THE CANADIAN CYSTIC FIBROSIS REGISTRY

2014 ANNUAL REPORT

Cystic Fibrosis Canada™

CYSTIC FIBROSIS

Cystic fibrosis (CF) is the most common fatal genetic disease affecting Canadian children and young adults. It is a multi-system disease that affects mainly the lungs and the digestive system. In the lungs, where the effects are most devastating, a build-up of thick mucous causes severe respiratory problems. Mucous also builds up in the digestive tract, making it difficult to digest and absorb nutrients from food. As improved therapies have helped to address the malnutrition issues, ultimately most deaths related to cystic fibrosis are due to lung disease. There is no cure.

CYSTIC FIBROSIS CANADA

Cystic Fibrosis Canada is a national charitable not-for-profit corporation established in 1960, and is one of the world's top three charitable organizations committed to finding a cure for cystic fibrosis. As an internationally-recognized leader in funding cystic fibrosis research, innovation, and clinical care, we invest more funding in life-saving CF research and care than any other non-governmental agency in Canada.

Since 1960, Cystic Fibrosis Canada has invested more than $235 million in leading research, innovation and care, resulting in one of the world's highest survival rates for Canadians living with cystic fibrosis. For more information, visit www.cysticfibrosis.ca.

Our mission is to end cystic fibrosis. We will help all people living with CF by funding targeted world-class research, supporting and advocating for high-quality individualized CF care and raising and allocating funds for these purposes.

Our vision is a world without cystic fibrosis.

Cover page: Patient from a CF clinic in British Columbia

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THE CANADIAN CYSTIC FIBROSIS REGISTRY

The Canadian Cystic Fibrosis Registry (CCFR), also referred to as "the Registry", is a national database of CF clinical information within Canada. The Registry allows the CF research and clinical community to gain important insights into this disease with the ultimate goal of improving the lives of individuals living with CF. The Registry serves many purposes:

A powerful research tool: The Registry is used to monitor important epidemiological trends that help guide the direction of research.

Education: The summary statistics in the Registry help to graphically show clinical outcomes over time. These visuals are presented to the public, medical and allied healthcare professionals, and many other groups to share and increase the knowledge about this disease in Canada.

Better understanding of CF populations: CF clinics can access the Registry data to better understand their own CF clinic population and respond to emerging healthcare issues, including nutritional status, infectious pathogens, pulmonary treatment, and more.

Quality improvement: Clinics can compare pulmonary and nutritional outcomes of individuals followed at their clinic to the national median value. These efforts will ultimately translate into improved outcomes for people with CF.

Each of the 42 accredited CF clinics across Canada submits data on behalf of patients into the Registry. Given that the majority of CF patients attend one of these clinics, we are confident that the Registry includes data on virtually all Canadians diagnosed with CF — giving a comprehensive picture of the CF population in this country.

There are many reasons that influence the survival of Canadians living with CF and studies are currently being conducted to better understand what those may be. Without the data from the Registry, these types of studies would not be possible.

The Registry system was recently updated in 2015 and now includes reporting capabilities, enhanced security, better French language support, video tutorials, and many other features which will better inform our CF community about this disease.

THANK YOU!

The continued cooperation and participation of CF clinics and those living with CF, along with the generous support of Cystic Fibrosis Canada's many friends, volunteers and donors is incredible. Thank you to everyone involved with the Registry. Without you all, this Registry could not exist and would not be the integral and significant resource that it has become. Everyone can be very proud of this accomplishment.

2014 HIGHLIGHTS

Over **4,100 Canadians** with cystic fibrosis received care at one of the **42 specialized CF clinics** based in hospitals across Canada

THE MEDIAN AGE
OF CANADIANS WITH CYSTIC FIBROSIS IS
21.9 YEARS OF AGE

There were **120 new diagnoses made in 2014:** 52 were through newborn screening and 18 were over 18 years of age

58.8% of CF patients are diagnosed within their first year of life

ALMOST 60% OF ALL PEOPLE
WITH CYSTIC FIBROSIS
IN CANADA **ARE ADULTS**

Cumulatively, CF patients underwent **867 courses of home IV therapy** in 2014

CUMULATIVELY, CF PATIENTS SPENT ALMOST
25,000 DAYS IN HOSPITAL
AND ATTENDED OVER
15,500 CLINIC VISITS IN 2014

FEV_1 percent predicted (a measure of lung function) is improving for persons with cystic fibrosis: **half of all 30 year olds** with cystic fibrosis had an **FEV_1 greater than 62.3%** in 2014 compared to **47.4%** two decades ago

THE **MEDIAN AGE OF SURVIVAL**
FOR CANADIANS WITH CYSTIC FIBROSIS
IS CURRENTLY **ESTIMATED** TO BE
51.8 YEARS OF AGE

86.2% of Canadians with cystic fibrosis must take **pancreatic enzymes** to digest food and absorb nutrients

28.7% of female adults with cystic fibrosis and **18.9% of male adults** with cystic fibrosis are classified as **underweight**

42.3% of female children and **41.9% of male children** with cystic fibrosis are above the national goal of 50th BMI percentile

33 CF PATIENTS
RECEIVED TRANSPLANTS
IN **2014**

47.4% and **37.4% of all patients** with cystic fibrosis are **infected in their lungs with harmful bacteria** such as ***Pseudomonas aeruginosa*** and ***Staphylococcus aureus*** respectively

24.0% of all CF patients have CF-related diabetes, and 40.0% of these individuals are 35 years of age and older

Over **2,000 different mutations** in the *CFTR* gene have been identified; however **89.7% of CF patients in Canada** carry at least one copy of the most common CF-causing mutation, **F508del**

OF THE 54 PATIENTS WHO DIED
IN 2014, **HALF WERE UNDER**
32.4 YEARS OF AGE

MESSAGE FROM NORMA BEAUCHAMP

PRESIDENT AND CEO, CYSTIC FIBROSIS CANADA

The Canadian Cystic Fibrosis Registry is one of our most outstanding assets of crucial and informative patient data on the Canadian CF population. This year, the Registry has gathered information from more than 4,100 Canadians with CF. This data is compiled anonymously and published to enhance knowledge and highlight key trends that lead to better CF research and care.

The Registry has become an indispensable resource in our efforts to ensure all Canadians with CF receive the highest quality, specialized care and the most effective treatments at the 42 CF clinics across the country. By capturing a broad range of data on the health of those living with CF, the Registry provides critical information to help advance many important initiatives including improvements in the quality of CF care and establishing Canada-wide standards for CF care and treatment.

This year's report shows the estimated median age of survival has now reached 51.8 years of age while almost 60 per cent of Canadians with CF are now 18 or older. These are incredible milestones and a challenge as we strive to serve the needs of an ever-increasing number of adults living with CF and its associated complications.

The tremendous success of the Registry would not be possible without the vital contributions of many. Most notably the individuals with CF and their families who generously agree to share their data and the clinic team members who collect and enter the data. We are deeply grateful to all who have helped and continue to make the Registry a success to improve the lives of Canadians with cystic fibrosis.

Together, let's END CF.

MESSAGE FROM DR. ANNE STEPHENSON MD, PHD

MEDICAL DIRECTOR, REGISTRY, CYSTIC FIBROSIS CANADA
CF PHYSICIAN, ST. MICHAEL'S HOSPITAL, TORONTO

I am proud to present the *Canadian CF Registry 2014 Annual Report*. The Registry continues to be a national resource that is being used for patient care, quality improvement initiatives, retrospective observational studies, and advocacy work. Over time, the *Canadian CF Registry* has evolved and expanded to adapt to the needs of the CF community and has positioned itself to ensure it is flexible for future modifications to the data capture so as to reflect the issues that affect individuals living with CF today. This past year, the Registry platform was revised with many new features including a secure, web-based application that supports the collection and reporting of real-time patient data, new reporting tools that provide users with the capability to create their own custom views of the underlying data and the ability to show individual patient trends over time. National CF registries are incredible resources that have the potential to advance care and improve our understanding of this disease at both the patient-level and the population-level. For example, using the Registry data, we were able to show the benefits of newborn screening (NBS) for CF in terms of nutrition and growth which can be used as an advocacy tool to ensure that NBS programs are implemented in all provinces across Canada.

The annual report provides summary statistics to graphically show important clinical outcomes of the Canadian CF population. Although the revised Registry platform allows clinics to collect information on individuals with CFTR-related disease, this report only summarizes information for those with a confirmed diagnosis of CF. Some of the data represents cross-sectional information for the specific year while others show longitudinal information and trends over time. Incorporating these summary statistics into presentations for the public, medical and allied health care professionals, and many other groups can increase knowledge about Canadians with CF and facilitate fundraising efforts. In addition, the Registry continues to be used to conduct exciting research within Canada and in collaboration with other countries. The number of peer-reviewed publications using the Registry data continues to grow. International collaborations are ongoing with the USA, United Kingdom and Europe to better understand variations in health outcomes of the CF population.

We would like to thank all the patients and families who participate in the Registry and all the CF clinics across the country who take care and time to enter data each and every year. The Registry is comprehensive and has a low rate of loss to follow up which is a testament to the hard work of each clinic across the country. We want the Registry to meet the needs of the CF community and we welcome input and suggestions to improve this resource for all Canadians living with CF.

HOW TO READ THE REPORT

All data presented in this report have been re-calculated for each year indicated in order to include data that might have been updated or missed in previous years. This ensures that data can be compared accurately between different years within this report. It also means that discrepancies might occur when comparing historical reports with this current one.

Patients who were reported on by any of the 42 CF clinics in 2014 were included in this report.

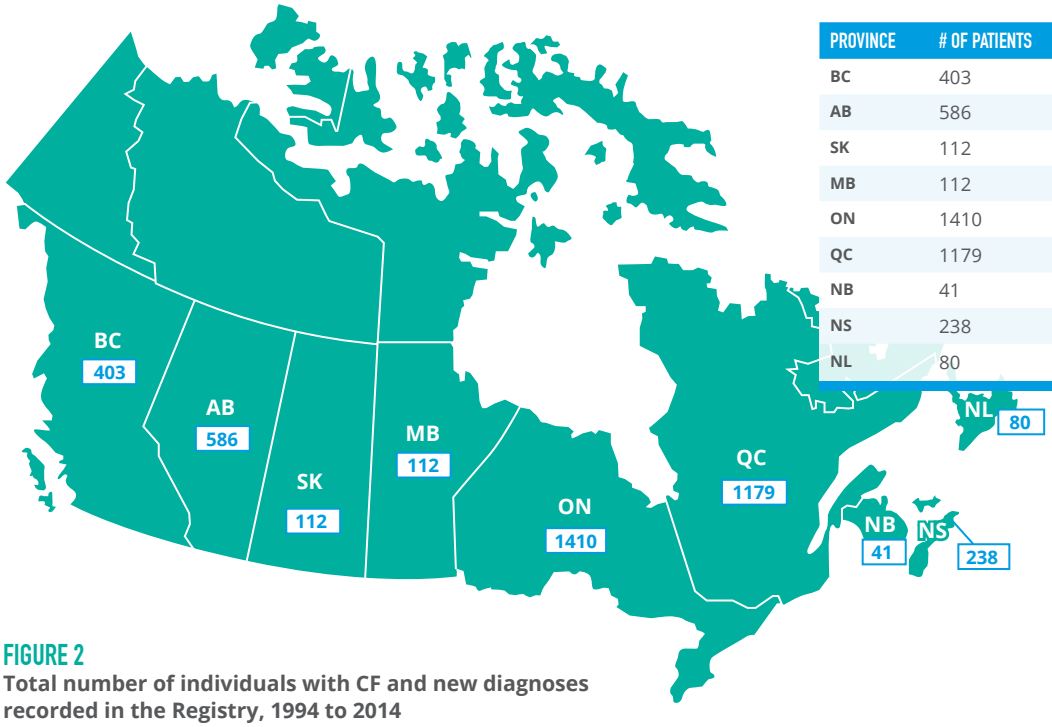
For those who are under 18 years of age, those individuals are categorized as *children* and those 18 years of age or older are categorized as *adults*. For the purposes of this report, age is calculated as of December 31, 2014.

DEMOGRAPHIC DATA

NUMBER OF CANADIANS WITH CYSTIC FIBROSIS

Across Canada, a total of 4,128 individuals with cystic fibrosis attended one of the 42 CF clinics in 2014 (Figure 1). Individuals will be counted in multiple provinces if they attended CF clinics in different provinces but they are only counted once (*i.e.* unique individuals) in the data analyses of this report. Since 1994, the total Canadian CF population has increased by almost 40% and in 2014, there were 120 new diagnoses of cystic fibrosis in Canada (Figure 2).

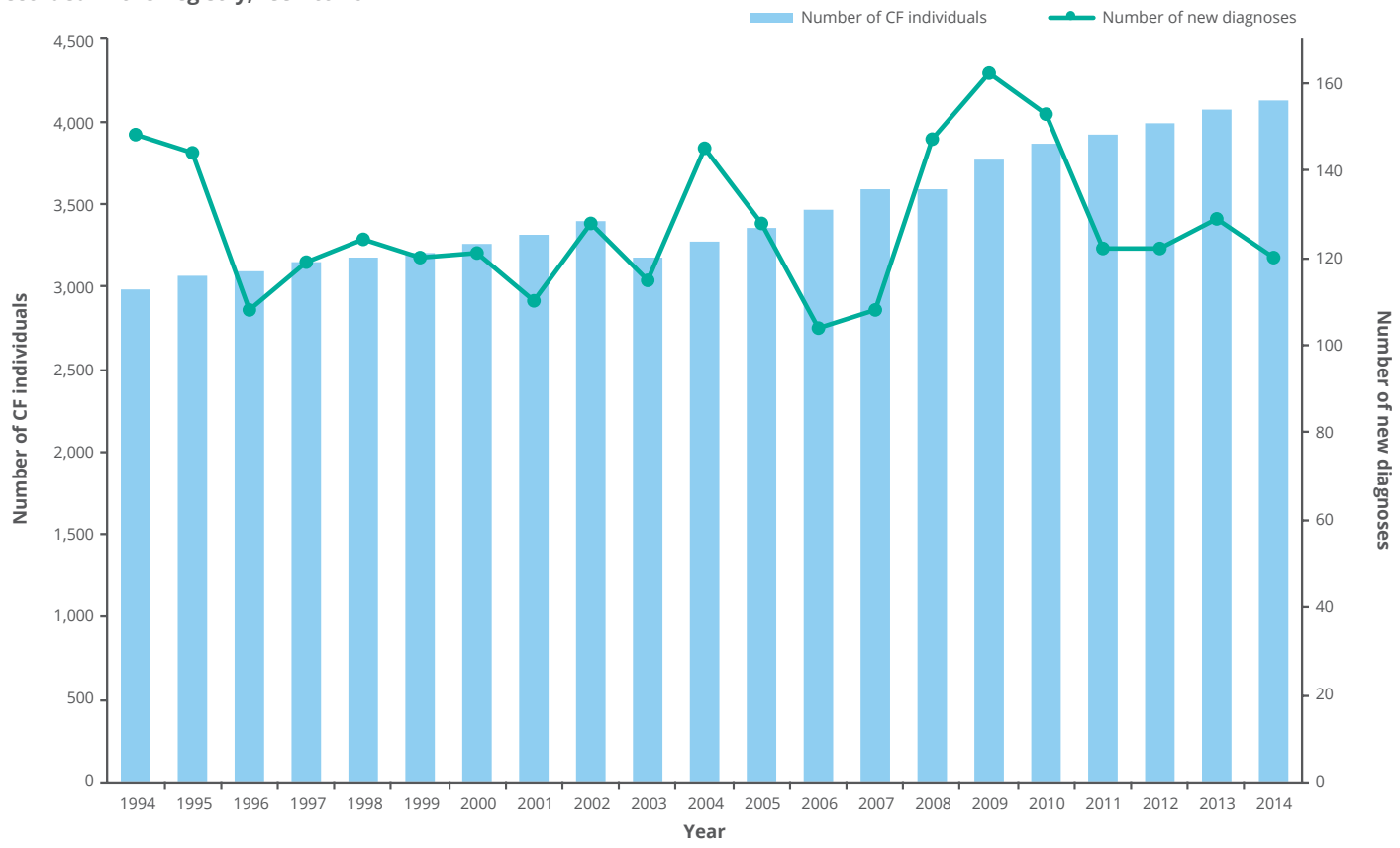
FIGURE 1



PROVINCE	# OF PATIENTS	FEMALE	MALE	ADULTS	CHILDREN
BC	403	170	233	243	160
AB	586	293	293	318	268
SK	112	48	64	62	50
MB	112	46	66	59	53
ON	1410	691	719	853	557
QC	1179	551	628	736	443
NB	41	21	20	27	14
NS	238	105	133	137	101
NL	80	31	49	52	28

FIGURE 2

Total number of individuals with CF and new diagnoses recorded in the Registry, 1994 to 2014



