# THE CANADIAN CYSTIC FIBROSIS REGISTRY

Cystic Fibrosis Canada™

## 2016 ANNUAL DATA REPORT

## CYSTIC FIBROSIS

Cystic fibrosis (CF) is a rare disease affecting over 4,200 Canadians or roughly 1 in 3,600 live births. CF is a progressive, degenerative multi-system disease that affects mainly the lungs and digestive system. In the lungs, where the effects are most devastating, a build-up of thick mucous causes severe respiratory problems. Mucous and protein also build up in the digestive tract, making it difficult to digest and absorb nutrients from food. In addition to the physical effects of the disease, mental health concerns are emerging and being addressed as anxiety and depression are common among this population. Individuals with CF may reach the point where they require a lung transplant; most fatalities of people with CF are due to lung disease. Currently, 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 CF. As an internationally-recognized leader in funding CF research, innovation, and clinical care, we invest more funding in life-saving CF research and care than any other non-government agency in Canada.

Since 1960, Cystic Fibrosis Canada has invested more than $244 million in leading research, innovation and care, resulting in one of the world's highest survival rates for Canadians living with CF. For more information, visit www.cysticfibrosis.ca.

Our mission is to end CF. 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.**

This publication is also available online. Please visit us at www.cysticfibrosis.ca

Cover page: CF individual from Manitoba


*This document is made from 100% recycled paper.*
*Join us in reducing our impact on the environment by choosing to recycle.*

*Published: November, 2017*

# TABLE OF CONTENTS

# THE CANADIAN CYSTIC FIBROSIS REGISTRY

The *Canadian Cystic Fibrosis Registry* (CCFR) is a collection of national CF data used to support and improve our knowledge and understanding of CF. This extensive resource has been involved in many important studies resulting in achievements in health outcomes for those living with CF.

Participating CF patients who attend any of the accredited 42 CF clinics across Canada are represented in the CCFR. Data are submitted by the CF clinics on behalf of patients. Given that the majority of CF patients attend one of these clinics, we are confident that the CCFR includes data on virtually all Canadians diagnosed with CF — giving a comprehensive picture of the CF population in this country.

Cystic Fibrosis Canada publishes the Canadian CF Registry Annual Data Report on national summary statistics to further educate and promote awareness of CF. We would like to acknowledge the involvement and continued participation of CF patients who consent to having their data submitted, and the exceptional effort and contribution from CF clinic team members who collect and enter the data.

**The Canadian Cystic Fibrosis Registry provides a yearly opportunity for our CF community to identify CF care progress, and to celebrate and respond to the data collected. This year's data indicates continual improvement in health outcomes for the Canadian CF population. With these results, Cystic Fibrosis Canada is as motivated as ever to support patients and families as we strive for excellence and ultimately, a cure or control. Our commitment has propelled Canada to be a leader in CF research and care, with a steady median age of survival among the highest in the world.**

**We are extremely grateful to the patients and clinicians who dedicated their time to collecting and entering these data. Time and time again, our community demonstrates its dedication, resiliency and tenacity towards ending CF. Without your support and commitment, this report and our impact would not be possible.**

**Over my tenure at Cystic Fibrosis Canada, we have accomplished so much – from a climbing median age of survival, to increasing the number of diagnoses made within the first year of life, to decreasing the amount of CF patients who are classified as underweight. CF Canada continues to prove that in this fight we are stronger together. I am certain that the strides we have made together over the course of my time at Cystic Fibrosis Canada will have an incredible impact on our community, and I look forward to seeing that impact reflected in future reports.**

**Together, we will create a world without cystic fibrosis.**

**With sincere gratitude and appreciation,**

**NORMA BEAUCHAMP**
PRESIDENT & CEO, CYSTIC FIBROSIS CANADA

---

**The information contained within the Canadian CF Registry is critically important and invaluable to the CF community. It has influenced research and clinical studies, changed the direction of healthcare and enhanced advocacy efforts. To everyone involved with the Canadian CF Registry, we thank you for your support.**

**DR. ANNE STEPHENSON**
MEDICAL DIRECTOR, REGISTRY, CYSTIC FIBROSIS CANADA
AND CF PHYSICIAN, ST. MICHAEL'S HOSPITAL, TORONTO

## HOW TO READ THE REPORT

All the data analyses presented in this report have been recalculated 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 the current one.

Patients who were reported by any of the 42 accredited Canadian CF clinics in 2016 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, 2016.

# 2016 HIGHLIGHTS

Over **4,200 Canadians** with CF received care at one of the **42 specialized CF clinics** based in hospitals across Canada

**122 new CF diagnoses made in 2016:** 66 were through newborn screening and 20 were over 18 years of age

**59.1%** of CF patients are diagnosed within their first year of life

## THE **CURRENT MEDIAN AGE** OF CANADIANS WITH CF IS **22.7 YEARS**

**60.8%** of all people with CF in Canada are **adults**

**20.1%** of CF patients **travelled more than 250km to receive CF care** in 2016

Cumulatively, CF patients underwent **over 1,000 courses of home IV therapy** in 2016

## CUMULATIVELY, CF PATIENTS VISITED A CLINIC **MORE THAN 19,000 TIMES** AND SPENT ALMOST **29,000 DAYS IN HOSPITAL IN 2016**

$FEV_1$ percent predicted (a measure of lung function) is improving for persons with CF: **half of all 30 year olds** with CF had an **$FEV_1$ greater than 72.2%** in 2016 compared to **53.3%** two decades ago

## OF THE 42 PATIENTS WHO DIED IN 2016, **HALF WERE UNDER 38.9 YEARS OF AGE**

## THE **MEDIAN AGE OF SURVIVAL** FOR CANADIANS WITH CF IS **ESTIMATED** TO BE **53.3 YEARS** OF AGE

**84.8%** of Canadians with CF must take **pancreatic enzymes** to digest food and absorb nutrients

## **22.8%** OF ALL **CF PATIENTS** HAVE **CF-RELATED DIABETES**

**12.8% of female adults** with CF and **6.3% of male adults** with CF are classified as **underweight** (BMI < 18.5 $kg/m^2$)

**49.6% of all children under 2 years** and **45.6% of all children between 2-17 years** are above the national goal of **50$^{th}$ BMI percentile**

## **45** CF PATIENTS **RECEIVED TRANSPLANTS** IN **2016** AND HAD A **MEDIAN AGE OF 31.2 YEARS** AT THE TIME OF TRANSPLANT

**37.0%** and **53.4% of all patients** with CF are **infected in their lungs with harmful bacteria** such as ***Pseudomonas aeruginosa*** and ***Staphylococcus aureus*** respectively

Over **2,000 different mutations** in the *CFTR* gene have been identified; however **89.2% of CF patients in Canada** carry at least one copy of the most common CF-causing mutation, **F508del**

# DEMOGRAPHIC DATA
## CANADIANS WITH CYSTIC FIBROSIS

In 2016, there were a total of 4,246 individuals with CF who attended one of the 42 accredited CF clinics across Canada (Figure 1) with 122 of those being new CF diagnoses. Overall, the total Canadian CF population has been steadily increasing and in the last two decades, has grown by 37.3% (Figure 2). Individuals attending CF clinics in different provinces will be counted in each of those provinces but are only counted once (i.e. unique individuals) in the national reported numbers.

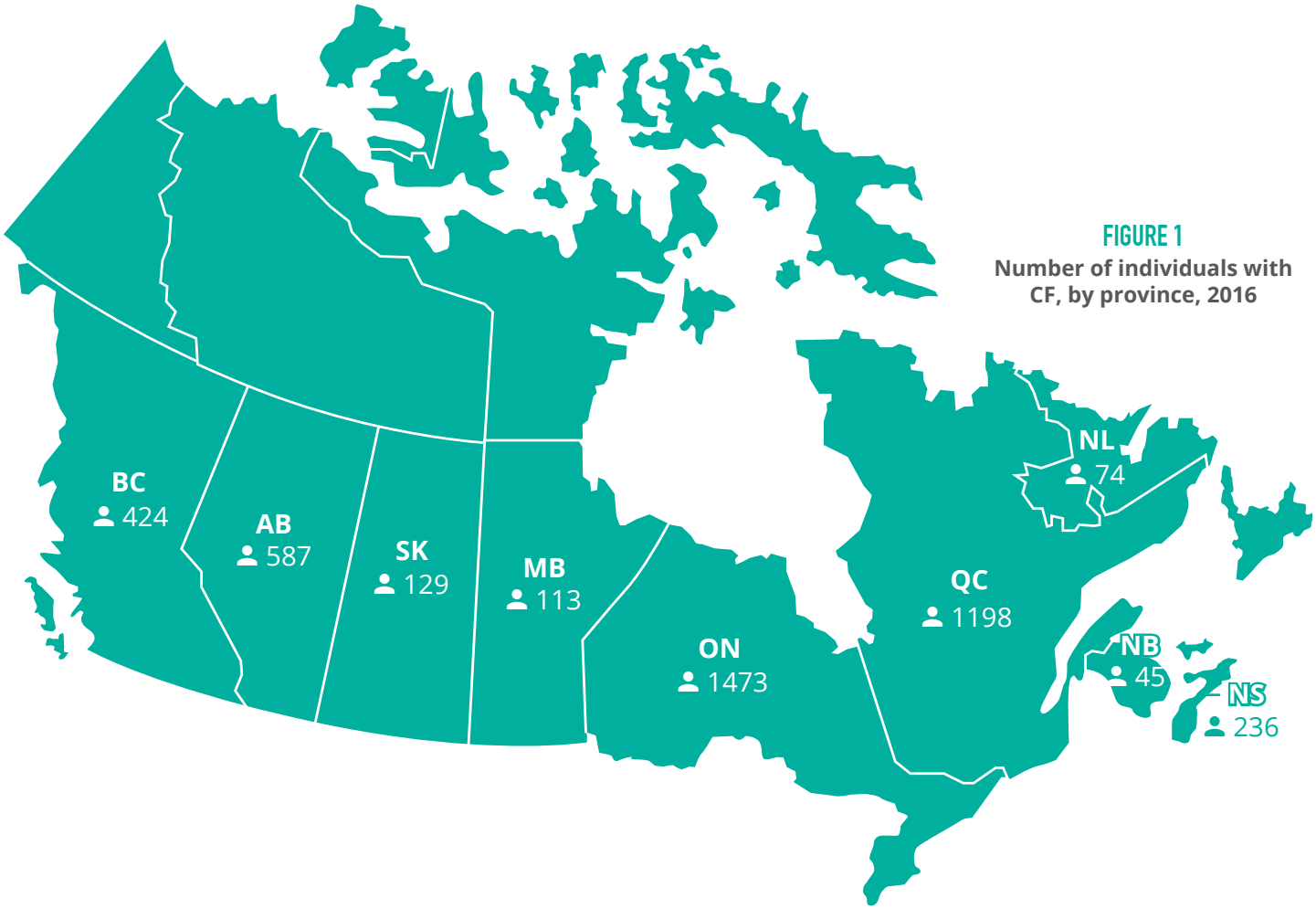


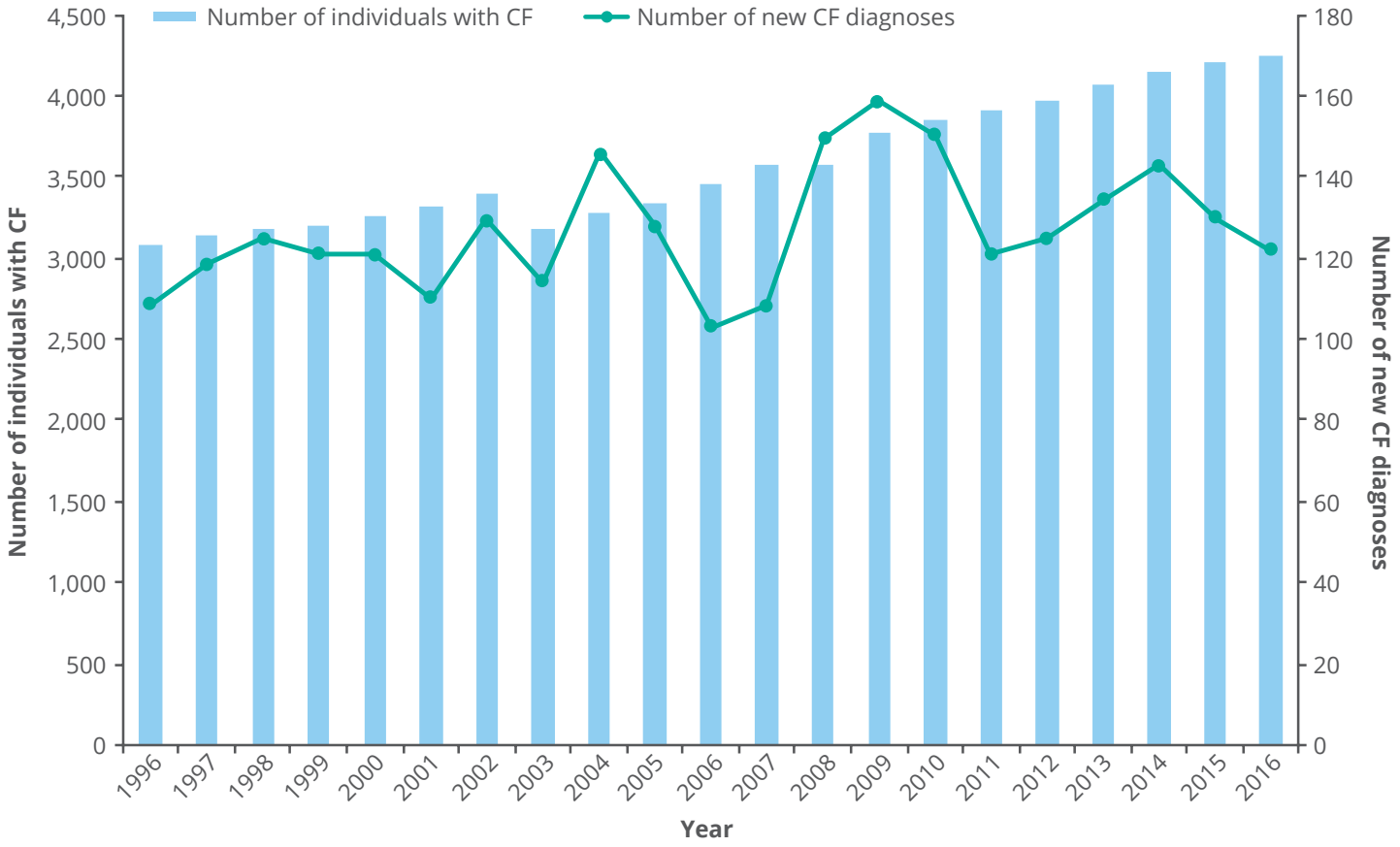

**FIGURE 1**
**Number of individuals with CF, by province, 2016**

| PROVINCE* | # OF PATIENTS | FEMALE | MALE | ADULTS | CHILDREN |
|---|---|---|---|---|---|
| AB | 587 | 279 | 308 | 335 | 252 |
| BC | 424 | 180 | 244 | 258 | 166 |
| MB | 113 | 48 | 65 | 57 | 56 |
| NB | 45 | 24 | 21 | 32 | 13 |
| NL | 74 | 29 | 45 | 54 | 20 |
| NS | 236 | 112 | 124 | 145 | 91 |
| ON | 1473 | 714 | 759 | 885 | 588 |
| QC | 1198 | 552 | 646 | 761 | 437 |
| SK | 129 | 51 | 78 | 69 | 60 |

* individuals with CF living in provinces or territories not listed here are included if reported on by other CF clinics

# DEMOGRAPHIC DATA
## NUMBER OF CANADIANS WITH CYSTIC FIBROSIS

**FIGURE 2**
**Total number of individuals with CF and new CF diagnoses, 1996 to 2016**



# DEMOGRAPHIC DATA
## PROVINCIAL POPULATION CHANGE

Over the past two decades, eight of the nine provinces with CF clinics had an increase in their CF population (Figure 3) with Manitoba experiencing the largest percent growth of over 75%.

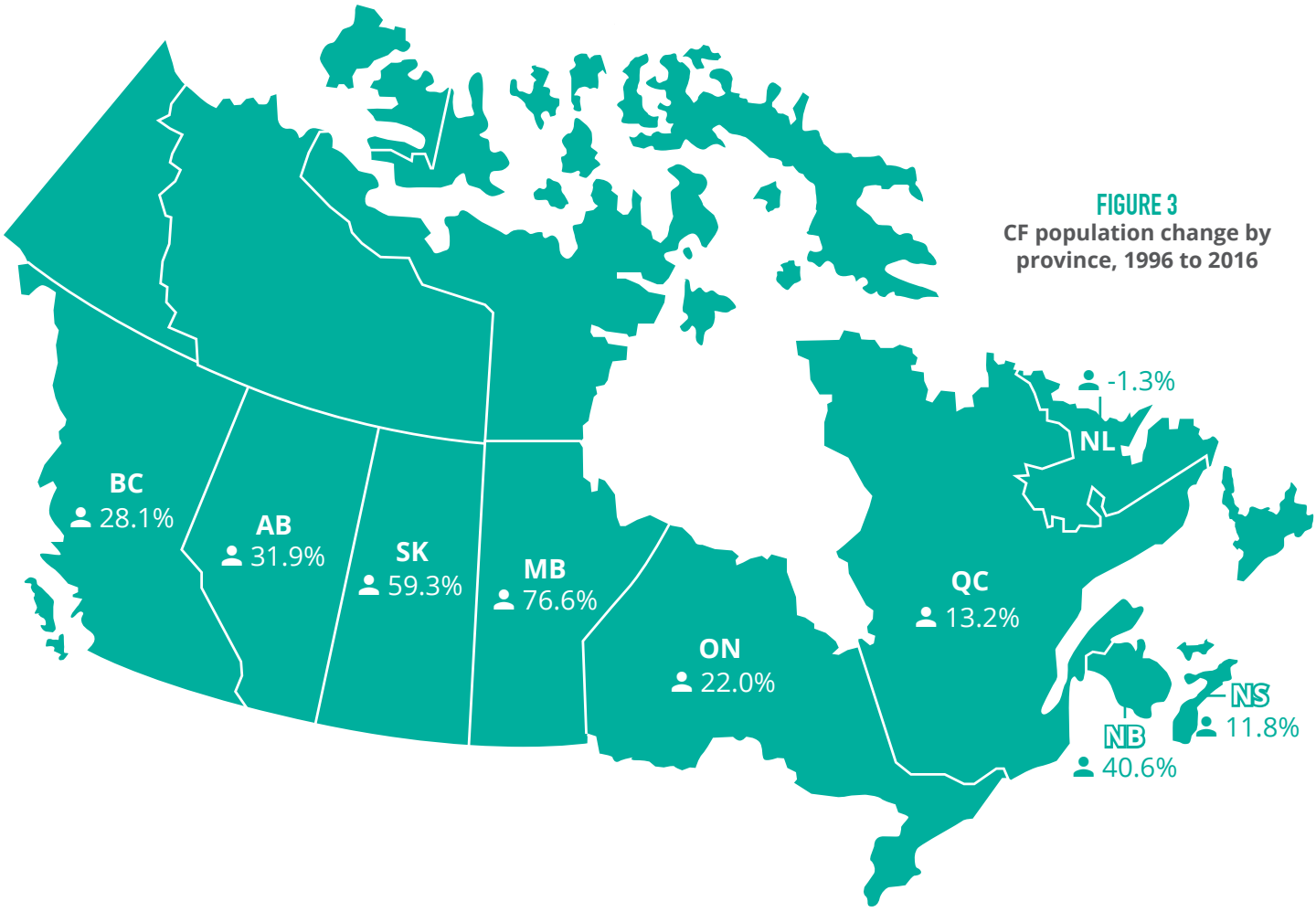



**FIGURE 3**
**CF population change by province, 1996 to 2016**

| PROVINCE* | 1996 | 2016 | PERCENT CHANGE |
|---|---|---|---|
| AB | 445 | 587 | 31.9% |
| BC | 331 | 424 | 28.1% |
| MB | 64 | 113 | 76.6% |
| NB | 32 | 45 | 40.6% |
| NL | 75 | 74 | -1.3% |
| NS | 211 | 236 | 11.8% |
| ON | 1207 | 1473 | 22.0% |
| QC | 1058 | 1198 | 13.2% |
| SK | 81 | 129 | 59.3% |

