Patient Registry

Annual Data Report
to the Center Directors

2013

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
2013 Annual Data Report to the Center Directors
Bethesda, Maryland
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PHOTOGRAPHY BY

Derek Smith

SPECIAL ACKNOWLEDGEMENTS

Those who contributed to the maintenance of PortCF, analysis of data and creation of this report:
Bruce Marshall
Alexander Elbert
Kristofer Petren
Mary Grimes
Aliza Fink
Vincent Myers
Ase Sewall

CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

September 2014

Dear Friends and Colleagues:

It is a pleasure to share the 2013 Patient Registry Annual Data Report with you. The state of the Cystic Fibrosis Foundation Patient Registry is stronger than ever. Registry data continue to inform many important initiatives, including: clinical trial design, quality improvement, retrospective observational studies, prospective "registry-embedded" observational studies, safety and effectiveness studies of newly approved therapies and comparative effectiveness research. Ongoing collaborations with registry teams in the United Kingdom and Canada are providing opportunities to compare outcomes and practice patterns across countries and health care systems. A steady stream of high-quality publications based on the Registry data is appearing in the peer-reviewed medical literature. The CF Foundation Registry was featured as a case study in the recently published 3rd edition of the *AHRQ Handbook: Registries for Evaluating Patient Outcomes, A User's Guide*, and was highlighted as "an outstanding registry" by Larsson et al in a global assessment of patient registries (Health Affairs 31:220-27, 2012).

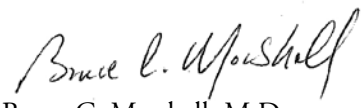
The tremendous success of the Registry would not be possible without the vital contribution of people with CF and their families who generously agree to share their information, as well as registry coordinators and care team members who collect and enter the data. Our recent audit studies confirm the 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 efforts to improve the health and quality of life for those with CF.

In this year's report, we've again expanded the number of longitudinal analyses and mutation class-specific analyses. Of note, we continue to see favorable trends in pulmonary function and nutritional status, as well as a continuing decrease in the prevalence of *Pseudomonas aeruginosa* among people with CF. Also notable is the decreased prevalence of MRSA in 2013, reversing the trend of the last 15 years.

We continue to see an increase in the percentage of new CF diagnoses derived from newborn screening, providing an opportunity to help get these infants off to a strong start in life. One worrisome finding, however, is the increasing number of newly diagnosed patients without sweat test results in the Registry. In the era of newborn screening, a complete diagnostic work-up is even more critical as we move towards earlier therapeutic interventions.

We hope that you find this year's report rich and interesting and that you participate in the discussions generated by the data. This is an exciting time in CF, with advances in health care delivery and new therapeutics with the potential to transform our field. Together, we will track these important developments in the Registry.

Thank you all for your hard work throughout the year on behalf of people with CF 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

TABLE OF CONTENTS *continued*

ABOUT THIS REPORT

Each year, we strive to improve the Annual Data Report in order to effectively convey the health status of individuals with cystic fibrosis (CF) and the care they receive at CF Foundation-accredited care centers. Last year, we made several substantial changes to the report. Historically, figures had primarily focused on showing center-level variation by providing the mean or median value of the outcome for each center. Beginning in the 2012 report, we also included tables and figures showing the data for all patients both cross-sectionally (using only data from the current year) and longitudinally (using data from multiple years). We have continued this approach in the 2013 report. Another change in the 2012 report was the addition of box-and-whisker plots to complement the histogram for displaying center-level variation. Since box-and-whisker plots provide more information about center-level variation, we have used them exclusively in this year's report. Corresponding histograms will be included in the reports sent to individual care centers.

Graphics in blue show center-level variation

Graphics in purple show patient-level data

This year, enhancements to the report include the use of new population standards, for both nutritional and lung function predicted values. More detail on the rationale for and impact of these changes is provided below.

Report Inclusion and Exclusion Criteria

This report is based on the 2013 data entered into the CF Foundation Patient Registry. Figures are either cross-sectional (2013 data only) or longitudinal (data over several years). When possible, longitudinal graphs include data from 1986 through 2013. However, for some figures, data from different years are included. In some cases, it is because the variable was added to the Registry later than 1986. In others, the way the variable was collected was modified or enhanced at a point and we can only show trends since the modification or enhancement.

Registry data are updated and processed every year, therefore, we encourage you to compare the 2013 data with the revised results from previous years displayed within this report rather than referring to previously published reports.

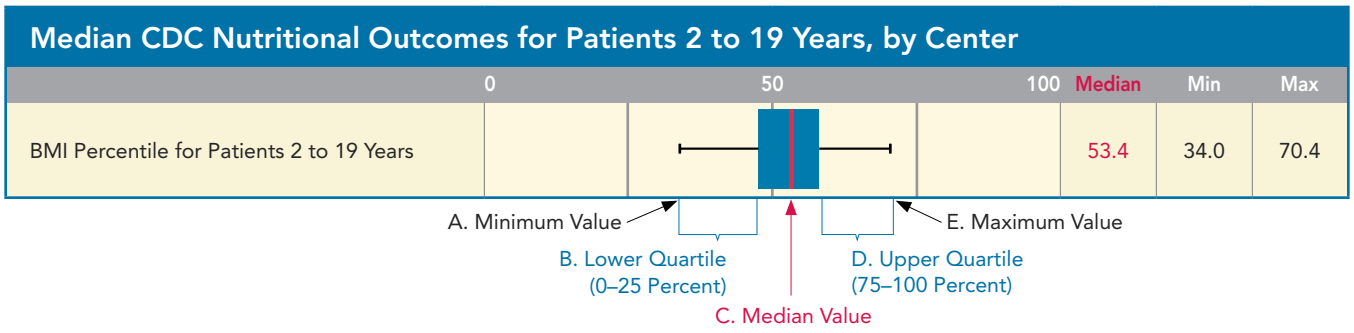
The report contains the data from individuals diagnosed with CF who have consented to participate in the Registry and who were seen in a CF center in 2013, or who were born, diagnosed or died in 2013. Data from individuals with a diagnosis of CFTR-related metabolic syndrome (CRMS) or CFTR-related disorders were excluded from all figures except the one figure specifically related to new diagnoses in 2013. 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 included populations represented in the figures vary and are based on the eligibility criteria described in the title and/or footnotes for the figure.

Figures presenting data on center-level variation include only those centers reporting on at least 10 eligible patients. Exceptions to this are figures showing center-level variation for infants, patients with G551D mutations, CFRD patients and patients with an exacerbation; for these figures, centers reporting on five or more eligible patients are included.

Using Box-and-Whisker Plots 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 was created using data looking at the variation across centers of the median body mass index (BMI) percentile among individuals ages 2 to 19:



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

A. Minimum: The lowest median BMI percentile.
B. 0–25th percentile: 25 percent of observations fall below.
C. Median: 50 percent of observations fall below and above. Median values, shown by a red line, are preferable to mean values because they are not skewed by extreme values.
D. 75th–100th percentile: 75 percent of values fall below.
E. Maximum: The highest median BMI percentile.

When reading these plots, there are a few things to look for. First, the width of the box indicates the amount of variation in the outcome across centers — the wider the box the more variation. Second, the position of the box indicates the values where the majority of centers fall on that particular measure. In addition, the shading of the chart area indicates the age group examined. An advantage of the compactness of box-and-whisker plots is that we can display a group of plots together on the same page, allowing for a comparison in both the width and position of the boxes across related outcomes.

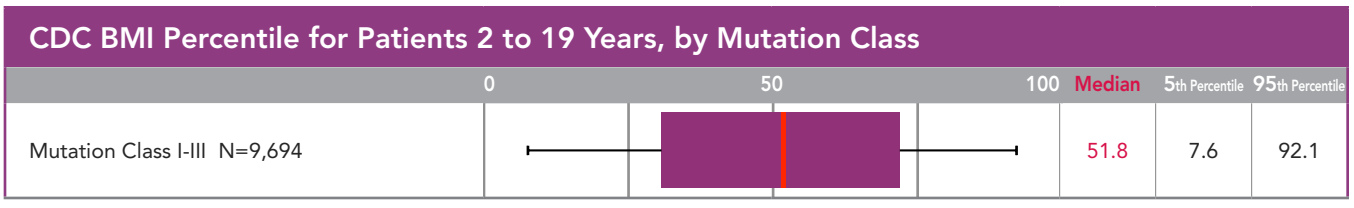
Plots with no shading show data for all patients

Plots with gray shading show data for infants

Plots with yellow shading show data for children

Plots with blue shading show data for adults

The box-and-whisker plot above displays center-level variation. For these plots we determine the median value for, or percentage of patients with, the outcome at each center. We then create the box-and-whisker plots using the summary numbers from each center. Box-and-whisker plots are also used to show the distribution of patient-level outcomes throughout the report. An example is the figure below, which also displays the variation in BMI percentile among individuals ages 2 to 19. In this case, each individual patient's data is included in the box-and-whisker plot. As a result, and as can be seen by comparing the two figures, there is much wider variation in the population-level box-and-whisker plot as compared to the center-level.



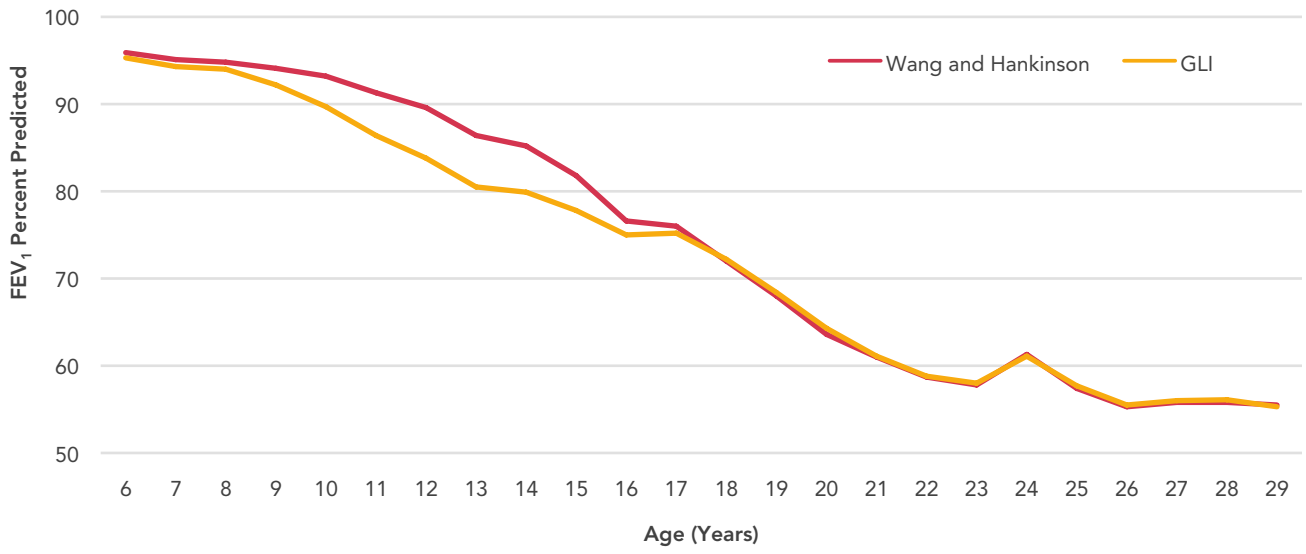
Adoption of Global Lung Initiative (GLI) Equations for Lung Function Assessment

In 2012, the Global Lung Initiative (GLI) released lung function reference equations. These equations have a number of advantages over the Wang[1] and Hankinson[2] reference equations, which have been used since 2004. The GLI reference equations were developed using data obtained from healthy, non-smoking individuals around the world and span 3 to 95 years of age, thus eliminating the need to use separate pediatric and adult equations.[3] As a result, FEV_1 percent predicted based on the GLI reference equations will be used in this report as well as future reports. More information about the GLI can be found at http://lungfunction.org/files/GLI-2012_Reference_values.pdf.

To understand the impact of using GLI reference equations to calculate lung function, we used data from 85,105 encounters that occurred in 2013 among individuals with CF ages 6 to 29 years with valid spirometry test results entered into the Registry.

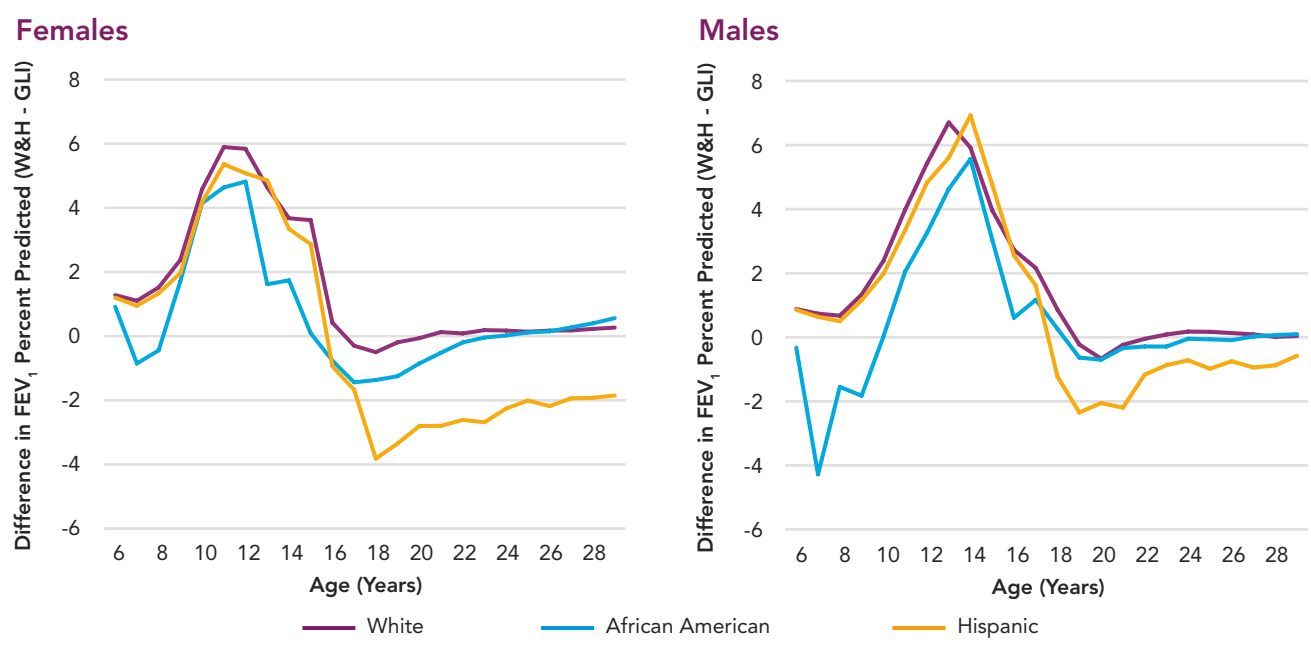
The figure below displays the mean FEV_1 percent predicted for individuals ages 6 to 29 using the Wang and Hankinson reference equations and the GLI reference equations. The graph indicates that there is no clinically meaningful difference in the FEV_1 percent predicted between the two reference equations for adults with CF. The patients most impacted by the change in reference equations are preteens, for whom the FEV_1 percent predicted using the GLI equations is on average lower than that obtained from the Wang and Hankinson equations. Our findings are comparable to what has been reported in a study by Stanojevic et al., using data from individuals with CF in the United Kingdom.[4]

Median FEV_1 Percent Predicted — Wang and Hankinson and GLI Reference Equations



The next two graphs show the median difference in FEV_1 percent predicted using the two different reference equations for each individual according to sex and the three main racial/ethnic groups in the Registry population (i.e., Hispanics, Non-Hispanic Whites and Non-Hispanic African Americans). Median differences greater than zero indicate that the Wang and Hankinson equations lead to higher estimates of FEV_1 percent predicted. Median differences less than zero indicate that the GLI equations lead to higher estimates of FEV_1 percent predicted. Again, this shows that Wang and Hankinson equations produced higher values for FEV_1 percent predicted during early adolescence for all racial/ethnic groups. Among adults, the group impacted the most by the changing the reference equations are Hispanic females, for whom GLI equations provide higher estimates of FEV_1 percent predicted.

Median Difference between Wang and Hankinson and GLI FEV_1 Percent Predicted Values

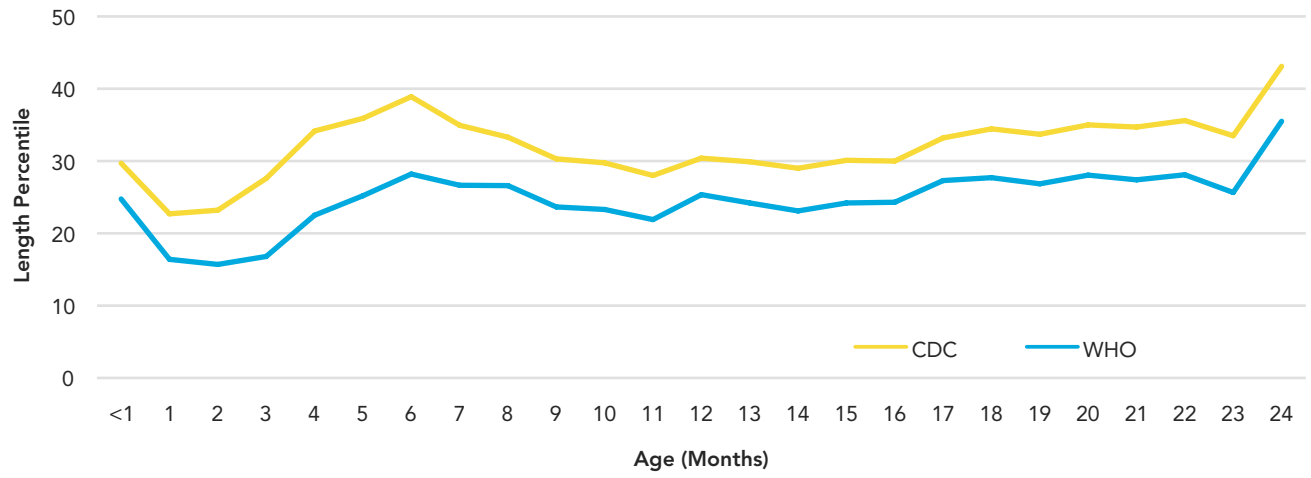


Adoption of World Health Organization (WHO) Growth Standards for Infants Under 2 Years of Age

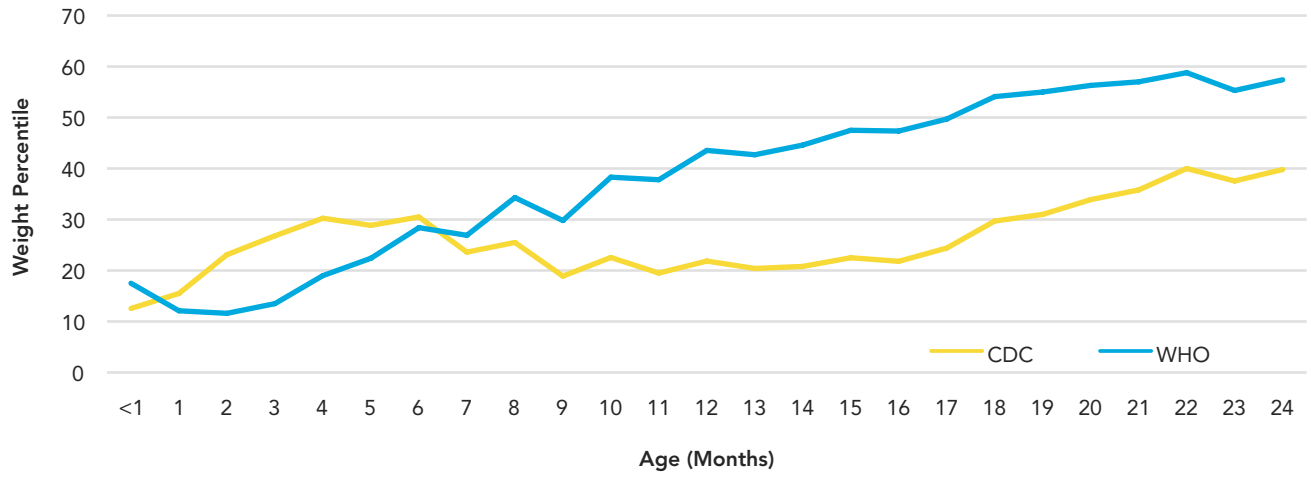
In the past, growth charts developed by the Centers for Disease Control and Prevention (CDC) were used to calculate height, weight, weight-for-length and BMI percentiles. For this year's report, we continue to use the CDC growth charts for individuals ages 2 to 19, but have switched to World Health Organization (WHO) growth charts for individuals younger than age 2, as recommended by the CDC.[5] The rationale for the CDC's recommendation was based on both the methodology of the WHO project and its larger sample size and more complete data. The CDC growth charts are based on data of how children in the United States grow as they age. In contrast, WHO charts are based on the physiology of how infants and toddlers should grow in optimal situations. The WHO charts use the growth of breastfed infants as the norm.

To understand the impact of using WHO growth charts to calculate length, weight and weight-for-length percentiles, we used data from 9,790 encounters that occurred in 2013 among individuals under the age of 2. For each measure by age, we calculated the median value using CDC growth charts and WHO growth charts. For length, percentiles using WHO growth charts are consistently lower than those using CDC growth charts. For weight, percentiles are lower using WHO growth charts for the first 6 months of life, but higher after the 6 months. Weight-for-length percentiles are generally comparable during the first year of life but increasingly diverge in the second year of life, with WHO percentiles being consistently higher.

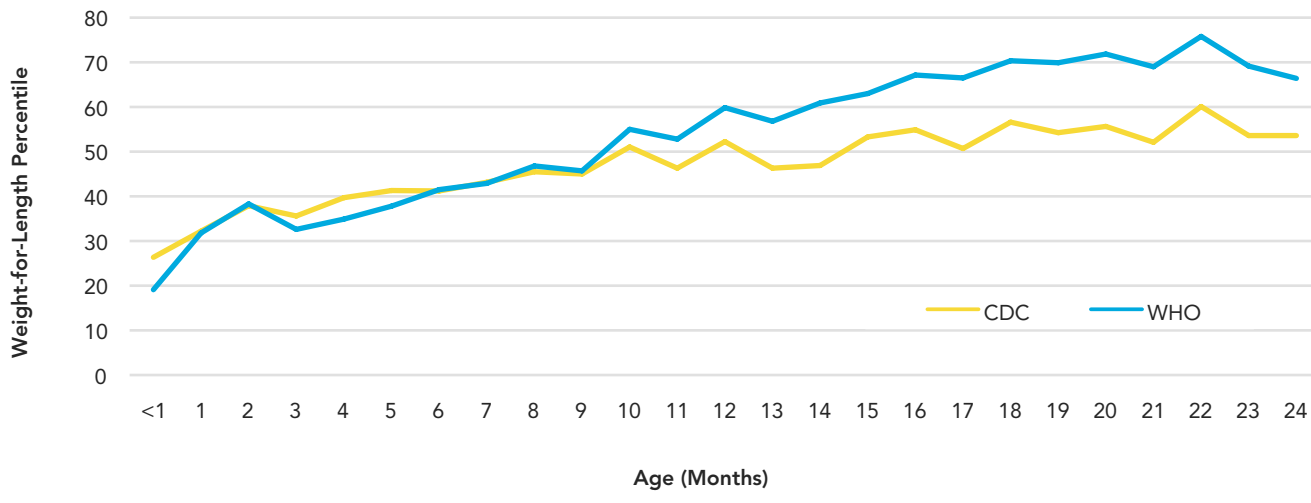
Median Length Percentile by Age — CDC and WHO Reference Equations



Median Weight Percentile by Age — CDC and WHO Reference Equations



Median Weight-for-Length Percentile by Age — CDC and WHO Reference Equations



Data Audit Summary

The CF Foundation conducted an external audit of the data entered into the Registry in 2012. Twenty-eight centers of varying size and geographic location participated. The audit reviewed data for 1,606 patients and included 8,247 encounters and 1,471 care episodes. For key information, such as demographic, microbiological, treatment, and hospitalization variables, the data entered for a patient in the Registry were compared with the data in their electronic medical record (EMR) and evaluated for completeness and accuracy. Overall, the Registry contained 96.5 percent of the encounters and 89.7 percent of the hospitalizations that were recorded in EMRs. Among the key variables examined, the accuracy of the data in the Registry was over 95 percent for date of birth, sex and CFTR mutations. Microbiology was recorded accurately for 93.1 percent of cultures and medications were recorded accurately with some variability by type — over 95 percent for dornase alfa and azithromycin; over 90 percent for hypertonic saline and aztreonam; and over 85 percent for inhaled tobramycin.

Considerations for Data Interpretation

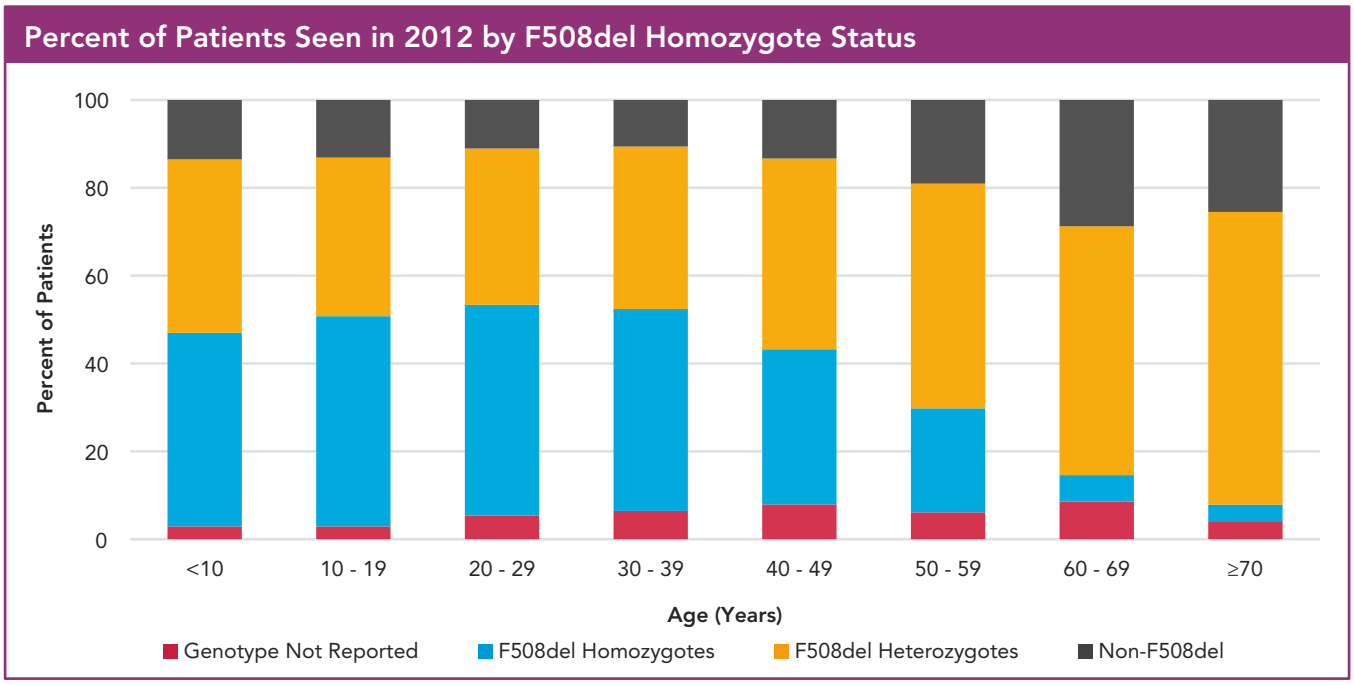
As the audit shows, the data in the Registry are complete and accurate, but some issues intrinsic to observational data need to be considered when interpreting Registry data.

Dynamic Population

Each year, the Registry report examines individuals who have consented to share their information in the Registry and who were seen in a CF care center or were born, diagnosed or died during that year. Each year, new children and adults with CF are added or return to the Registry, while others are no longer captured in the Registry due to death or loss to follow-up. These year-to-year changes impact the overall profile of the patient population in the Registry. To quantify the extent to which patients remain in the Registry, we selected a cohort of individuals with CF who were included in the Registry in 2008 and examined their status from 2008 to 2012. Of those in the 2008 cohort who were, to the best of our knowledge, alive in 2012, 91 percent were included in the Registry in 2012, and 87 percent of the cohort were included in the Registry for all five years. Among patients without five years of data, 36 percent returned to the Registry after a one-year gap, and an additional 9 percent returned after a two- or three-year gap.

Survival Bias

In previous reports, we have included figures based on cross-sectional data that show trends in different outcomes as individuals with CF age. To show improvements over time, we included charts showing FEV_1 or BMI for different age groups in three different years; however, if one looks at data from different age groups for a single year, the comparison may be affected by what is referred to as survival bias. This bias is an artifact of cross-sectional data. Older patients currently in the Registry have survived and are likely healthier, and, therefore, are not representative of other patients who were in the same birth cohort at younger ages. The figure on the next page, which shows the proportion of patients by age group who are F508del homozygous, can be used to highlight the possible effect of survival bias. Typically, F508del homozygous patients have more severe disease. As patients age, the proportion of patients who are F508del homozygous decreases, since some patients with more severe disease do not survive to be included in the older age groups.



In an effort to prevent distorted interpretation of data due to survival bias, we have modified several figures in the report that had previously displayed outcomes by age to now display outcomes over time for different age groups. Survival bias needs to be kept in mind when reviewing the data in this report, particularly for the adult population. Figures that include all adults or all patients are less likely to be impacted by this bias since the "older" patients represent a relatively small proportion of the population.

Impact of Newborn Screening

Universal newborn screening for CF has been in place since 2010, with many states having introduced it earlier. Therefore, the clinical characteristics of very young patients included in the Registry in recent years are different than those of young patients included in the Registry previously. Prior to newborn screening, most infants were diagnosed by way of clinical symptoms. Now, asymptomatic and potentially healthier infants are being diagnosed with CF and are included in the Registry much earlier than they previously would have been. As a result, when examining cohorts of individuals with CF over time, we need to be aware of the changing case mix in the Registry as the proportion of individuals diagnosed through newborn screening increases.

Summary of the Cystic Fibrosis Foundation Patient Registry, 1998-2013

Demographics	1998	2003	2008	2012	2013
CF patients (n)	21,066	21,488	25,408	27,904	28,103
Newly diagnosed patients (n)	992	1,044	1,161	1,055	959
Detected by newborn screening (%)	5.7	11.7	42.7	60.0	62.0
Mean age at diagnosis (years)	3.1	3.1	3.5	3.7	3.7
Median age at diagnosis (months)	6	6	5	4	4
Mean age (years)	16.4	17.1	18.9	19.8	20.2
Median age (years)	14.2	15.1	16.9	17.7	17.9
Adults ≥ 18 years (%)	36.9	39.7	46.4	49.0	49.7
Race (not mutually exclusive)					
White (%)	95.6	95.3	94.6	94.0	93.9
African American (%)	3.7	3.8	4.2	4.5	4.6
Other race (%)	1.3	1.8	2.4	3.0	3.1
Hispanic (any race) (%)	4.9	5.8	6.5	7.8	7.9
Males (%)	53.1	51.9	51.7	51.7	51.5
Mortality					
Total deaths (n)	388	355	434	425	414
Annual mortality rate (per 100)	1.8	1.7	1.7	1.5	1.5
Predicted median survival (years)	32.2	33.4	36.6	41.3	40.7
95% confidence interval (years)	30.3-34.9	30.9-36.0	34.6-39.5	37.5-43.1	37.7-44.1
Median age at death (years)	25.8	26.0	26.6	27.4	27.5
GI/Nutrition					
BMI percentile, patients 2 to 19 years (median)	39.1	44.1	49.1	52.6	53.3
Weight < 10th CDC percentile, patients 2 to 19 years (%)	26.3	21.4	16.6	13.7	13.3
Height < 5th CDC percentile, patients 2 to 19 years (%)	17.0	14.7	12.5	10.8	10.5
BMI patients 20 to 40 years (median)	20.7	21.4	21.9	22.2	22.2
Pancreatic enzyme supplements (% of patients)	96.2	95.3	90.9	87.5	87.2
Supplemental feeding - tube (%)	-	8.9	11.5	11.4	11.2
Supplemental feeding - oral only (%)	-	35.2	40.9	43.0	42.7
Pulmonary					
FVC % predicted (mean)[A]	81.5	83.4	86.2	87.3	87.4
FEV_1 % predicted (mean)[A]	70.1	72.9	74.8	75.9	76.1
Respiratory Microbiology					
P. aeruginosa (PA) (%)[B]	60.7	57.3	52.9	49.6	48.7
Multidrug-resistant *P. aeruginosa* (MDR-PA) (%)[C]	-	10.7	9.4	9.5	9.2
B. cepacia complex (%)	3.5	3.0	2.8	2.5	2.6
S. aureus (SA) (%)[D]	44.8	59.3	66.0	69.0	69.3
Methicillin-sensitive *S. aureus* (MSSA) (%)	42.2	51.0	50.7	52.3	51.7
Methicillin-resistant *S. aureus* (MRSA) (%)	3.3	11.9	22.6	26.5	25.6
S. maltophilia (%)	5.5	11.2	12.7	13.4	13.7
Mycobacterial species (%)[E]	-	-	-	11.9	12.1

Table continues on the next page

Summary of the Cystic Fibrosis Foundation Patient Registry, 1998-2013 *continued*					
Health Care Utilization and Pulmonary Exacerbations[F]	**1998**	**2003**	**2008**	**2012**	**2013**
Outpatient visits to CF centers reported per year (mean)	5.3	4.1	4.3	4.6	4.6
Treated for a pulmonary exacerbation (%)	-	33.2	36.8	34.7	35.3
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)[G]	-	29.2	32.9	29.5	31.0
Number of days of home IV treatment for pulmonary exacerbation per year (mean)[G]	-	12.3	14.0	10.9	11.9
Number of days of hospitalization for pulmonary exacerbation per year (mean)[G]	-	17.0	18.8	18.6	19.1
Pulmonary Therapies[H]					
Dornase alfa (≥ 6 years) (%)	56.5	67.6	79.6	83.8	85.0
Inhaled tobramycin (PA+ and ≥ 6 years) (%)[I]	52.6	67.3	70.0	65.7	63.0
Inhaled aztreonam (PA+ and ≥ 6 years) (%)	-	-	2.5	39.0	41.5
Azithromycin (PA+ and ≥ 6 years) (%)[J]	-	41.2	66.1	70.6	69.2
Hypertonic Saline (≥ 6 years) (%)	-	-	43.6	60.5	63.2
Ibuprofen (6–17 years with FEV_1 ≥ 60 percent) (%)	11.9	6.6	4.6	3.6	3.3
Ivacaftor (≥ 6 years with G551D mutation)	-	-	-	77.7	86.8
Oxygen (%)[K]	-	-	11.4	10.8	11.4
Non-invasive ventilation (%)	-	-	2.1	2.5	2.8
Transplants					
Lung (all procedures) (n)	133	152	166	213	246
Liver (n)	14	13	8	20	8
Kidney (n)	1	10	8	11	10

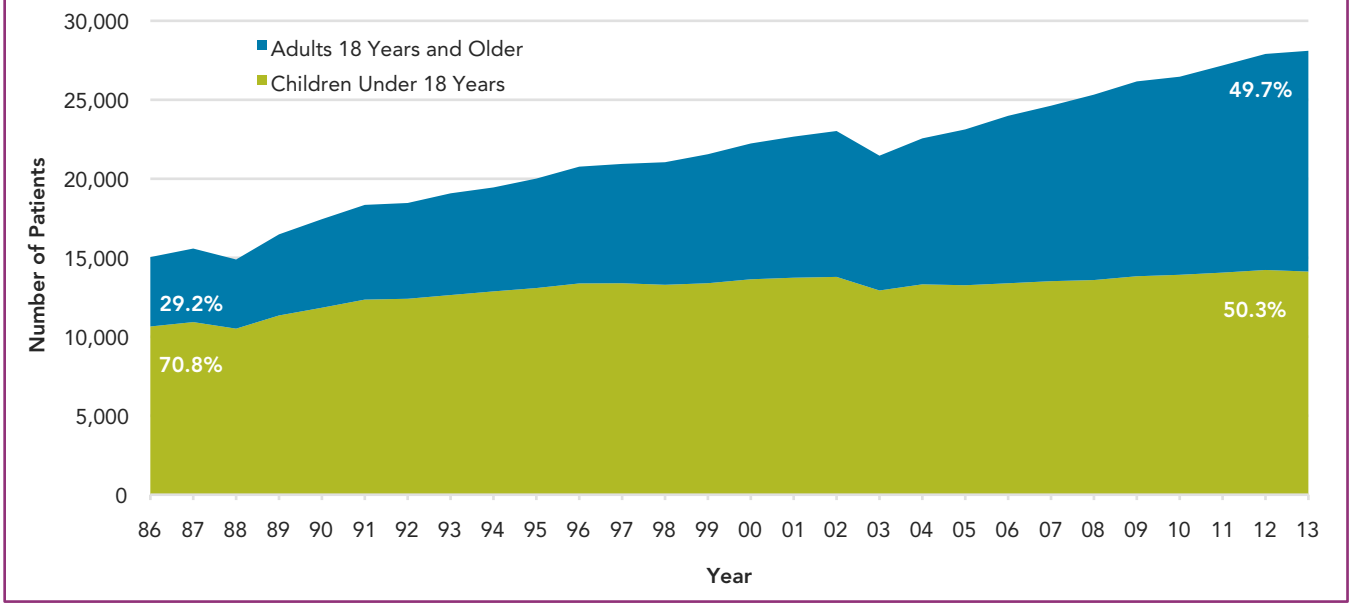
[A] *Pulmonary function data throughout this report reflect the use of GLI equations[3] for both children and adults.*
[B] *Includes PA and multidrug-resistant PA, found in any culture during the year.*
[C] *Defined as resistant to all antibiotics tested in two or more classes.*
[D] *Includes MSSA and MRSA and reflects the prevalence of* S. aureus *among patients 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.*
[E] *Percent of patients 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.*
[F] *Defined as a period of treatment with intravenous (IV) antibiotics in the hospital and/or at home.*
[G] *Among those with one or more pulmonary exacerbations in the year.*
[H] *Percent of patients on therapy at any encounter in the year. All patients noted as intolerant or having an allergy to a specific therapy were excluded.*
[I] *Includes TOBI®, TOBI® Podhaler™ and Bethkis® in 2013 — in prior years, only TOBI® was available.*
[J] *Patients were considered eligible if they met the selection criteria used in the U.S. azithromycin trial.[6]*
[K] *Includes continuous, nocturnal or with exertion.*

DEMOGRAPHICS

The Registry in its current form contains data on patients from 1986 to 2013. Over that time, substantial changes in the care people with CF receive have led to improved survival. This section displays the current and longitudinal distribution of demographic characteristics of individuals with CF in the Registry.