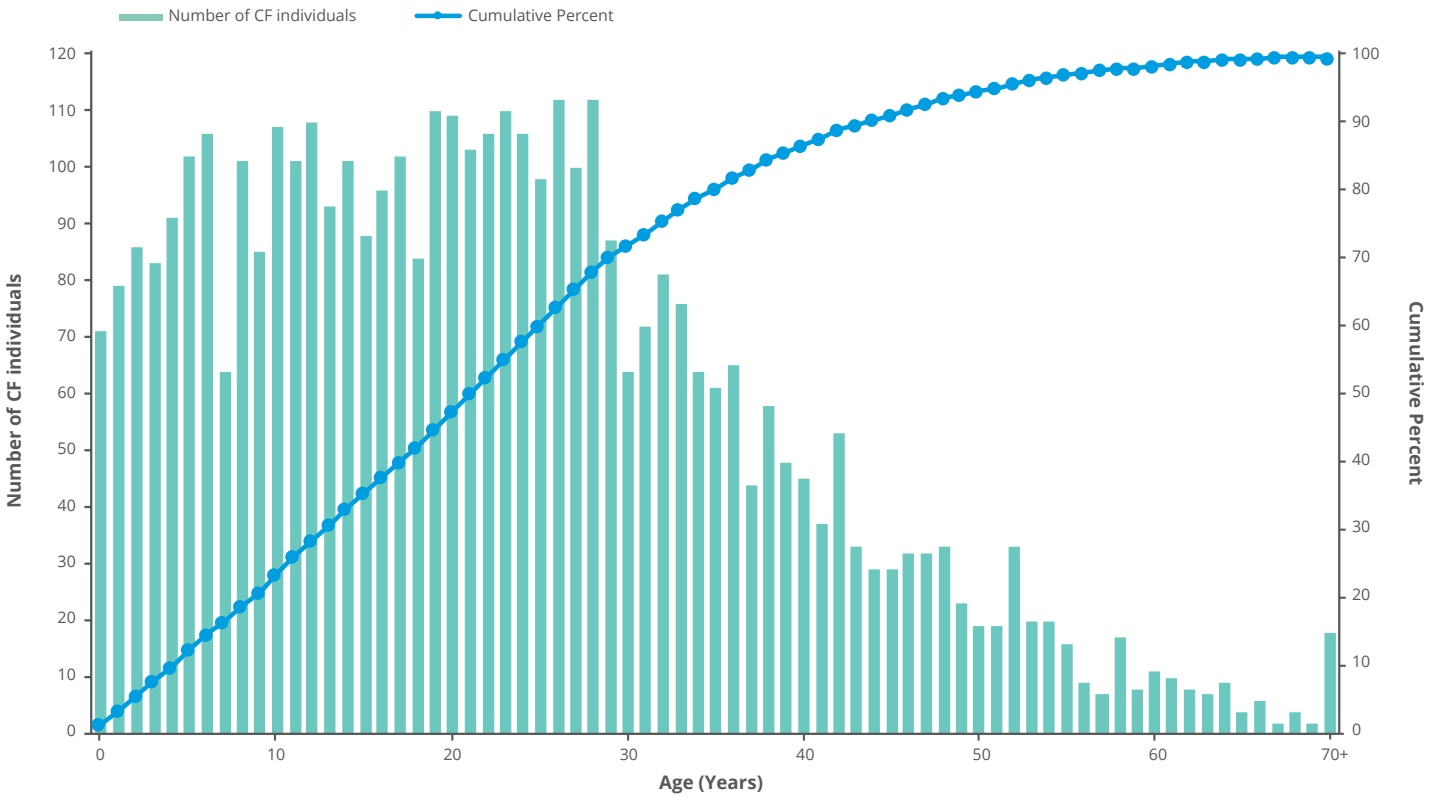
DEMOGRAPHIC DATA

AGES OF CANADIANS WITH CYSTIC FIBROSIS

Figure 3 shows the age distribution of the Canadian CF population in 2014. The ages of individuals with cystic fibrosis range from birth to almost 80 years old. The median age of all individuals reported on in 2014 was 21.9 years, with 59.7% of individuals over 18 years of age (Figure 6) and 14.4% over 40 years of age.

FIGURE 3

Age distribution of the CF population, 2014



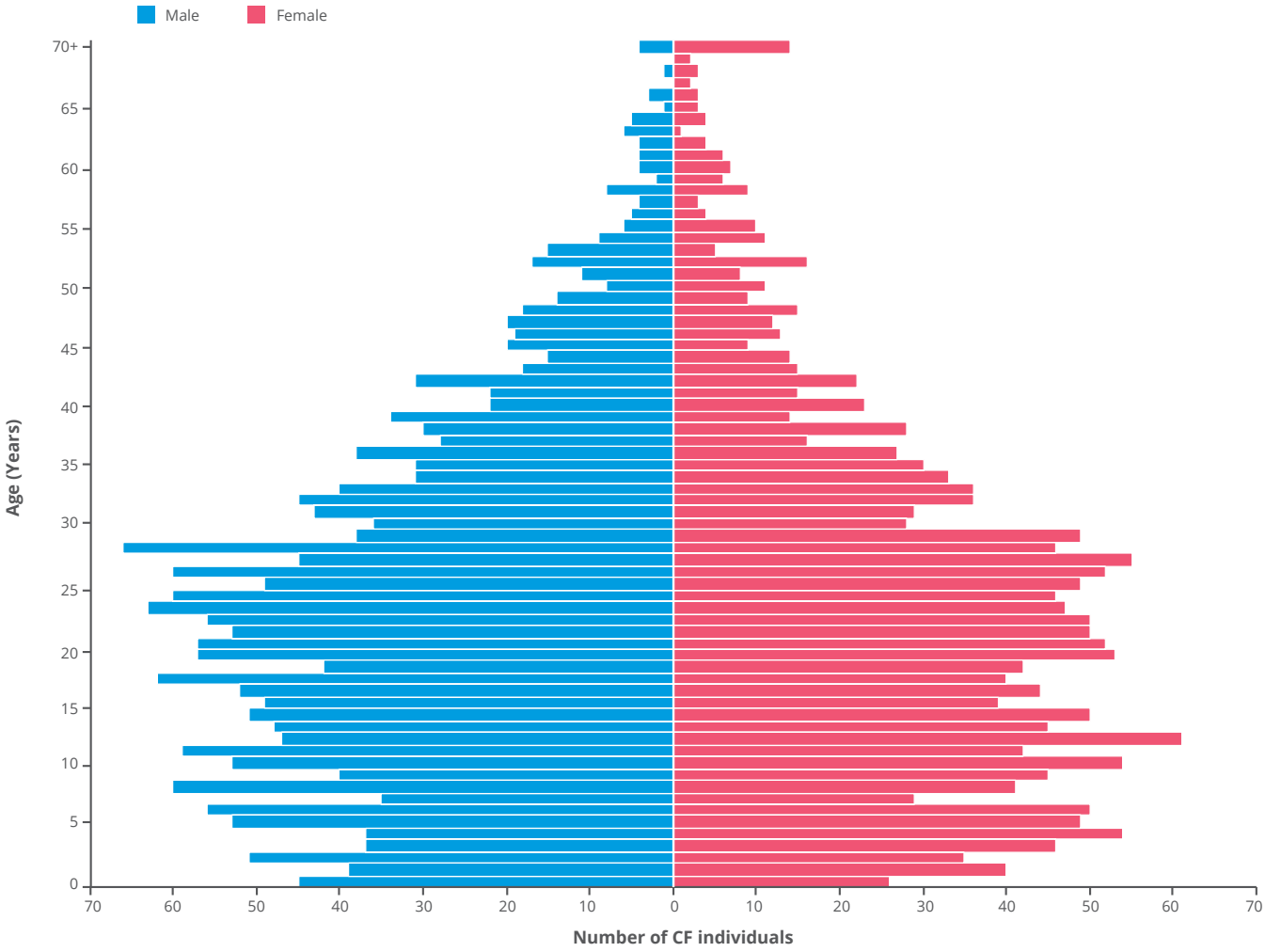
DEMOGRAPHIC DATA

AGE AND SEX DISTRIBUTION OF CANADIANS WITH CYSTIC FIBROSIS

In 2014, males accounted for 53.1% of individuals in the Registry with 7.7% of males and 6.8% of females over the age of 40 (Figure 4).

FIGURE 4

Population distribution by age and sex of the CF population, 2014



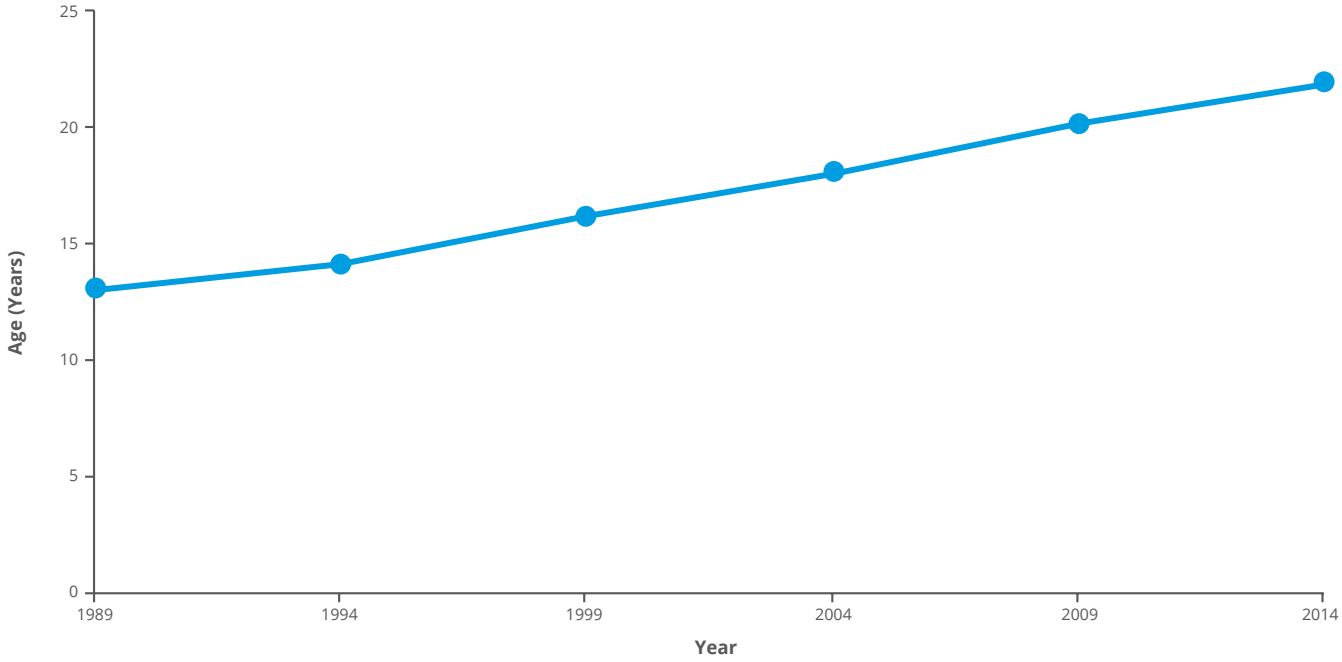
DEMOGRAPHIC DATA

MEDIAN AGE OF CANADIANS WITH CYSTIC FIBROSIS

The current median age of individuals with CF reported on in 2014 is 21.9 years, almost nine years higher than it was in 1989 (Figure 5).

FIGURE 5

Median age of CF individuals reported on from 1989 to 2014

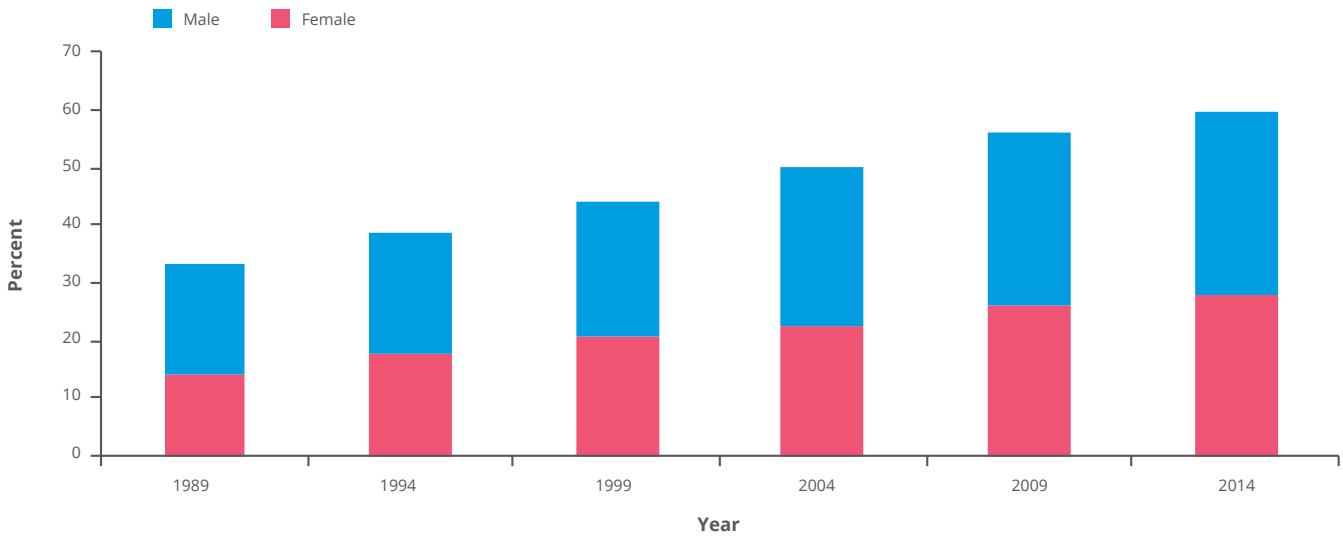


CANADIAN ADULTS WITH CYSTIC FIBROSIS

Adults (individuals 18 years of age or older) account for 59.7% of individuals in the Registry in 2014 with 27.8% adult females and 31.9% adult males (Figure 6).

FIGURE 6

Proportion of CF adults, by sex, 1989 to 2014



DIAGNOSIS

AGE AT DIAGNOSIS

By one year of age, 58.8% of individuals are diagnosed with CF, and over two thirds (66.8%) are diagnosed by the age of two years (Figure 7). The median age of diagnosis has been declining slowly since 1989 which can be attributed to both improved diagnostic tools and the implementation of provincial newborn screening programs for CF (Figure 8). Adults diagnosed later in life (over the age of 40 years) account for only 2% of all diagnoses.

As newborn screening (NBS) programs for cystic fibrosis continue to be introduced in Canadian provinces (at the time of publication, it is available in all provinces except Quebec), the majority of individuals with cystic fibrosis will be diagnosed at birth. Figure 9 shows the percentage of newborns diagnosed through the NBS program over the last 7 years. In 2014, 52 (43.3%) of all new diagnoses were made through the NBS program.

FIGURE 7

Age at diagnosis, all individuals with CF reported on in the Registry as of December 31, 2014

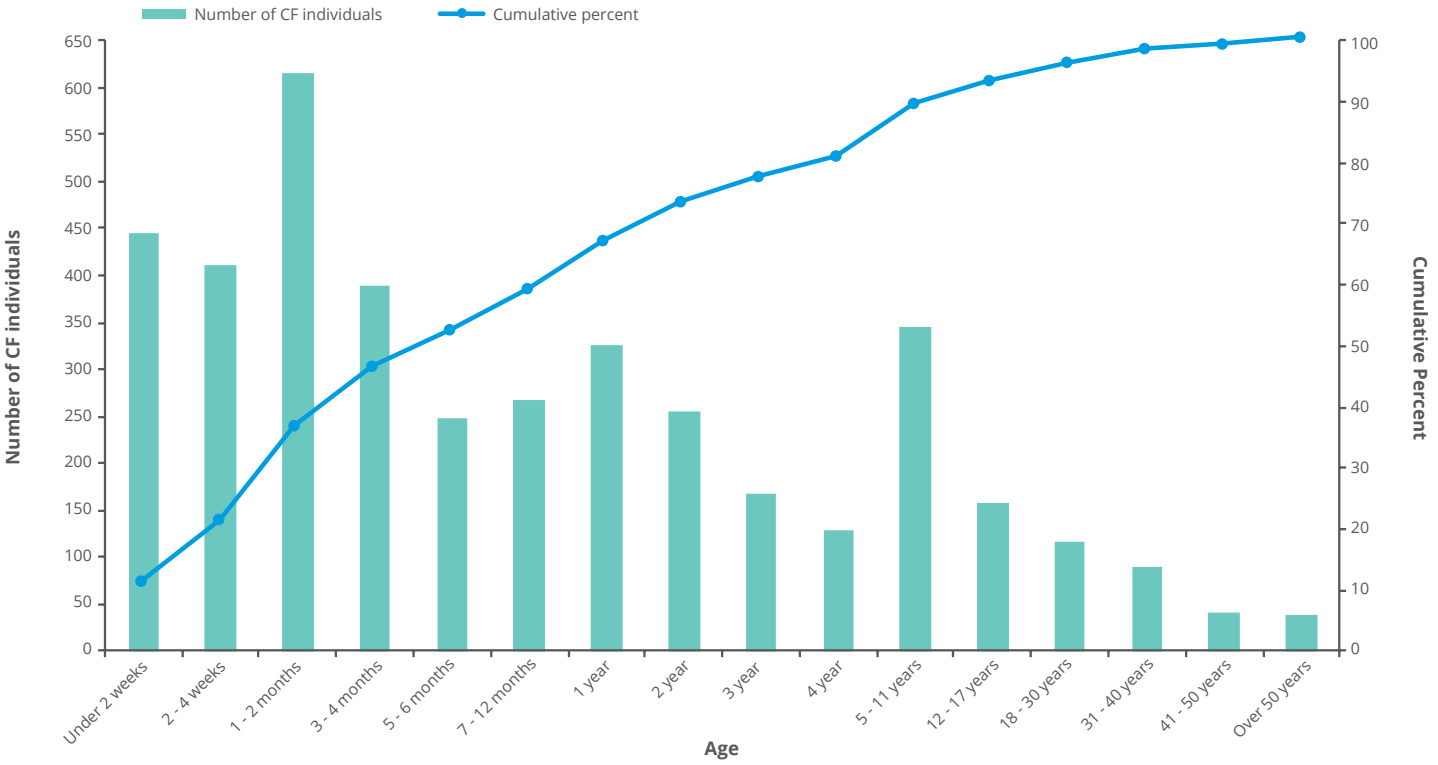


FIGURE 8

The median age at diagnosis for individuals with CF reported on from 1989 to 2014