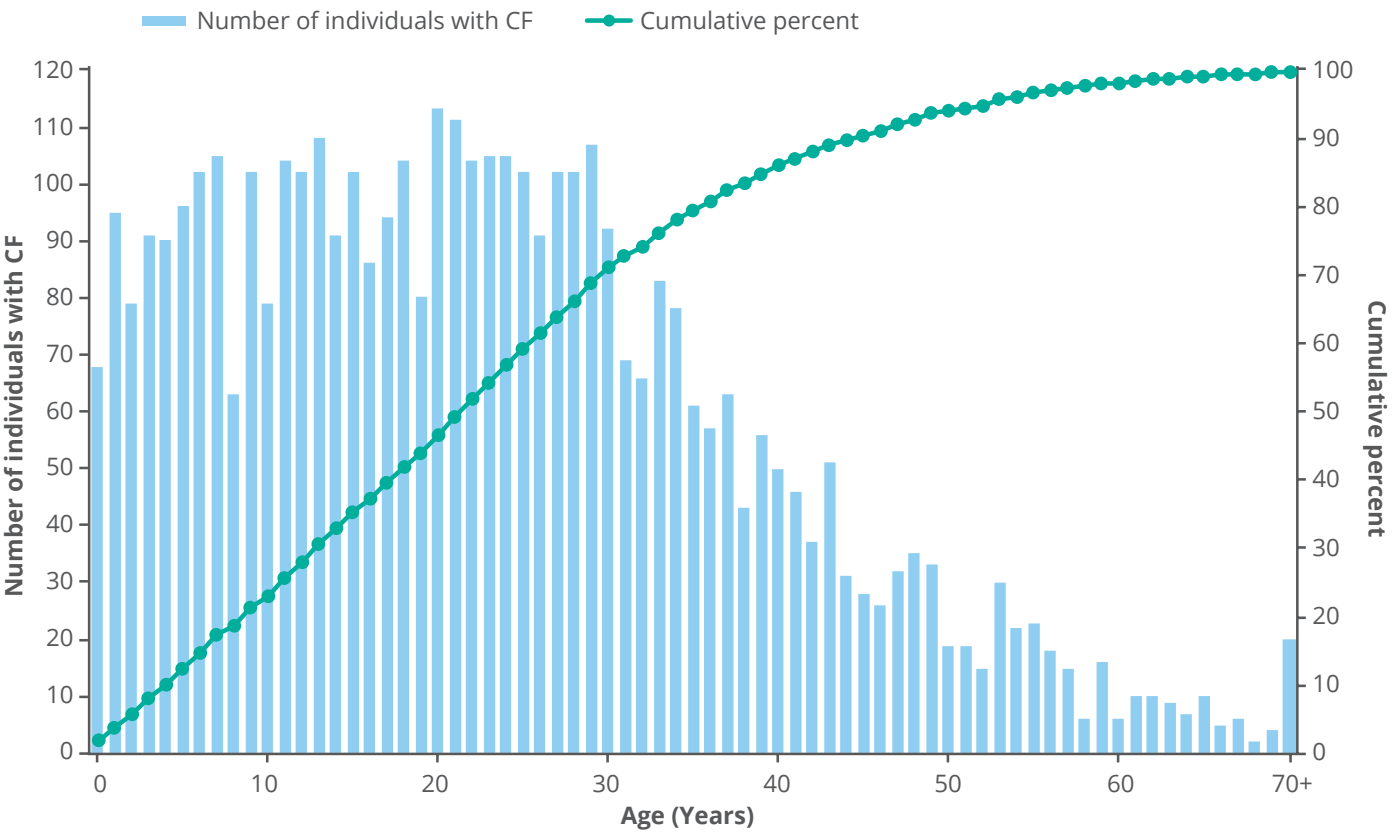
* individuals with CF living in provinces or territories not listed here are included if reported on by other CF clinics

# DEMOGRAPHIC DATA

## AGE DISTRIBUTION OF CANADIANS WITH CYSTIC FIBROSIS

Figure 4 shows the age distribution of the Canadian CF population in 2016. The median age of all individuals reported on in 2016 was 22.7 years with 60.8% of individuals over 18 years of age (Figure 7), 16.0% over 40 years of age and 0.5% over 70 years of age.

**FIGURE 4**
**Age distribution of individuals with CF, as of December 31, 2016**



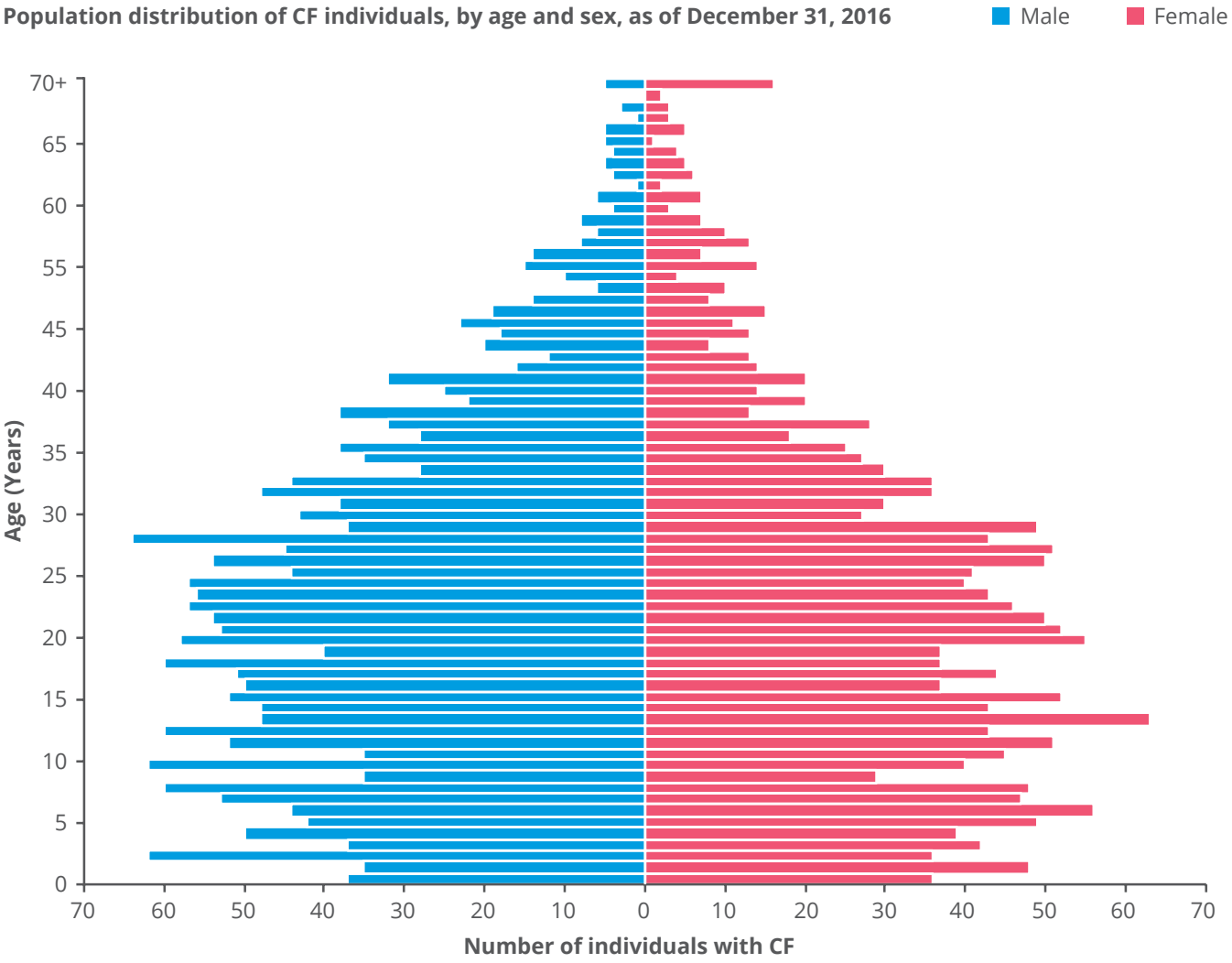
# DEMOGRAPHIC DATA

## AGE AND SEX DISTRIBUTION OF CANADIANS WITH CYSTIC FIBROSIS

Males accounted for 53.6% of individuals reported on in 2016 with 9.1% of males and 7.4% of females over the age of 40 (Figure 5).

**FIGURE 5**

**Population distribution of CF individuals, by age and sex, as of December 31, 2016**



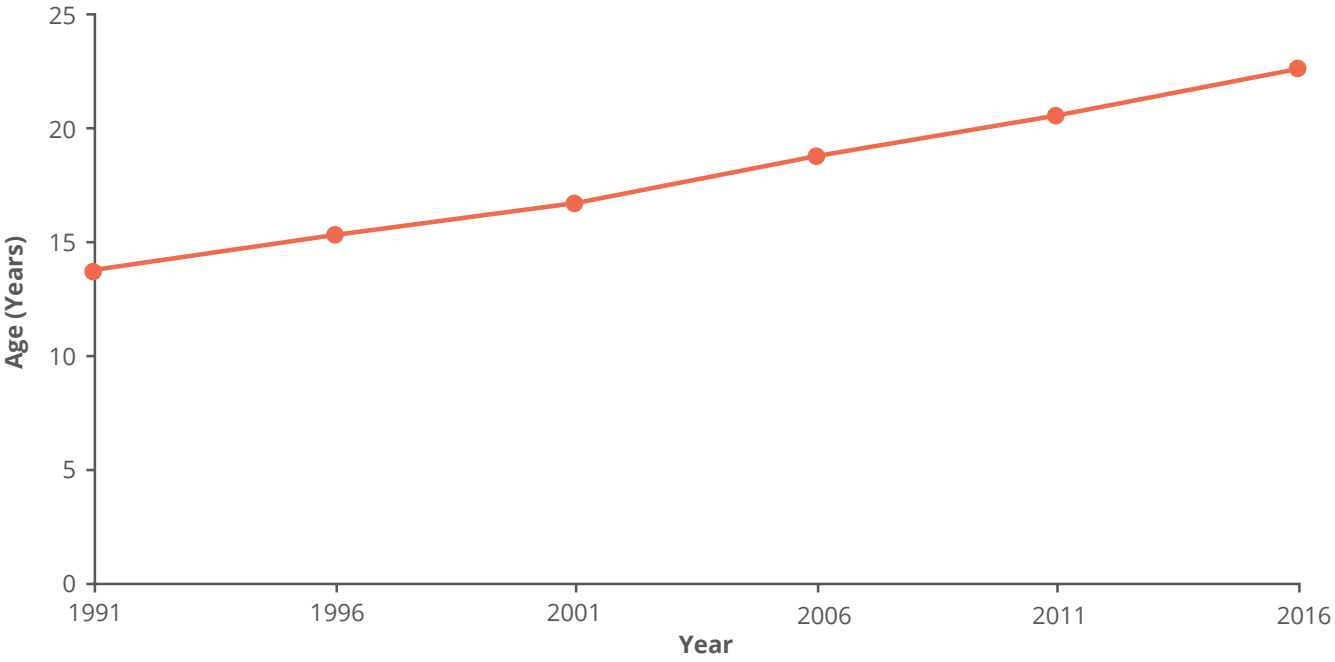
# DEMOGRAPHIC DATA

## MEDIAN AGE OF CANADIANS WITH CYSTIC FIBROSIS

The current median age of individuals with CF reported on in 2016 was 22.7 years, more than seven years higher than it was two decades ago (Figure 6).

**FIGURE 6**

**Median age of individuals with CF,1991 to 2016**

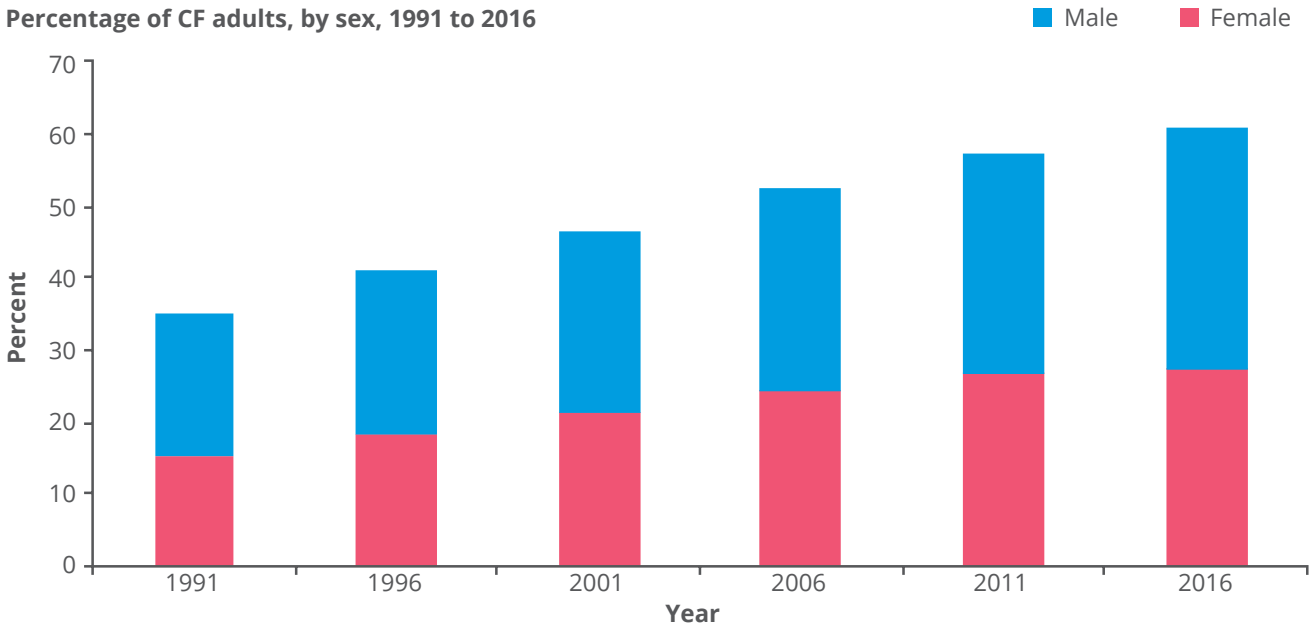



## CANADIAN ADULTS WITH CYSTIC FIBROSIS

In 2016, there were 2,580 (60.8%) adults (individuals 18 years of age or older) and among those adults, 45.2% were females and 54.8% were males (Figure 7).

**FIGURE 7**

**Percentage of CF adults, by sex, 1991 to 2016**



# DIAGNOSIS
## AGE AT DIAGNOSIS

The majority (59.1%) of individuals with CF reported in 2016 were diagnosed by one year of age and by 18 years of age, 92.4% had been diagnosed (Figure 8). Adults diagnosed later in life (18 years or older) account for only 7.6% of all diagnoses.

Figure 9 shows the percentage of newborns diagnosed through provincial newborn screening (NBS) programs since 2007 when NBS for CF started in Alberta. Back then, less than 10% of new CF diagnoses were identified through NBS. Now, in 2016, over half of those newly diagnosed (66, 54.1%) have been diagnosed through NBS. All provinces in Canada now screen newborns for CF (Quebec will add CF testing to their NBS program in 2018).

**FIGURE 8**
**Age at diagnosis of CF individuals, as of December 31, 2016 (N = 4,181)**

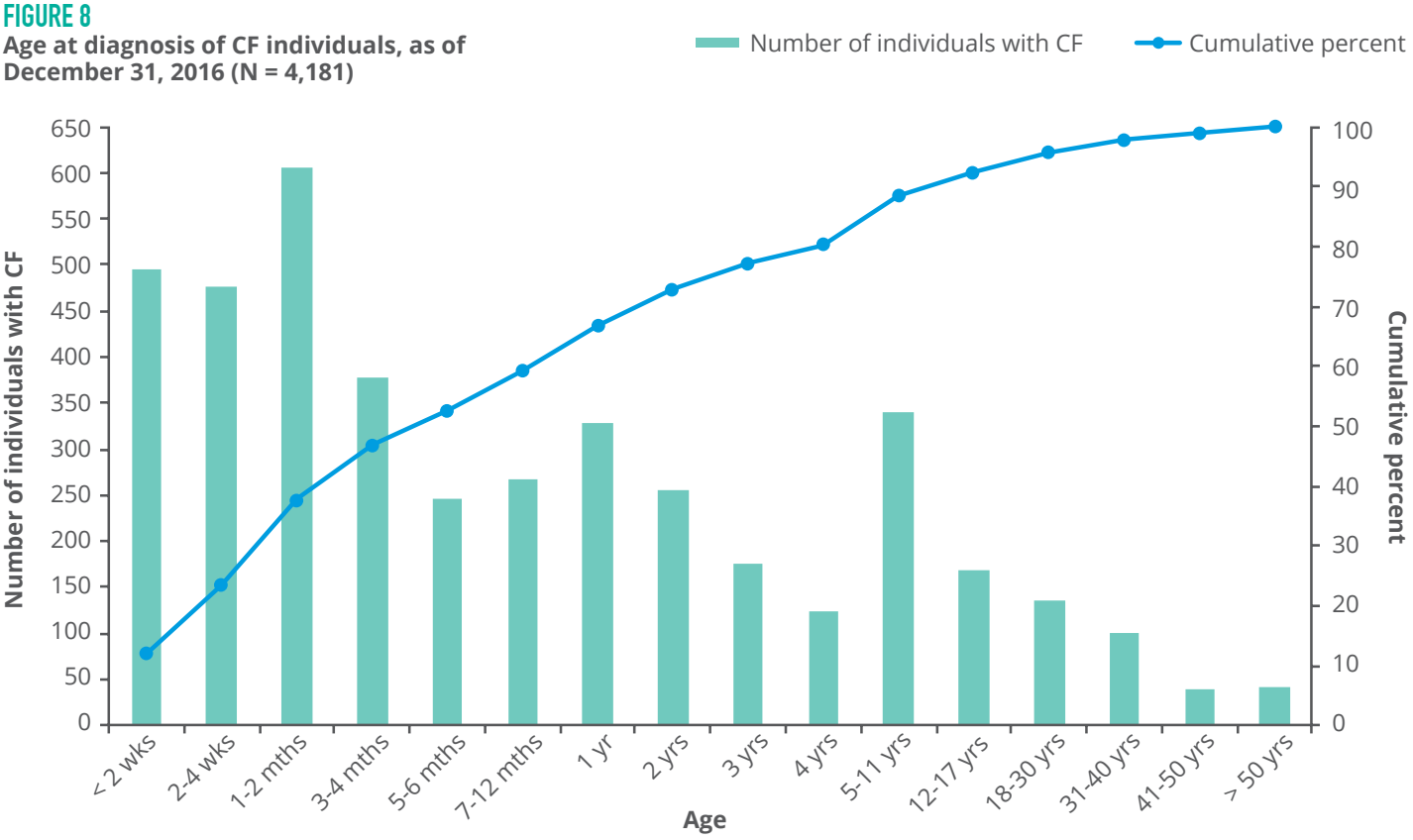
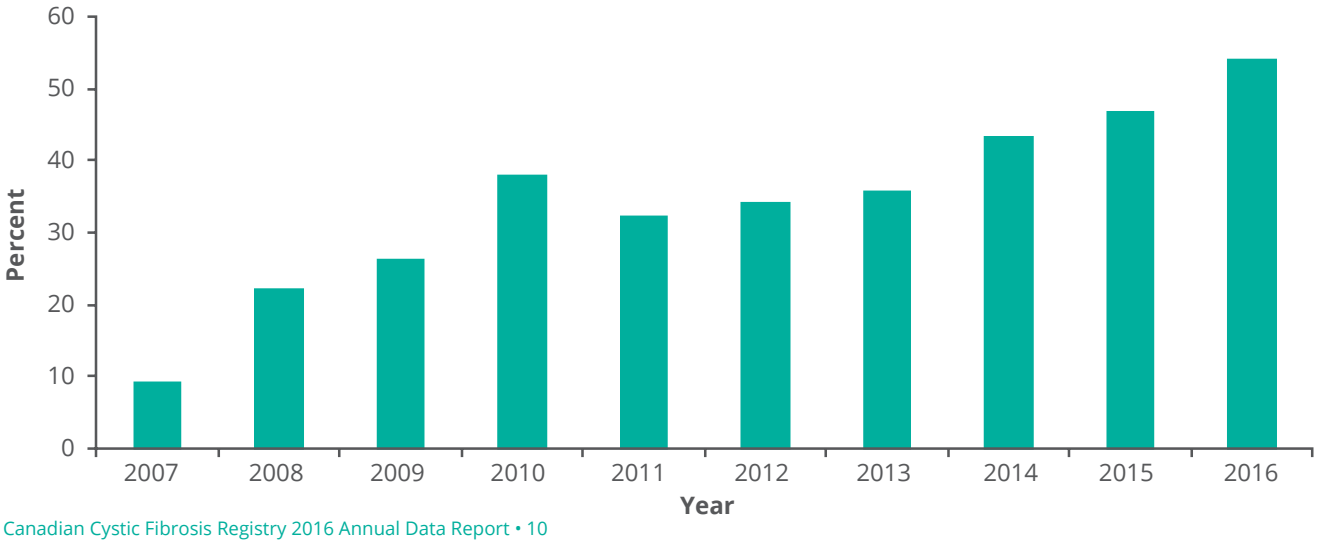


