs, including over 50 percent of children under age 10. We see an increase in the number of people with CF on Medicare around age 20. Though the overall prevalence of Medicare use is low, the program covers between 20 and 40 percent of adults each age from 30 to 65 years. Individuals under age 65 who receive Medicare have met the federal criteria for disability.

Medicare/Indian Health Service vs. Medicaid/State Programs by Age, 2014



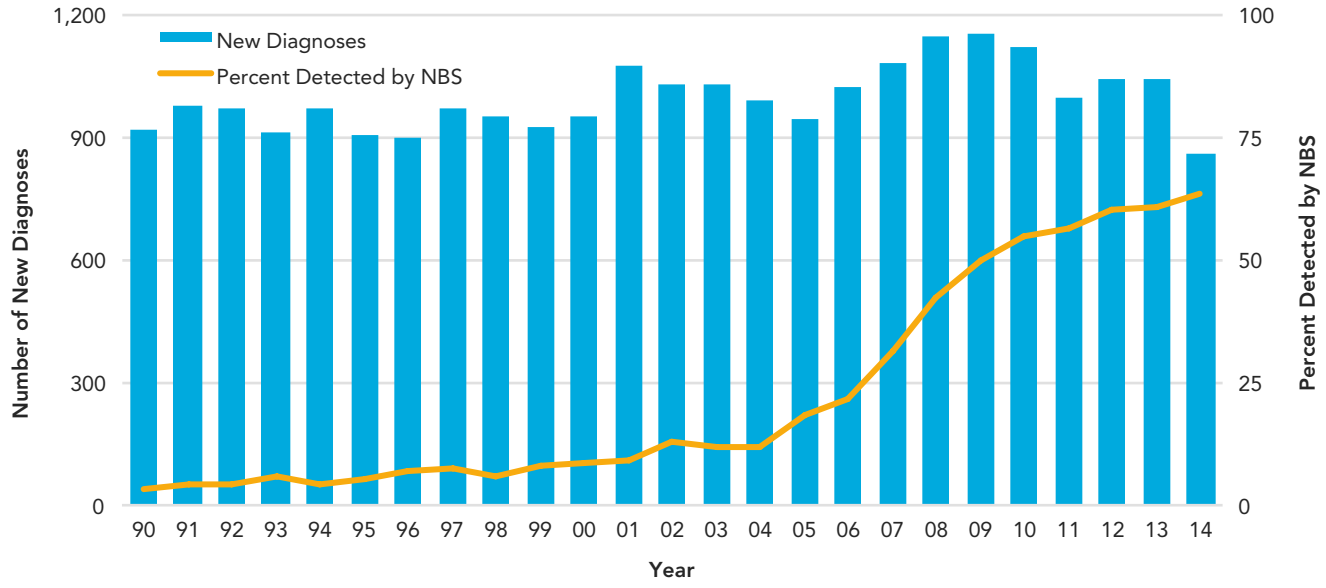
DIAGNOSIS

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

Characteristics of Diagnoses among Individuals with CF

In 2014, 63.7 percent of new diagnoses were 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 care centers to partner with community physicians and families to ensure the best possible care and outcomes for infants with CF.

Number of New CF Diagnoses, 1990–2014

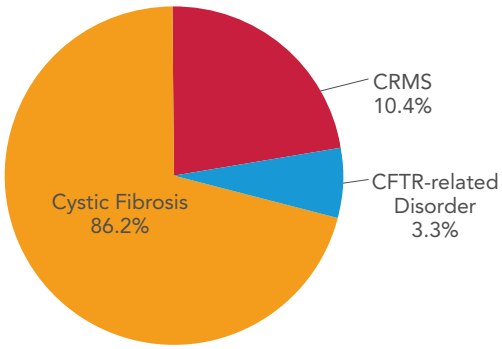


The new diagnoses for years prior to 2014 have been adjusted to include individuals first reported to the Registry in the years after their diagnosis year. As in previous reports, we anticipate that the number of new diagnoses in 2014 will increase when the 2015 data are available.

According to CF Foundation guidelines, infants with a positive NBS who have inconclusive sweat test results and less than two CF-causing mutations should be diagnosed with CFTR-related metabolic syndrome (CRMS).[6] CRMS was added to the Registry as a diagnostic option in 2010. The entry of a diagnosis of CF versus CRMS into the Registry is a clinical decision; there is no validation that individuals meet published diagnostic criteria for CF or CRMS. A comparison of clinical diagnoses of CF and CRMS in 2010 and 2011 showed that 41 percent of individuals who met the diagnostic criteria for CRMS were entered into the Registry with a diagnosis of CF.[7]

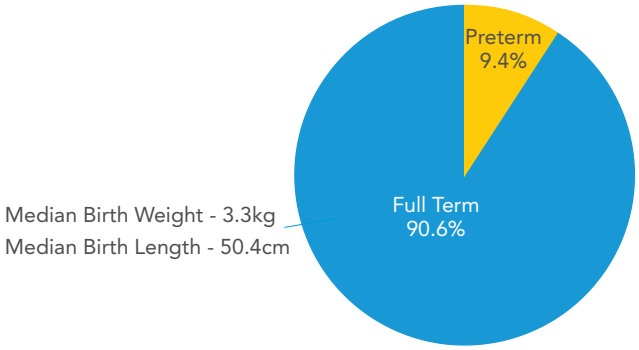
In 2014, data were entered into the Registry for 608 individuals diagnosed with CRMS, 103 of whom were given this diagnosis during 2014. In addition to CRMS, individuals can be diagnosed with a CFTR-related disorder. This option has also been available in the Registry since 2010. Individuals with this diagnosis do not meet the diagnostic criteria for CF or CRMS but are affected by CF-related conditions such as congenital bilateral absence of the vas deferens (CBAVD), and they often have mutations in the CFTR gene.[8] Collection and analysis of data from these individuals will provide new and important information for these distinct populations.

CF, CRMS and CFTR-related Disorder Diagnoses in 2014



In 2014, 586 infants were born and diagnosed with CF. Of those with a known gestational age at birth, 90.6 percent were born full term. This rate is comparable to that of the general U.S. population.[9] The mean birth weight for full-term infants with CF is about the same as that of the U.S. population,[10] suggesting that babies born with CF do not initially show any nutritional deficiencies. The gestational age of 106 infants born and diagnosed with CF in 2014 is not known (18.1 percent).

Gestational Age of Infants Born and Diagnosed with CF in 2014



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 the time of diagnosis. Among the 14% of infants diagnosed in 2014 under age 1 with meconium ileus (or other intestinal obstruction), 21.1 percent had bowel perforation. Those diagnosed after age 1 often present with acute or persistent respiratory abnormalities.

Presentation at Diagnosis

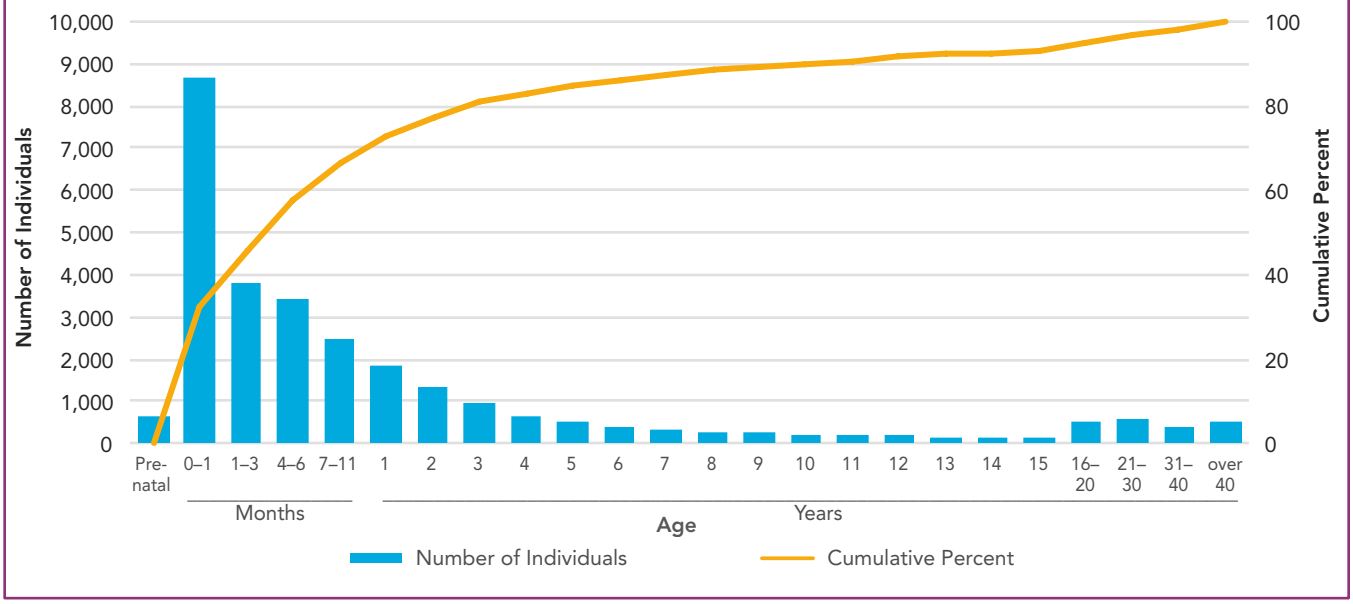
	Diagnosed in 2014 (%)	Diagnosed in 2014 Age < 1 (%)	Diagnosed in 2014 Age ≥ 1 (%)	All People with CF (%)
Number of Individuals	**855**	**640**	**215**	**28,676**
Asymptomatic				
DNA analysis	18.5	17.1	22.8	10.2
Family history	9.4	8.4	12.6	15.2
Newborn (neonatal) screening	63.7	82.9	6.0	20.4
Prenatal screening (CVS,[A] amniocentesis)	3.0	4.0	0.0	2.3
Symptomatic				
Meconium ileus/other intestinal obstruction	10.7	14.0	0.9	18.2
Acute or persistent respiratory abnormalities	15.5	2.0	55.8	39.2
CBAVD[B] or infertility/GU[C] abnormalities	1.6	0.0	6.5	0.4
Digital clubbing	1.4	0.0	5.6	0.4
Edema	0.1	0.0	0.5	0.6
Electrolyte imbalance	0.5	0.5	0.5	3.5
Failure to thrive/malnutrition	6.8	4.8	12.6	30.9
Liver problems	0.6	0.2	1.9	1.1
Nasal polyps/sinus disease	3.0	0.0	12.1	3.6
Rectal prolapse	0.6	0.3	1.4	2.9
Steatorrhea/abnormal stools/malabsorption	6.5	4.2	13.5	24.1
Other	4.9	2.6	11.6	4.5

Note: Data are not mutually exclusive. In addition, we anticipate that additional 2014 diagnoses will be entered into the Registry in 2015.

[A]*Chorionic villus sampling*
[B]*Congenital bilateral absence of the vas deferens*
[C]*Genitourinary abnormalities*

Previous figures in this section refer to infants born or diagnosed in 2014; the figure below includes all individuals followed in the Registry in 2014.

Age at Diagnosis of All Individuals with CF Seen in 2014



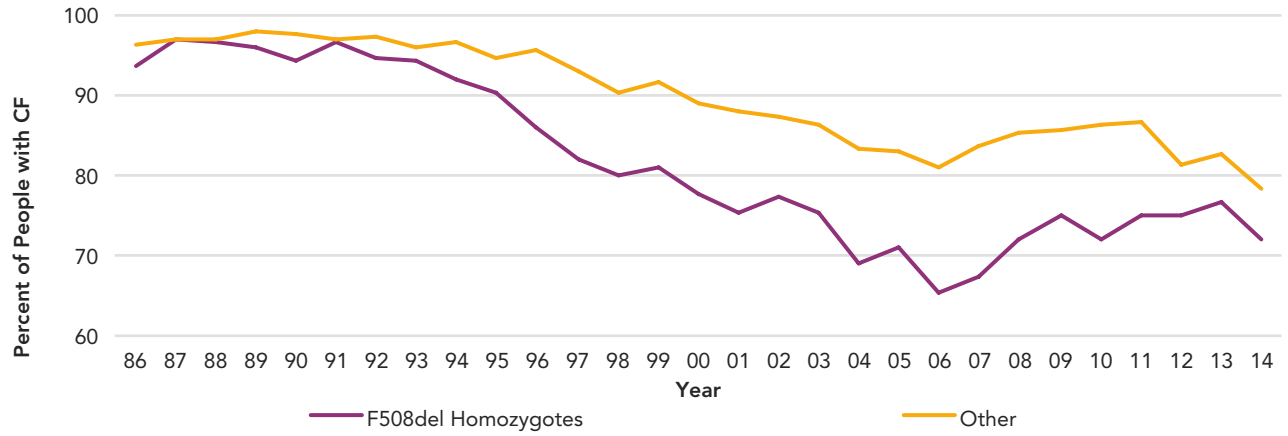
Among all individuals in the Registry in 2014, 66.4 percent were diagnosed in the first year of life.

Diagnostic Tests

Sweat Chloride Testing

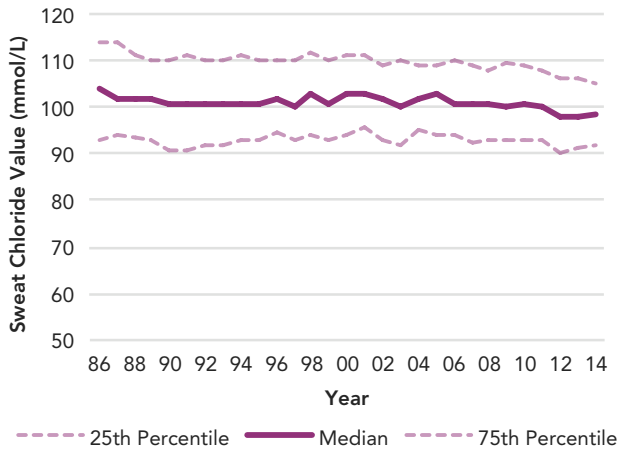
Sweat chloride testing is an important diagnostic test recommended for all individuals regardless of genotype.[11] In 2014, 83.3 percent of individuals in the Registry had a sweat chloride test result recorded. We see a decreasing trend over time in the percent of individuals with a sweat test entered into the Registry. Individuals who are homozygous for F508del are less likely to have sweat values in the Registry than those who are not F508del homozygotes. A baseline sweat test is becoming increasingly important as a change in sweat chloride is viewed as an indicator of the physiological effect of a CFTR modulator.

Percent of People with CF with a Sweat Chloride Reported by Year of Diagnosis, 1986–2014

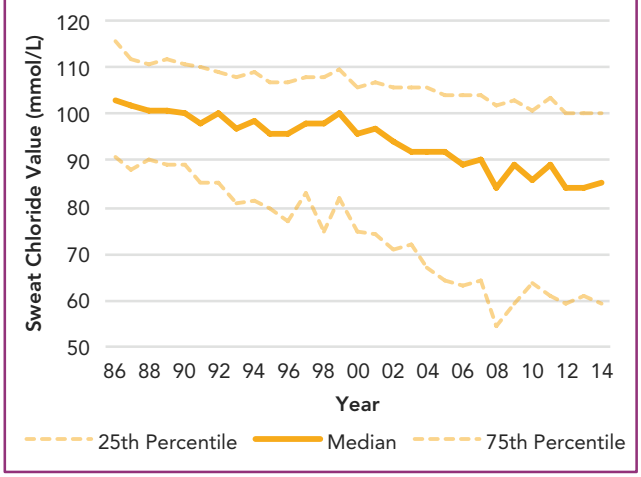


Among those with a sweat chloride test, the median sweat chloride test results have remained consistent for individuals who are F508del homozygotes. In contrast, there has been a steady decline in the median sweat chloride value among individuals who are not homozygous for F508del, suggesting that the Registry is including more individuals with milder diseases in recent years.

Sweat Chloride Value of F508del Homozygotes by Year of Diagnosis, 1986-2014



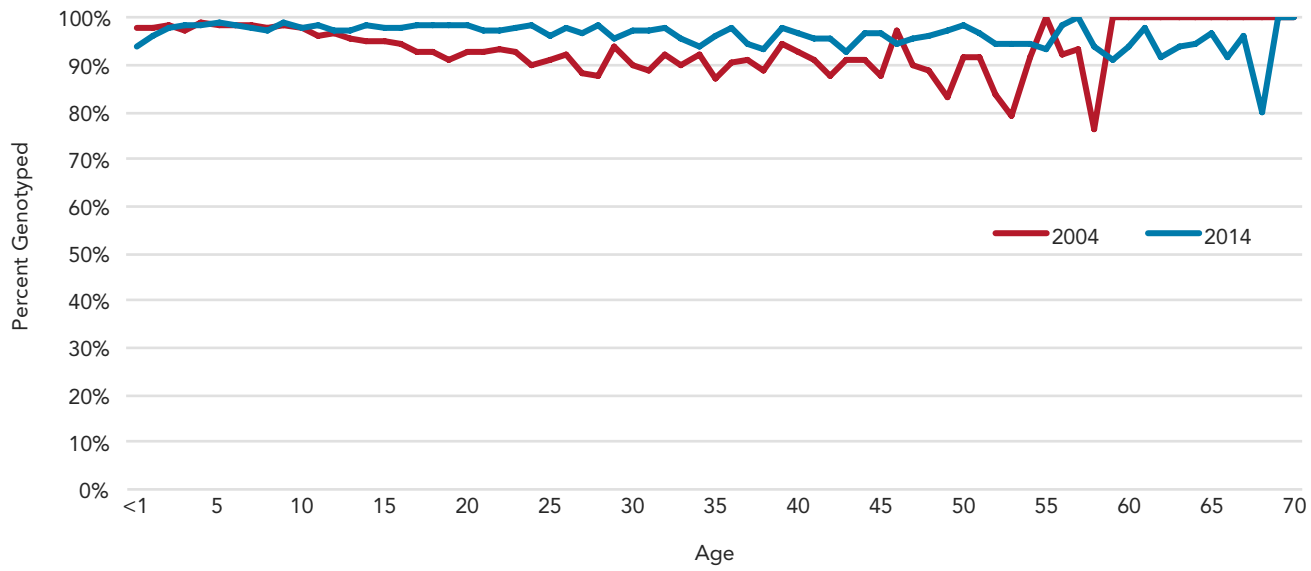
Sweat Chloride Value of Patients Not Homozygous for F508del by Year of Diagnosis, 1986-2014



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 been a key component of the diagnostic work-up. In addition, with the introduction of CFTR modulators, genotyping all people with CF is increasingly important to research and clinical care. In 2014, 97.4 percent of individuals (n= 27,935) in the Registry have been genotyped. However, even among those who have been genotyped, 7.3 percent have one or more alleles entered as "Unknown."

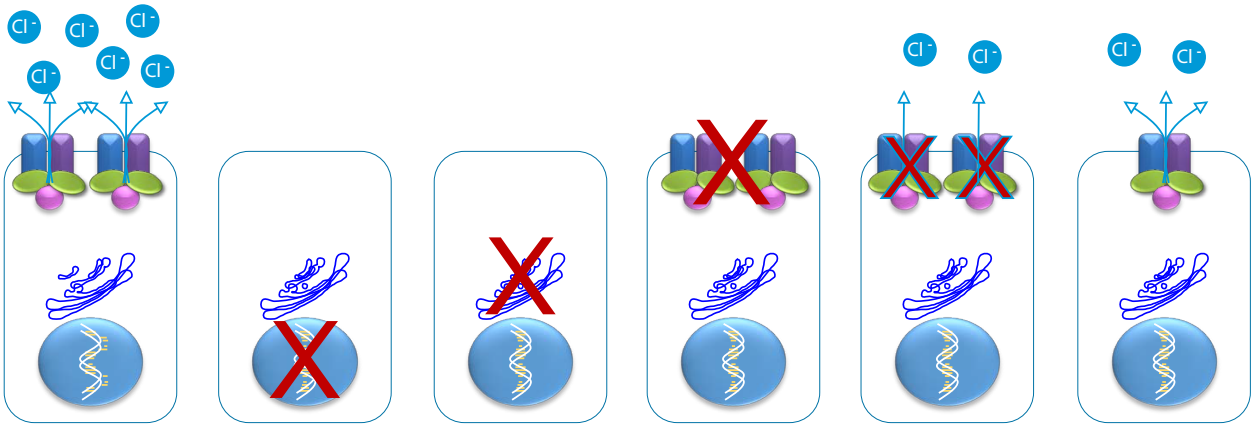
Percent of People with CF Genotyped by Age, 2004 vs. 2014



CFTR GENE MUTATIONS

To date, more than 1,800 mutations have been found in the CFTR gene.[12] Different mutations disrupt the normal production, delivery to the cell surface and function of the CFTR protein by distinct mechanisms. Some mutations result in virtually no CFTR function and others are associated with some residual CFTR function. To help categorize different mutations based on the resulting functional impact, researchers have categorized CF disease-causing mutations into five main classes.[13-15] This classification schema is an oversimplification of reality as some mutations lead to more than one defect in CFTR function. In addition, the functional status has not been determined for all mutations. As a result, we use the term "class not identified" to refer to individuals who have been diagnosed with CF and genotyped but have one or more mutations whose functional consequences have not yet been determined.

One Way of Classifying CFTR Mutations



	Normal	Class I	Class II	Class III	Class IV	Class V
DESCRIPTION	CFTR is created, reaches cell surface and functions properly, allowing transfer of chloride and water.	No functional CFTR created.	CFTR protein is created, but misfolded, keeping it from reaching the cell surface.	CFTR protein is created and reaches cell surface, but does not function properly.	The opening in the CFTR protein ion channel is faulty.	CFTR is created in insufficient quantities.
EXAMPLES		G542X W1282X R553X	F508del N1303K I507del	G551D S549N V520F	R117H D1152H R347P	3849+10kbC->T 2789+5G->A A455E

Adapted from: http://www.umd.be/CFTR/W_CFTR/gene.html

The most common CFTR mutation is F508del: 86.5 percent of individuals in the Registry 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 CF population.

Prevalence of the 25 Most Common CFTR Mutations in People with CF Seen in 2014

Mutation	Number of Individuals	Percent of All People with CF
F508del	24,157	86.5
G542X	1,289	4.6
G551D	1,219	4.4
R117H	784	2.8
N1303K	676	2.4
W1282X	631	2.3
R553X	503	1.8
1717-1G->A	445	1.6
621+1G->T	429	1.5
3849+10kbC->T	405	1.4
2789+5G->A	360	1.3
3120+1G->A	273	1.0
I507del	227	0.8
D1152H	205	0.7
R1162X	202	0.7
3659delC	195	0.7
1898+1G->A	184	0.7
G85E	179	0.6
R347P	164	0.6
R560T	164	0.6
2184insA	152	0.5
A455E	146	0.5
R334W	138	0.5
Q493X	130	0.5
E60X	117	0.4

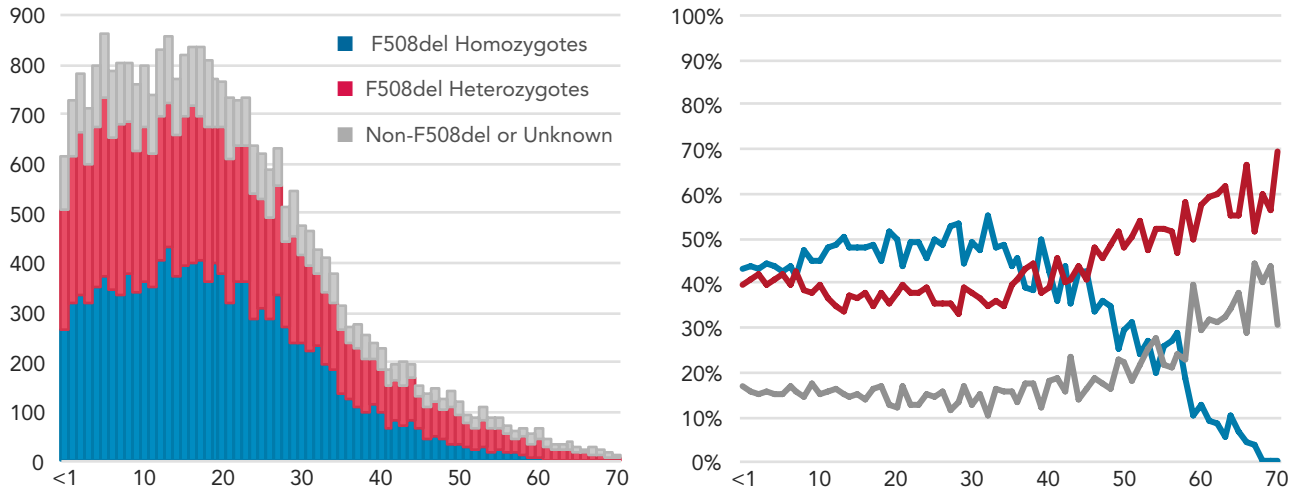
F508del homozygotes (%) – 46.4

F508del heterozygotes (%) – 40.1

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

Since F508del is the most common mutation, we examined the distribution of individuals by age and their F508del status; two F508del mutations (homozygote), one F508del mutation (heterozygote) and no F508del mutations. A larger proportion of non-F508del carriers and individuals with one F508del mutation in the older ages could be due both to late diagnosis of a mild form of the disease or survivor bias of individuals with mild CFTR mutations.

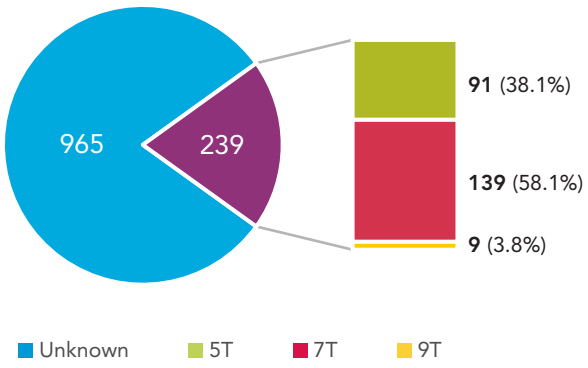
F508del Mutation Status by Age, 2014 *(Stacked Bar Chart)*



Of the 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 almost 5 percent of those genotyped in 2014. Several factors could influence the shift in the distribution of mutations, such as a change in the ethnic distribution of the population or the introduction of newborn screening.

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 higher likelihood of having CF.[16,17] Unfortunately, the Registry has incomplete information on the poly-T tract for 965 of the 1,204 individuals with CF with R117H who ever had a record in the Registry.

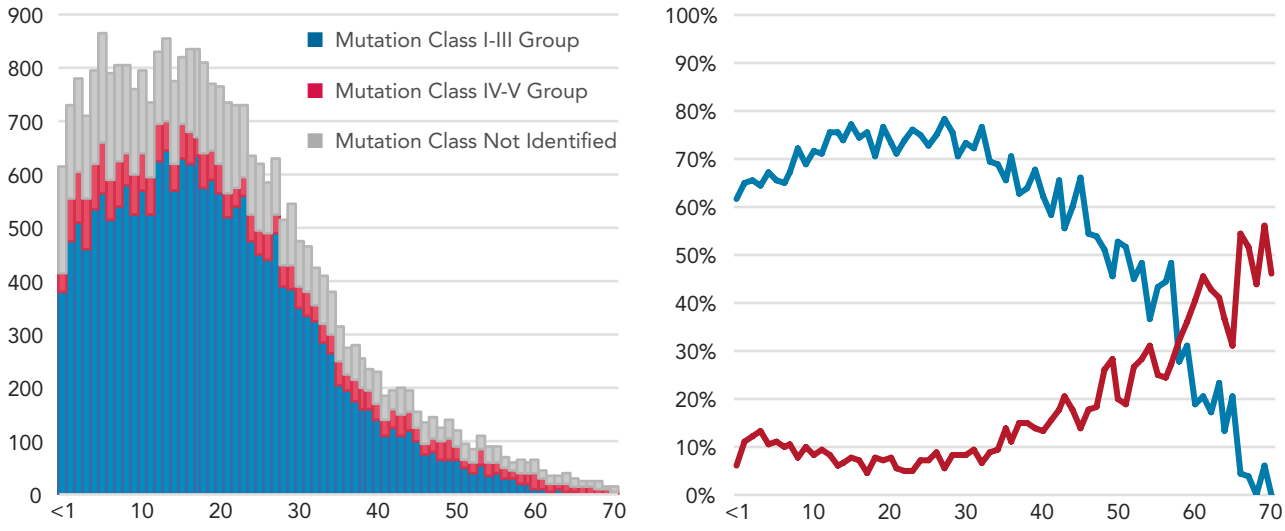
Poly-T Tract Status of Individuals with an R117H Mutation



Throughout this report, we use the categories of mutation classes. Specifically, individuals with two mutations in classes I, II or III are grouped together because their mutations typically lead to little or no CFTR function. Individuals with one or two mutations in classes IV or V are grouped together because these mutations are typically associated with residual CFTR function. Previous research has shown that this grouping of classes is associated with meaningful clinical differences between the groups.[13,15]

Individuals in the mutation class I-III group comprise the majority of the population of children and young adults with CF. The number and proportion of individuals in this group decreases in older ages. Conversely, we see a greater number of individuals with a genotype in the class IV-V group who are under age 10, likely a result of newborn screening identifying these individuals prior to a clinical presentation of CF. This chart shows a similar pattern to the chart on F508del mutation status above, likely because F508del homozygotes comprise the majority of those in the mutation class I-III group.