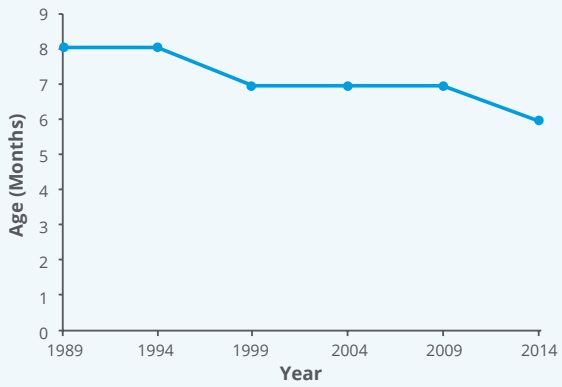


FIGURE 9

Proportion of all new diagnoses made through the NBS program, 2008 to 2014

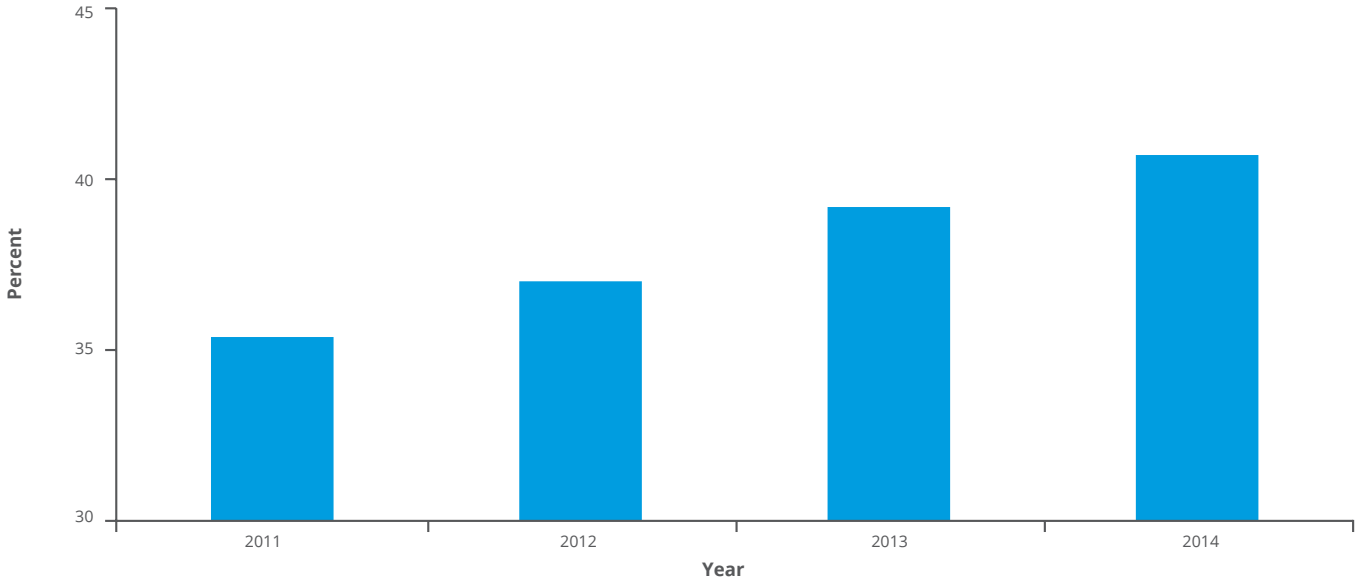
DIAGNOSIS

SWEAT CHLORIDE TESTING

Sweat chloride testing is used in the diagnosis of CF. Individuals with CF have higher levels of chloride in their sweat and these tests measure the amount of chloride in the sweat. Typically, two sweat chloride test results greater than 60 mmol/L are needed to confirm a CF diagnosis. The Registry began capturing sweat chloride test results in 2011. In 2014, 1,679 (40.7%) individuals with CF had at least one sweat chloride test result recorded in the Registry (Figure 10).

FIGURE 10

Proportion of individuals with CF with at least one sweat chloride test result in the Registry, 2011 to 2014

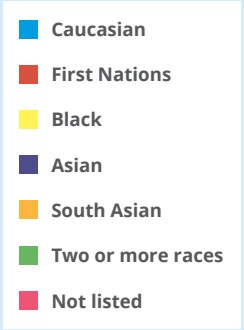


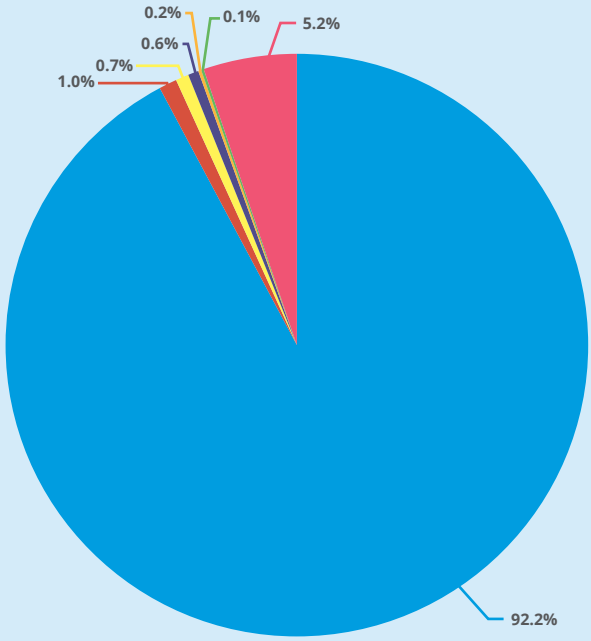
ETHNICITY

The majority of the Canadian CF population is Caucasian (92.2%). Of those remaining who have an identified ethnicity (Figure 11), they are divided among four other ethnic groups (First Nations, Black, Asian and South Asian).

FIGURE 11

Ethnicity, 2014





GENOTYPE

Cystic fibrosis is caused by one or more mutations in a single gene located on chromosome 7, termed the Cystic Fibrosis Transmembrane Regulator (*CFTR*) gene. The *CFTR* gene codes for the CFTR protein which functions as a chloride channel and is involved in many cellular functions. To date, more than 2,000 different mutations in the *CFTR* gene have been identified.

The most common CF mutation worldwide is a three base-pair deletion in the *CFTR* gene resulting in the deletion of the phenylalanine (F) residue at position 508 in the CFTR protein, commonly referred to as **F508del**. CF disease-causing mutations can be classified into five major categories depending on the how the mutation impacts the production and function of the CFTR protein (Table 1). There are some mutations where the impact on the CFTR protein is not clear or unknown therefore these cannot be classified. CFTR protein modulator medications target specific classes of mutations.

TABLE 1
Classification of CFTR mutations based on the impact on the CFTR protein

CLASS	HOW CFTR PROTEIN IS AFFECTED	EXAMPLES
I	No functional CFTR protein is made	G542X, W1282X, 621+1G->T
II	CFTR protein is abnormal and destroyed by the cell before it reaches the cell membrane	F508del, G85E
III	CFTR protein reaches the cell membrane but the channel is blocked	G551D
IV	CFTR protein reaches the cell membrane but the channel does not move chloride the way it should	R117H, R334W
V	The CFTR protein is made and works properly but the quantity of protein made is insufficient	3849+10kbC->T

Of those individuals with genetic information recorded within the Registry and reported on in 2014, 49.9% carry two F508del mutations (Figure 12) and 89.7% carry at least one F508del mutation (Table 2). The genotype distribution is similar between adults (18+ years) and children (0-17 years) (Figure 13). There are 4,996 individuals in the entire Registry that are reported as being alive and out of those, 4,631 (92.7%) individuals have at least one CF mutation recorded.

FIGURE 12
Genotype (based on N = 4,042), 2014

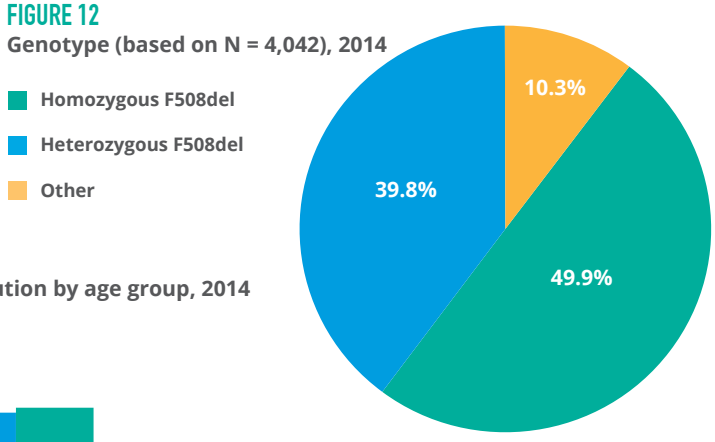


FIGURE 13
Genotype distribution by age group, 2014

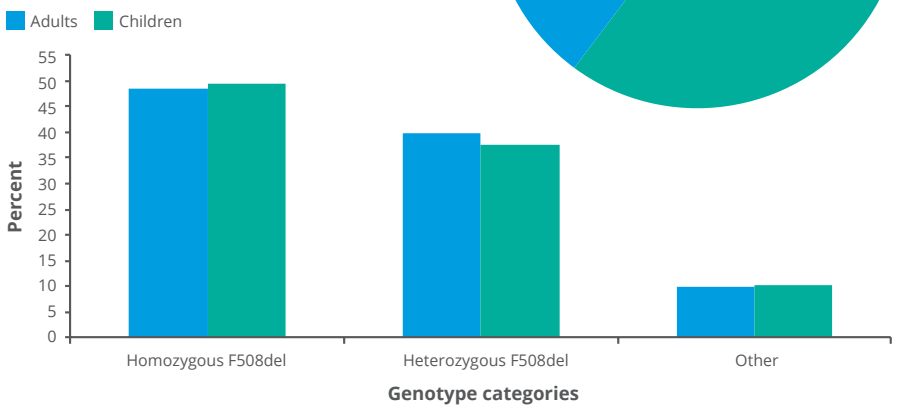


TABLE 2
Frequency of CF mutations on one or both alleles (top ten)

GENOTYPE	NUMBER	PERCENT
F508del	3,625	89.7
621+1G->T	246	6.1
G542X	131	3.2
G551D	119	2.9
711+1G->T	107	2.6
A455E	100	2.5
N1303K	90	2.2
R117H	81	2.0
G85E	63	1.6
M1101K	56	1.4

RESPIRATORY
MEDIAN FEV_1 PERCENT PREDICTED

Respiratory measures are needed to evaluate lung health. FEV_1 (forced expiratory volume in one second) is the volume of air that a person can forcibly blow out in one second. FEV_1 percent predicted for an individual is calculated by comparing it to the average FEV_1 of a healthy population of similar age, height and sex. Lung function is reliably measured starting at six years of age.

In previous reports, we have used the Wang[1] and Hankinson[2] reference equations in order to calculate the percent predicted FEV_1 values for paediatric and adult patients respectively. New this year, we have changed to the Global Lung Initiative[3] (GLI) equations because the GLI reference equations span the full age spectrum from 3 to 95 years of age which means that we do not have to use two different reference equations for child and adult populations.

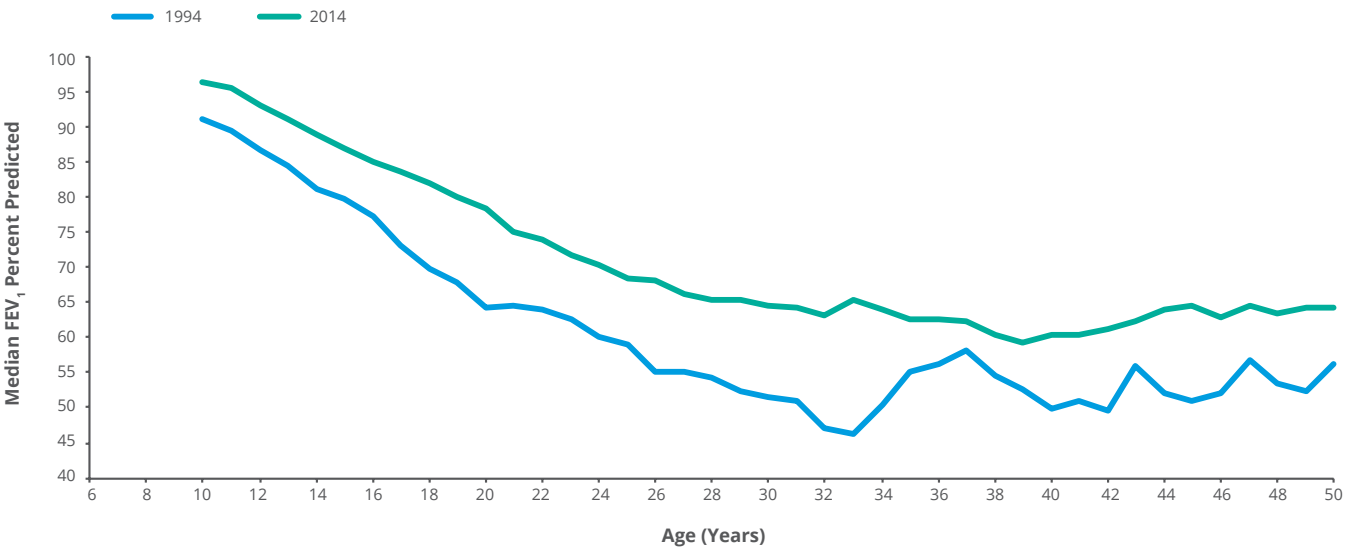
We found that while there was little difference between FEV_1 percent predicted values whether you use the Hankinson or the GLI reference equation for the adult population, applying the GLI to the paediatric population resulted in a lower values compared to Wang equations. This is because the GLI equations predict a higher lung volume for children compared to the Wang equations. For comparison, the national median FEV_1 percent predicted for adults (ages 18 years and older) using GLI was 66.5% compared to 66.2% using Hankinson. For children (ages 6-17 years), the national median FEV_1 percent predicted using GLI was 90.8% compared to 94.5% using Wang.

Figure 14 shows in a 5-year moving average window, the median FEV_1 percent predicted from the ages 6 to 50 years. While there is a tendency for lung function to decline with age, the median FEV_1 percent predicted at 30 years of age in 2014 was 62.3% compared to 47.4% in 1994. From the ages of 6 to 30, the data for 1994 shows a higher average annual decline in lung function of 2.0% compared to 1.6% for 2014. The largest declines occur during the teenage years, indicating that the transition from adolescent/youth to adult is a particularly vulnerable time for individuals with cystic fibrosis.

Figure 15 shows that individuals who were born recently have a higher median FEV_1 percent predicted and the rate of decline is slower than those born earlier (average annual decline of 0.8% in the 2005-2009 birth cohort compared to 1.2% in the 1985-1989 birth cohort).

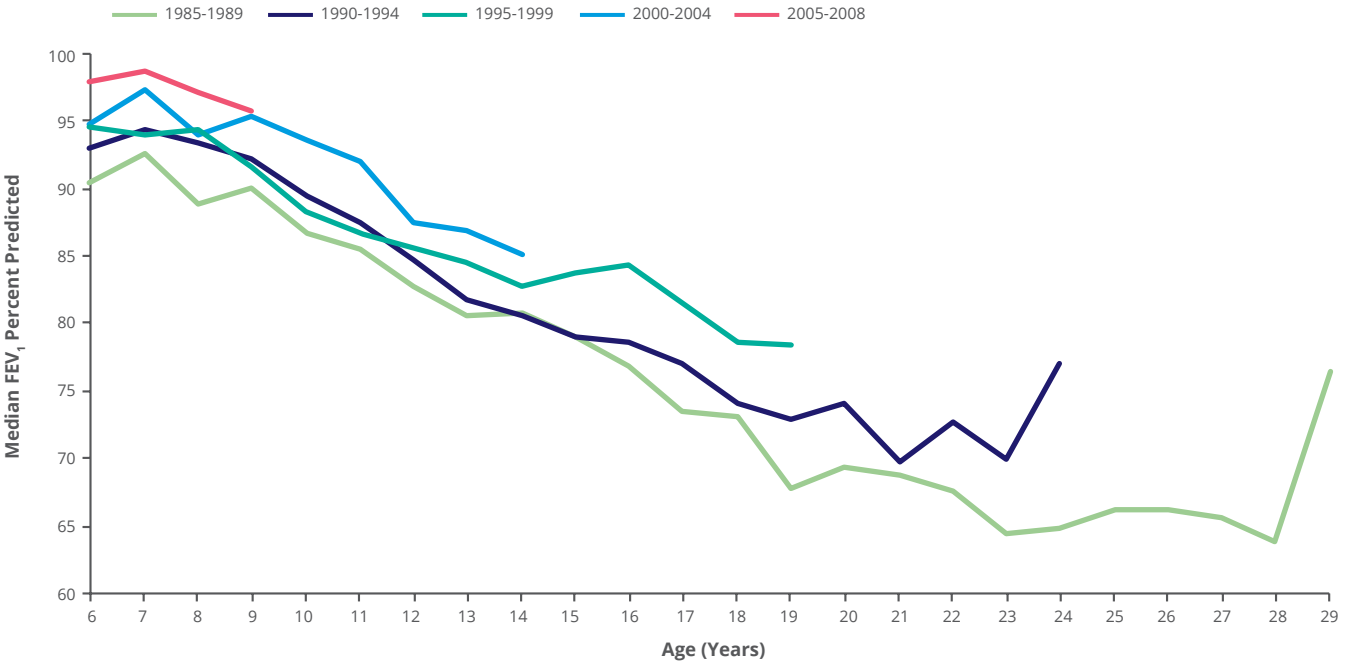
FIGURE 14

Median FEV_1 percent predicted vs. age (in a 5-year moving window), 1994 and 2014*



**GLI reference equations used to calculate FEV_1 percent predicted values*

FIGURE 15
Median FEV_1 percent predicted by birth cohorts*



**GLI reference equations used to calculate FEV_1 percent predicted values*

RESPIRATORY

RESPIRATORY STATUS

Table 3 summarizes the FEV_1 percent predicted classified by lung function severity and includes data from all patients reported on in 2014 including those who are post-transplant. For children ages 6 to 17 years, the majority (51.8%) have normal lung function (FEV_1 percent predicted greater than or equal to 90% predicted). For adults, the majority (37.5%) have lung function classified as moderate (Figure 16). Median FEV_1 percent predicted has been steadily increasing over time for both age groups (Figure 17).