In 2013, there were 28,103 individuals with CF followed in the Registry. The number of adults with CF (individuals ages 18 and older) continues to increase, while the number of children has remained relatively stable over the past decade. In 2013, adults comprised 49.7 percent of the CF population, compared with 29.2 percent in 1986.

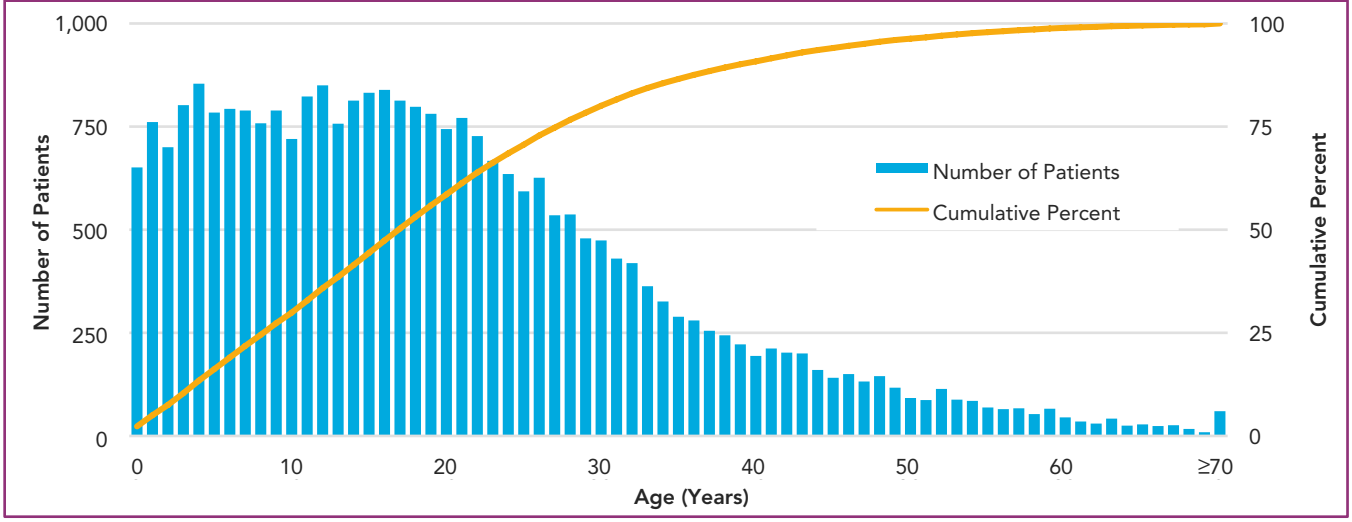
Number of Children and Adults with CF, 1986–2013



The decrease in the number of patients in 2003 is due to a delay in obtaining patient consents before the close of the calendar year at some care centers.

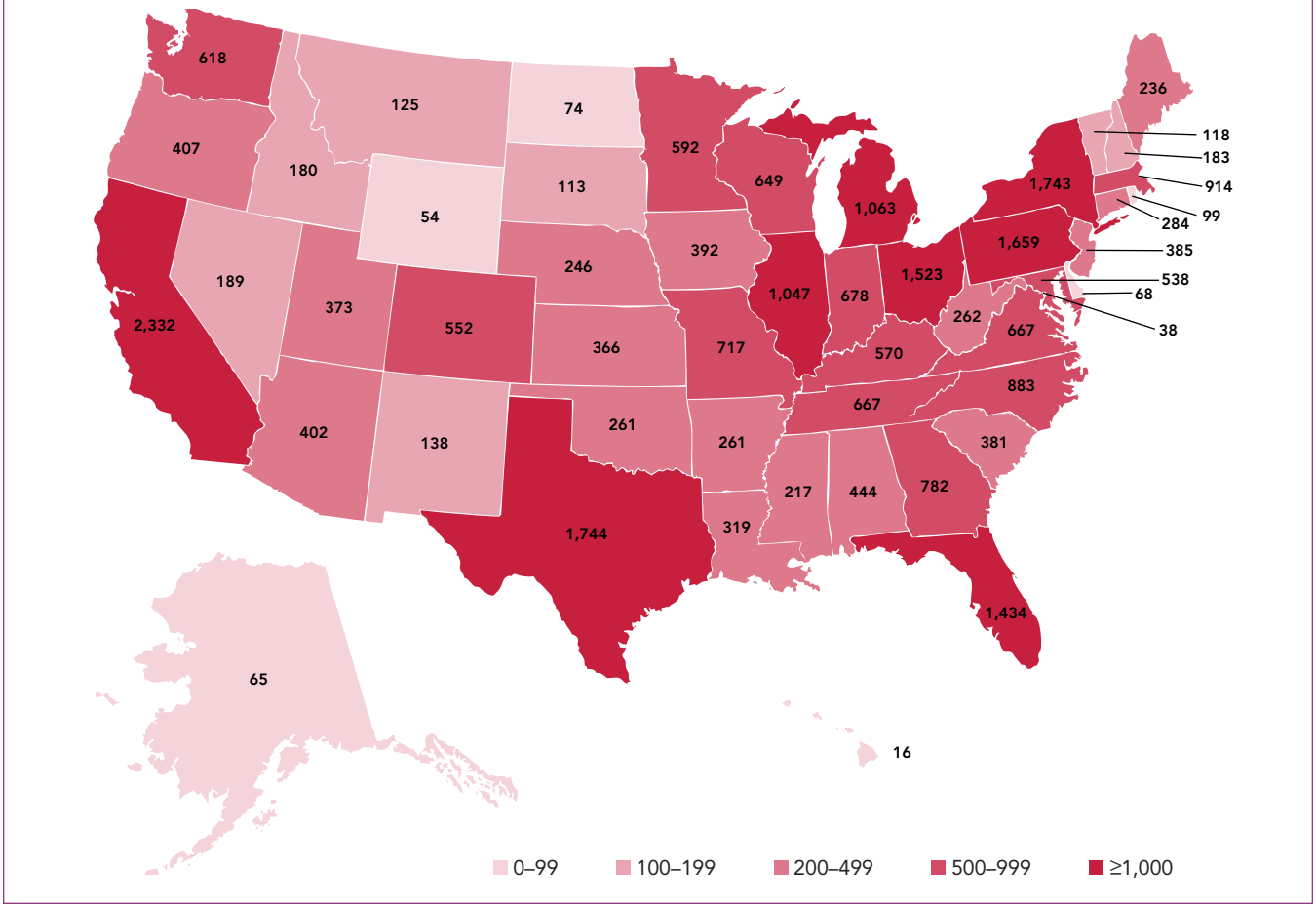
The median age of people currently in the Registry is 17.9 years. The range is from birth to 85 years. Despite gains in survival, the age distribution remains markedly skewed toward younger patients.

Age Distribution of the CF Population in 2013



The map below displays the number of individuals with CF residing in each state.

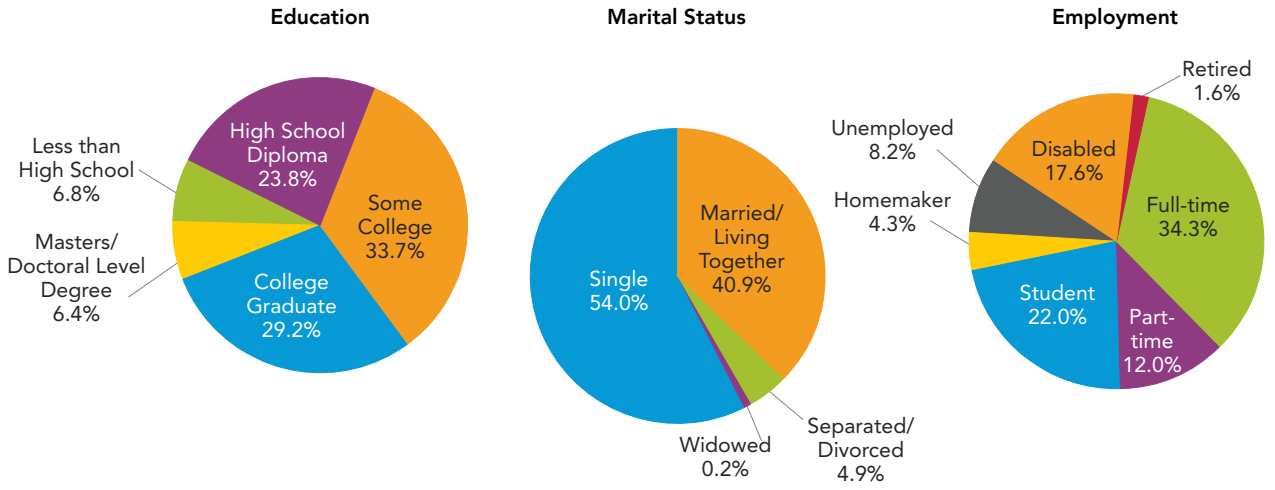
Number of Individuals with CF Residing in Each State in 2013



Characteristics of Adults with CF 18 Years and Older

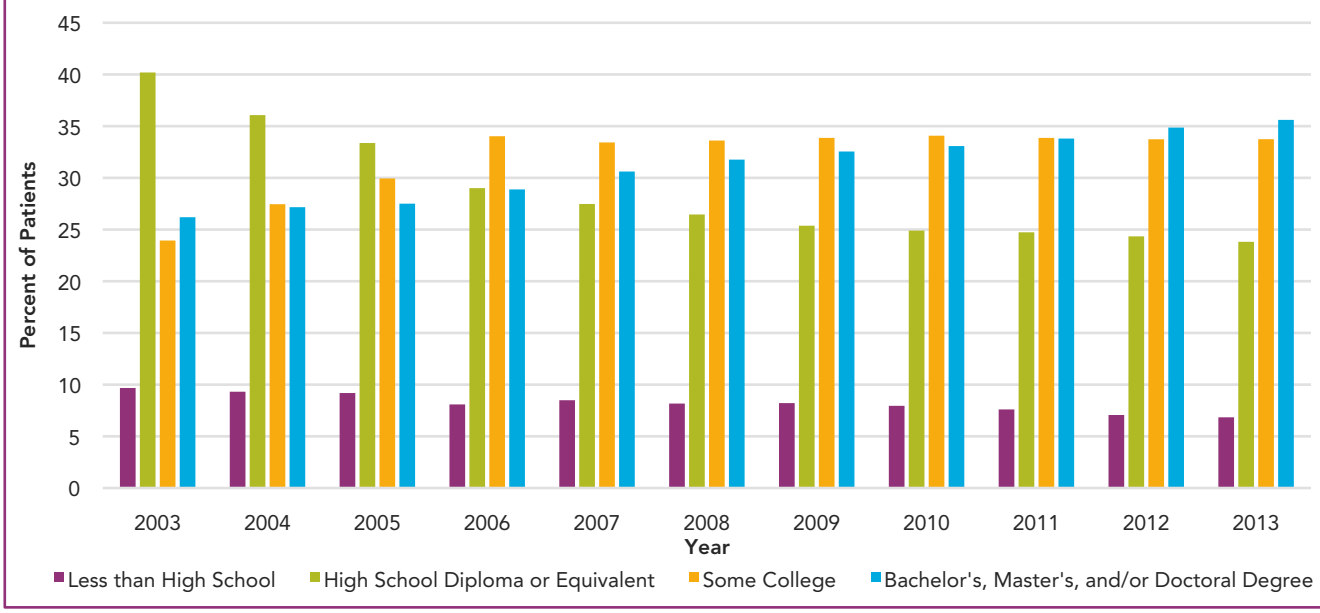
As a larger proportion of individuals with CF enter adulthood, it is encouraging to note that many of them are pursuing higher education and employment and are in committed relationships and having children of their own. About two-thirds of adults are either students or working.

Socioeconomic Characteristics of Adults 18 Years and Older with CF in 2013



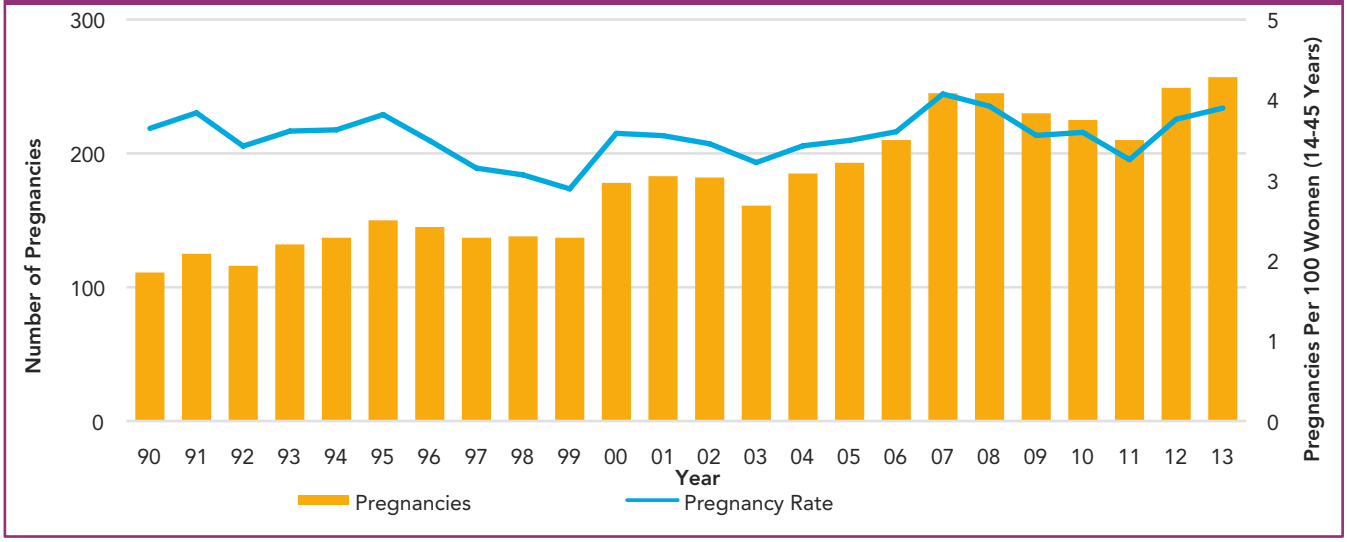
Currently, about 35 percent of individuals in the Registry are college graduates, and this percentage has increased over the past 10 years.

Educational Attainment of the Adult CF Population, 2003–2013



The number of pregnancies among women with CF has steadily increased since the 1990s — in 2013, a total of 257 women with CF were pregnant. During this time, the overall pregnancy rate among women with CF has remained relatively constant due to the balance of additional pregnancies and additional women surviving to be included in the denominator. In contrast, the pregnancy rate in the general United States population is declining over time.[7]

Pregnancies and Pregnancy Rate in Women Ages 14 to 45 Years with CF, 1990–2013



Insurance Information

Insurance Coverage in 2013

	Under 18 Years	18 to 25 Years	26 Years and Older
Number of patients (n)	13,742	5,552	7,990
Health insurance policy (e.g. private insurance) (%)	54.9	64.3	66.4
Medicare/Indian Health Services (%)	0.7	7.3	25.7
Medicaid/state programs (%)	53.8	41.0	27.1
TriCare or other military health plan (%)	3.1	2.7	1.6
Other (%)	1.3	1.7	1.8
No health insurance (%)	0.5	2.2	1.3

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 2013

Patients who participated in a patient assistance program (%)	25.4
Patients 18 to 25 years covered under parents' insurance (%)	57.0

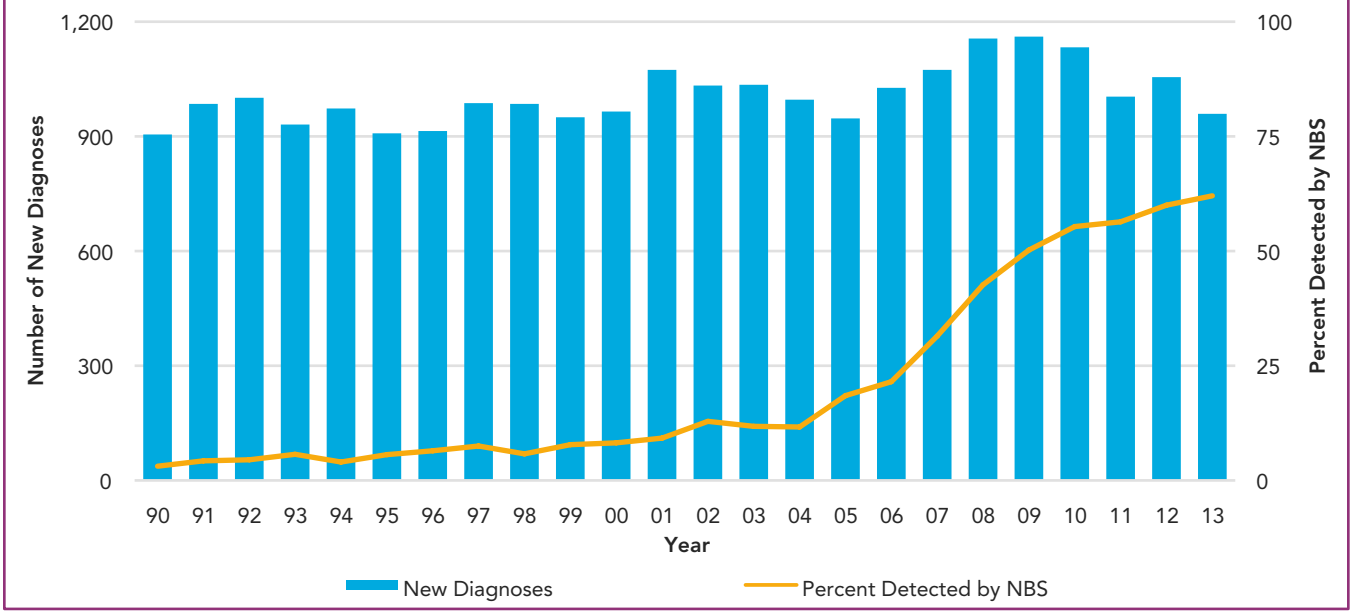
"Patient assistance program" refers to any program that provides free medication or co-pay assistance.

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.

In 2013, 62.0 percent of new diagnoses were detected by newborn screening (NBS). There is evidence that patients diagnosed prior to the onset of symptoms have better lung function and nutritional outcomes later in life.[8] 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, 1990–2013

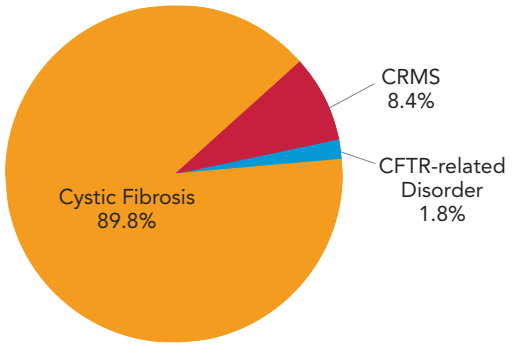


The number of new diagnoses for years prior to 2013 has been adjusted to include patients first reported to the Registry in the year after their diagnosis year. As in previous reports, we anticipate that the number of new diagnoses in 2013 will increase when the 2014 data are available.

According to CF Foundation guidelines, infants with a positive NBS but indeterminate sweat tests or less than two CF causing mutations should be diagnosed with CFTR-related metabolic syndrome (CRMS).[9] CRMS was added to the Registry as a diagnostic option in 2010, with 719 patients with this diagnosis entered since then. In 2013, data were entered for 502 patients diagnosed with CRMS, 89 of whom were diagnosed during that year. Of those CRMS patients with a genotype entered (98.4%), 62.5 percent had one F508del mutation and 32.4 percent had one R117H mutation.

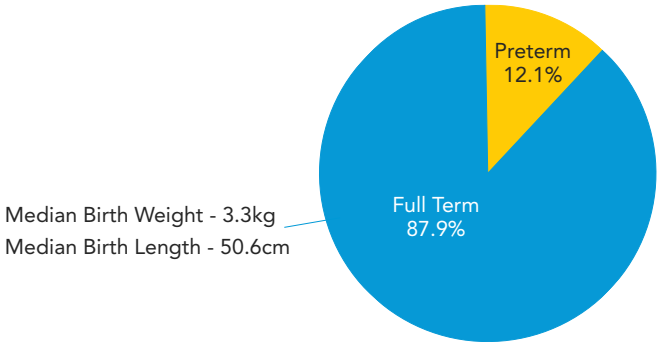
In addition to CRMS, patients can be identified as having a CFTR-related disorder. This option has also been available in the Registry since 2010. Patients with this diagnosis do not meet the diagnostic criteria for CF but are affected by CF-related conditions such as congenital bilateral absence of the vas deferens (CBAVD) and often have mutations in the CFTR gene.[10] Collection and analysis of data from these individuals will provide new and important information for these patient populations.

CF, CRMS and CFTR-related Disorder Diagnoses in 2013



In 2013, 651 infants were born and diagnosed with CF. Of those with a known gestational age at birth, 87.9 percent were born full term. This rate is comparable to that of the general U.S. population.[11] The mean birth weight for full term infants with CF is approximately the same as that of the U.S. population.[12] The gestational age of 112 infants born and diagnosed with CF in 2013 is not known.

Birth Characteristics of Infants Born and Diagnosed with CF in 2013



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.

Other than those presenting with meconium ileus, the great majority of those diagnosed under the age of 1 year are asymptomatic or minimally symptomatic at the time of diagnosis. Those diagnosed after age 1, however, often present with symptoms such as acute or persistent respiratory abnormalities.

Presentation at Diagnosis

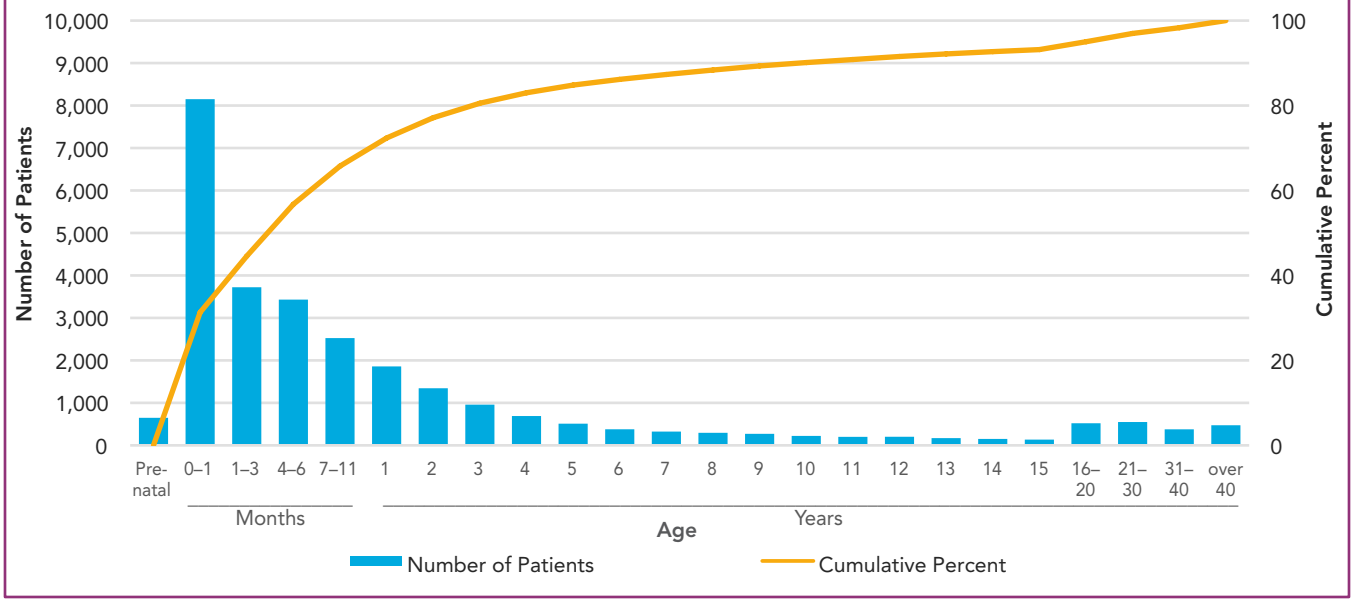
	Diagnosed in 2013 (%)	Diagnosed in 2013 Age < 1 (%)	Diagnosed in 2013 Age ≥ 1 (%)	All Patients (%)
Asymptomatic				
DNA analysis	21.0	18.8	26.9	10.1
Family history	9.3	7.9	13.0	15.6
Newborn (neonatal) screening	62.0	83.0	3.6	19.1
Prenatal screening (CVS, amniocentesis)	4.1	5.2	0.8	2.3
Symptomatic				
Meconium ileus/other intestinal obstruction	10.3	13.5	1.6	18.5
Acute or persistent respiratory abnormalities	18.4	2.1	63.6	40.5
CBAVD or infertility/GU abnormalities	2.1	0.0	7.9	0.3
Digital clubbing	1.6	0.1	5.5	0.4
Edema	0.1	0.0	0.4	0.6
Electrolyte imbalance	0.4	0.3	0.8	3.6
Failure to thrive/malnutrition	5.4	3.7	10.3	32.0
Liver problems	0.4	0.1	1.2	1.1
Nasal polyps/sinus disease	3.2	0.0	12.3	3.7
Rectal prolapse	0.5	0.0	2.0	3.0
Steatorrhea/abnormal stools/malabsorption	5.6	4.1	9.9	24.9
Other	4.6	2.5	10.3	4.5

Data are not mutually exclusive.

Among those diagnosed in 2013 under the age of 1 with meconium ileus or another intestinal obstruction, 23.2 percent had meconium ileus with perforation, 57.9 had meconium ileus without perforation and the remaining 18.9 percent had another neonatal bowel obstruction or it was unknown if perforation of the bowel had occurred.

Previous figures in this section refer to infants born in 2013, the rest of the section relates to all patients followed in the Registry in 2013.

Age at Diagnosis of Individuals with CF in 2013



Among patients in the Registry in 2013, 72.4 percent were diagnosed in the first year of life.

Genotype Data

With the introduction of genotype-specific cystic fibrosis transmembrane conductance (CFTR) modulators, genotyping all patients is increasingly important to CF research and clinical care. In 2013, 96.7 percent of patients (27,165) in the Registry had been genotyped. Of the more than 1,800 mutations that have been identified in the CFTR gene,[13] the most common is the F508del mutation — 86.4 percent of patients in the Registry have at least one copy of this mutation. There is a substantial drop 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 2013

Mutation	Number of Patients	Percent of Patients
F508del	23,478	86.4
G542X	1,252	4.6
G551D	1,182	4.4
R117H	767	2.8
N1303K	672	2.5
W1282X	625	2.3
R553X	493	1.8
621+1G->T	437	1.6
1717-1G->A	425	1.6
3849+10kbC->T	411	1.5
2789+5G->A	369	1.4
3120+1G->A	267	1.0
I507del	220	0.8
D1152H	196	0.7
R1162X	193	0.7
3659delC	189	0.7
1898+1G->A	187	0.7
G85E	178	0.7
R560T	165	0.6
R347P	158	0.6
2184insA	151	0.6
R334W	145	0.5
A455E	142	0.5
Q493X	129	0.5
2184delA	116	0.4

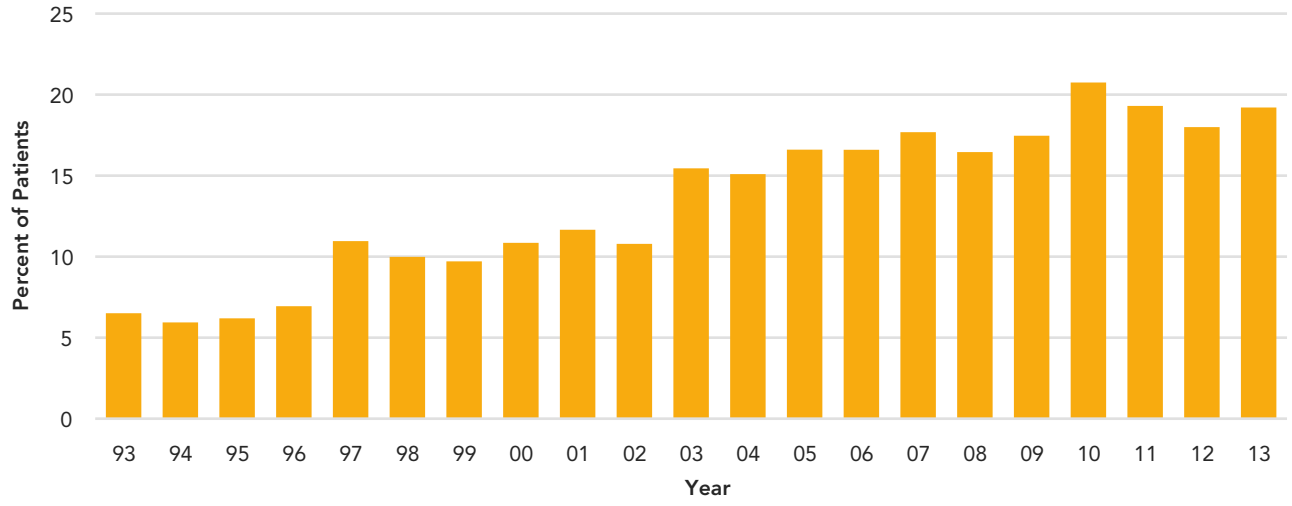
homozygotes - 46.5%
heterozygotes - 39.9%

The number and percent of patients with a mutation includes patients with one or two copies of the mutation.

Among patients with genotyping information in the Registry, 1.1 percent of patients have one or more allele entered as "Unknown".

Over time, the distribution of CFTR mutations among patients diagnosed with CF has changed, with the proportion of patients who do not have at least one F508del mutation increasing.

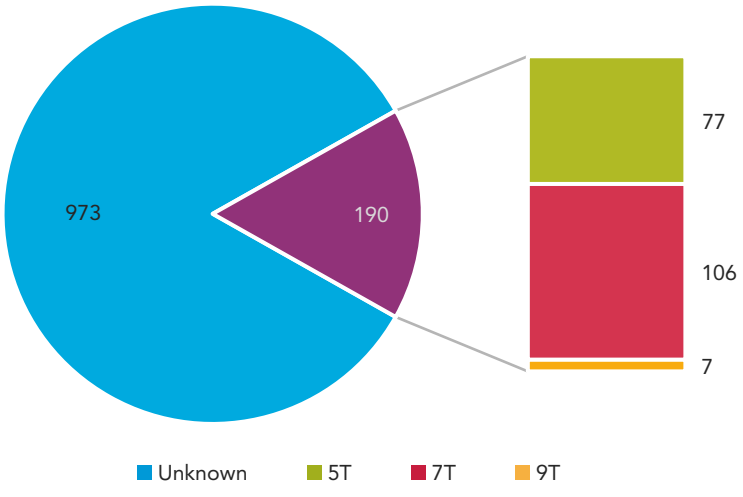
Percent of Patients with No F508del Mutations by Year of Genotyping,1993–2013



Of the less common mutations, there has been a consistent increase in the number of individuals with an R117H mutation. Among those genotyped in 1993, less than 1 percent of the population had an R117H mutation compared to almost 5 percent in 2013. There are many factors that could influence the shift in the distribution of mutations, such as the change in the ethnic distribution of the population or the introduction of newborn screening.

The clinical significance of the R117H mutation is highly dependent on the poly-T tract variant (5T, 7T or 9T) on the chromosome. Research indicates that a shorter poly-T tract is associated with higher disease penetrance.[14,15] Unfortunately, the Registry does not have information on the poly-T repeat groups for 973 of the 1,163 patients with R117H ever followed in the Registry. We hope to reduce the amount of missing data for this important modifier of the R117H mutation phenotype.