Mutation Class Status by Age, 2014 *(Stacked Bar Chart)*



Of all individuals who were genotyped, 70.7 percent were classified in the mutation class I-III group, 10.4 percent were classified in the mutation class IV-V group and 18.9 percent could not be classified. As expected, individuals in the mutation class I-III group are younger and are more likely to be prescribed pancreatic enzyme replacement therapy than individuals with a mutation in class IV or V.

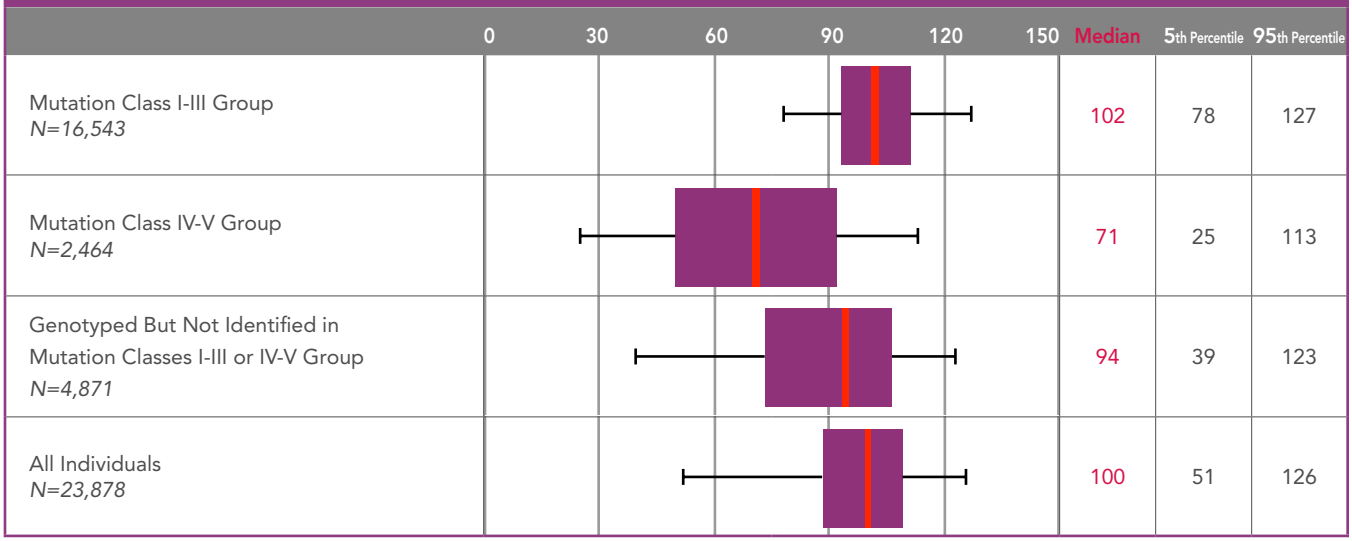
CFTR Mutation Class Comparisons

	Class I-III	Class IV-V	Unclassified
Individuals with a sweat test (%)	86.6	86.3	93.5
Age (years)	17.9	21.5	17.7
Individuals taking PERT* (%)	98.5	37.7	71.8

** Pancreatic Enzyme Replacement Therapy*

The I-III and IV-V mutation class groups appear to correlate with sweat test values: higher sweat test values are observed among individuals in the I-III group as compared to the IV-V group. Also of note, there is more variation in the IV-V group.

Sweat Chloride Value (mmol/L), by Mutation Class Group



GUIDELINES: CARE, SCREENING AND PREVENTION

The CF Foundation has developed clinical practice guidelines for routine care and screening for individuals with CF during infancy, childhood and adulthood. In accordance with guidelines for people with CF over age 6,[18,19] many centers report four office visits and two pulmonary function tests annually for the majority of their CF patients.

However, adherence to the recommendation that centers perform quarterly respiratory cultures continues to be lower and more variable across the care center network.[20] 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 by the CF Foundation.[18]

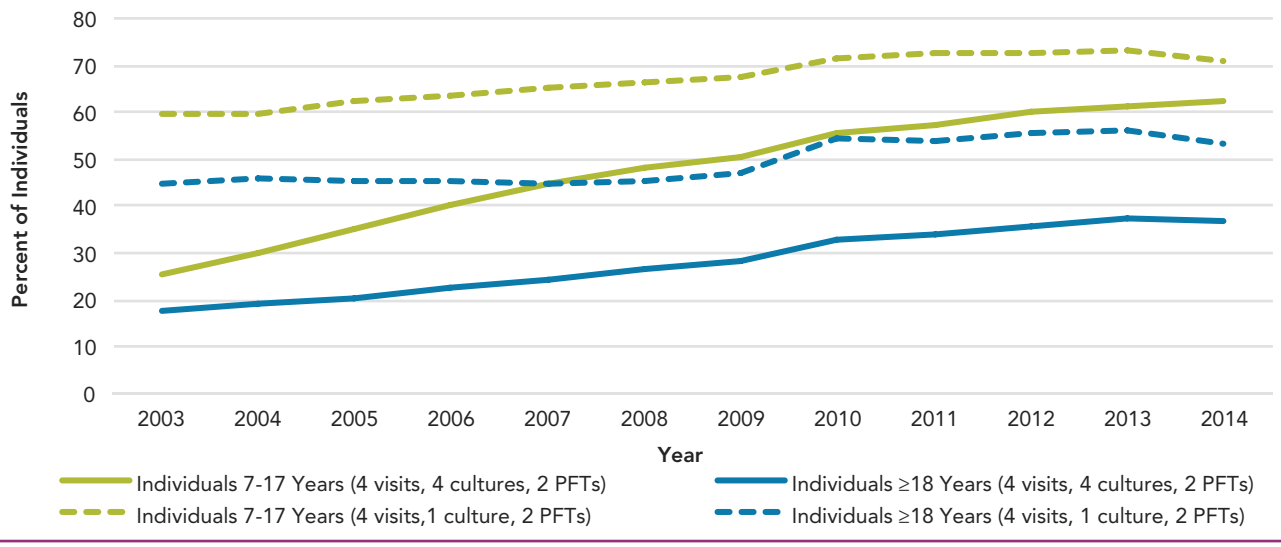
There is significant center-level variation in several key screening measures, including measurement of immunoglobulin E (IgE) for allergic bronchopulmonary aspergillosis (ABPA) and dual-energy X-ray absorptiometry (DXA) scan for osteopenia/osteoporosis. The influenza vaccination rate for people with CF 6 months and older remains high across the CFF care center network. Smoking and secondhand smoke exposure remain challenging problems, particularly for young adults.

Patient Care Guidelines

The percentage of individuals receiving care that meets CF Foundation care guidelines has increased in recent years. Because individuals should be able to perform reliable pulmonary function tests (PFTs) at age 6 and older, we use guidelines criteria for those ages 7 and older throughout this section to ensure individuals were eligible to perform a reliable PFT for the entire year.

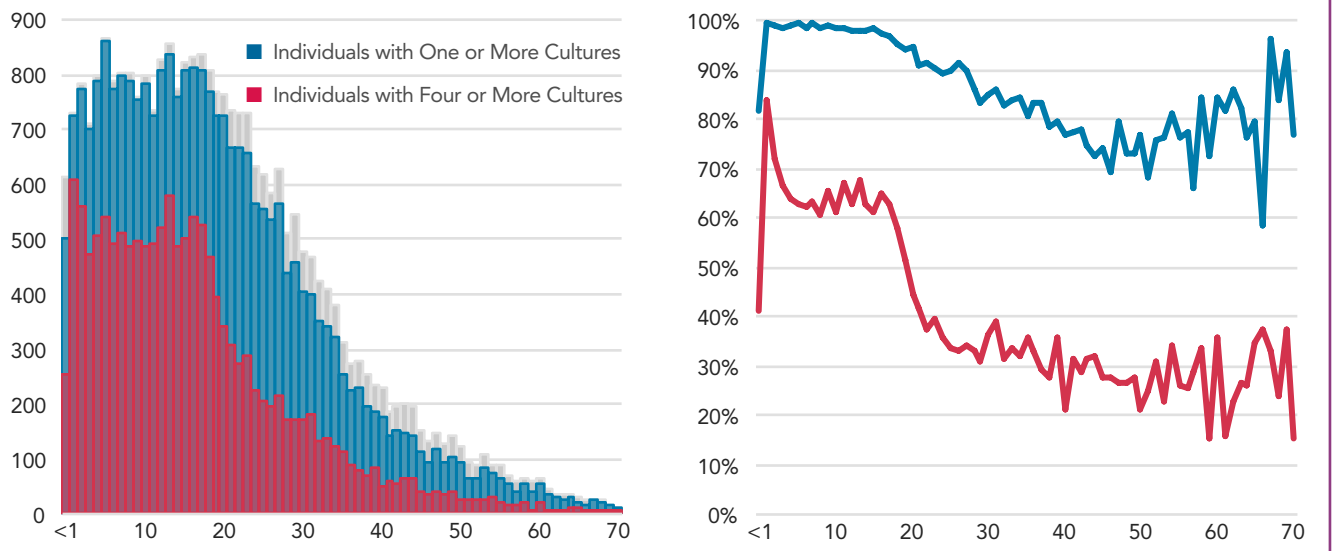
Over the past decade, the number of children and adults receiving the recommended four visits, four respiratory cultures and two PFTs has doubled.[19,20] The percentage of adults who receive care that meets guidelines criteria remains lower than the percentage observed in children.

Percent of Individuals Meeting Guidelines for Visits, Cultures and PFTs, 2003–2014



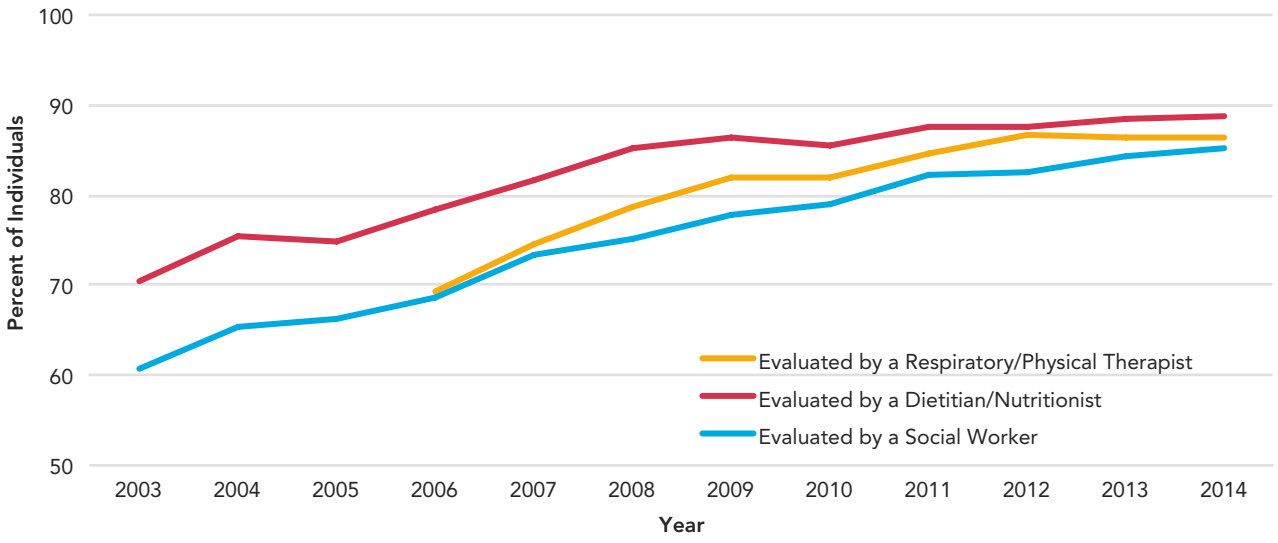
The guidelines on infection prevention and control recommend that individuals with CF have quarterly respiratory cultures.[20,21] Nearly 92 percent of individuals received at least one culture, and 50 percent of individuals had four or more respiratory cultures in 2014. Those under age 18 were more likely to meet the recommendation for four cultures.

Number of Cultures by Age, 2014



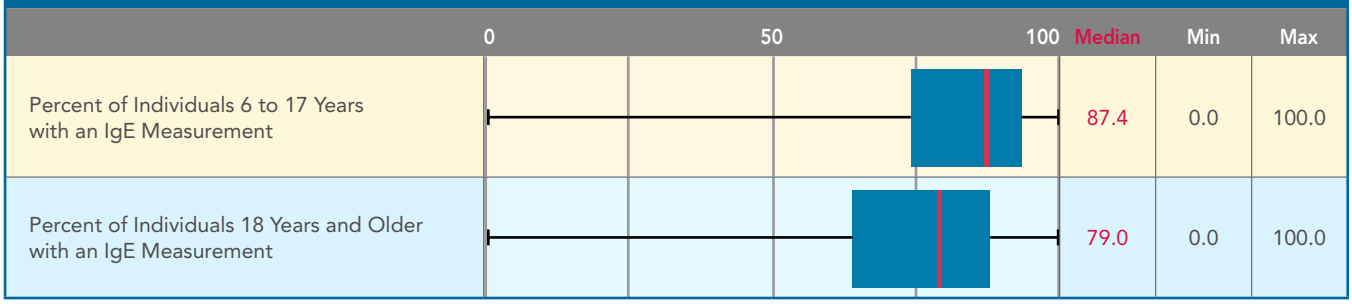
The multidisciplinary care team plays an important role in CF care. Foundation-accredited care centers continue to increase the percentage of individuals who see a dietitian/nutritionist, physical/respiratory therapist and social worker each year. More than 85 percent of individuals with CF are evaluated at least yearly by a respiratory therapist, dietitian and social worker, and 70.5 percent were seen by all three specialists in 2014.

Percent of Individuals Evaluated by Multidisciplinary Care Team Members, 2003–2014



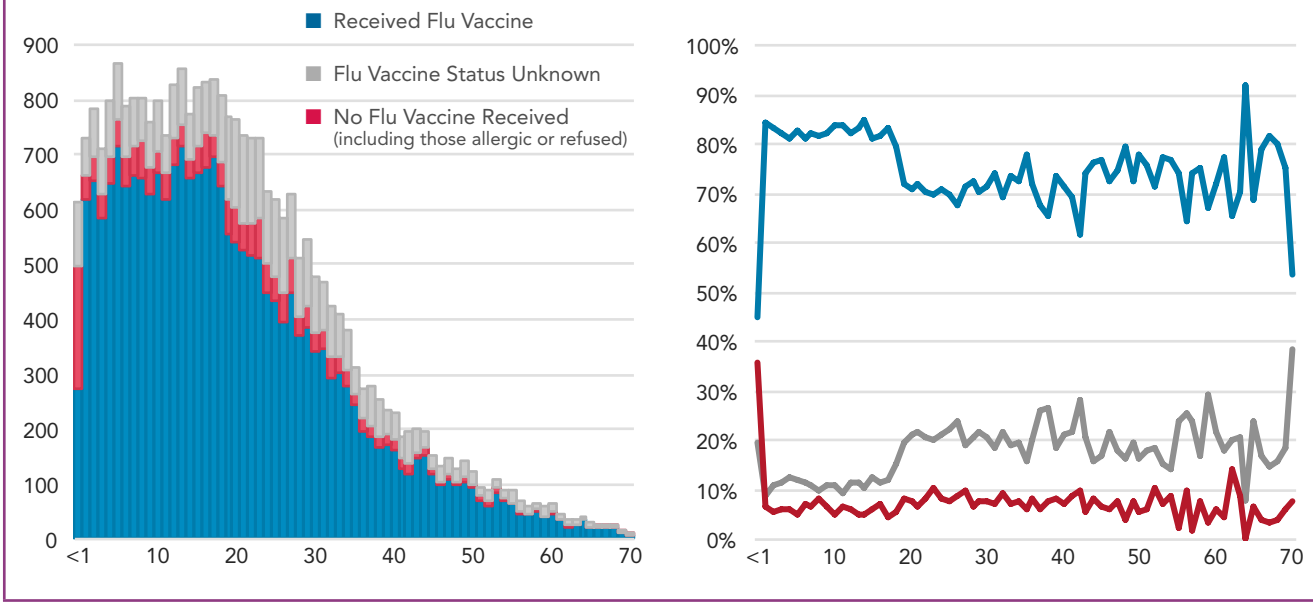
The CF Foundation's consensus statement on ABPA recommends screening individuals 6 years and older for ABPA by annual measurement of total serum IgE concentration.[22]

Percent of Patients with an IgE Measurement, by Center



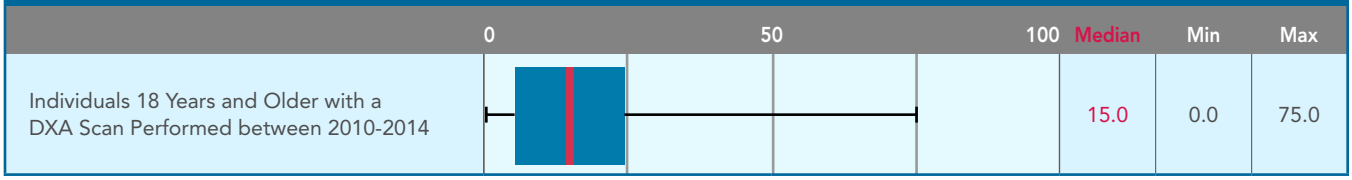
The Centers for Disease Control's Advisory Committee on Immunization Practices recommends influenza vaccination for all individuals with CF ages 6 months and older.[23] The influenza vaccination rate of people with CF 6 months and older is about 80 percent of the total population and about 91 percent if individuals with a vaccination status of "Unknown" (16 percent) are excluded from this analysis.

Flu Vaccine Status by Age, 2014 *(Stacked Bar Chart)*



The CF Foundation consensus statement on bone health and disease recommends screening all adults 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 high DXA z-scores, whereas those with low and intermediate scores are recommended for retesting in 5 year and 2 to 4 years, respectively. Therefore, we would not expect all individuals to have been screened in a given year.

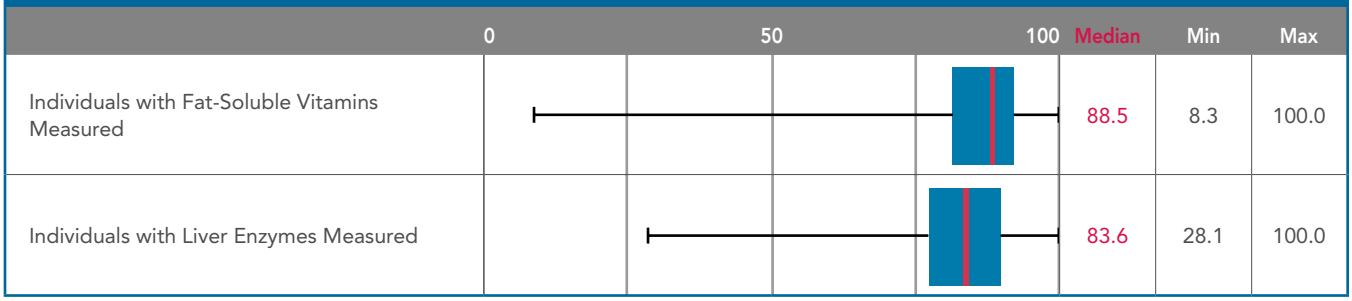
Percent of Individuals with a DXA Scan, by Center



Includes any DXA scans performed 2010–2014.

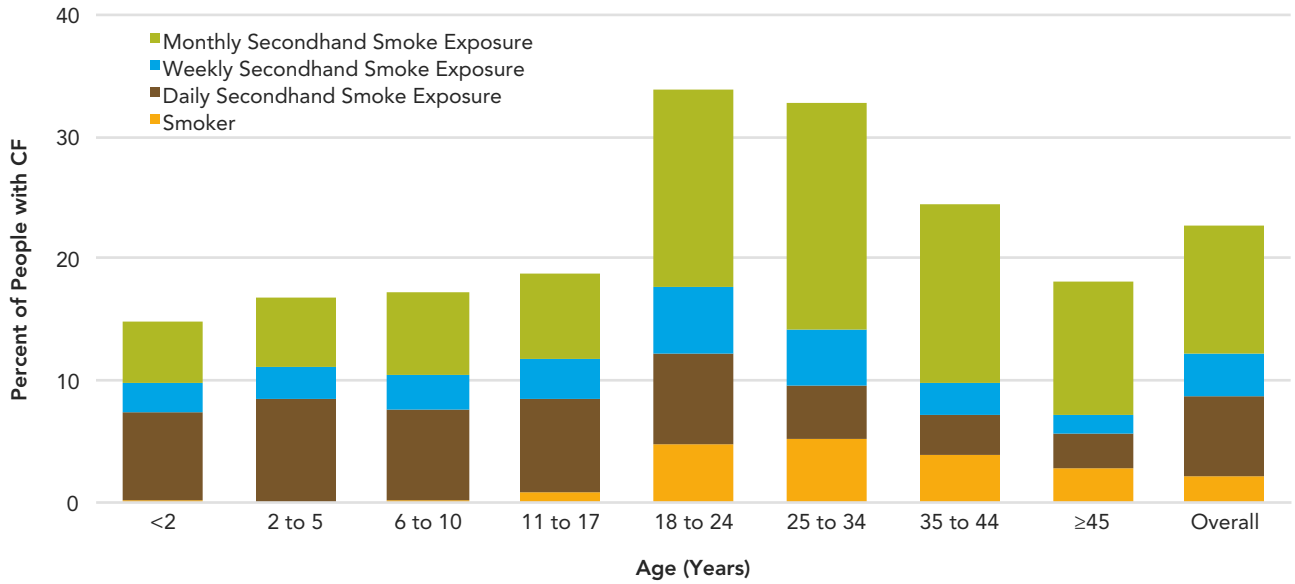
CF Foundation guidelines recommend annual measurement of fat-soluble vitamins to screen for vitamin deficiency.[19,25] The CF Foundation Hepatobiliary Disease Consensus Group recommends a yearly panel of liver blood tests for all people with CF to screen for possible liver disease. Registry data suggest that these tests are being done on the majority of individuals.[26]

Percent of Individuals Screened by or Monitored with Annual Labs, by Center



In 2014, 22.7 percent of individuals with CF reported monthly or more frequent exposure to tobacco smoke, either secondhand or as a smoker themselves. Exposure to tobacco smoke is a substantial problem that causes disease and premature death in children and adults.[27] Cigarette smoking prevalence is lower in the CF population than in the general U.S. population — only 4.6 percent of people with CF 18 years and older are smokers, compared with 19.0 percent in the general population in 2013.[28] However, smoking and secondhand smoke exposure remain a significant concern, especially for infants and young adults. Smoke exposure was unknown for 38.4 percent of individuals with CF. They were excluded from the analyses.

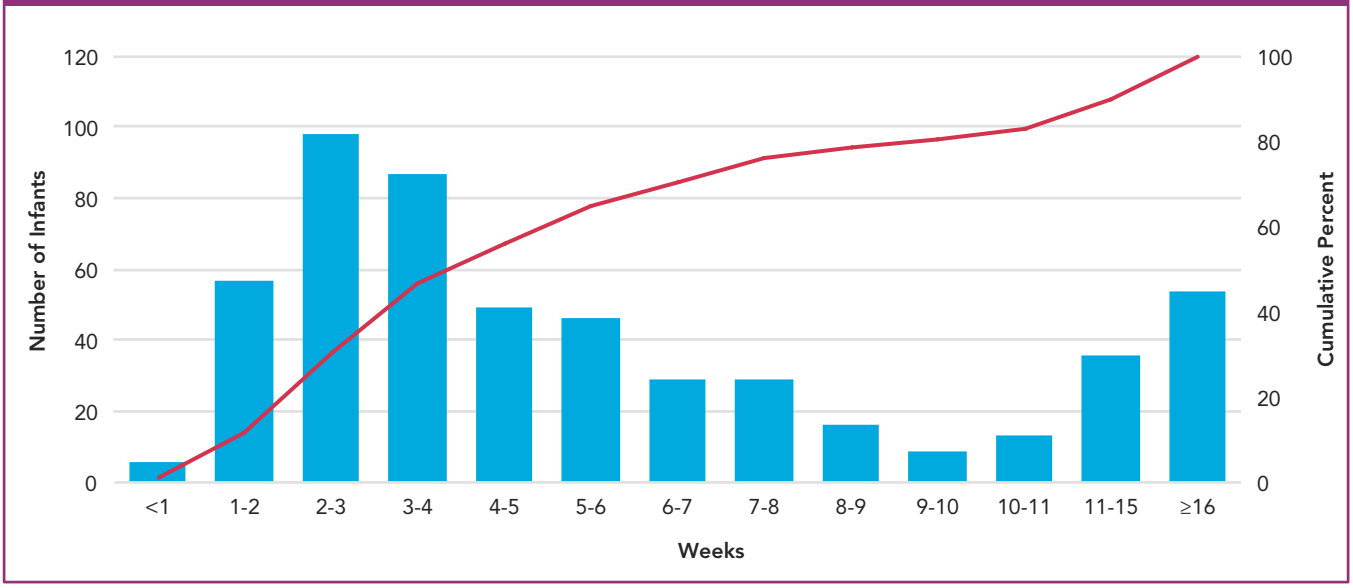
Tobacco Smoke Exposure by Age in 2014



Infant Care Guidelines

The CF Foundation guidelines for diagnosis of CF recommend that infants with a positive newborn screen undergo a sweat test. It is important to make a definitive diagnosis as quickly as possible so families can be educated about the disease, and treatment can be started.[5]

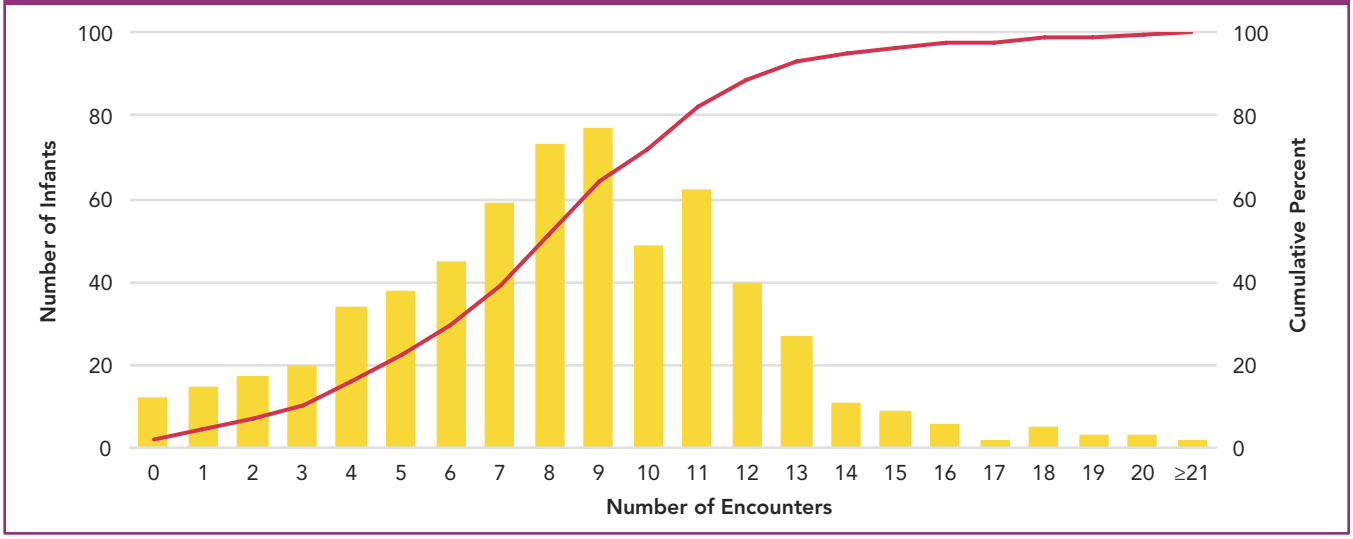
Time from Birth to First Recorded Sweat Test for Infants with CF Born in 2013 and Detected by Newborn Screening (n=529)



The chart shows data for children born in 2013 because a full year of data is available for these individuals. Median time to first sweat test for these individuals is 30 days, but 80 (13.1 percent) of infants born in 2013 and detected by newborn screening had not reported a sweat chloride test to the Registry by the end of 2014 and thus are not included in this analysis.

The CF Foundation infant care guidelines recommend monthly care center visits during the first 6 months of life and every one to two months in the second 6 months.[5] Therefore, we expect infants with CF to have around nine visits in the first year of life, which is reflected in the chart below. There is marked variation in the number of encounters for individuals in the first year of life across the care center network.