FIGURE 16
Respiratory status of children and adults with CF, 2014

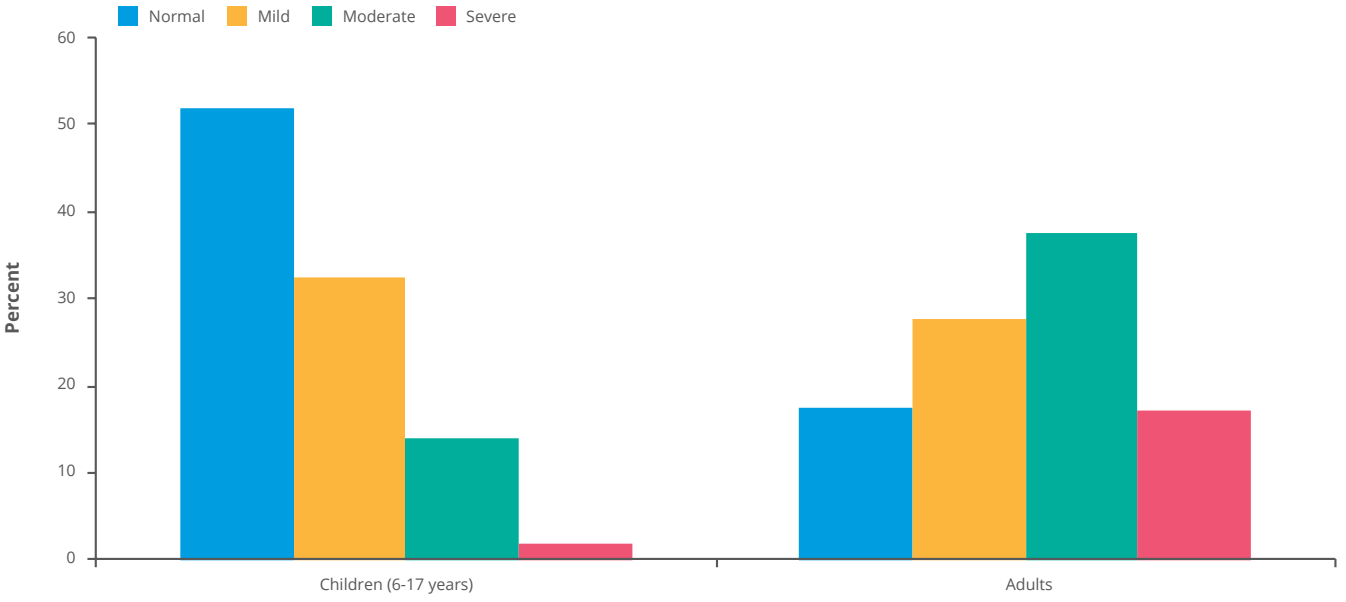


FIGURE 17

Median FEV_1 percent predicted values for children (6 to 17 years) and adults with cystic fibrosis, 1989 to 2014

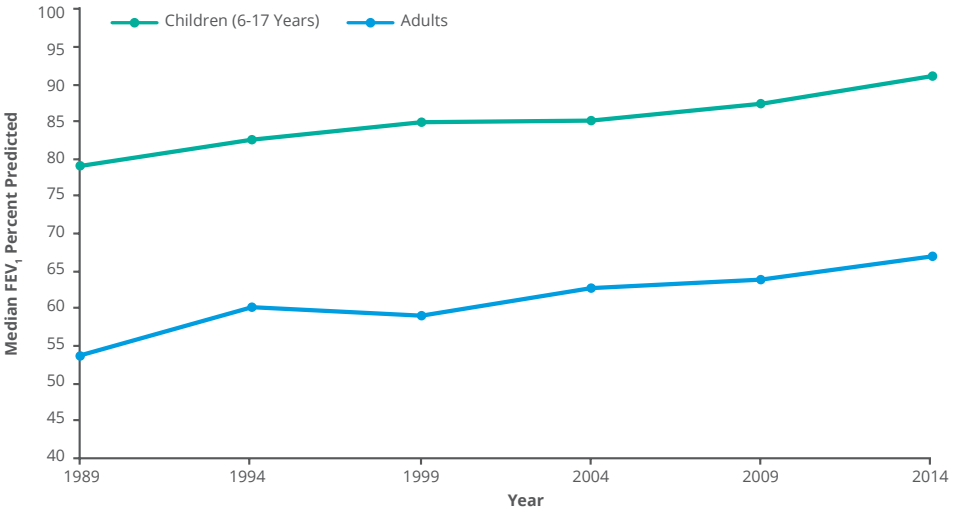


TABLE 3

FEV_1 percent predicted classification

CLASSIFICATION	RANGE
Normal	≥ 90%
Mild	70 – 89%
Moderate	40 – 69%
Severe	< 40%

RESPIRATORY

RESPIRATORY STATUS BY SEX

Figure 18 and Figure 19 show that the proportion of people within each lung function category is generally similar between males and females.

FIGURE 18

Respiratory status of children (6 to 17 years) with CF, by sex, 2014

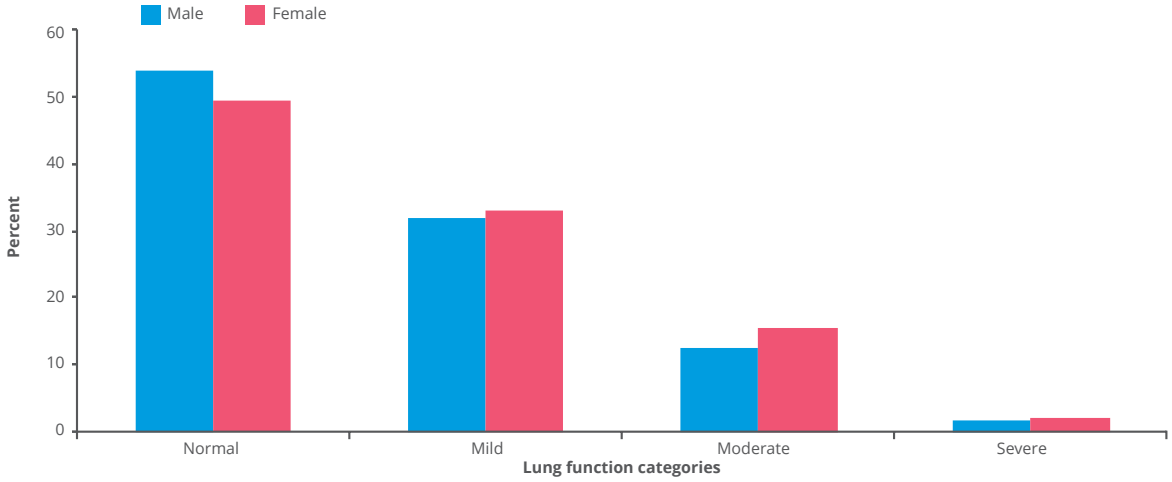
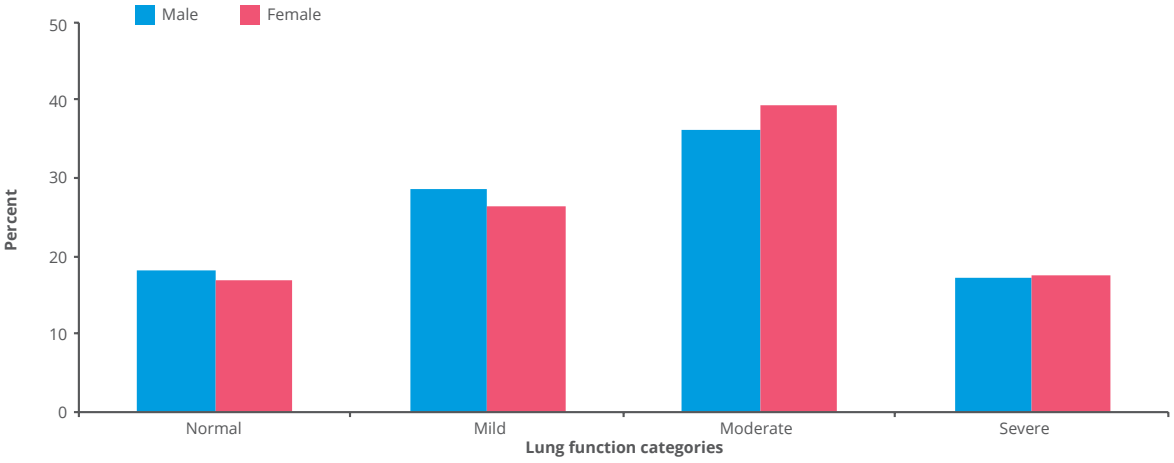


FIGURE 19

Respiratory status of adults (18 years of age and older) with CF, by sex, 2014



NUTRITION
PANCREATIC STATUS

Malnutrition is common in individuals with cystic fibrosis as a result of pancreatic insufficiency. Pancreatic enzymes are given as supplements to help with digestion and absorption of nutrients. In 2014, 86.2% of individuals with cystic fibrosis were taking supplemental pancreatic enzymes (pancreatic insufficient), whereas 13.8% did not require oral pancreatic enzyme supplementation to digest their food (pancreatic sufficient) (Figure 20).

For individuals 40 years of age or older, 32.6% were pancreatic sufficient (Figure 21). This is a reflection of the fact that individuals diagnosed with cystic fibrosis as adults are more likely to have milder mutations that are associated with pancreatic sufficiency.

FIGURE 20
Pancreatic sufficiency in individuals with cystic fibrosis, 2014

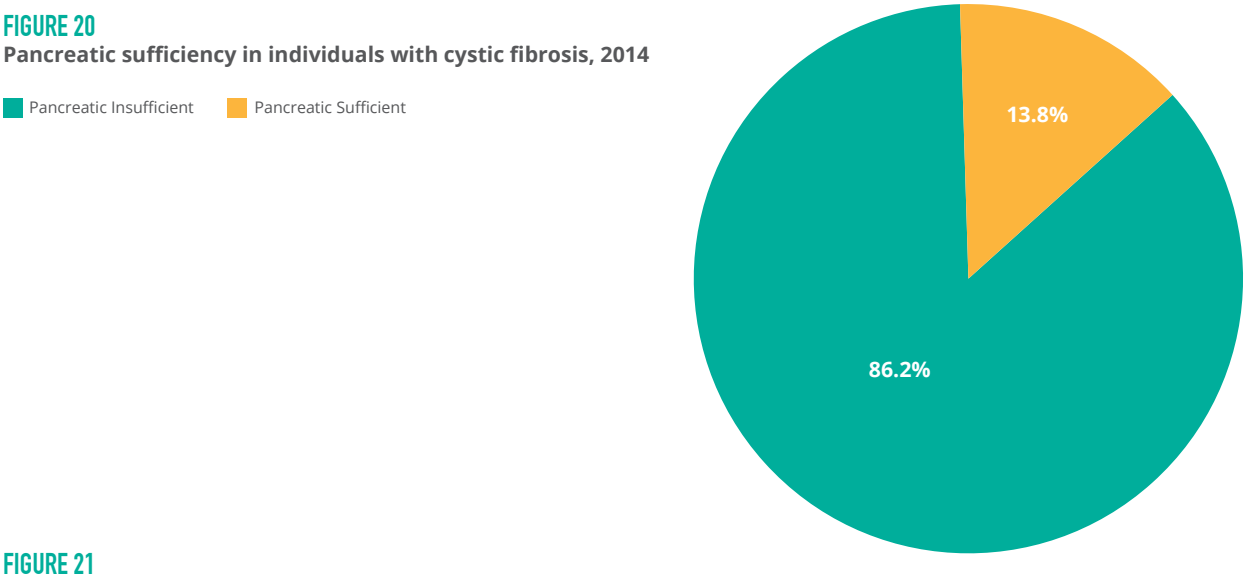
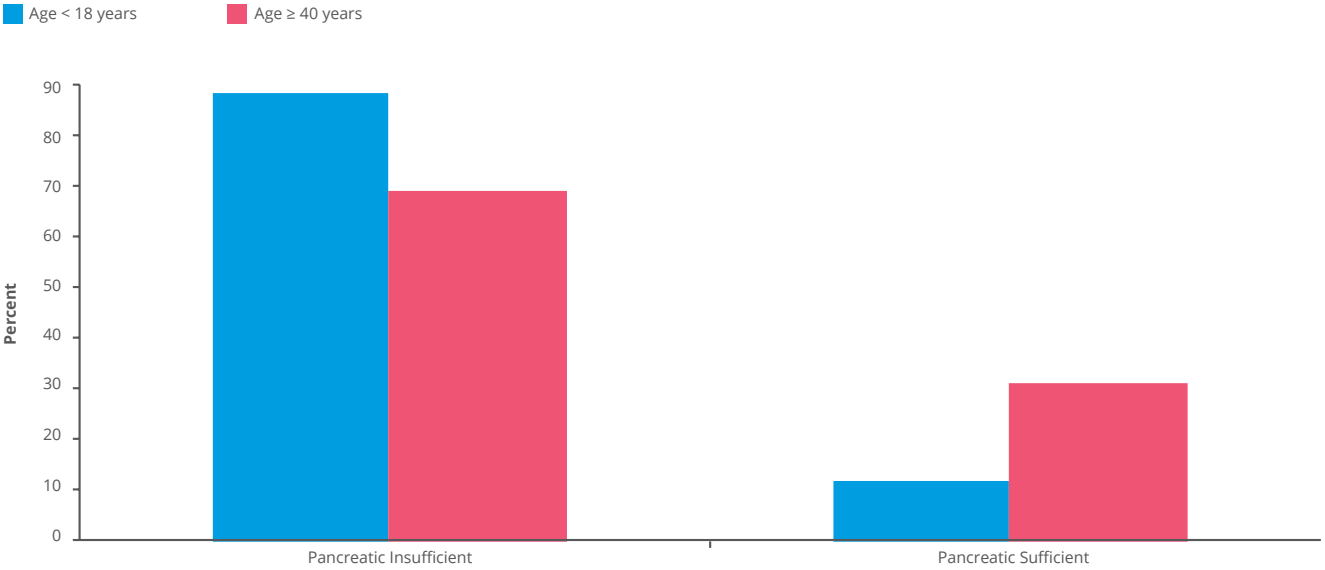


FIGURE 21
Pancreatic status by age group, 2014



NUTRITION
BMI PERCENTILE

For children ages 2 to 17 years, BMI percentiles are calculated comparing the individual's height and weight to those of children who are the same age and sex following the Centers for Disease Control and Prevention guidelines[4]. BMI percentile is not calculated for those under the age of two years. Table 4 summarizes the BMI percentile classification categories[5].

The national median BMI percentile for children is 43.9 (ages 2-17). The majority (77.5%) of children with CF have an adequate weight with a small proportion considered overweight (10.0%) (Figure 22). The national goal for children with cystic fibrosis (ages 2-17) is 50th BMI percentile. 42.1% of all children (ages 2-17) with cystic fibrosis are above the national goal with 51.3% of those being male.