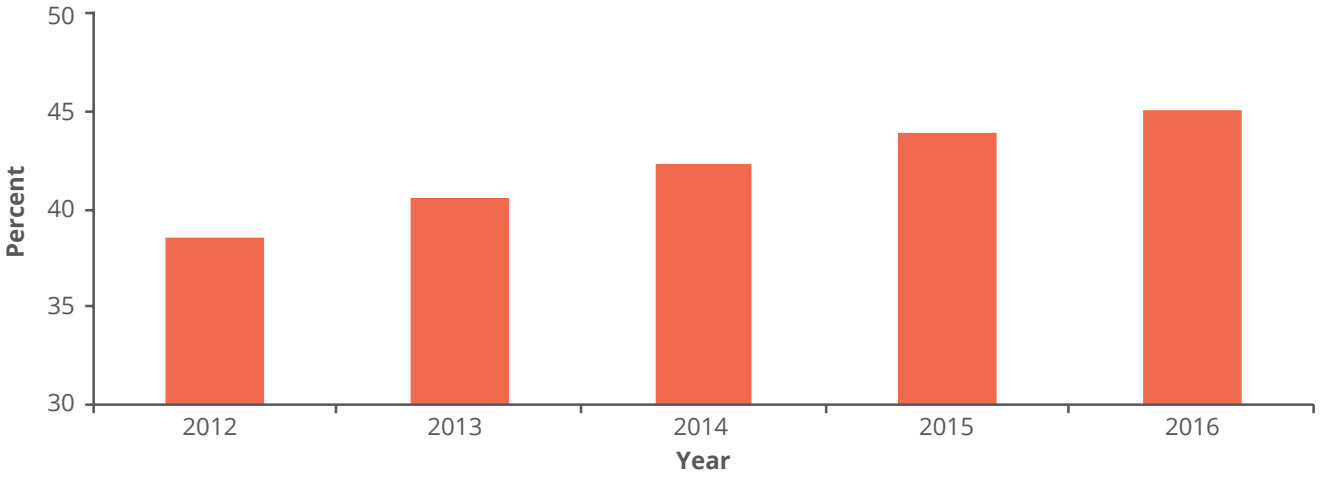

**FIGURE 9**
**Percentage of all new CF diagnoses made through the NBS program, 2007 to 2016**



# DIAGNOSIS
## SWEAT CHLORIDE TESTING

Sweat chloride testing is used in the diagnosis of CF. Individuals with CF typically have a sweat chloride value greater than 60 mmol/L whereas values between 40 and 59 mmol/L are indeterminate. Values lower than 40 mmol/L are considered in the normal range. The CCFR began capturing sweat chloride test results in 2011. In 2016, there were 1,912 (45.0%) individuals with CF with at least one sweat chloride test result recorded (Figure 10). While this percentage has been gradually increasing, it does not reflect those who have been diagnosed more recently. In fact, of those newly diagnosed in 2016, 106 (86.8%) had at least one sweat chloride test result recorded.

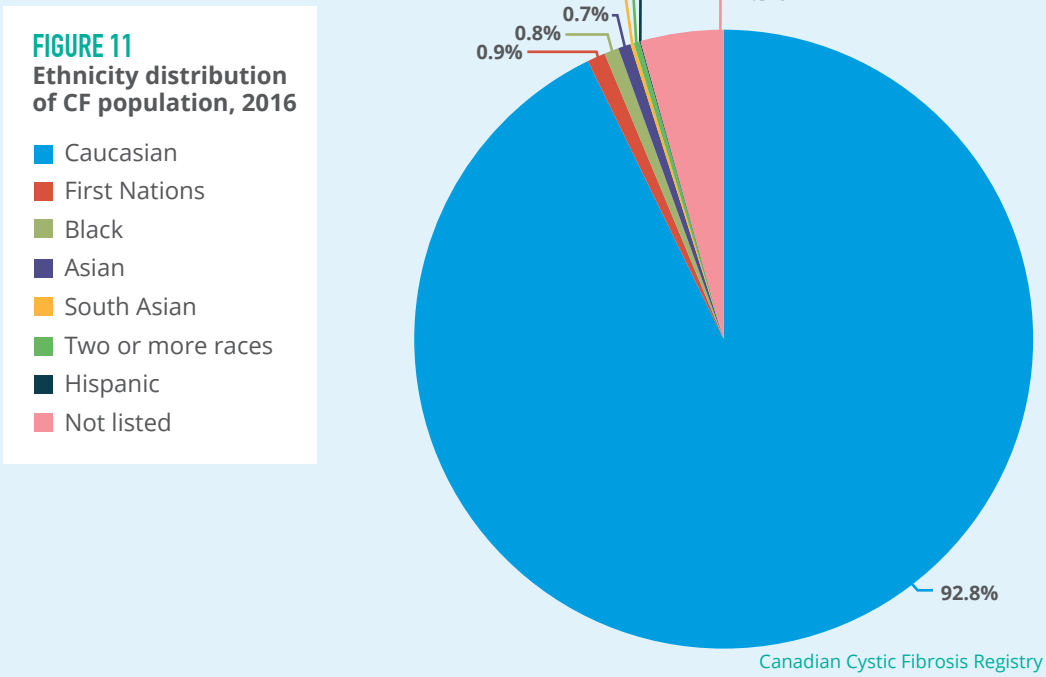
**FIGURE 10**
**Percentage of individuals with CF with at least one sweat chloride test result, 2012 to 2016**




# ETHNICITY

The majority of the Canadian CF population is Caucasian (92.8%). Of those remaining who have an identified ethnicity (Figure 11), they are divided among five other ethnic groups (First Nations, Black, Asian, South Asian and Hispanic). Ethnicity is captured through self-report.

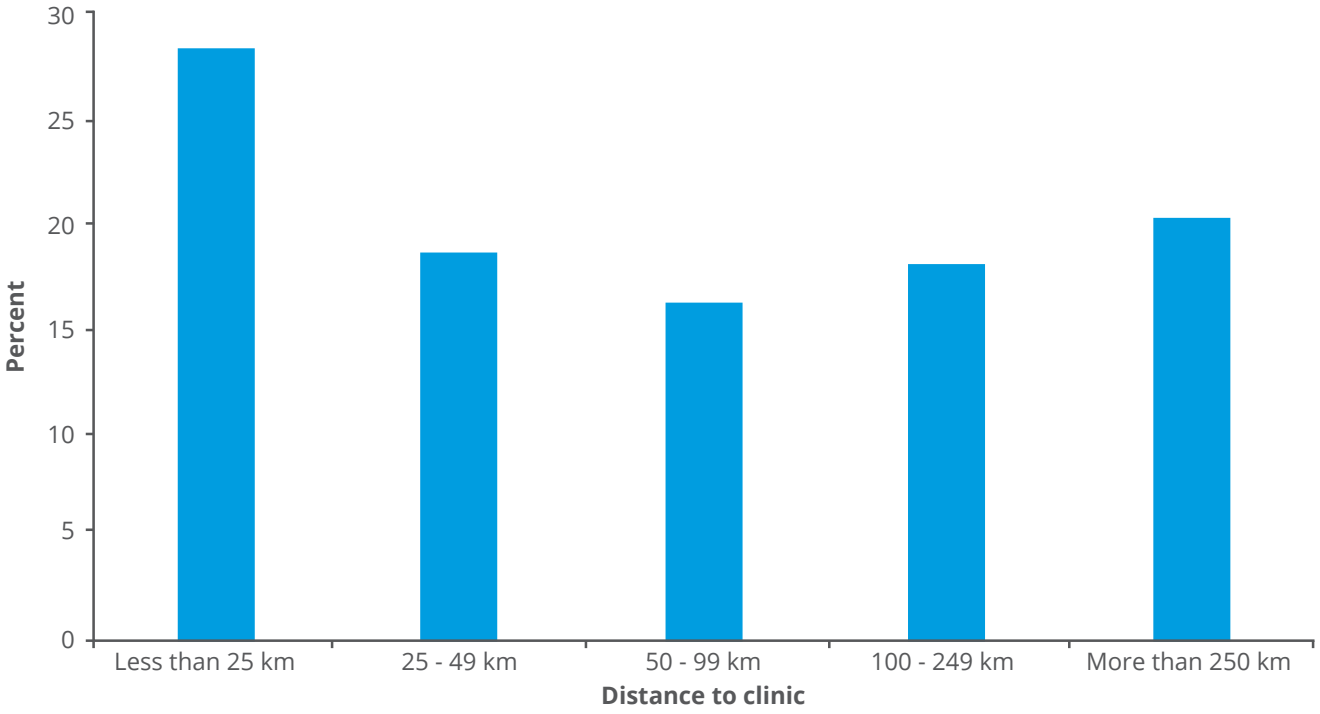
**FIGURE 11**
**Ethnicity distribution of CF population, 2016**



# DISTANCE TO CLINICS

The general location (the first three characters of the postal code) of where individuals with CF live was added to the CCFR in 2015. There were 1,201 (28.3%) CF individuals with at least one valid location recorded. Distances to the reporting clinic were calculated in kilometers and assumed that driving was the mode of transportation with the fastest route taken. All reported locations in 2016 were included in (Figure 12). The majority (62.9%) of those with a reported location attend a CF clinic within 100km of where they live while 20.1% travel more than 250 km for their CF care.

**FIGURE 12**
**Distance travelled to clinic for individuals with CF, 2016**




# MENTAL HEALTH

In 2016, 484 (11.4%) individuals with CF were reported to have a clinical diagnosis of depression and/or anxiety. Of those individuals, 41 were children and 443 were adults. These prevalence rates are in line with findings from The International Depression/Anxiety Epidemiology Study (TIDES)[1,2] which showed elevated rates of depression and anxiety among individuals with CF and their parents/caregivers. The data recorded in the Registry may be an underestimation of the true number of CF individuals with mental health illness as the definition of depression and/or anxiety can vary greatly.

# GENOTYPE

CF 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.

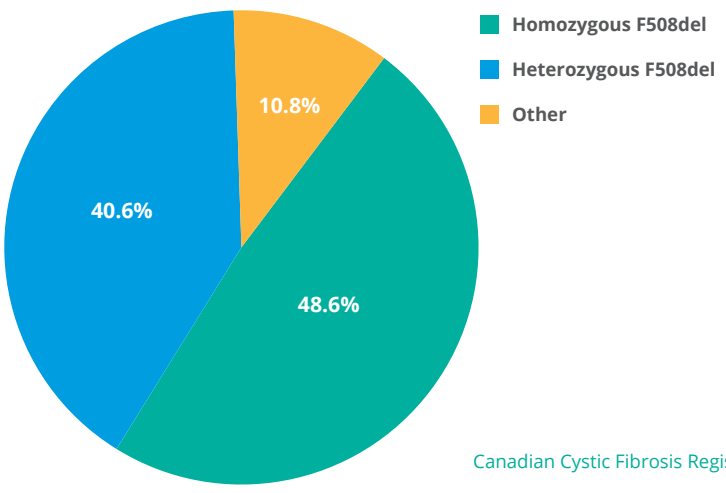
The most common CF mutation worldwide is a three base-pair deletion in the *CFTR* gene resulting in the deletion of the phenylalanine (F) residue at position 508 in the CFTR protein, commonly referred to as **F508del**. CF disease-causing mutations can be classified into five major categories depending on the how the mutation impacts the production and function of the CFTR protein. 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 |

Nearly all (4,175, 98.3%) individuals with CF reported in 2016 had at least one CF mutation recorded. Almost half (2,027, 48.6%) have two copies of the F508del mutation and almost 90% carry at least one copy of the F508del mutation (Figure 13). The genotype distribution is nearly identical between adults (18+ years) and children (0-17 years) (Figure 14). In the entire CCFR, 93.1% of all individuals with CF reported as being alive have at least one CF mutation recorded and 86.9% of those individuals with no mutations reported are adults. The CCFR has genotype data for almost all recently reported individuals with CF (especially among children).

**FIGURE 13**
**Genotype distribution of CF population, (N = 4,175), 2016**



# GENOTYPE

**FIGURE 14**
**Genotype distribution of individuals with CF, by age group, 2016**

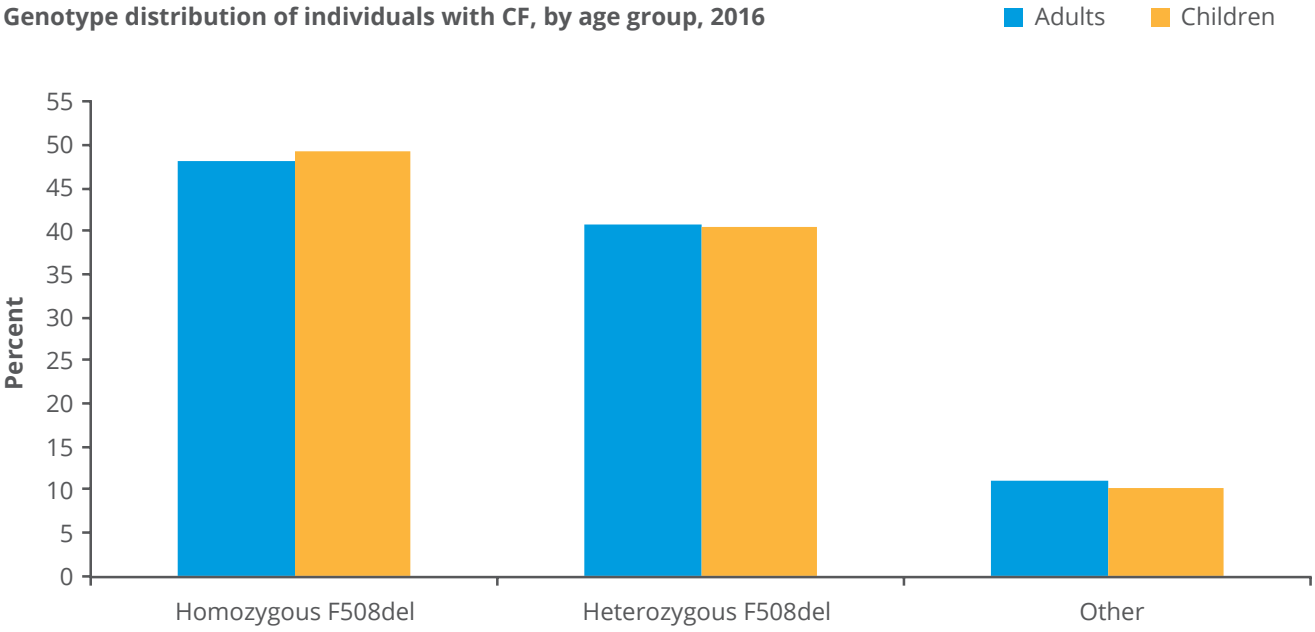



Table 2 lists the most common mutations for individuals with CF reported in 2016. After F508del, 621+1G->T is the next most frequent mutation identified in 6.1% of the population.

**TABLE 2**
**Frequency of the top 10 most common CF mutations on one or both alleles of CF individuals (N = 4,175), 2016**

| GENOTYPE | NUMBER | PERCENT |
|---|---|---|
| F508del | 3,724 | 89.2 |
| 621+1G->T | 253 | 6.1 |
| G542X | 147 | 3.5 |
| G551D | 126 | 3.0 |
| 711+1G->T | 110 | 2.6 |
| A455E | 101 | 2.4 |
| L206W | 91 | 2.2 |
| N1303K | 87 | 2.1 |
| R117H | 87 | 2.1 |
| W1282X | 84 | 2.0 |

# RESPIRATORY
## MEDIAN $FEV_1$ PERCENT PREDICTED

Lung function measurements are critical for evaluating lung health and are reliably measured starting at six years of age. $FEV_1$ (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 their $FEV_1$ to the average $FEV_1$ of a healthy population of similar age, height, race and sex.

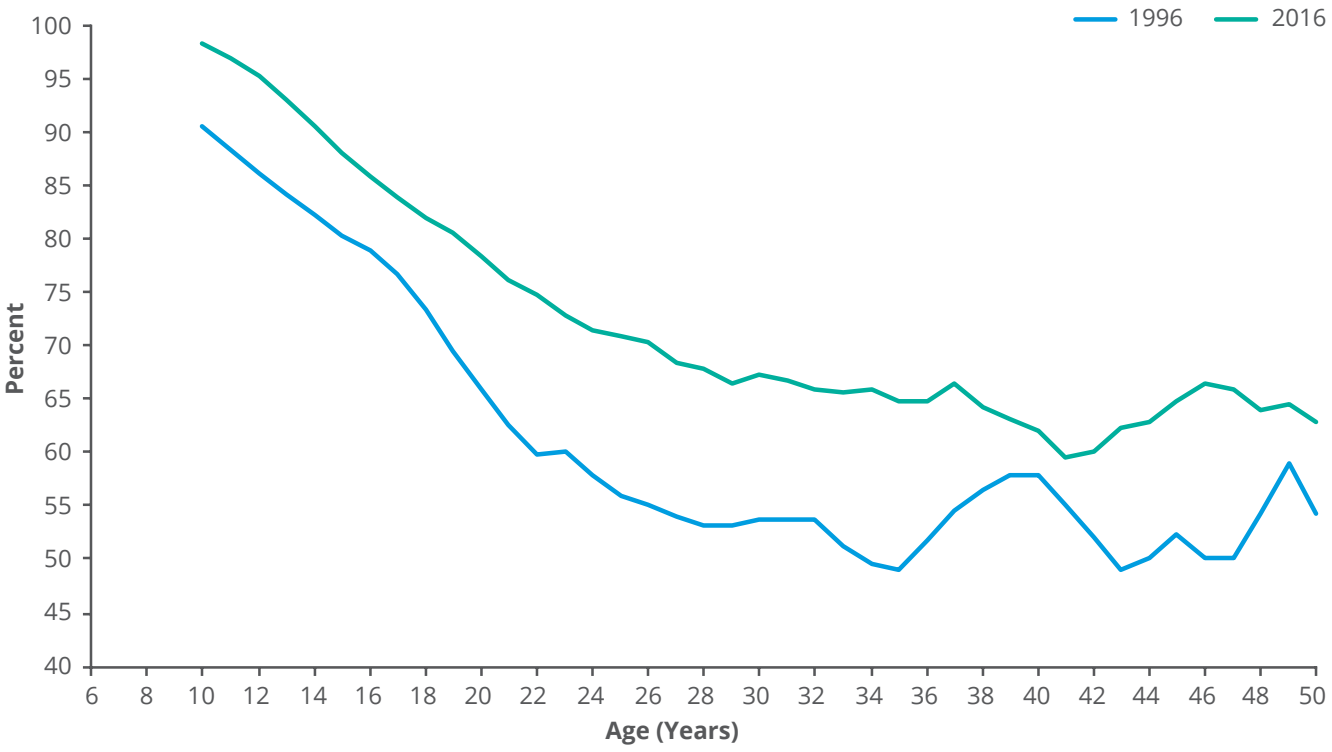
Global Lung Initiative (GLI) equations[3] are used to calculate the percent predicted $FEV_1$ values. In this report, the first complete stable lung measurement of the year was used per individual with CF to summarize lung function, otherwise, the first complete measurement regardless of the lung status was used.