Poly-T Tract Status of Patients with an R117H Mutation



Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Mutation Classes

Researchers have categorized CF disease-causing mutations into five classes based on how the mutation affects the function or production of the cystic fibrosis transmembrane conductance regulator (CFTR) protein.[16–18]

CFTR Mutations and Their Functional Effects

Class	Impact on CFTR Protein	Examples of Mutations
Class I	No functional CFTR protein created	G542X, W1282X, R553X, 621+1G->T, 1717-1G->A
Class II	CFTR protein is created, but misfolded, keeping it from reaching the cell surface	F508del, N1303K, I507del, G85E, R560T
Class III	CFTR protein is created and reaches cell surface, but does not function properly	G551D, S549N, V520F, L1077P, G1244E
Class IV	The opening in the CFTR protein ion channel is faulty	R117H, D1152H, R347P, R334W, L206W
Class V	CFTR protein is created in insufficient quantities	3849+10kbC->T, 2789+5G->A, A455E, 3272-26A->G, 3120G->A

Mutation class comparisons have been included in this report. Mutation Classes I, II and III and Classes IV and V, respectively, are grouped together throughout this report. Patients included in the Class I-III group have two mutations in Classes I, II or III. These are considered more severe genotypes with little to no CFTR function. Patients with one or two mutations in Classes IV or V are considered to have milder genotypes with some residual CFTR function. The differences between these genotype classes lead to important clinical differences between the two groups.[16,18]

CFTR Mutation Class Comparisons

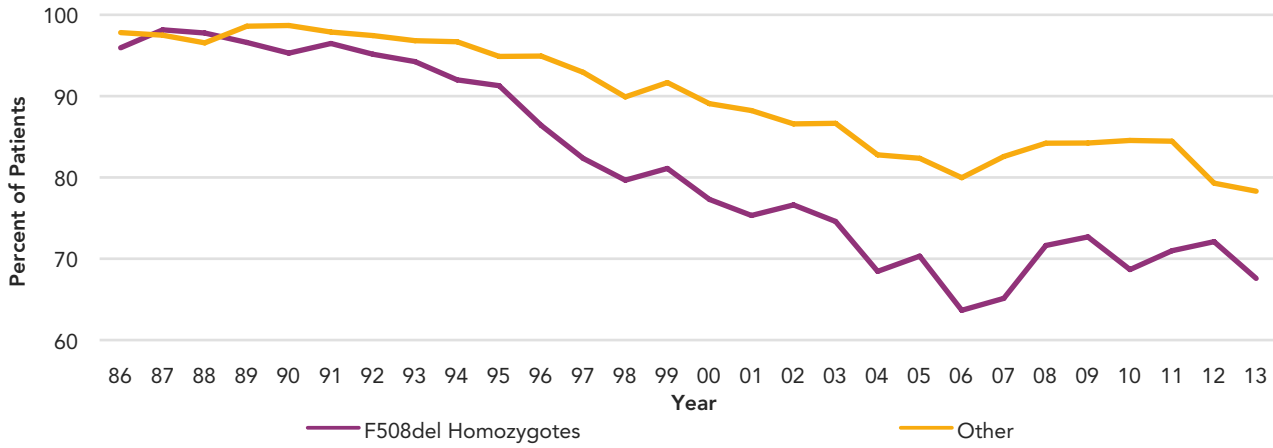
	Classes I-III	Classes IV-V	Class Not Identified
Patients genotyped (%)	71.1	10.5	18.4
Patients with a sweat test (%)	84.2	84.6	92.7
Age (median)	17.5	20.9	17.4
FEV_1 for patients 6 to 17 years (median)	90.7	97.1	92.6
FEV_1 for patients 18 to 30 years (median)	70.7	85.2	75.2
BMI percentile for patients 2 to 19 years (median)	51.8	64.9	56.0
BMI for patients 20 to 40 years (median)	21.8	24.2	22.8
Patients taking enzymes (%)	98.4	37.1	71.5

Class not identified, in this table as well as others throughout the report, refers to patients diagnosed with CF who were genotyped but the functional consequences of one or both of their mutations has not yet been determined.

Sweat Chloride Testing

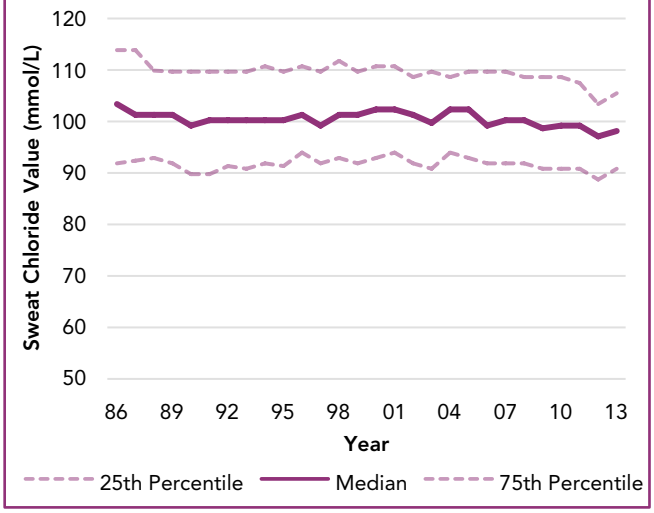
Sweat chloride testing continues to be an important diagnostic test and is recommended for all patients regardless of genotype.[19] In 2013, 85.6 percent of patients in the Registry had a sweat chloride test result recorded. We see a decreasing trend over time in the percent of patients with a sweat test entered into the Registry, which to the best of our knowledge is not the result of incomplete data entry. Individuals who are homozygous for F508del are substantially less likely to have a sweat chloride result entered in the Registry than those who are not F508del homozygotes.

Percent of Patients with a Sweat Chloride Reported by Year of Diagnosis, 1986–2013

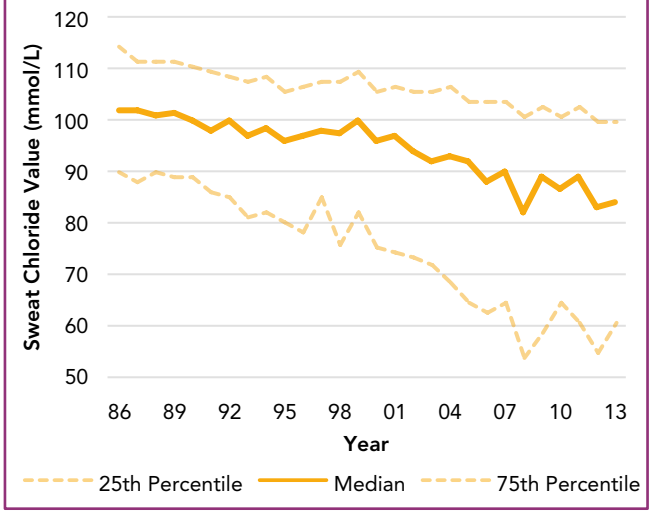


Among those with a sweat chloride test, the median sweat chloride test results have remained consistent for patients who are F508del homozygotes with minimal variation. In contrast, there has been a steady decline in the median sweat chloride result among individuals who are not homozygous for F508del.

Sweat Chloride Value of F508del Homozygotes by Year of Diagnosis, 1986–2013

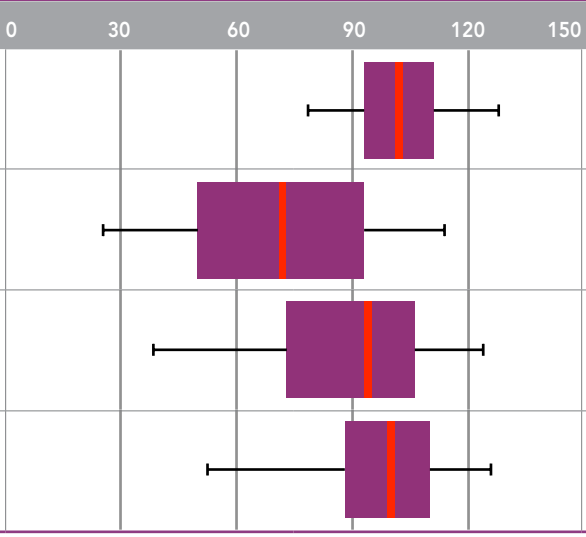


Sweat Chloride Value of Patients Not Homozygous for F508del by Year of Diagnosis, 1986–2013



Patients with a severe genotype (Class I-III) have higher median sweat chloride values than those with milder genotypes (Class IV-V), indicative of residual CFTR function in many of the Class IV-V patients.

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



	Median	5th Percentile	95th Percentile
Mutation Class I-III N=16,168	102	78	128
Mutation Class IV-V N=2,407	72	25	114
Genotyped but not identified in Mutation Classes I-III or IV-V N=4,623	94	38	124
All Patients N=23,198	100	52	126

GUIDELINES: CARE, SCREENING AND PREVENTION

The CF Foundation has developed guidelines for routine care and screening for individuals with CF during infancy, childhood and adulthood. In accordance with care guidelines for patients over age 2,[20,21] 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 much lower and more variable across the care center network.[22] Care centers report that respiratory therapists/physical therapists, dietitians/nutritionists, and social workers evaluate most patients at least once per year, as recommended by the CF Foundation.[20]

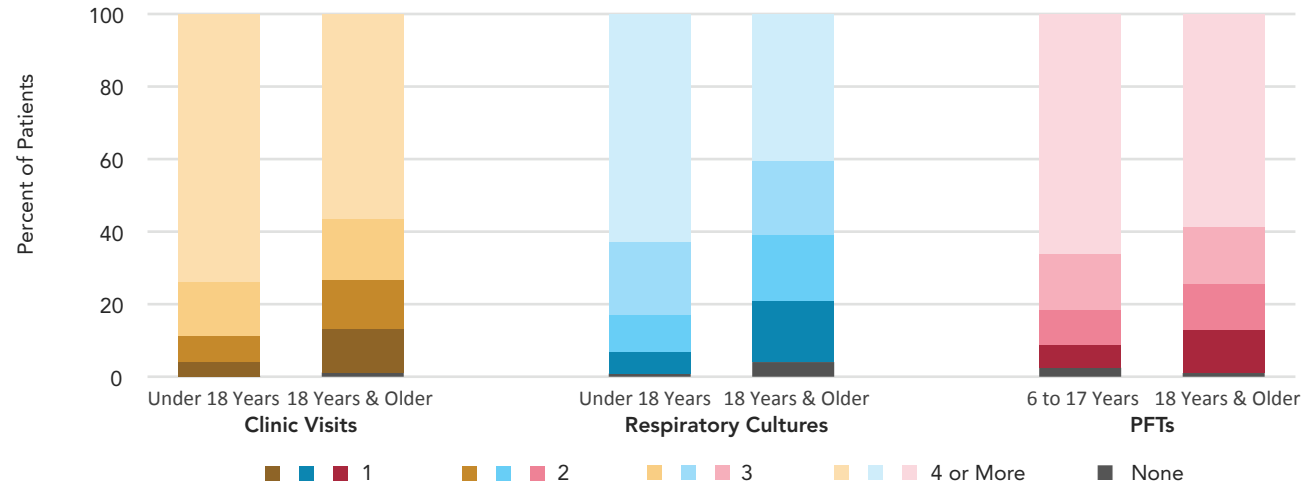
There is significant center-level variation in several key screening measures, including measurement of IgE for allergic bronchopulmonary aspergillosis (ABPA) and DXA scan for osteopenia/osteoporosis. The influenza vaccination rate is remarkable at 91.2 percent; however, the vaccination status of 16.2 percent of patients was reported as unknown. Smoking and secondhand smoke exposure remain challenging problems, particularly for young adults.

Patient Care Guidelines

Over time, the percentage of patients meeting the CF Foundation care guidelines has increased. Because patients should be able to perform reliable PFT tests at the age of 6 and older, we use the age of 7 for meeting guidelines criteria throughout this section to ensure individuals were eligible to perform a reliable PFT for the entire reporting year of 2013.

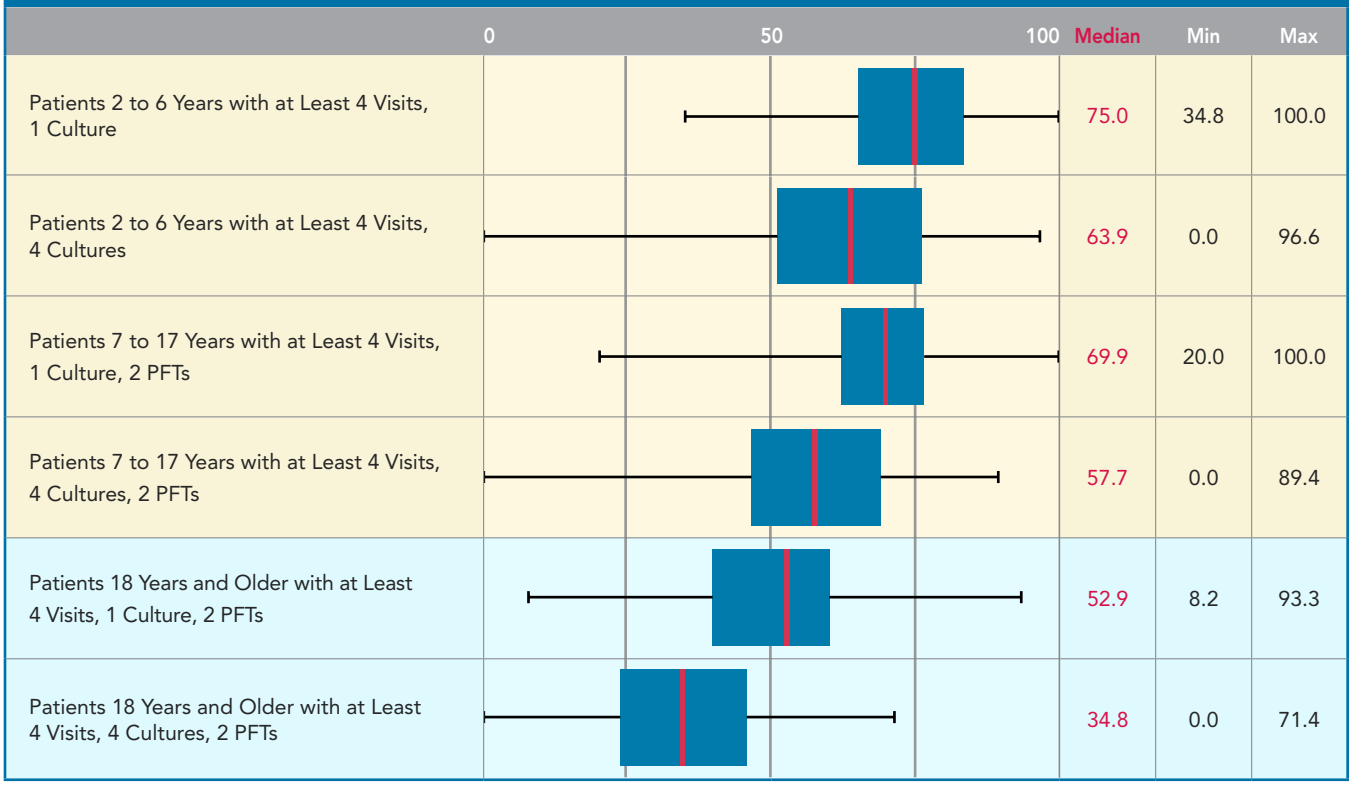
In 2003, 25.1 percent of children ages 7 to 17 years had four visits, four respiratory cultures and two PFTs, as recommended by the guidelines.[21,22] In 2013, the percent of children receiving recommended care rose to 60.0 percent. Among adults 18 years of age and older, 16.7 percent had four visits, four respiratory cultures and two PFTs in 2003, while 33.8 percent met these guidelines in 2013.

Number of Clinic Visits, Respiratory Cultures and PFTs in 2013

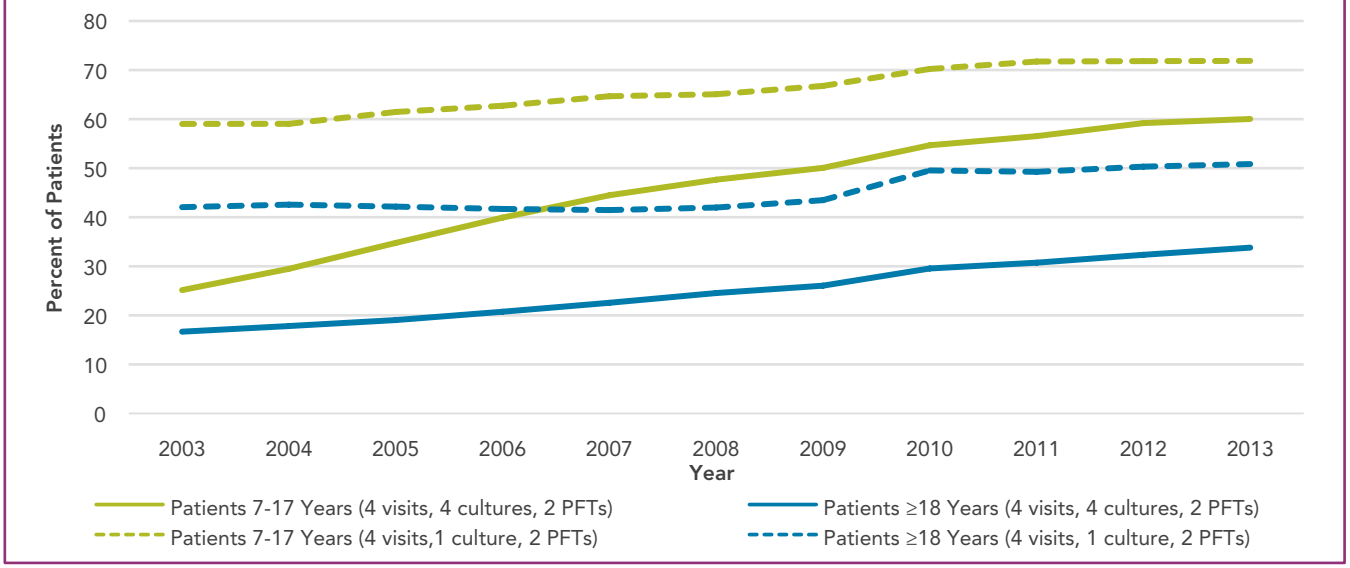


Patients needed to have one or more clinic visits in 2013 to be included in the report.

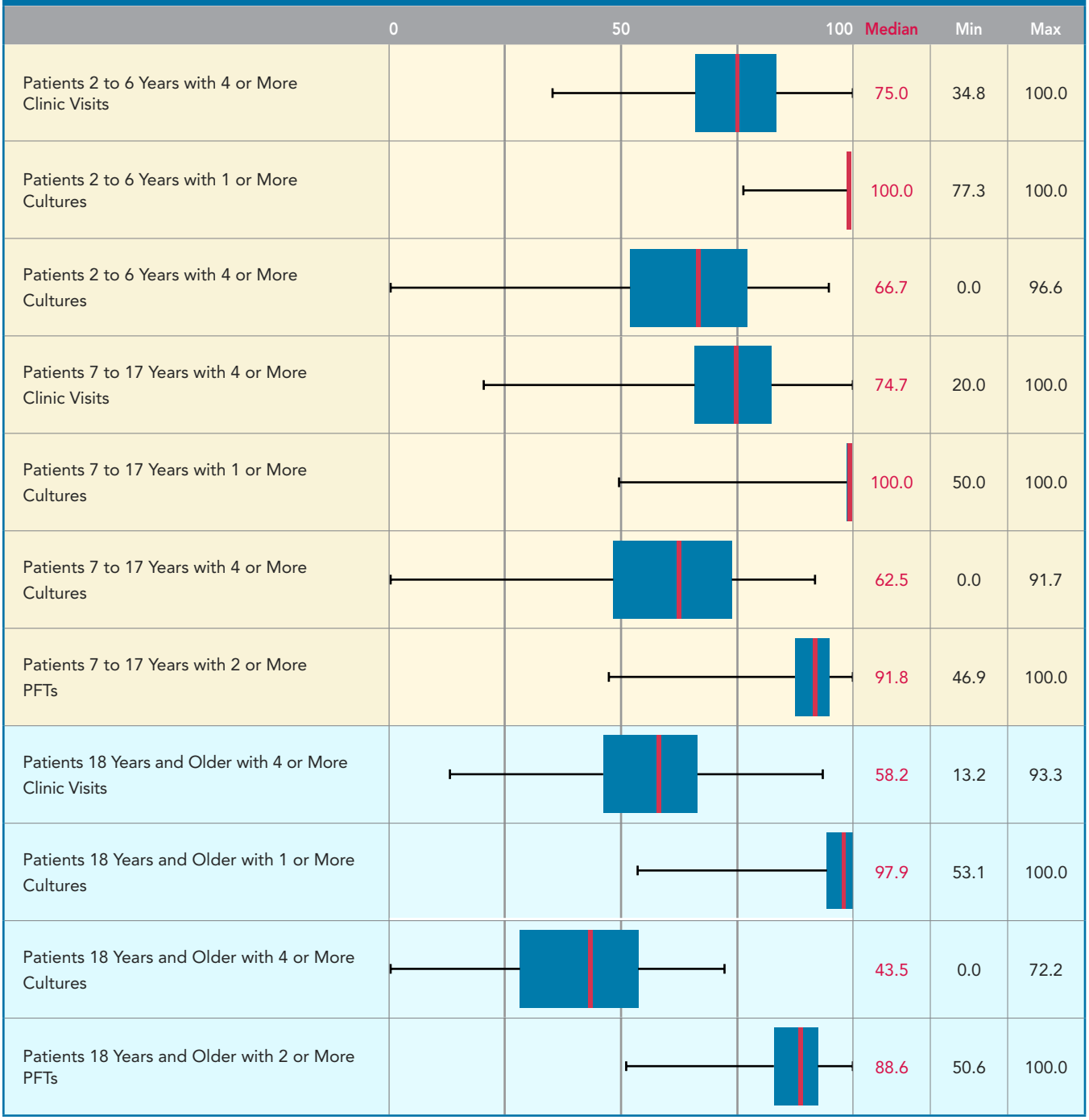
Percent of Patients Meeting Guidelines for Visits, Cultures and PFTs, by Center



Percent of Patients Meeting Guidelines for Visits, Cultures and PFTs, 2003–2013



Percent of Patients Meeting Individual Guideline Criteria , by Center



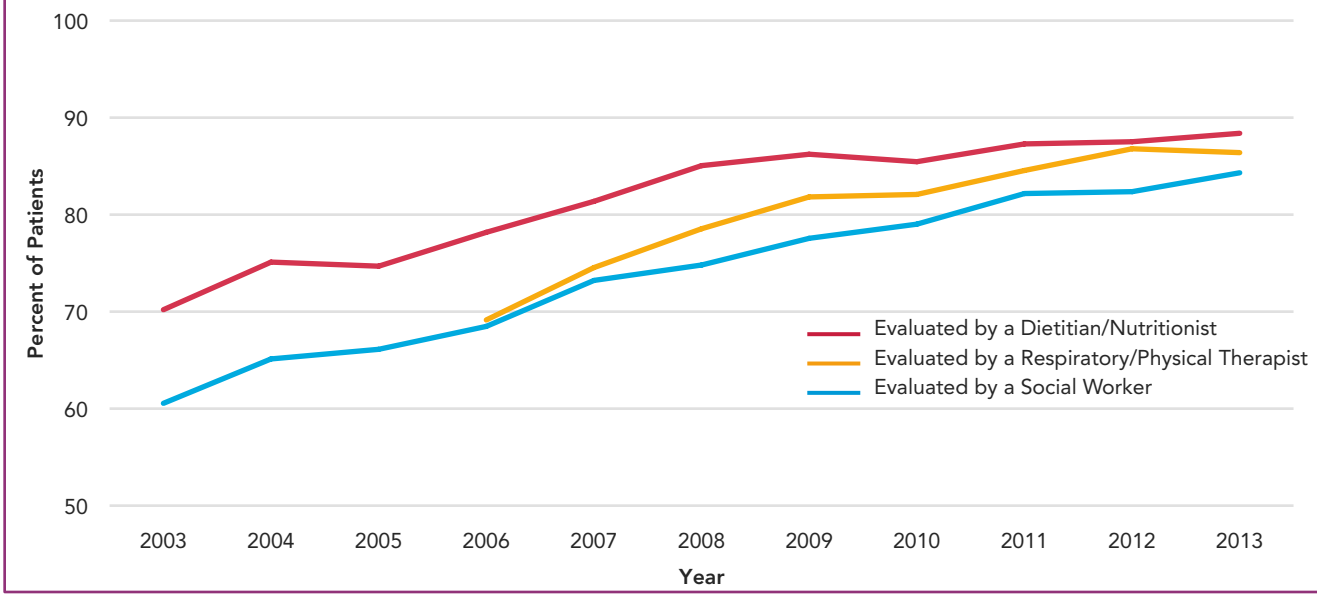
The infection prevention and control guidelines recommend that patients have at least quarterly respiratory cultures.[22,23] Overall, 52.2 percent of patients had four or more respiratory cultures in 2013. Patients under the age of 18 were more likely to meet this recommendation.

The multidisciplinary care team plays an important role in CF care. CF care centers continue to increase the percentage of patients who see a dietitian/nutritionist, physical/respiratory therapist and social worker each year.

Percent of Patients Evaluated by Multidisciplinary Care Team Members, by Center

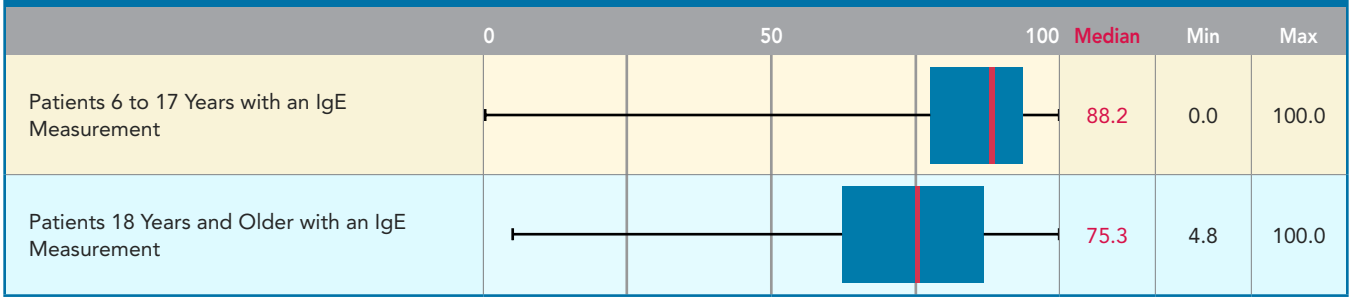
	0 — 50 — 100	Median	Min	Max
Patients Under 18 Years Evaluated by a Respiratory Therapist/Physical Therapist		96.0	0.0	100.0
Patients 18 Years and Older Evaluated by a Respiratory Therapist/Physical Therapist		95.2	0.0	100.0
Patients Under 18 Years Evaluated by a Dietitian/Nutritionist		97.6	0.0	100.0
Patients 18 Years and Older Evaluated by a Dietitian/Nutritionist		88.9	0.0	100.0
Patients Under 18 Years Evaluated by a Social Worker		95.0	0.0	100.0
Patients 18 Years and Older Evaluated by a Social Worker		85.5	0.0	100.0

Percent of Patients Evaluated by Multidisciplinary Care Team Members, 2003–2013



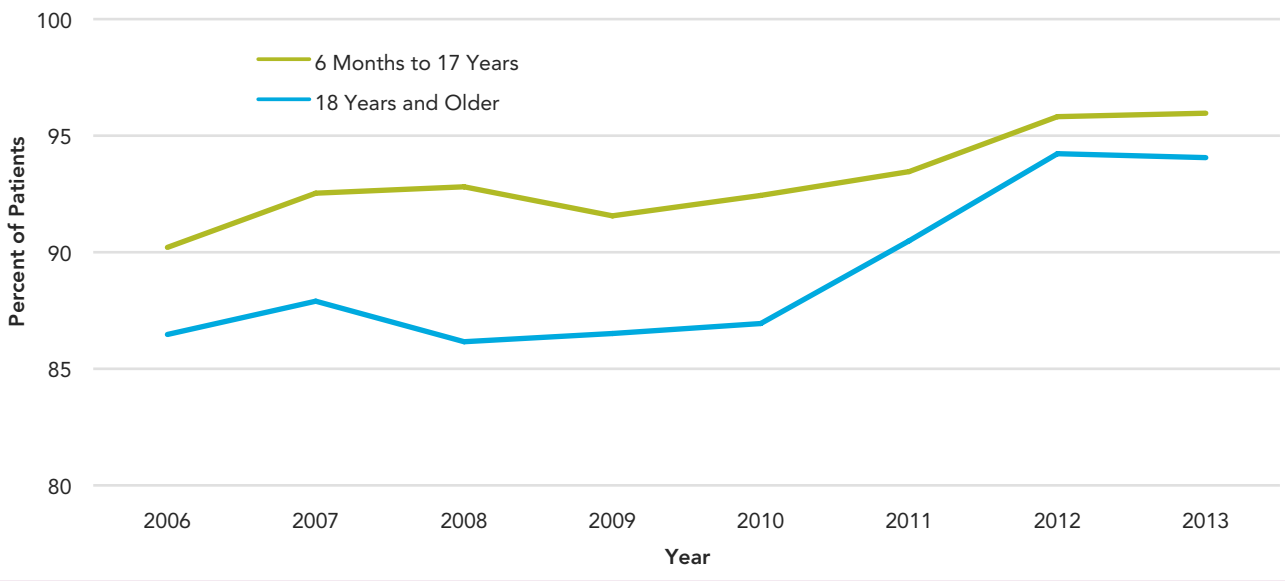
The CF Foundation Consensus Statement on ABPA recommends screening patients 6 years and older for ABPA by annual measurement of total serum IgE concentration.[24]

Percent of Patients with an IgE Measurement, by Center



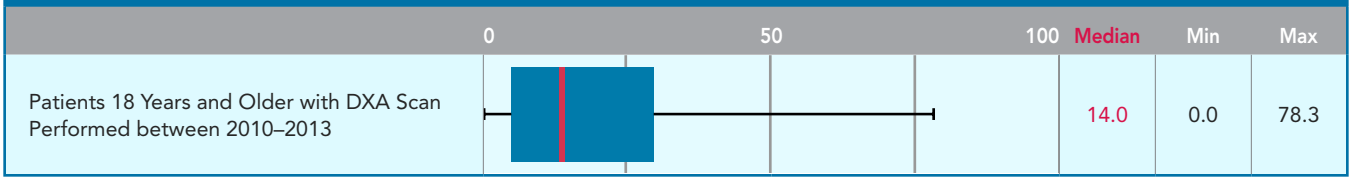
The CDC's Advisory Committee on Immunization Practices recommends influenza vaccination for all CF patients ages 6 months and older.[25] Patients with unknown vaccination status (16.2%) and patients reported as "allergic/refused" (2.7%) were excluded from the analyses.

Percent of Patients Receiving an Influenza Vaccine, 2006–2013



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 scan.[26] Note that patients may have had a DXA scan in a previous year.

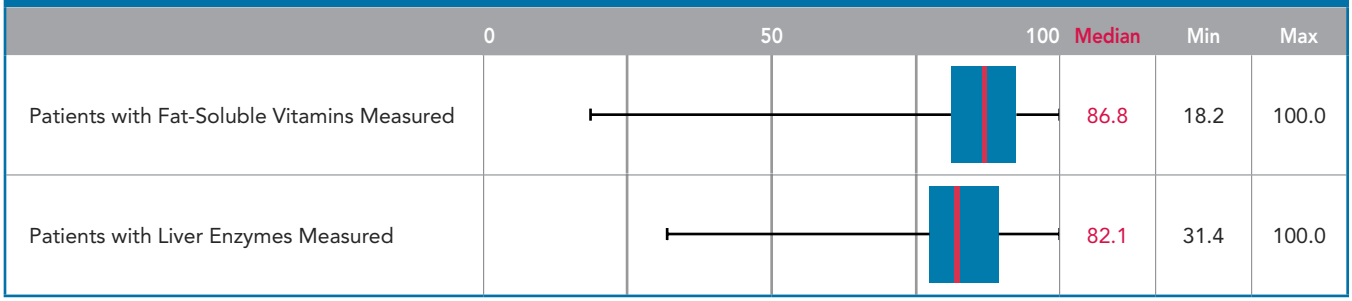
Percent of Patients Screened with a DXA Scan, by Center



Includes any DXA scans performed 2010–2013.

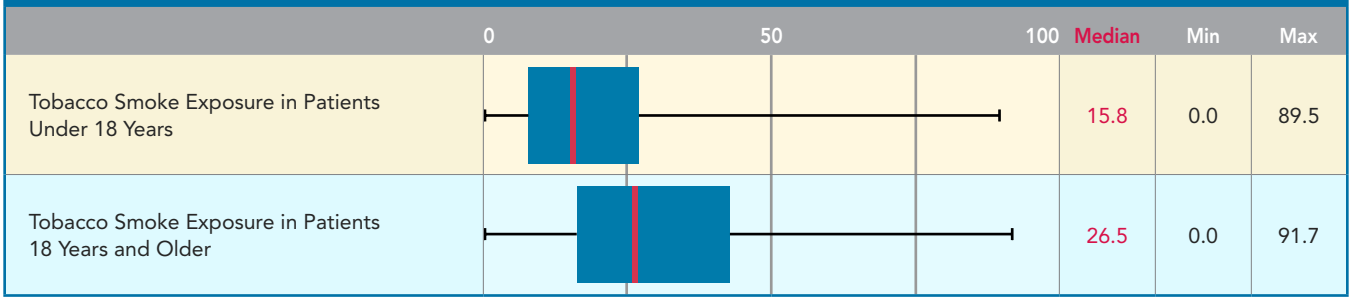
CF Foundation guidelines recommend annual measurement of fat-soluble vitamins to screen for vitamin deficiency.[21,27] The CF Foundation Hepatobiliary Disease Consensus Group recommends a yearly panel of liver blood tests for all CF patients to screen for possible liver disease.[28]

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



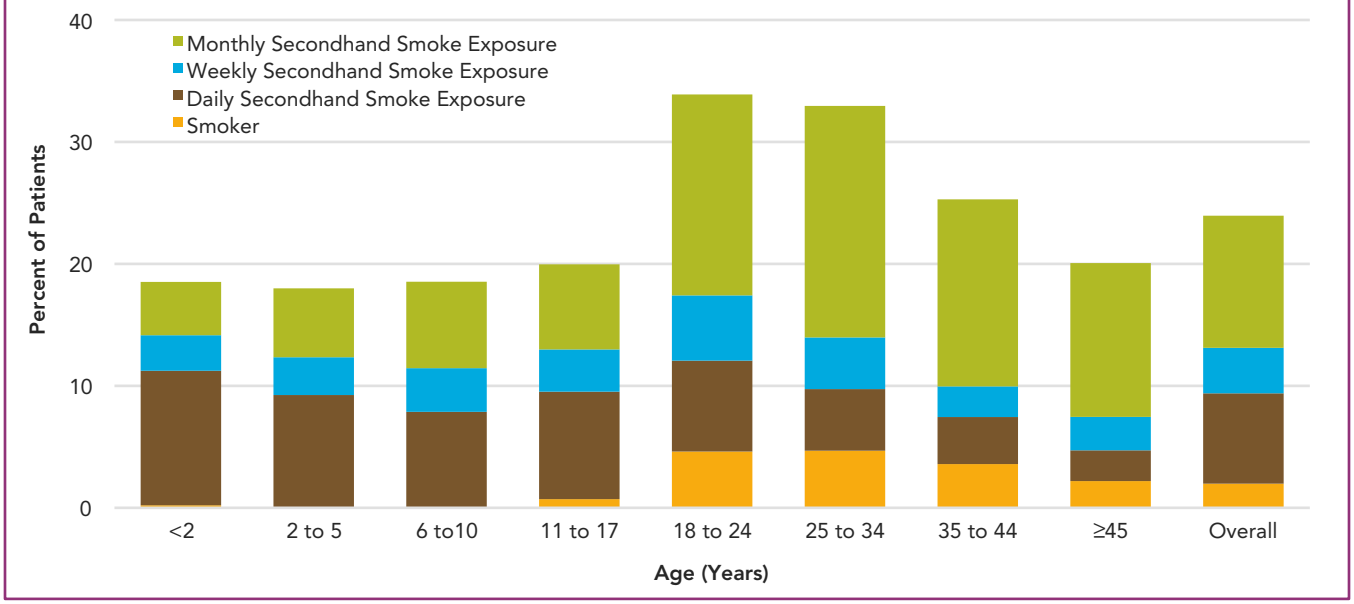
In 2013, 23.5 percent of individuals with CF reported monthly or more frequent exposure to tobacco smoke, either secondhand or as a smoker themselves. Exposure to tobacco smoke is a substantial problem that causes disease and premature death in children and adults.[29] Cigarette smoking prevalence is lower in the CF population than in the general U.S. population — only 4.6 percent of CF patients 18 years and older are smokers, compared with 18.1 percent in the general population in 2012.[30] However, smoking and secondhand smoke exposure remain a significant concern, especially for infants and young adults. Smoke exposure was unknown for 36.0 percent of patients. These patients were excluded from analyses.