FIGURE 22
BMI percentile classification for children with cystic fibrosis, 2014

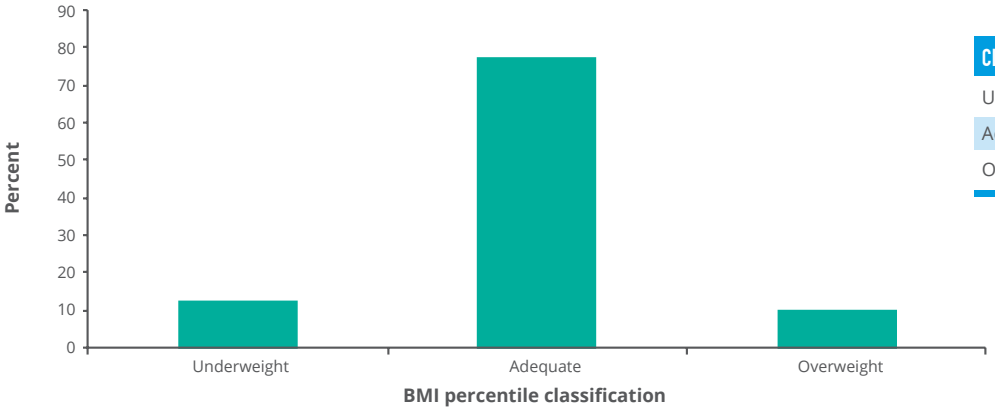
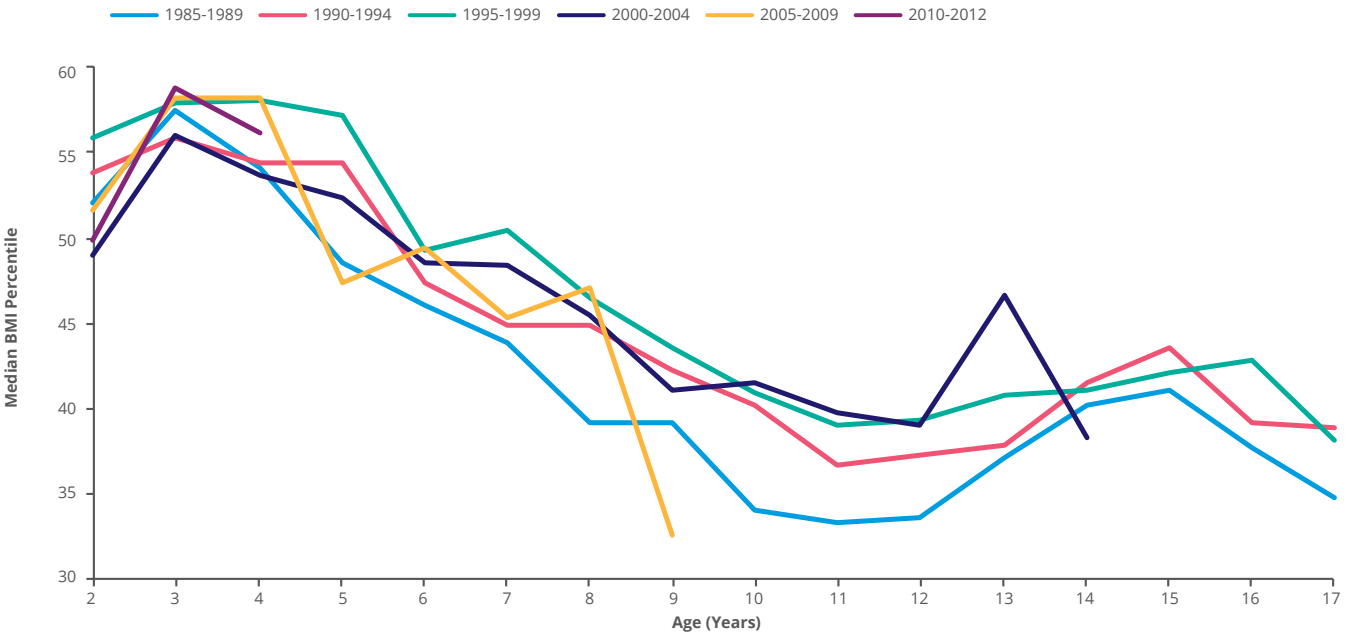


TABLE 4
BMI percentile classification

CLASSIFICATION	RANGE
Underweight	≤ 10th percentile
Adequate	10th percentile - 84th percentile
Overweight	≥ 85th percentile

FIGURE 23
Median BMI percentile for children by birth cohort



NUTRITION
BMI PERCENTILE BY SEX

Figure 24 shows the breakdown of BMI percentile classifications for males and females between the ages of 2 and 17. There are slightly more females with an adequate weight than males (80.1% vs. 75.1%). BMI percentiles have been increasing over time for both males and females, however BMI percentiles for females have risen at a faster rate than males since 1989 (Figure 25).

FIGURE 24
BMI percentile classification for children with cystic fibrosis, by sex, 2014

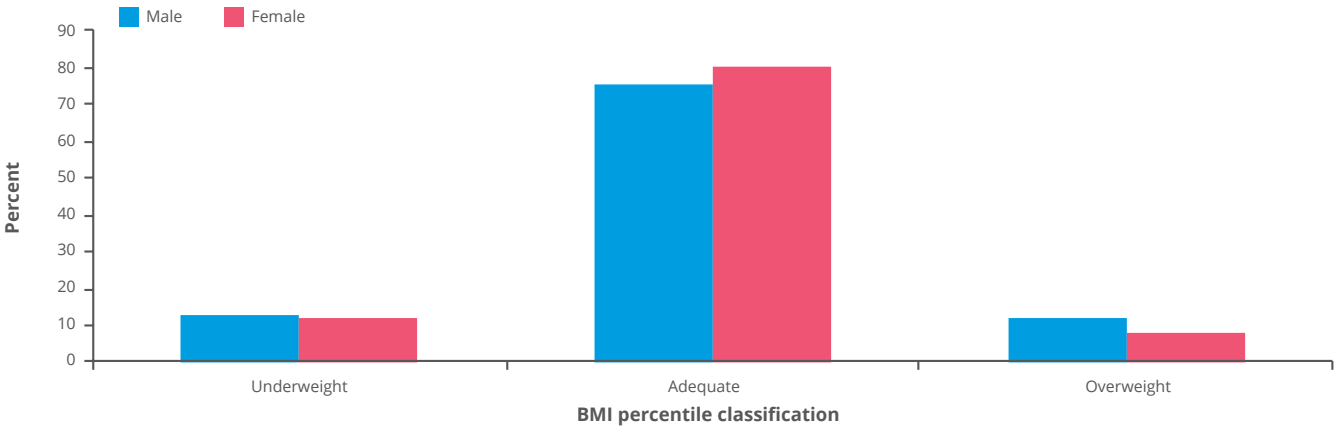
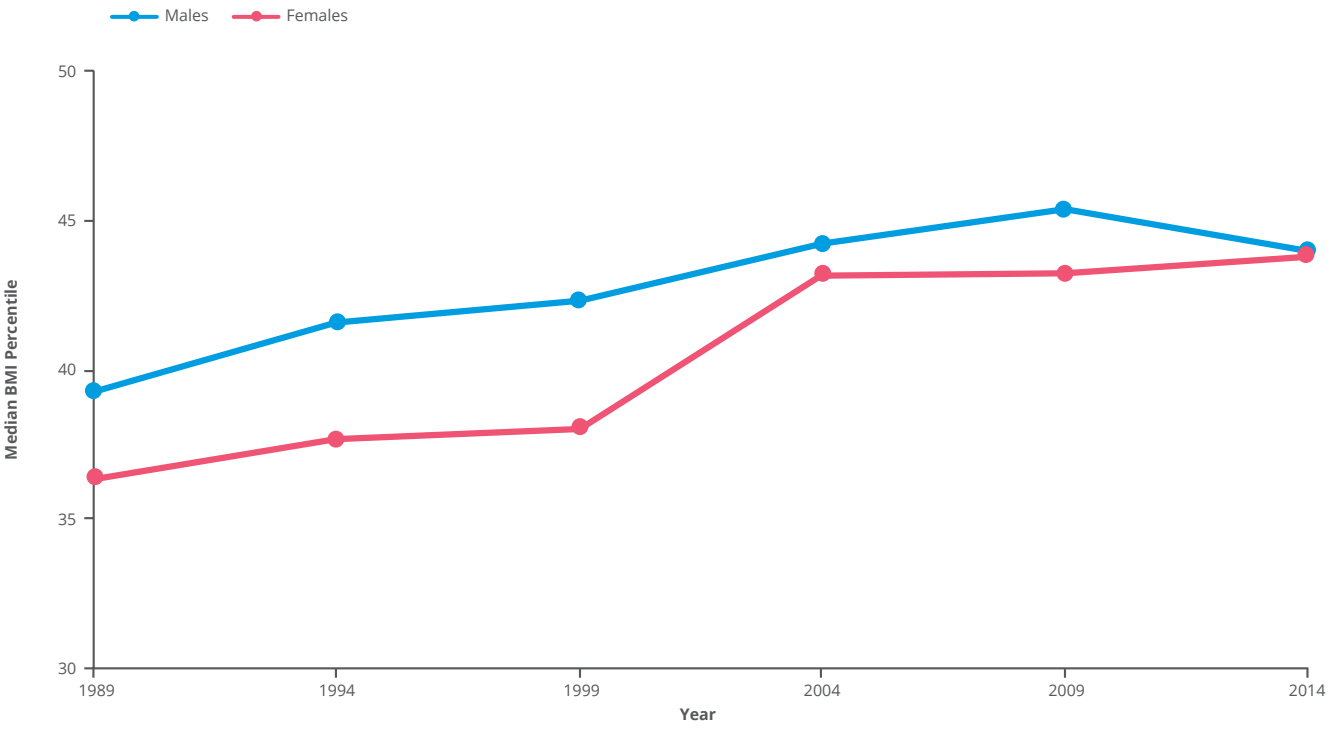


FIGURE 25
Median BMI percentiles for children with cystic fibrosis, by sex, 1989 to 2014



NUTRITION
BODY MASS INDEX (BMI)

Body mass index (BMI) is a measurement of nutrition and is based on a person's weight (in kilograms) and height (in metres). Typically, this is calculated for adults only because they have attained their maximal height. Children are rapidly growing and therefore, one must consider the child's age when assessing their nutritional status.

The national median BMI for adults (≥ 18 years) is 22.2 kg/m^2. Table 5 below describes the BMI classifications and their BMI ranges. In 2014, the majority (60.3%) of the adult CF population had an adequate weight while 23.4% were considered underweight and 4.8% were considered obese (Figure 26).

FIGURE 26
BMI classification for adults with cystic fibrosis, 2014

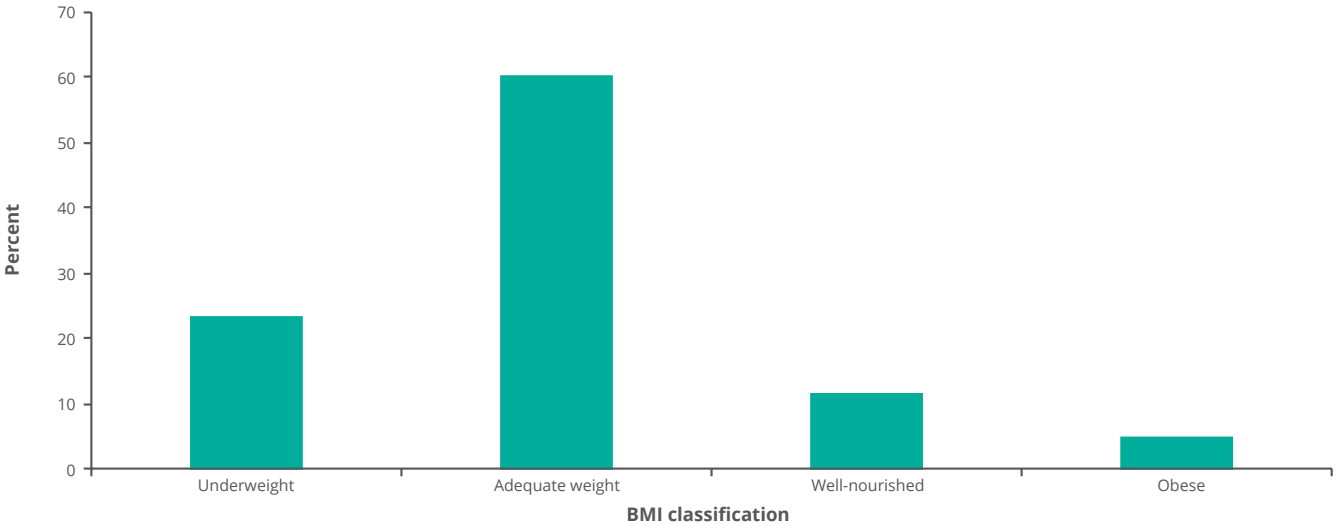


TABLE 5
BMI classification

CLASSIFICATION	RANGE
Underweight	< 20.0 kg/m^2
Adequate weight	20.0 - 25.9 kg/m^2
Well-nourished	26 - 29.9 kg/m^2
Obese	≥ 30 kg/m^2

NUTRITION
BMI BY SEX

Figure 27 shows the breakdown of BMI categories (see previous page for definitions) for adult males and females. Individuals who are muscular may have a BMI between 26-29 kg/m^2 due to increased weight from high muscle mass. In 2014, a larger proportion of females (28.7%) are considered underweight (BMI < 20 kg/m^2) compared to males (18.9%). However, in the last 25 years, median BMI has been steadily rising within the CF population (Figure 28) and can be attributed to the decline in individuals considered malnourished (Figures 29 and 30).

FIGURE 27
BMI classification for adults with cystic fibrosis, by sex, 2014

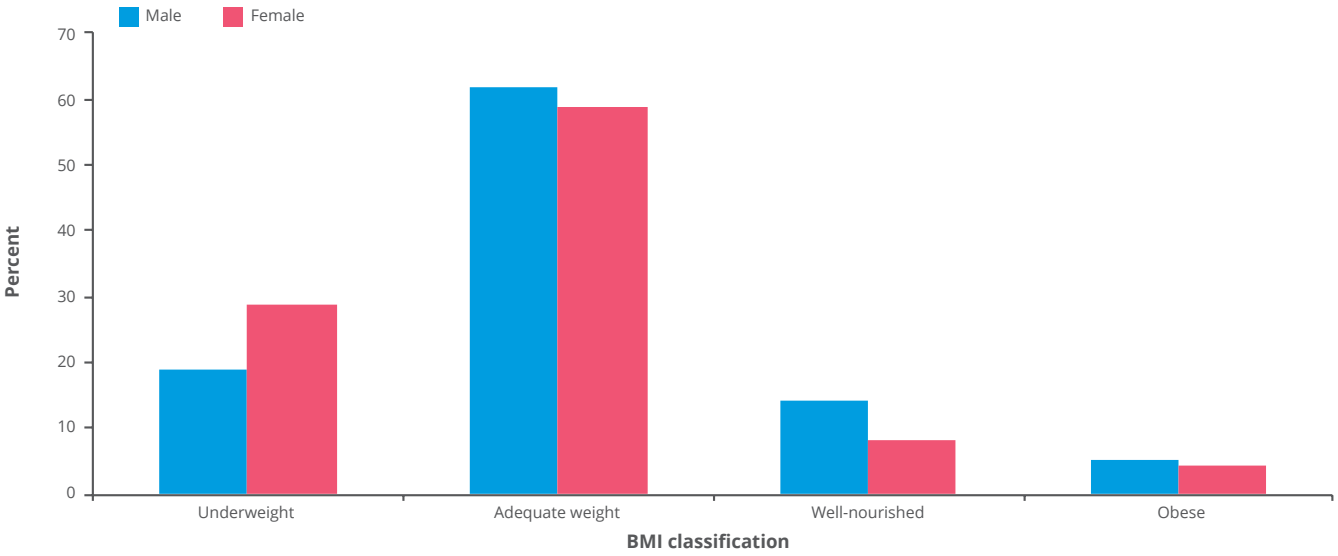


FIGURE 28
Median BMI values for adults with cystic fibrosis, by sex, 1989 to 2014