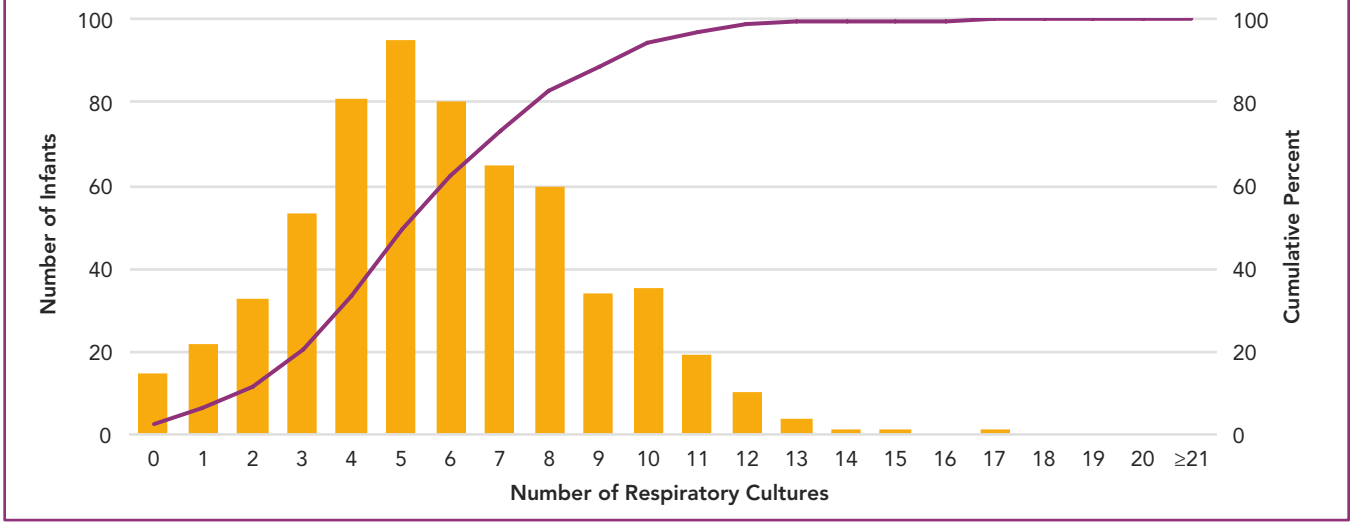
Number of Encounters in the First Year of Life for Infants with CF Born in 2013 and Detected by Newborn Screening (n=609)



The chart shows data for children born in 2013 because a full year of data is available for these individuals. The median number of visits in the first year of life is eight.

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

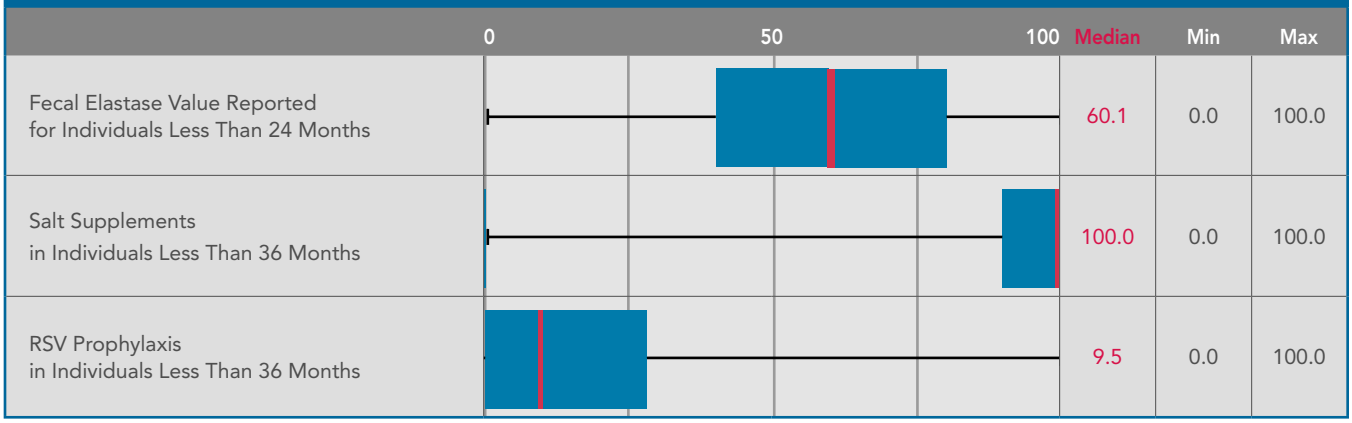
Number of Respiratory Cultures in the First Year of Life for Infants with CF Born in 2013 and Detected by Newborn Screening (n=609)



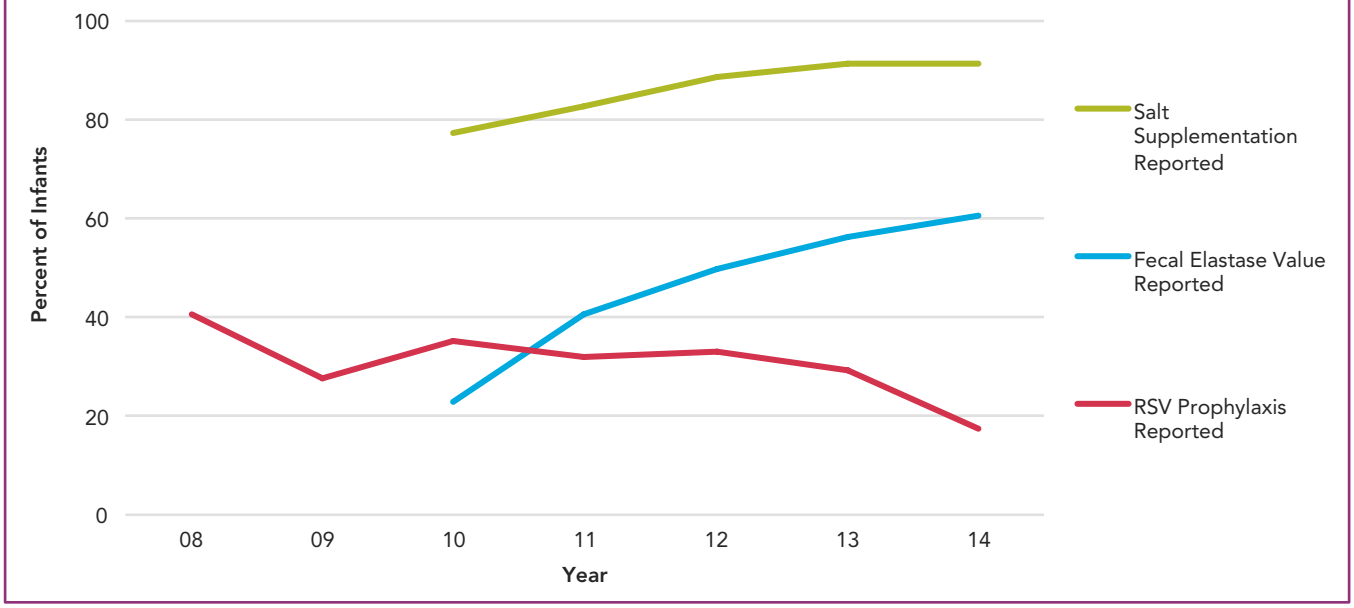
The chart shows data for children born in 2013 because a full year of data is available for these individuals. The median number of cultures is five.

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 care center network. The guidelines also recommend that infants begin salt supplements after diagnosis, and this is widely followed across the care center network. We observe substantial variation in the utilization of palivizumab (RSV prophylaxis) across the care center network. The current American Academy of Pediatrics (AAP) recommendation is that palivizumab should not be routinely used in individuals with CF. The infant care guidelines recommend that its use be considered for infants with CF.[5] Nearly all centers are prescribing the therapy for some infants, but there has been a decrease in use in recent years.

Infant Care Guidelines, by Center



Testing and Therapies for Individuals Under 24 Months of Age, 2008-2014



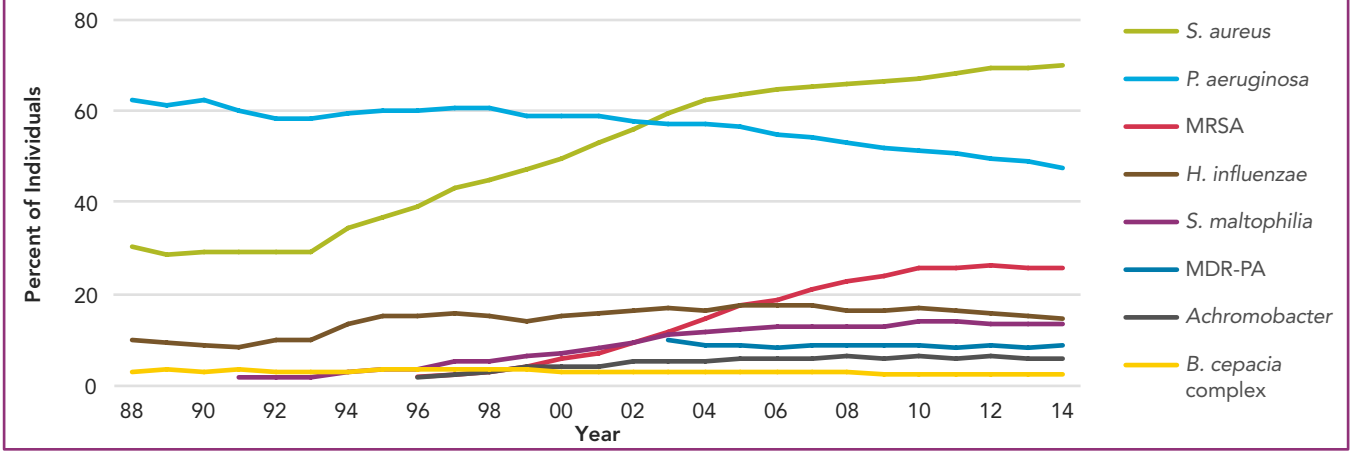
MICROBIOLOGY

Bronchiectasis with chronic pulmonary infections represents a serious problem for most individuals with CF. This section provides information on trends in CF pathogens over time and by age group. Updated infection prevention and control guidelines provide the current best practices for reducing exposure to CF pathogens in the health care setting and in everyday life.[21]

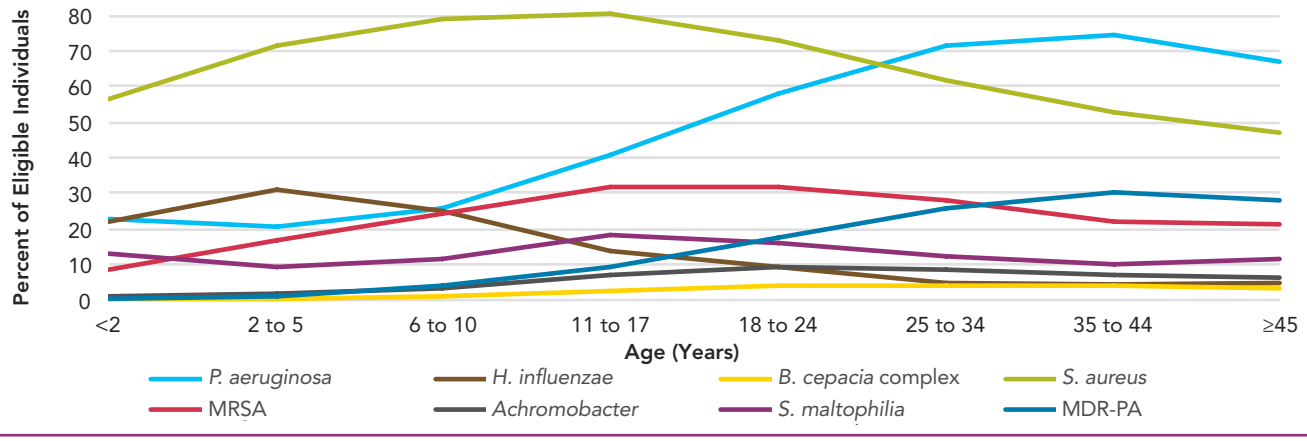
The prevalence of P. aeruginosa *continues to decrease. This may in part relate to widespread implementation of therapy to eradicate initial acquisition of* P. aeruginosa.[21,29]

Some of the increase in S. aureus *and MRSA may be due to improved microbiologic practices for the detection of Gram-positive organisms. From 2000 to 2014 there was about a five-fold increase in the numbers of individuals with CF with a culture positive for MRSA. Since 2010 the prevalence appears to be plateauing. The increases in prevalence of MRSA likely mirrors the increases that have been seen in the general population. Research has shown that about two thirds of individuals with MRSA had strains associated with hospital acquired infections while one third has strains associated with community acquired infections.*[30-32] *The stabilization of the prevalence is potentially due to increased awareness and infection prevention and control strategies.*

Prevalence of Respiratory Microorganisms, 1988–2014



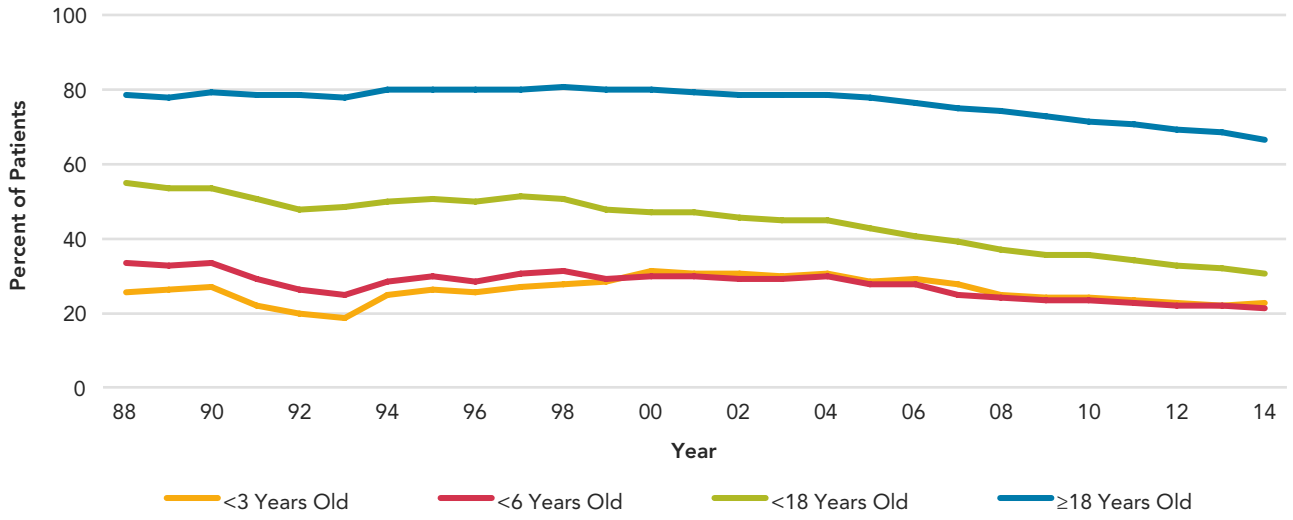
Prevalence of Respiratory Microorganisms by Age Cohort, 2014



Pseudomonas aeruginosa

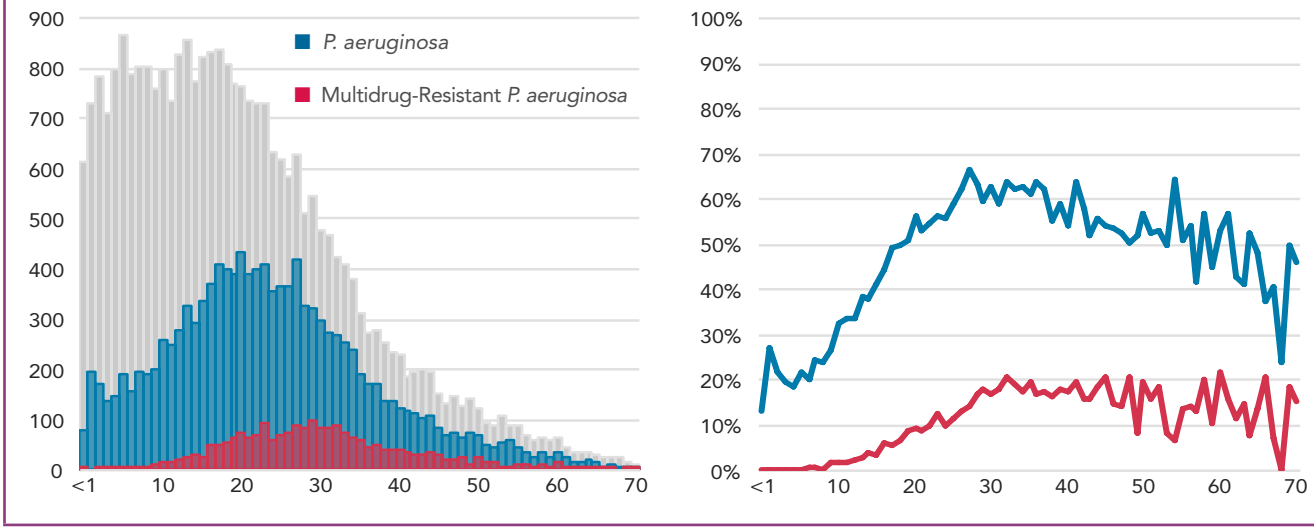
P. aeruginosa has continued to decline over time with the largest decrease observed among individuals 6 to 17 years old. Many individuals with CF now transition to adult care without *P. aeruginosa* in their respiratory tract.

P. aeruginosa Infection by Age Cohort, 1988–2014



Rates of multidrug-resistant *P. aeruginosa* infection are most notable in older adolescents and adults with CF. These findings likely reflect cumulative exposure to antibiotics. The clinical significance of this drug resistance is unclear. Multidrug resistance is defined as resistance to all antibiotics tested in two or more classes in a single culture. Currently, 18.1 percent of individuals with a *P. aeruginosa* infection have MDR-PA. (In this year's report, we have improved the accuracy of our calculation of MDR-PA, which has led to a decrease from what was reported previously.)

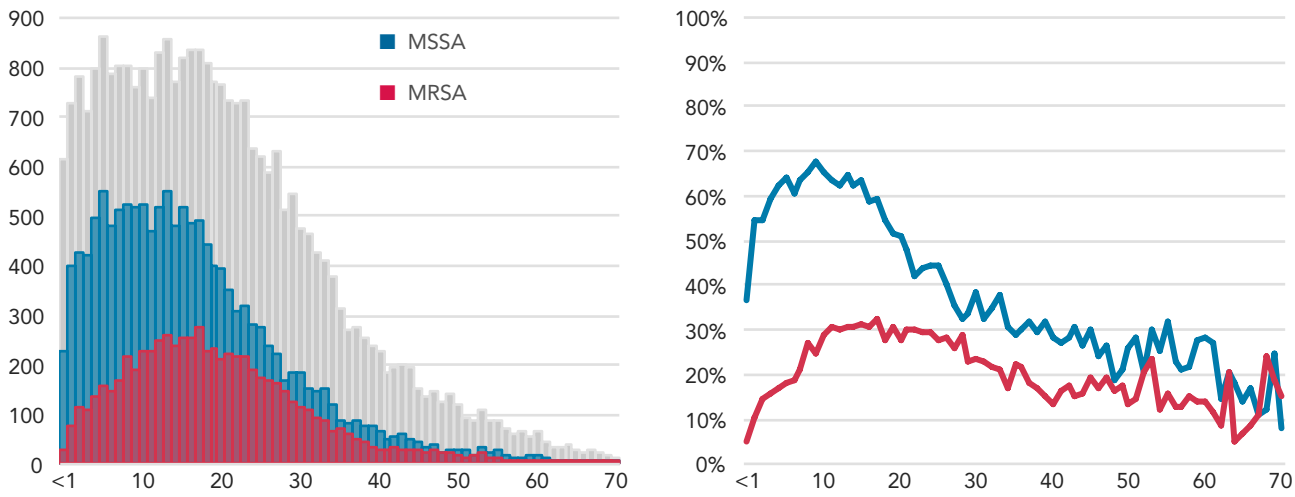
P. aeruginosa and Multidrug-Resistant *P. aeruginosa* by Age, 2014



Staphylococcus aureus

The prevalence of methicillin-resistant *S. aureus* (MRSA) has markedly increased over the last 25 years, which reflects trends in the general population. This chart shows that the highest prevalence of MRSA occurs in individuals between the ages of 10 and 30.

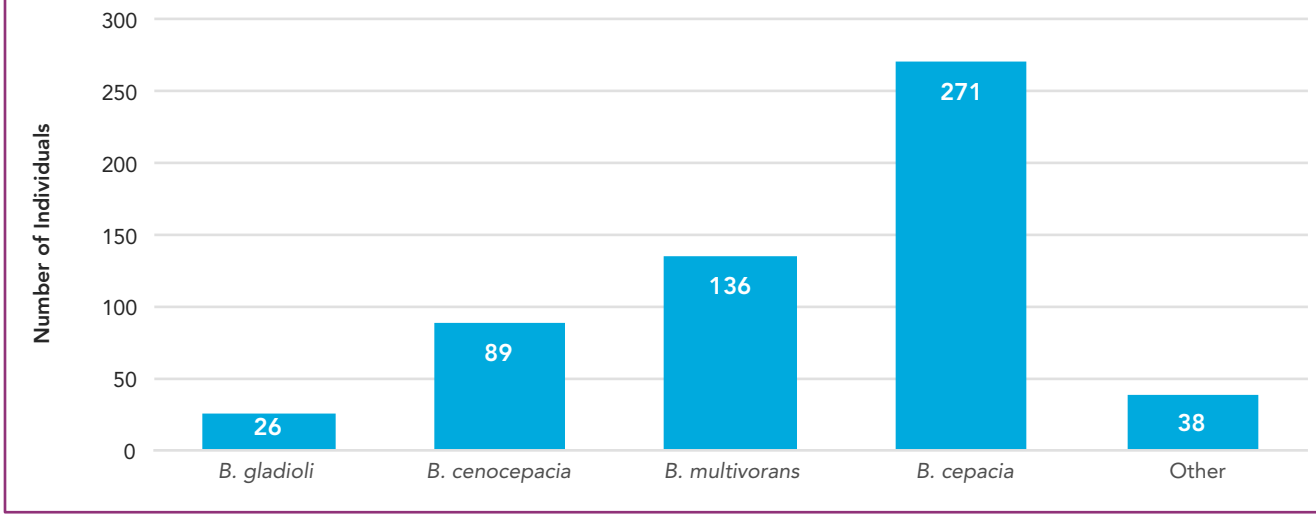
Mutation Class Status by Age, 2014 *(Stacked Bar Chart)*



Burkholderia cepacia complex

In 2014, 664 people with CF had a culture positive for *B. cepacia* complex: 93.6 percent of those isolates were confirmed at the CF Foundation *B. cepacia* Research Laboratory and Repository at the University of Michigan.

***Burkholderia* Species Confirmed at the *B. cepacia* Research Lab in 2014**



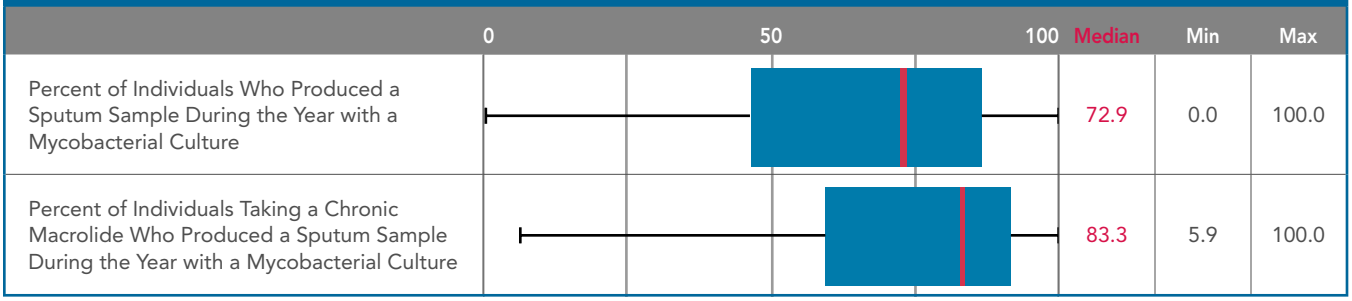
Data are not mutually exclusive. Some individuals have more than one species.
Note that B. gladioli is not part of the B. cepacia complex.

Nontuberculous Mycobacteria

The prevalence of nontuberculous mycobacteria (NTM) infections is increasing in the general population.[33] Since 2010, the Registry has collected more robust information on mycobacterial cultures and NTM infections.

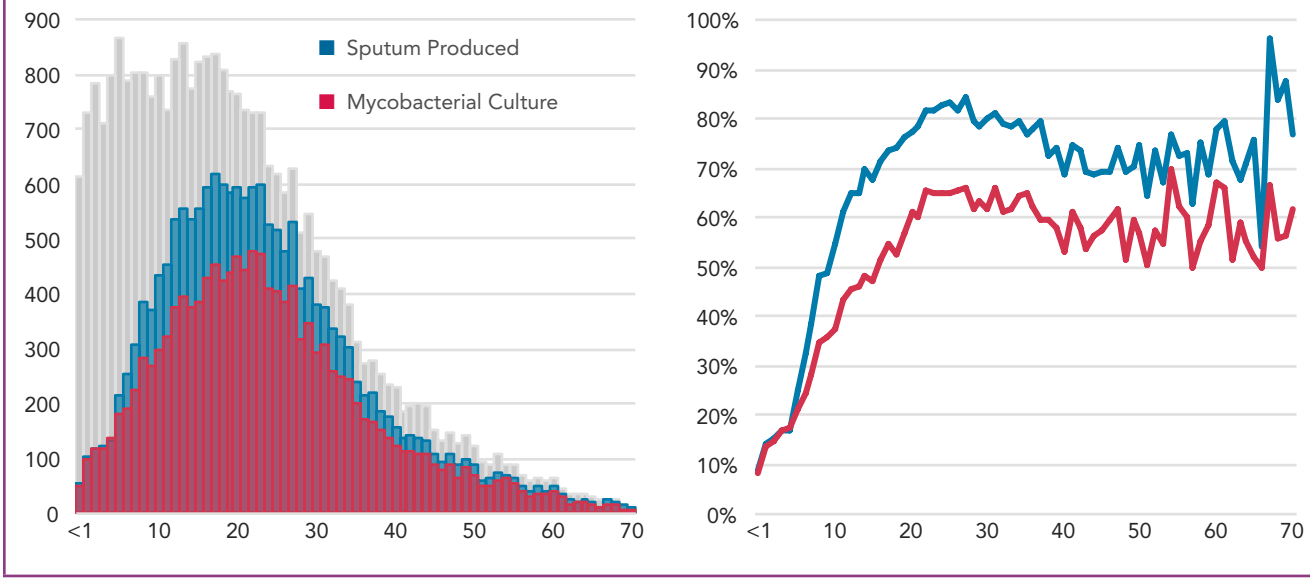
The CF Foundation/European Cystic Fibrosis Society Guidelines Committee recommends that individuals with CF who are able to expectorate be cultured for NTM infections annually.[34] Individuals should also be screened before and 6 months after beginning azithromycin and annually thereafter.[2] The data show improvement in screening rates over time, but wide center-level variation persists in these measures.

Mycobacterial Culture Data, by Center



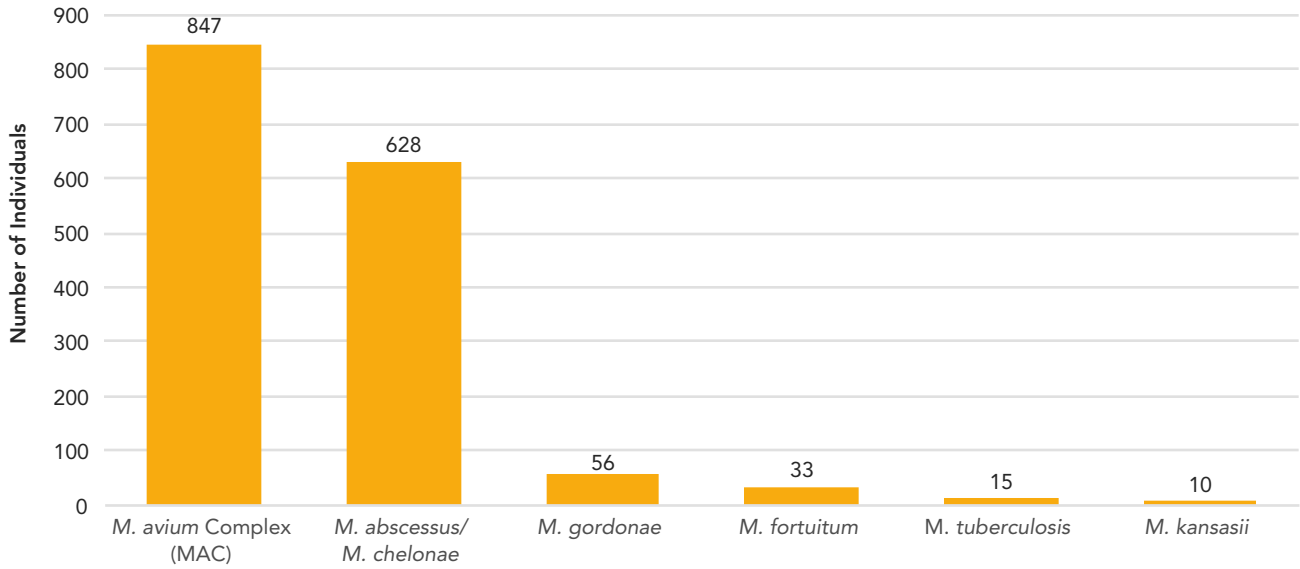
A throat swab is insufficient for a mycobacterial culture, so a patient must be able to produce sputum in order for this culture to be performed. As shown in the chart below, a majority of the individuals who produced a sputum culture for a bacterial culture also had a mycobacterial culture performed during the year.

Sputum Produced and Mycobacterial Cultures by Age, 2014



Of the 13,602 individuals who had a mycobacterial culture performed in 2014, 1,657 (12.2 percent) had a mycobacterial species isolated one or more times. The relative proportion of *M. abscessus* isolated in 2014 is higher than that reported over a decade ago in the CF Foundation-supported multicenter prevalence study.[35]

Mycobacterial Species Isolated in 2014



Data are not mutually exclusive. Some individuals have more than one species.