Percent of Patients Exposed to Tobacco Smoke, by Center



Includes any exposure to tobacco smoke reported in the Registry, i.e., exposure to secondhand smoke (daily, weekly, monthly) and patients who are smokers.

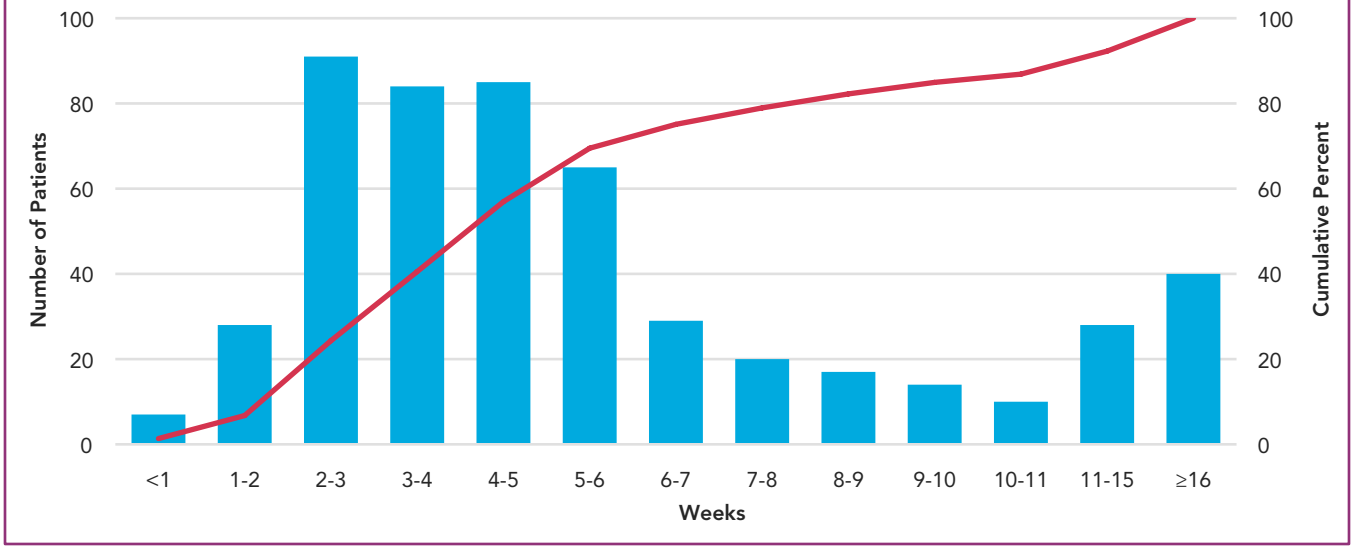
Tobacco Smoke Exposure by Age in 2013



Infant Care Guidelines

The CF Foundation guidelines for diagnosis of cystic fibrosis recommend that infants with a positive newborn screen for CF 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 begin.[8]

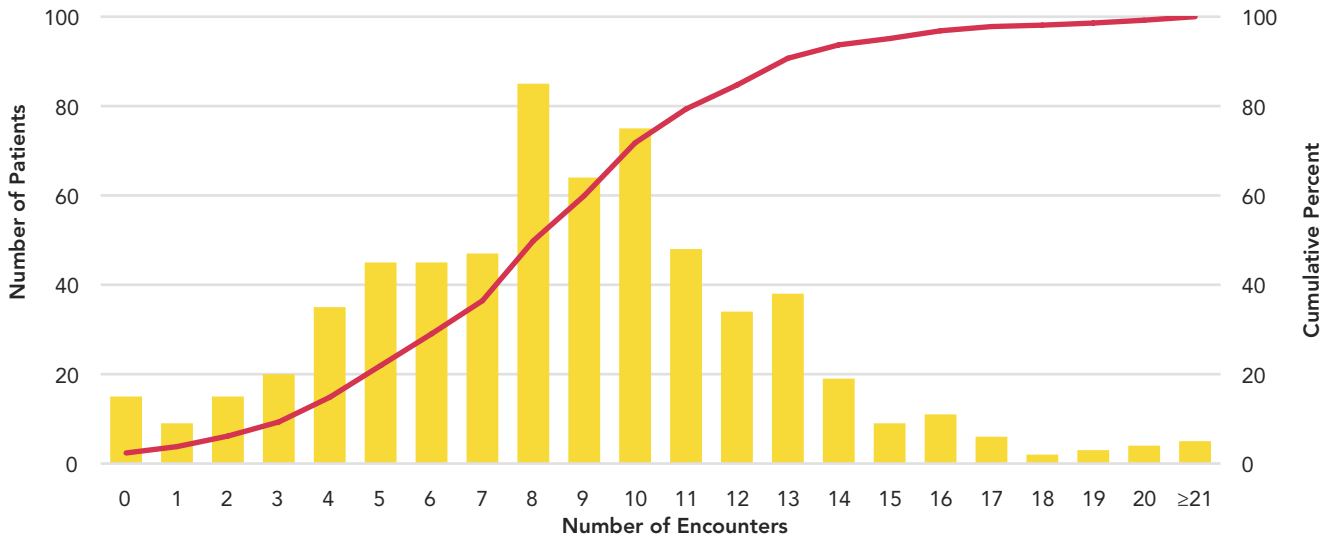
Time from Birth to First Recorded Sweat Test for Infants with CF Born in 2012 and Detected by Newborn Screening (n=518)



The chart shows data for children born in 2012 because a full year of data is available for these patients. There were 116 infants with CF born in 2012 and detected by newborn screening not represented in this chart for whom a sweat test value has not been reported in the Registry.

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.[8] We would therefore expect patients to have around 9 visits in the first year of life, which is reflected in the chart below. There is marked variation in the number of encounters across the care center network among patients in the first year of life.

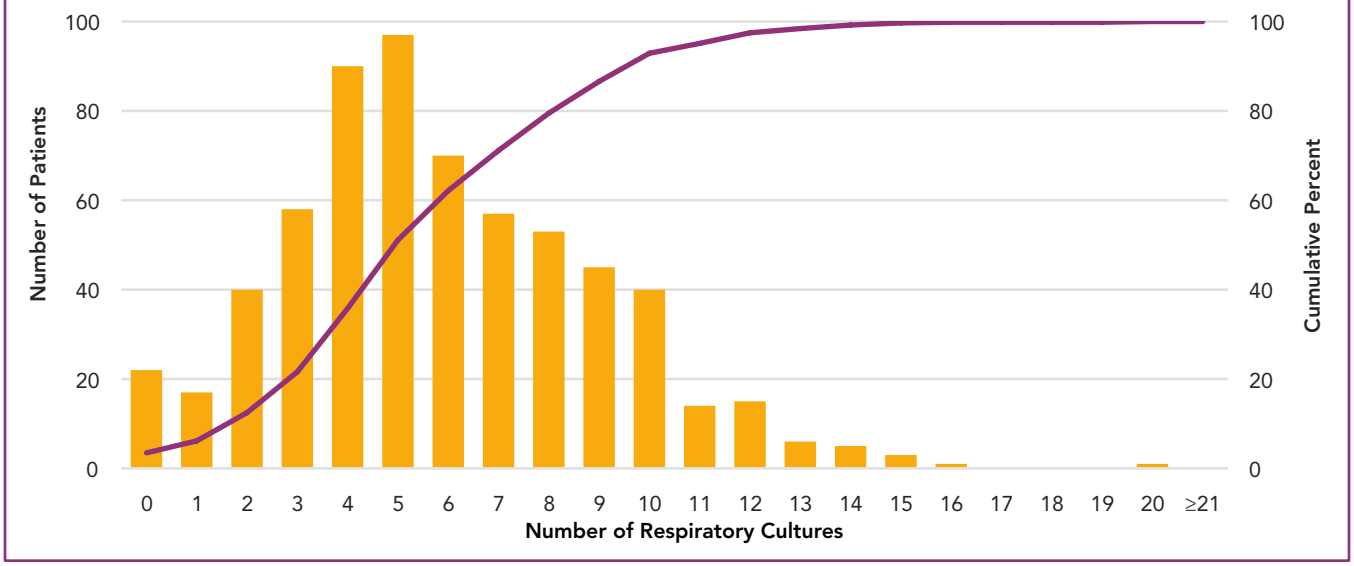
Number of Encounters in the First Year of Life for Infants with CF Born in 2012 and Detected by Newborn Screening (n=634)



The chart shows data for children born in 2012 because a full year of data is available for these patients.

Respiratory cultures are being collected at the majority of clinic visits. Guidelines recommend cultures be performed at least quarterly during the first two years of life.[8]

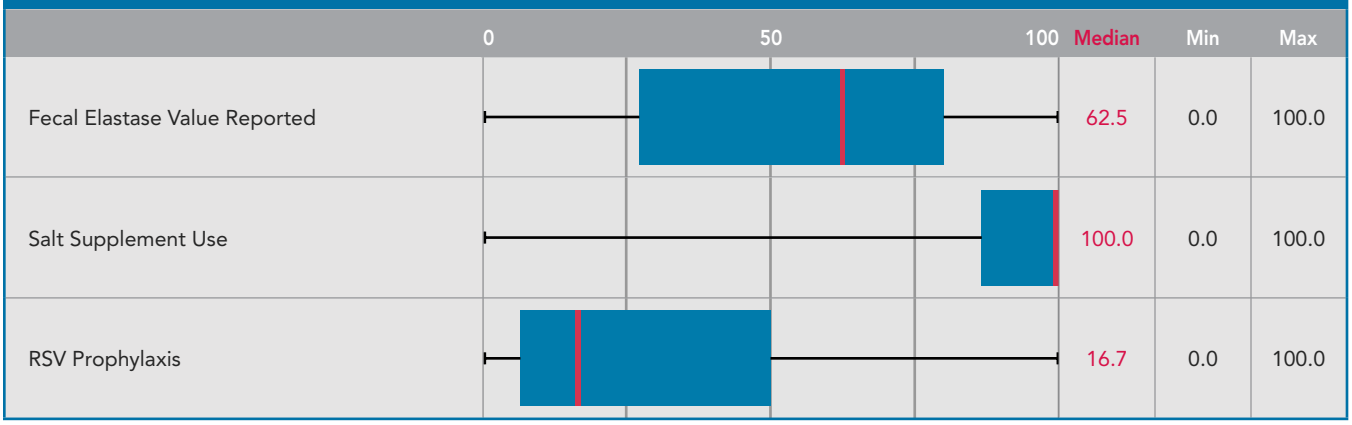
Number of Respiratory Cultures in the First Year of Life for Infants with CF Born in 2012 and Detected by Newborn Screening (n=634)



The chart shows data for children born in 2012 because a full year of data is available for these patients.

Fecal elastase testing, an objective measure of pancreatic function, is recommended in the infant care guidelines.[8] 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 across the care center network. Despite the current lack of compelling evidence supporting the efficacy of palivizumab in children with CF,[31] the infant care guidelines recommend that its use be considered for infants with CF.[8] Nearly all centers are prescribing the therapy for some of their infants.

Percent of Patients Under 24 Months Meeting Guidelines, by Center

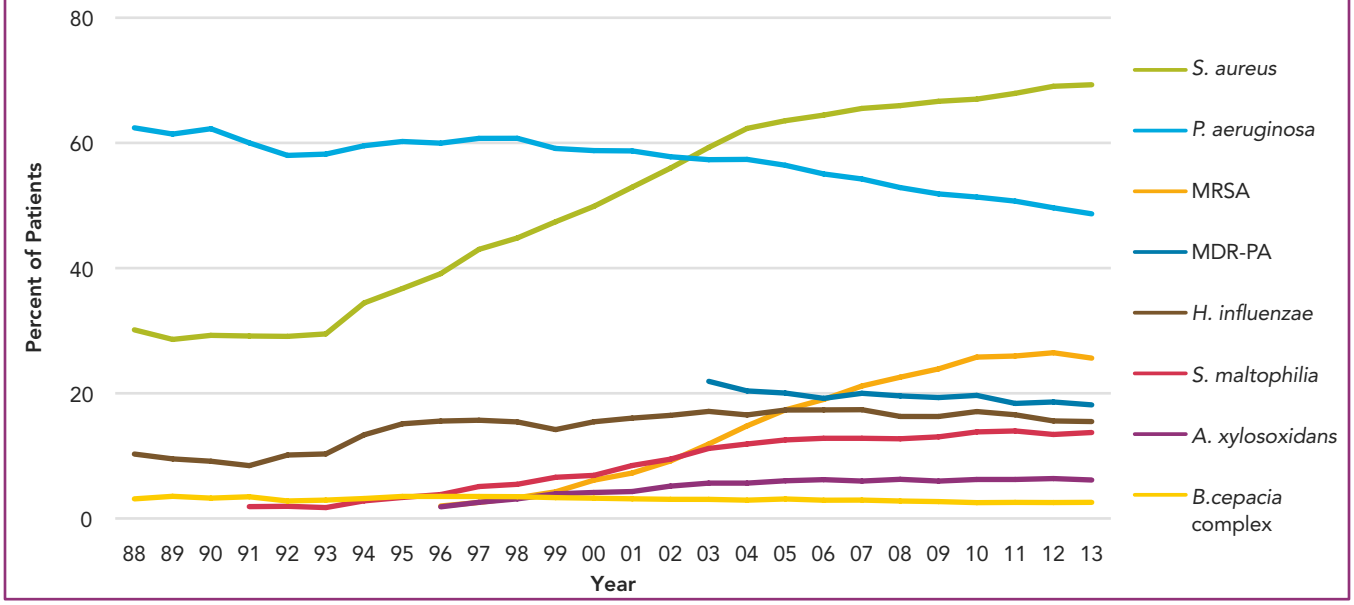


MICROBIOLOGY

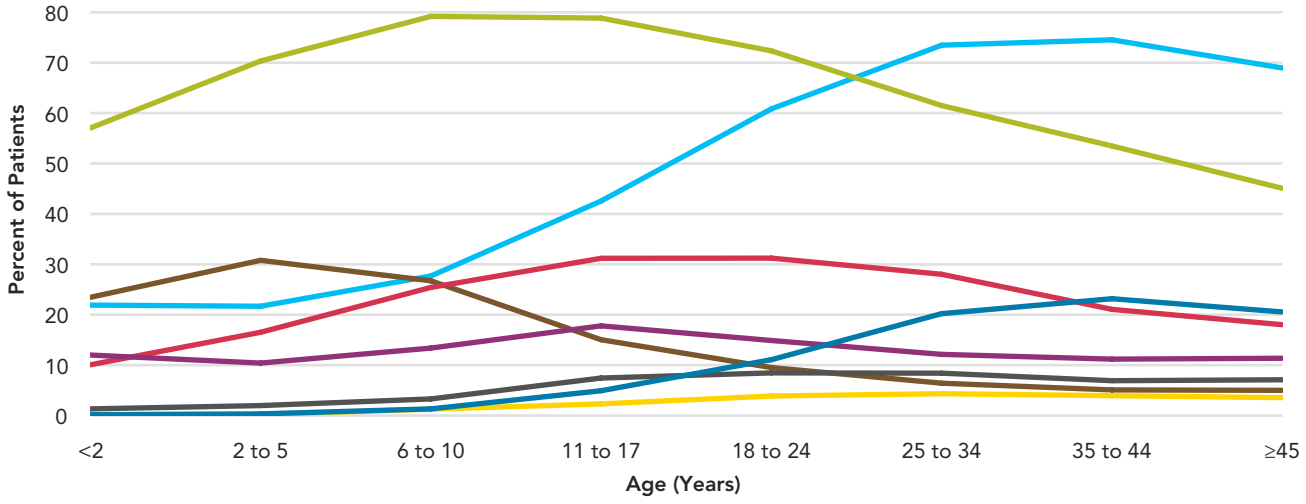
Pulmonary infections represent a serious and chronic problem for most individuals with CF. This section provides information on the trends in CF pathogens over time and by age groups. Updated infection prevention and control guidelines provide the current best practices for reducing exposure to CF pathogens in the health care setting and in everyday life.[23]

The prevalence of P. aeruginosa *has been steadily decreasing and, as of 2003, is no longer the most common pathogen cultured in individuals with CF, while increases in the prevalence of* S. aureus, *both MRSA and MSSA, and* S. maltophilia *have been observed. The observed decrease in the prevalence of* P. aeruginosa *may in part reflect the widespread adoption of eradication strategies for initial acquisition of the organism. Some of the increase in* S. aureus *and MRSA may be due to improved microbiologic practices for the detection of Gram-positive organisms.*

Prevalence of Respiratory Microorganisms, 1988–2013



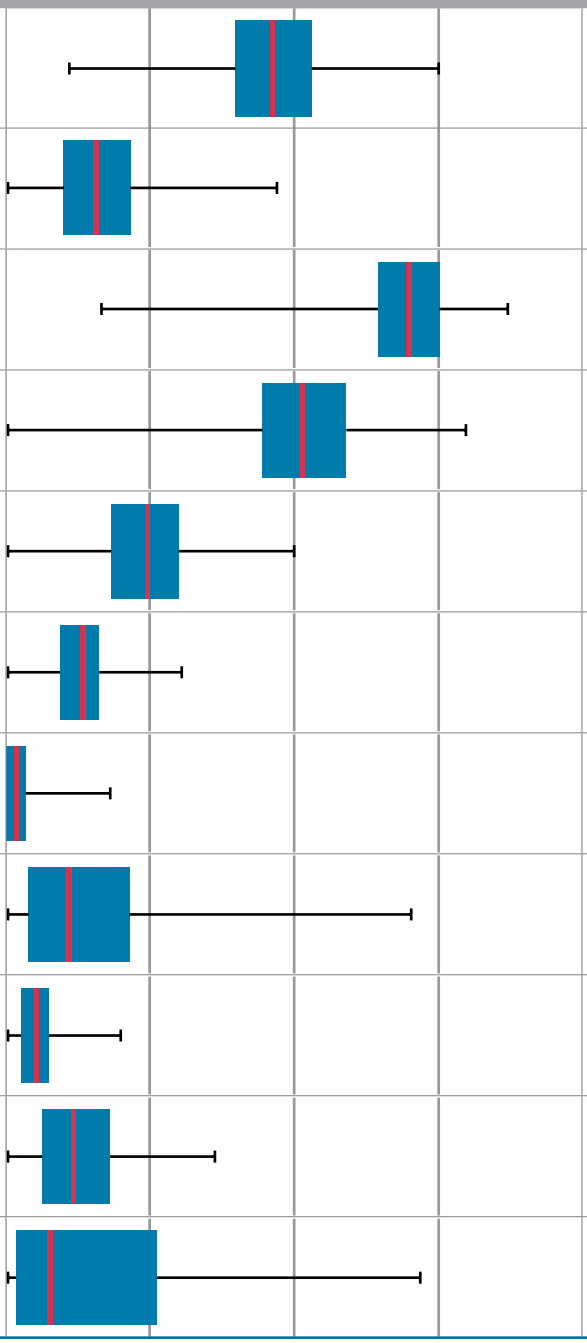
Prevalence of Respiratory Microorganisms by Age in 2013



Rates of multidrug-resistant *P. aeruginosa* infection have increased substantially in older CF patients. These findings likely reflect cumulative exposure to antibiotics; the clinical significance is unclear. Multidrug resistance is defined as resistance to all antibiotics tested in two or more classes.

Variation in the prevalence of some microorganisms across the care center network exposes opportunities to improve adherence to CF Foundation infection prevention and control guidelines.[32,33]

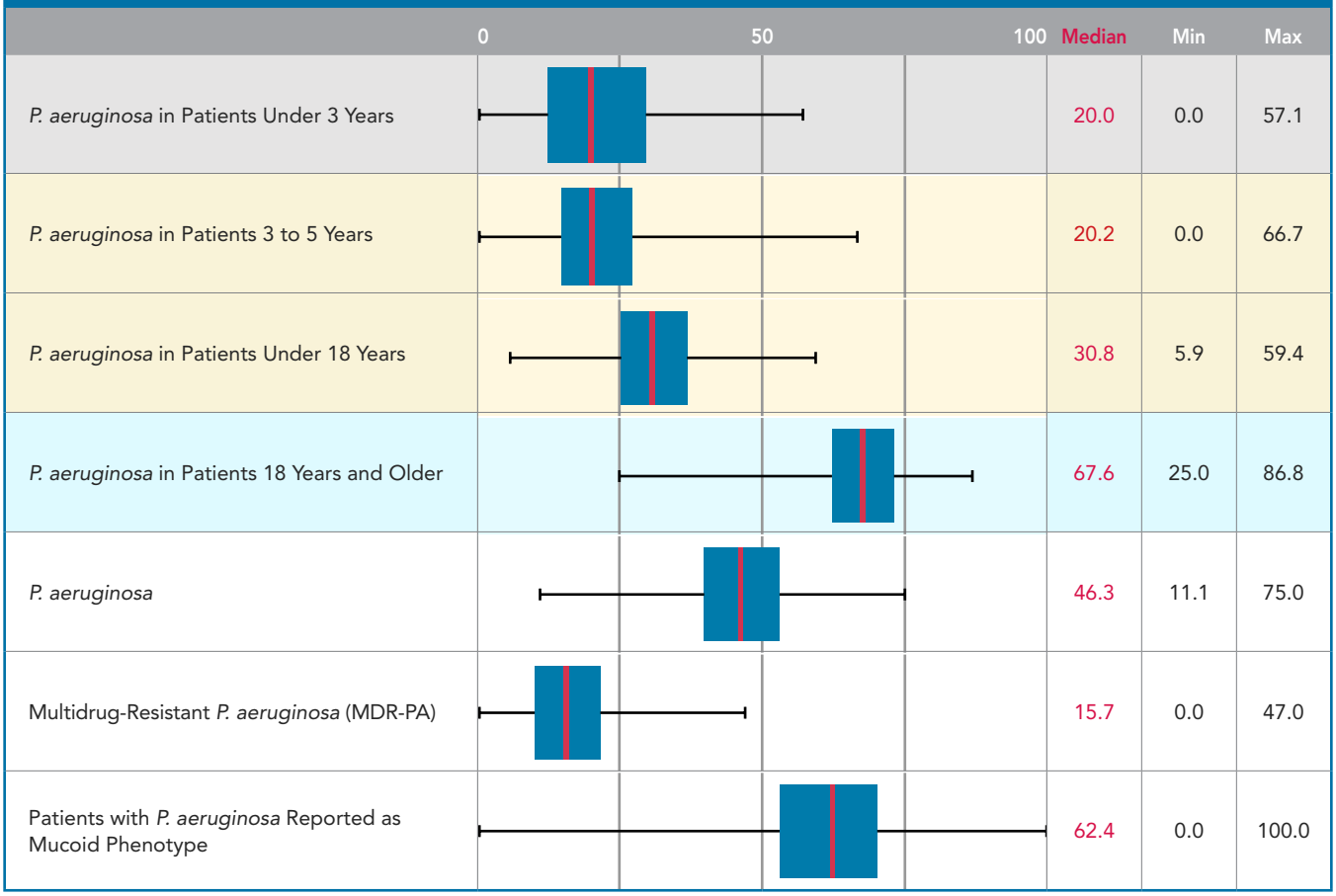
Percent of Patients with Cultures Positive for Respiratory Microorganisms, by Center



	Median	Min	Max
P. aeruginosa	46.3	11.1	75.0
Multidrug-Resistant *P. aeruginosa* (MDR-PA)	15.7	0.0	47.0
S. aureus	69.9	16.7	87.0
Methicillin-Sensitive *S. aureus* (MSSA)	51.5	0.0	79.7
Methicillin-Resistant *S. aureus* (MRSA)	24.6	0.0	50.0
S. maltophilia	13.5	0.0	30.6
B. cepacia complex	2.0	0.0	18.2
H. influenzae	11.0	0.0	70.2
A. xylosoxidans	5.5	0.0	20.0
Aspergillus	11.9	0.0	36.3
Candida	7.8	0.0	71.8

A large percentage of adolescents and adults with CF become chronically infected with *P. aeruginosa*, and there is less variation observed across centers. Among these patients, however, there is wide variation in the number of patients reported as having a mucoid phenotype. This may in part reflect differences in reporting the colony phenotype among microbiology labs.

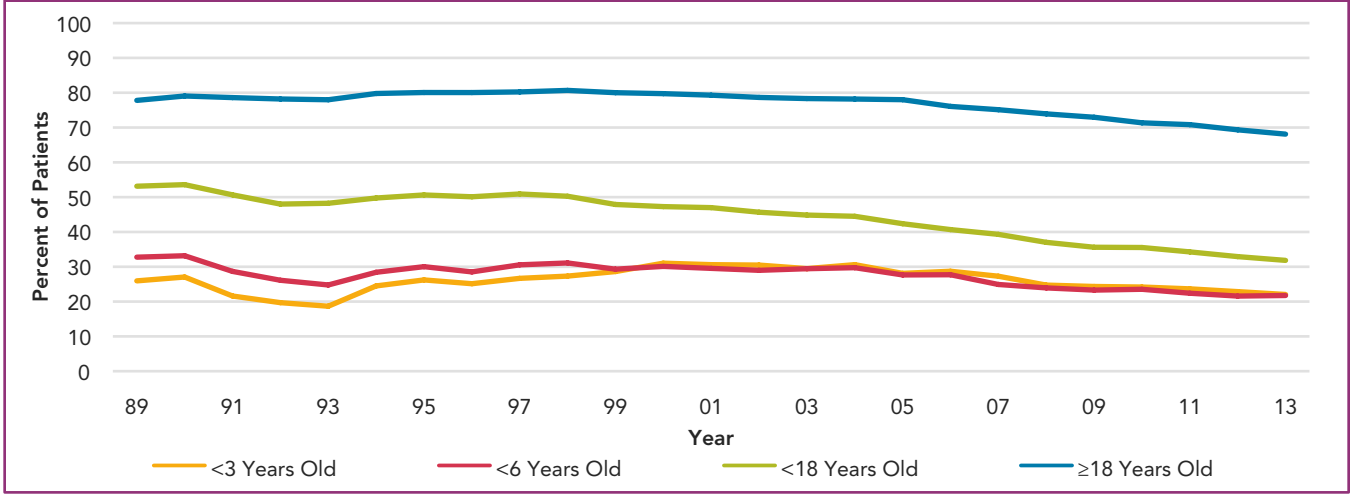
Percent of Patients with Cultures Positive for *P. aeruginosa*, by Center



	Median	Min	Max
P. aeruginosa in Patients Under 3 Years	20.0	0.0	57.1
P. aeruginosa in Patients 3 to 5 Years	20.2	0.0	66.7
P. aeruginosa in Patients Under 18 Years	30.8	5.9	59.4
P. aeruginosa in Patients 18 Years and Older	67.6	25.0	86.8
P. aeruginosa	46.3	11.1	75.0
Multidrug-Resistant *P. aeruginosa* (MDR-PA)	15.7	0.0	47.0
Patients with *P. aeruginosa* Reported as Mucoid Phenotype	62.4	0.0	100.0

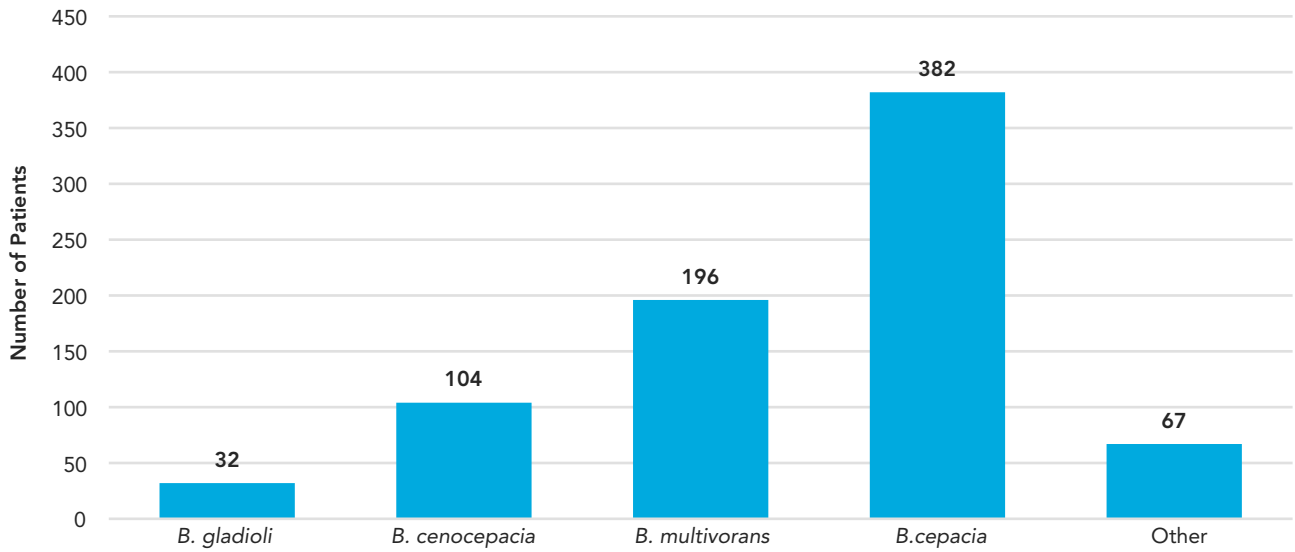
The largest decrease over time is observed among individuals under the age of 18, 6 to 17 year olds in particular.

P. aeruginosa Infection by Age Cohort, 1989–2013



In 2013, 662 patients had a culture positive for *B. cepacia* complex: 94.3 percent of those isolates were confirmed at the CF Foundation *Burkholderia cepacia* Research Laboratory and Repository at the University of Michigan.

Burkholderia Species Confirmed at the *B. cepacia* Research Lab in 2013



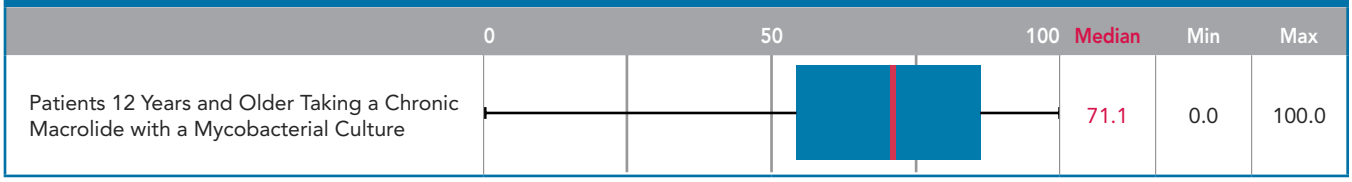
Data are not mutually exclusive. Some patients have more than one species.
Note that B. gladioli *is not part of the* B. cepacia *complex.*

Nontuberculous Mycobacteria (NTM)

The prevalence of nontuberculous mycobacteria (NTM) infections is increasing in the general population.[34] Since 2010, the Registry has collected more robust information on mycobacterial cultures and NTM infections.

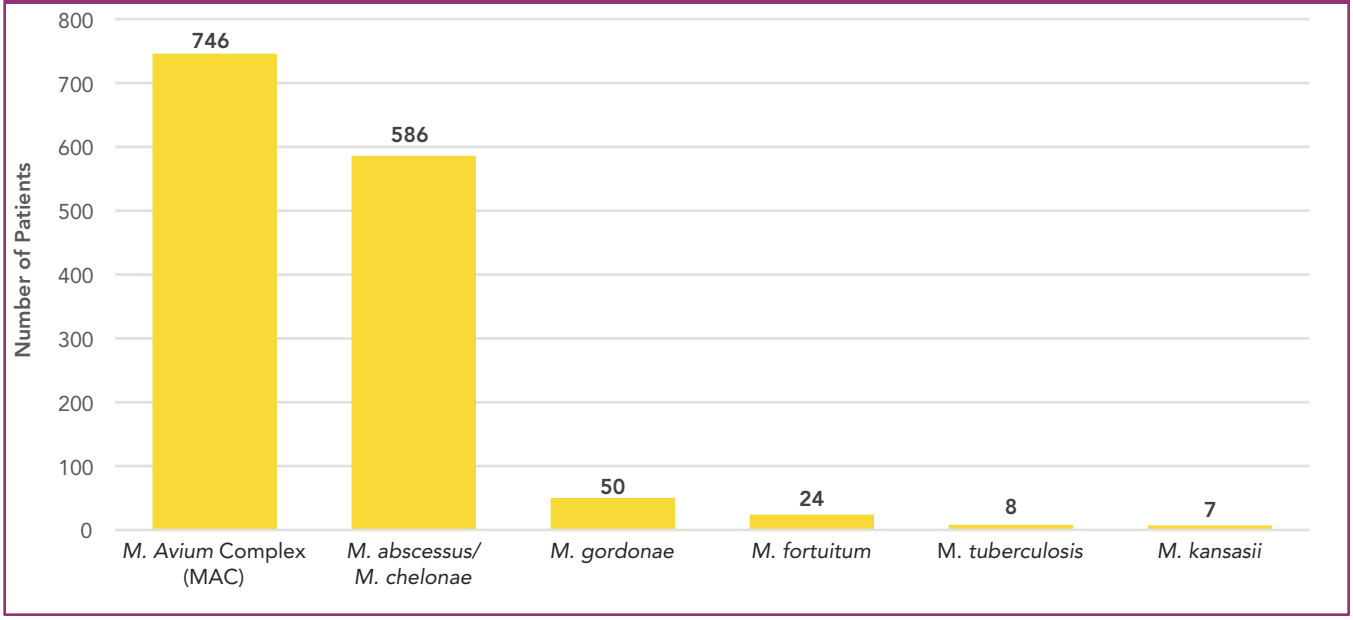
Patients should be screened for nontuberculous mycobacteria before and 6 months after beginning azithromycin and annually thereafter.[6] The data show wide center-level variation in this measure.

Percent of Patients with a Mycobacterial Culture, by Center



Of the 12,873 patients who had a mycobacterial culture in 2013, 1,543 (12.0%) had a mycobacterial species isolated one or more times. The relative proportion of *M. abscessus* isolated in 2013 is higher than that reported over a decade ago in the CF Foundation-supported multicenter prevalence study.[35]

Mycobacterial Species Isolated in 2013



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

Because patients may not have a mycobacterial culture each year, mycobacterial culture data from 2010 to 2013 were examined as well. The percent of patients with a mycobacterial culture at any time from 2010 to 2013, regardless of age or chronic macrolide use, is 59.3 percent. Of the 18,807 patients who were cultured, 3,069 had one or more mycobacterial species isolated (16.3%).

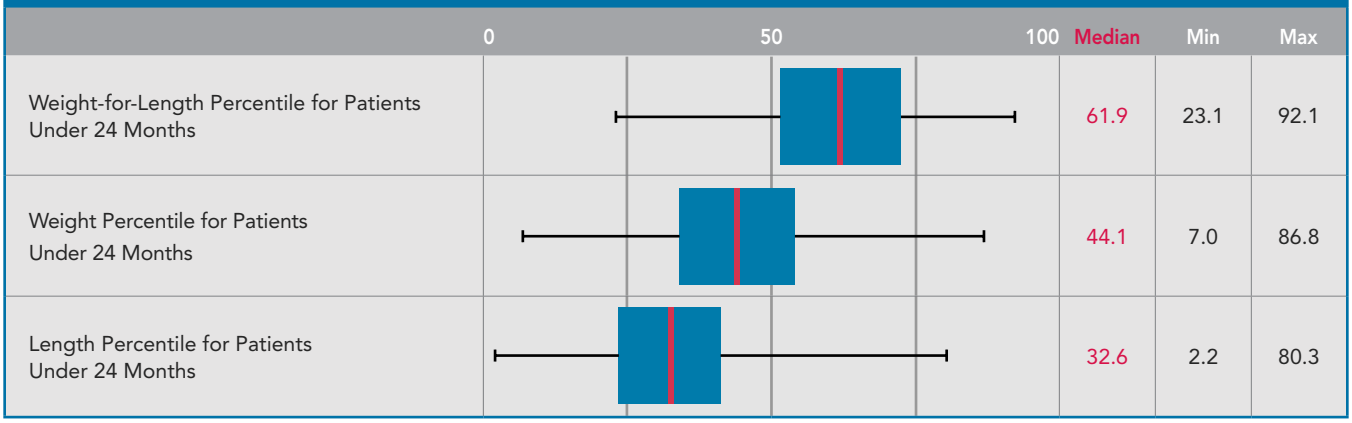
NUTRITION

Nutritional outcomes are a key measure of health in individuals with CF. Since 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. In addition to measures of nutritional status, data are displayed on pancreatic enzyme replacement therapy and other nutritional interventions.