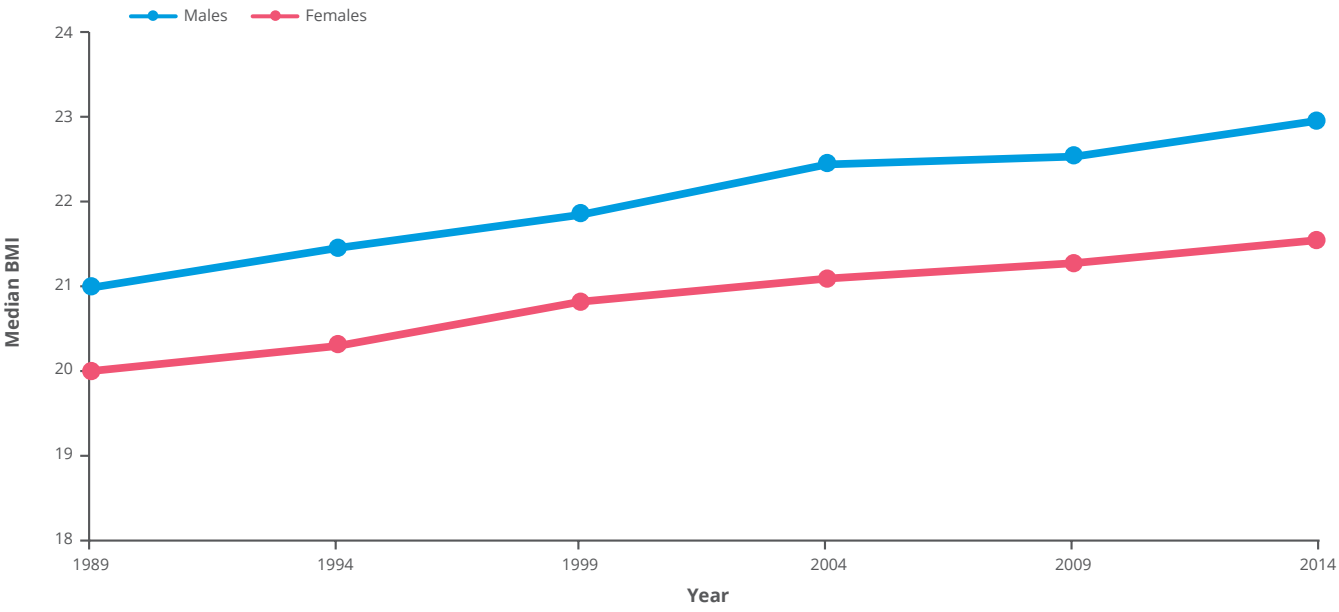


FIGURE 29
Percentage of male adults per BMI classification, 1989 to 2014

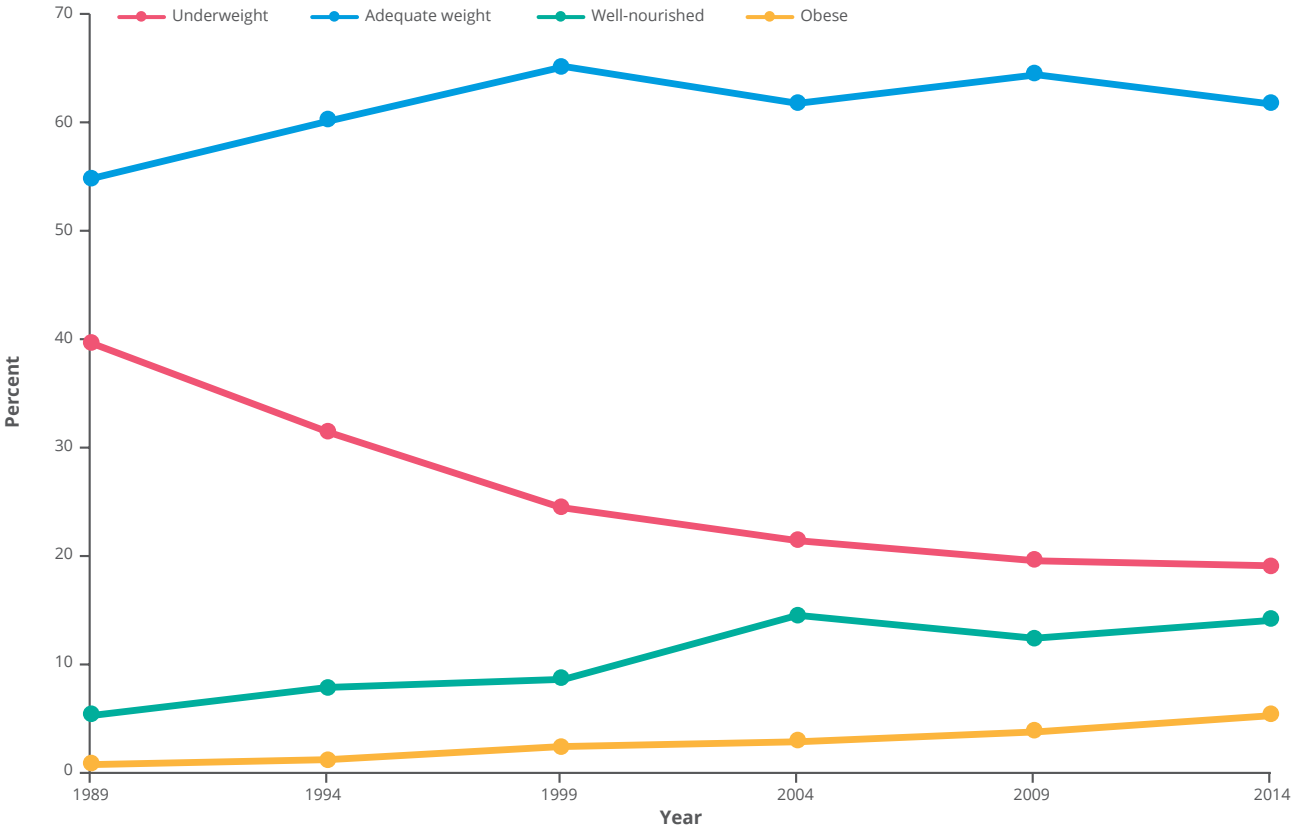
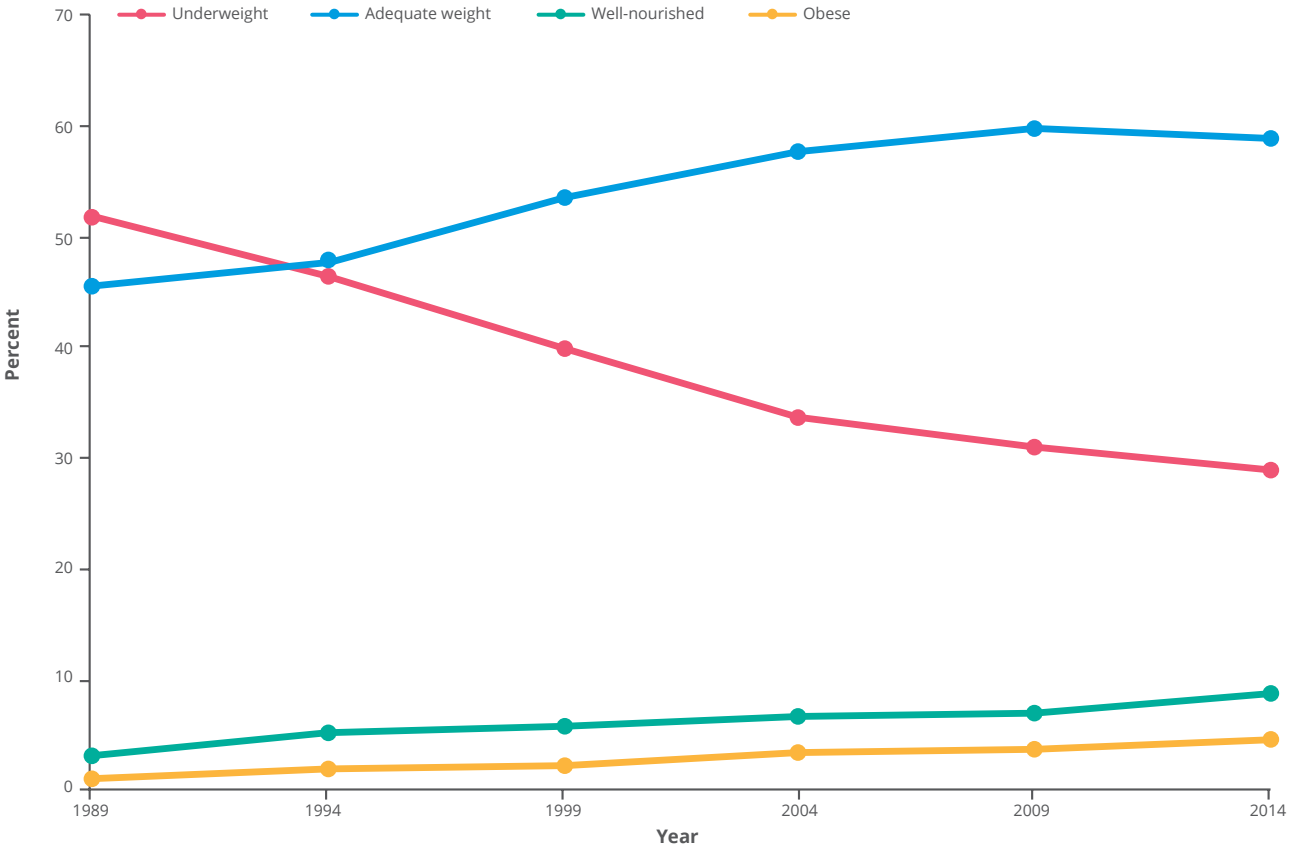
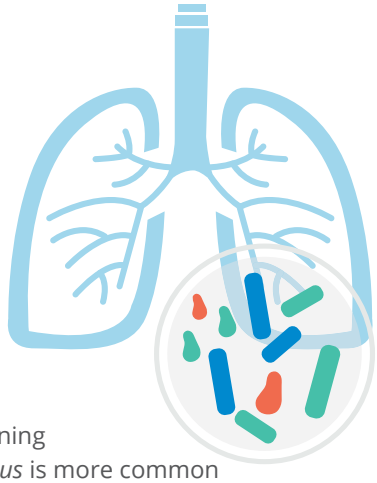


FIGURE 30
Percentage of female adults per BMI classification, 1989 to 2014



MICROBIOLOGY

BACTERIAL SPECIES AND RESPIRATORY INFECTIONS



Overall, *Pseudomonas aeruginosa* and *Staphylococcus aureus* are the most common pulmonary pathogens in Canadians with cystic fibrosis (Figure 31). MRSA was added to the Registry as of 2003. In 2011, clinics began to record additional microbiology data including the prevalence of *Alcaligenes (achromobacter)* species and atypical mycobacteria.

Over time, the prevalence of the more common pulmonary pathogens appear to be slowly declining (Figure 32). This may, in part, be due to increased surveillance. As expected, *Staphyloccocus aureus* is more common in children with CF whereas *Pseudomonas aeruginosa* is more common in the adult CF population (Figure 33). The prevalence of *Stenotrophomonas maltophilia* is highest in the teen years (11-17 years) and appears to be lower in older individuals. The prevalence of *Burkholderia cepacia* complex (BCC) is low (3.8%) and is more commonly seen in older individuals with cystic fibrosis. New acquisition of BCC in general has decreased substantially over the years, due to infection control practices, making its prevalence low in children. However, those individuals who previously acquired *B. cepacia* complex are aging, making the prevalence of this organism higher in older individuals.

FIGURE 31

Prevalence of bacterial species cultured from airways of CF individuals (all ages), 2014

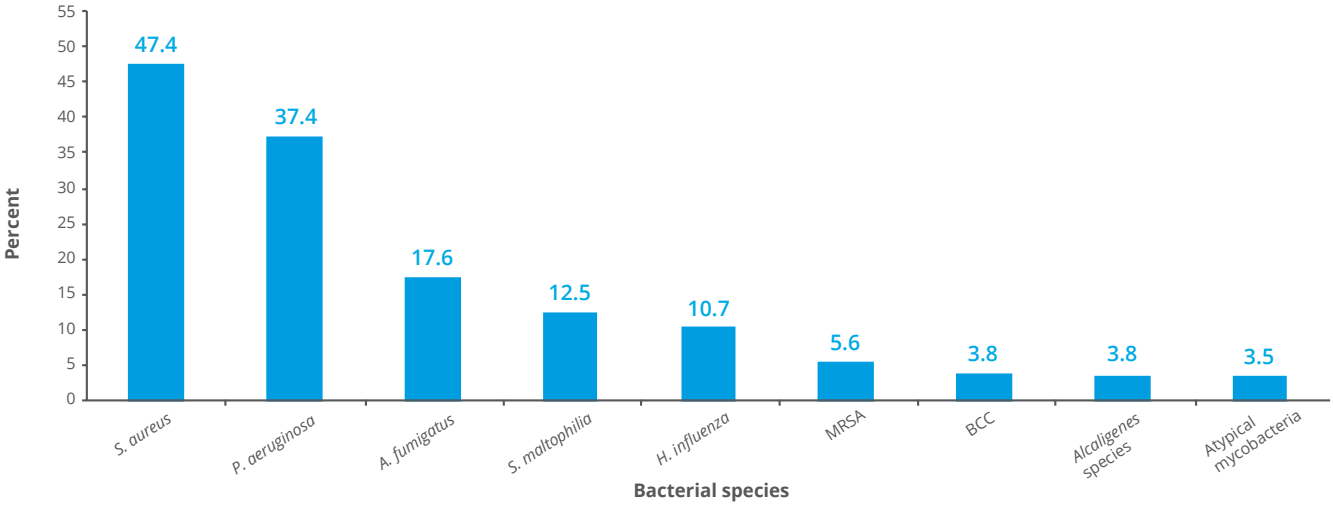


FIGURE 32

Prevalence of respiratory infections, 2010 to 2014

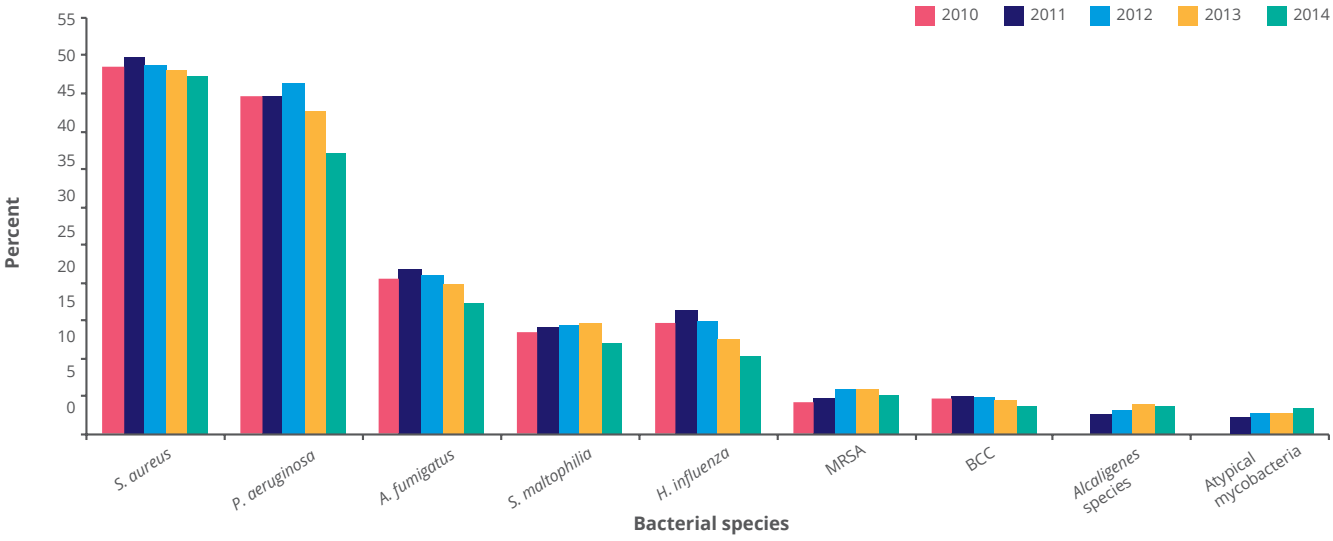
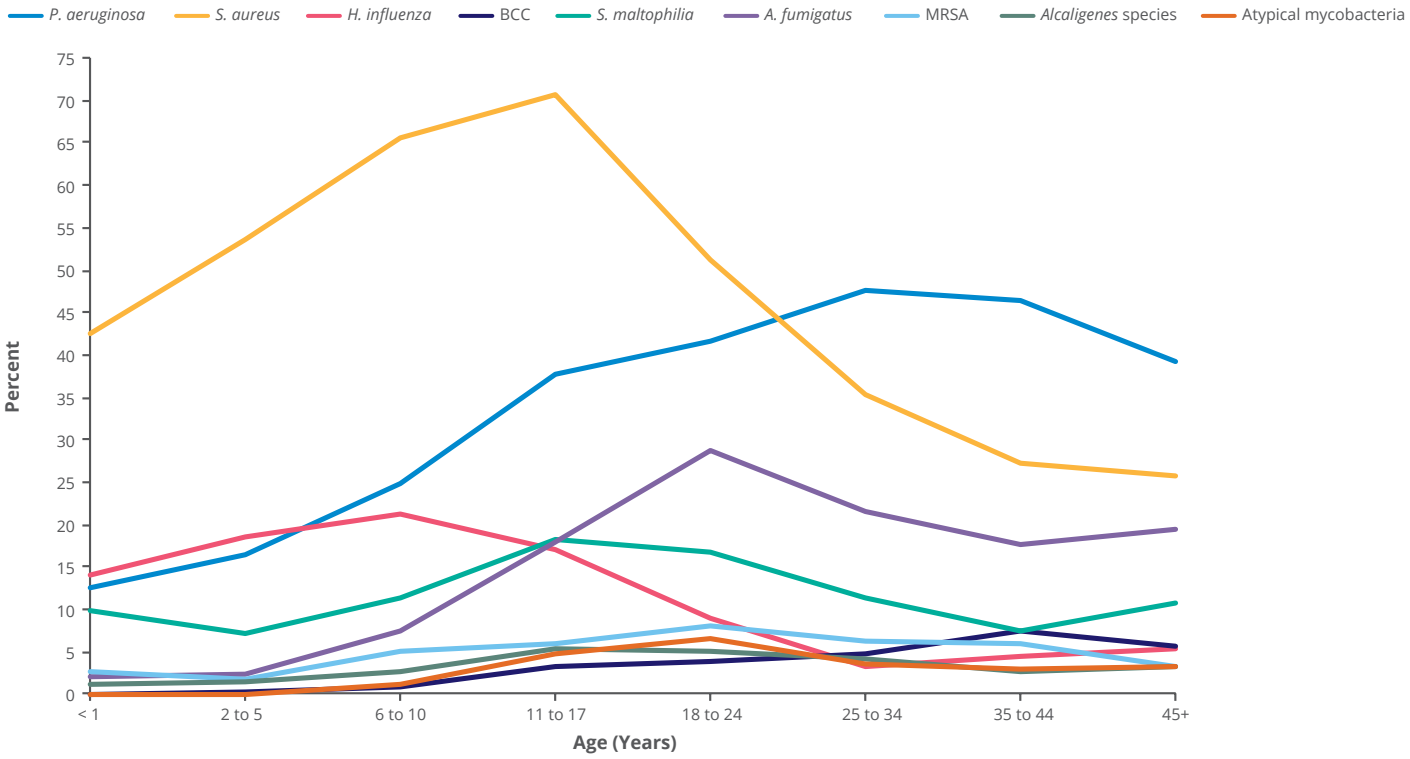


FIGURE 33
Age-specific prevalence of respiratory infections in CF individuals, 2014



BURKHOLDERIA CEPACIA COMPLEX (BCC)

There were 156 (3.8%) individuals with CF who grew *Burkholderia cepacia* complex (BCC) species in 2014. *B. cenocepacia* and *B. multivorans* were the two most common types of BCC species (Figure 34). Of the individuals with BCC in 2014, 129 (82.7%) were adults with 30.2% over the age of 40 (Figure 35). Not all BCC bacteria have been speciated. 8.9% of the BCC species in the Registry were classified as unknown. Although the Registry has captured BCC for decades, the ability to specify the type of BCC species was added to the Registry in 2011.

Note: The prevalence of *B. gladioli* was 5.7%, though it was not included in Figure 34 because it is not officially recognized as part of the BCC.