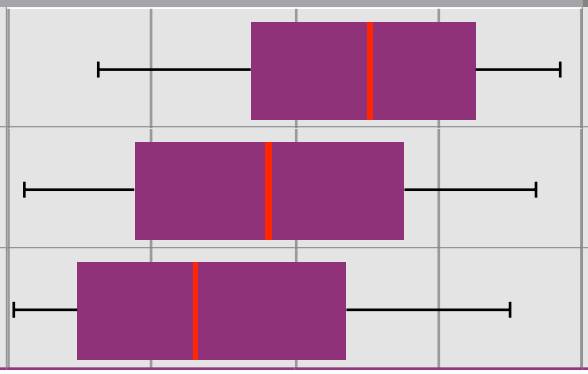
Because individuals may not have a mycobacterial culture each year, data from 2010 to 2014 were combined to allow a more robust analysis of mycobacterial species prevalence among people with CF. Of the 20,880 individuals who were cultured in this time period, 3,775 had one or more mycobacterial species isolated (18.1 percent).

NUTRITION

Nutritional outcomes are a key measure of health in people with CF. Because there is no consistent nutritional measurement that can be used across the lifespan, this section is divided into three age groups: infants younger than 2, children ages 2 to 19 and adults 20 years and older.

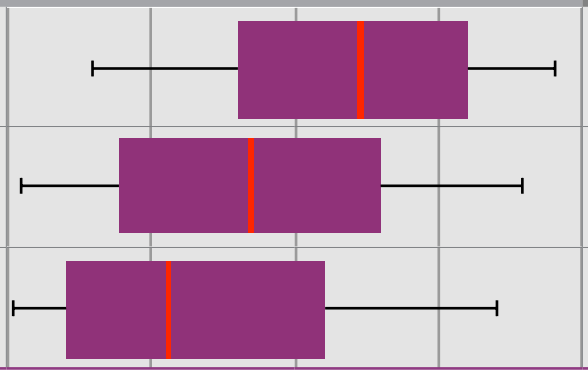
Below you can see the population-level variation for this age group for WHO weight-for-length, weight percentile and height percentiles in all individuals, those in the mutation class I-III group, and those in mutation class IV-V group. All three of these groups show a median weight-for-length value well above the 50th percentile, however, individuals in the mutation class I-III group have lower weight and substantially lower height percentiles than individuals in the mutation class IV-V group. This suggests that growth is not optimal in these infants, but trends over time are showing improvement.

All Individuals, WHO Nutritional Outcomes for Individuals Under 24 Months



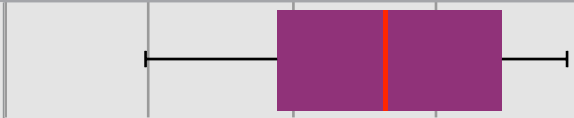
	Median	5th Percentile	95th Percentile
Weight-for-Length *N=1,870*	63.0	15.6	96.3
Weight Percentile *N=1,875*	45.3	2.8	91.9
Length Percentile *N=1,870*	32.6	0.8	87.4

Mutation Class I-III Group, WHO Nutritional Outcomes for Individuals Under 24 Months

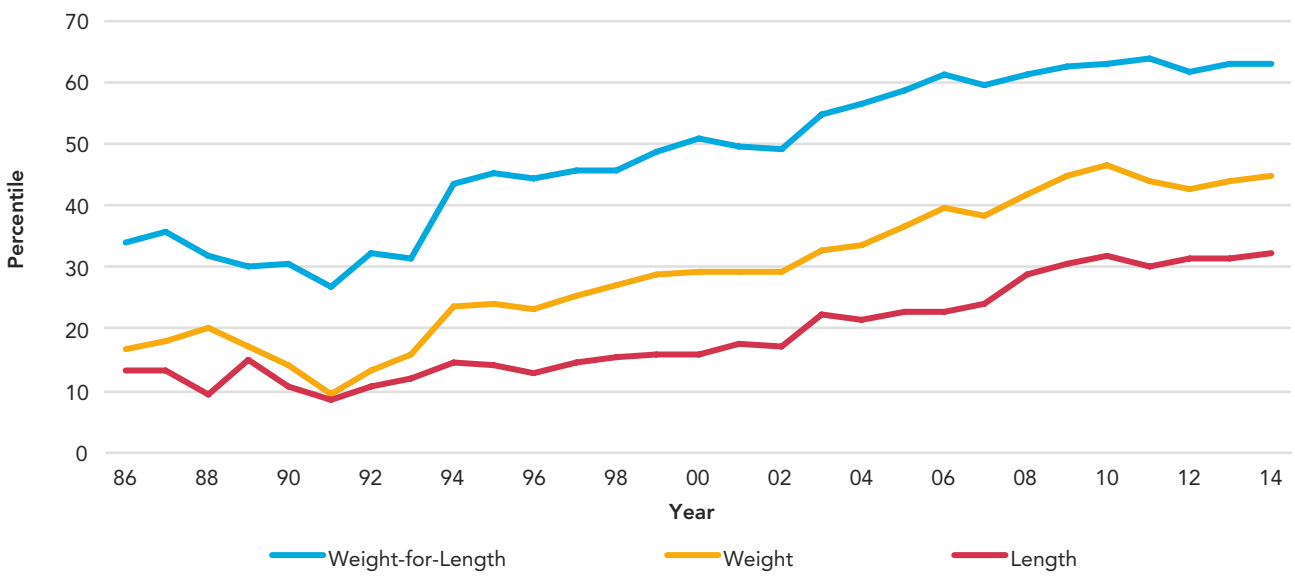


	Median	5th Percentile	95th Percentile
Weight-for-Length *N=1,255*	61.4	14.7	95.2
Weight Percentile *N=1,258*	42.3	2.3	89.5
Length Percentile *N=1,255*	27.9	0.7	85.3

Mutation Class IV-V Group, WHO Nutritional Outcomes for Individuals Under 24 Months

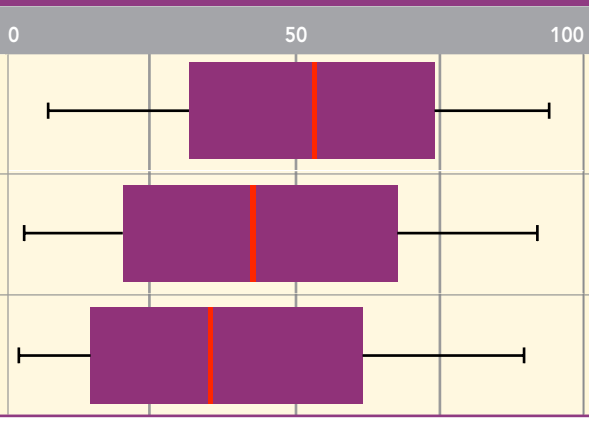
	0 — 50 — 100	Median	5th Percentile	95th Percentile
Weight-for-Length *N=187*		66.1	24.2	97.8
Weight Percentile *N=188*		58.7	11.3	95.7
Length Percentile *N=187*		49.3	3.2	92.6

Median WHO Nutritional Outcome Percentiles for Patients Under 24 Months, 1986–2014



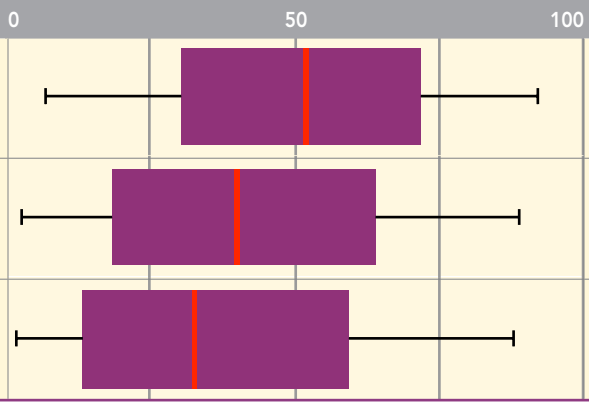
The goal established by the CF Foundation nutrition guidelines for children 2 to 19 years of age is a BMI at or above the 50th percentile.[25] The median BMI percentile is above the 50th percentile for this age group. The median weight percentile is approaching the recommendation, but the median height percentile still has room for improvement.

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



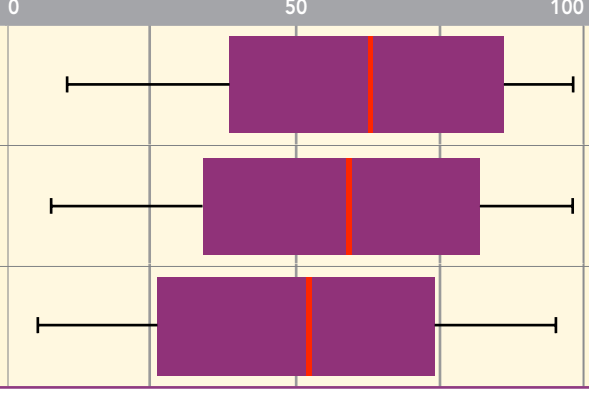
	Median	5th Percentile	95th Percentile
BMI Percentile *N=10,495*	53.5	7.5	94.0
Weight Percentile *N=11,332*	42.8	3.2	91.9
Height Percentile *N=11,366*	35.3	2.1	89.6

Mutation Class I-III Group, CDC Nutritional Outcomes for Individuals 2 to 19 Years



	Median	5th Percentile	95th Percentile
BMI Percentile *N=1,245*	51.9	7.0	92.1
Weight Percentile *N=1,374*	40.2	2.8	89.0
Height Percentile *N=1,373*	32.8	1.8	87.9

Mutation Class IV-V Group, CDC Nutritional Outcomes for Individuals 2 to 19 Years

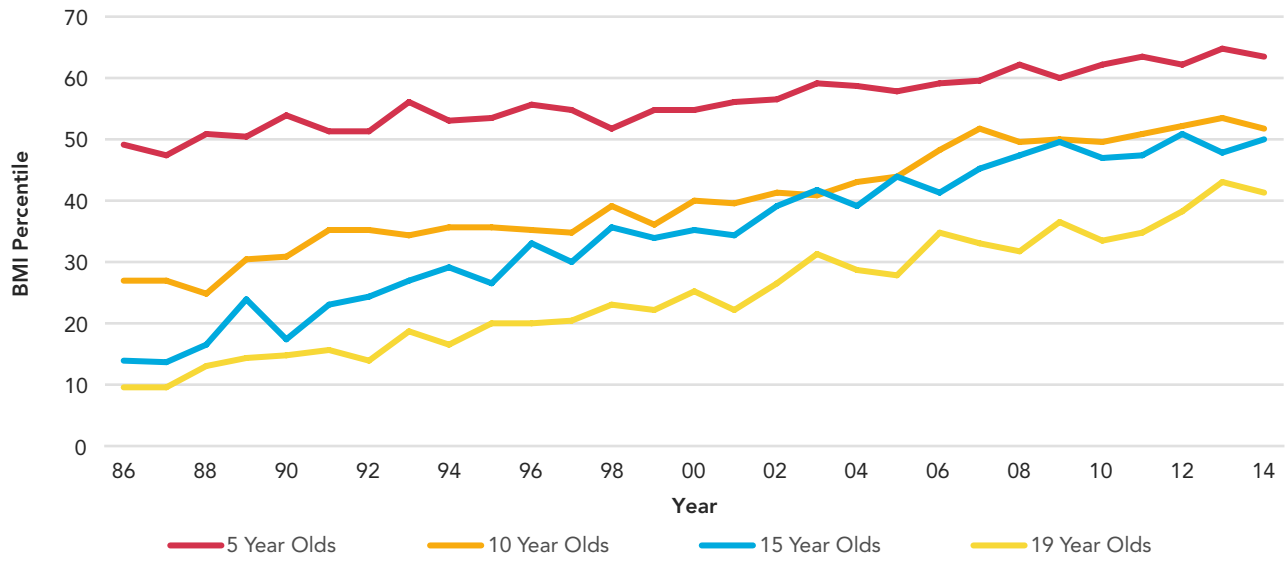


	Median	5th Percentile	95th Percentile
BMI Percentile *N=14,401*	63.2	10.4	98.1
Weight Percentile *N=15,651*	59.4	7.7	98.0
Height Percentile *N=15,697*	52.6	5.5	95.1

People with CF ages 2-19 years in the mutation class IV-V group have higher BMI percentiles than those in the mutation class I-III group, but there is substantial variation in the outcomes and significant overlap in outcomes between the two.

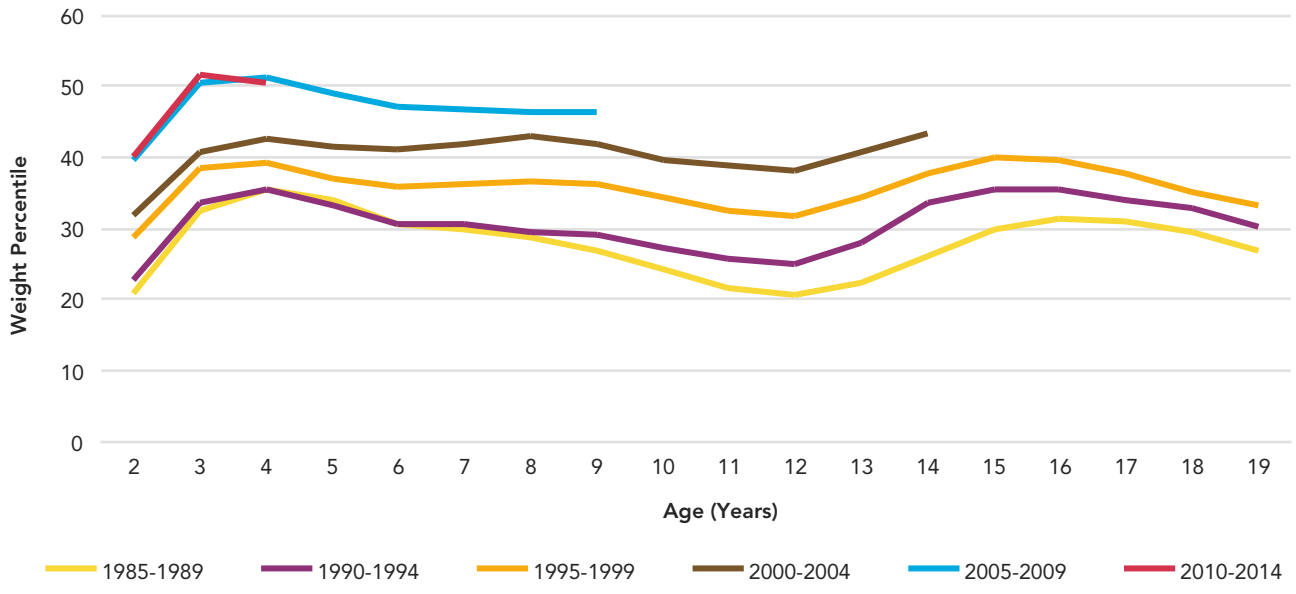
Since 1986, median BMI percentiles have increased steadily among people with CF ages 2 to 19. The greatest increase is seen in 15-year-olds. As individuals age, their BMI percentile drops, but the gap has been getting smaller in recent years.

Median CDC BMI Percentile by Age, 1986–2014

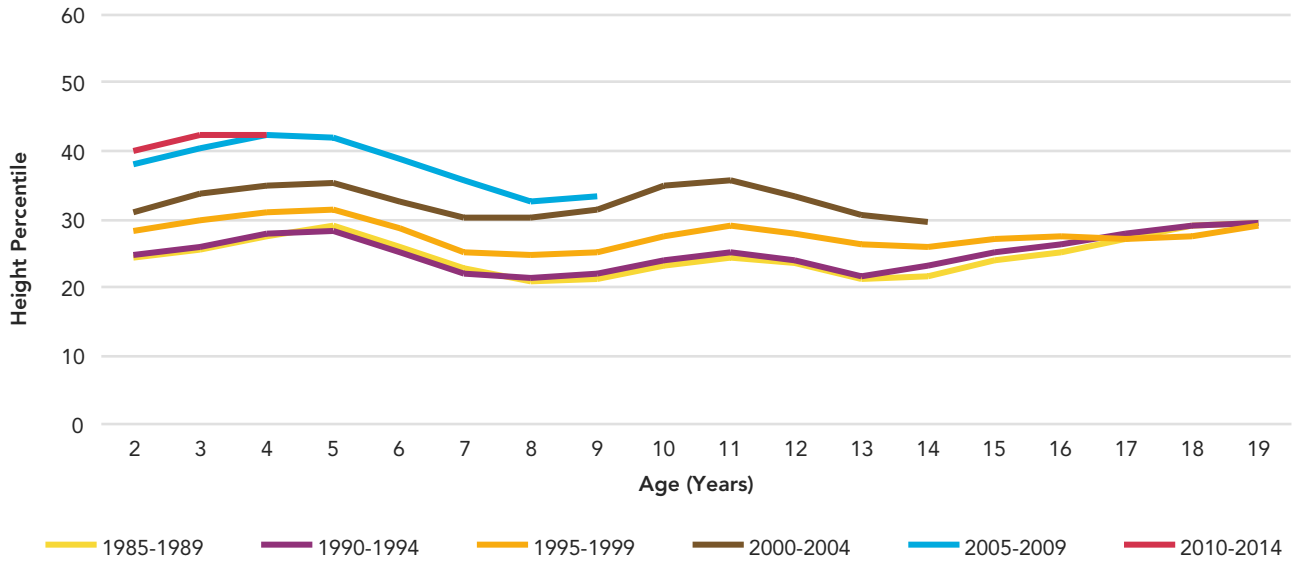


Successive birth cohorts show improved weight and height percentiles, most notably in the youngest cohorts. Multiple factors may be contributing to the improvements in the youngest cohorts including implementation of newborn screening with early intervention.

Median CDC Weight Percentile vs. Age, by Birth Cohort

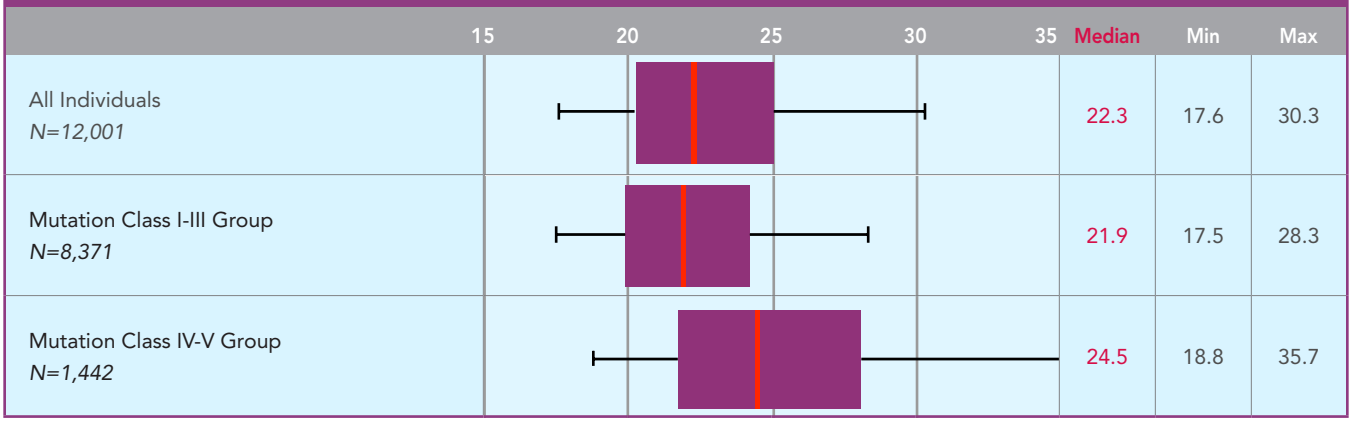


Median CDC Height Percentile vs. Age, by Birth Cohort



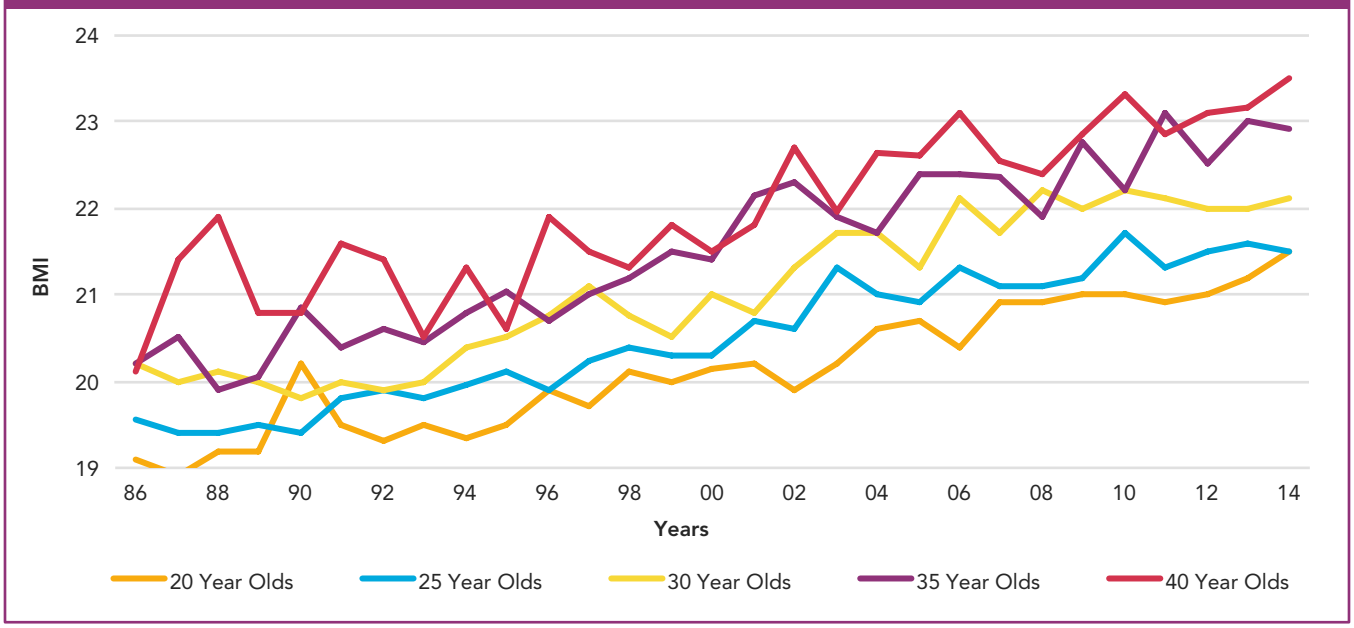
The goal established by the CF Foundation nutrition guidelines is a BMI at or above 22 for females and 23 for males age 20 and older.[25] Among individuals in the mutation class I-III group, median BMI is below the goal, whereas individuals in the class IV and V mutation group have a median BMI above the goal. Considerable variation in BMI exists within each genotype group, with significant overlap between individuals in the mutation class I-III group and individuals in the mutation class IV-V group. Of note, a substantial proportion of those in class IV-V group are overweight (BMI 25 to 29.9), and some are obese (BMI 30+).

BMI Value for Individuals 20 Years and Older, by Mutation Class Group



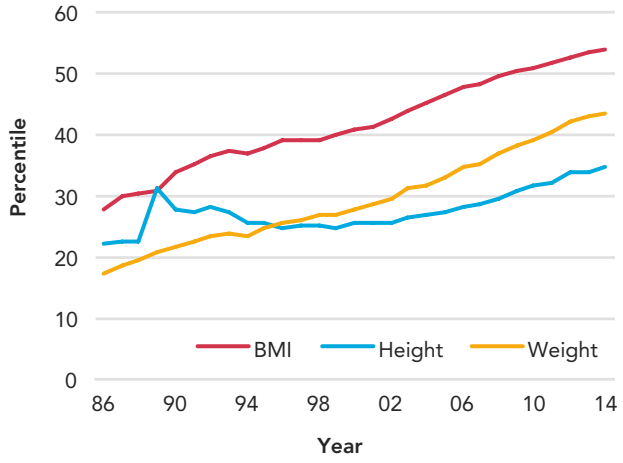
The nutritional outcomes of young adults has improved markedly over the past two decades. Small numbers of individuals at each age lead to fluctuations year to year, but overall, the trend is one of increasing median BMI. Increases in BMI at older ages may in part relate to an increase in adult diagnoses and the better survival of individuals with milder disease.

Median BMI Value by Age, 1986–2014

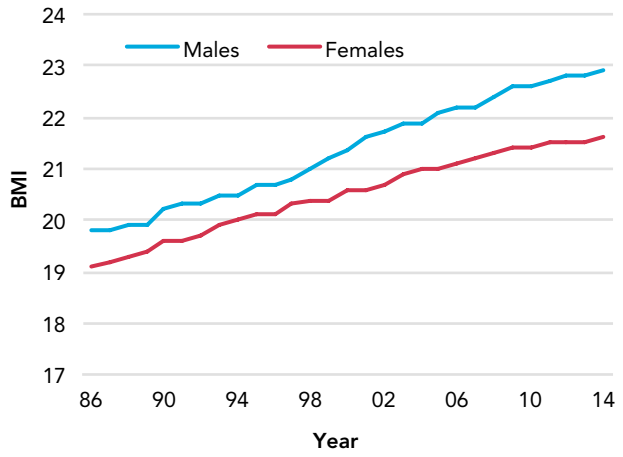


Since the 1980s, significant progress in nutritional outcomes has been made for both the pediatric and adult CF populations. Since 2008, the median BMI percentile of individuals with CF ages 2 to 19 has met the CF Foundation goal of the 50th percentile. The aging of the CF population and a greater number of late diagnoses with genotypes associated with milder disease may also be contributing to this trend in adults.

Median Nutritional Outcomes Percentiles for Individuals 2 to 19, 1986–2014



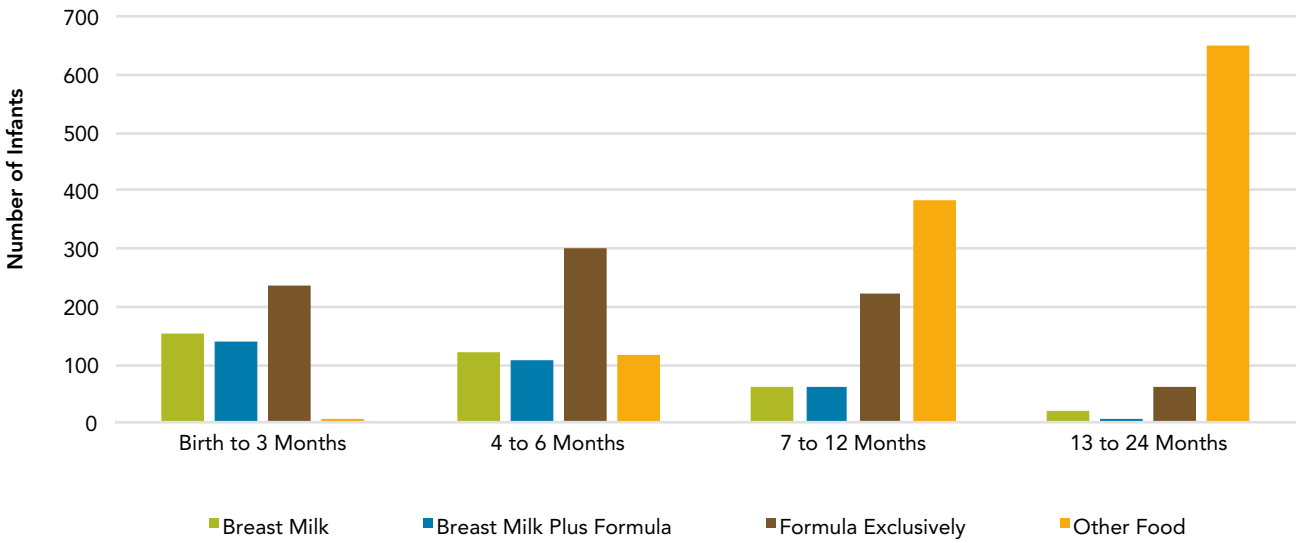
Median BMI Value for Individuals 20 Years and Older, 1986–2014



Infant Feeding

The majority of infants with CF receive formula feeding as the primary form of feeding or as a supplement to breast-feeding. Cow's milk-based formula with the standard 20 cal/oz caloric density is the most common feeding used from birth to 3 months of age. 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 2014*



**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*

GASTROINTESTINAL (GI) THERAPIES

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

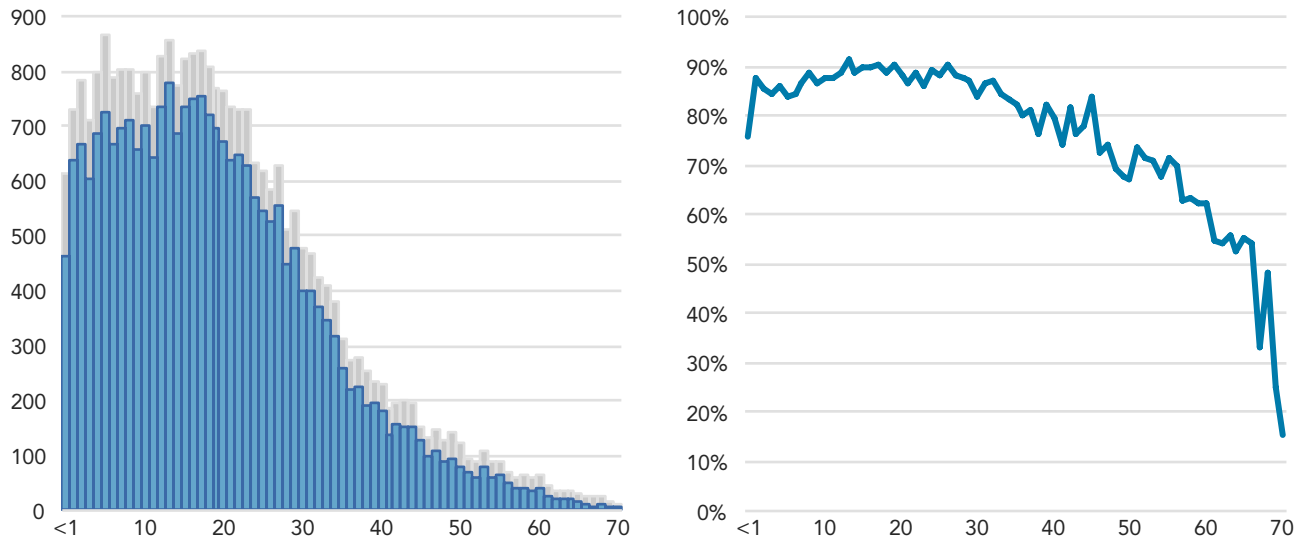
For infants with CF under age 2, the guidelines recommend assessment of pancreatic functional status by measurement of fecal elastase.[5] Data on fecal elastase test results have been collected in the Registry since 2010 and we have seen an increase in the number of individuals with a fecal elastase test. Almost 60 percent of infants were tested in 2014. Almost all individuals with a fecal elastase value of less than 100 and the vast majority of individuals with a fecal elastase value between 100 and 200 have been prescribed PERT. Approximately one-quarter of individuals with fecal elastase values greater than 200 were prescribed pancreatic enzymes.