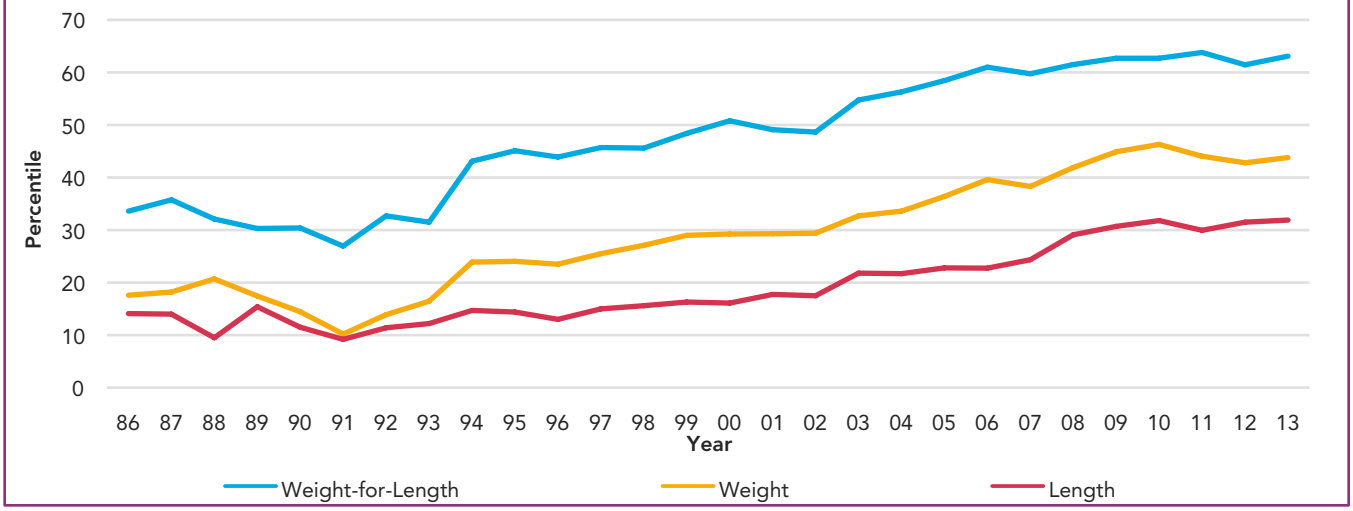
Center-level data show significant variation in nutritional outcomes. Epidemiologic evidence suggests that nutritional status early in life is predictive of future pulmonary function.[36] The data also show significant variation in the use of pancreatic enzymes, nutritional supplements, and acid blockers across the care center network.

The goal established by the CF Foundation nutrition guidelines is a weight-for-length at or above the 50th percentile by 2 years of age.[27] Over 50 percent of centers are meeting this goal. Median weight and length percentiles are well below the 50th percentiles but improving over time.

Median WHO Nutritional Outcomes for Patients Under 24 Months, by Center

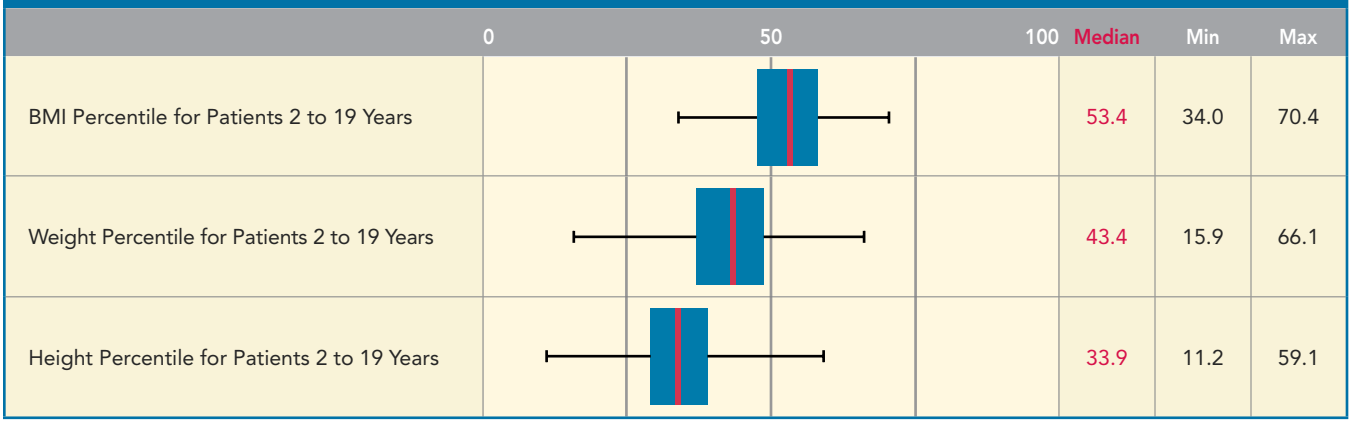


Median WHO Nutritional Outcome Percentiles for Patients Under 24 Months, 1986–2013



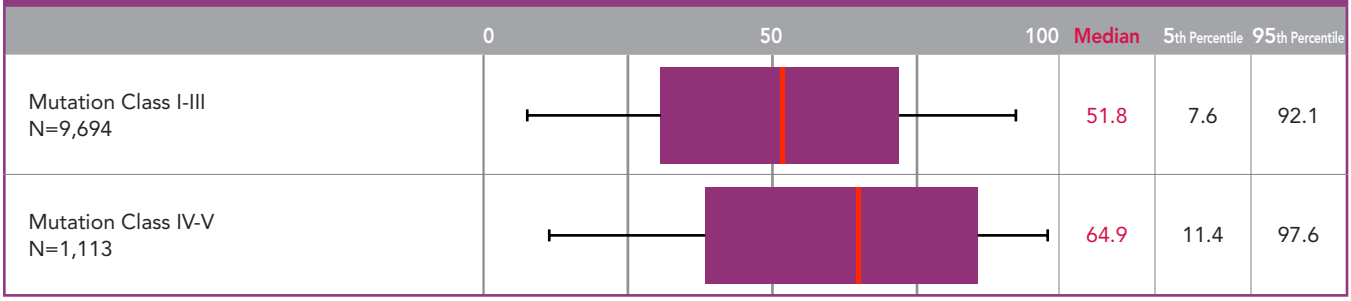
The goal established by the CF Foundation nutrition guidelines for children 2 to 19 years of age is a BMI at or above the 50th percentile.[27] The median BMI percentile at more than half of the centers meet the guideline goal. Median weight and height percentiles are below the 50th percentile.

Median CDC Nutritional Outcomes for Patients 2 to 19 Years, by Center



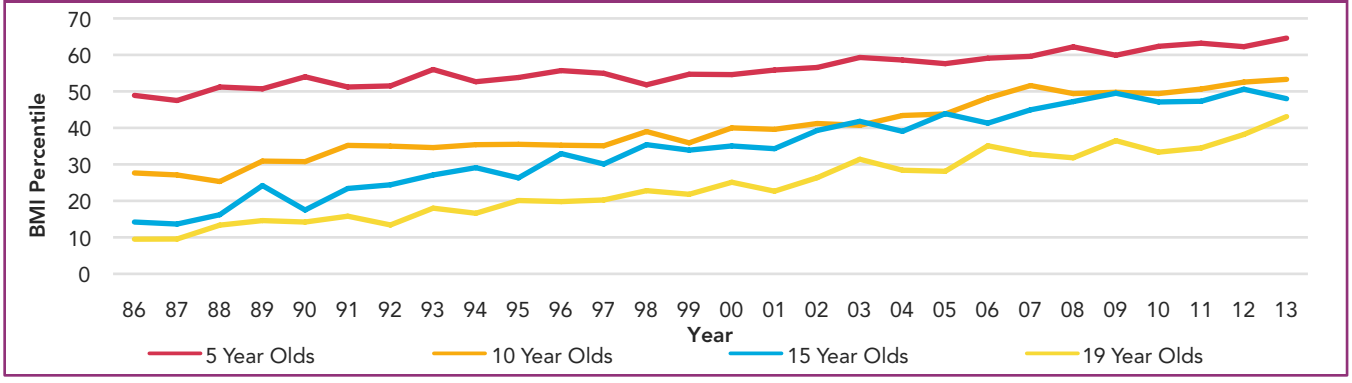
Children grouped in mutation Class IV-V have higher BMI percentiles than those in Class I-III, but there is substantial variation in the outcomes with significant overlap between the two classes.

CDC BMI Percentile for Patients 2 to 19 Years, by Mutation Class



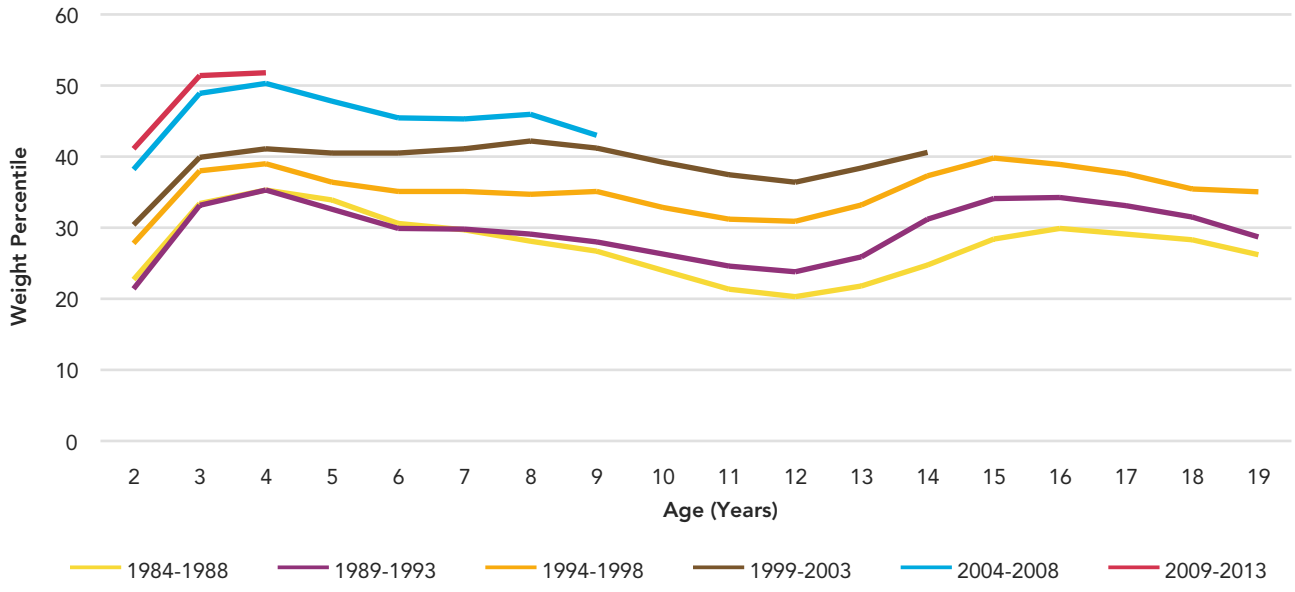
Since 1986, there have been steady increases in median BMI percentile among 2 to 19-year-olds. BMI percentiles decrease with age, but as the result of steeper increases among adolescents ages 15 and 19 than children ages 5 and 10, there is less variation across ages in 2013 as compared to previous years.

Median CDC BMI Percentile by Age, 1986–2013

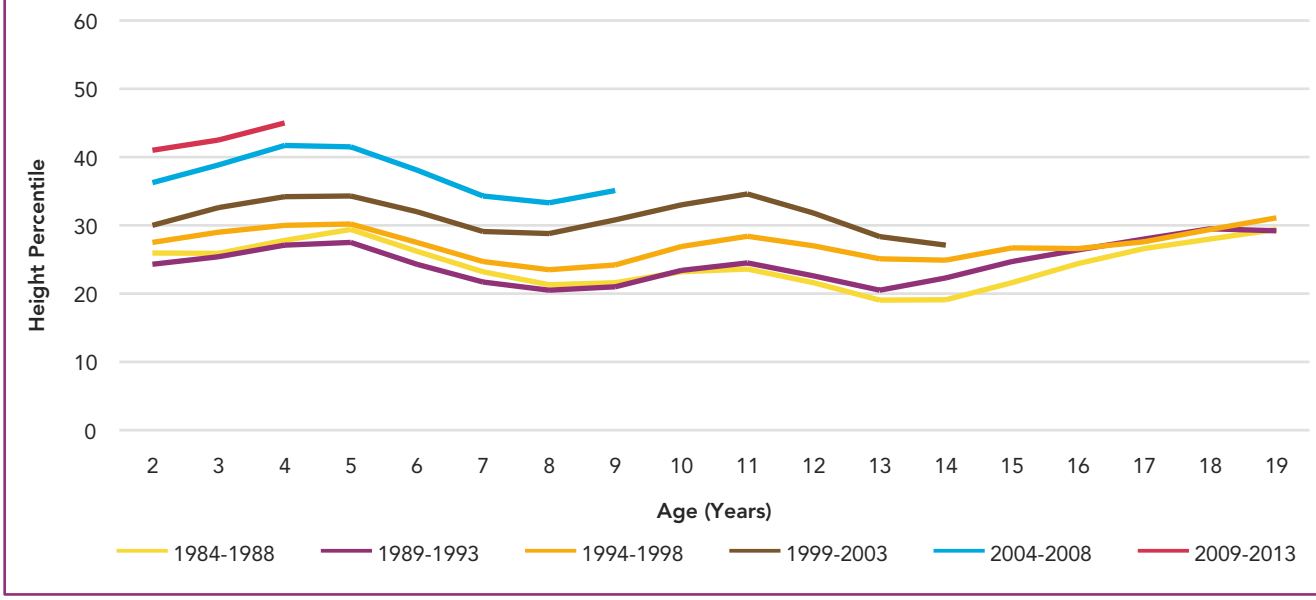


Successive birth cohorts show improved weight and height percentiles, most notably in the youngest cohorts. This is most likely due to widespread implementation of newborn screening.

Median CDC Weight Percentile vs. Age by Birth Cohort

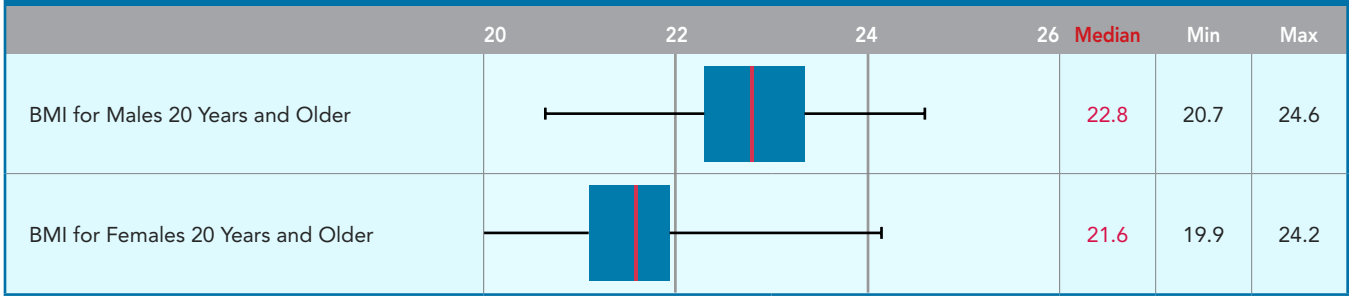


Median CDC Height Percentile vs. Age by Birth Cohort



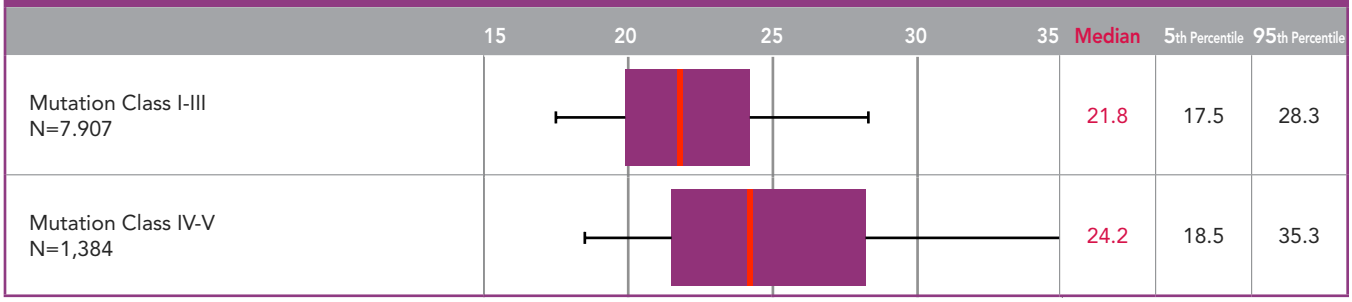
The goal established by the CF Foundation nutrition guidelines is a BMI at or above 22 for females and 23 for males age 20 and older.[27]

Median BMI Value for Patients 20 Years and Older, by Center



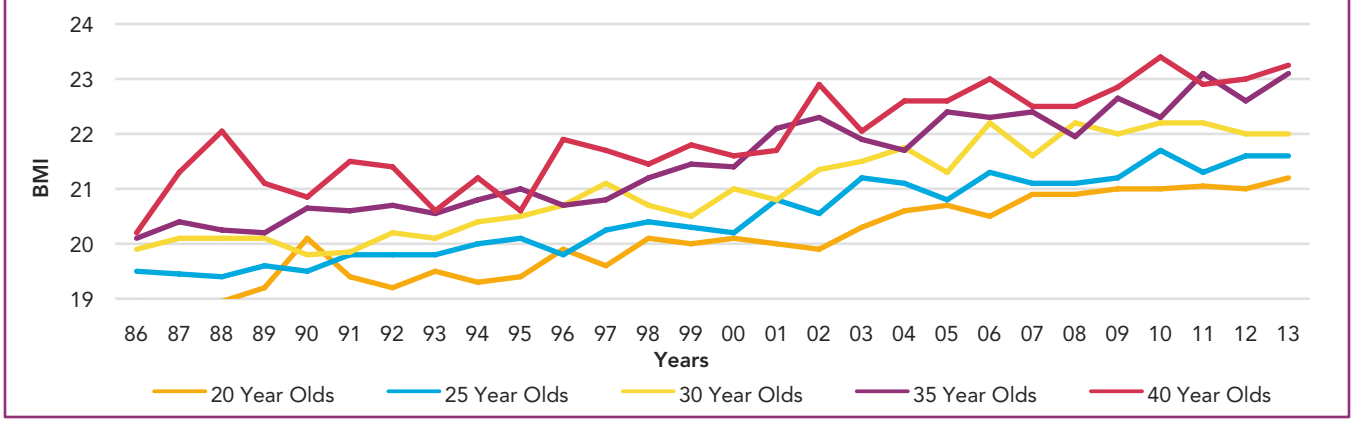
Adults in mutation Class IV-V have higher BMI values than adults in Class I-III.

BMI Value for Patients 20 Years and Older, by Mutation Class



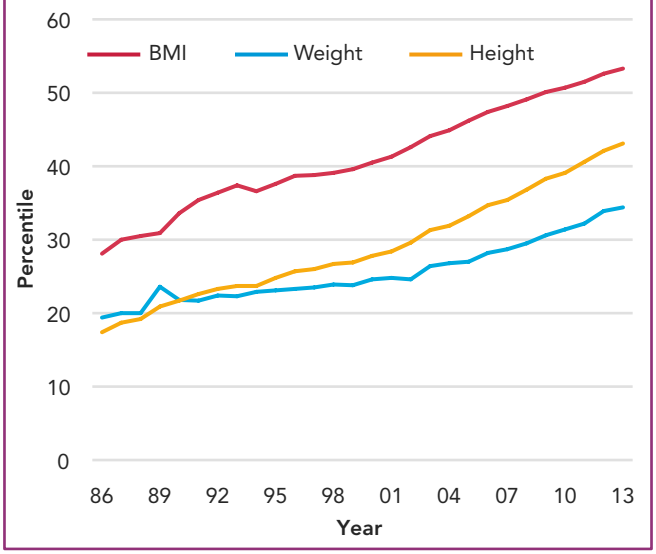
The average BMI of young adults has improved markedly over the past two decades. Small numbers of patients at each age lead to fluctuation year to year, but overall, for each of the ages examined, the trend is one of increasing median BMI. Increases in BMI at older ages may in part relate to an increase in adult diagnoses with mutations associated with milder disease.

Median BMI Value by Age, 1986–2013

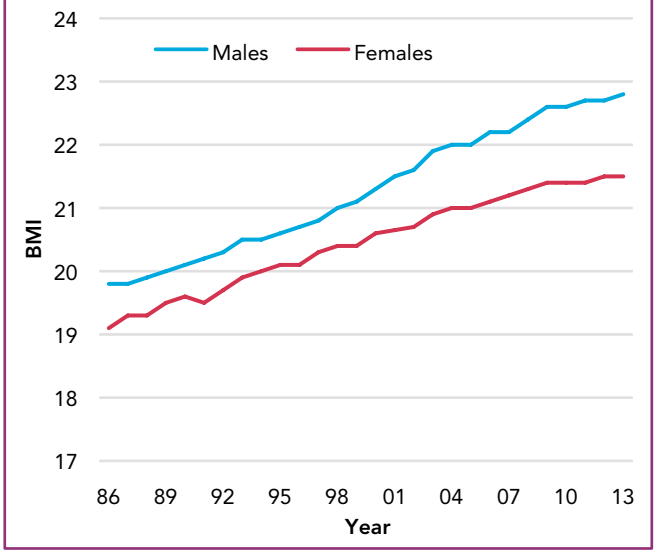


Significant progress has been made since the 1980s for both the pediatric and adult CF populations. Since 2008, the median BMI percentile of CF patients ages 2 to 19 years has met the CF Foundation goal of the 50th percentile. These analyses show dramatic improvements in nutritional status. The aging of the patient population and a greater number of late diagnoses with milder genotypes may also be contributing to this trend.

Median Nutritional Outcome Percentiles for Patients 2 to 19 Years, 1986–2013



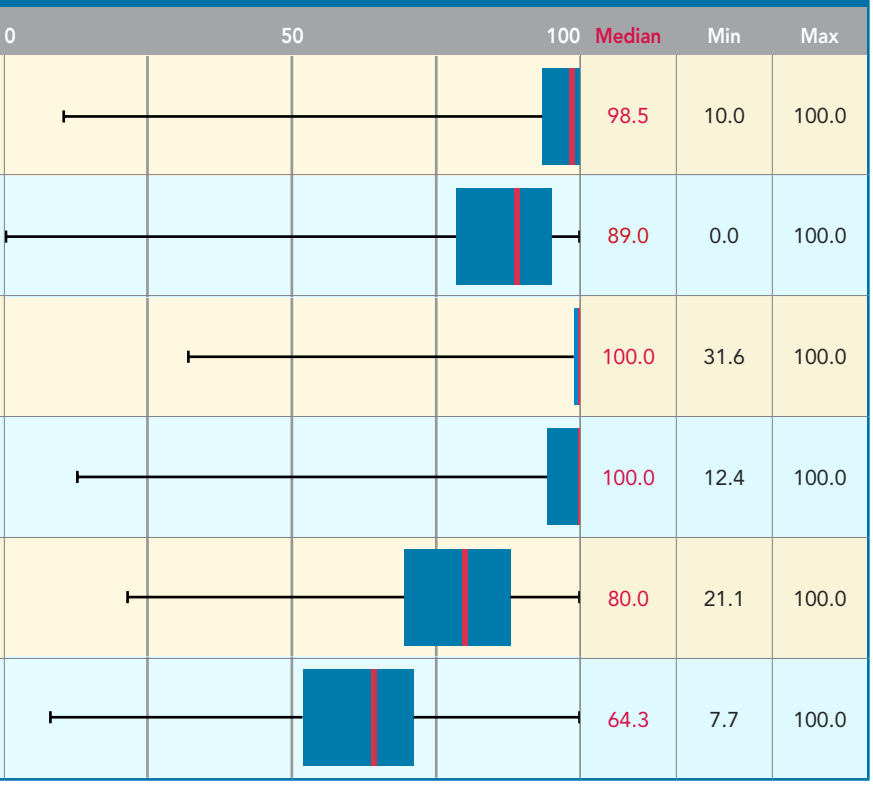
Median BMI Value for Patients 20 Years and Older, 1986–2013



The CF Foundation nutrition guidelines recommend the use of nutritional supplements in addition to usual dietary intake for adults and children with weight deficits.[27] While there have been substantial improvements in nutritional outcomes over time, the median percent of patients who did not meet nutritional goals is 45.3 for children and 52.6 for adults with CF.

Overall, patients who are not meeting nutritional goals as set out in the nutrition guidelines[27] have access to a dietitian and have had their oral intake assessed. Oral or tube supplemental feeding is used in the majority of centers, more frequently for children than adults.

Assessment and Treatment of Patients Not Meeting Nutrition Goals, by Center



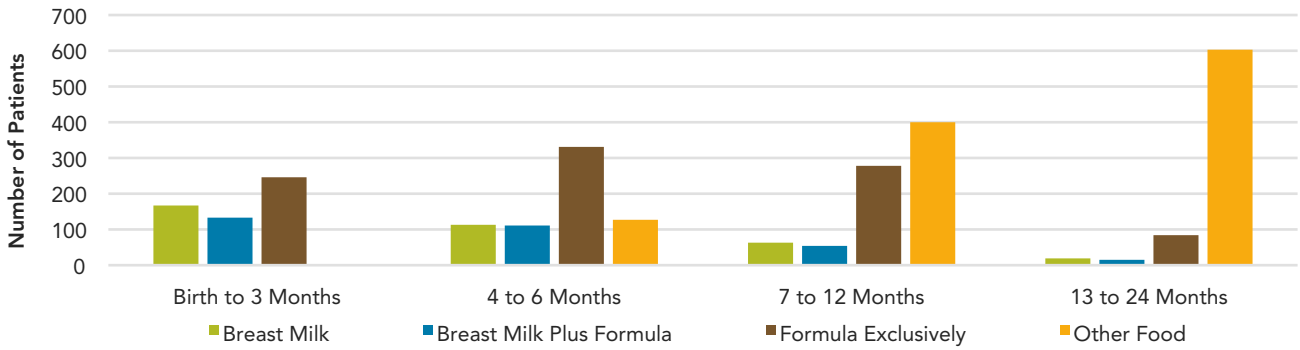
	Median	Min	Max
Patients 2 to 19 Years with BMI Below the 50th Percentile Seen by a Dietitian/Nutritionist	98.5	10.0	100.0
Patients 20 Years and Older with BMI Less than 22 for Females or Less than 23 for Males Seen by a Dietitian/Nutritionist	89.0	0.0	100.0
Oral Intake Assessed in Patients 2 to 19 Years with BMI Below the 50th Percentile	100.0	31.6	100.0
Oral Intake Assessed in Patients 20 Years and Older with BMI Less than 22 for Females or Less than 23 for Males	100.0	12.4	100.0
Oral or Tube* Supplemental Feeding in Patients 2 to 19 Years with BMI Below the 50th Percentile	80.0	21.1	100.0
Oral or Tube* Supplemental Feeding in Patients 20 Years and Older with BMI Less than 22 for Females or Less than 23 for Males	64.3	7.7	100.0

**Includes nasogastric (NG) tube, gastrostomy tube/button (G-tube), jejunal tube (J-tube) and total parenteral nutrition (TPN).*

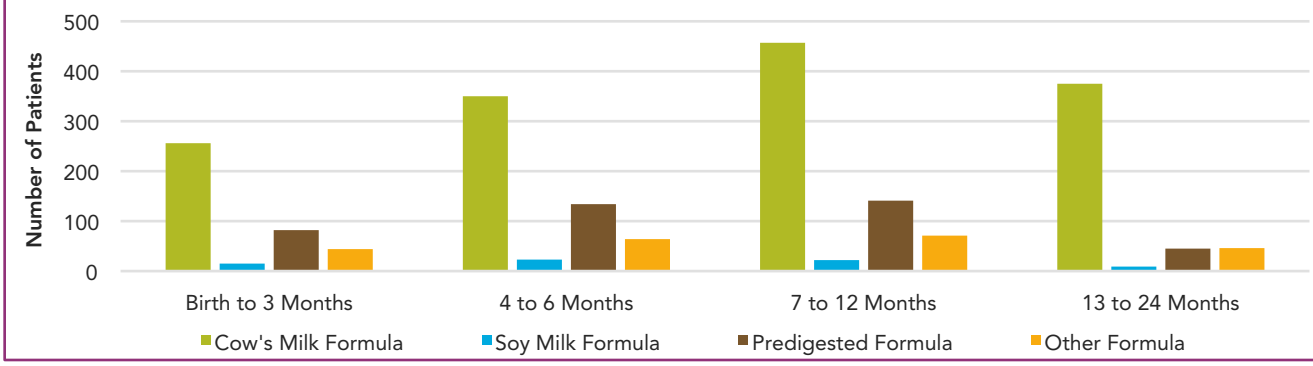
Infant Feeding

The majority of infants with CF receive formula 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.[8]

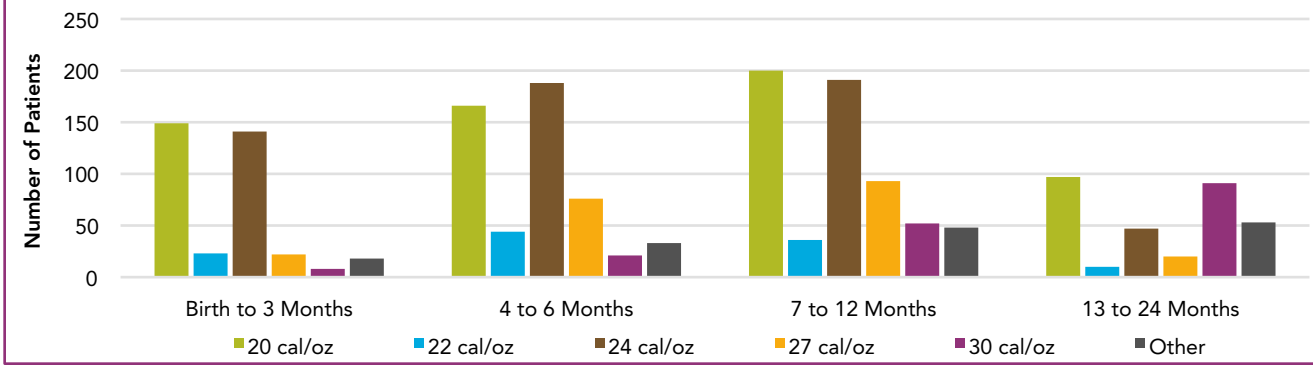
Form of Feeding by Age in 2013*



Type of Formula Feeding by Age in 2013*



Caloric Density of Feeding by Age in 2013*



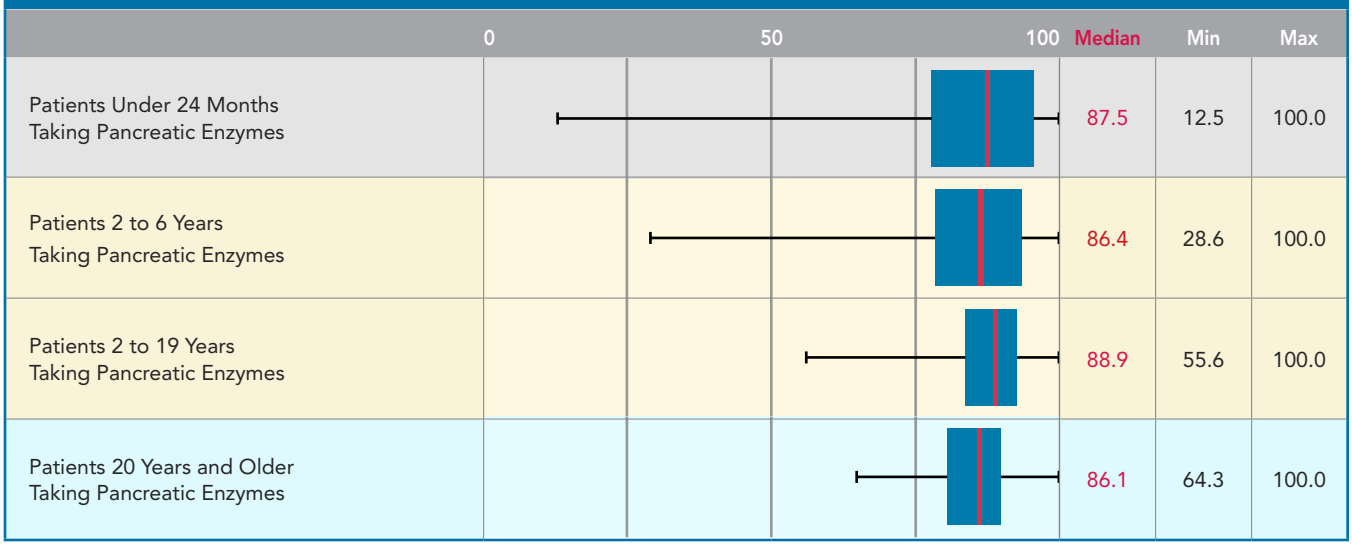
**Infants may be included in more than one age category. They may also be counted more than once within an age category if different answers were entered in separate encounters while within the same age category.*

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.[8]

The greatest variation in enzyme use across the care center network occurs in infants.

Percent of Patients Taking Pancreatic Enzymes, by Center



For infants with CF under age 2, the guidelines recommend assessment of pancreatic function status by fecal elastase.[8] Data on fecal elastase test results have been entered into the Registry since 2010. Uptake of this test is increasing and half of patients under the age of 2 have a fecal elastase test result in the Registry. Among patients with fecal elastase testing results available, almost all patients with a fecal elastase value of less than 100 and the vast majority of patients with a fecal elastase value between 100 and 200 have been prescribed PERT. Approximately one–quarter of patients with fecal elastase values greater than 200 are prescribed pancreatic enzymes.

Percent of Patients Taking Enzymes in 2013 by Fecal Elastase Value

Most Recent Fecal Elastase Value	Patients Under 24 Months	Patients Under 4 Years	All Patients
Less than 100	98.6	98.5	96.9
Between 100 and 200	89.2	89.7	88.3
Greater than or equal to 200	24.2	26.2	28.2
Percent of patients with a fecal elastase value	51.0	37.4	9.9

The infant care guidelines recommend infants detected by newborn screening with two CFTR mutations associated with pancreatic insufficiency, or clinical or laboratory evidence of pancreatic insufficiency, be started on 2,000 to 5,000 lipase units per feeding (total lipase dose) with adjustments as the infant grows.[8]

Lipase Units per Largest Meal for Infants Taking Pancreatic Enzymes, by Center

	Median	Min	Max
Lipase Units per Largest Meal for Patients Under 24 Months Taking Enzymes	13,862	5,121	26,988

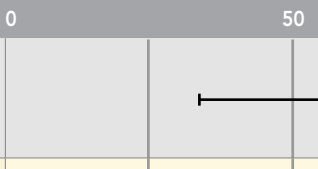
For patients 2 years of age and older, the recommended upper limit for enzyme dosing is 2,500 lipase units/kg/meal and a total of 10,000 lipase units/kg/day.[27]

Lipase Units per Kilogram per Largest Meal for Patients Taking Pancreatic Enzymes, by Center

	Median	Min	Max
Lipase Units per Kilogram per Largest Meal for Patients 2 to 6 Years Taking Enzymes	1,853	1,007	2,740
Lipase Units per Kilogram per Largest Meal for Patients 2 to 19 Years Taking Enzymes	1,846	1,061	2,751
Lipase Units per Kilogram per Largest Meal for Patients 20 Years and Older Taking Enzymes	1,697	958	2,558

The CF Foundation guidelines recommend supplementation with fat-soluble vitamins due to the high prevalence of fat-soluble vitamin deficiency.[8,21,37] The data indicate this recommendation is followed at the vast majority of centers, especially among younger patients.