Figure 15 shows the median $FEV_1$ percent predicted from the ages 6 to 50 years in a 5-year moving average window. While at an individual patient level, lung function tends to decline with age, at a population level the median $FEV_1$ percent predicted has increased over the years.

In 2016, the median $FEV_1$ was 72.2% at 30 years of age compared to 53.3% in 1996 marking an improvement of nearly 19% over the last two decades. Interestingly, the trends between these two time periods are similar. From ages 6 to 30 years, there is a steady decline in annual lung function, with a slightly larger average annual drop in 1996 (2.0%) than in 2016 (1.6%). Perhaps as expected, while the largest average annual drop in lung function (3.3% in 1996 and 2.1% in 2016) occurs during the teenage years (13 to 20 years) the rate of decline is less than it was 20 years ago. This could be because this age group typically undergoes a challenging transition period to adulthood which may include relocating to a new city, attending a new school and transferring to another CF clinic.

Individuals born recently have a higher median $FEV_1$ percent predicted and a slower rate of decline than those born earlier. While the 1987-1991 birth cohort has an average annual lung function drop of 1.3%, the most recent birth cohort (2007-2011) shows a small average lung function growth of 0.8% which could indicate that the historical trend of declining lung function may be delayed (Figure 16). Across all birth cohorts (with the exception of the most recent 2007-2011 group), all have an average annual lung function decline of 1-2%.

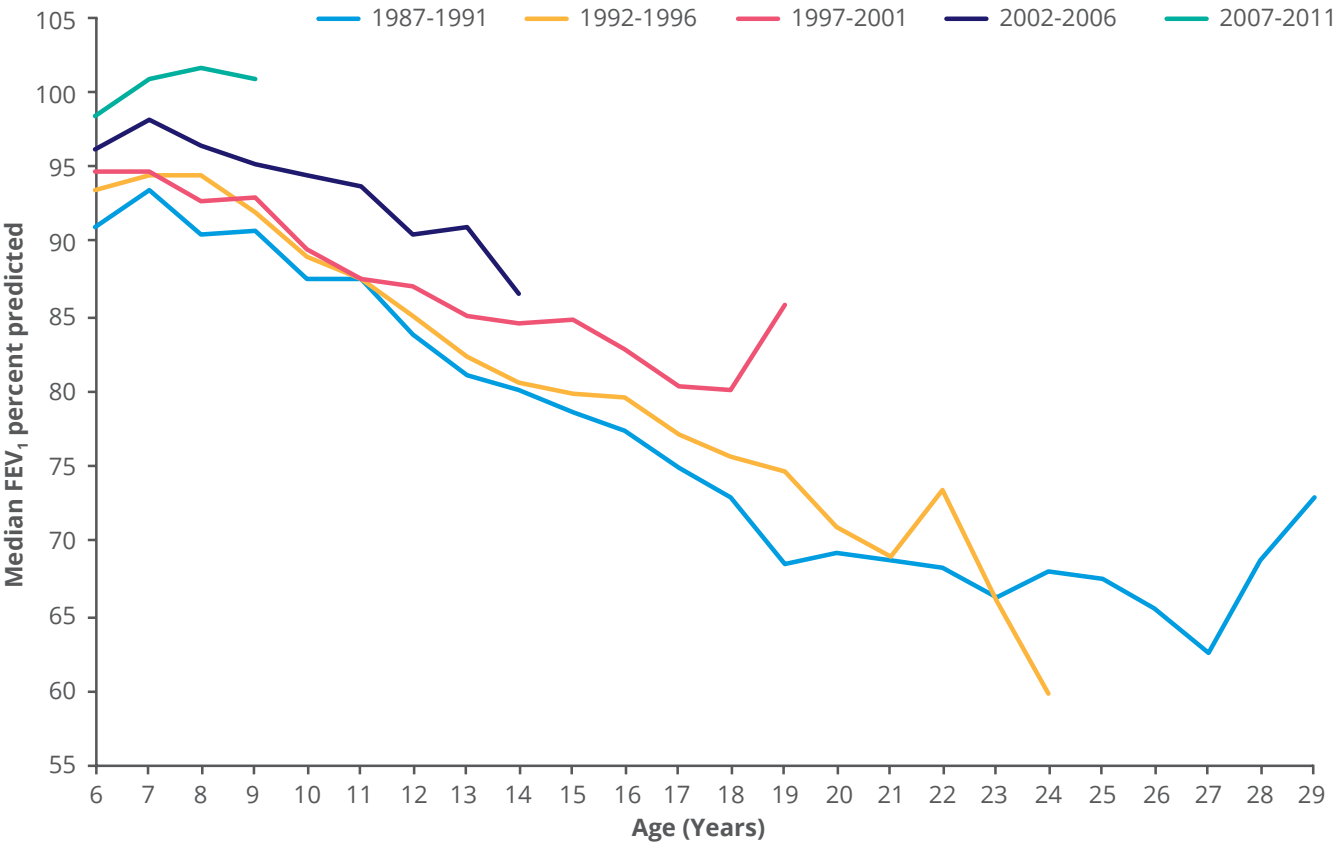
### FIGURE 15
**Median FEV1 percent predicted vs. age of CF individuals (5-year moving window), 1996 and 2016***




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

## FIGURE 16

**Median $FEV_1$ percent predicted of individuals with CF, by birth cohort, 2016***




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

Figure 17 shows that the majority (53.6%) of children, ages 6 to 17 years, have normal lung function while the majority (37.0%) of adults have moderate lung function. Figure 18 shows that over time, the median $FEV_1$ percent predicted has been steadily increasing for both age groups and in 2016, these values were 67.7% for adults and 91.5% for children (6-17 years of age). Both figures include data from all those reported on in 2016, including those who are post-transplant. Table 3 summarizes the $FEV_1$ percent predicted classification categories.

**TABLE 3**
**Lung function classification by $FEV_1$ percent predicted values**

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

**FIGURE 17**
**Respiratory status of children and adults with CF, 2016**

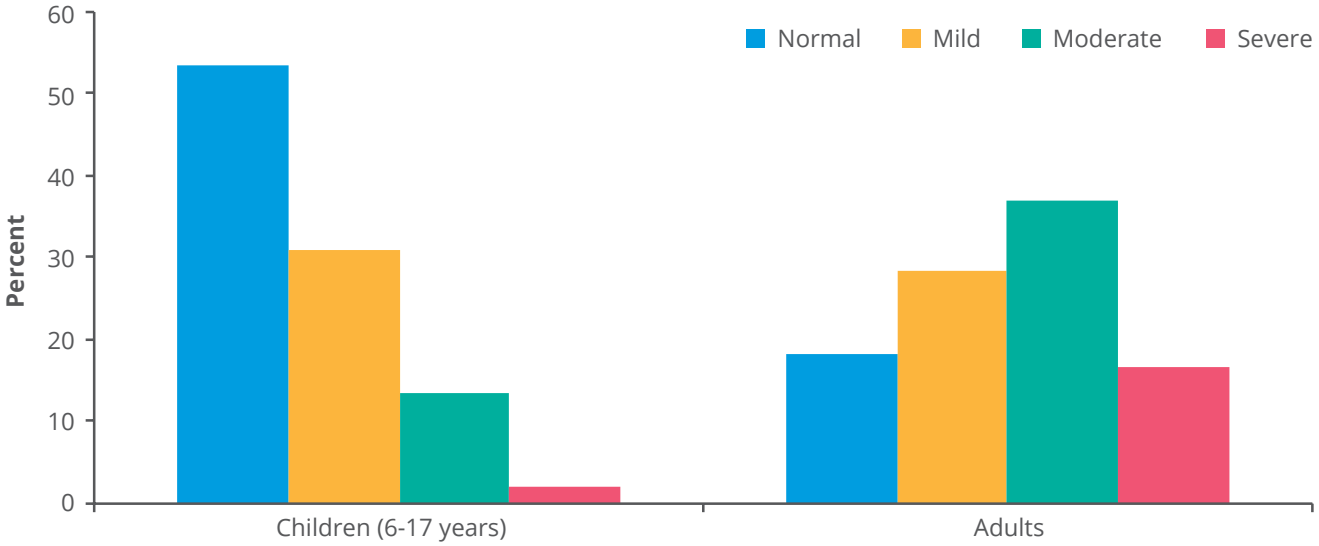
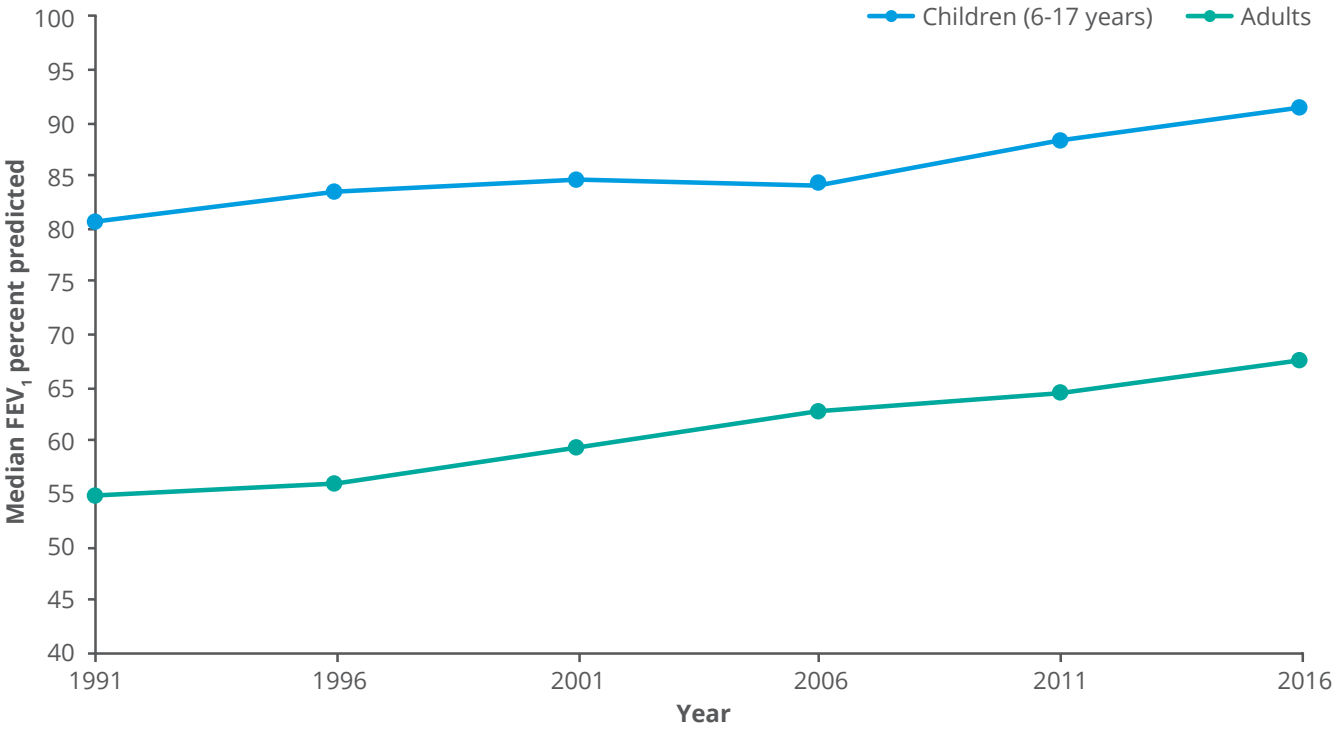


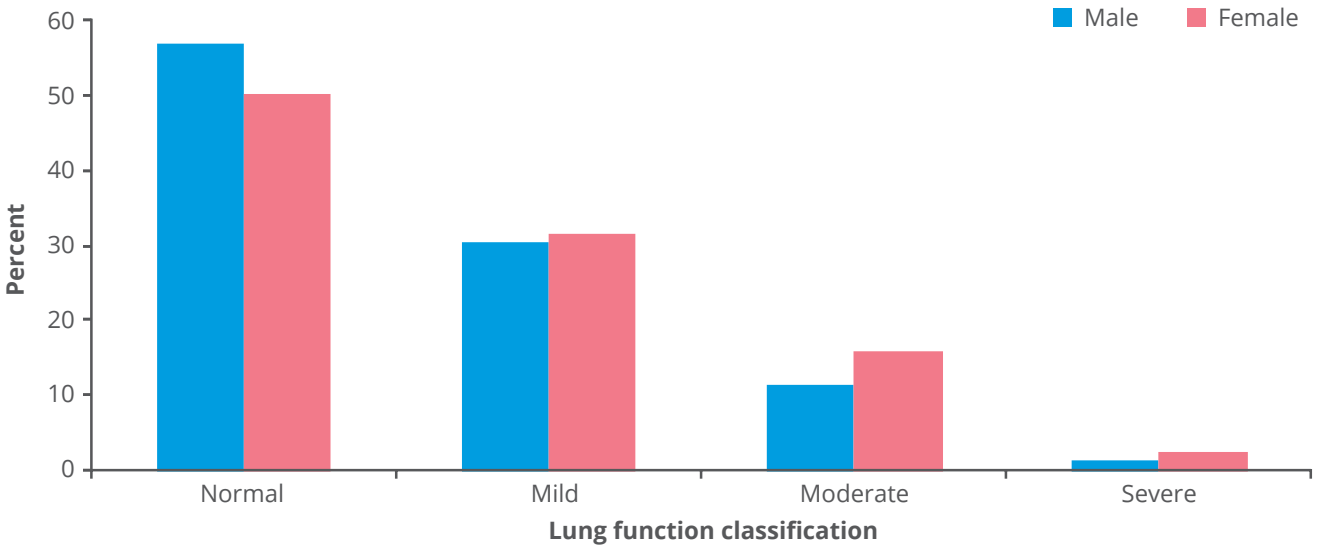

**FIGURE 18**
**Median $FEV_1$ percent predicted values for children and adults with CF, 1991 to 2016**



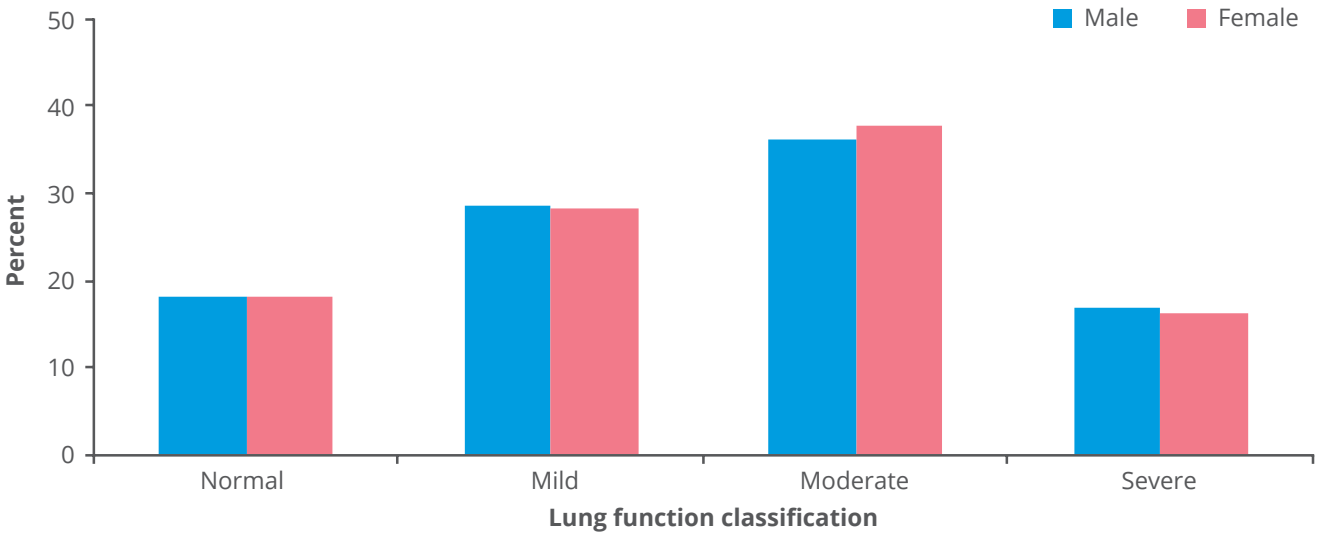
## RESPIRATORY STATUS BY SEX

Figures 19 and 20 show that for both age groups (children age 6-17 years and adults), the distribution is similar between males and females within each lung function category.

### FIGURE 19
**Respiratory status of children (6 to 17 years) with CF, by sex, 2016**




### FIGURE 20
**Respiratory status of adults (18 years of age and older) with CF, by sex, 2016**



# NUTRITION
## PANCREATIC STATUS

Malnutrition is common in individuals with CF as a result of pancreatic insufficiency. Pancreatic enzymes are given as supplements to help with digestion and absorption of nutrients. In 2016, 84.8% of individuals with CF were taking supplemental pancreatic enzymes (pancreatic insufficient) (Figure 21).

For individuals 40 years of age or older, 30.0% were pancreatic sufficient (Figure 22). This is a reflection of the fact that individuals diagnosed with CF as adults are more likely to have milder mutations that are associated with pancreatic sufficiency.