Percent of Individuals Taking Enzymes in 2014 by Fecal Elastase Value

Most Recent Fecal Elastase Value	Individuals Under 24 Months	All People with CF
Less than 100	97.6	99.1
Between 100 and 200	90.3	94.2
Greater than or equal to 200	22.2	22.2
Percent of individuals with a fecal elastase value	59.9	12.4

A large proportion of individuals of all ages are prescribed PERT. The proportion of individuals prescribed PERT remains over 80 percent until age 40, when the proportion in each age begins to decrease. The decrease in the proportion of older CF individuals prescribed PERT is most likely due to survival bias.

PERT Use by Age, 2014

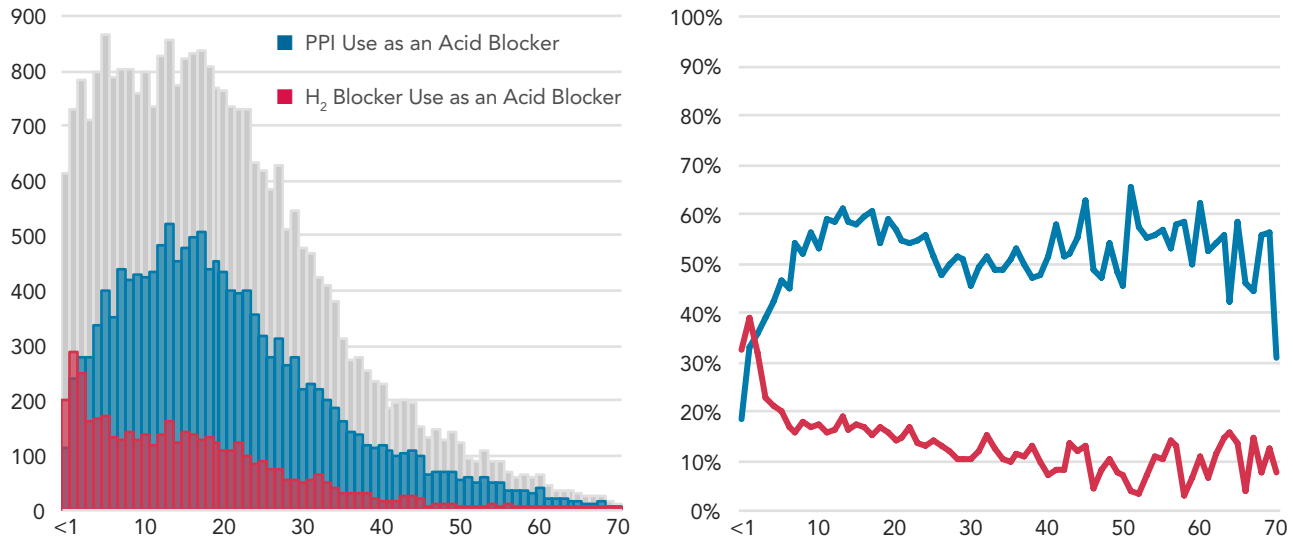


Infants with evidence of pancreatic insufficiency are recommended to receive 2,000 to 5,000 lipase units per feeding (total lipase dose), with adjustments as the infant grows.[5] The Registry data show that the mean highest dose of lipase among children younger than age 2 is 14,310 total lipase units per largest meal. The low height percentiles suggest that the dosing and delivery of PERT may be suboptimal in this age group.

For individuals ages 2 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 of individuals 2 to 19 years is 1883.7 and individuals 20 years and older is 1740.5.

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 (51.3 percent of individuals) than H_2 blockers (16.3 percent of individuals). H_2 blockers are used more frequently in younger individuals and their use tapers among older individuals. In contrast, use of PPIs is lowest among younger individuals and consistently around 50 percent among individuals ages 20 and older.

PPI and H_2 Blocker Use by Age, 2014



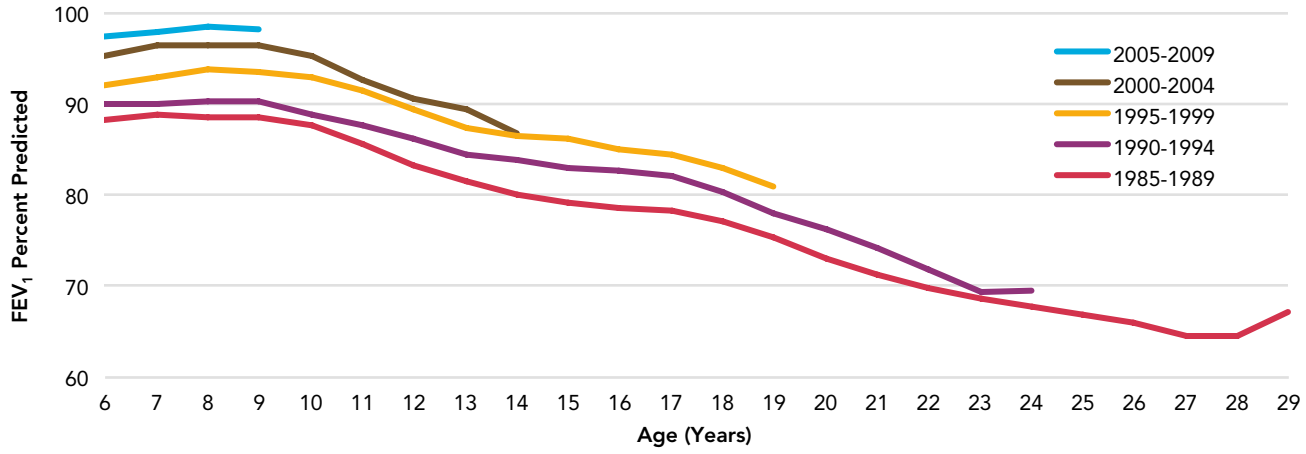
CF-specific vitamins also play an important role in the overall regiment of GI therapies for an individual with CF. In 2014, almost 92 percent of individuals 2 to 19 and over 80 percent of individuals 20 years and older were prescribed CF-specific vitamins.

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, as well as variations in pulmonary function across care centers and by mutation class. Pulmonary function is measured using FEV_1 percent predicted and calculated using the Global Lung Initiative (GLI) reference equations.[1]

Successive birth cohorts show improved pulmonary function, and cross-sectional analyses from 1994 to 2014 show improved FEV_1 percent predicted across all ages. The majority of 18-year-olds — a typical age of transition to adult care — now have normal lung function or mild obstruction, defined as an FEV_1 percent predicted greater than or equal to 70.

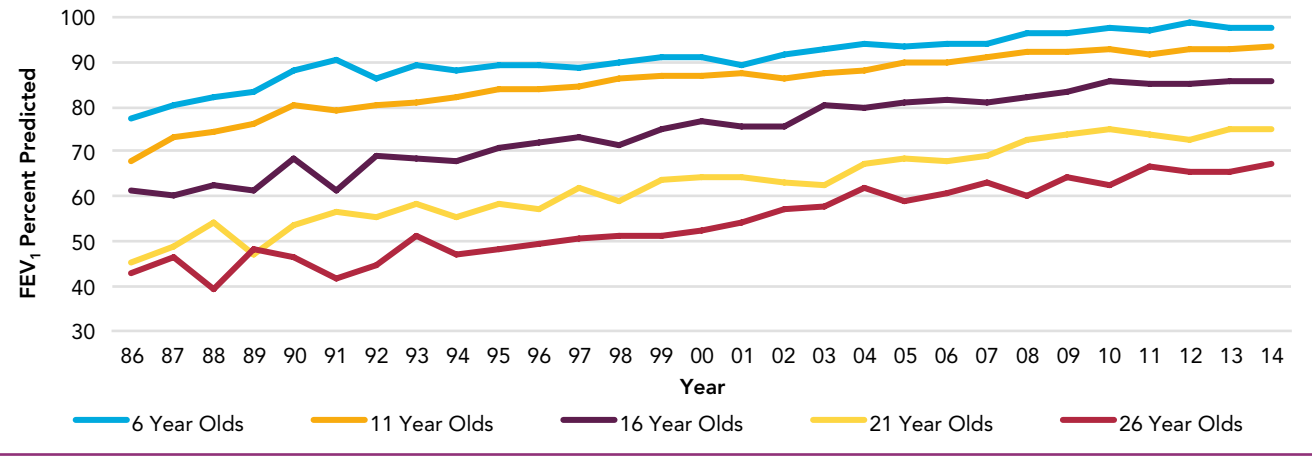
Median FEV_1 Percent Predicted vs. Age by Birth Cohort



FEV_1 percent predicted is steadily improving and currently is above 90 percent predicted into early adolescence.

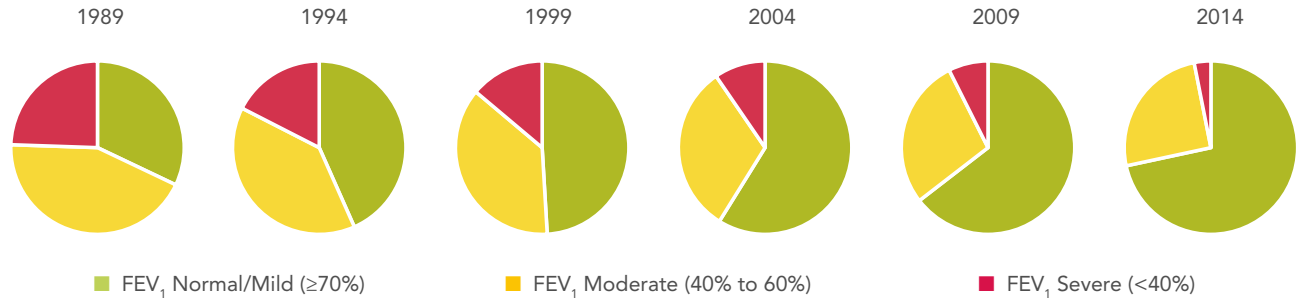
Median FEV_1 percent predicted has improved more than 10 percentage points for people with CF of all ages since 1986; however, the lines are nearly parallel, suggesting that the rate of decline in adolescence remains the same.

Median FEV_1 Precent Predicted by Age, 1986–2014



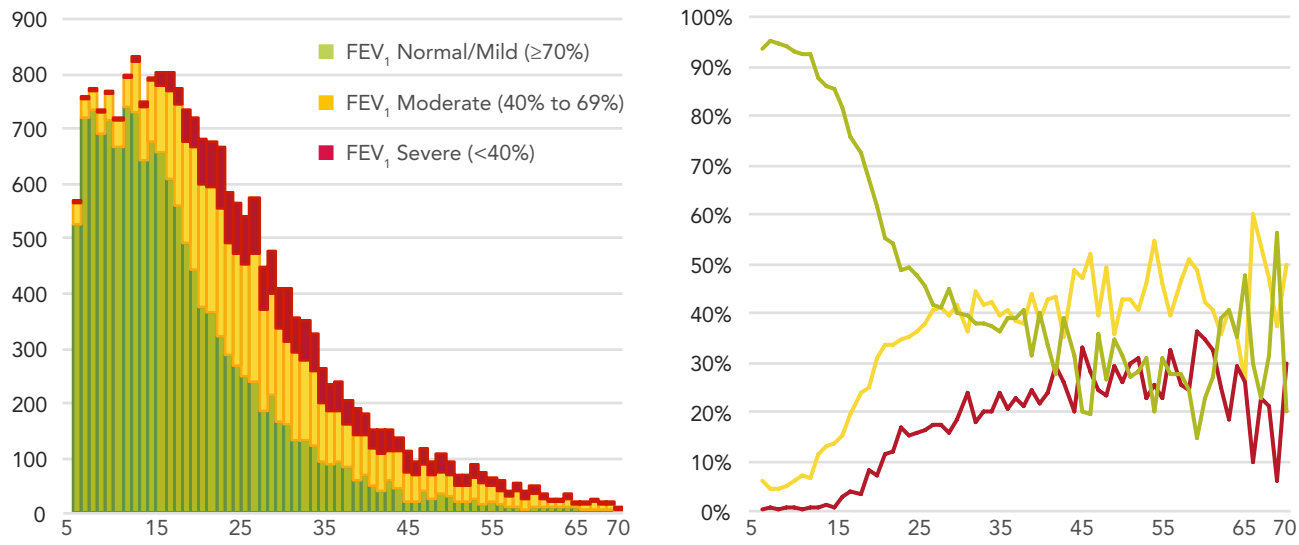
The proportion of 18-year-olds in the normal/mild category (FEV_1 ≥70 percent predicted) has increased from 31.1 percent in 1989 to 71.6 percent in 2014, while the proportion in the severe category (FEV_1<40 percent predicted) has decreased from 24.5 percent to 3.1 percent.

Median FEV_1 Percent Predicted in 18-Year-Olds, 1989–2014



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 lung disease. This proportion decreases with age until the age of 45, when the population has nearly equal proportions of individuals with mild, moderate and severe lung disease.

Lung Disease Severity by Age, 2014 *(Stacked Bar Chart)*

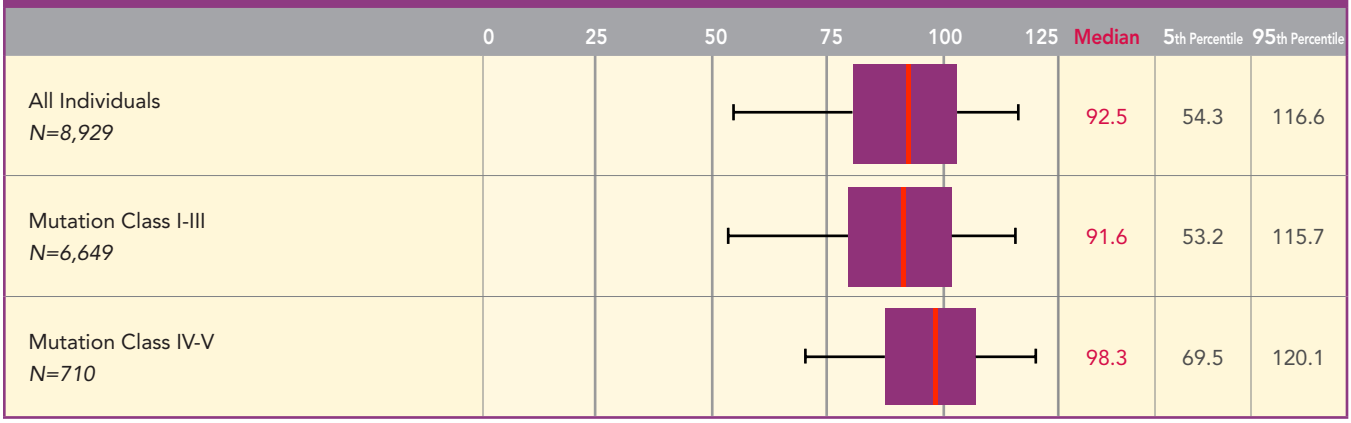


Mutation Class Variation in FEV_1 Outcomes

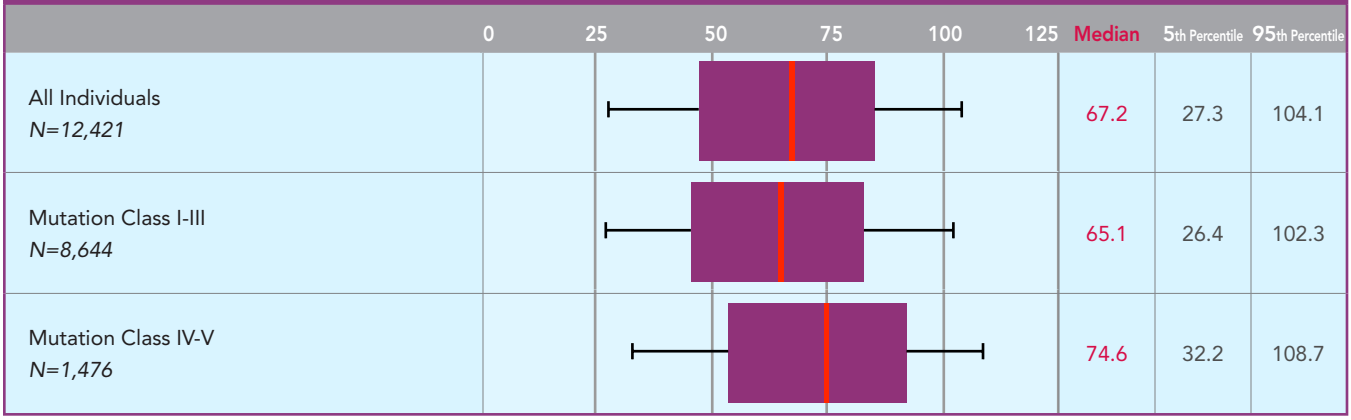
As the majority of individuals with CF fall into mutation class I-III (70.7 percent of those genotyped), the outcomes of this group drive national averages.

In children and adults with CF, median lung function is lower among individuals in the mutation class I–III group compared with individuals in mutation class IV-V (6.7 percent lower in children and 9.5 percent lower in adults). However, there is considerable variation among individuals within each mutation class group and substantial overlap between the two groups.

FEV_1 Percent Predicted for Individuals 6 to 17 Years, by Mutation Class Group



FEV_1 Percent Predicted for Individuals 18 Years and Older, by Mutation Class Group



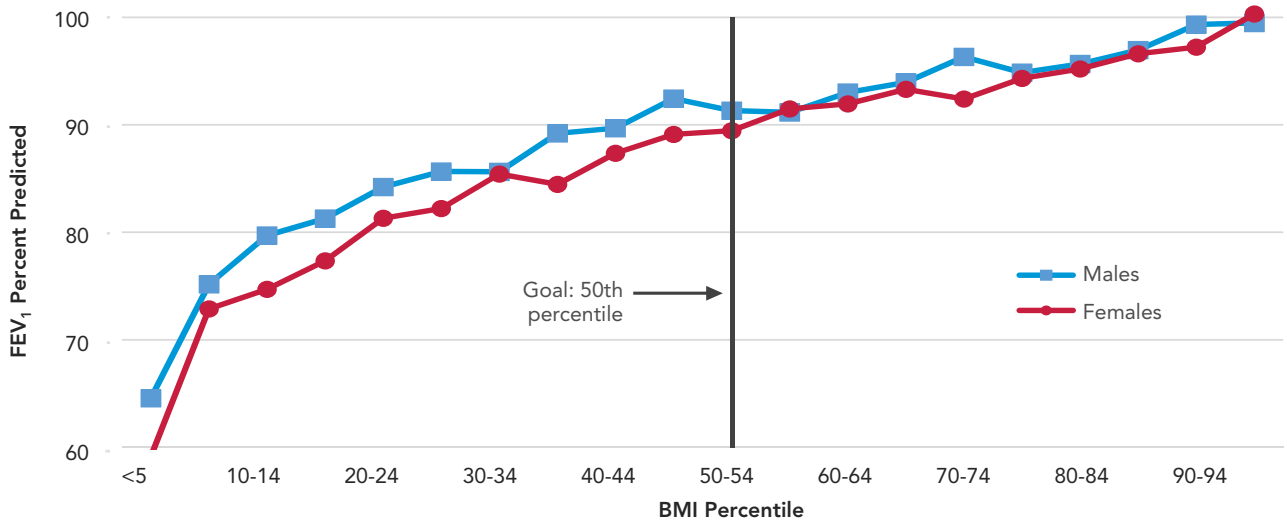
FEV_1 AND BMI OUTCOMES

Pulmonary and nutritional outcomes are two key metrics of health among individuals with CF and are therefore the main focus of quality improvement work within the CF care network. The data show that, for both children and adults with CF, pulmonary function and nutrition status are related and improvements in one metric are associated with improvements in the other.

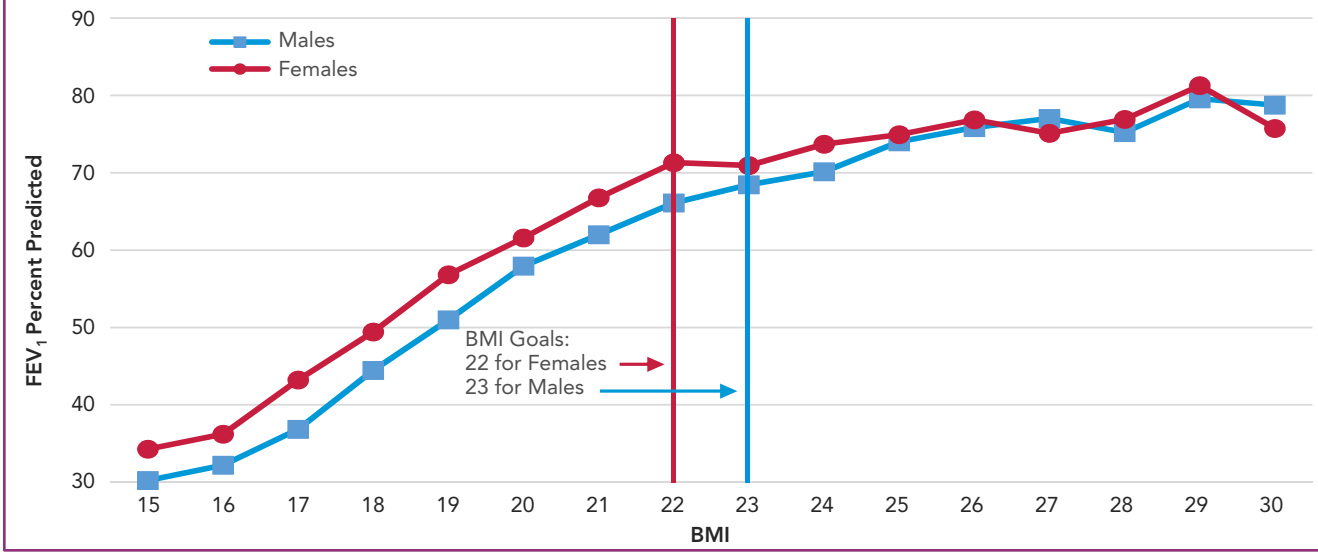
The pulmonary and nutritional goals are:

- *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 greater than or equal to 22 for females and 23 for males.*[25]

FEV_1 Percent Predicted vs. BMI Percentile for Children 6 to 19 Years in 2014

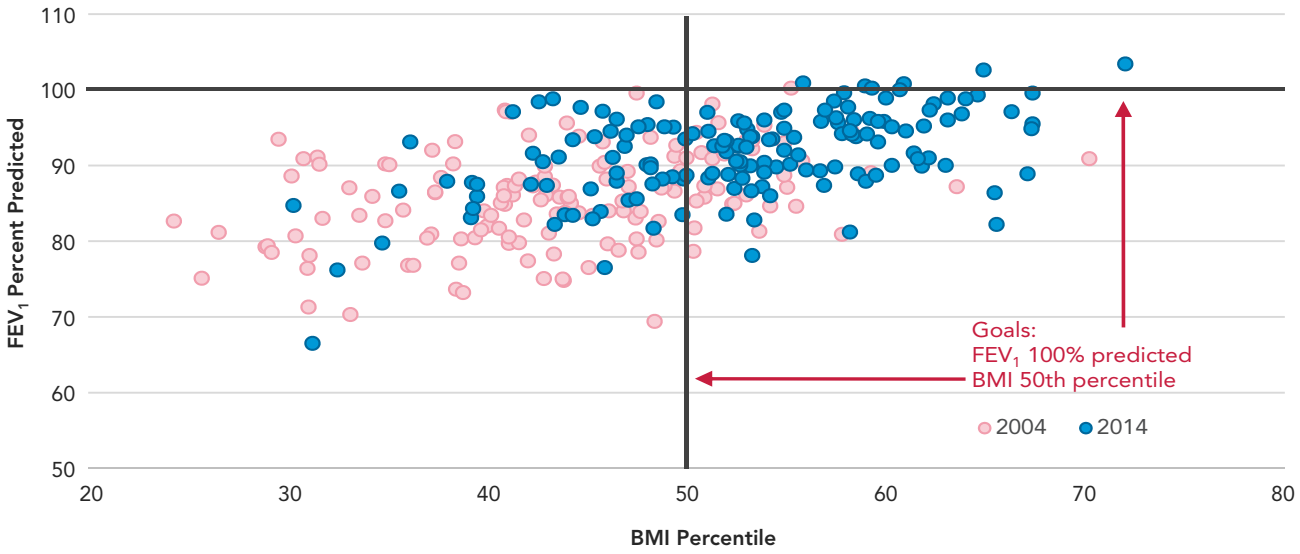


FEV_1 Percent Predicted vs. BMI Value for Adults 20 to 40 Years in 2014

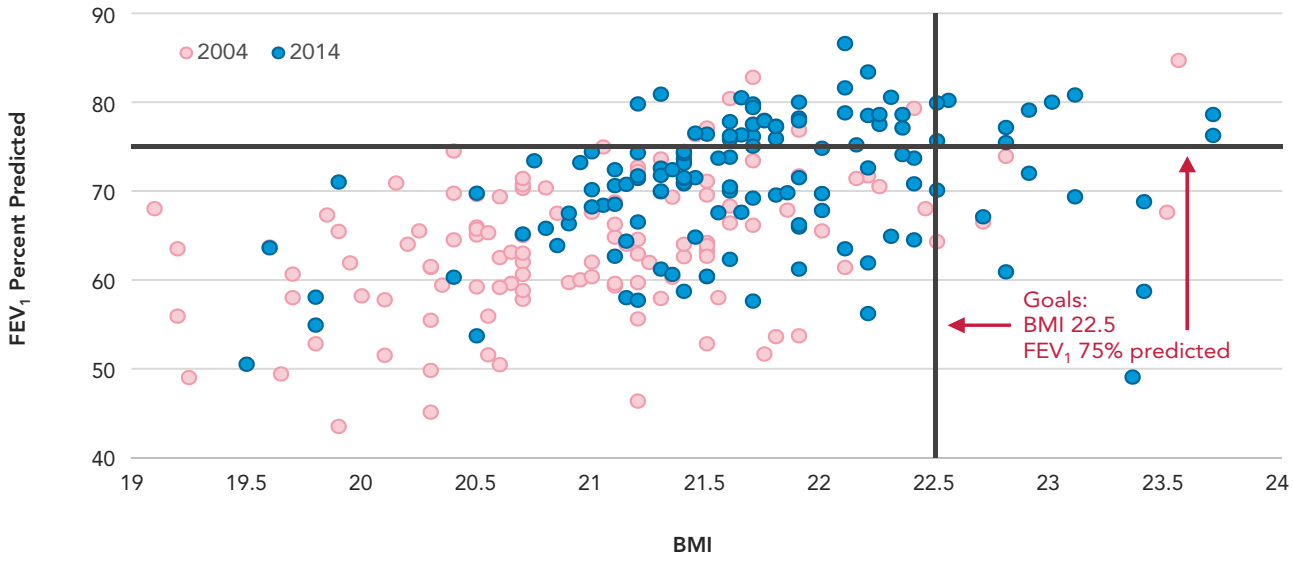


The figure below shows the distribution of centers with regard to their median nutritional and pulmonary outcomes and the change in the distribution between 2004 and 2014. Each dot in the figure below represents a value from an accredited care center or affiliate program. Ideally, centers would be in the upper right quadrant of the graph, which represents centers that are meeting both pulmonary function and nutritional goals. In 2014, the majority of pediatric centers are meeting nutritional guidelines with improvements in median pulmonary function during the past 10 years. Among adult centers, 38.6 percent are meeting the pulmonary function goals with progression toward more centers meeting the nutritional goals.