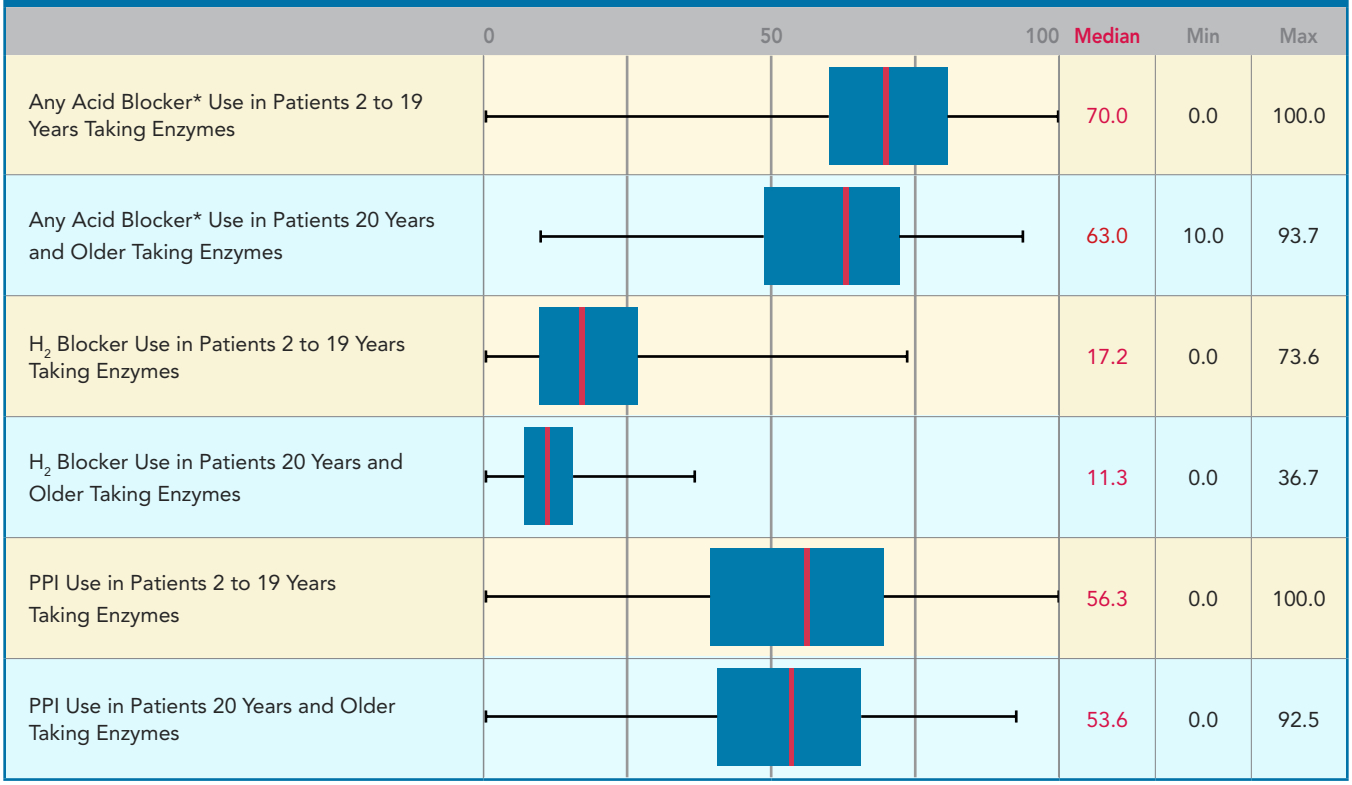
Percent of Patients Taking CF-Specific Vitamins, by Center



	Median	Min	Max
Patients Under 24 Months Taking CF-Specific Vitamins	95.3	33.3	100.0
Patients 2 to 19 Years Taking CF-Specific Vitamins	93.8	21.1	100.0
Patients 20 Years and Older Taking CF-Specific Vitamins	82.2	0.0	100.0

Acid blockers are commonly prescribed in patients with CF to treat gastroesophageal reflux disease (GERD) and/or to increase the effectiveness of PERT. There is wide variability across centers, but the median percentage prescribed an acid blocker is approximately two-thirds. Proton pump inhibitors (PPIs) are prescribed more often than H_2 blockers with substantial variability across centers.

Acid Blocker Use, by Center



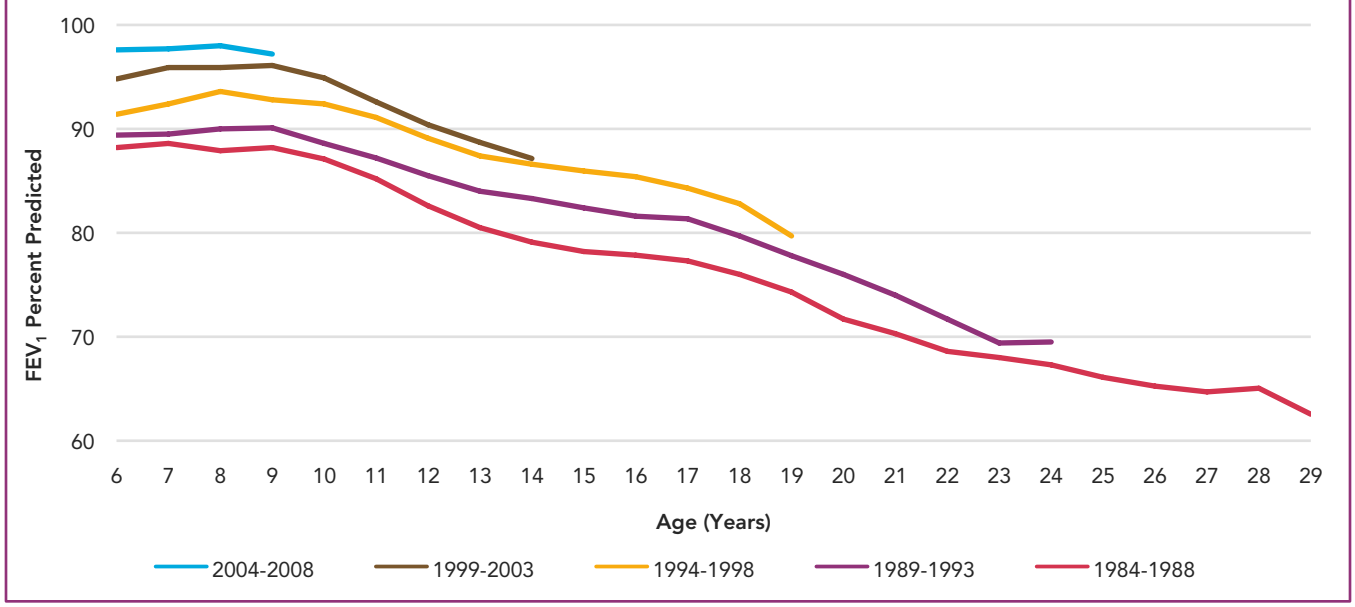
**H_2 blocker or proton pump inhibitor (PPI).*

PULMONARY FUNCTION

Pulmonary function is a crucial clinical indicator of the health of individuals with CF. This section provides information on trends in pulmonary function over time and by age. Variations in pulmonary function across care centers and by mutation class are also examined. This report uses FEV_1 percent predicted as the measurement to describe lung function; all measurements were calculated using the Global Lung Initiative (GLI) reference equations. More information about the effect of this change of reference equations can be found in the About This Report *section on page 8.*

Some noteworthy observations are that successive birth cohorts show improved pulmonary function, and analyses from 1993 to 2013 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. Center-level data show significant variation in pulmonary outcomes, highlighting opportunities for improvement.

Median FEV_1 Percent Predicted by Age and Birth Cohort

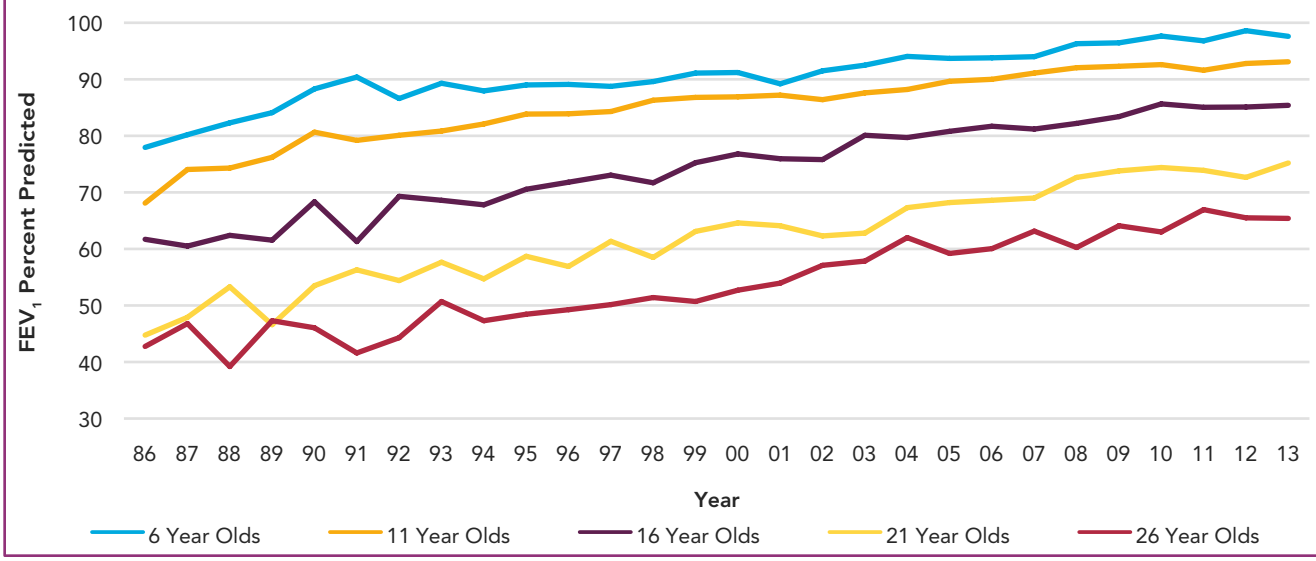


GLI reference equations were used to calculate FEV_1 percent predicted.

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 all ages over time; however, the lines are near parallel, suggesting that the rate of decline in adolescence remains the same.

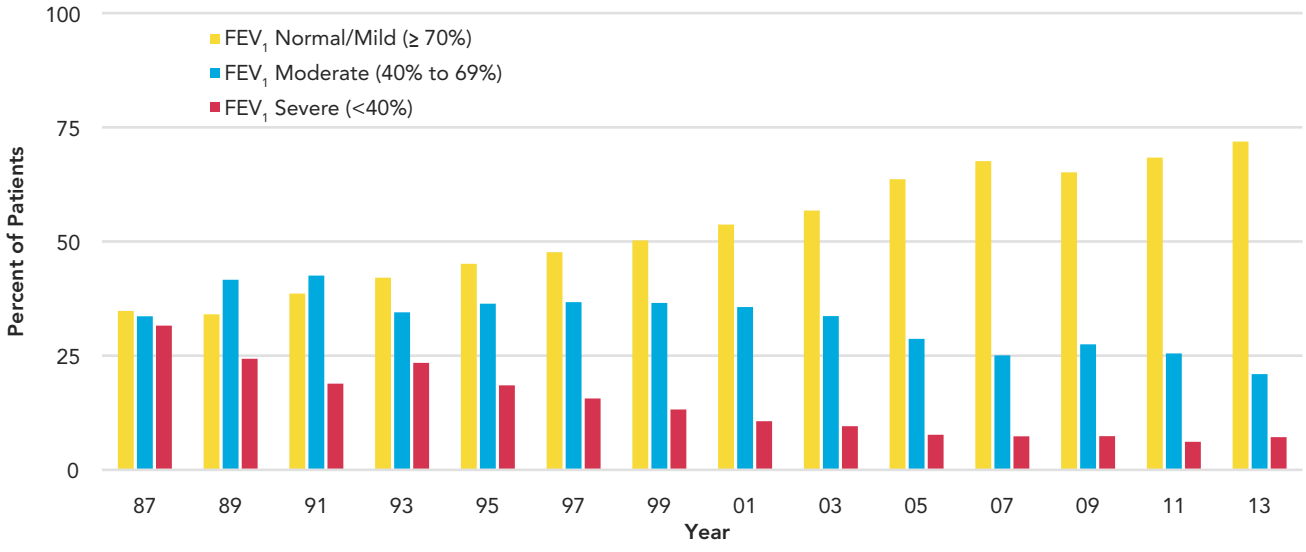
Median FEV_1 Precent Predicted by Age, 1986–2013



GLI reference equations were used to calculate FEV_1 percent predicted.

The proportion of 18-year-olds in the normal/mild categories (FEV_1 ≥70 percent predicted) has increased from 34.8 percent in 1987 to 71.9 percent in 2013, while the proportion in the severe category (FEV_1 <40 percent predicted) has decreased from 31.6 percent to 7.2 percent.

Median FEV_1 Percent Predicted in 18-Year-Olds, 1987–2013

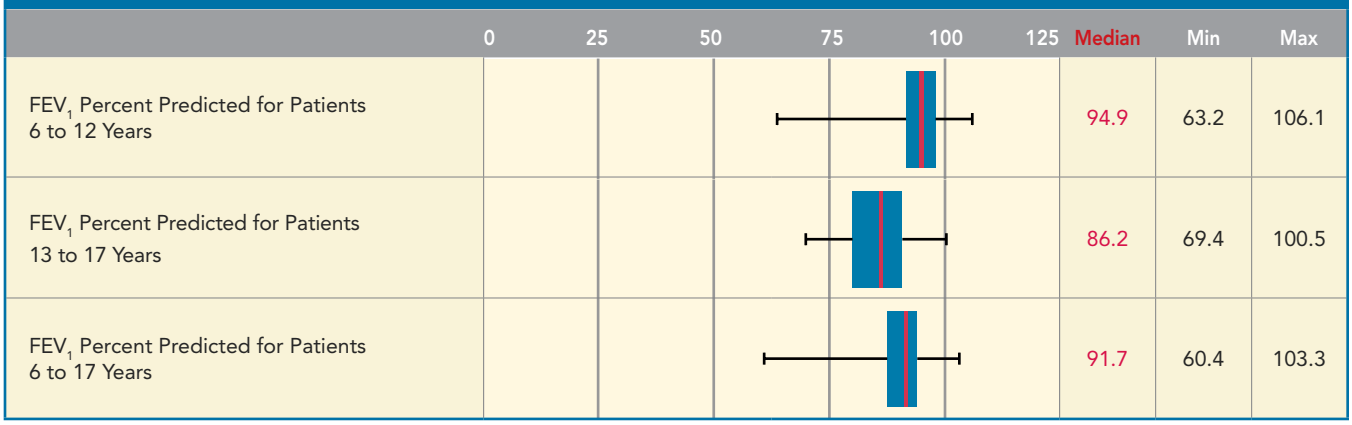


GLI reference equations were used to calculate FEV_1 percent predicted.

Center-Level Variation in FEV_1 Outcomes

The national goal is an FEV_1 of 100 percent predicted for children under age 18. There is minimal variation across the care center network with regard to pediatric pulmonary outcomes. The data show an improvement from 10 years ago, when the median FEV_1 percent predicted by center for patients 6 to 17 years was 85.4 percent predicted.

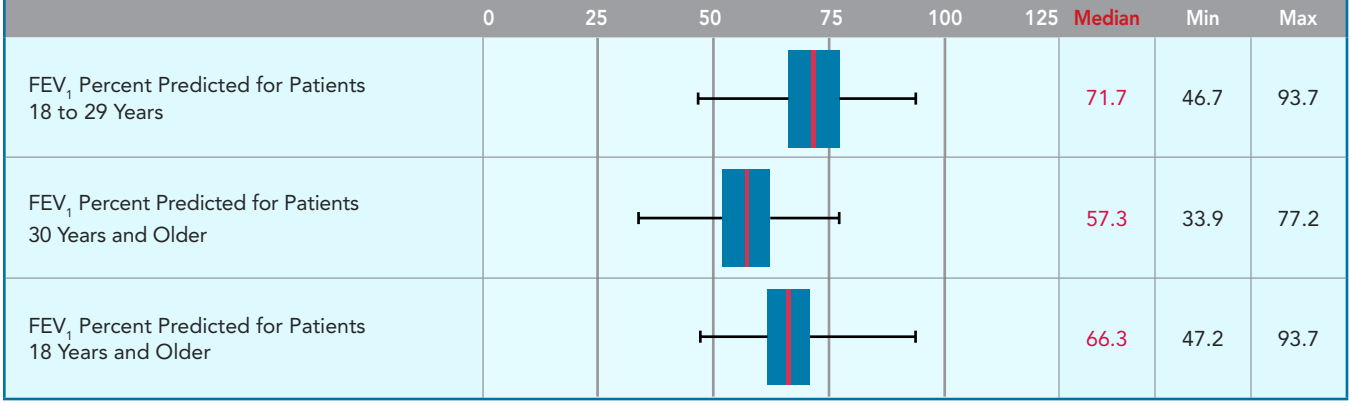
Median FEV_1 Percent Predicted for Children, by Center



GLI reference equations were used to calculate FEV_1 percent predicted.

The national goal is an FEV_1 of 75 percent predicted for adults 18 and older. Median FEV_1 percent predicted for patients 18 years and older has improved substantially, from 59.9 percent predicted in 2003 to 66.8 percent predicted in 2013. There is more variability across adult centers than pediatric centers.

Median FEV_1 Percent Predicted for Adults, by Center



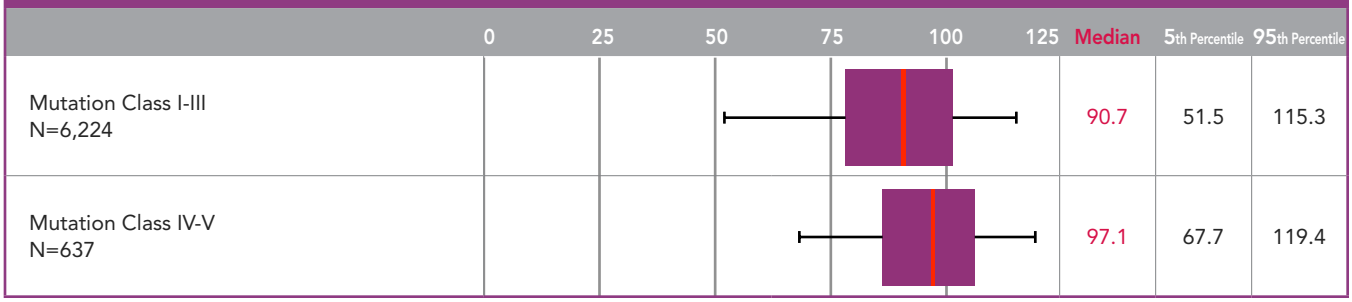
GLI reference equations were used to calculate FEV_1 percent predicted.

Mutation Class Variation in FEV_1 Outcomes

As the majority of patients fall into mutation Class I-III, the outcomes of this group drive national averages.

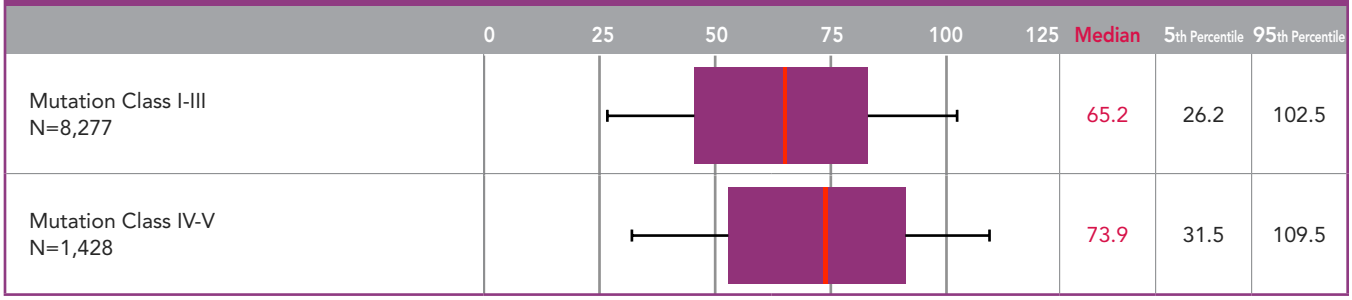
Among children and adolescents, there is more variability in outcomes among individuals with Class I-III mutations, with a substantial overlap in FEV_1 percent predicted between the two mutation class groups (I-III and IV-V) at all ages. Nevertheless, both children and adults in Class IV-V have higher lung function than those in Class I-III.

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



GLI reference equations were used to calculate FEV_1 percent predicted.

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



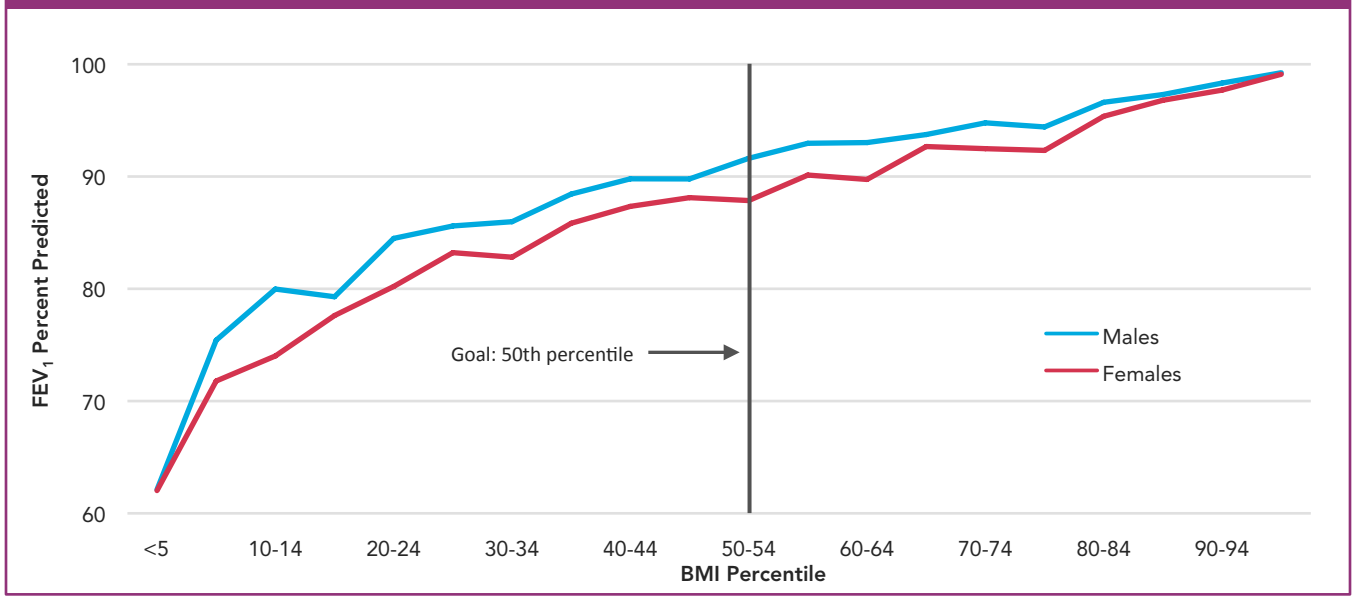
GLI reference equations were used to calculate FEV_1 percent predicted.

FEV_1 AND BMI OUTCOMES

Pulmonary and nutritional outcomes are two main focuses of quality improvement work within the CF care network. The data show that pulmonary function and nutritional status increase proportionally for both pediatric and adult patients.

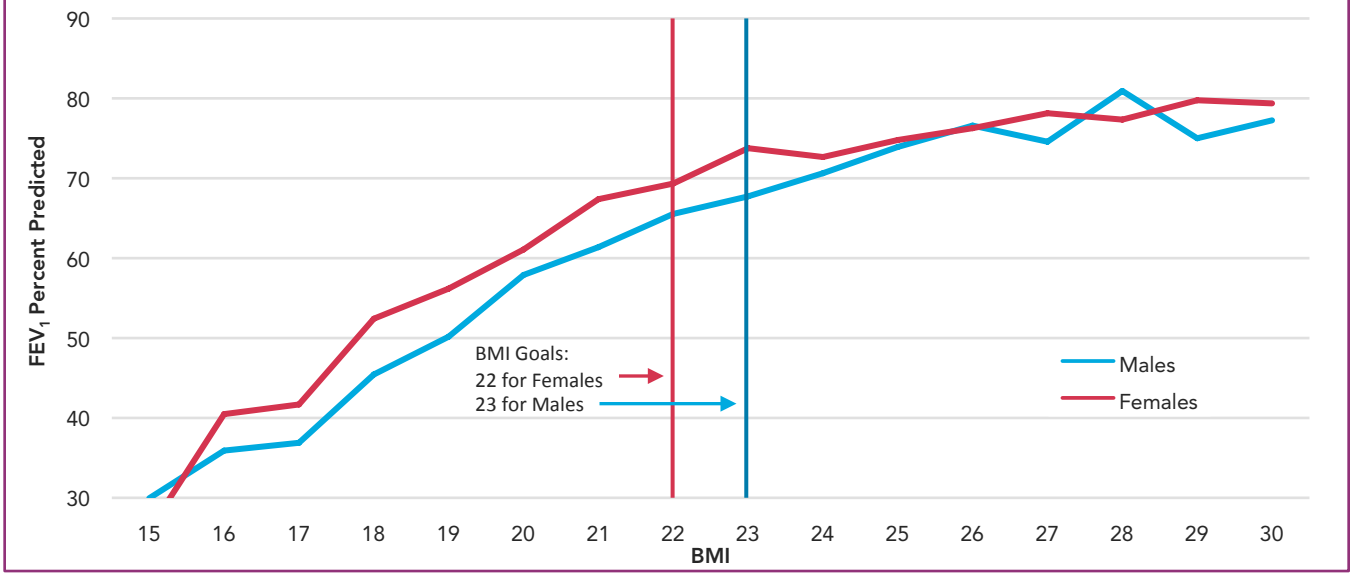
Established pulmonary and nutritional goals are: for children, FEV_1 percent predicted greater than or equal to 100 and BMI percentile meeting or exceeding the 50th percentile, and for adults, FEV_1 percent predicted greater than or equal to 75 and BMI greater than or equal to 22 for females and 23 for males.[27]

Median FEV_1 Percent Predicted vs. Median BMI Percentile for Children 6 to 19 Years in 2013



GLI reference equations were used to calculate FEV_1 percent predicted.

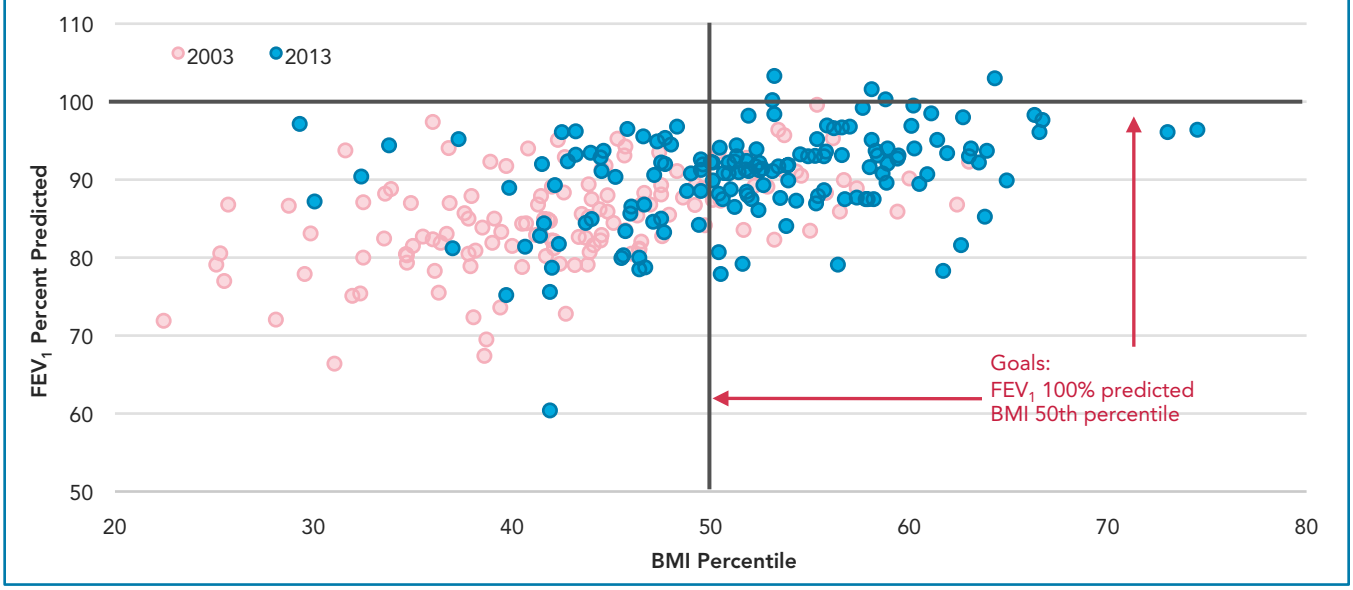
Median FEV_1 Percent Predicted vs. Median BMI Value for Adults 20 to 40 Years in 2013



GLI reference equations were used to calculate FEV_1 percent predicted.

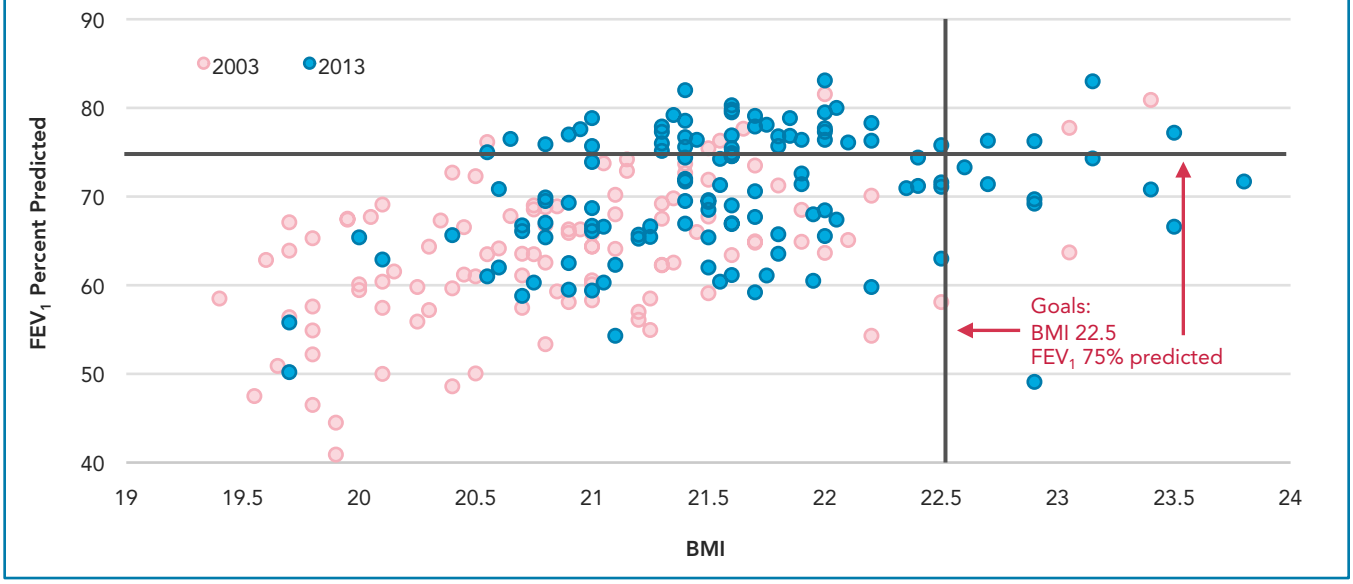
Each dot in the figure below represents values from an accredited care center or affiliate program. This figure shows the distribution of centers with regard to their median nutritional and pulmonary outcomes and the change in distribution between 2003 and 2013. Many more centers in 2013 are approaching the upper right quadrant than 10 years ago.

Median FEV_1 Percent Predicted vs. Median BMI Percentile for Patients 6 to 17 Years — 2003 vs. 2013



GLI reference equations were used to calculate FEV_1 percent predicted.

Median FEV_1 Percent Predicted vs. Median BMI Value for Patients 18 to 30 Years — 2003 vs. 2013



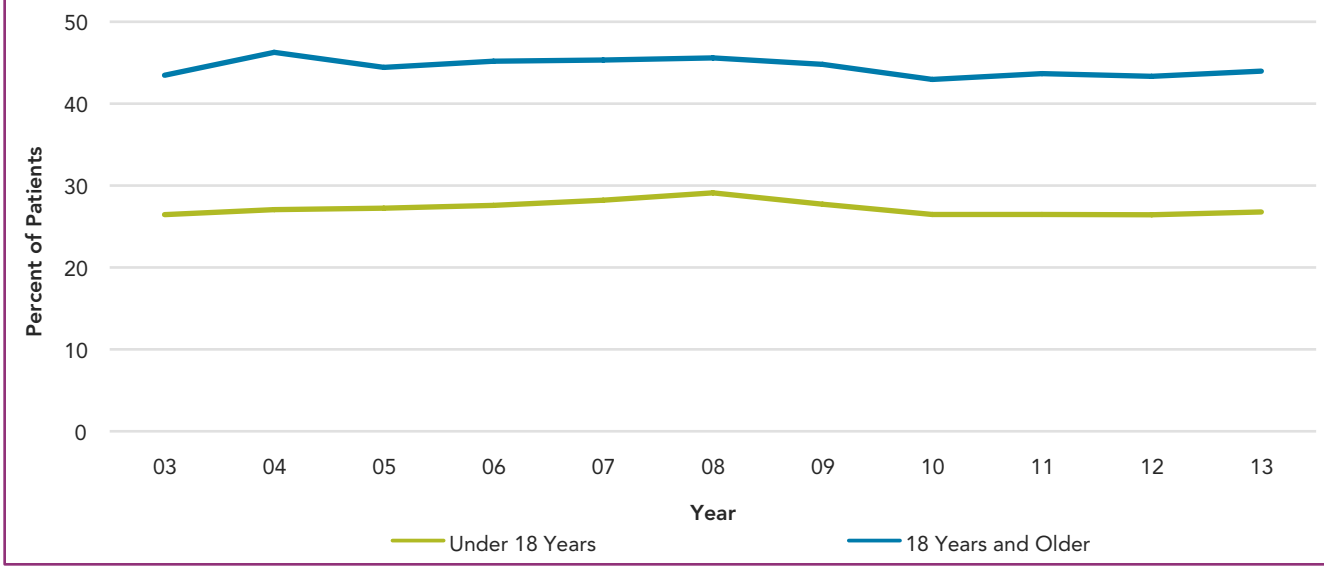
GLI reference equations were used to calculate FEV_1 percent predicted.