**FIGURE 21**
**Pancreatic status of individuals with CF, 2016**

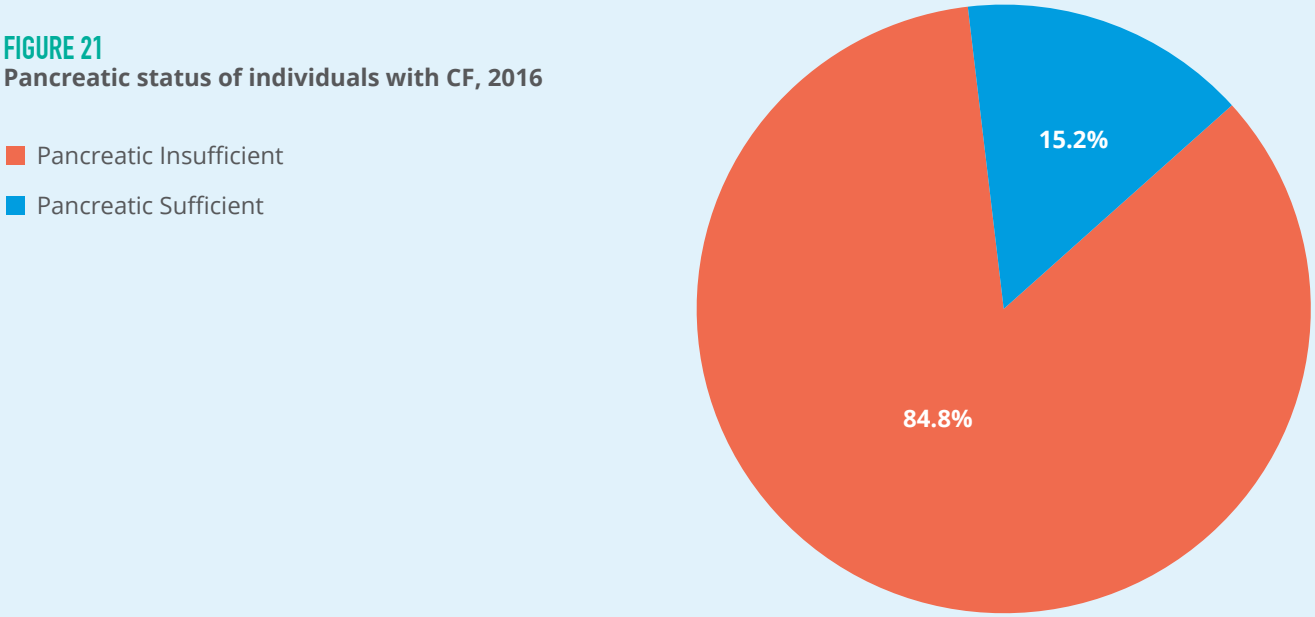
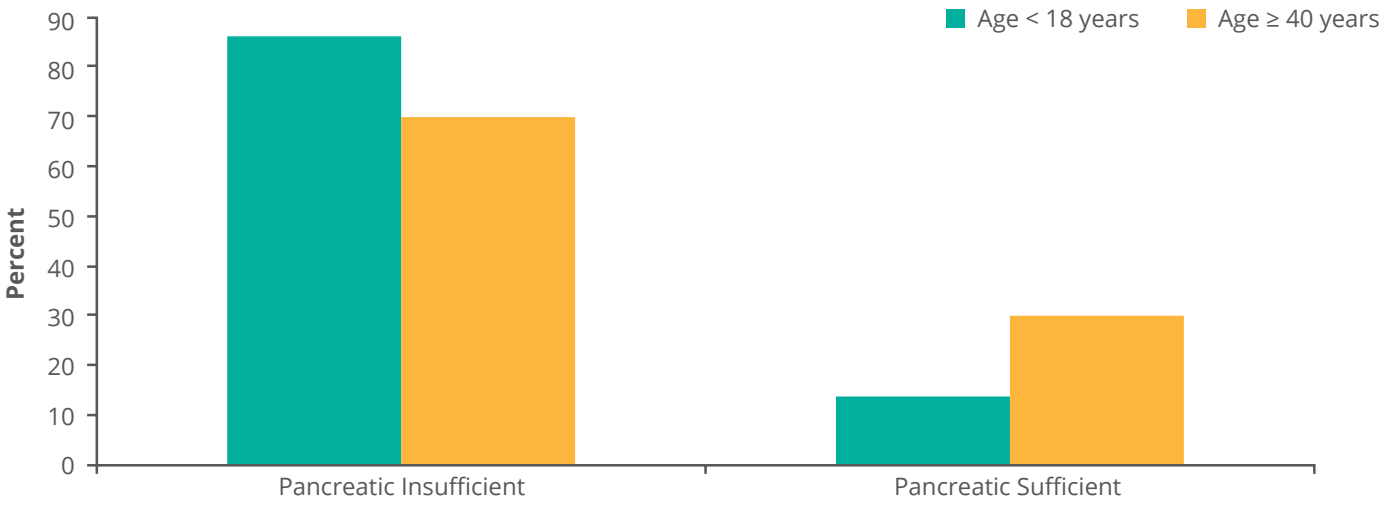



**FIGURE 22**
**Pancreatic status of individuals with CF, by age group 2016**



# NUTRITION
## BMI PERCENTILE

BMI percentiles[4] are calculated for children under 2 years of age following the World Health Organization (WHO) guidelines and for children ages 2 to 17 years, the Centers for Disease Control and Prevention (CDC) guidelines are followed. BMI percentiles allow comparisons to be made between the individual's height and weight and other children who are the same age and sex. Table 4 summarizes the BMI percentile classification categories following the respective WHO or CDC guidelines[5]. As such, the proportions of BMI percentile classifications will be different from those described in previous reports.

The national median BMI percentile for babies is 49.1 (under 2 years of age) and 45.3 for children (ages 2-17 years). The vast majority of children with CF (67.5% of children under 2 years and 76.3% of children 2-17 years) have an adequate weight (Figure 23). The national goal for children with CF is 50th BMI percentile and 49.6% of children under 2 years and 45.6% of children 2-17 years are above the national goal.

**FIGURE 23**
**BMI percentile status for children with CF, 2016**

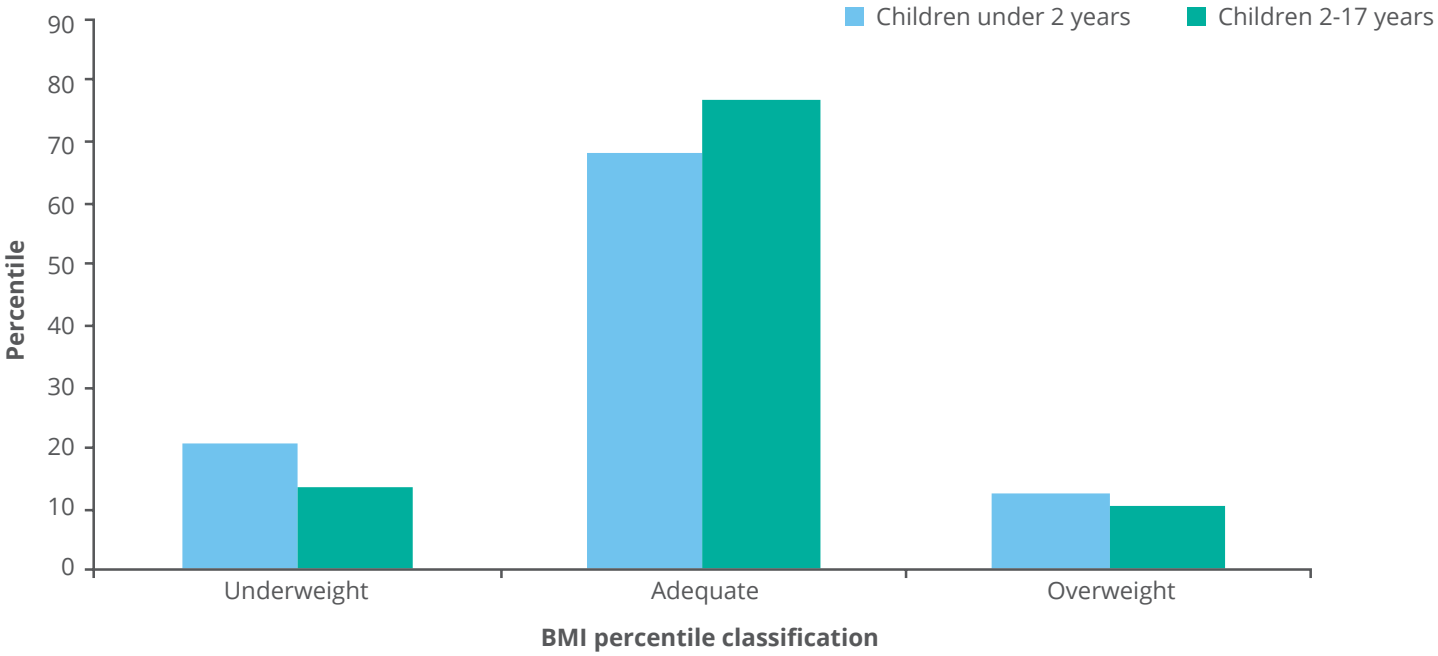
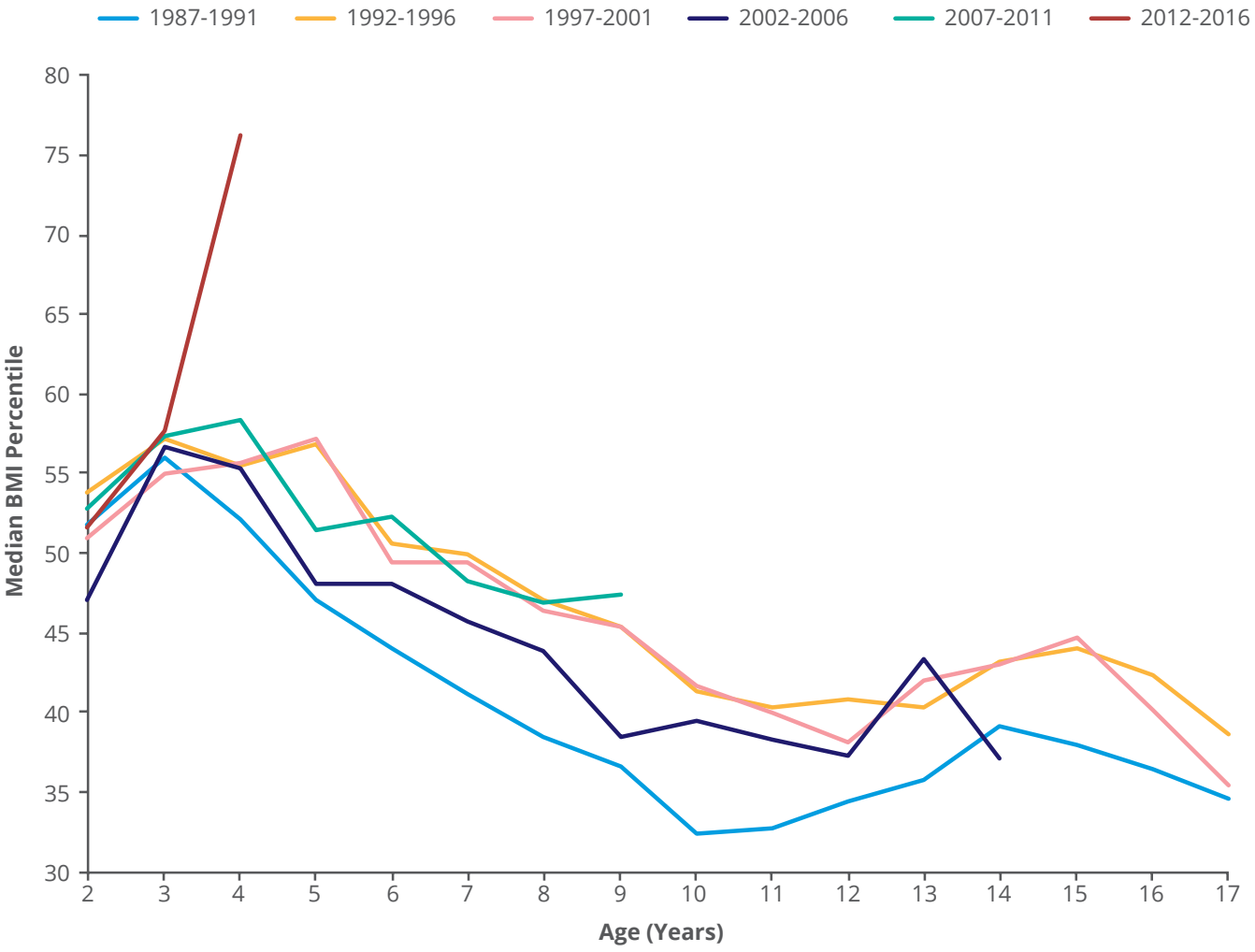



**TABLE 4**
**BMI percentile classification**

| CLASSIFICATION | RANGE |
|---|---|
| Underweight | ≤ 12th percentile |
| Adequate | 13th percentile - 84th percentile |
| Overweight | ≥ 85th percentile |

For children 2-17 years of age, Figure 24 shows that the median BMI percentiles over time for those born before 2012 have similar trends. Those earlier birth cohorts have comparable average median BMI percentile decreases of between 1.2 and 1.4 percentile per year. The most recent birth cohort (2012-2016) has relatively few data points which may explain the large spike for those who are 4 years of age but it is expected that the data will stabilize with the collection of more information in the coming years. BMI percentile appears to decline starting at age 3 years and by 10 years of age, there is evidence of stabilization with flattening of the curves.

**FIGURE 24**
**Median BMI percentile for children (2-17 years) with CF, by birth cohort, 2016**



# NUTRITION
## BMI PERCENTILE BY SEX

Figures 25 and 26 show the BMI percentile status for males and females in children under 2 years (N = 228) and children 2-17 years (N = 1,499). In both age groups, the sex distribution is quite similar. As well, median BMI percentiles have been increasing over time for both males and females with both sexes showing similar trends (Figure 27).

**FIGURE 25**
**BMI percentile status for children (under 2 years) with CF, by sex, 2016**

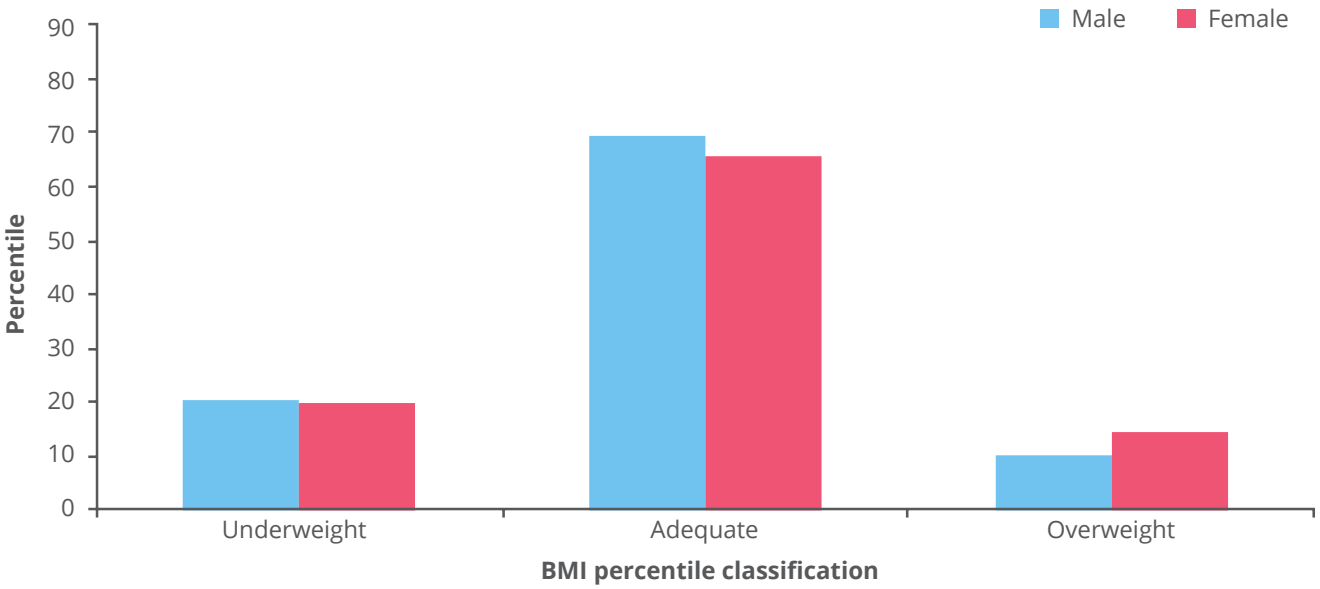



**FIGURE 26**
**BMI percentile status for children (2-17 years) with CF, by sex, 2016**

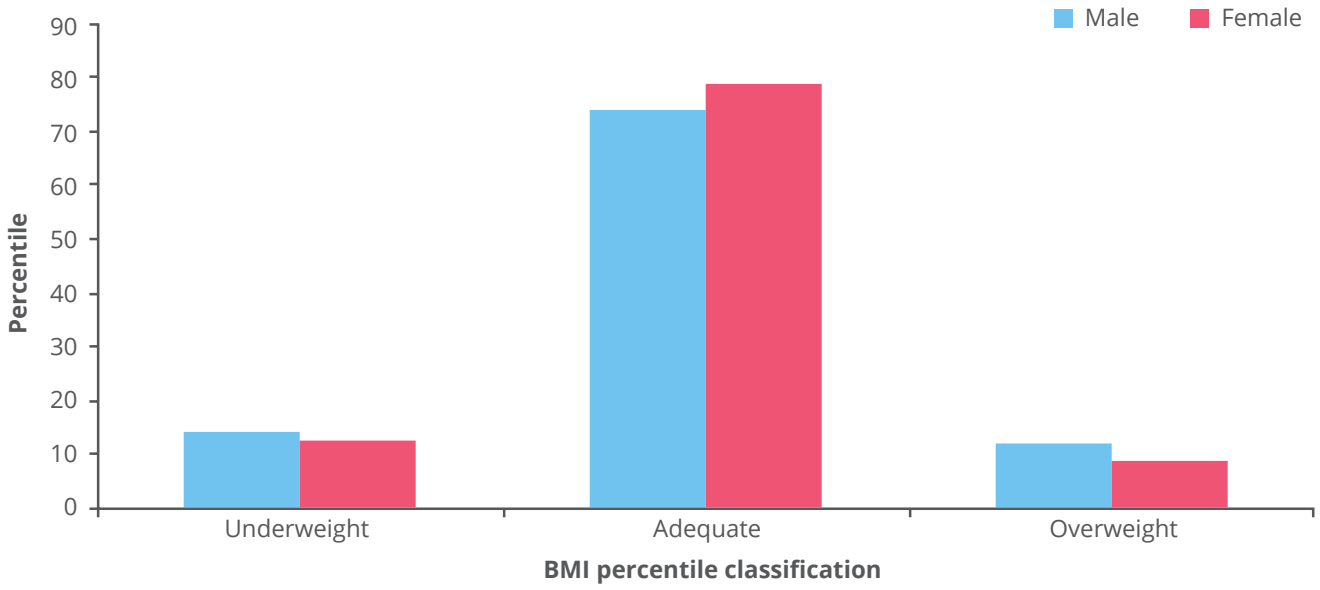
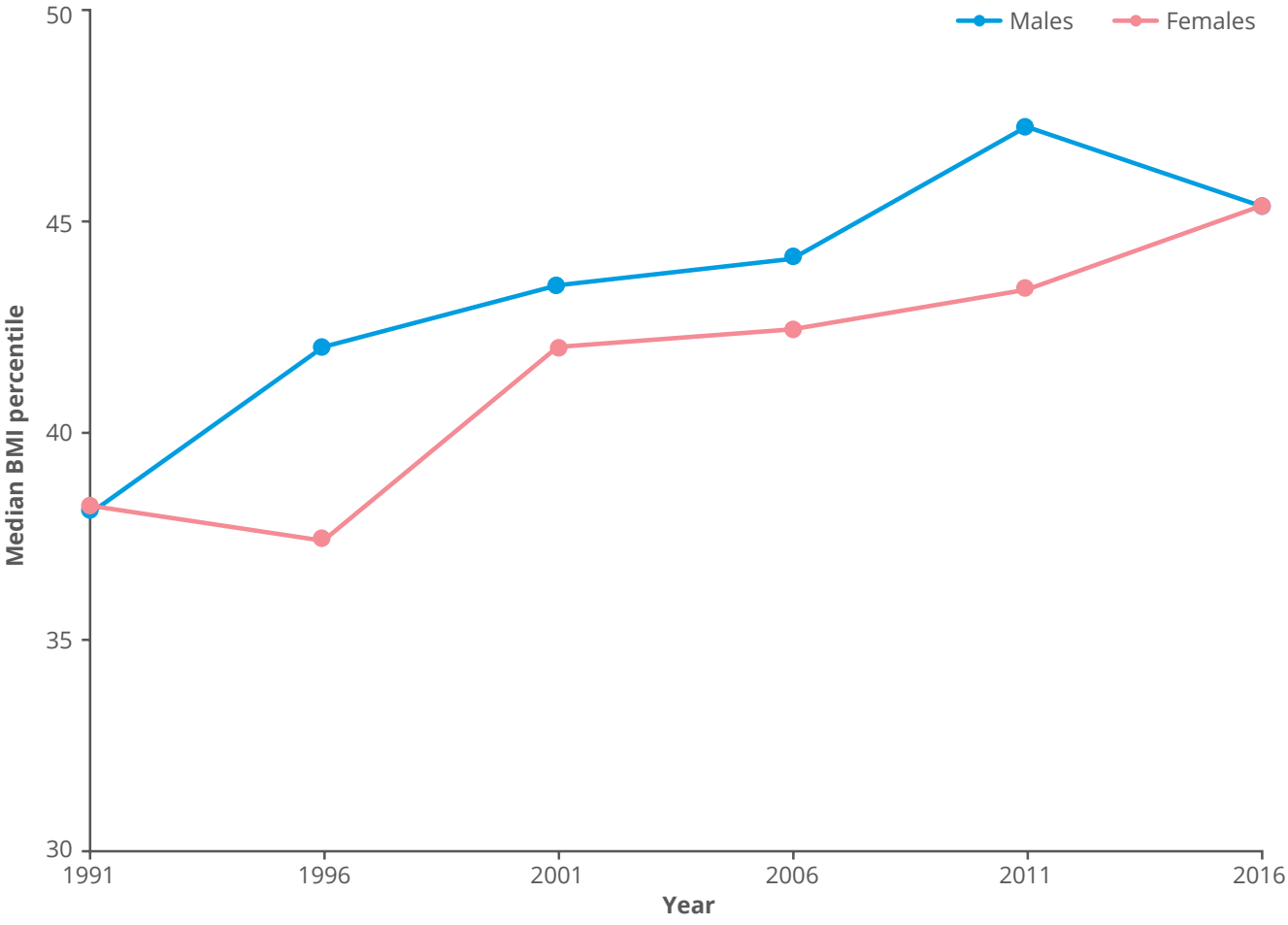


FIGURE 27
**Median BMI percentiles for children (2-17 years) with CF, by sex, 1991 to 2016**



# NUTRITION
## BODY MASS INDEX (BMI)

Body mass index (BMI) is a measure of a person's nutritional status and is based on their 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.