Median FEV_1 Percent Predicted vs. Median BMI Percentile for Individuals 6 to 17 Years, 2004 vs. 2014



Median FEV_1 Percent Predicted vs. Median BMI Value for Individuals 18 to 30 Years, 2004 vs. 2014

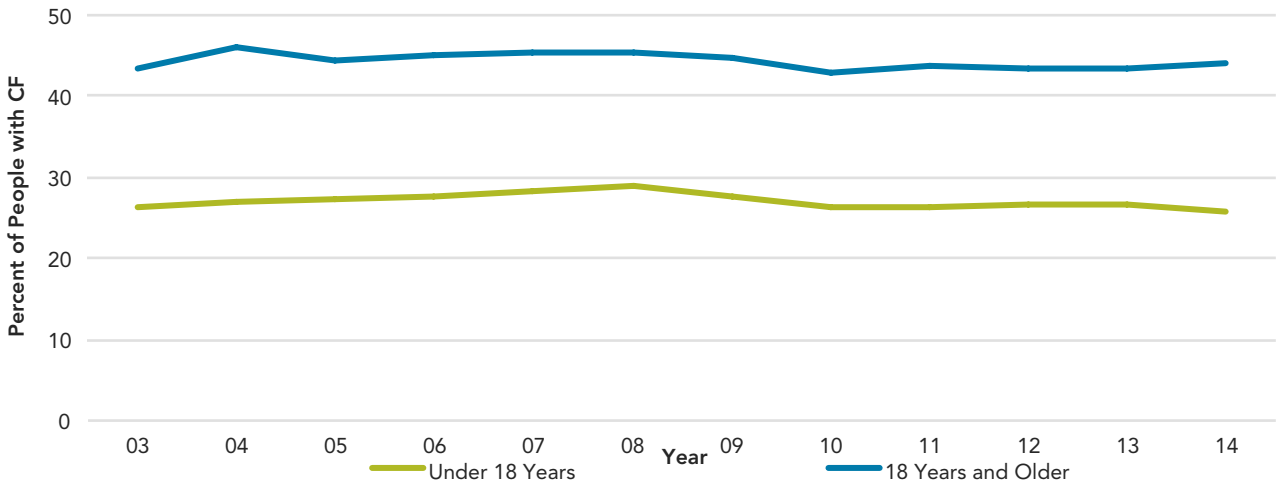


PULMONARY EXACERBATIONS

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 the cost of care. This section displays trends in the rate of pulmonary exacerbations over time and by age group. Center variation with regard to exacerbation rates and treatment characteristics is also shown.

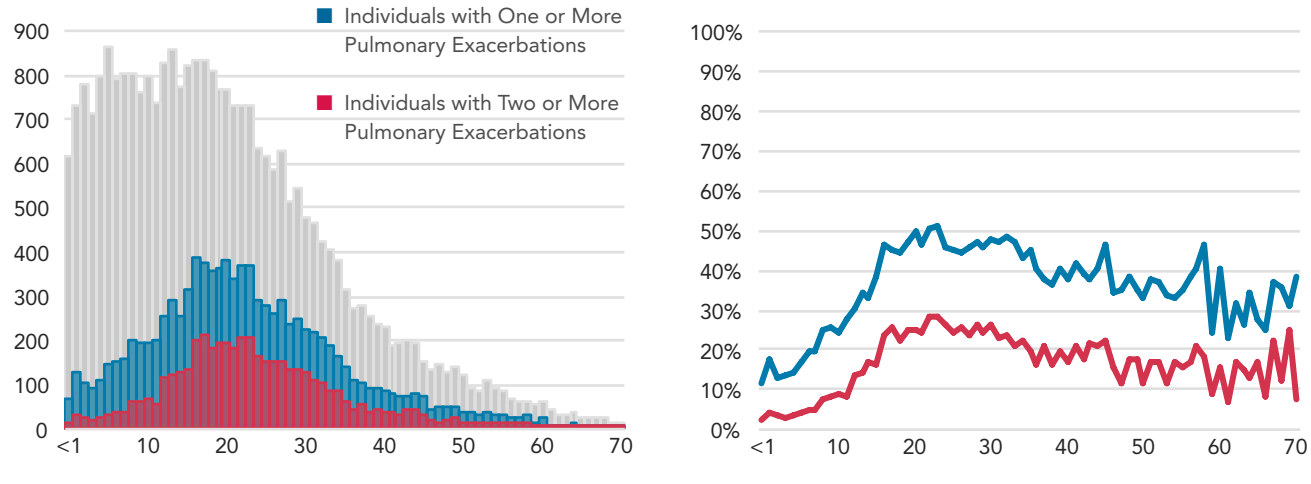
Despite the notable improvements in pulmonary function and nutritional status over the past decades, a significant proportion of individuals are still treated with IV antibiotics for pulmonary exacerbations, and during that time, there has been no reduction in the proportion of individuals with CF who experience at least one exacerbation during the calendar year.

Patients Treated with IV Antibiotics for a Pulmonary Exacerbation, 2003–2014



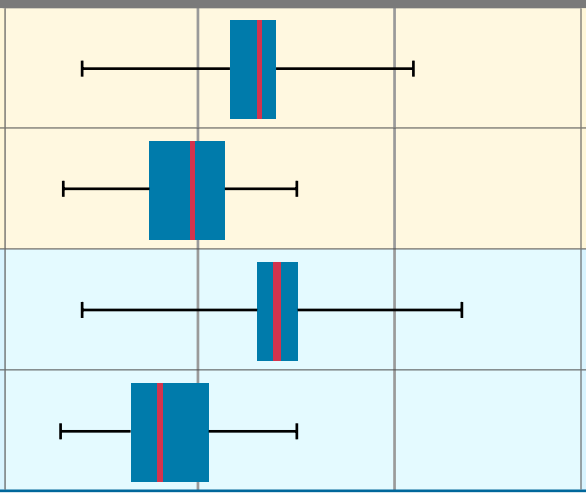
Individuals with CF who are between the ages of 15 and 30 are the most likely to experience an exacerbation during the year, compared with other age groups.

Pulmonary Exacerbations by Age, 2014



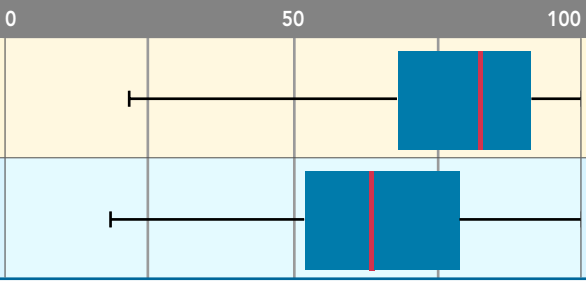
When the CF Foundation developed guidelines for the treatment of pulmonary exacerbations in 2009, there was little published literature or data available upon which to base recommendations.[36] Current practice within the CF Foundation care center network is a median treatment duration of about two weeks, with adults more likely to complete some of their treatment at home. Further research is underway to develop best practices for the treatment of pulmonary exacerbations.

Exacerbation Treatment Duration in Days, by Center



	Median	Min	Max
Median Total Duration of IV Antibiotic Treatment for a Pulmonary Exacerbation in Individuals Less than 18 Years	13.1	4.0	21.0
Median Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Individuals Less than 18 Years	9.7	3.0	15.0
Median Total Duration of IV Antibiotic Treatment for a Pulmonary Exacerbation in Individuals 18 Years and Older	14.0	4.0	23.5
Median Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Individuals 18 Years and Older	8.0	2.9	15.0

Percent of Total Treatment Duration in Hospital, by Center



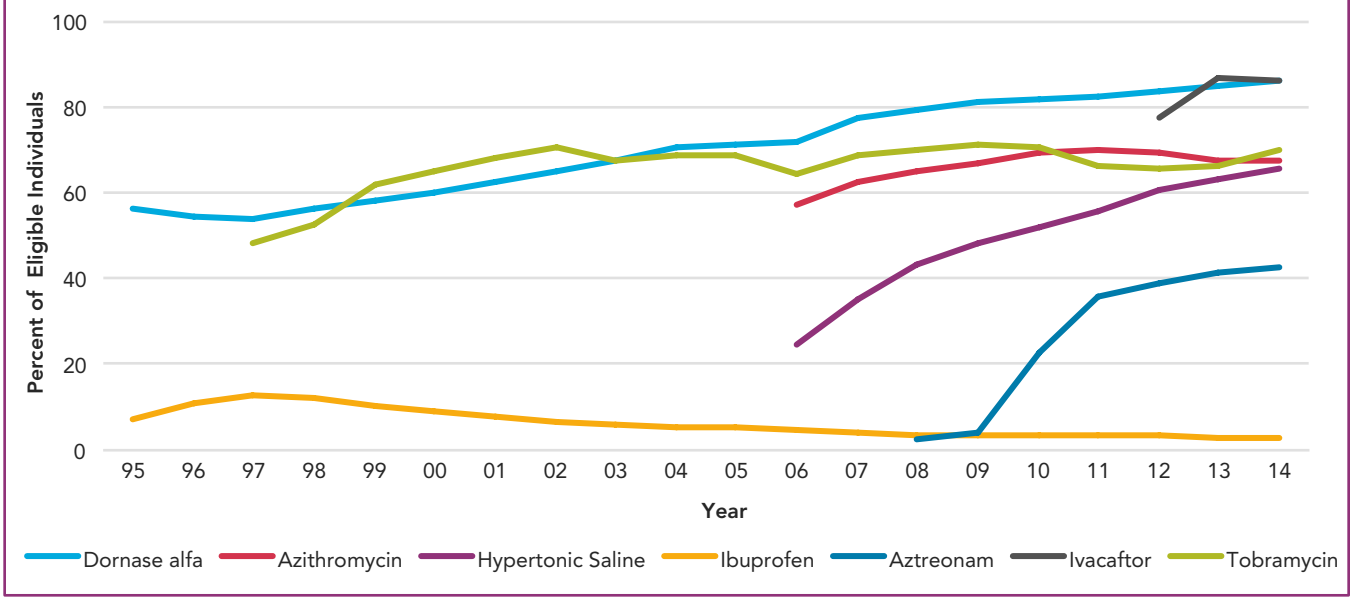
	Median	Min	Max
Percent of Total Treatment Duration in Hospital in Individuals < 18 Years	82.4	21.4	100.0
Percent of Total Treatment Duration in Hospital in Individuals ≥ 18 Years	63.6	18.5	100.0

PULMONARY THERAPIES

Chronic pulmonary therapies are a major component of the treatment regimen for individuals with CF. This section provides data on the uptake of and trends in the prescription of pulmonary medications recommended for chronic use by the CF Foundation pulmonary guidelines committee. Data are also provided on medications that are not recommended and for those which the committee did not find sufficient evidence to recommend for or against chronic use.[37]

Use of CF therapies is typically between 60 to 80 percent of the eligible population with use of most therapies increasing over time. Over the last few years, additional formulations of inhaled tobramycin have become available, so the chart below includes all formulations. Chronic oral antibiotics are used infrequently (by only 13.7 percent of the CF population). The availability of multiple pulmonary therapies for CF is beneficial; however, it also contributes to treatment complexity and the overall burden on individuals with CF and their caregivers.

Chronic Medication Use in Eligible Individuals, 1995–2014

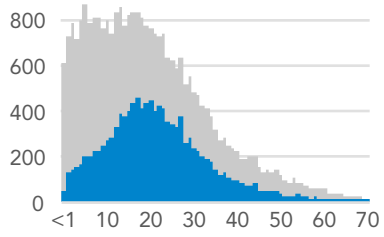


Only individuals with a G551D mutation were eligible for ivacaftor in 2012 and 2013, but that eligibility was extended by the FDA to include those with at least one of eight additional gating mutations in 2014.

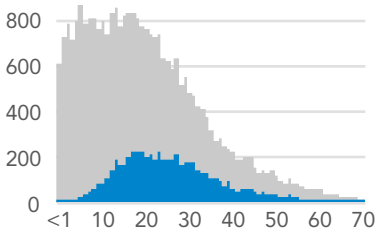
Prescriptions for pulmonary medications by age are shown below. The vast majority of the population is prescribed dornase alfa and inhaled bronchodilators. Use of dornase alfa is more widespread than hypertonic saline, especially among younger individuals. Use of inhaled antibiotics is highest among adolescents and young adults.

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, the peak in use occurs during adolescence and young adulthood.

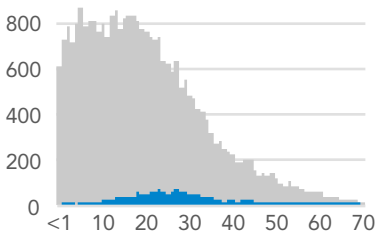
Any Tobramycin



Aztreonam

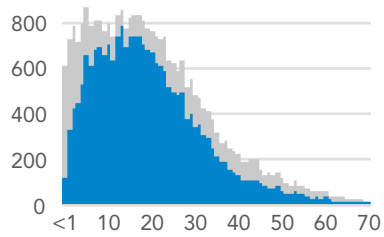


Colistin

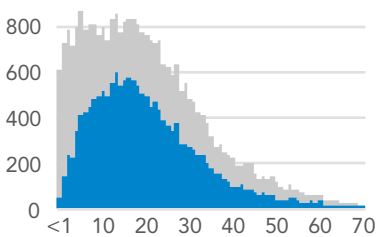


Dornase alfa is prescribed for the majority of individuals with CF, and more than half of them are prescribed hypertonic saline either in place of, or in addition to, dornase alfa. Azithromycin is also widely used, with the peak in use occurring at slightly older ages, compared with use of dornase alfa and hypertonic saline.

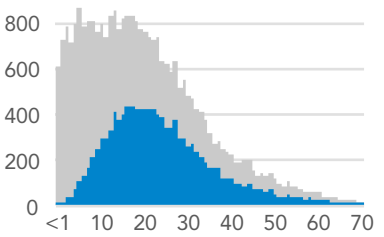
Dornase Alfa



Hypertonic Saline

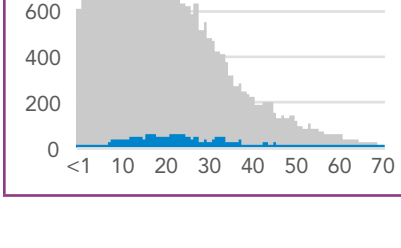


Azithromycin

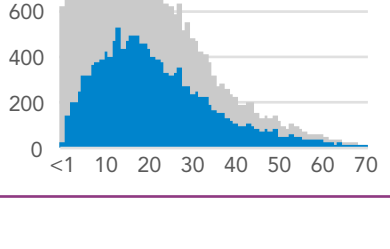


A substantial proportion of individuals with CF is prescribed inhaled corticosteroids and, to a lesser degree, leukotriene modifiers. Oral corticosteroids are used infrequently.

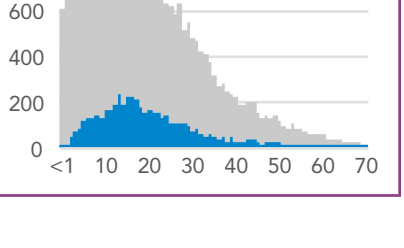
Oral Corticosteroids



Inhaled Corticosteroid

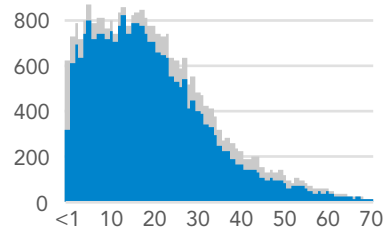


Leukotriene Modifiers

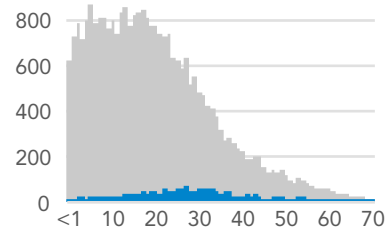


Bronchodilators are used extensively among individuals with CF. Almost all people with CF are prescribed beta agonists, except for a very small percentage who are prescribed an anticholinergic.

Inhaled Beta Agonist

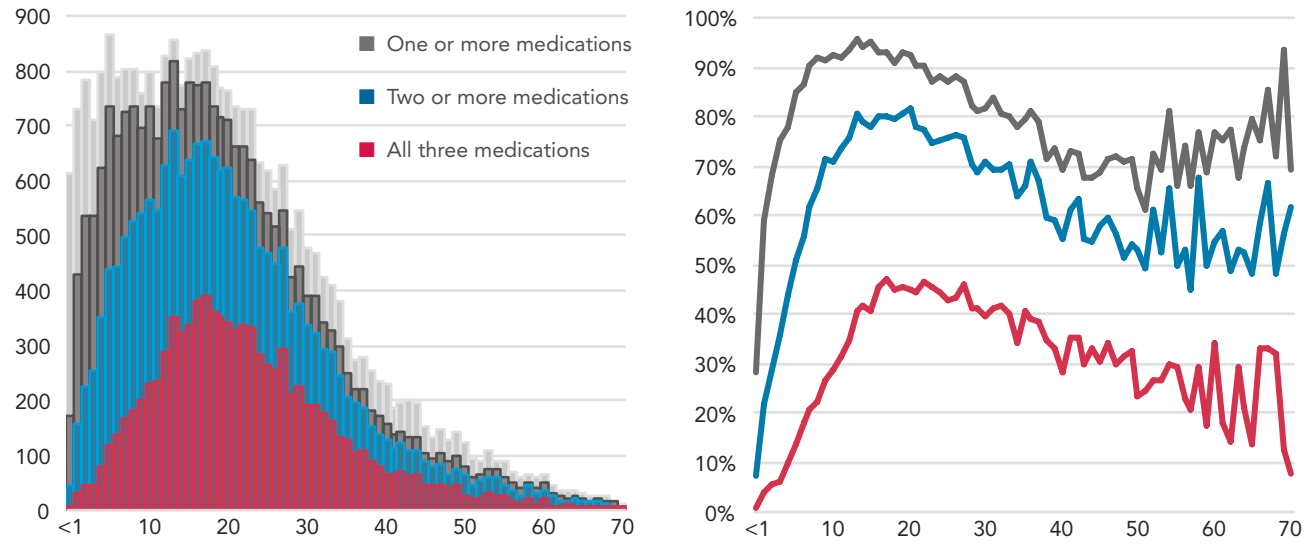


Inhaled Anticholinergic



Multiple pulmonary therapies are available for individuals with CF. Inhaled medications are effective treatments for pulmonary disease, but these require extensive time to prepare, administer and clean after treatment. All people with CF are eligible for dornase alfa and hypertonic saline prescriptions. Those with a *P. aeruginosa* infection are eligible for an inhaled antibiotic. Almost all individuals are prescribed at least one of these medications, and over half of those ages 15 and older are prescribed two or more of these therapies.

Inhaled Medication Use (Dornase Alfa, Hypertonic Saline, Inhaled Antibiotic) Use by Age, 2014

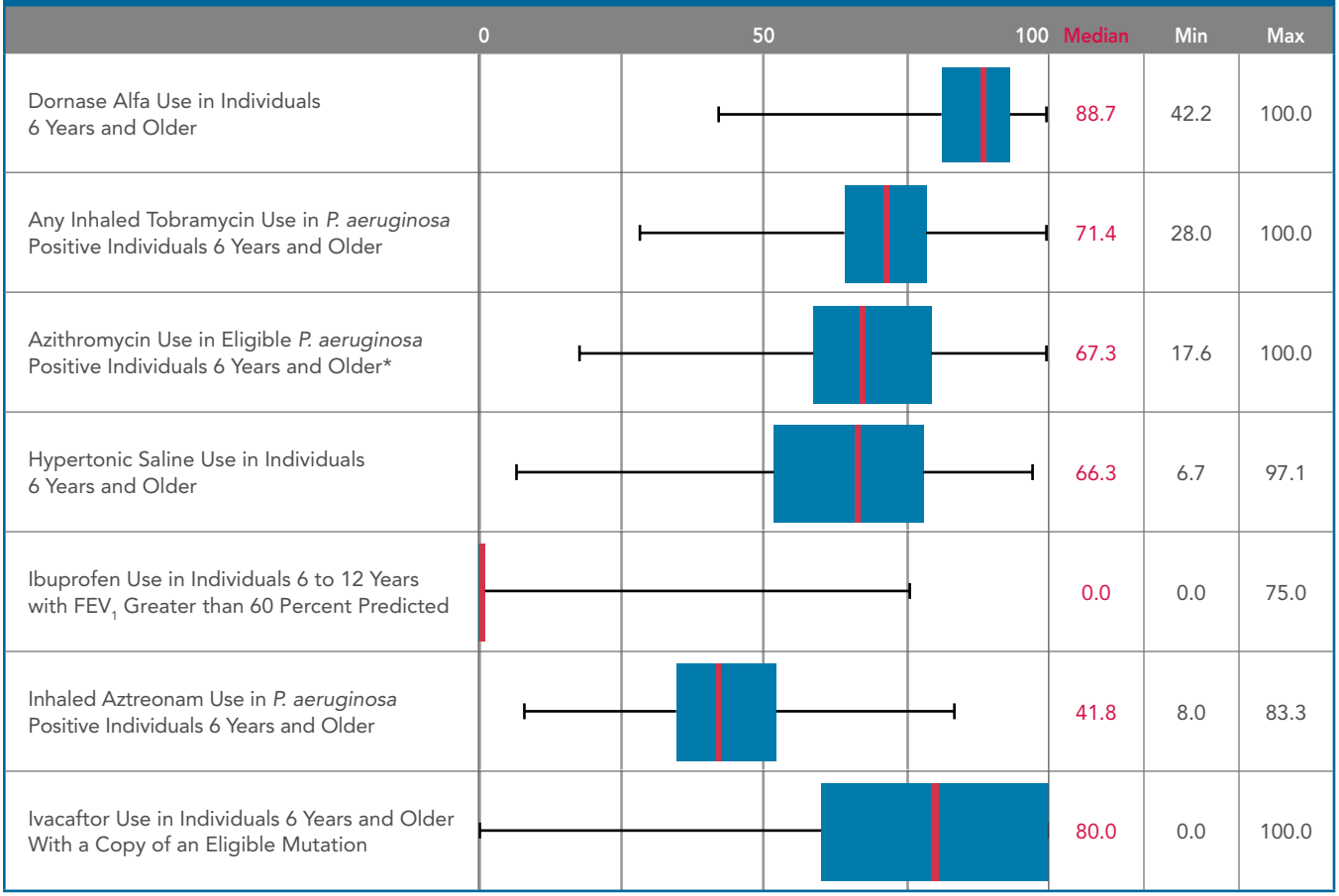


Inhaled Antibiotic includes the use of Tobramycin, Aztreonam, Colistin or Other Aminoglycosides

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. Ivacaftor is used by the majority of individuals eligible for the therapy.

Pulmonary Therapies Recommended for Chronic Use, by Center

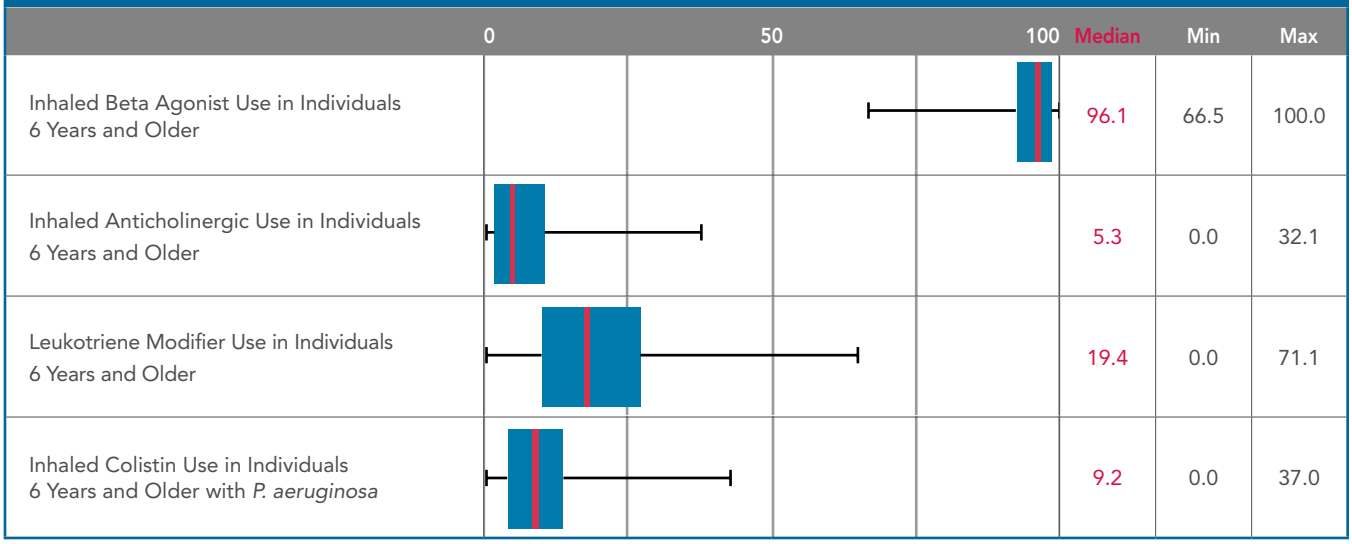


**Individuals were considered eligible if they met the selection criteria used in the U.S. azithromycin trial.[2]*

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, leukotriene modifiers and inhaled colistin to improve lung function, reduce exacerbations or improve quality of life.[37] Inhaled beta agonists are used consistently across the care center network for the vast majority of individuals with CF. Use of colistin has decreased in recent years. The other medications are used infrequently.

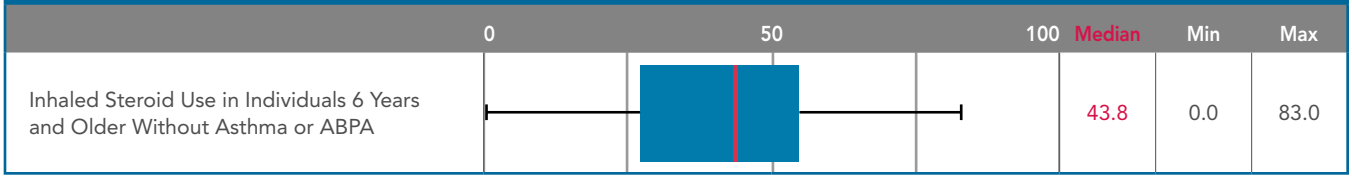
Pulmonary Therapies with Insufficient Evidence to Recommend for or Against Chronic Use, by Center



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 ABPA.

Pulmonary Therapies Not Recommended for Chronic Use, by Center



Medication Use in Young Children

Guidelines for chronic pulmonary medications exist only for individuals ages 6 years and older; however, guidelines are in development for children ages 2 to 5 years. The chart below shows the use of these medications among children younger than 6.

Medication Use in Individuals Under 6 Years, 2014

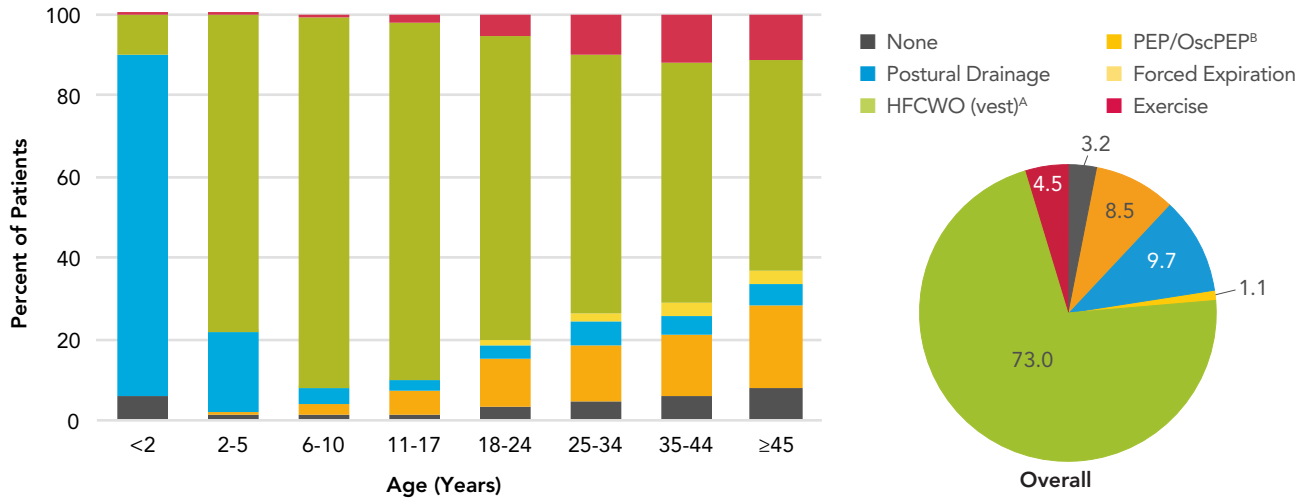
	Individuals Under 3 Years (%)	Individuals 3 to 5 Years (%)
Number of Individuals (n)	**2,038**	**2,354**
Dornase alfa	42.7	69.8
Hypertonic saline	21.0	41.6
Inhaled bronchodilators	79.2	92.2
Inhaled corticosteroids	18.0	32.3
Inhaled tobramycin	15.1	21.4
Azithromycin	2.2	9.2
Inhaled aztreonam	1.5	3.1

Most children under the age of 6 are prescribed inhaled bronchodilators. Dornase alfa is prescribed in 42.7 percent of children younger than age 3 and in almost 70 percent of children ages 3 to 5.