FIGURE 34
***Burkholderia cepacia* complex species, 2014**

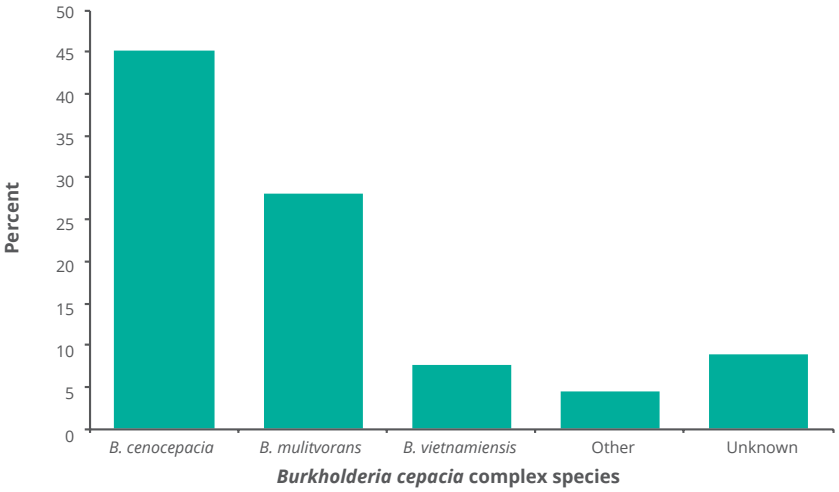
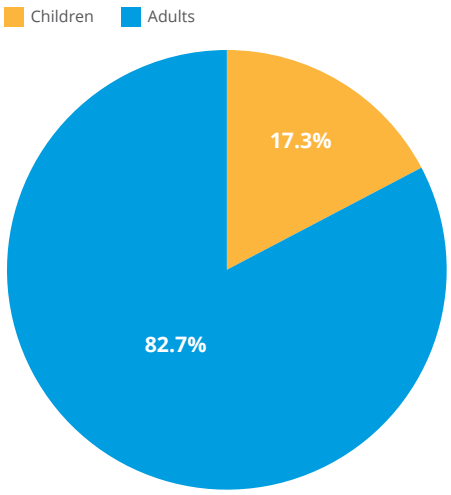


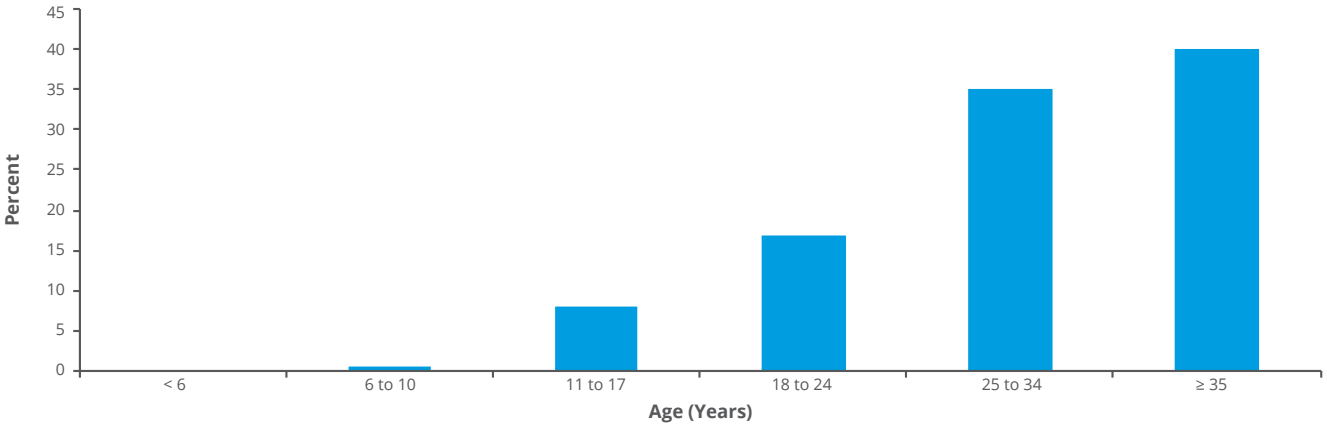
FIGURE 35
***Burkholderia cepacia* complex distribution by age, 2014**



CF-RELATED DIABETES (CFRD)

The prevalence of CFRD increases with age (Figure 36). In 2014, CFRD was reported in 989 (24.0%) individuals with cystic fibrosis. Of those individuals, 21.4% have had a transplant, 51.4% were female and 40.0% were 35 years of age or older.

FIGURE 36
Proportion of CF individuals with CFRD by age, 2014

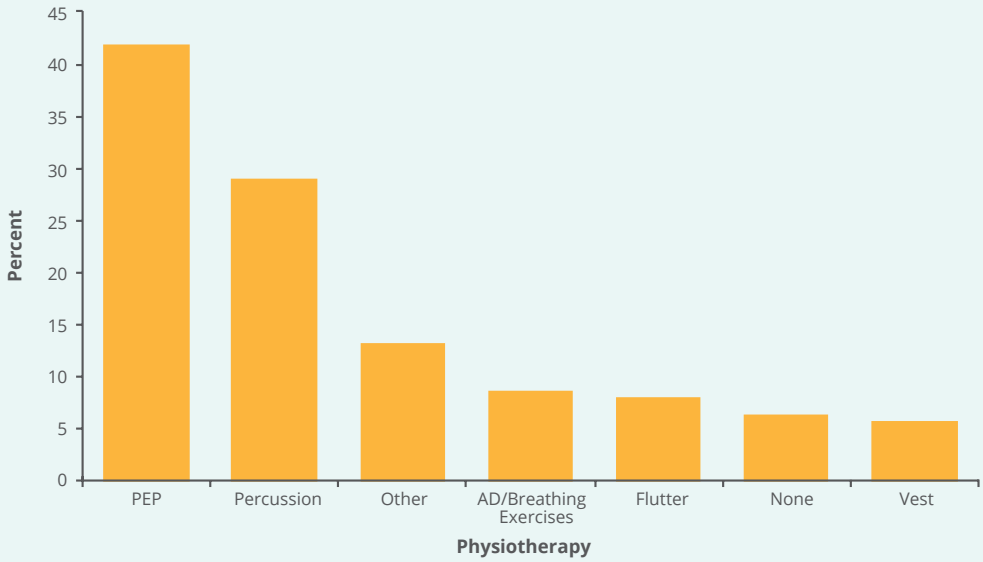


PHYSIOTHERAPY

Physiotherapy is done to help clear mucous from airways using a variety of methods. Multiple forms of physiotherapy can be used with positive expiratory pressure (PEP) and percussion being the most commonly used by Canadian CF individuals (Figure 37).

Note: Individuals who have ever received a lung transplant (6.5%) were excluded from these calculations because, typically, chest phyisotherapy is not part of routine post-transplant treatment.

FIGURE 37
Physiotherapy (based on N = 3,859), 2014



MEDICATIONS

In 2014, there were a total of 3,347 individuals over the age of 6 years (1,145 children over 6 years and 2,202 adults) who have never received a transplant. Of those, 1,743 (52.1%) are on a mucolytic therapy (hypertonic saline and/or Pulmozyme®) (Figure 38).

Individuals over the age of 6 years who have never received a transplant and were reported to have *Pseudomonas aeruginosa* in the reporting year include 373 children (6-17 years) and 999 adults. There were 291 children (6-17 years) (78.0%) and 766 adults (76.7%) who were prescribed inhaled antibiotic treatment, and 81 children (6-17 years) (21.7%) and 615 adults (61.6%) who were prescribed macrolide therapy (azithromycin) (Figure 39).

There are 23 children and 44 adults with a G551D mutation who are currently taking KALYDECO® (ivacaftor) recorded in the Registry in 2014.

FIGURE 38
Proportion on mucolytics, by age group, 2014

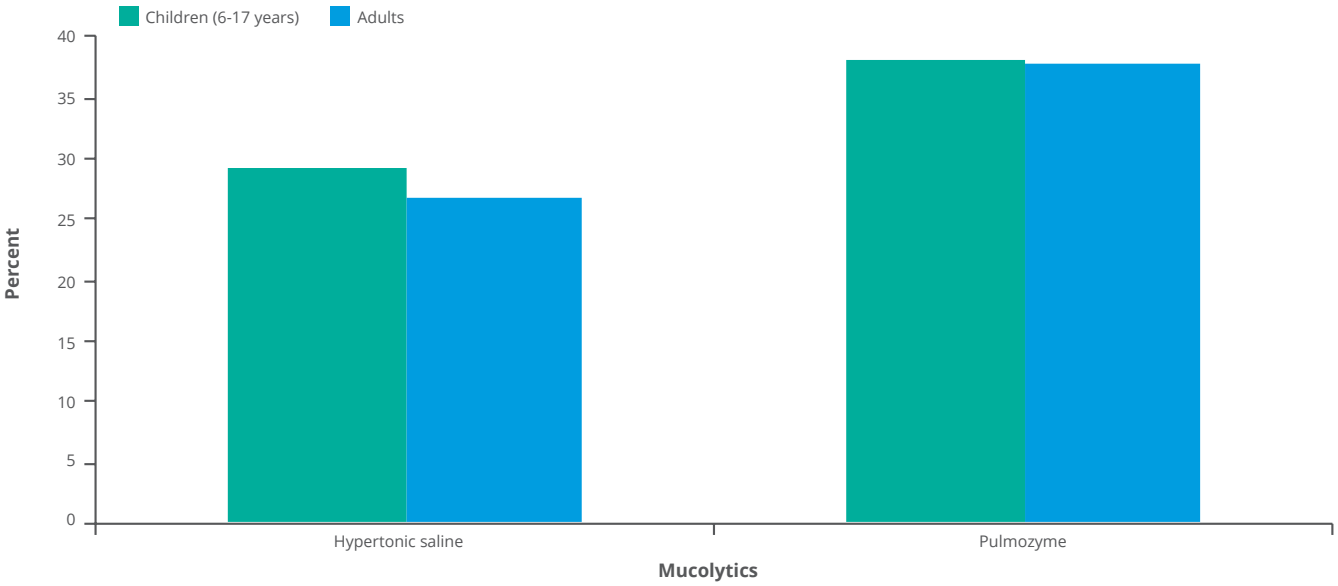
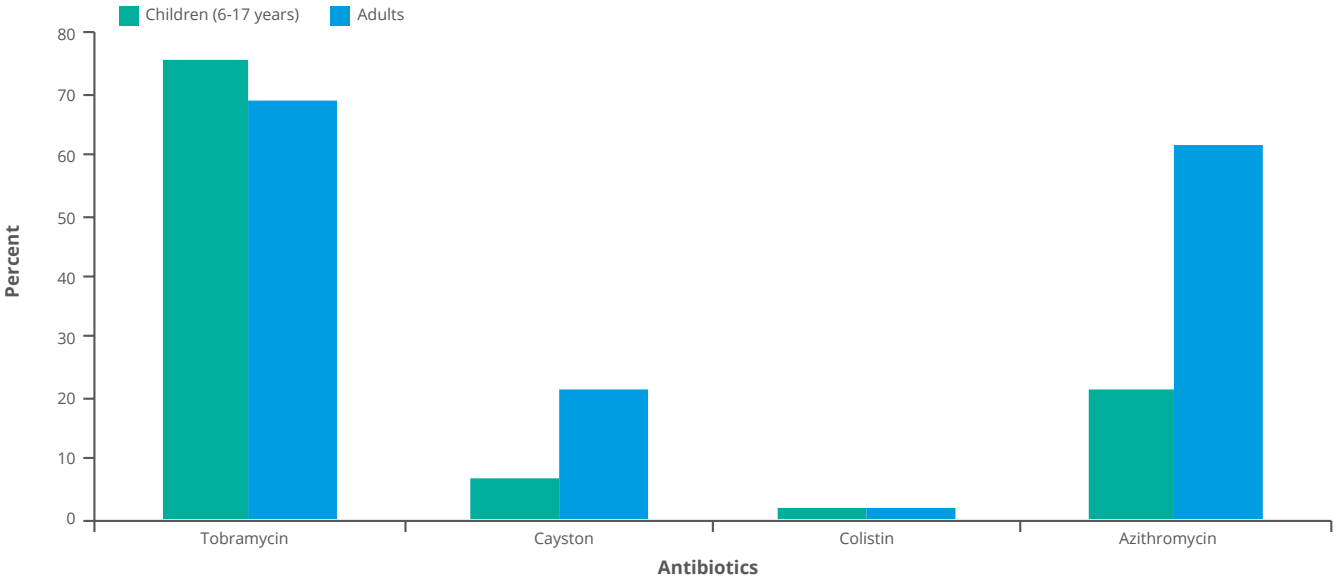


FIGURE 39
Proportion on antibiotics, by age group, 2014



HOSPITALIZATION AND HOME IV

In 2014, 1,793 hospitalizations were recorded in the Registry (Table 6). In total, 867 courses of home IV therapy were recorded in the Registry. In 2014, 4,062 (96.9%) individuals with CF had at least one clinc visit and 2,927 (70.9%) individuals had three or more clinic visits. Of those having three or more clinic visits, 1,349 (46.1%) were children under 18 and 1,578 (53.9%) were adults.

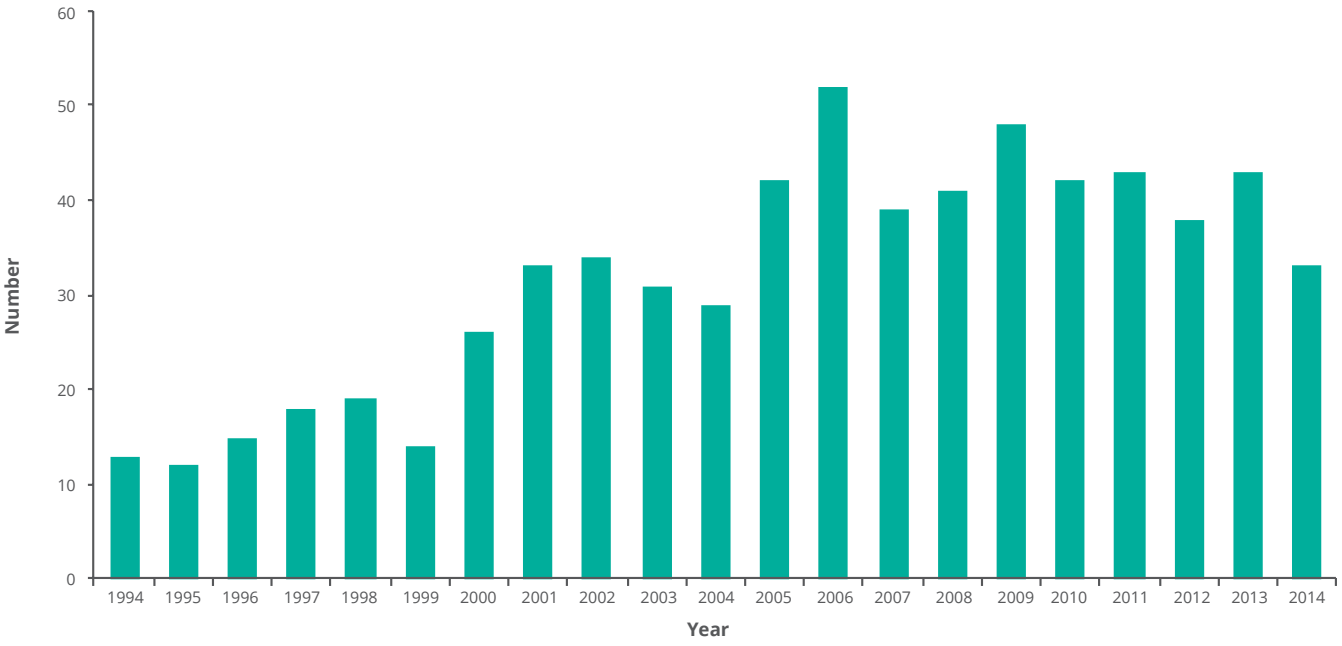
TABLE 6
Number of hospital days and home IV courses, 2014

	TOTAL NUMBER
Hospital Days	24,900
Hospitalizations	1,793
Clinic Visits	15,790
Home IV Courses	867
Home IV Days	13,781

TRANSPLANTS

Figure 40 shows the number of transplants carried out per year as reported in the Registry. In 2014, 33 CF individuals received a transplant with a median age of 29.0 years at the time of transplant. Although the numbers provided represent primarily lung transplants, individuals who received other combinations (e.g. lung-liver, liver, heart-lung, etc.) are also included in the total. As of December 31, 2014, there were 665 CF individuals recorded in the Registry as having received one or more transplants. Of those individuals, the median age was 28.3 years at the time of transplant and 390 individuals were reported as being alive with 57.2% of them being male.

FIGURE 40
Number of transplants per year, 1994 to 2014



SURVIVAL

There were 54 deaths recorded in the Registry in 2014. Since there are relatively few deaths per year, the sum of all deaths from 2010 to 2014 has been included in Figure 41. The median age at death in 2014 was **32.4 years of age** (Figure 42). In other words, of those who died, half died before the median age at death and half died later than the median age at death. Median age at death is calculated by taking into account all patients who died in a given year, placing them in ascending order based on the age of death, and determining which age is the middle number. The most common cause of death was related to pulmonary complications and 30 of the 54 individuals with CF (55.6%) who passed away in 2014 were post-transplant.