PULMONARY EXACERBATIONS

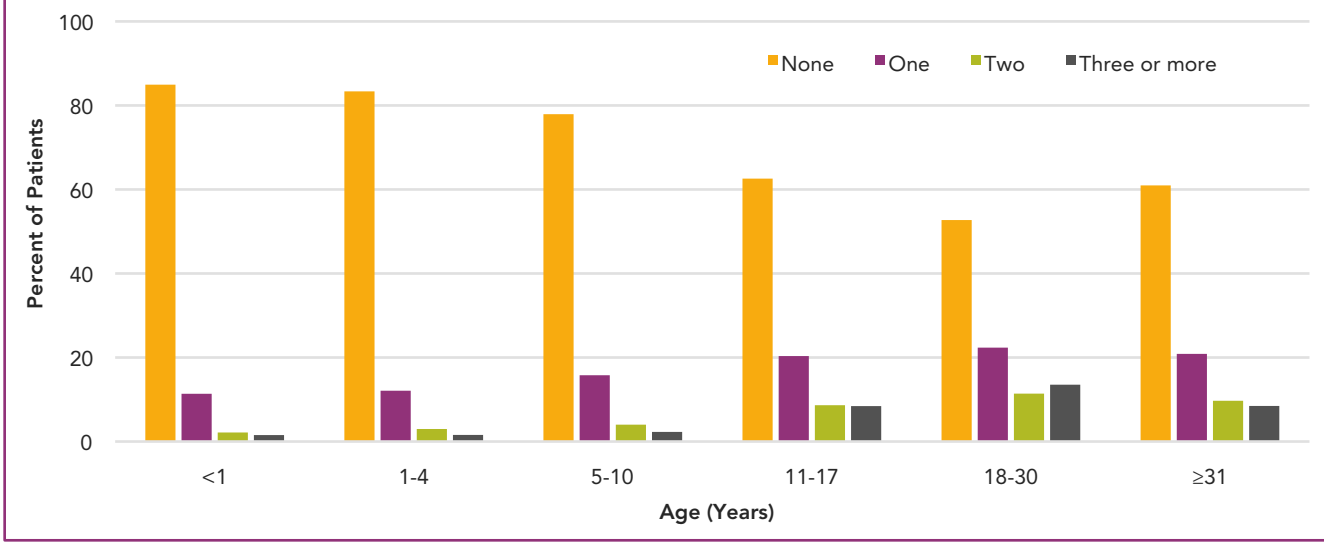
Pulmonary exacerbations, defined as treatment in the hospital and/or at home with intravenous (IV) antibiotics, are associated with morbidity, mortality and decreased quality of life, and they are a major driver of the cost of care. This section displays the trends in the rate of pulmonary exacerbations over time and by age group. Center variation with regard to exacerbation rates and treatment characteristics are also displayed.

Despite the notable improvements in pulmonary function and nutritional status over the past two decades, a significant proportion of patients are still treated with IV antibiotics for pulmonary exacerbations and there has been no reduction over time in the proportion of individuals with CF who experience an exacerbation.

Patients Treated with IV Antibiotics for a Pulmonary Exacerbation, 2003–2013



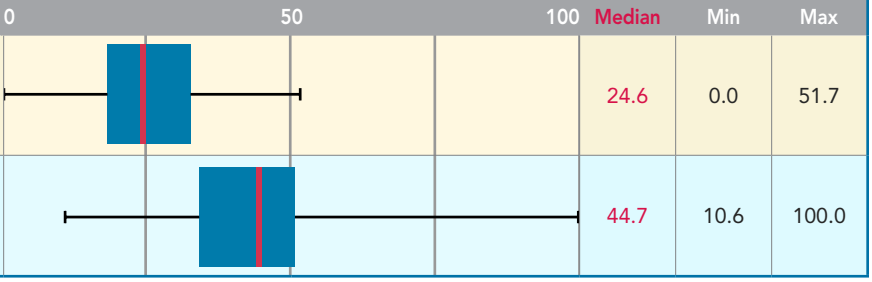
Pulmonary Exacerbations by Age Group in 2013



In 2013, 73.2 percent of children and 56.0 percent of adults with CF — 64.7 percent of all patients — did not have a pulmonary exacerbation. Adults ages 18 to 30 were the most likely to experience at least one exacerbation in 2013, with over 10 percent experiencing three or more exacerbations.

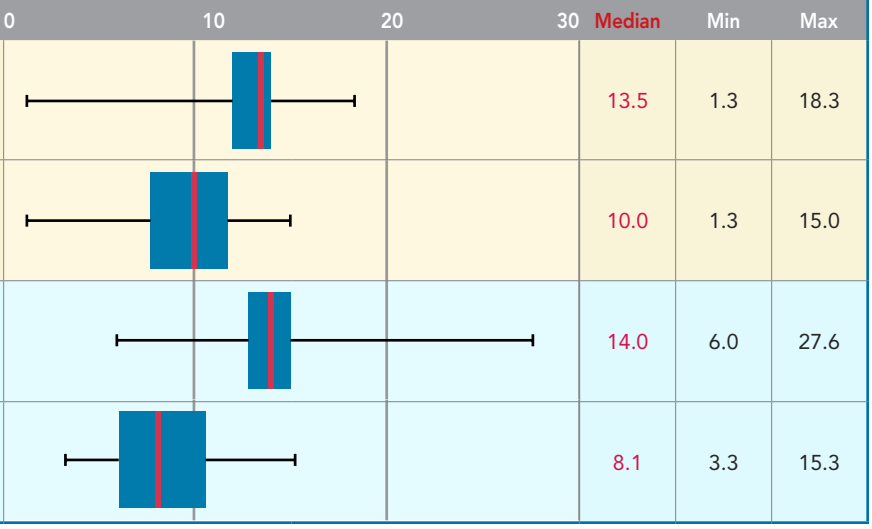
While adults ages 18 and older were more likely to have an exacerbation, the percentage varied by center. The median length of treatment for both children and adults with CF was approximately two weeks. Center-level data show marked variation in the treatment of exacerbations, highlighting opportunities for further research and quality improvement.

Percent of Patients with One or More Pulmonary Exacerbations, by Center



	Median	Min	Max
Patients Under 18 Years with One or More Pulmonary Exacerbations	24.6	0.0	51.7
Patients 18 Years and Older with One or More Pulmonary Exacerbations	44.7	10.6	100.0

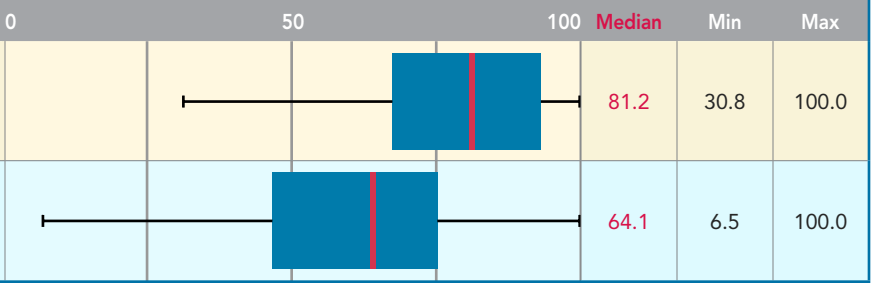
Median Exacerbation Treatment Duration in Days, by Center



	Median	Min	Max
Total Duration of IV Antibiotic Treatment for a Pulmonary Exacerbation in Patients Under 18 Years	13.5	1.3	18.3
Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Patients Under 18 Years	10.0	1.3	15.0
Total Duration of IV Antibiotic Treatment for a Pulmonary Exacerbation in Patients 18 Years and Older	14.0	6.0	27.6
Duration of Hospital Stay for Treatment of a Pulmonary Exacerbation in Patients 18 Years and Older	8.1	3.3	15.3

The data show more center-level variation in the percentage of IV treatment in the hospital versus in the home among adults with pulmonary exacerbations than children.

Percent of Total Treatment Duration in Hospital, by Center

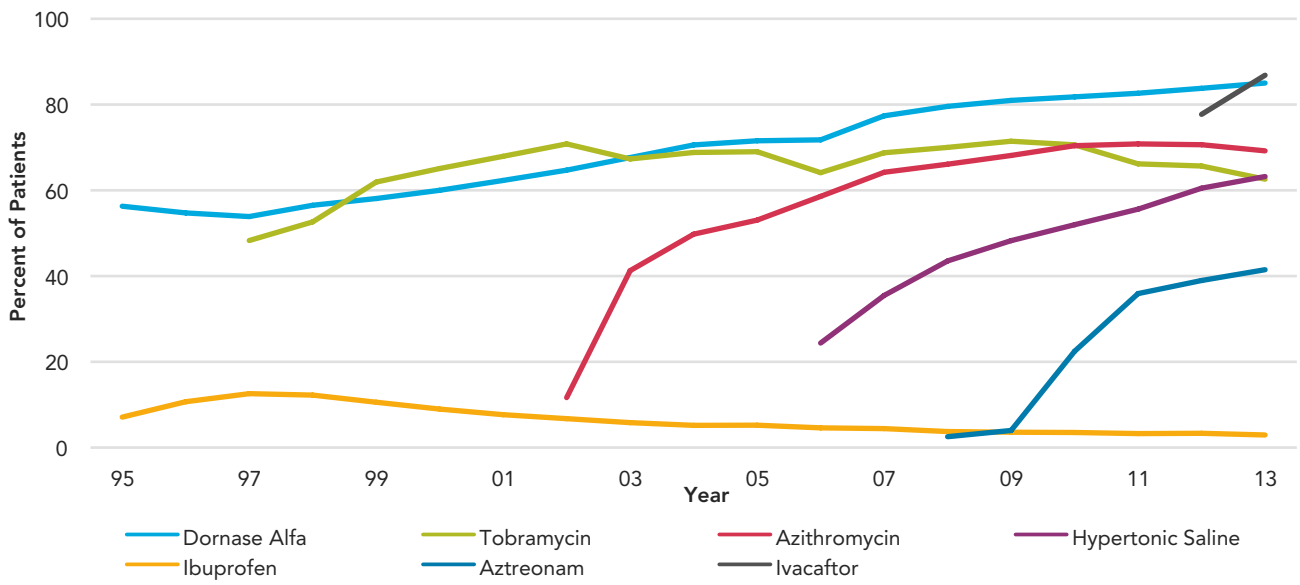


	Median	Min	Max
Percent of Total Treatment Duration in Hospital in Patients Under 18 Years	81.2	30.8	100.0
Percent of Total Treatment Duration in Hospital in Patients 18 Years and Older	64.1	6.5	100.0

PULMONARY THERAPIES

Chronic pulmonary therapies are a major component of the treatment regimen for individuals with CF. This section provides data on the uptake and trends in usage of pulmonary medications recommended for chronic use by the CF Foundation pulmonary guidelines committee, as well as further information about the use of each of the recommended medications. 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.[38]

Chronic Medication Use in Eligible Patients, 1995–2013

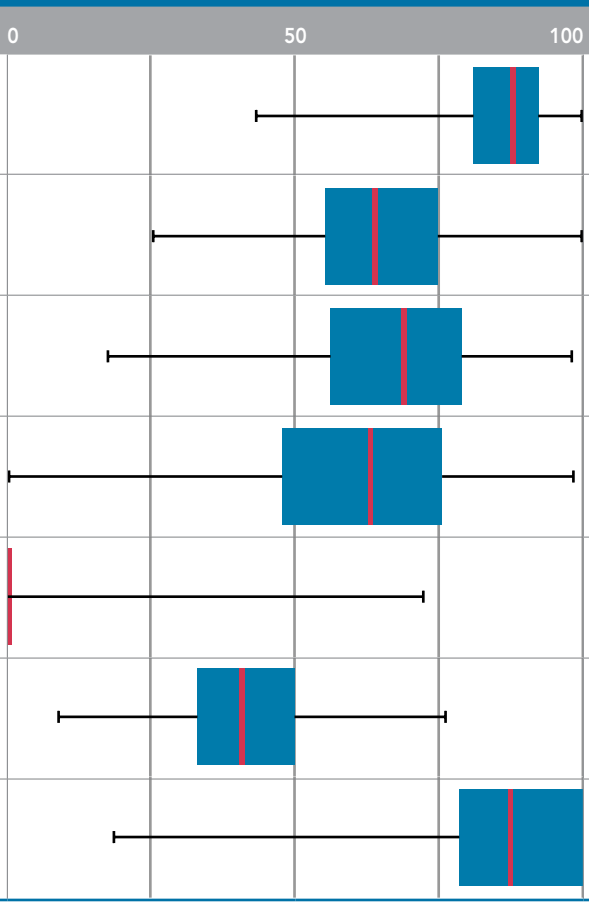


Patients are included in the percent of eligible patients if they were prescribed the specific therapy at any encounter during the year. Among recommended medications, the use of dornase alfa, hypertonic saline, aztreonam and ivacaftor are increasing over time, while ibuprofen and tobramycin are decreasing.

Medications Recommended for Chronic Use

Recommended therapies are widely prescribed with the exception of ibuprofen. Hypertonic saline use continues to increase (from 24.4 percent in 2006 to 63.2 percent in 2013); however, its use is more variable across the care center network than the other widely used therapies. The use of inhaled aztreonam continues to increase. Ivacaftor is used by the majority of eligible patients with the G551D mutation.

Percent of Patients Prescribed Medications Recommended for Chronic Use, by Center



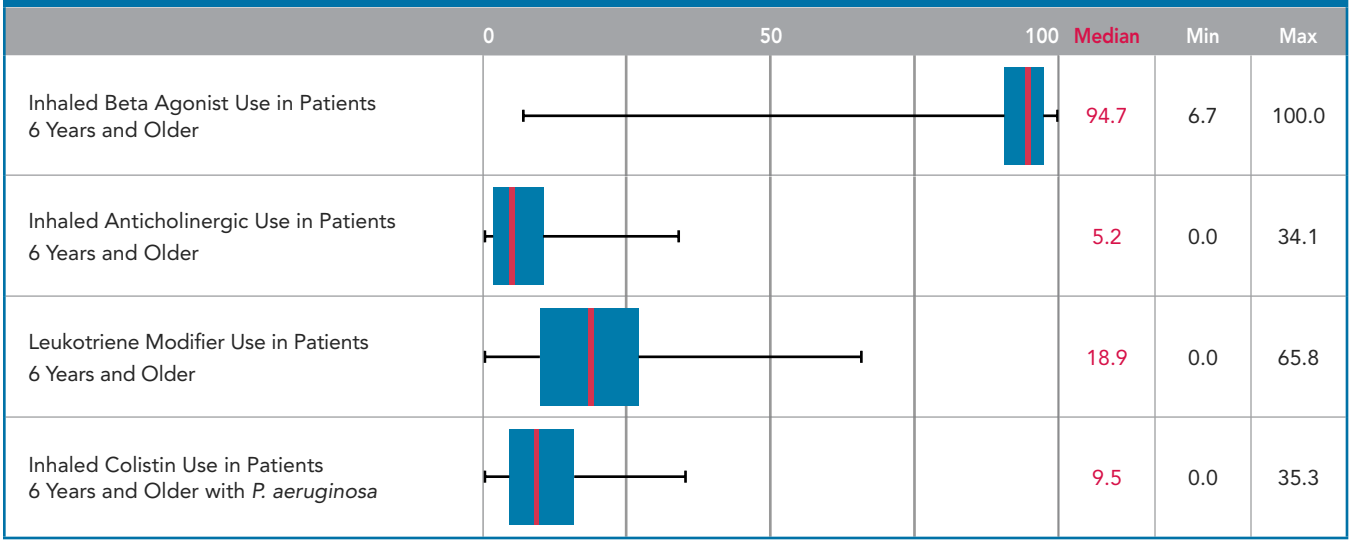
	Median	Min	Max
Dornase alfa Use in Patients 6 Years and Older	87.9	42.9	100.0
Inhaled Tobramycin Use in *P. aeruginosa* Positive Patients 6 Years and Older	64.0	25.0	100.0
Azithromycin Use in Eligible *P. aeruginosa* Positive Patients 6 Years and Older*	69.0	17.6	98.1
Hypertonic Saline Use in Patients 6 Years and Older	63.2	0.0	98.4
High-dose Ibuprofen Use in Patients 6 to 17 Years with FEV_1 Greater Than or Equal to 60 Percent Predicted	0.0	0.0	73.6
Inhaled Aztreonam Use in *P. aeruginosa* Positive Patients 6 Years and Older	40.9	9.1	76.2
Ivacaftor Use in Patients 6 Years and Older with a Copy of the G551D Mutation	87.5	18.2	100.0

**Patients were considered eligible if they met the selection criteria used in the U.S. azithromycin trial.*[6]

Medications with Insufficient Evidence to Recommend For or Against Chronic Use

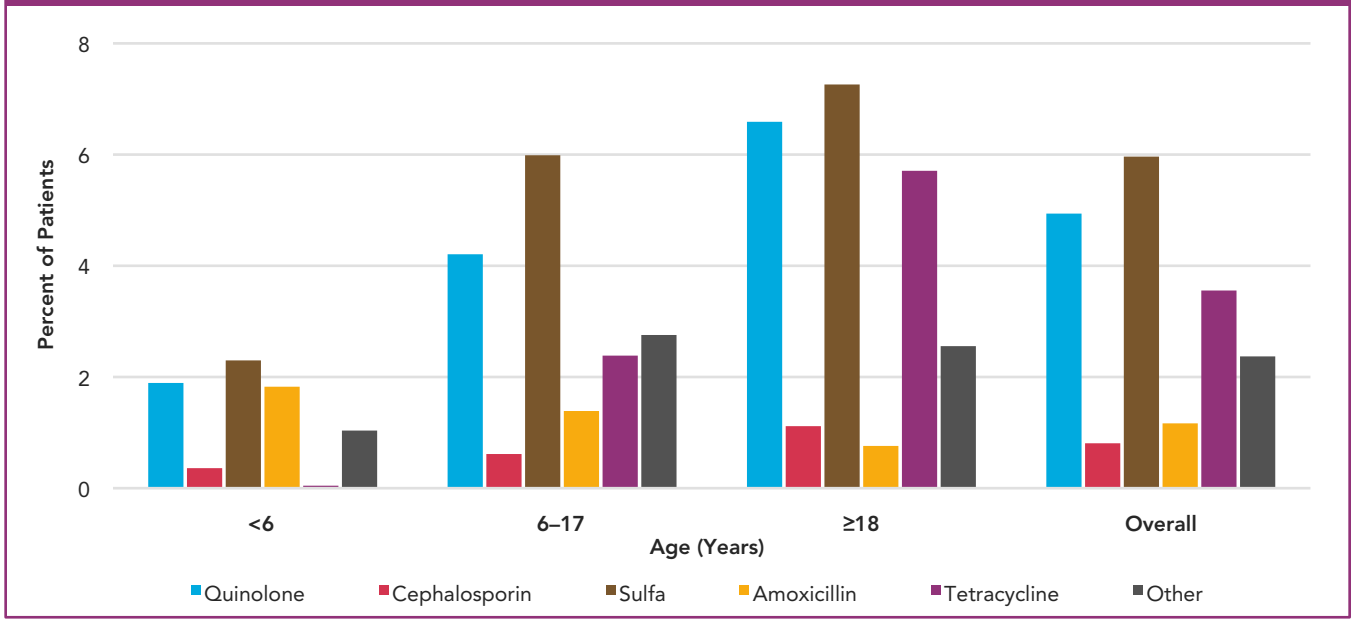
For the updated CF Foundation pulmonary guidelines, the guidelines committee determined that there was insufficient evidence to recommend for or against the chronic use of inhaled beta agonists, inhaled anticholinergics, leukotriene modifiers and inhaled colistin to improve lung function, reduce exacerbations or improve quality of life.[38] Most of these medications are used infrequently.

Percent of Patients Prescribed Medications with Insufficient Evidence to Recommend For or Against Chronic Use, by Center



In 2013, 85.9 percent of patients did not use any chronic oral antibiotics.

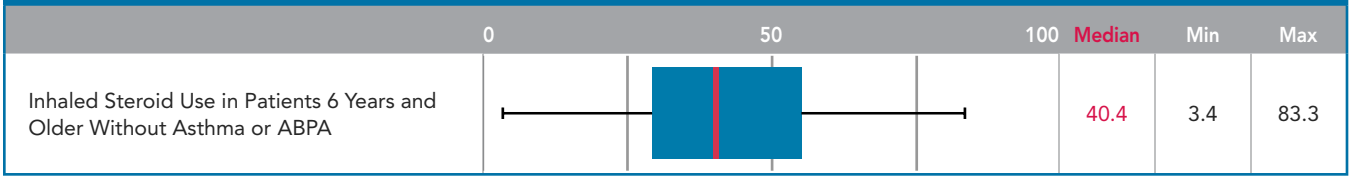
Chronic Oral Antibiotic Use in 2013



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.

Percent of Patients Prescribed Medications Not Recommended for Chronic Use, by Center



Medication Use in Young Children

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

Medication Use in Patients Under 6 Years in 2013

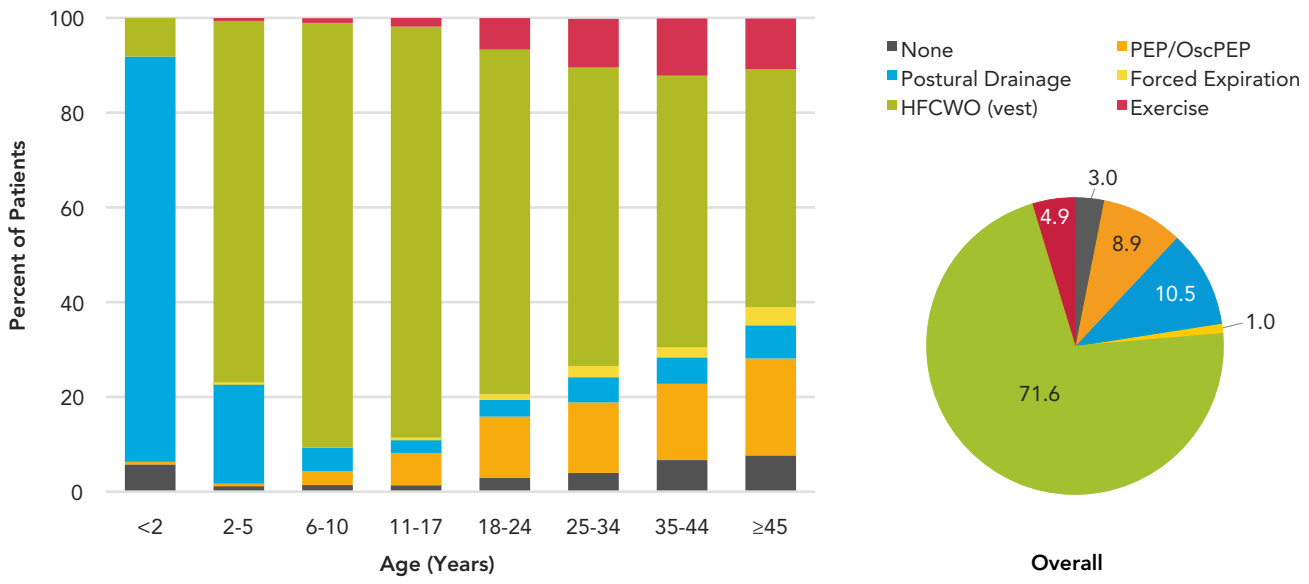
	Patients Under 3 Years (%)	Patients 3 to 5 Years(%)
Number of Patients (n)	**2,026**	**2,423**
Dornase alfa	40.5	68.5
Hypertonic saline	18.2	39.7
Inhaled bronchodilators	76.7	89.1
Inhaled corticosteroids	17.6	33.1
Inhaled tobramycin	15.6	22.9
Azithromycin	3.1	9.8
Inhaled aztreonam	1.2	2.7

Most patients under the age of 6 years are prescribed inhaled bronchodilators. Dornase alfa is prescribed in 40.5 percent of patients younger than 3 years of age and over two-thirds of patients ages 3 to 5 years.

Airway Clearance Techniques

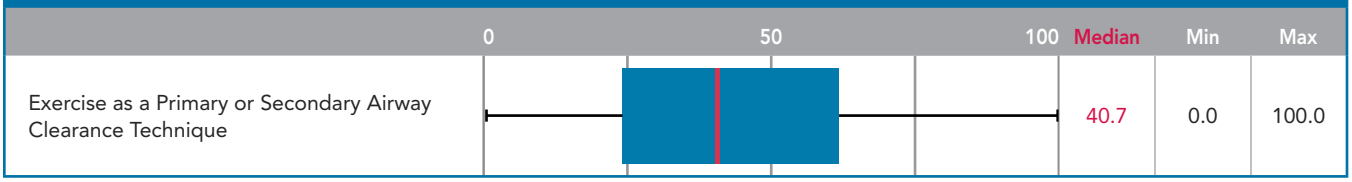
The CF Foundation pulmonary guidelines recommend airway clearance for all patients.[39] High-frequency chest wall oscillation vest is the most widely used airway clearance technique beyond the infant years.

Primary Airway Clearance Techniques by Age and Overall in 2013



The CF Foundation pulmonary guidelines recommend aerobic exercise as an adjunct therapy for airway clearance and for its additional benefits to overall health.[39]

Percent of Patients Using Exercise as an Airway Clearance Technique, by Center



COMPLICATIONS

Management of complications secondary to CF 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.

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 and depression are two other complications of CF more common among older adults.

Complications of CF in 2013

	< 18	≥ 18	All
Number of patients	14,128	13,975	28,103
Percent with no complications	27.6	6.6	17.1
Percent with complications not reported[A]	2.6	3.8	3.2
Cystic Fibrosis-Related Diabetes	**< 18 (%)**	**≥ 18 (%)**	**All (%)**
Cystic fibrosis-related diabetes (CFRD)[B]	6.5	34.3	20.3
Hepatobiliary			
Gall stones	0.2	0.9	0.5
Gall stones, requiring surgery/procedure	0.2	1.3	0.7
Liver disease, cirrhosis[C]	2.0	2.9	2.5
Liver disease, non- cirrhosis	4.9	5.1	5.0
Hepatic steatosis	0.3	0.5	0.4
Liver disease, other	2.8	3.1	3.0
Bone/Joints			
Arthritis/arthropathy	0.5	5.7	3.1
Bone fracture	0.2	0.4	0.3
Osteopenia	1.8	20.9	11.2
Osteoporosis	0.7	9.4	5.0
Pulmonary			
Allergic bronchopulmonary aspergillosis (ABPA)	3.2	7.0	5.0
Asthma	25.2	27.5	26.3
Hemoptysis, massive	0.3	2.2	1.2
Pneumothorax requiring chest tube	0.1	0.8	0.5
GI			
Distal intestinal obstruction syndrome (DIOS)	4.1	6.1	5.1
Gastroesophageal reflux disease (GERD)	28.1	34.5	31.3
GI bleed requiring hospitalization (non-variceal)	0.0	0.1	0.1
Pancreatitis	0.6	2.8	1.7
Peptic ulcer disease	0.1	0.3	0.2
Rectal prolapse	0.9	0.3	0.6
Other Complications			
Anxiety disorder	1.6	11.1	6.2
Cancer confirmed by histology	0.0	0.8	0.4
Depression	2.3	22.6	12.3
Hearing loss	0.8	2.7	1.7
Hypertension	0.4	7.8	4.0
Kidney stones	0.2	2.7	1.5
Nasal polyps requiring surgery	3.7	5.2	4.4
Renal failure requiring dialysis[D]	0.0	0.4	0.2
Sinus disease	17.4	44.3	30.7

[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 77 for secondary complications.*

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

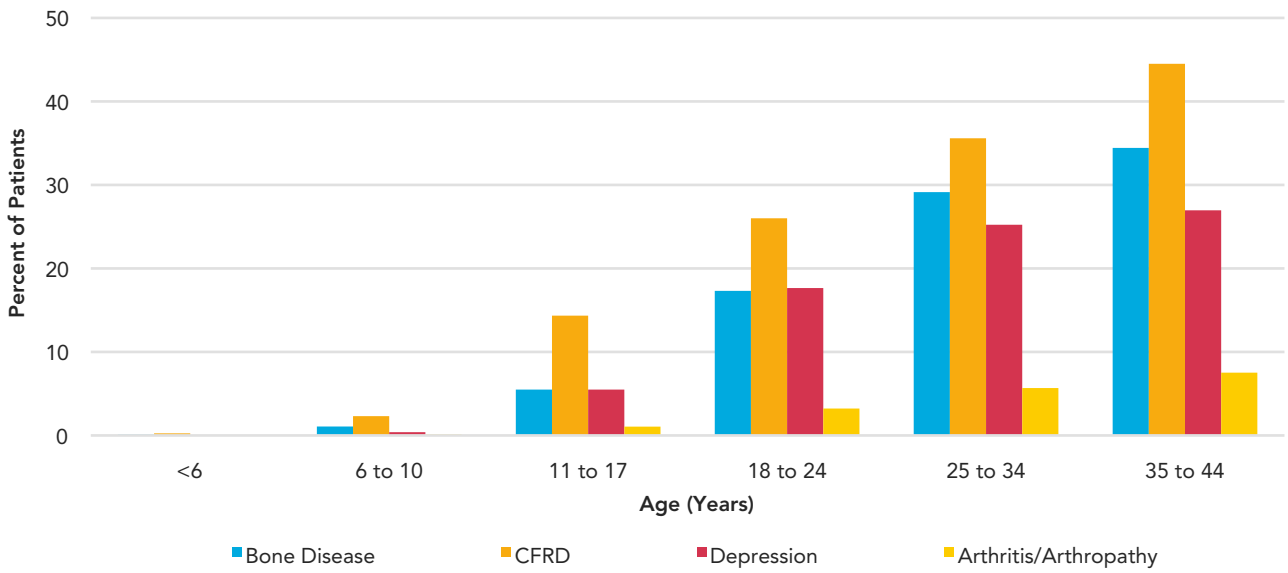
[D] *Cause other than CFRD.*

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

Complications of Liver Disease, Cirrhosis in 2013 (n=678)

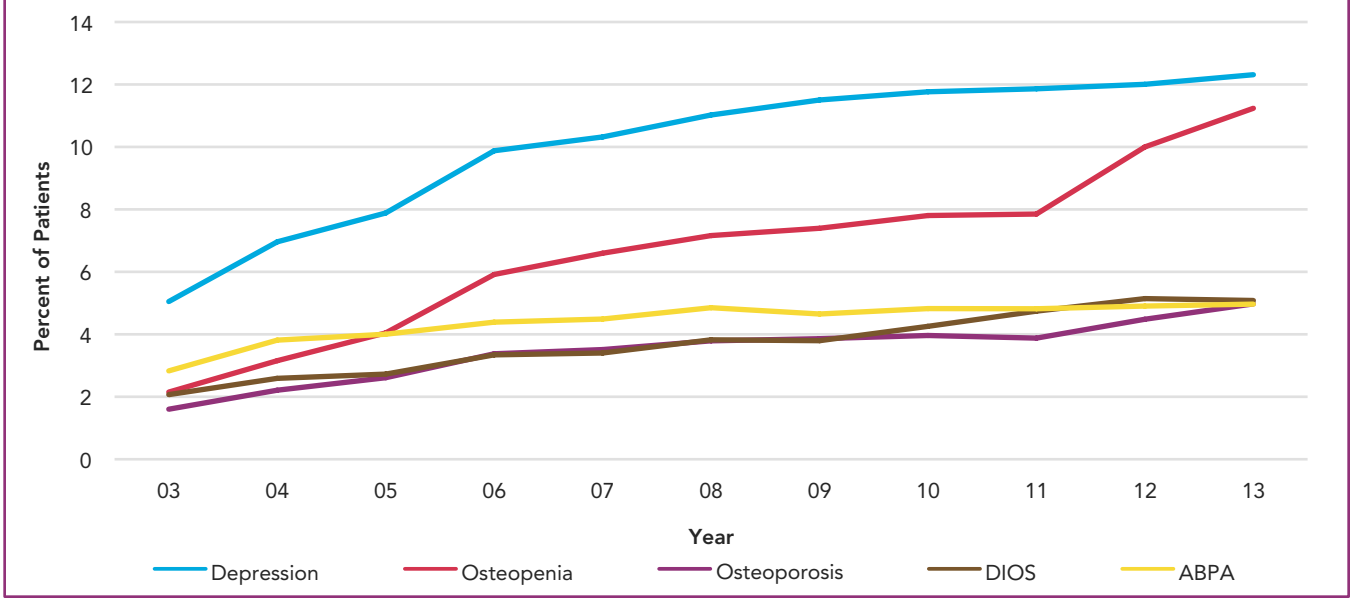
	All (n)	All (%)	< 18 (%)	≥ 18 (%)
Esophageal varices	148	21.8	20.9	22.5
Gastric varices	30	4.4	4.3	4.5
GI bleed related to varices	18	2.7	2.2	3.0
Splenomegaly	224	33.0	39.6	28.5
Hypersplenism	79	11.7	12.6	11.0
Ascites	48	7.1	5.4	8.3

Prevalence of Common Complications by Age in 2013



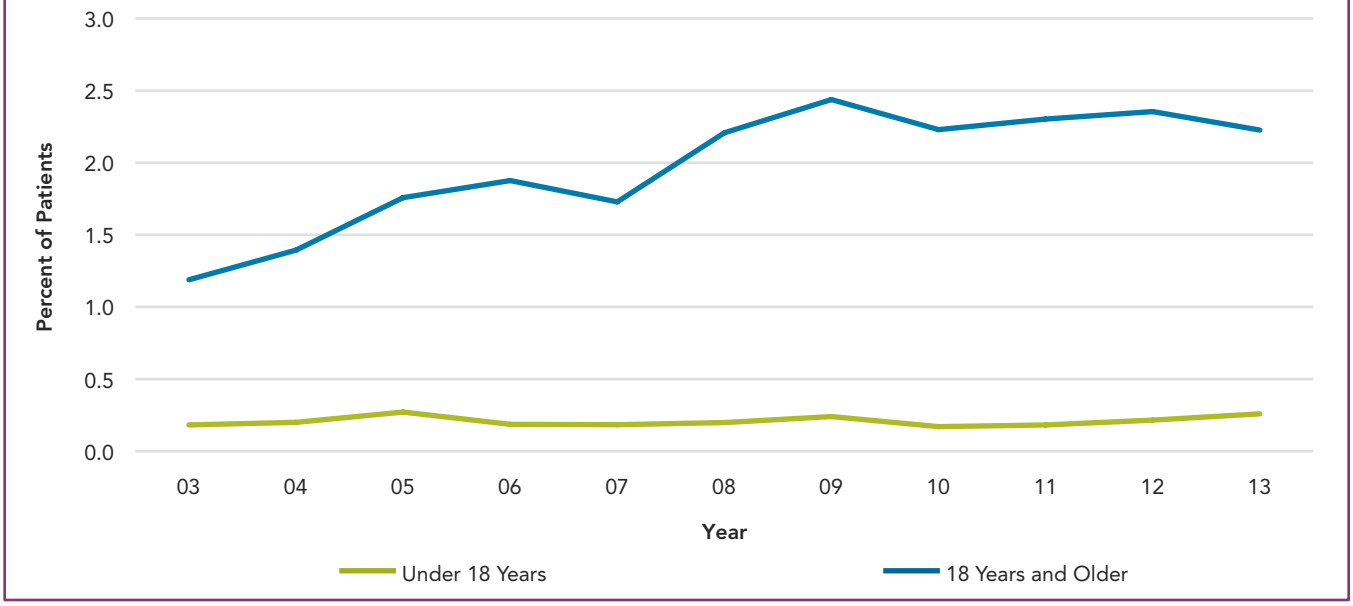
The increased prevalence of depression and bone disease likely relates to increased awareness of these important complications and more widespread screening. Aging of the population may also be a contributing factor.

Prevalence of Complications, 2003–2013



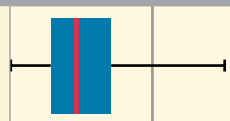
Between 2003 and 2013, the overall percentage of patients reporting massive hemoptysis remained low, though increasing in patients age 18 and older.

Prevalence of Hemoptysis, 2003–2013



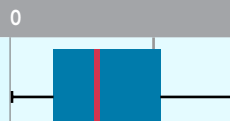
Differences in the prevalence of complications may reflect differences in the case mix across centers. However, for some complications, particularly CFRD, bone disease, and anxiety and depression, marked center-level variation may reflect differences in screening for these treatable complications.