Airway Clearance Techniques

The CF Foundation pulmonary guidelines recommend airway clearance for all individuals with CF.[38] A high-frequency chest wall oscillation vest is the most widely used airway clearance technique beyond infancy.

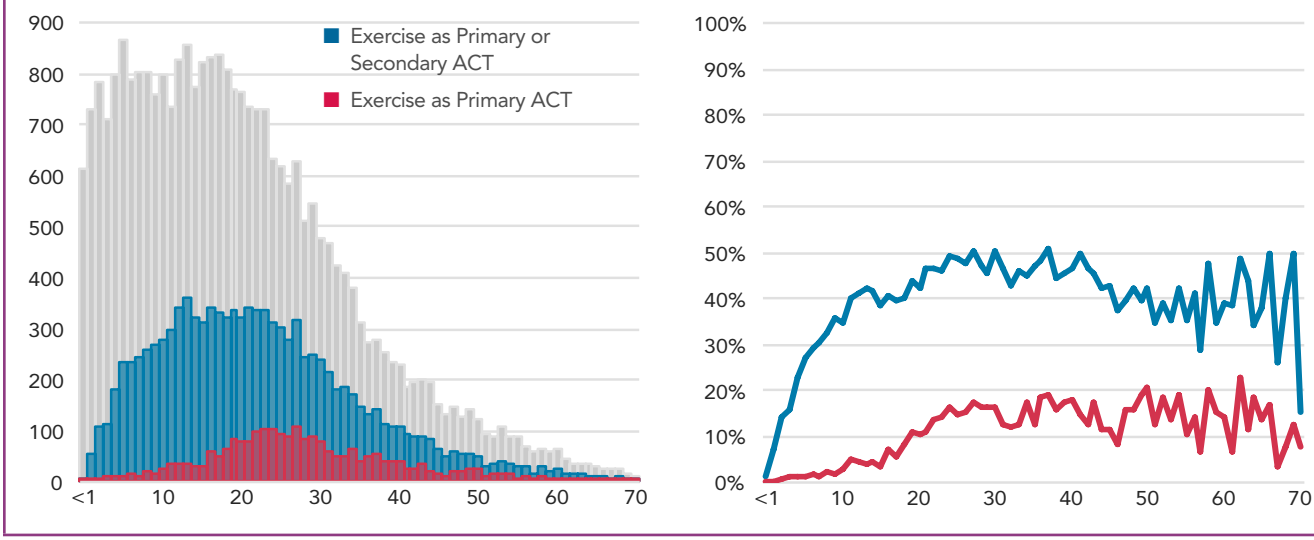
Primary Airway Clearance Techniques by Age and Overall, 2014



A *High frequency chest wall oscillation*
B *Positive expiratory pressure / Oscillating positive expiratory pressure*

The CF Foundation pulmonary guidelines recommend aerobic exercise as an adjunct therapy for airway clearance and for its additional benefits to overall health.[38] Many individuals with CF report exercising in addition to their primary method of airway clearance, with 30.4 percent of children and 45.2 percent of adults identifying exercise as one of their methods of airway clearance. The reporting of exercise seems lower than expected and may not reflect actual use of the method.

Exercise as an Airway Clearance Technique by Age, 2014



COMPLICATIONS

Management of CF secondary complications is important for maintaining an individual's health and quality of life. Complications of CF can impact many different organ systems and can be the direct result of the malfunction of the CFTR protein or a downstream effect of the disease or its treatment.

Cystic fibrosis-related diabetes (CFRD) remains an important and highly prevalent complication that greatly impacts a person's quality of life and is associated with increased morbidity and mortality. Bone disease, sinus disease and depression are other complications of CF that are more common among older adults.

Complications of CF in 2014

	< 18	≥ 18	All
Number of Individuals	14,137	14,539	28,676
Percent with no complications	26.0	5.2	15.5
Percent with complications not reported[A]	2.2	3.2	2.7
Cystic Fibrosis-Related Diabetes	**< 18 (%)**	**≥ 18 (%)**	**All (%)**
Cystic fibrosis-related diabetes (CFRD)[B]	6.7	34.5	20.7
Hepatobiliary			
Gallstones	0.2	1.0	0.6
Gallstones, requiring surgery/procedure	0.2	1.3	0.8
Liver disease, cirrhosis[C]	2.0	2.9	2.5
Liver disease, non-cirrhosis	5.2	5.1	5.1
Hepatic steatosis	0.4	0.6	0.5
Liver disease, other	3.0	3.3	3.1
Bone/Joints			
Arthritis/arthropathy	0.6	5.5	3.0
Bone fracture	0.3	0.5	0.4
Osteopenia	1.7	20.6	11.3
Osteoporosis	0.6	9.2	4.9
Pulmonary			
Allergic bronchopulmonary aspergillosis (ABPA)	3.1	7.0	5.0
Asthma	27.1	29.3	28.2
Hemoptysis, massive	0.2	2.5	1.3
Pneumothorax requiring chest tube	0.1	0.8	0.5
GI			
Distal intestinal obstruction syndrome (DIOS)	4.6	6.1	5.3
Gastroesophageal reflux disease (GERD)	29.9	35.4	32.7
GI bleed requiring hospitalization (non-variceal)	0.0	0.2	0.1
Pancreatitis	0.6	3.1	1.9
Peptic ulcer disease	0.0	0.3	0.2
Rectal prolapse	1.1	0.3	0.7

Table continues on the next page

Complications of CF in 2014 (continued)			
	< 18	≥ 18	All
Other Complications			
Anxiety disorder	1.9	12.4	7.2
Cancer confirmed by histology	0.0	1.0	0.5
Depression	2.4	23.1	12.8
Hearing loss	0.9	2.8	1.9
Hypertension	0.4	7.7	4.1
Kidney stones	0.2	2.6	1.4
Nasal polyps requiring surgery	3.9	5.5	4.7
Renal failure requiring dialysis[D]	0.0	0.4	0.2
Sinus disease	18.1	46.2	32.3

[A] *Patients who did not have a complications case report form completed were considered to not have any complications, as in previous years.*
[B] *See table on page 70 for secondary complications.*
[C] *See table below for secondary complications.*
[D] *Cause other than CFRD.*

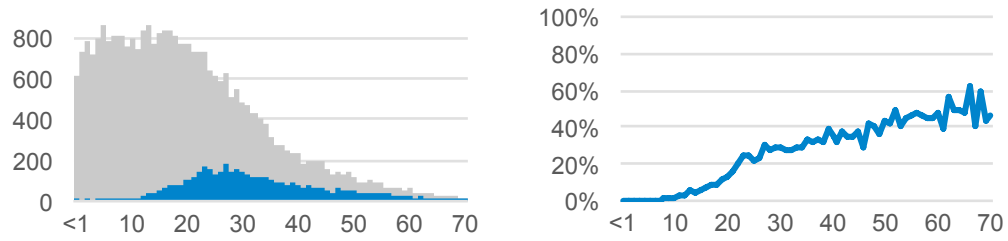
The table below highlights the prevalence of the clinical manifestations of portal hypertension among individuals with cirrhosis.

Complications of Liver Disease, Cirrhosis in 2014 (n=691)				
	All (n)	All (%)	< 18 (%)	≥ 18 (%)
Esophageal varices	170	24.6	23.9	25.1
Gastric varices	34	4.9	4.3	5.3
GI bleed related to varices	23	3.3	1.8	4.3
Splenomegaly	220	31.8	38.4	27.5
Hypersplenism	77	11.1	12.3	10.4
Ascites	50	7.2	5.4	8.4

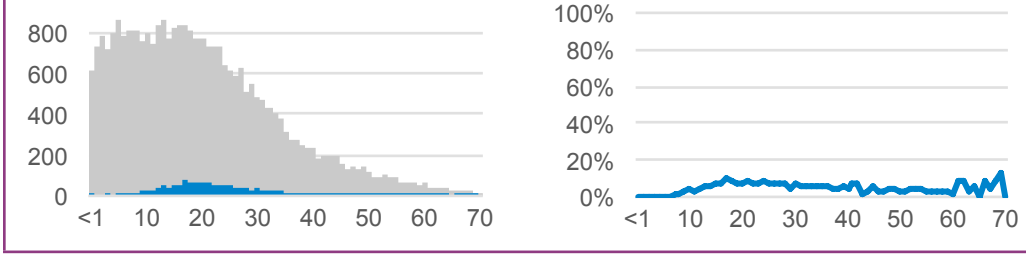
CF Complications by Age, 2014

Addressing complications of CF is becoming an increasingly important component of the treatment and care for people with CF. The prevalence of bone disease and GERD is higher among older age groups. Sinus disease, asthma and depression are higher among older children and adolescents, but then stabilizes among adults of all ages. The prevalence of CFRD peaks around age 45. ABPA, distal intestinal obstruction syndrome (DIOS), and anxiety are less prevalent and appear to remain consistent across all age groups. Liver disease is more prevalent in children.

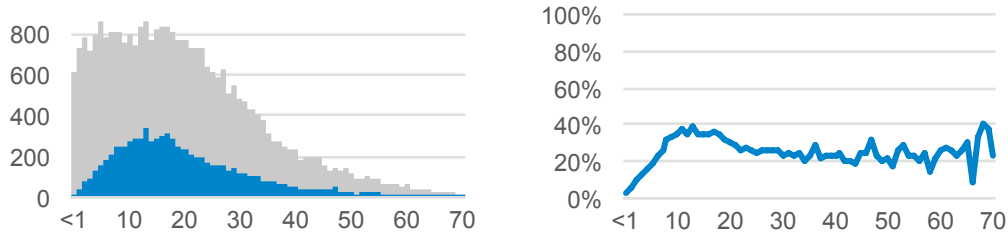
Bone Disease (Osteopenia, Osteoporosis or Bone Fracture)



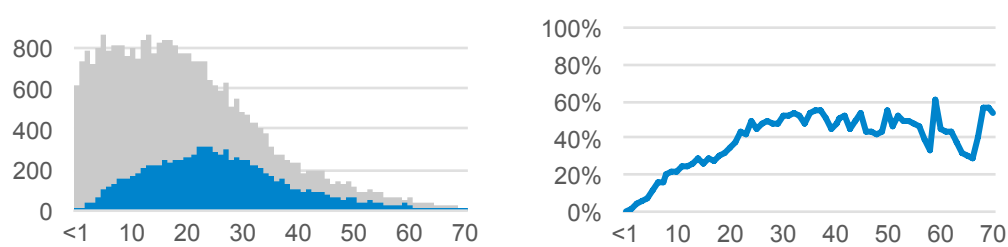
Allergic Bronchopulmonary Aspergillosis (ABPA)



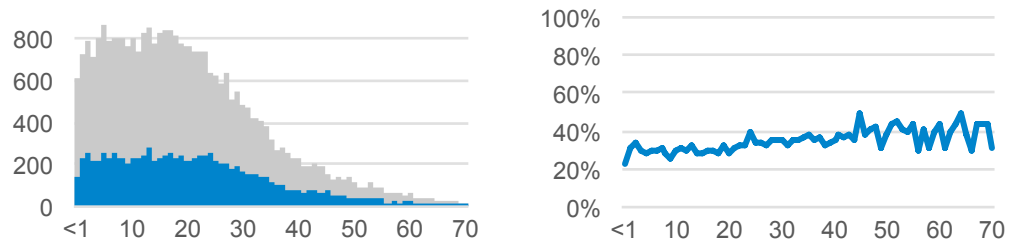
Asthma



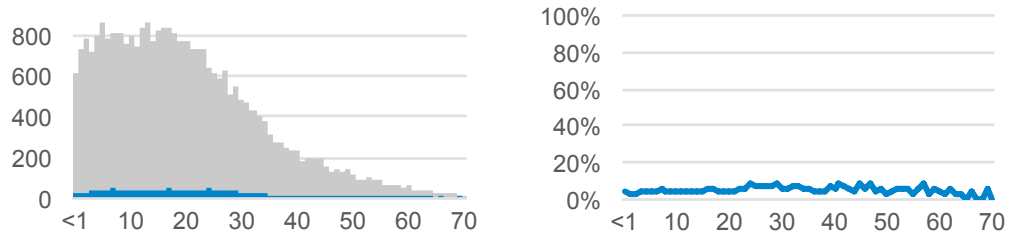
Sinus Disease



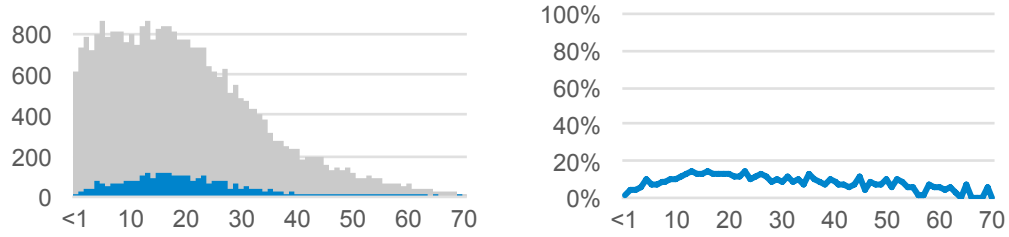
Gastroesophageal Reflux Disease (GERD)



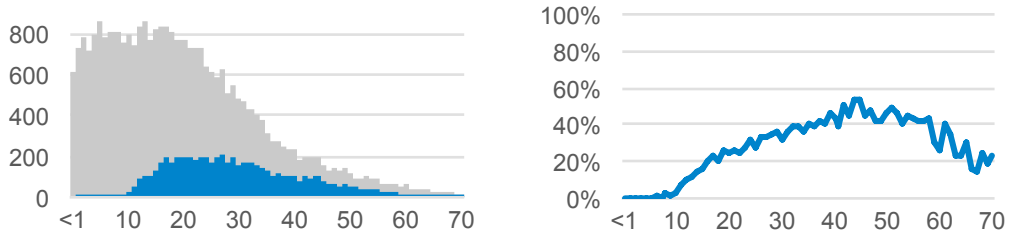
Distal Intestinal Obstruction Syndrome (DIOS)



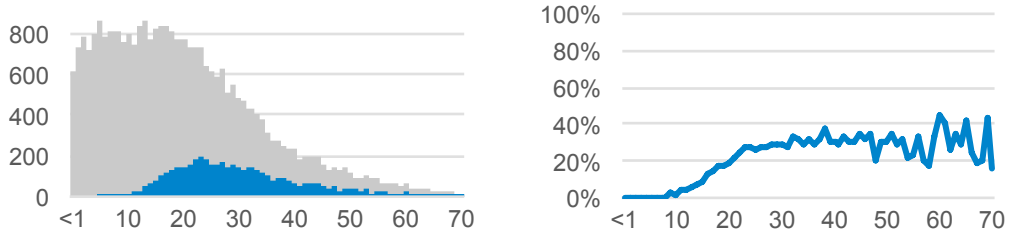
Liver Disease



Cystic Fibrosis Related-Diabetes (CFRD)

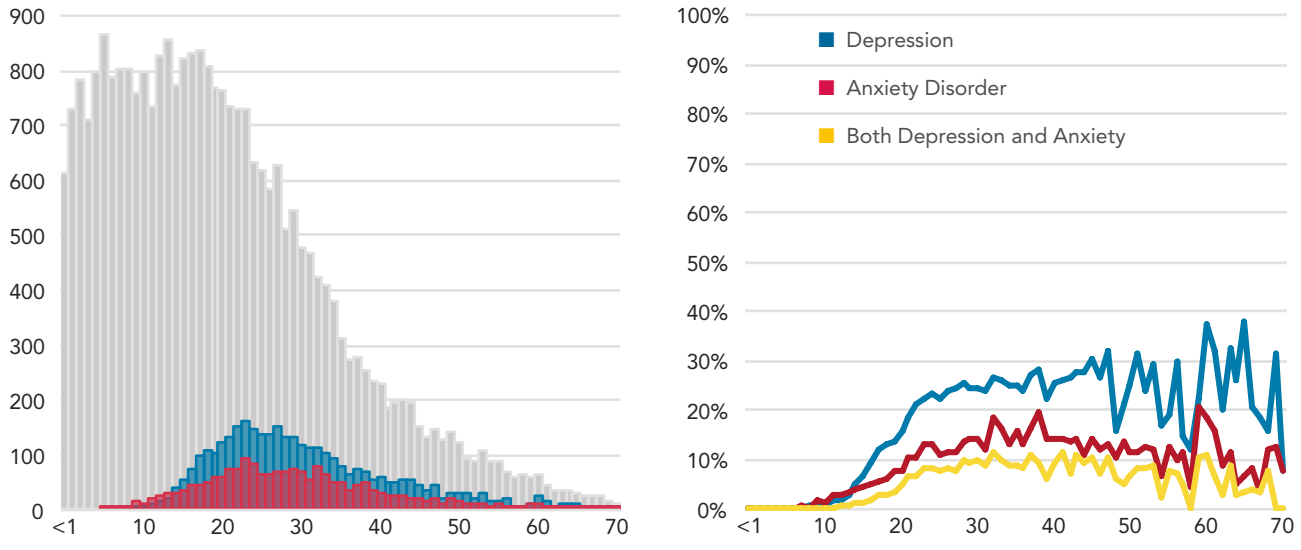


Depression or Anxiety



Addressing the mental health of all individuals with CF is critical to maintaining physical health and quality of life. Substantial proportions of individuals living with CF report anxiety and/or depression. This number is likely an underestimate, as mental health screenings are not consistently performed across the care center network. Prevalence is highest in early adulthood, a time when lung disease often worsens. Almost 10 percent of the adult CF population reports having both depression and anxiety.

Depression and Anxiety by Age, 2014



The table below displays complications by mutation class. Over time, the percentage of individuals reporting no complications has decreased. This observation is potentially the result of improved screening for complications, more consistent reporting of these complications in the Registry and increased survival. CFRD, liver disease, meconium ileus and DIOS are more prevalent among individuals in the mutation class I-III group. In contrast, pancreatitis is more common among individuals in the mutation class IV-V group. It is interesting to note that the prevalence of anxiety and depression do not differ depending on mutation class.

Complications of CF in 2014, by Mutation Class Group

	Class I-III Group	Class IV-V Group
Number of Individuals	**19,754**	**2,900**
Percent with no complications	13.6	22.1
Percent with complications not reported [A]	2.0	4.3
Cystic Fibrosis-Related Diabetes	**Class I-III Group (%)**	**Class IV-V Group (%)**
CFRD [B]	24.3	6.6
Hepatobiliary		
Liver disease, cirrhosis [C]	2.8	0.6
Liver disease, non-cirrhosis	6.1	1.5
Liver disease, other	3.7	1.2
Bone/Joints		
Osteopenia	11.5	11.2
Osteoporosis	4.9	6.0
Pulmonary		
Allergic bronchopulmonary aspergillosis (ABPA)	5.2	3.9
Asthma	28.9	26.0
Hemoptysis, massive	1.4	1.2
Pneumothorax requiring chest tube	0.5	0.4
GASTROINTESTINAL		
Distal intestinal obstruction syndrome (DIOS)	6.0	1.9
Gastroesophageal reflux disease (GERD)	34.9	25.7
Pancreatitis	0.4	9.2
Rectal prolapse	0.8	0.2
Other Complications		
Anxiety disorder	7.2	6.7
Cancer confirmed by histology	0.4	0.9
Depression	13.0	12.3
Hypertension	3.8	5.6
Kidney stones	1.6	1.0
Nasal polyps requiring surgery	5.2	2.9
Renal failure requiring dialysis [D]	0.2	0.2
Sinus disease	32.6	33.1
Complications at Birth		
Meconium ileus or other neonatal bowel obstruction	22.0	2.8

[A] *Individuals who did not have a complications case report form completed were considered to not have any complications, as in previous years.*

[B] *See table on page 70 for secondary complications.*

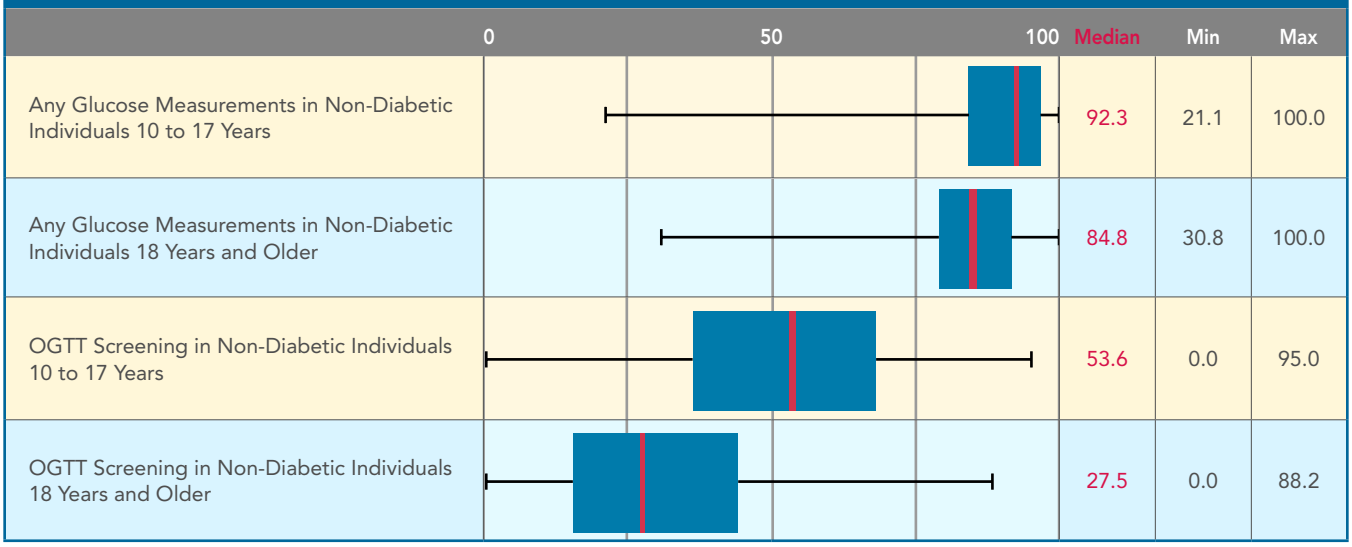
[C] *See table on page 63 for secondary complications.*

[D] *Cause other than CFRD.*

Cystic Fibrosis-Related Diabetes (CFRD)

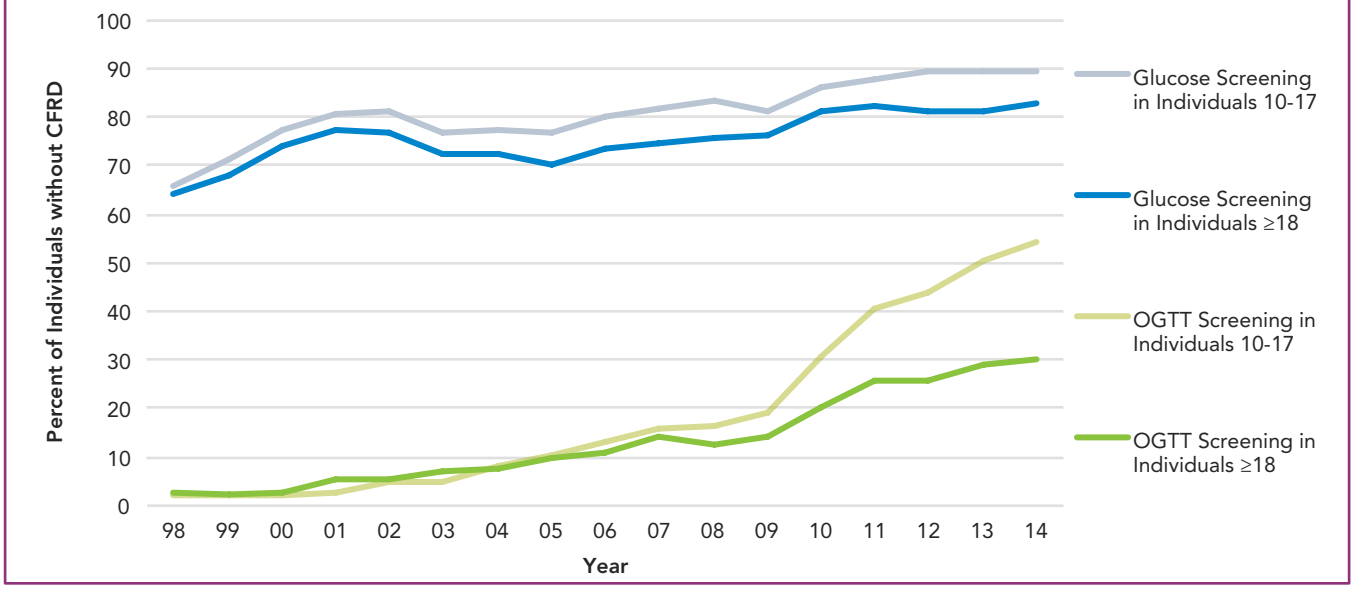
CFRD is associated with weight loss, lung function decline and increased mortality.[39] Early diagnosis and treatment may minimize the impact of CFRD. The CF Foundation CFRD guidelines recommend screening all individuals annually, starting at age 10, with an oral glucose tolerance test (OGTT).

Glucose Testing in Non-Diabetic Individuals, by Center



CFRD screening using blood glucose tests is routinely performed at the vast majority of centers. However, there is not as much use of the recommended Oral Glucose Tolerance Test (OGTT), with substantial variation across centers.

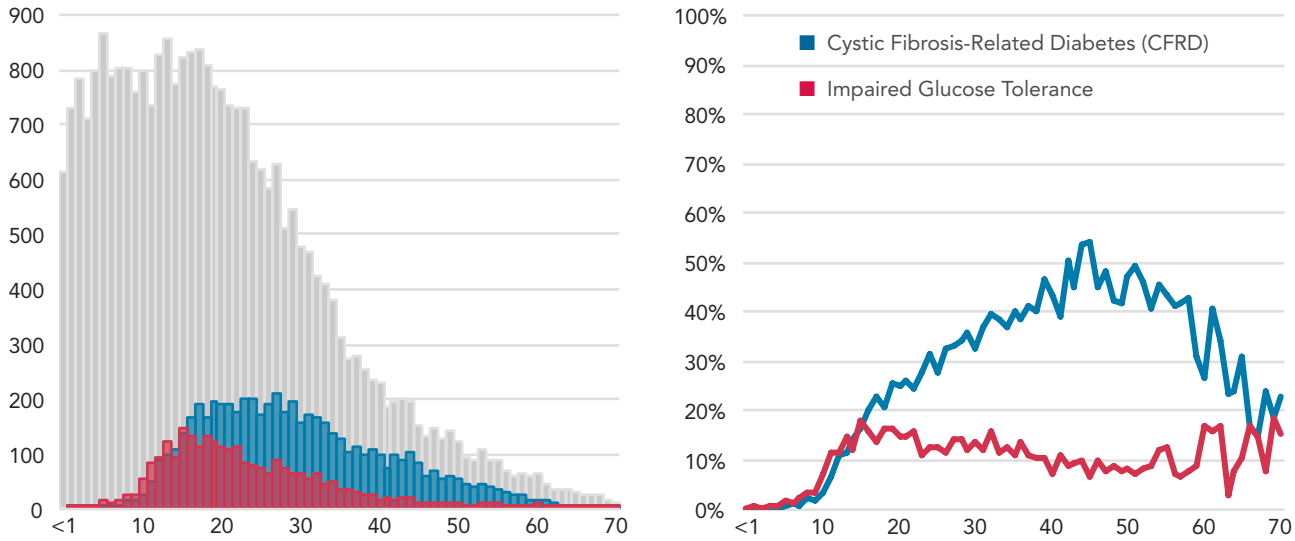
Blood Glucose and OGTT Screening for Individuals without CFRD, 1998–2014



It is encouraging to note that rates of screening for CFRD using the OGTT have increased since the publication of the CF Foundation CFRD guidelines in 2010.[39]

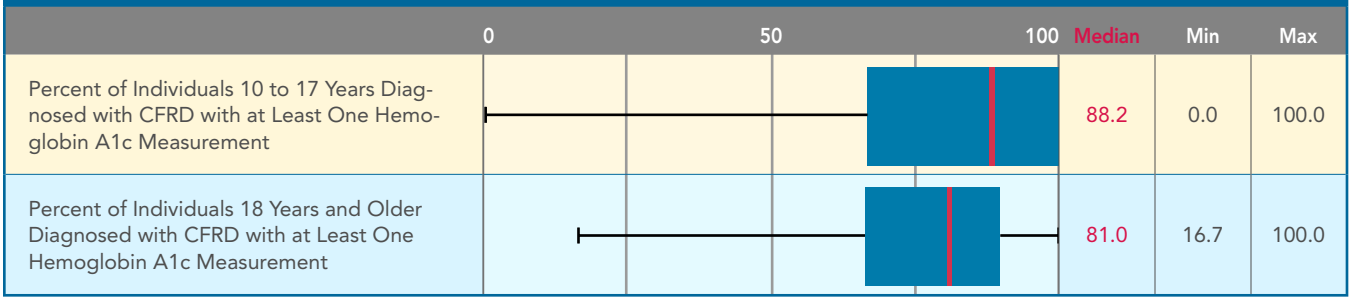
The prevalence of CFRD is higher among adults with CF than it is among children with CF. The great majority of all individuals with CFRD are treated with insulin to maintain normal blood glucose levels. In addition to individuals with CFRD, 10 to 20 percent of the population has impaired glucose tolerance. These individuals are at increased risk for developing CFRD and may benefit from increased monitoring.