FIGURE 41
Age at death, 2010-2014

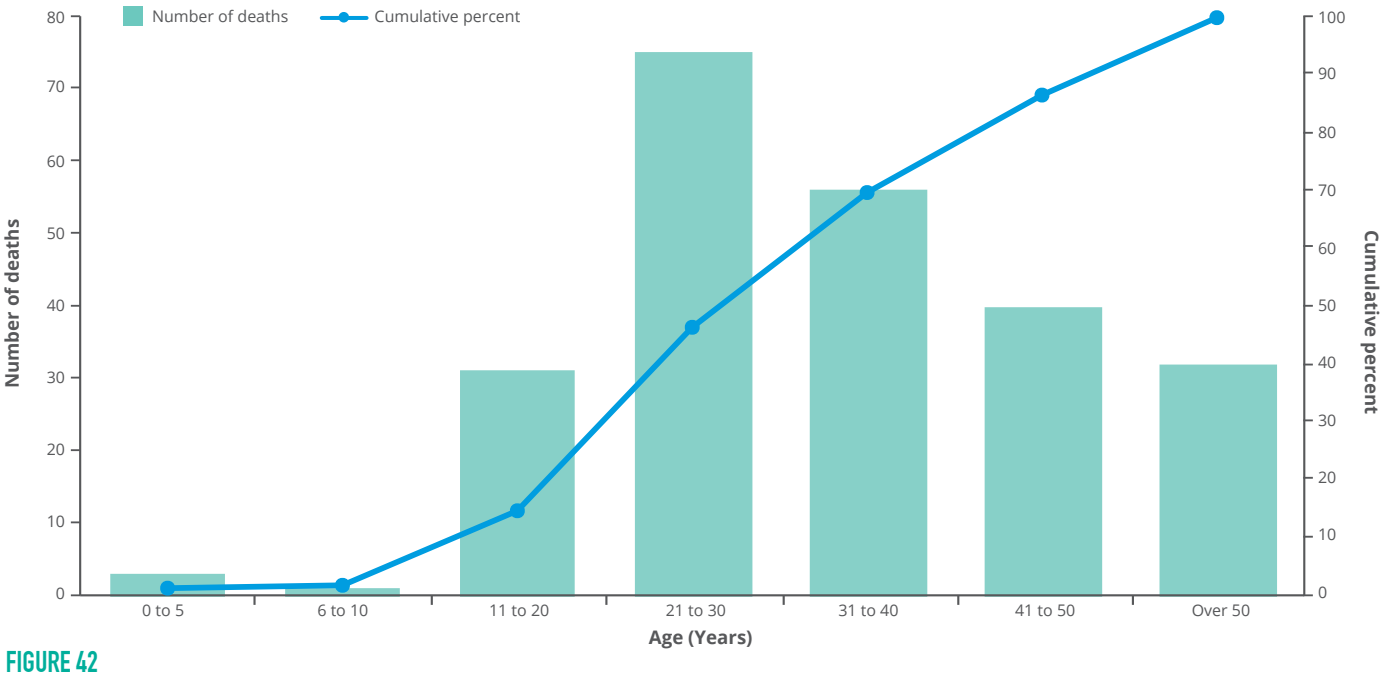
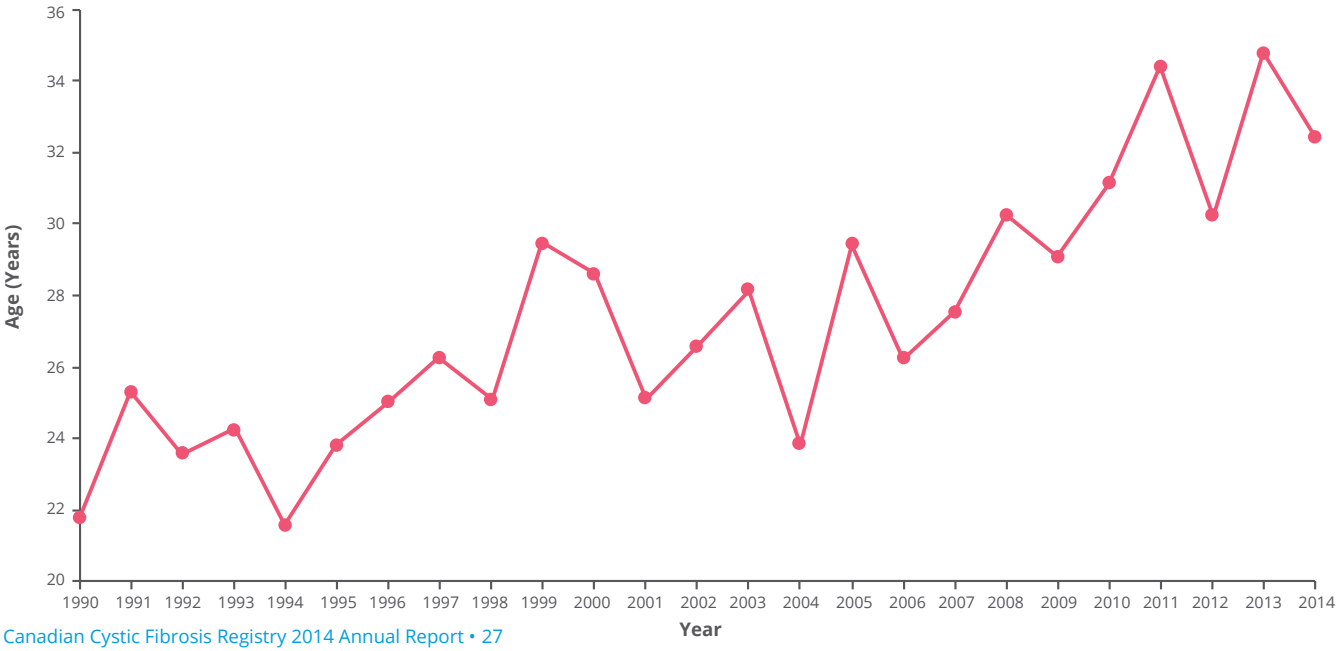


FIGURE 42
Median age at death, 1990 to 2014



SURVIVAL
ESTIMATED MEDIAN AGE OF SURVIVAL

The estimated median age of survival for Canadians with cystic fibrosis is calculated using the Cox proportional hazards model. Because there are relatively few deaths per year in Canada, a 5-year rolling window was used to calculate the median age of survival. This allows for more stable estimates over time. The most recent 5-year window (2010-2014) included 4,599 people with CF and 235 deaths. The number of individuals with CF lost-to-follow-up was 237 (5.2%). Transplanted individuals are included in the analysis as this is considered a form of therapy for end-stage cystic fibrosis and excluding deaths post-transplant would bias the survival estimates resulting in an overestimation of survival[6]. The median predicted age of survival is the age to which half of the CF population would be expected to survive to given their current ages and assuming that mortality rates do not change.

In 2014, the median age of survival is currently estimated to be **51.8 years of age** (Figure 43). Males continue to have a higher median age of survival compared to females (Figure 44). The cause of lower survival in females is not well understood but has been documented in the published CF literature. Survival by birth cohort is presented in Figure 45 and indicates that survival is higher for those born more recently.

FIGURE 43
Median age of survival for a moving 5-year window with 95% confidence intervals, 1980 to 2014

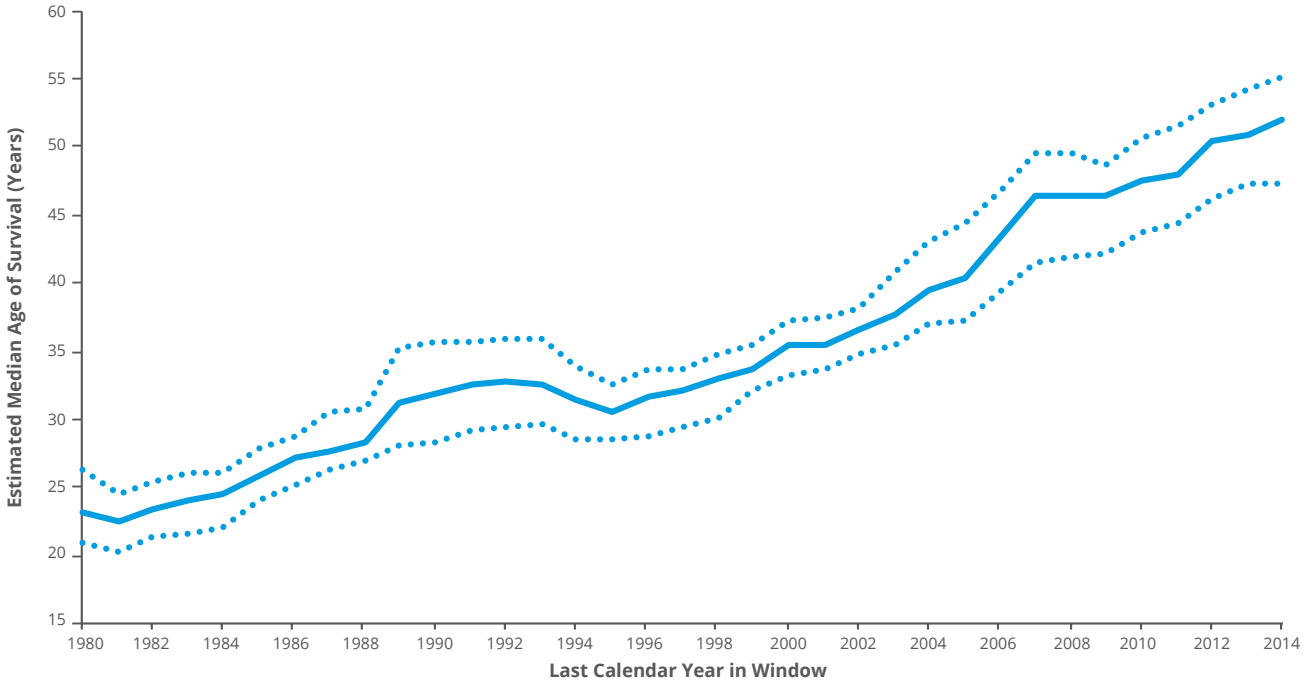


FIGURE 44

Median age of survival for a moving 5-year window with 95% confidence intervals, by sex, 1980 to 2014

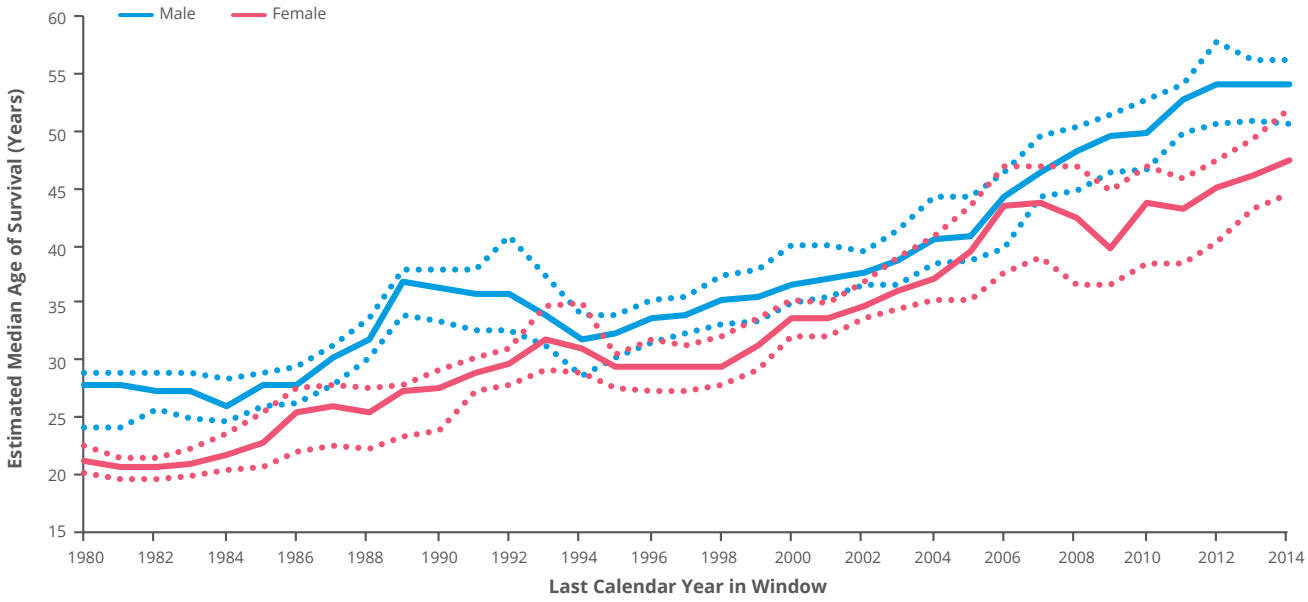
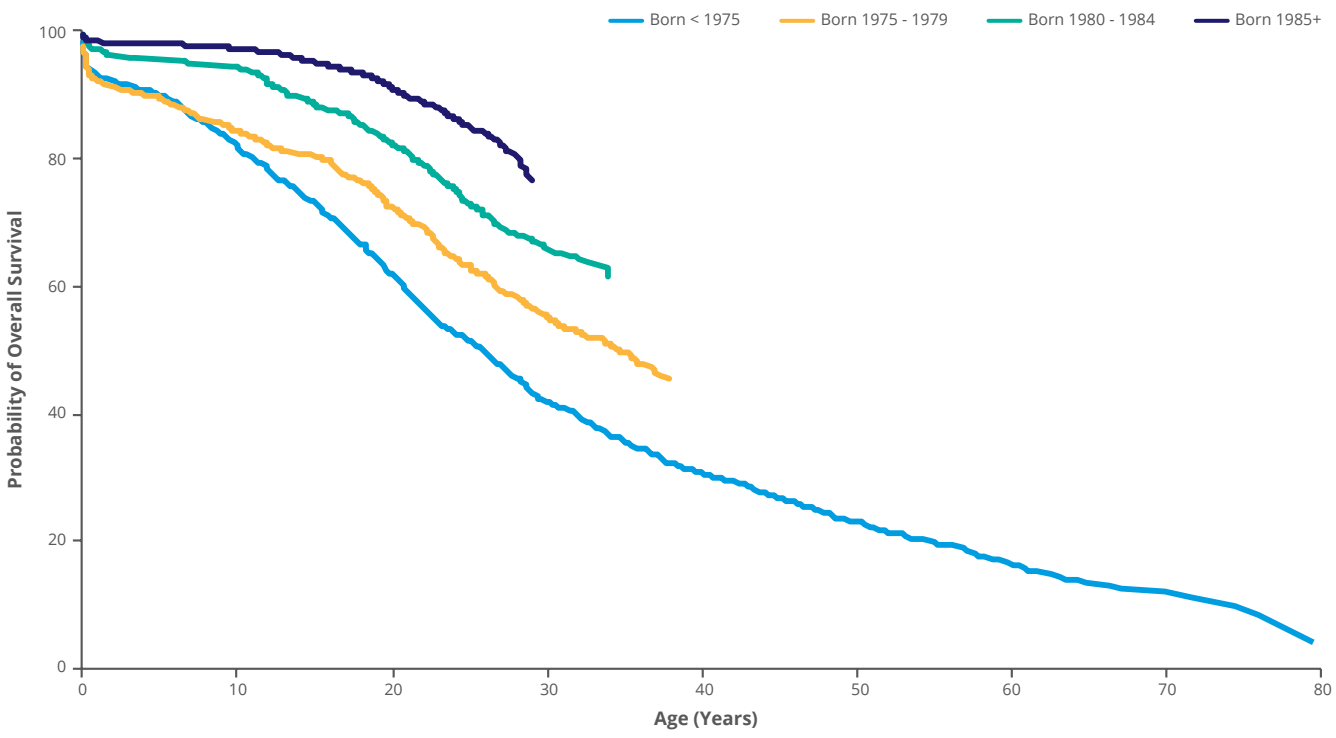


FIGURE 45

Overall survival by birth cohorts



SURVIVAL
GLOSSARY OF TERMS

LIFE EXPECTANCY

The life expectancy is the average age to which someone can be expected to live. In other words, it is the **expected average length of life based on current age-specific mortality rates**. For the general population born today, life expectancy in Canada is 80 years for males and 84 years for females based on data from World Health Organization[7]. This means that, *on average*, a male baby born today will be expected to live 80 years and a female baby, *on average*, will be expected to live to 84 years of age. In comparison, the median age of survival is the estimated age beyond which 50 percent of the population will live - it is not an average.

Life expectancy is not the same as median age of survival. This measurement uses the mean (average) and not the median. For example, the average life expectancy for women in Canada is 84 years of age. This means that a baby girl born today will be expected to live until the age of 84 years, *on average* (i.e. some girls will die before the age of 84 years and some will live beyond the age of 84 years but, on average, women will live 84 years).

It is possible to calculate the life expectancy in CF but we do not usually do it because it is influenced by extreme values more so than the median age of survival. For example, the life expectancy may change significantly if one or two people in the population lived until a very old age because it is calculating a mean age whereas the median age is less sensitive to extreme values and is a more robust measurement.

MEDIAN AGE AT DEATH

The median age at death is very different than the median age of survival. Median age at death is calculated simply by taking into account all deaths in a given year, placing them in ascending order, and determining which age is the middle number. The median age at death is **calculated using only those individuals who have died in a given year**. In other words, of those who died in the year, half died before the median age at death and half died later than the median age at death.

This calculation does not provide information about the individuals who are still alive. You need to know the ages of those still living to get information on median survival.

MEDIAN AGE OF SURVIVAL

Median age of survival is calculated based on cross-sectional data (i.e. data taken across different age groups) of the CF population and takes into consideration data from both individuals who have died AND those who are still alive. It is the **estimated age beyond which 50 percent of the CF population would be expected to live, assuming the mortality rate in CF remained constant**. This is NOT the age at which people with CF would be expected to die, (i.e. how long someone can expect to live, on average - see *life expectancy* below). Median age of survival is simply one way to evaluate survival in the CF population; however, there are other measures that provide us with additional information about how long people with CF are living (for example, median age at death and annual death rate).

When we say that the median age of surival in 2014 is 51.8 years, we are saying that if a child with CF is born in Canada in 2014, they have a 50 percent probability of living beyond 51.8 years of age based on current mortality rates. In other words, *half* of the CF population would be expected to live to an age older than 51.8 years. Of course, mortality rates are not static and are constantly changing as new therapies and medicines for CF become available. Thus, this estimate is a reflection of the most accurate data that is available today.

Keep in mind that these survival estimates apply to a population of individuals and do not necessarily apply to any one individual.

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The Hospital for Sick Children, Toronto	Janeway Children's Health Centre, St. John's
St. Michael's Hospital, Toronto	Health Sciences Centre, St. John's

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