Table 5 below describes the BMI classifications and their BMI ranges which have been updated to follow the WHO guidelines[6]. As such, the proportions of BMI classifications will be different from those described in previous reports. In 2016, the national median BMI for adults (≥ 18 years) was 22.4 kg/m$^2$. The majority (66.0%) of the adult CF population had a normal weight while 9.2% were considered underweight and 5.7% were considered obese (Figure 28).

**FIGURE 28**
**BMI status for adults with CF, 2016**

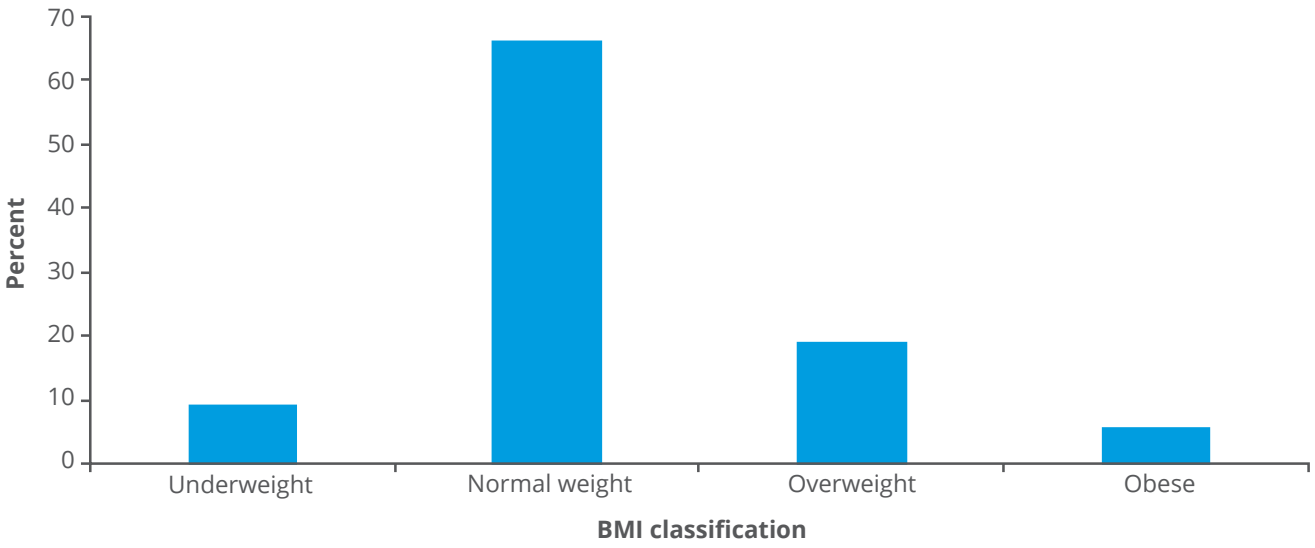



**TABLE 5**
**BMI classification**

| CLASSIFICATION | RANGE |
|---|---|
| Underweight | < 18.5 kg/m$^2$ |
| Normal weight | 18.5 - 24.9 kg/m$^2$ |
| Overweight | 25 - 29.9 kg/m$^2$ |
| Obese | ≥ 30 kg/m$^2$ |

# NUTRITION
## BMI BY SEX

Figure 29 shows the breakdown of BMI categories for adult males and females. Individuals who are muscular may have a higher BMI due to increased weight from larger amounts of muscle mass.

In 2016, while more females (12.8%) were considered underweight compared to males (6.3%), the median BMI over the past 25 years has been steadily rising within the CF adult population for both sexes (Figure 30) and can be attributed to fewer individuals who are underweight and more adults classified as either overweight or obese (Figures 31 and 32).

**FIGURE 29**
**BMI status for adults with CF, by sex, 2016**

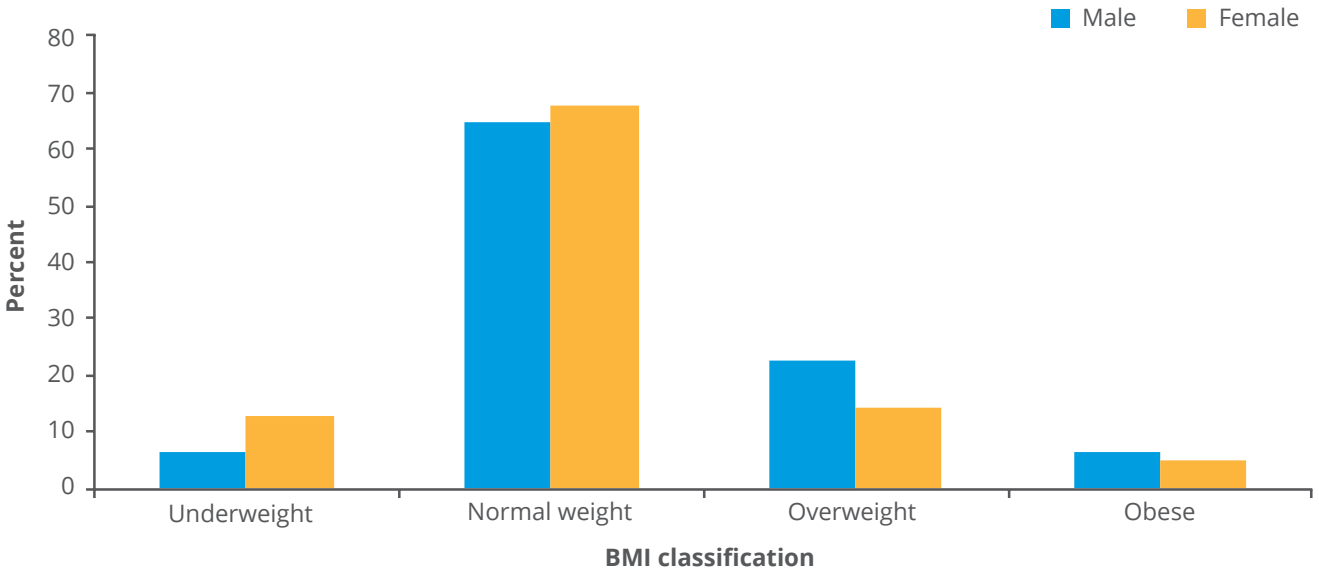



**FIGURE 30**
**Median BMI values for adults with CF, by sex, 1991 to 2016**

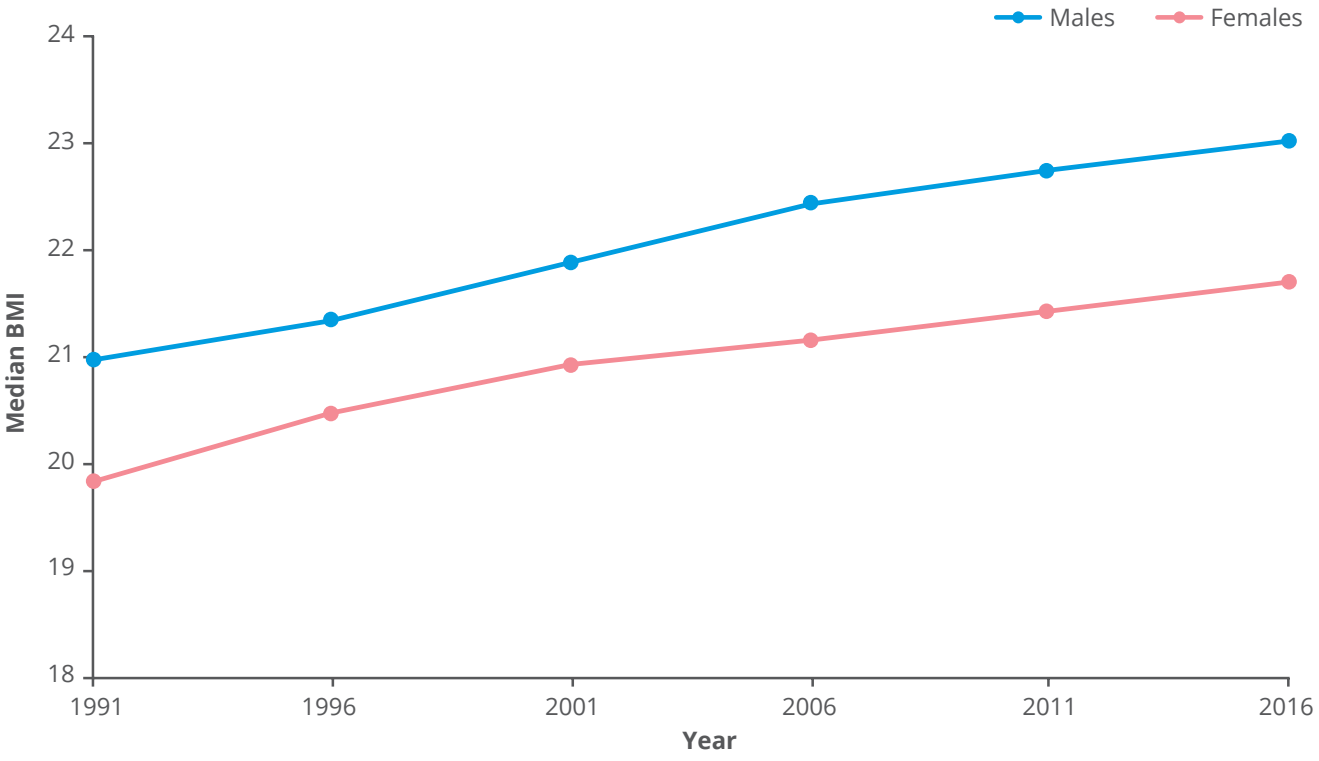


FIGURE 31
**Percentage of male adults with CF, by BMI status, 1991 to 2016**

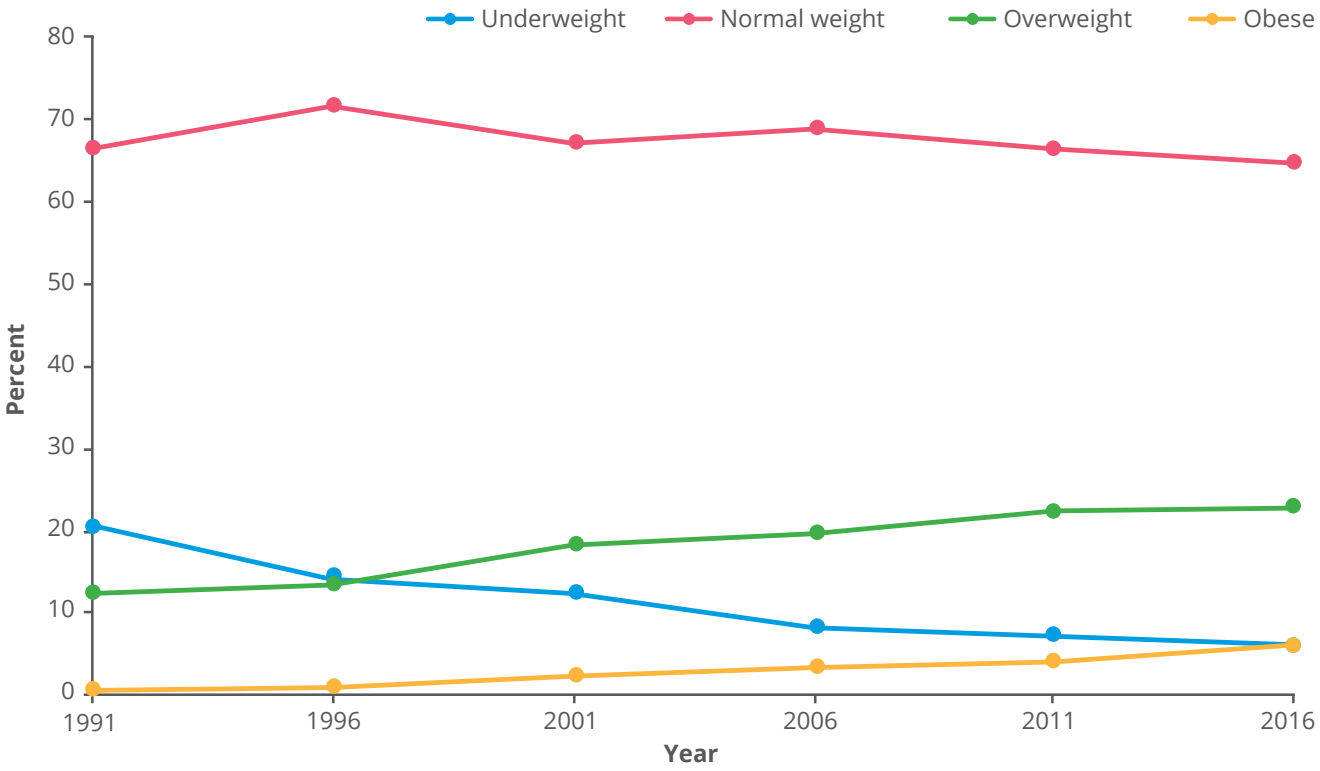
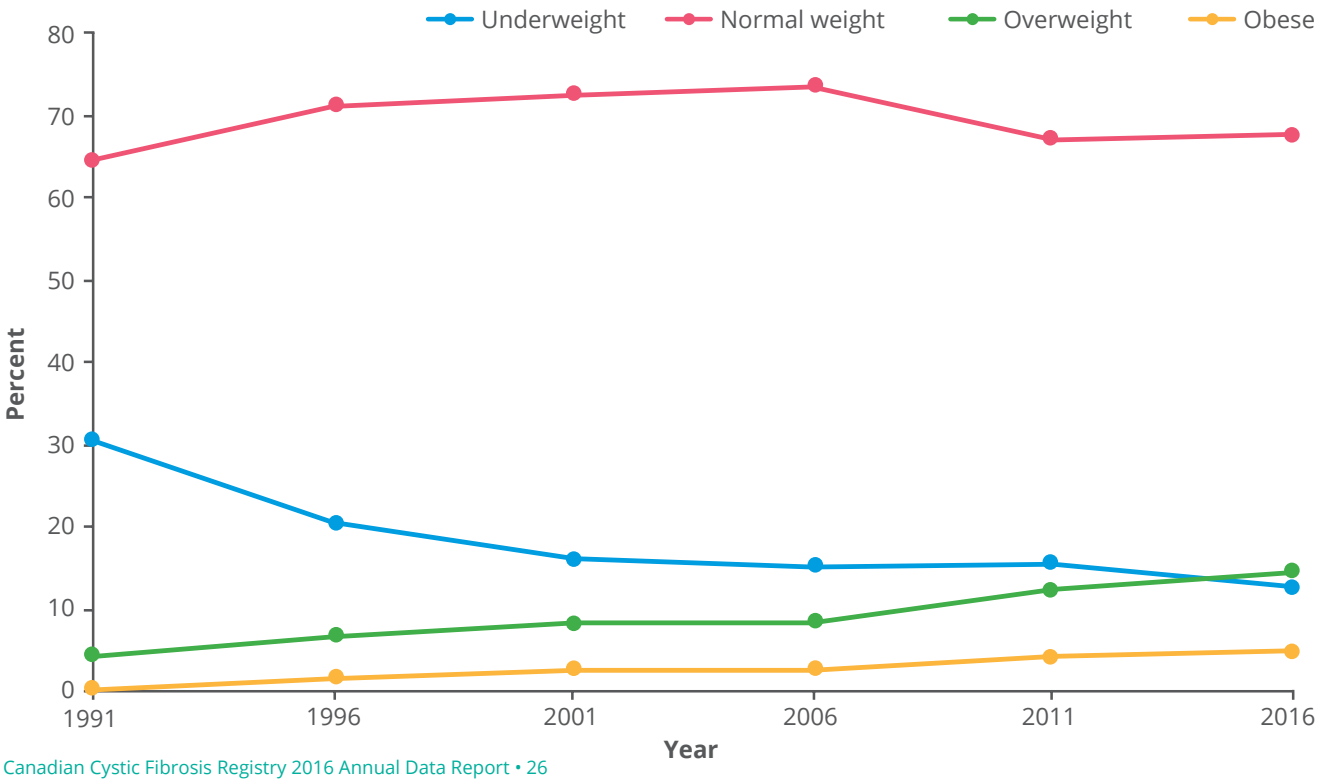



FIGURE 32
**Percentage of female adults with CF, by BMI status, 1991 to 2016**



# MICROBIOLOGY
## BACTERIAL SPECIES AND RESPIRATORY INFECTIONS

*Staphylococcus aureus* (53.4%) and *Pseudomonas aeruginosa* (37.0%) are the most common pulmonary pathogens in Canadians with CF (Figure 33). The CCFR aims to track relevant bacterial species for the CF population and several have been added in recent years including MSRA (2003), *Alcaligenes* (*achromobacter*) species (2011) and Atypical *mycobacteria* (2011).

**FIGURE 33**
**Prevalence of bacterial species cultured from airways of individuals with CF (all ages), 2016**

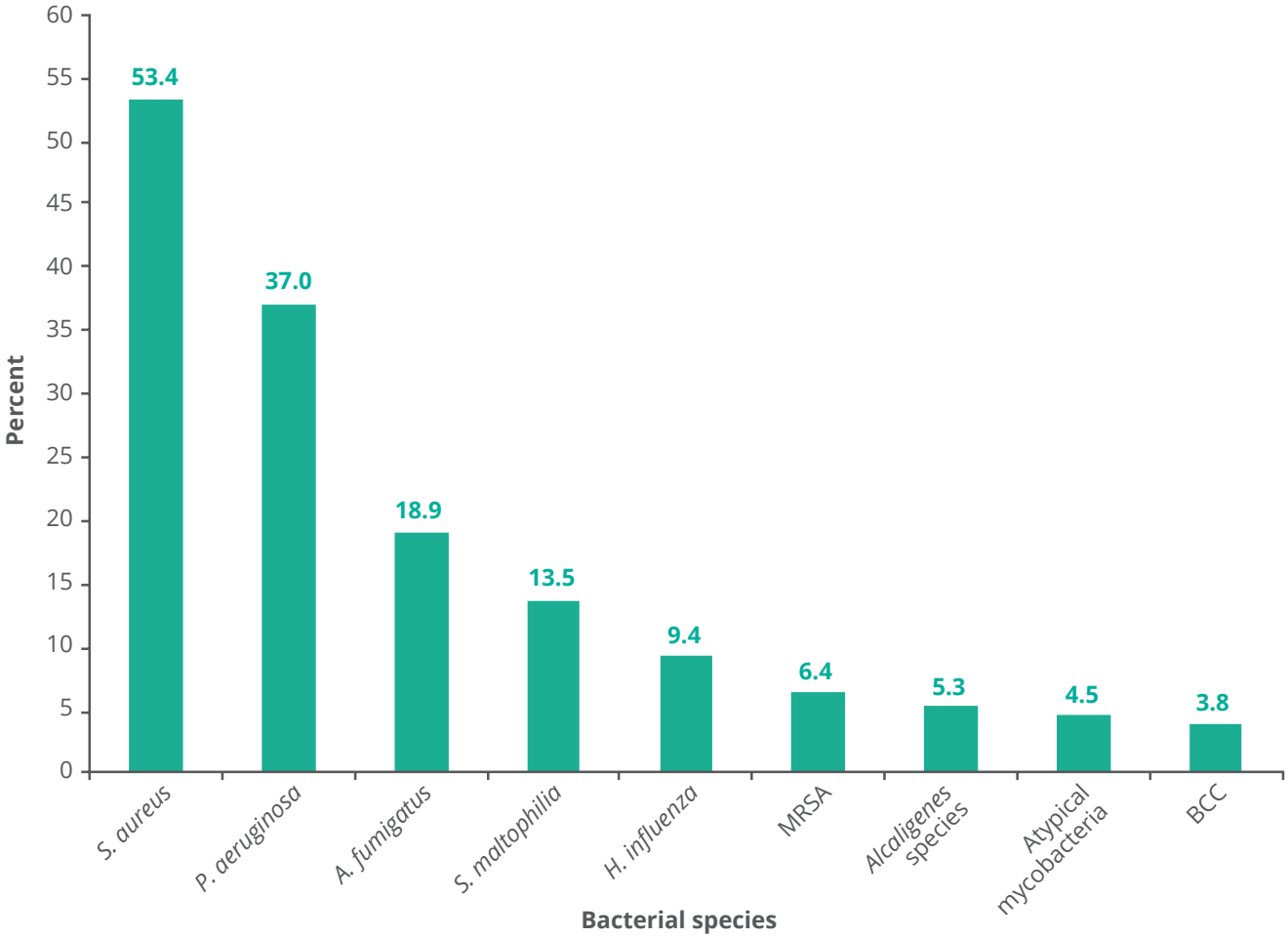


Figure 34 shows that over the past several years, there has been a minor decline in prevalence for some of the more common pulmonary pathogens but a minor increase in the less frequently found pathogens such as *Alcaligenes* species and Atypical mycobacteria. When examining the prevalence of pathogens by age (Figure 35), it appears that *Staphyloccocus aureus* is more common in CF children and *Pseudomonas aeruginosa* is more common in the adult CF population. *Burkholderia cepacia* complex (BCC) is more commonly seen in older individuals with CF but the prevalence is low for the entire CF population (3.8%). 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 BCC are aging, making the prevalence of this organism higher in older individuals.