CFRD and Impaired Glucose Tolerance by Age, 2014



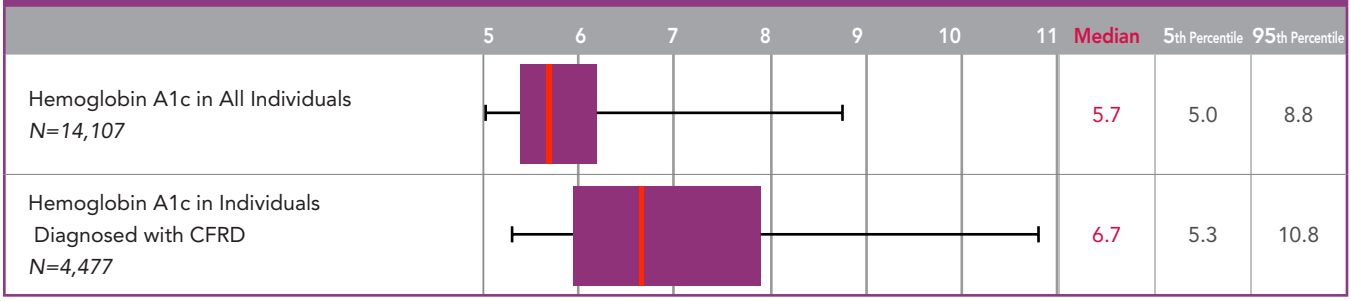
The CFRD guidelines recommend regular hemoglobin A1c (HgbA1c) measurements for individuals with CFRD.[39] Center-level variation in the percentage of individuals with CFRD with one or more hemoglobin A1c measurements during the year indicates that a majority of centers are testing their patients at least annually.

Percent of Individuals with CFRD with at Least One Hemoglobin A1c Measurement, by Center



The goal established by the CF Foundation CFRD guidelines is a hemoglobin A1c less than 7.0 percent for individuals with CFRD.[39] More than half of individuals with CFRD are meeting this guideline.

Hemoglobin A1c Lab Values Reported, 2014



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 CFRD guidelines.[39]

Complications of CFRD in 2014 (n=5,811)

	All (n)	All (%)	< 18 (%)	≥ 18 (%)
Retinopathy	49	0.8	0.3	0.9
Microalbuminuria	101	1.7	0.3	2.0
Chronic renal insufficiency	269	4.7	0.2	5.5
Chronic renal failure requiring dialysis	21	0.4	0.0	0.4
Peripheral neuropathy	52	0.9	0.2	1.0
Any episodes of severe hypoglycemia	215	5.0	3.9	5.2

TRANSPLANTATION

Lung transplantation remains an option for some individuals with severe disease. The annual number of lung transplant procedures for CF fluctuates yearly, with an overall upward trend. The bilateral lung transplant is by far the most common procedure.

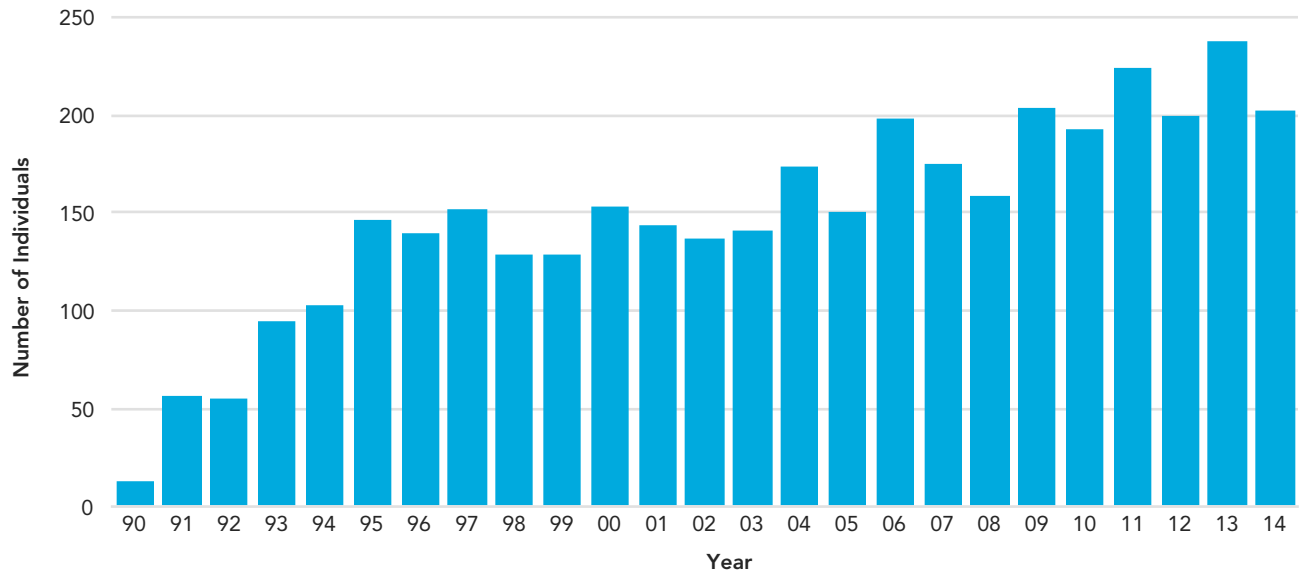
There are 1,463 individuals in the Registry in 2014 who have received a lung, kidney, heart or liver transplant.

Transplant Status of People with CF in 2014 (All organs)

	Number of Individuals
Accepted, on waiting list	182
Evaluated, final decision pending	376
Evaluated, rejected	94
Received transplant this year	220
Received transplant in prior years	1,243

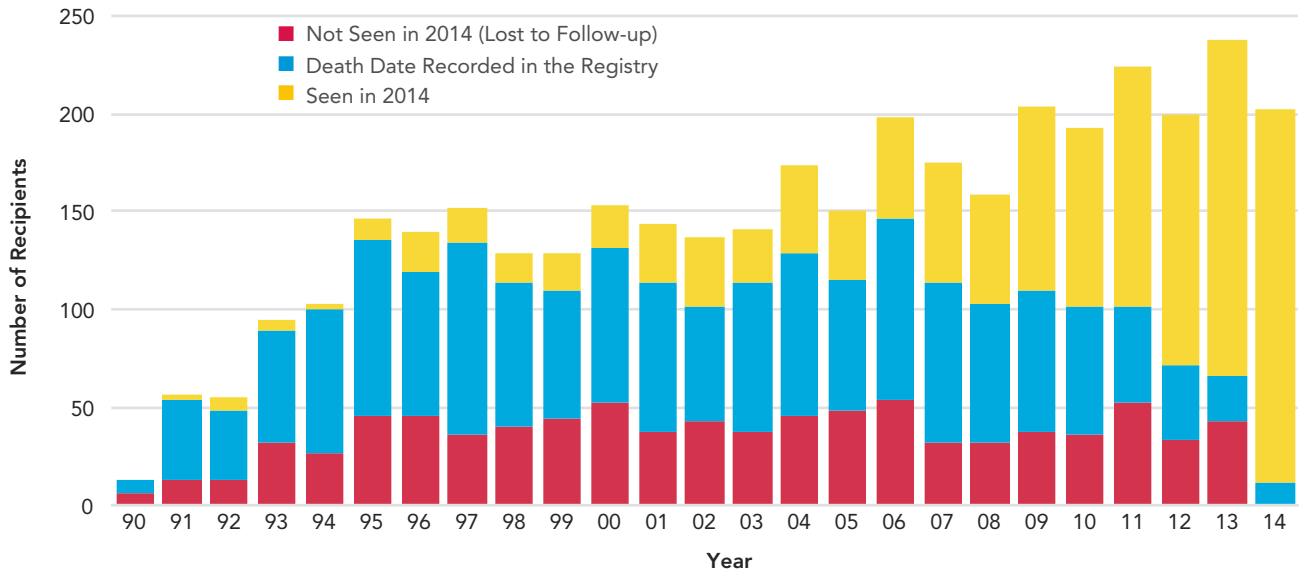
There are 1,305 individuals in the Registry in 2014 who have ever had a lung transplant. This includes 202 individuals who received a lung transplant in 2014.

Number of People with CF Receiving a Lung Transplant, 1990–2014



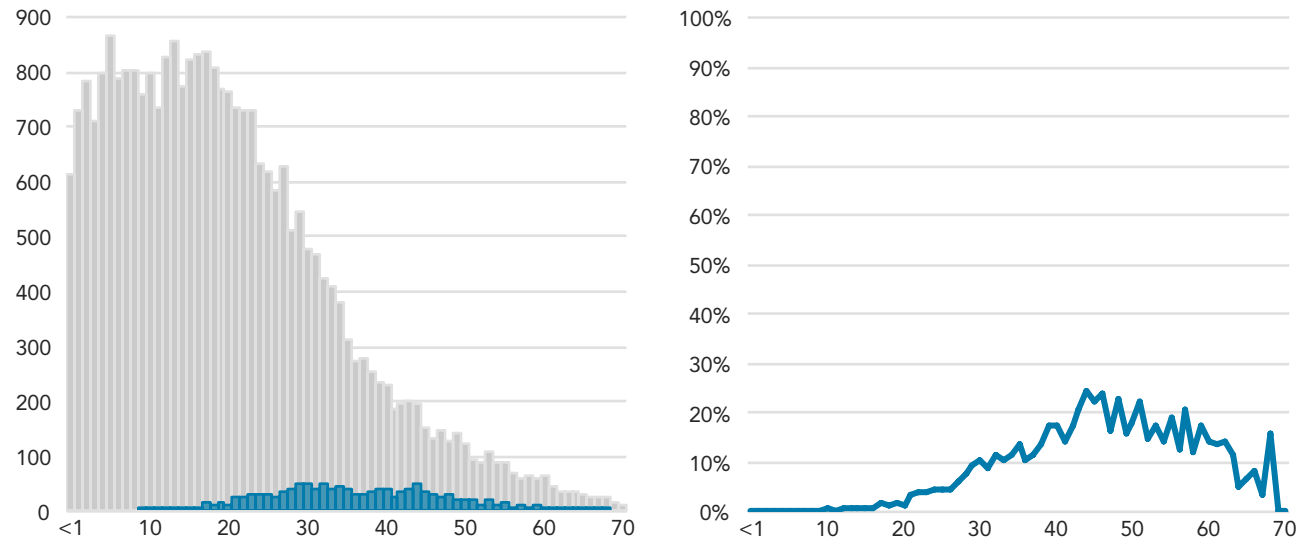
There is concern that the Registry may have incomplete information on post-transplant individuals if they receive all of their care at a transplant center. The figure below shows that data were not entered into the Registry in 2014 for a sizable proportion of lung transplant recipients. This may impact our survival calculations.

2014 Status of Lung Transplant Recipients by Year of Transplant, 1990–2014



Overall, lung transplant recipients are a small proportion of individuals included in the Registry and are most likely ages 30 and older.

Lung Transplant Distribution in People with CF Seen in 2014

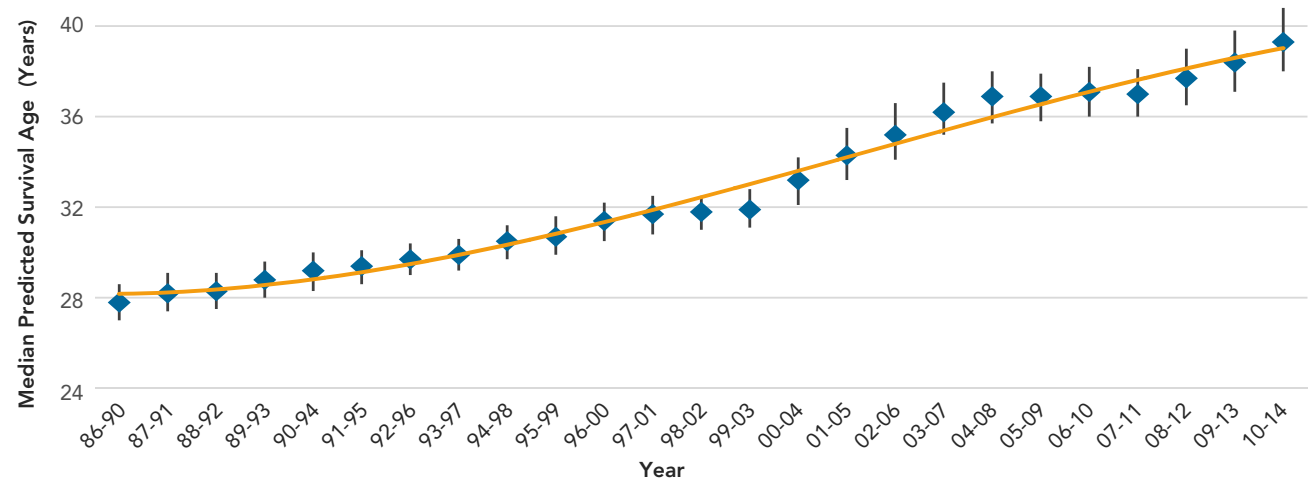


SURVIVAL

The key metric used for calculating survival is the median predicted survival age. This is generated by life table analysis and represents the age to which half of the current Registry population would be expected to survive, given their ages in the time period and assuming that mortality rates do not change. Factors that impact this calculation are the number of deaths during the time period, the ages at which the deaths occurred and the age distribution of the entire population.

The median predicted survival age in 2014 is 39.3 years (95 percent confidence interval: 37.3–41.4 years). This means that 50 percent of individuals with CF in the Registry in 2014 are expected to live to 39.3 years of age. This estimate decreased slightly from 40.4 in 2013. This decline is likely temporary and caused by fluctuations in numbers of deaths from year to year. The median age at death continues to increase and is almost one year higher than in 2013. Annual estimates can be unstable, so we group the data into five-year increments. The graph below shows that, based on five-year increments, there have been gains in median predicted survival from 1986 to 2014. The median predicted survival age for 2010 to 2014 is 39.3 years (95 percent confidence interval: 38.0–40.8 years).

Median Predicted Survival Age, 1986–2014 In 5-Year Increments



The primary causes of death are respiratory/cardiorespiratory and transplant-related.

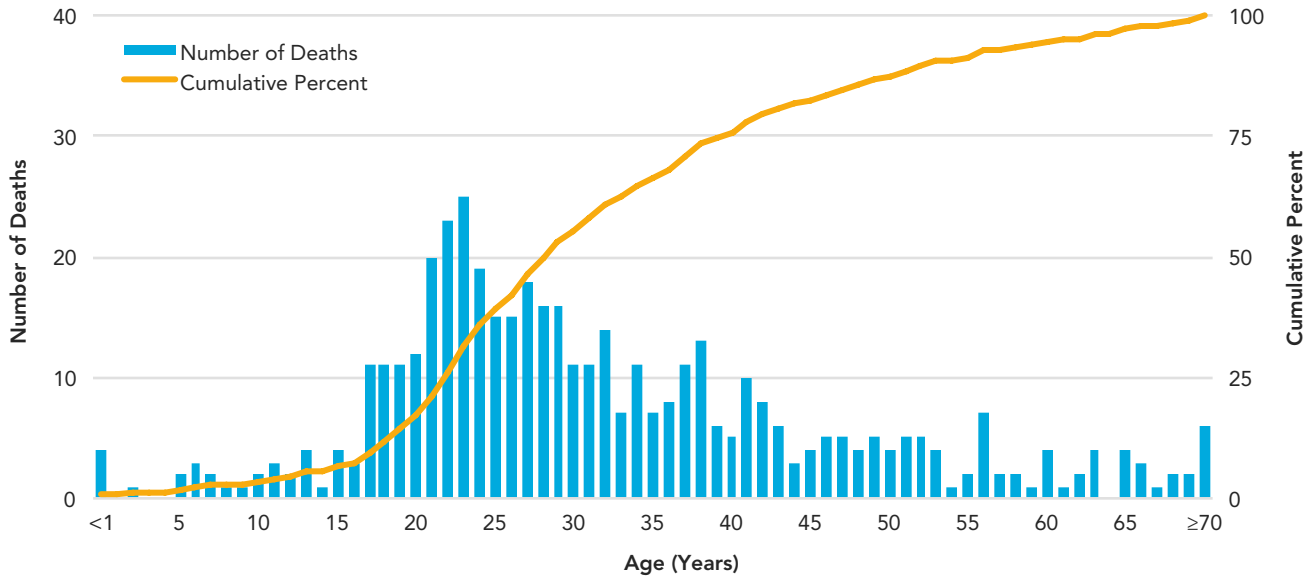
Primary Cause of Death in 2014

Cause	Number of Individuals	Percent
Respiratory/cardiorespiratory	325	70.5
Transplant-related: other	44	9.5
Other	42	9.1
Transplant-related: bronchiolitis obliterans	16	3.5
Unknown	15	3.3
Liver disease/liver failure	13	2.8
Suicide	4	0.9
Trauma	2	0.4

In 2014, over 50 percent of deaths among individuals in the Registry occurred among F508del homozygotes. Although less than 5 percent of the Registry population is post-transplant, transplant recipients represent 20 percent of all reported deaths.

The median predicted survival age is calculated using the entire 2014 Registry population. In contrast, the median age at death is calculated from the deaths reported in 2014. The median age at death for the 461 deaths reported in 2014 is 29.1 years.

Age at Death in 2014



Overall, survival among individuals with CF is continuing to improve. Median predicted survival among people with CF has been steadily increasing for several decades, and the median age at death has also been increasing. Infants with CF born in 2014 are expected to live longer than previous birth cohorts.

A recently published analysis of the Registry data suggests that survival will likely continue to improve in the coming years.[40] This prediction does not encompass the anticipated benefits of newborn screening and the availability of CFTR modulator drugs. While this provides hope for a brighter future, the registry data clearly demonstrate that we have much more work ahead of us.

REFERENCES

1. Quanjer, P.H., 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): p. 1324-43.
2. Saiman, L., et al., *Azithromycin in patients with cystic fibrosis chronically infected with Pseudomonas aeruginosa: a randomized controlled trial.* JAMA, 2003. 290(13): p. 1749-56.
3. U.S. Census Bureau, Population Division. The Hispanic Population in the United States: 2010. Table 1. Population by Sex, Age, Hispanic Origin, and Race. Available at: http://www.census.gov/population/hispanic/data/2010.html. Accessed August 13, 2015.
4. Curtin, S.C., et al., *Pregnancy rates for U.S. women continue to drop.* NCHS Data Brief, 2013(136): p. 1-8.
5. Borowitz, D., et al., *Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis*. J Pediatr, 2009. 155(6 Suppl): p. S73-93.
6. Borowitz, D., 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. 155(6 Suppl): p. S106-16.
7. Ren, C.L., et al., *Outcomes of infants with indeterminate diagnosis detected by cystic fibrosis newborn screening*. Pediatrics, 2015. 135(6): p. e1386-92.
8. Bombieri, C., et al., *Recommendations for the classification of diseases as CFTR-related disorders*. J Cyst Fibros, 2011. 10 Suppl 2: p. S86-102.
9. Martin JA, Osterman MJK, et al., *Births: Final data for 2012.*, in *National vital statistics reports.* 2013, National Center for Health Statistics: Hyattsville, MD.
10. Donahue, S.M., et al., *Trends in birth weight and gestational length among singleton term births in the United States: 1990-2005*. Obstet Gynecol, 2010. 115(2 Pt 1): p. 357-64.
11. Farrell, P.M., et al., *Guidelines for diagnosis of cystic fibrosis in newborns through older adults: Cystic Fibrosis Foundation consensus report*. J Pediatr, 2008. 153(2): p. S4-s14.
12. US CF Foundation, Johns Hopkins University, The Hospital for Sick Children. The Clinical and Functional TRanslation of CFTR (CFTR2). Available at: http://cftr2.org. Accessed August 13, 2015.
13. Welsh, M.J. and A.E. Smith, *Molecular mechanisms of CFTR chloride channel dysfunction in cystic fibrosis.* Cell, 1993. 73(7): p. 1251-4.
14. De Boeck, K., et al., *The relative frequency of CFTR mutation classes in European patients with cystic fibrosis.* J Cyst Fibros, 2014. 13(4): p. 403-9.
15. Green, D.M., et al., *Mutations that permit residual CFTR function delay acquisition of multiple respiratory pathogens in CF patients*. Respir Res, 2010. 11: p. 140.
16. Thauvin-Robinet, C., 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): p. 752-8.
17. Kiesewetter, S., et al., *A mutation in CFTR produces different phenotypes depending on chromosomal background.* Nat Genet, 1993. 5(3): p. 274-8.
18. Clinical Practice Guidelines for Cystic Fibrosis Committee. Clinical practice guidelines for cystic fibrosis. 1997, Bethesda, MD: Cystic Fibrosis Foundation.
19. Yankaskas, J.R., et al., *Cystic fibrosis adult care: consensus conference report.* Chest, 2004. 125(1 Suppl): p. 1s-39s.
20. Saiman, L. and J. Siegel, *Infection control recommendations for patients with cystic fibrosis: microbiology, important pathogens, and infection control practices to prevent patient-to-patient transmission.* Infect Control Hosp Epidemiol, 2003. 24(5 Suppl): p. S6-52.
21. Saiman, L., et al., *Infection prevention and control guideline for cystic fibrosis: 2013 update.* Infect Control Hosp Epidemiol, 2014. 35 Suppl 1: p. S1-S67.
22. Stevens, D.A., et al., *Allergic bronchopulmonary aspergillosis in cystic fibrosis--state of the art: Cystic Fibrosis Foundation Consensus Conference.* Clin Infect Dis, 2003. 37 Suppl 3: p. S225-64.
23. Fiore, A.E., et al., *Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008.* MMWR Recomm Rep, 2008. 57(Rr-7): p. 1-60.
24. Aris, R.M., et al., *Guide to bone health and disease in cystic fibrosis.* J Clin Endocrinol Metab, 2005. 90(3): p. 1888-96.

25. Stallings, V.A., 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. 108(5): p. 832-9.

26. Sokol, R.J. and P.R. Durie, *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: p. S1-13.

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. 2006, U.S. Dept. of Health and Human Services, Public Health Service, Office of the Surgeon General: Rockville, MD.

28. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data. Available from: http://wwwdev.cdc.gov/brfss/brfssprevalence/. Accessed Jul 23, 2015.

29. Mogayzel, P.J., Jr., 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): p. 1640-50.

30. Stone, A., et al., *Staphylococcus aureus nasal colonization among pediatric cystic fibrosis patients and their household contacts.* Pediatr Infect Dis J, 2009. 28(10): p. 895-9.

31. Glikman, D., et al., *Complex molecular epidemiology of methicillin-resistant staphylococcus aureus isolates from children with cystic fibrosis in the era of epidemic community-associated methicillin-resistant S aureus.* Chest, 2008. 133(6): p. 1381-7.

32. Champion, E.A., et al., *Antimicrobial susceptibility and molecular typing of MRSA in cystic fibrosis.* Pediatr Pulmonol, 2014. 49(3): p. 230-7.

33. Billinger, M.E., et al., *Nontuberculous mycobacteria-associated lung disease in hospitalized persons, United States, 1998-2005.* Emerg Infect Dis, 2009. 15(10): p. 1562-9.

34. Floto, R.A., et al., *Cystic Fibrosis Foundation and European Cystic Fibrosis Society Consensus Recommendations for the Management of Nontuberculous Mycobacteria in Individuals with Cystic Fibrosis.* In press.

35. Olivier, K.N., et al., *Nontuberculous mycobacteria. I: multicenter prevalence study in cystic fibrosis*. Am J Respir Crit Care Med, 2003. 167(6): p. 828-34.

36. Flume, P.A., et al., *Cystic fibrosis pulmonary guidelines: treatment of pulmonary exacerbations.* Am J Respir Crit Care Med, 2009. 180(9): p. 802-8.

37. Mogayzel, P.J., Jr., et al., *Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health.* Am J Respir Crit Care Med, 2013. 187(7): p. 680-9.

38. Flume, P.A., et al., *Cystic fibrosis pulmonary guidelines: airway clearance therapies*. Respir Care, 2009. 54(4): p. 522-37.

39. Moran, A., 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. 33(12): p. 2697-708.

40. MacKenzie, T., et al., *Longevity of patients with cystic fibrosis in 2000 to 2010 and beyond: survival analysis of the cystic fibrosis foundation patient registry*. Ann Intern Med, 2014. 161(4): p. 233-41.

2014 Cystic Fibrosos 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
○ 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

2014 Cystic Fibrosos 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 ○ Unknown
Poly TG repeats: ○ 9 ○ 10 ○11 ○12 ○13
○ Other/unknown/not done

Select Mutation 2: _____ Other genotype: _____
Poly T tract: ○ 5T ○ 7T ○ 9T ○ 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
Non-clinic start date: (MM/DD/YYYY)
Non-clinic end date: (MM/DD/YYYY)
Height : _____ ○ cm ○ inches
[Height Percentile _____]
Weight : _____ ○ kg ○ lb
[Weight Percentile _____]
[BMI value: _____]
[BMI Percentile: _____]
[Weight for Length percentile: _____]

Exacerbation Assessment
What was your assessment regarding pulmonary exacerbation at this visit?
○ Absent
○ Mild exacerbation
○ Moderate exacerbation
○ Severe exacerbation
Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

○ 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.)

Social Worker Consultation
☐ Patient consulted with a Social Worker at this visit

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

Pulmonary
☐ Patient was seen by a Respiratory therapist/physical therapist at this visit

Other
Record any additional information about this encounter:
Custom field 1:_____
Custom field 2:_____
Custom field 3: _____

Respiratory 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

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

2014 Cystic Fibrosos 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 Medication
Chronic Antibiotics (i.e. not prescribed to treat an exacerbation) – inhaled and/or oral
Tobramycin solution for inhalation (i.e. TOBI): ☐
Frequency: ○ 300 mg BID alternate month schedule
○ 300 mg BID continuous
○ Other regimen (different dose or freq)

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

Bethkis: ☐
Frequency: ○ 300 mg BID alternate month
○ Other regimen (different dose or freq)

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

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

2014 Cystic Fibrosos Foundation Patient Registry Questionnaire

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

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

Chronic oral macrolide antibiotic: ☐
☐ azithromycin (Zithromax)
☐ clarithromycin (Biaxin)

Other chronic 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 (e.g. Kalydeco, VX-770): ☐
Frequency: ○ 150mg BID
○ Other Regimen

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): ☐
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)

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

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)
☐ Tobramycin solution for inhalation (i.e. TOBI)
☐ Aztreonam
☐ Colistin
☐ Macrolide antibiotics
☐ High-dose ibuprofen
☐ Hypertonic saline

GI/Nutrition/Endrocrine Medications
This Patient is on enzyme medications: ○ Yes ○ No
For all enzymes, "capsules per largest meal" options are:
○ .5 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 ○ 10+
"Total capsules per day" is a numeric free text field.

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

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

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

2014 Cystic Fibrosos Foundation Patient Registry Questionnaire

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: ____

Pancrecarb
Pancrecarb MS-4: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Pancrecarb MS-8: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____
Pancrecarb MS-16: ☐
Number of capsules per largest meal of the day: ____
Total capsules per day: ____

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

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): _____
[Predicted value:_____]
[Reference equation:_____]
[% Predicted:_____]
[CF Specific FEV 1 percentile (ages 6-21):]

GI/Nutrition

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

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

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

2014 Cystic Fibrosos Foundation Patient Registry Questionnaire

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: ☐

CFRD Status

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

Hepatobiliary

☐ Gall stones
☐ Gall stones, requiring surgery/procedure
☐ Liver disease, cirrhosis
Please specify complications related to cirrhosis:
☐ Esophageal varices
☐ Gastric varices
☐ GI bleed related to varices
☐ Splenomegaly
☐ Hypersplenism (i.e., WBC <3.0 or platelets <100,000)
☐ Ascites
☐ Liver disease, non- cirrhosis
☐ Hepatic Steatosis
☐ Liver disease, other: _____

Bones/Joints

☐ Arthritis/Arthropathy
☐ Bone fracture
☐ Osteopenia
☐ Osteoporosis

Pulmonary

☐ Allergic Bronchial Pulmonary Aspergillosis (ABPA)
☐ Asthma
☐ Hemoptysis, massive
☐ 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

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: _____

Glucose Test

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

If OGTT performed:

OGTT Fasting glucose level (mg/dL):_____
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)

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

2014 Cystic Fibrosos Foundation Patient Registry Questionnaire

○ 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
☐ 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: [ ]
[Number of Care Episodes recorded by Care Center: [ ]
Number of Care Episodes recorded by Other Care Centers: [ ]
Key:
FORM NAME
○ radio buttons (select one option only)
☐ check box (multiple selections allowed)

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

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

2014 Cystic Fibrosos Foundation Patient Registry Questionnaire

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

Update on CFRD 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)
○ CF-related diabetes with or without fasting hyperglycemia (2-h PG >= 200)

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
○ 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: _____

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: ☐

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

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

2014 Cystic Fibrosos Foundation Patient Registry Questionnaire

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

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

NOTES

NOTES

NOTES

PATIENT REGISTRY ANNUAL DATA REPORT 2014

CYSTIC FIBROSIS FOUNDATION

CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

CYSTIC FIBROSIS FOUNDATION
6931 Arlington Road
Bethesda, MD 20814
1.800.FIGHT.CF
www.cff.org
info@cff.org