Percent of Patients with CFRD, by Center



	Median	Min	Max
Patients 10 to 17 Years with CFRD	11.9	0.0	37.5
Patients 18 Years and Older with CFRD	32.7	0.0	71.4

Percent of Patients with Bone Disease, by Center



	Median	Min	Max
Patients 18 Years and Older with Osteopenia	15.3	0.0	50.0
Patients 18 Years and Older with Osteoporosis	7.1	0.0	27.0

Percent of Patients with CF-Related Complications, by Center

	Median	Min	Max
Patients with Allergic Bronchopulmonary Aspergillosis (ABPA)	3.7	0.0	16.7
Patients with Depression or Anxiety Disorder	12.0	0.0	44.2
Patients with Distal Intestinal Obstruction Syndrome (DIOS)	3.5	0.0	19.1

This table shows complications by mutation class for selected complications. CFRD, liver disease and distal intestinal obstruction syndrome (DIOS) are more prevalent among individuals in mutation Class I-III. In contrast, pancreatitis is more common among patients in mutation Class IV-V. It is interesting to note that the prevalence of anxiety and depression does not differ depending on mutation class.

Complications of CF in 2013, by Mutation Class

	Mutation Class I-III	Mutation Class IV-V
Number of Patients	**18,128**	**2,734**
Percent with no complications	15.3	24.4
Percent with complications not reported[A]	2.5	4.9
Cystic Fibrosis-Related Diabetes	**I-III (%)**	**IV-V (%)**
Cystic fibrosis-related diabetes (CFRD)[B]	23.5	6.6
Hepatobiliary		
Liver disease, cirrhosis[C]	2.8	0.5
Liver disease, non-cirrhosis	6.0	1.1
Liver disease, other	3.5	1.3
Bone/joints		
Osteopenia	11.7	10.4
Osteoporosis	5.0	5.3
Pulmonary		
Allergic bronchopulmonary aspergillosis (ABPA)	5.2	4.0
Asthma	33.4	23.5
Hemoptysis, massive	1.3	0.9
Pneumothorax requiring chest tube	0.5	0.3
GI		
Distal intestinal obstruction syndrome (DIOS)	5.7	1.8
Gastroesophageal reflux disease (GERD)	33.4	24.5
Pancreatitis	0.4	8.3
Rectal prolapse	0.7	0.1
Other Complications		
Anxiety disorder	6.4	5.6
Cancer confirmed by histology	0.4	0.7
Depression	12.6	11.4
Hypertension	3.8	5.3
Kidney Stones	1.8	1.0
Nasal polyps requiring surgery	4.8	3.1
Renal failure requiring dialysis[D]	0.2	0.1
Sinus disease	30.9	31.8

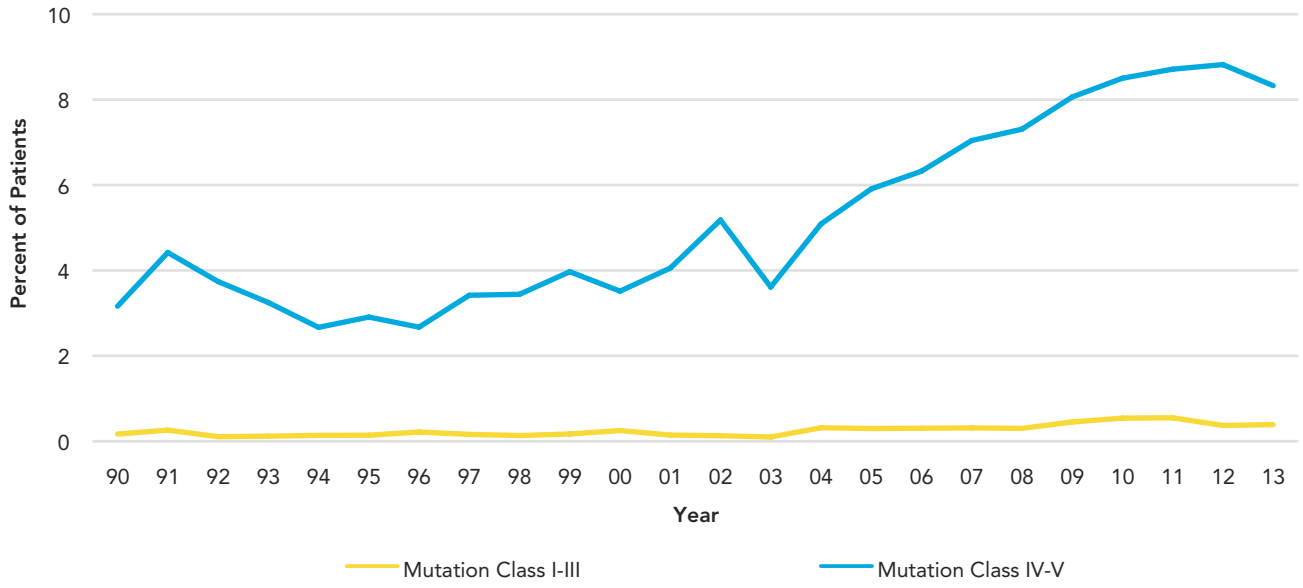
[A] *Patients who did not have a complications case report form completed were considered to not have any complications, as in previous years.*

[B] *See table on page 77 for secondary complications.*

[C] *See table on page 69 for secondary complications.*

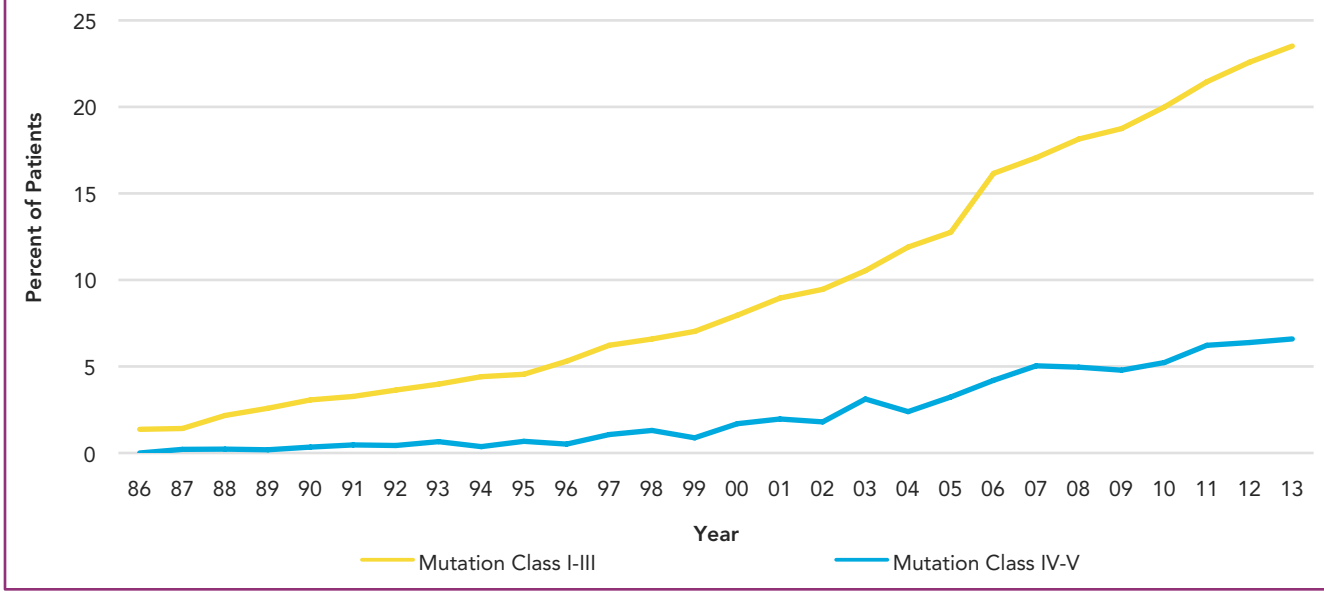
[D] *Cause other than CFRD.*

Prevalence of Pancreatitis by Mutation Class, 1990–2013



The increased prevalence of pancreatitis over time may reflect an increase in CF diagnoses in adolescents and adults with Class IV and V mutations.

Prevalence of CFRD by Mutation Class, 1986–2013



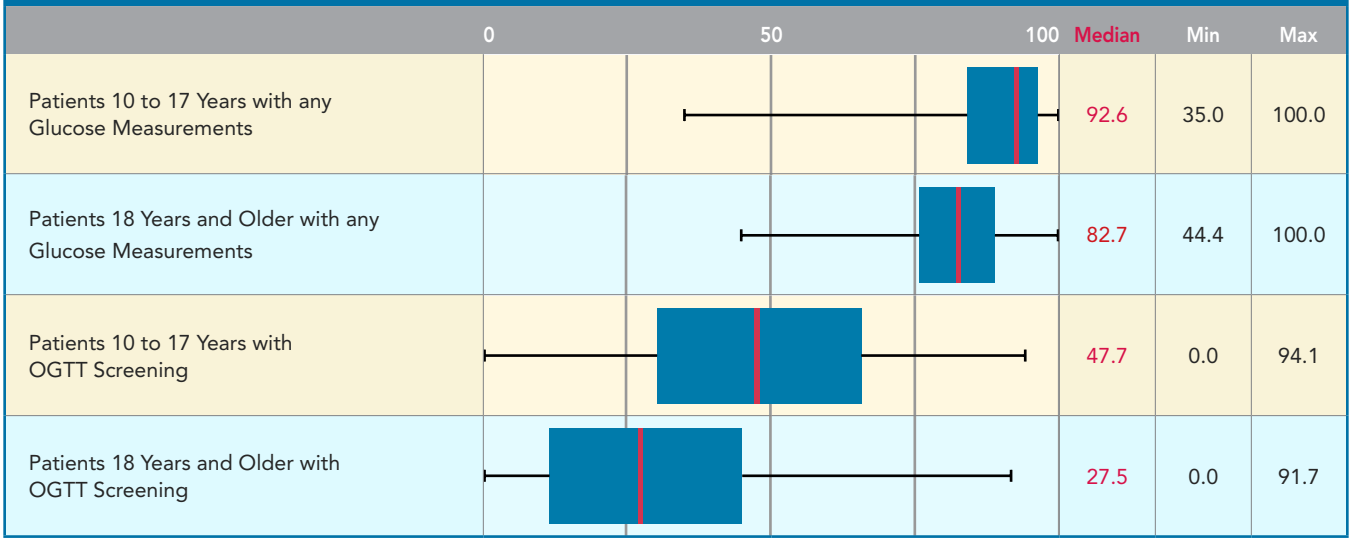
The increased prevalence of CFRD over time may reflect aging of the patient population and/or more systematic screening for this complication.

Cystic Fibrosis-Related Diabetes (CFRD)

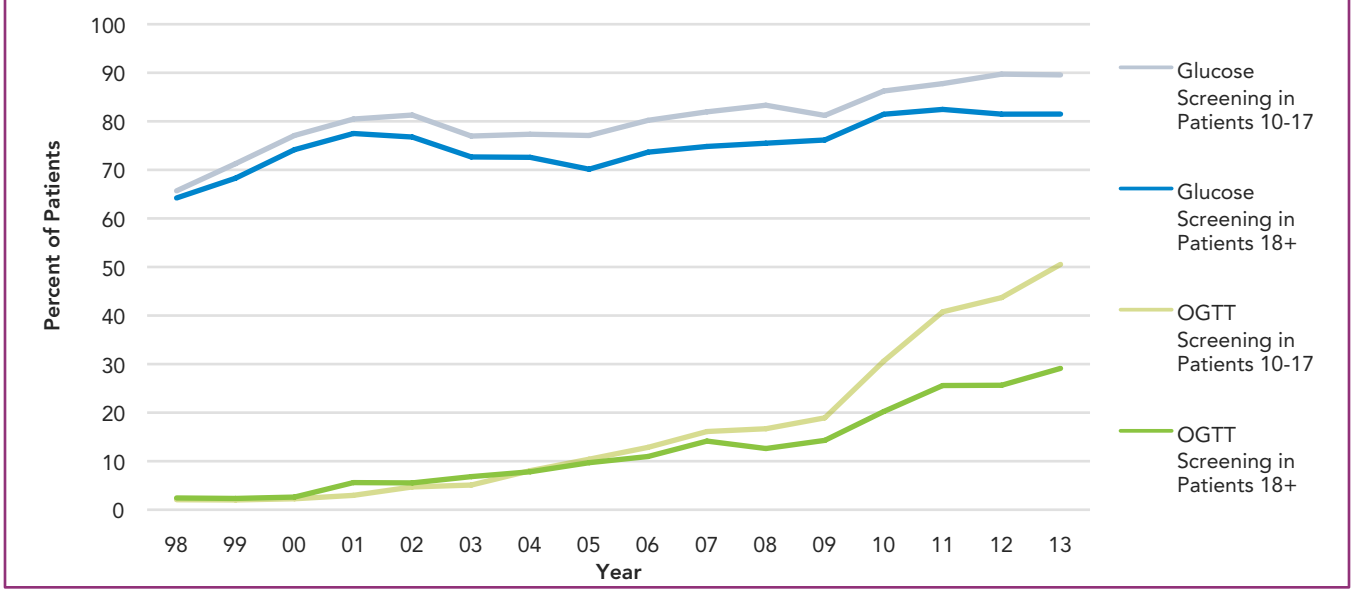
CFRD is associated with weight loss, lung function decline and increased mortality.[40] Early diagnosis and treatment may minimize the impact of CFRD. The CF Foundation CFRD guidelines recommend screening all patients annually, starting by the age of 10, with an oral glucose tolerance test (OGTT).[40]

CFRD screening using blood glucose tests are routinely performed at the vast majority of centers. However, there is less utilization of the recommended OGTT test, with substantial variation across centers. Among adult centers, 80.0 percent of centers report performing this test in less than half of their patients.

Percent of Non-CFRD Patients with Glucose Testing, by Center



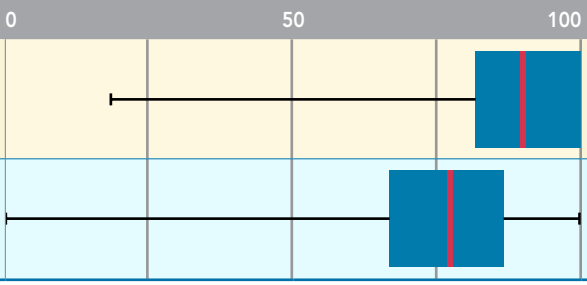
Random and Fasting Blood Glucose and OGTT Screening in Non-CFRD Patients, 1998–2013



Rates of OGTT screening for CFRD have increased since the publication of the CF Foundation CFRD guidelines[40] in 2010.

The CFRD guidelines recommend quarterly hemoglobin A1c (HgbA1c) measurements for patients with CFRD.[40] Center-level variation in the percentage of CFRD patients with one or more hemoglobin A1c measurement during the year indicate that a majority of centers are routinely testing their patients.

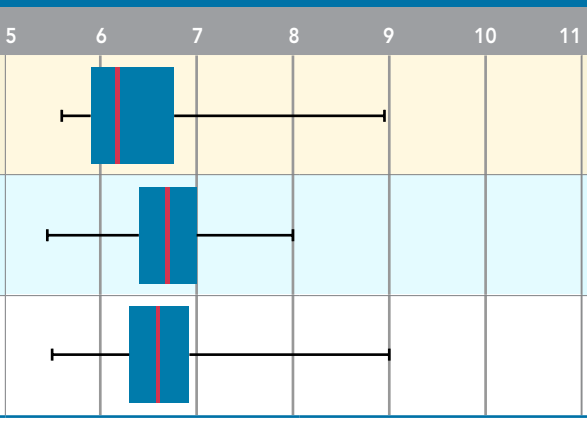
Percent of Patients with CFRD with at Least One Hemoglobin A1c Measurement, by Center



	Median	Min	Max
Patients 10 to 17 Years with at Least One Hemoglobin A1c Measurement	90.0	18.2	100.0
Patients 18 Years and Older with at Least One Hemoglobin A1c Measurement	77.4	0.0	100.0

The goal established by the CF Foundation CFRD guidelines is a hemoglobin A1c less than 7.0 percent for individuals with CFRD.[40]

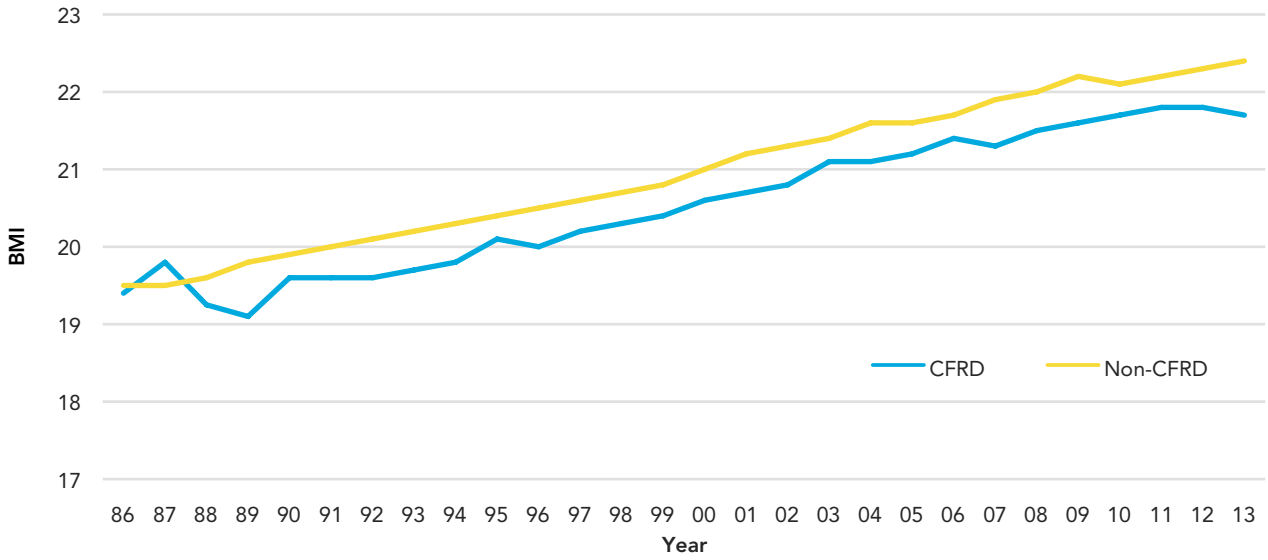
Median Hemoglobin A1c of Patients with CFRD, by Center



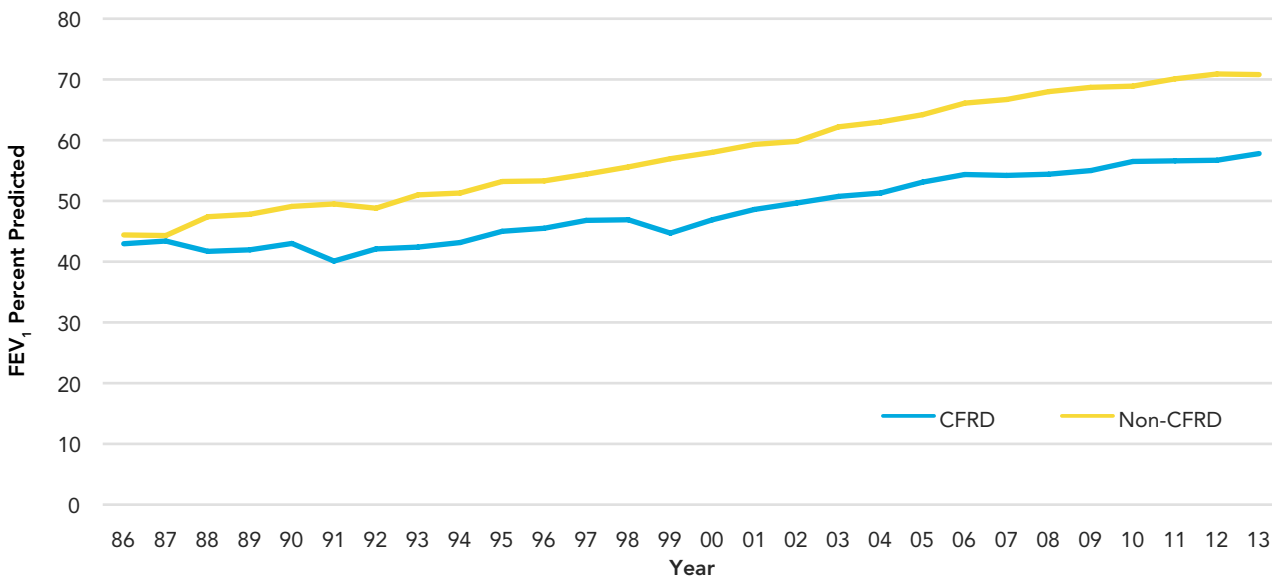
	Median	Min	Max
Hemoglobin A1c of Patients 10 to 17 Years with CFRD	6.2	5.6	9.0
Hemoglobin A1c of Patients 18 Years and Older with CFRD	6.7	5.5	8.0
Hemoglobin A1c of All Patients with CFRD	6.6	5.5	9.0

Adults who have been diagnosed with CFRD have a median BMI lower than that of patients who have not been diagnosed with CFRD, and this difference has persisted over time, even as median BMI has increased. Lung function is also lower among patients with CFRD and the difference between the two groups has increased over time.

Median BMI Value for Patients 20 Years and Older by CFRD Status, 1986–2013



Median FEV_1 Percent Predicted for Patients 18 Years and Older by CFRD Status, 1986–2013



GLI reference equations were used to calculate FEV_1 percent predicted.

Rates of secondary complications of CFRD, including retinopathy, microalbuminuria, kidney disease and neuropathy, remain low. As the CF population continues to age, adult care providers should continue to screen patients for these complications as recommended by the CFRD guidelines.[40]

Complications of CFRD in 2013 (n=5,542)

	All (n)	All (%)	< 18 (%)	≥ 18 (%)
Retinopathy	45	0.8	0.1	1.0
Microalbuminuria	90	1.7	0.3	2.0
Chronic renal insufficiency	266	5.0	0.7	5.8
Chronic renal failure requiring dialysis	18	0.3	0.0	0.4
Peripheral neuropathy	60	1.1	0.1	1.3
Any episodes of severe hypoglycemia	194	4.8	2.1	5.4

TRANSPLANTATION

Lung transplantation remains an option for some patients 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 1,426 individuals followed in the Registry in 2013 who have received a lung, kidney, heart or liver transplant.

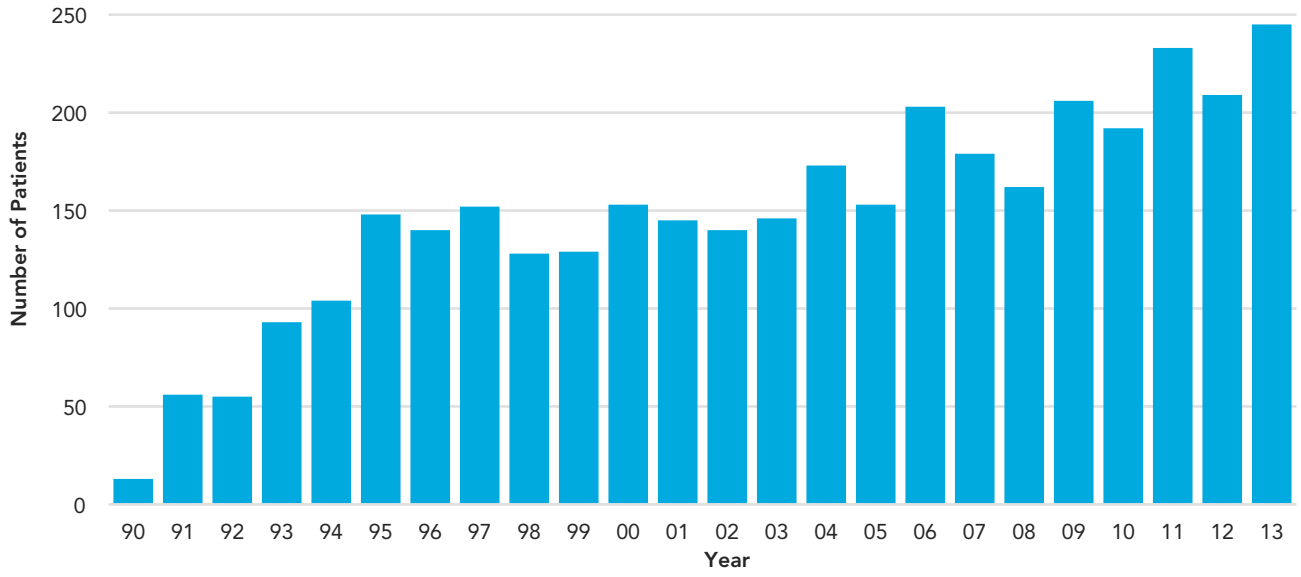
Transplant Status of Patients in 2013

	Number of Patients
Accepted, on waiting list	221
Evaluated, final decision pending	328
Evaluated, rejected	83
Received transplant this year	251
Received transplant in a prior year	1,175

Transplant status reflects all transplants, not just lung transplants.

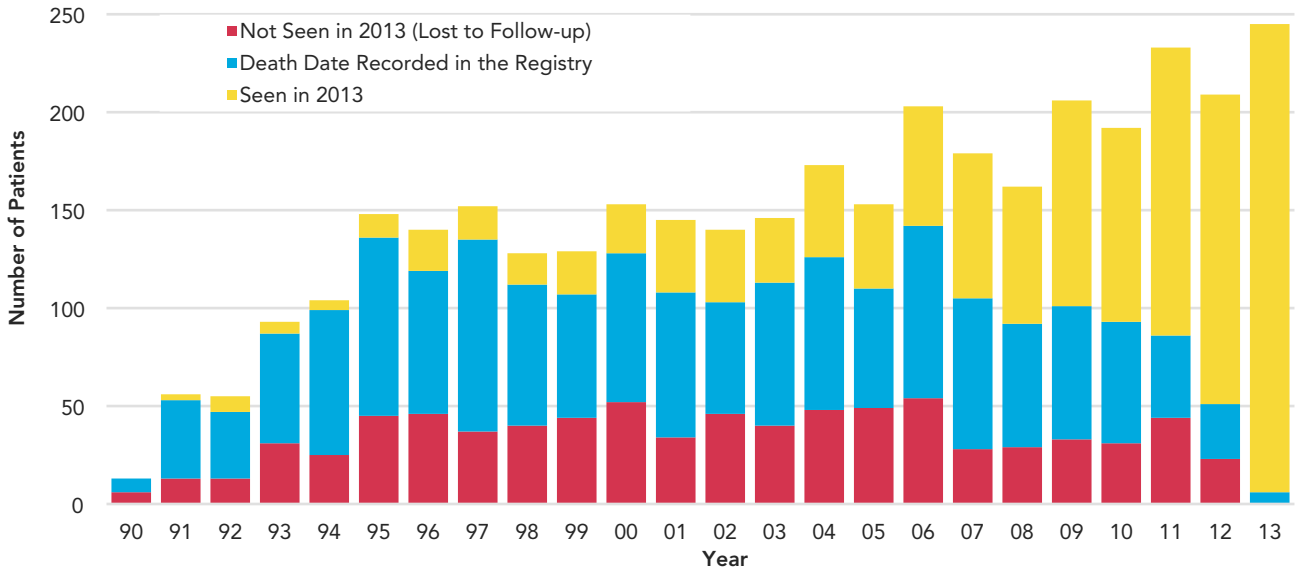
There are 1,291 patients who have had a lung transplant followed in the Registry in 2013, including the 245 patients who received a lung transplant in 2013.

Number of Patients Receiving a Lung Transplant, 1990–2013



There is concern that the Registry may have incomplete information on post-transplant patients if they receive all of their care at a transplant center. The figure below shows that data were not entered into the Registry in 2013 for a sizable proportion of lung transplant recipients. This may impact our survival calculations.

2013 Status of Lung Transplant Recipients by Year of Transplant, 1990–2013

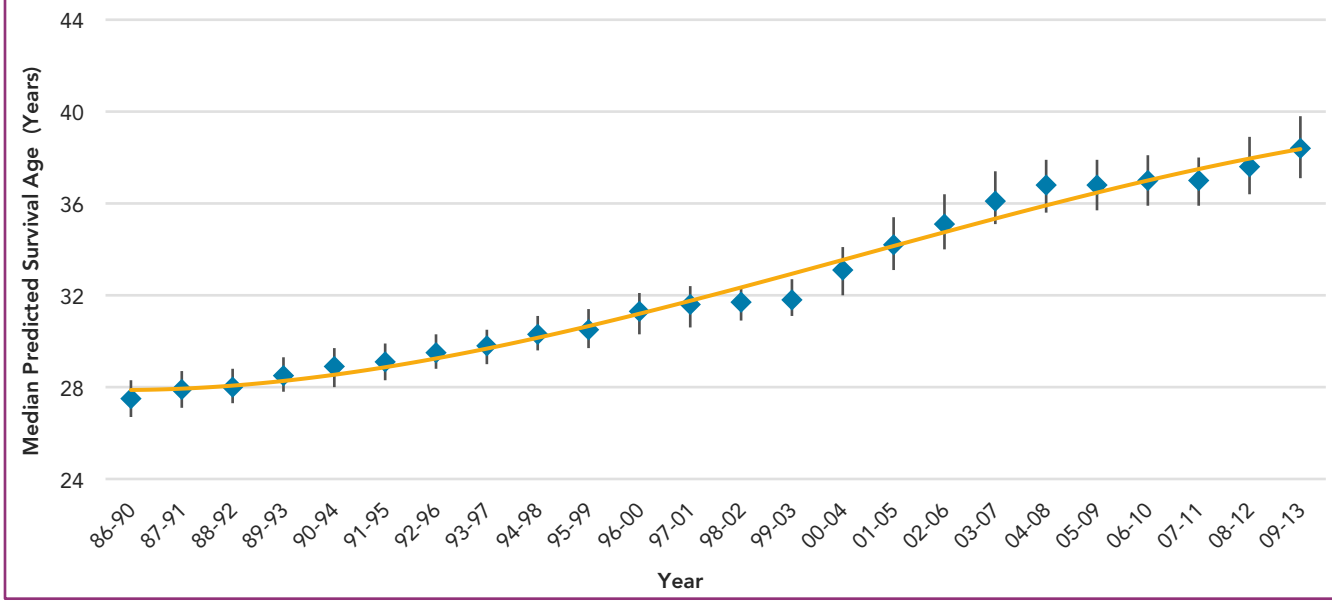


SURVIVAL

The median predicted survival age in 2013 is 40.7 years (95 percent confidence interval: 37.7–44.1 years). The median predicted survival age 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 2013 and assuming that mortality rates do not change.

The graph below shows the gains in median predicted survival from 1986 to 2013. By using five-year increments, the year-to-year variability decreases and the confidence bounds narrow. The median predicted survival age for 2009 to 2013 is 38.4 years (95 percent confidence interval: 37.1–39.8 years).

Median Predicted Survival Age, 1986–2013 In 5-Year Increments



The primary causes of death for patients with CF are respiratory/cardiorespiratory and transplant-related.

Primary Cause of Death in 2013

Cause	Number of Patients	Percent
Respiratory/cardiorespiratory	282	68.1
Transplant related: other	48	11.6
Other	35	8.5
Transplant related: bronchiolitis obliterans	20	4.8
Unknown	14	3.4
Liver disease/liver failure	12	2.9
Suicide	3	0.7
Trauma	0	0.0

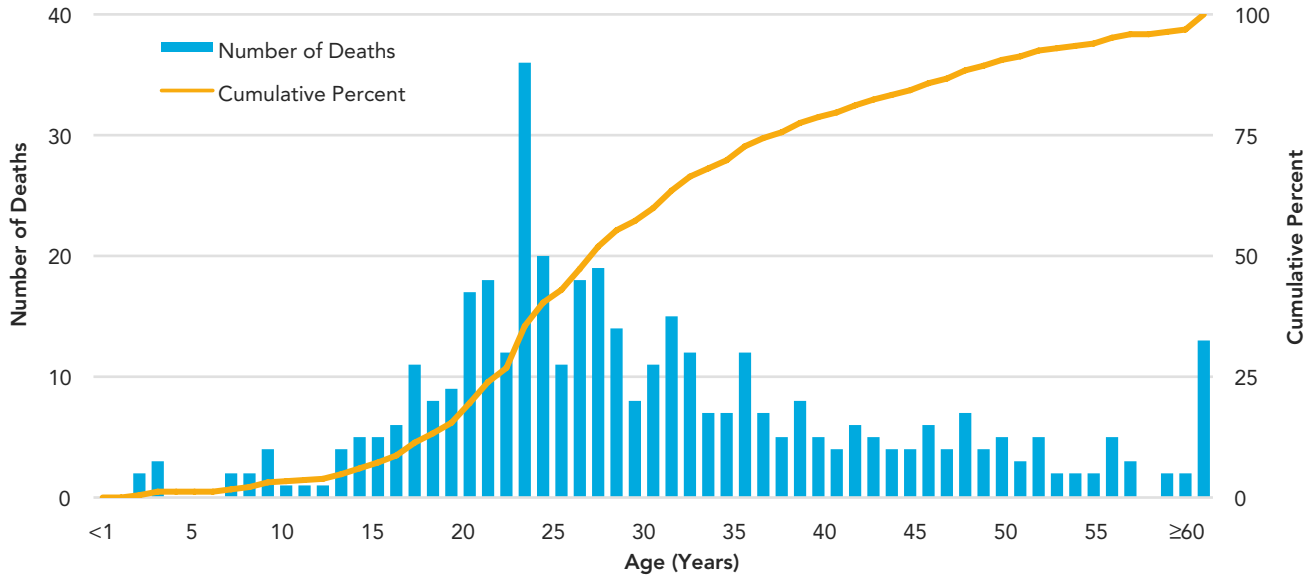
The table below displays the characteristics of the patients who died in 2013. Looking at the distribution, more women with CF died than men and a substantial number of those who died were diagnosed with CFRD or had undergone a lung transplant.

Characteristics of Patients Who Died in 2013

Female (%)	F508del Homozygous (%)	CFRD (%)	Lung Transplant Recipient (%)
53.1	51.2	65.2	22.0

The median predicted survival age is calculated using the entire 2013 Registry population. In contrast, the median age at death is calculated from the deaths reported in 2013. The median age at death for the 414 deaths reported in 2013 is 27.5 years.

Age at Death in 2013



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2013 Cystic Fibrosis Foundation Patient Registry Questionnaire

DEMOGRAPHIC DATA

Demographics

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

Race/Ethnicity Information

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

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

Death Information

Date of Death: (MM/DD/YYYY)

Check if date of death is approximate: ☐

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

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2013 Cystic Fibrosis Foundation Patient Registry Questionnaire

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

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

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

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

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

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

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

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

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

Other bacterial or fungal species: ☐
Specify: _____

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

Type of Specimen:
○ sputum ○ induced sputum ○ bronchoscopy

AFB Smear:
○ Positive ○ Negative ○ Not done

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

Mycobacterial Species:
☐ Mycobacterial tuberculosis
☐ Mycobacterium abscessus/chelonae
☐ Mycobacterium avium complex (MAC)
☐ Mycobacterium fortuitum group
☐ Mycobacterium gordonae
☐ Mycobacterium kansasii
☐ Mycobacterium marinum
☐ Mycobacterium terrae
☐ Other
Specify: _____
Please note: The option Mycobacterium avium complex (MAC) includes M. avium subsp. Avium, M. avium subsp. Hominissuis, M. avium subsp paratuberculosis, and M. intracellulare.

Medications

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

Pulmonary 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)

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2013 Cystic Fibrosis 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:____

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2013 Cystic Fibrosis 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)
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2013 Cystic Fibrosis 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)

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2013 Cystic Fibrosis 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

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2013 Cystic Fibrosis 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

2013 Cystic Fibrosis 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

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