**FIGURE 34**
**Prevalence of respiratory infections of individuals with CF, 2012 to 2016**

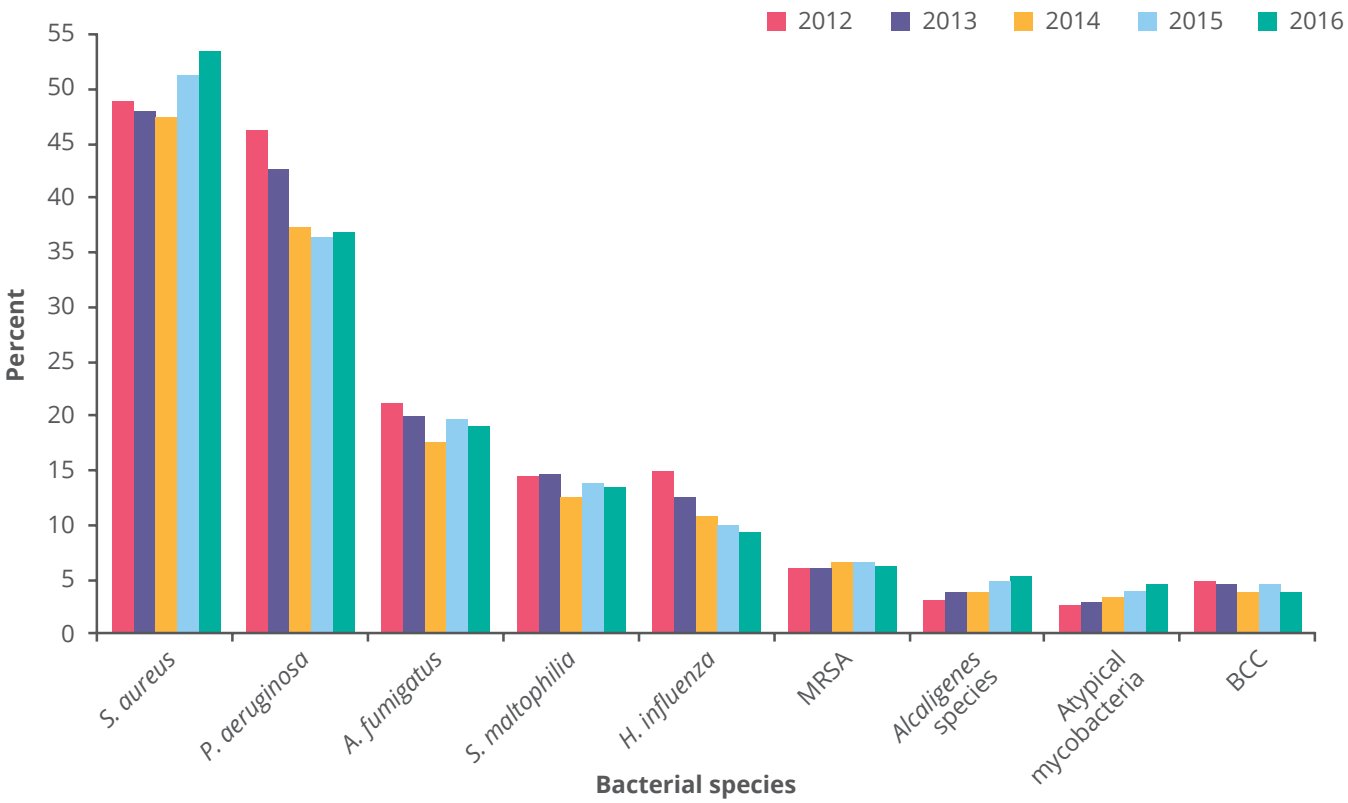
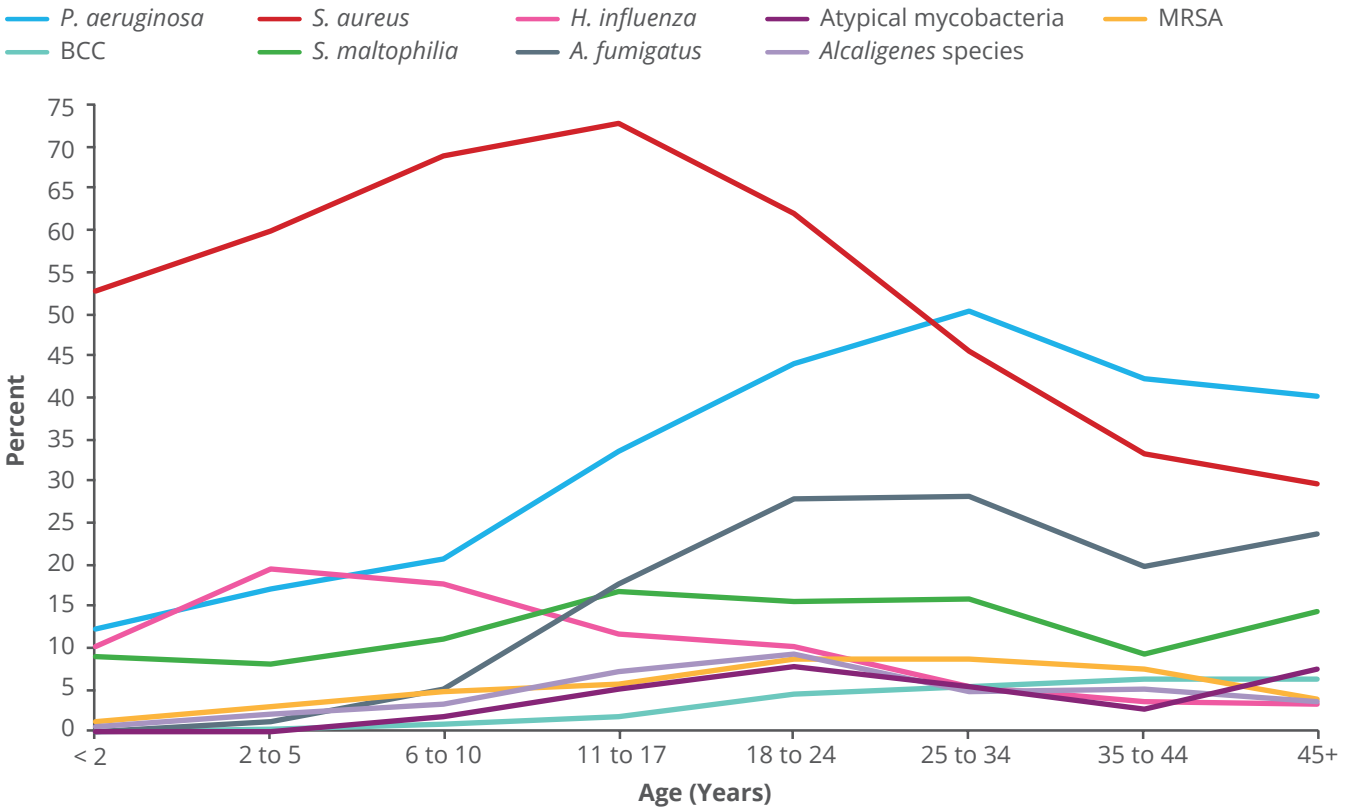


**FIGURE 35**
**Age-specific prevalence of respiratory infections in individuals with CF, 2016**



# MICROBIOLOGY
## *BURKHOLDERIA CEPACIA* COMPLEX (BCC)

In 2016, there were 160 (3.8%) unique individuals with CF who grew at least one *Burkholderia cepacia* complex (BCC) species. *B. cenocepacia* (38.6%) and *B. multivorans* (26.9%) were the two most common types of BCC species (Figure 36). Of the unique individuals who had BCC in 2016, 142 (88.8%) were adults and 45 (28.1%) adults were over the age of 40 (Figure 37). Not all BCC bacteria have been speciated as 12.2% of the BCC species in the CCFR were classified as unknown. Although BCC has been reported on for decades, the ability to specify the type of BCC species was added to the CCFR in 2011.

Note: The prevalence of *B. gladioli* was 10.2%, though it was not included in Figure 36 because it is not officially recognized as part of the BCC.

**FIGURE 36**
***Burkholderia cepacia* complex species prevalence in individuals with CF, 2016**

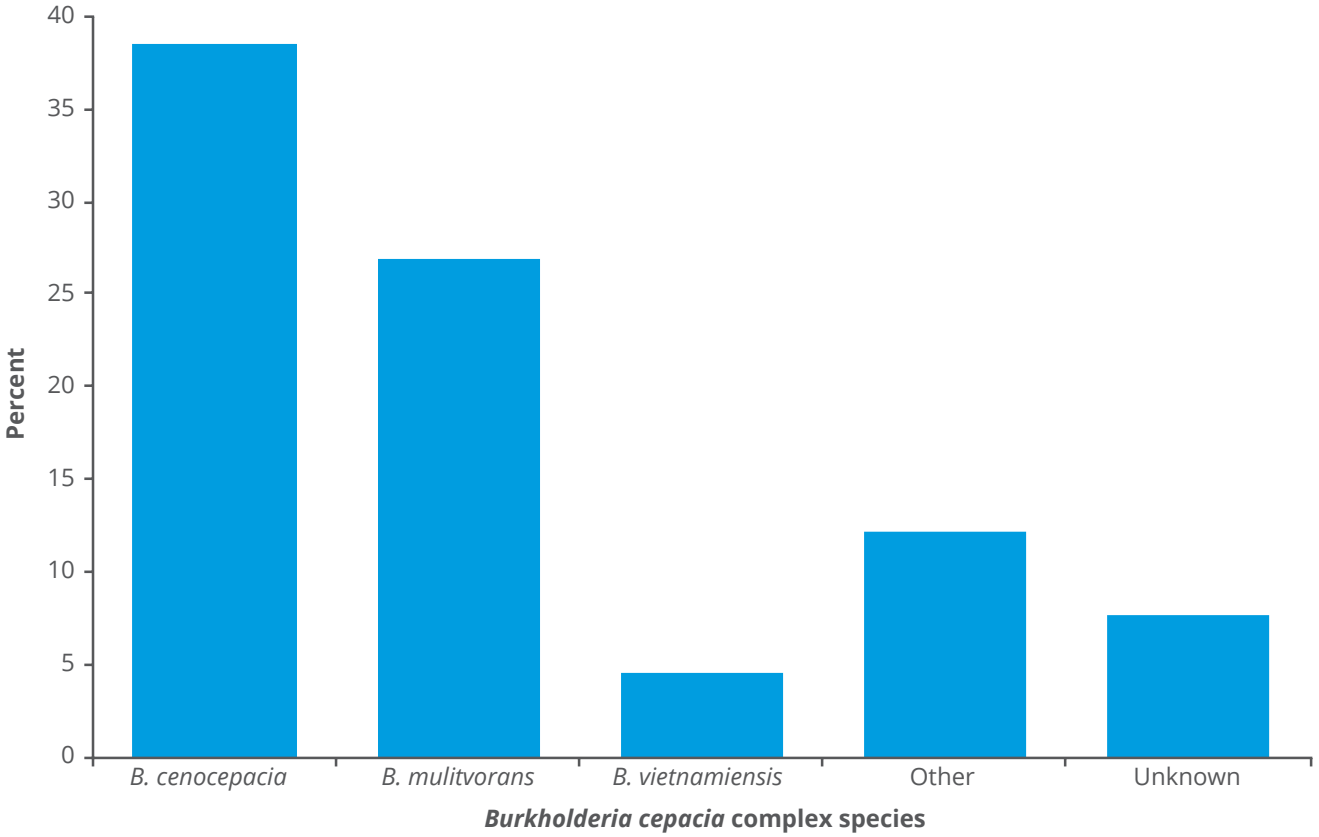
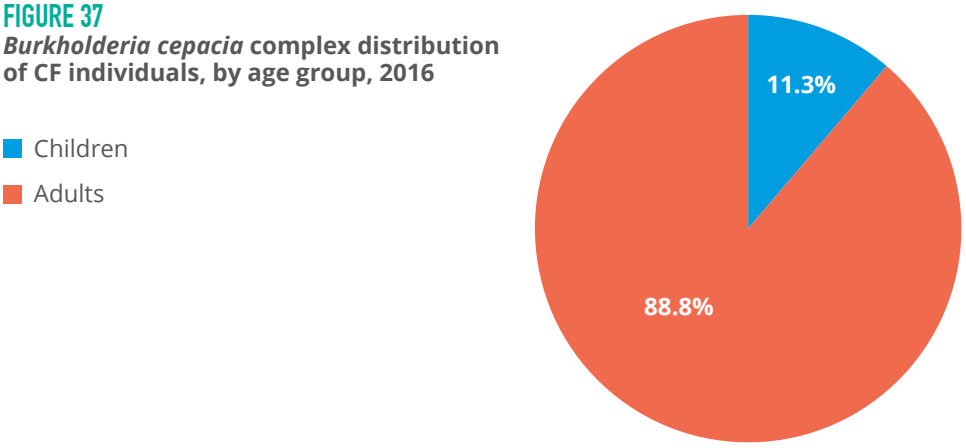


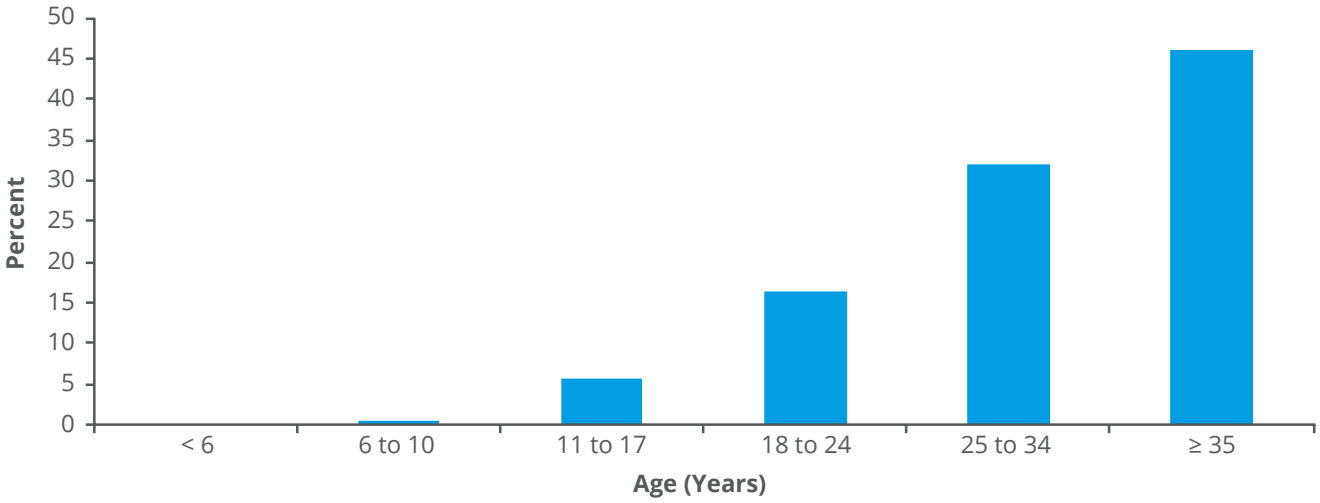

**FIGURE 37**
***Burkholderia cepacia* complex distribution of CF individuals, by age group, 2016**



# CF-RELATED DIABETES (CFRD)

Figure 38 shows the increasing prevalance of CFRD with age with no children under 6 years of age reported as having CFRD. In 2016, CFRD was reported in 966 (22.8%) individuals with CF and of those, 0.4% were under 11 years of age, 49.8% were female, 22.4% have received a transplant, and 46.1% were 35 years of age or older. Overall, 35.2% of all Canadian CF adults have CFRD.

**FIGURE 38**
**Percentage of CF individuals with CFRD by age (N = 966), 2016**

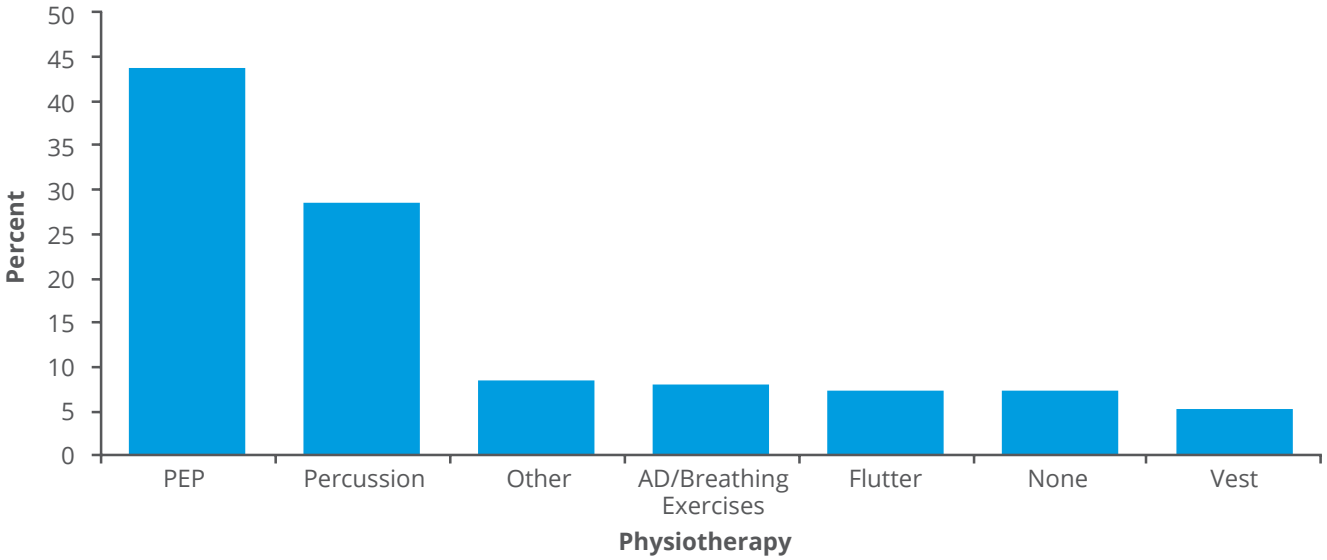



# PHYSIOTHERAPY

Physiotherapy is done to help clear mucous from airways using a variety of methods. Figure 39 shows the multiple forms of physiotherapy that are tracked in the CCFR. The most commonly used form of therapy are positive expiratory pressure (PEP) (43.7%) and percussion (28.4%) while 7.4% were reported as not doing any form of physiotherapy.

Note: Individuals who have ever received a lung transplant (7.1% of the 2016 reported CF population) were excluded from these calculations because, typically, chest phyisotherapy is not part of routine post-transplant treatment.

**FIGURE 39**
**Physiotherapy usage of CF individuals (N = 3,946), 2016**



# MEDICATIONS

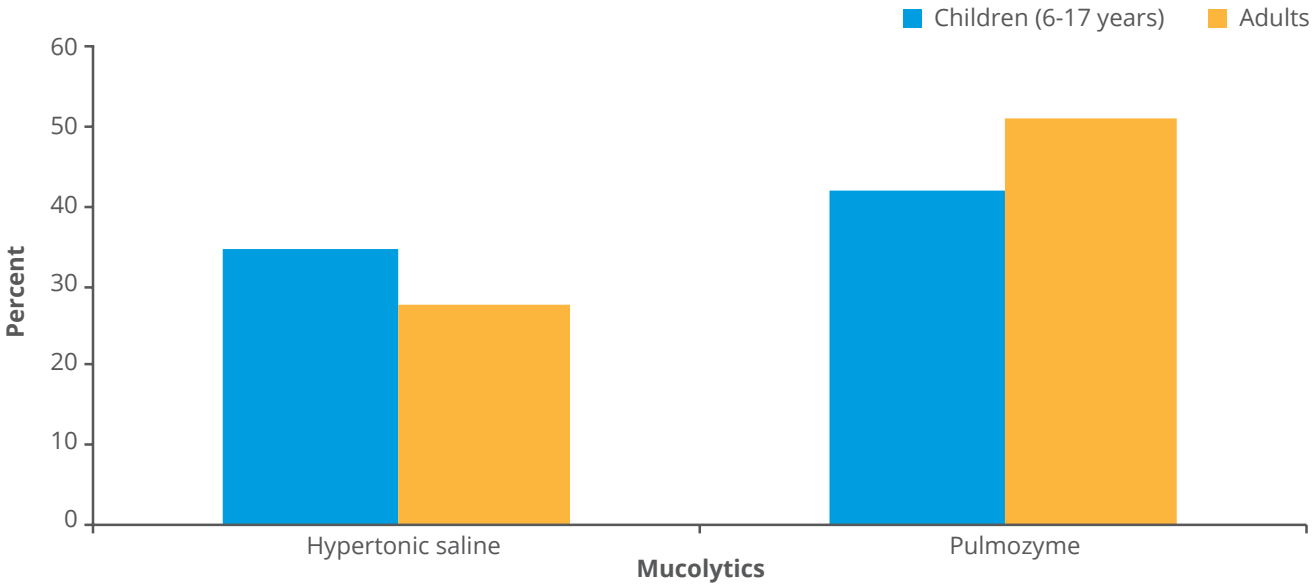
In 2016, there were a total of 3,475 individuals over the age of 6 years (1,150 children 6-17 years and 2,325 adults) who have never received a transplant. Figure 40 shows that of those individuals, 2,174 (62.6%) were prescribed mucolytic therapy during the calendar year (hypertonic saline and/or Pulmozyme®).

There were 1,418 individuals over the age of 6 years who have never received a transplant and were reported to have *Pseudomonas aeruginosa* in 2016 which include 325 children (6-17 years) and 1,093 adults. There were 240 children (6-17 years) (73.8%) and 886 adults (81.1%) who were prescribed inhaled antibiotic treatment, and 71 children (6-17 years) (21.8%) and 651 adults (59.6%) who were prescribed macrolide therapy (azithromycin) (Figure 41).

There were 41 children and 54 adults with a G551D mutation who are currently taking KALYDECO® (ivacaftor) in 2016.

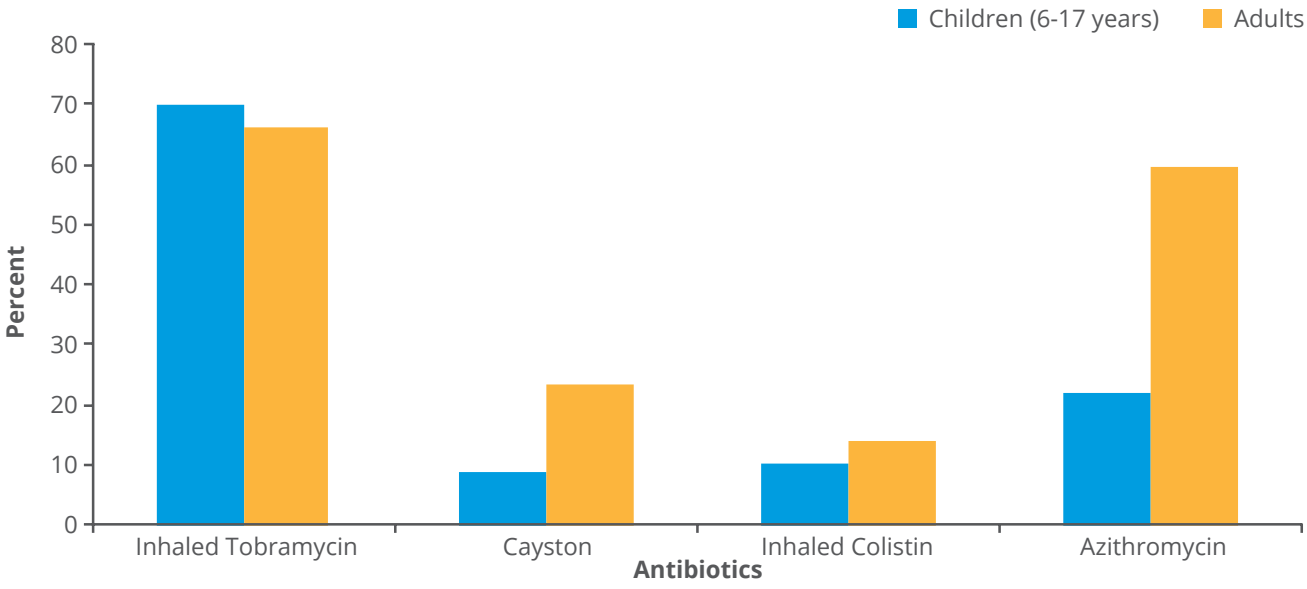
## FIGURE 40

**Percentage of CF individuals on mucolytics, by age group, 2016**




## FIGURE 41

**Percentage of CF individuals on antibiotics, by age group, 2016**



# HOSPITALIZATION AND HOME IV

In 2016, there were 2,191 hospitalizations recorded which added up to almost 29,000 days spent in hospital (Table 6) which do not include visits to the out-patient CF clinics. A total of 4,204 (99.0%) individuals with CF visited a CF clinic at least once with 3,288 (77.4%) having three or more clinic visits. Out of those reported with more than three clinic visits, 1,528 (91.7%) were children and 1,760 (68.2%) were adults. At home, individuals with CF had almost 1,100 courses of home IV therapy adding up to over 19,000 days on home IV antibiotics.

**TABLE 6**
**Total number of hospital days and home IV courses recorded for individuals with CF, 2016**

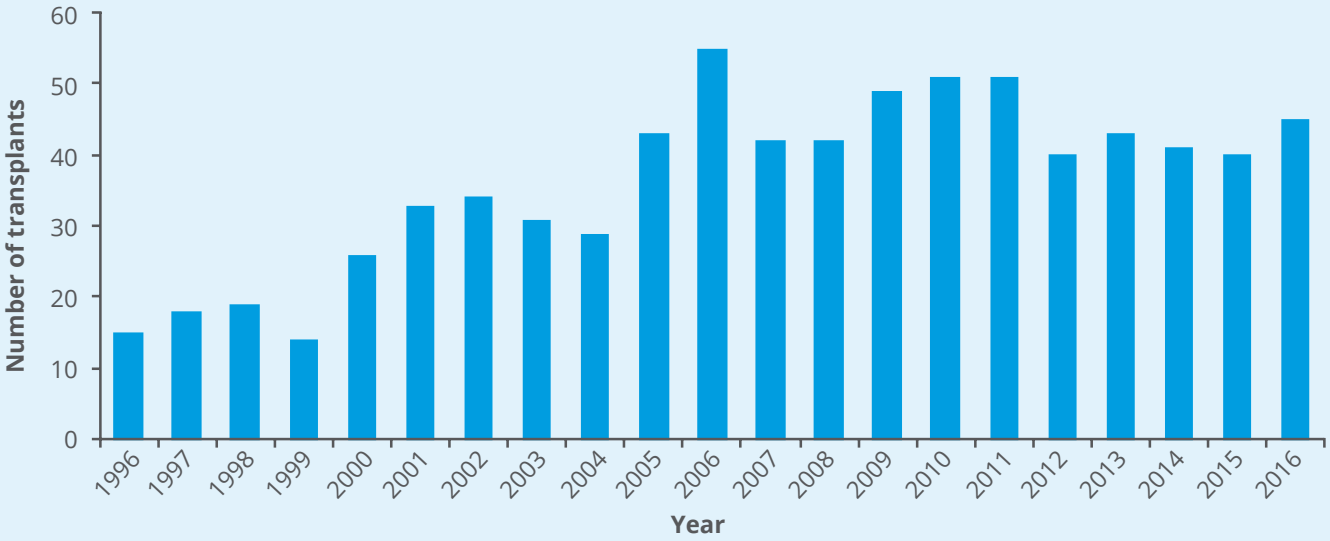
| | TOTAL NUMBER |
|---|---|
| Hospital Days | 28,963 |
| Hospitalizations | 2,191 |
| Clinic Visits | 19,326 |
| Home IV Courses | 1,098 |
| Home IV Days | 19,725 |

# TRANSPLANTS

Figure 42 shows the number of transplants carried out per year as reported in the CCFR. In 2016, 45 individuals with CF received a transplant having a median age of 31.2 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, 2016, there were 766 individuals with CF reported as having received one or more transplants with a median age of 28.6 years at the time of transplant and 43 (5.6%) have received at least two lung transplants, 453 (59.1%) were reported as being alive and 55.8% of them were male.

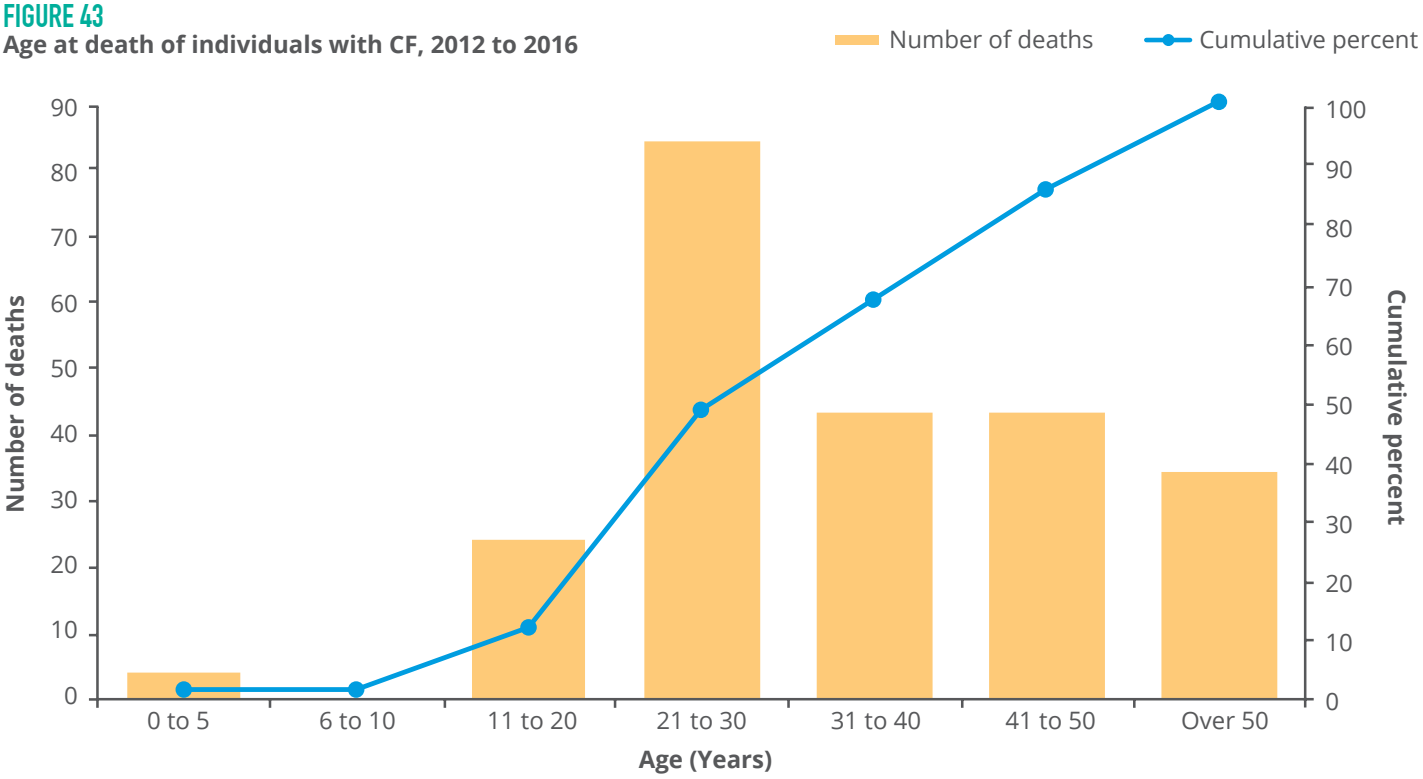
**FIGURE 42**
**Number of transplants per year of CF individuals, 1996 to 2016**



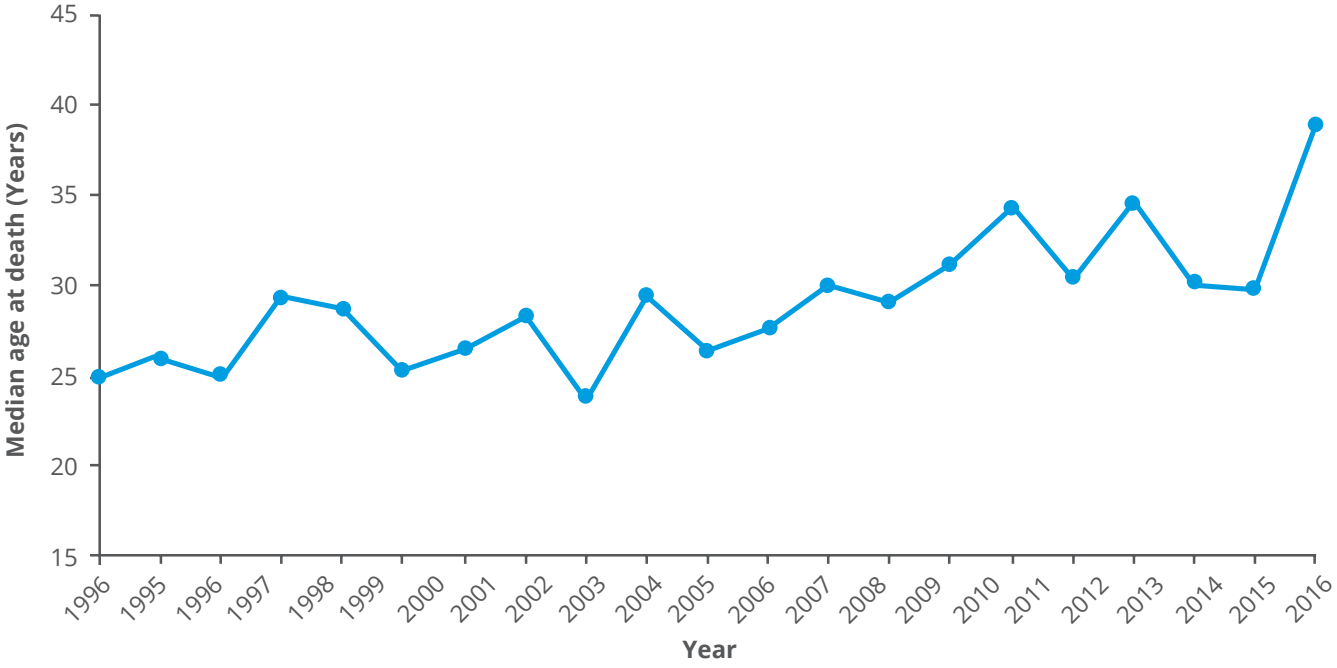
# SURVIVAL

There were 42 deaths recorded in the CCFR in 2016. Figure 43 shows the cumulative number of deaths and the age range from 2012 to 2016. Over the past two decades, a gradual increase in the median age of death can be seen. The median age of death was 38.9 years in 2016 compared to 25.0 years in 1996 (Figure 44). This number tells us that half of those who died were younger than 38.9 years of age and the other half who died were older. Large fluctuations in the median age of death can be seen each year because there are relatively few deaths in a given year. However, the annual death rate (calculated as the number of deaths divided by the total number of individuals reported in the year) has been steadily decreasing since 1996 (Figure 45). In 2016, the death rate was 0.99% marking the first time it has fallen below 1%. The most common cause of death was related to pulmonary complications and 20 (47.6%) individuals with CF who passed away in 2016 were post-transplant.

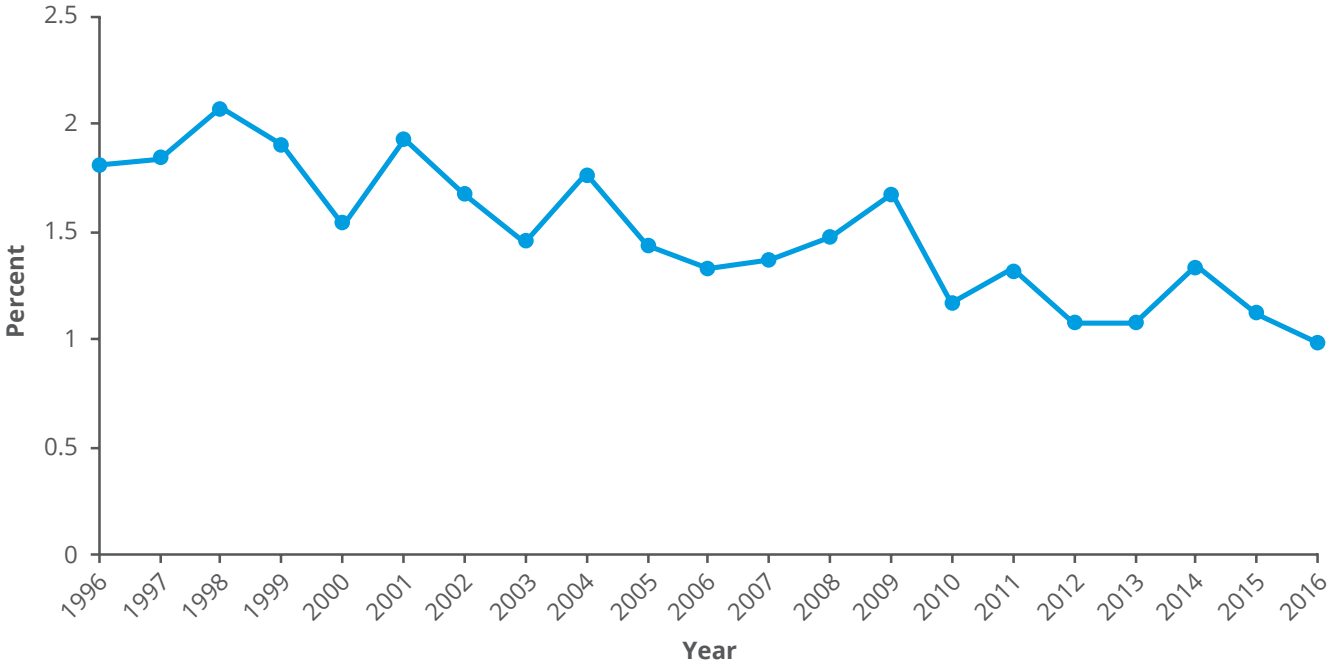
**FIGURE 43**
**Age at death of individuals with CF, 2012 to 2016**



## FIGURE 44
**Median age at death of CF individuals per year, 1996 to 2016**




## FIGURE 45
**Death rate of CF individuals per year, 1996 to 2016**



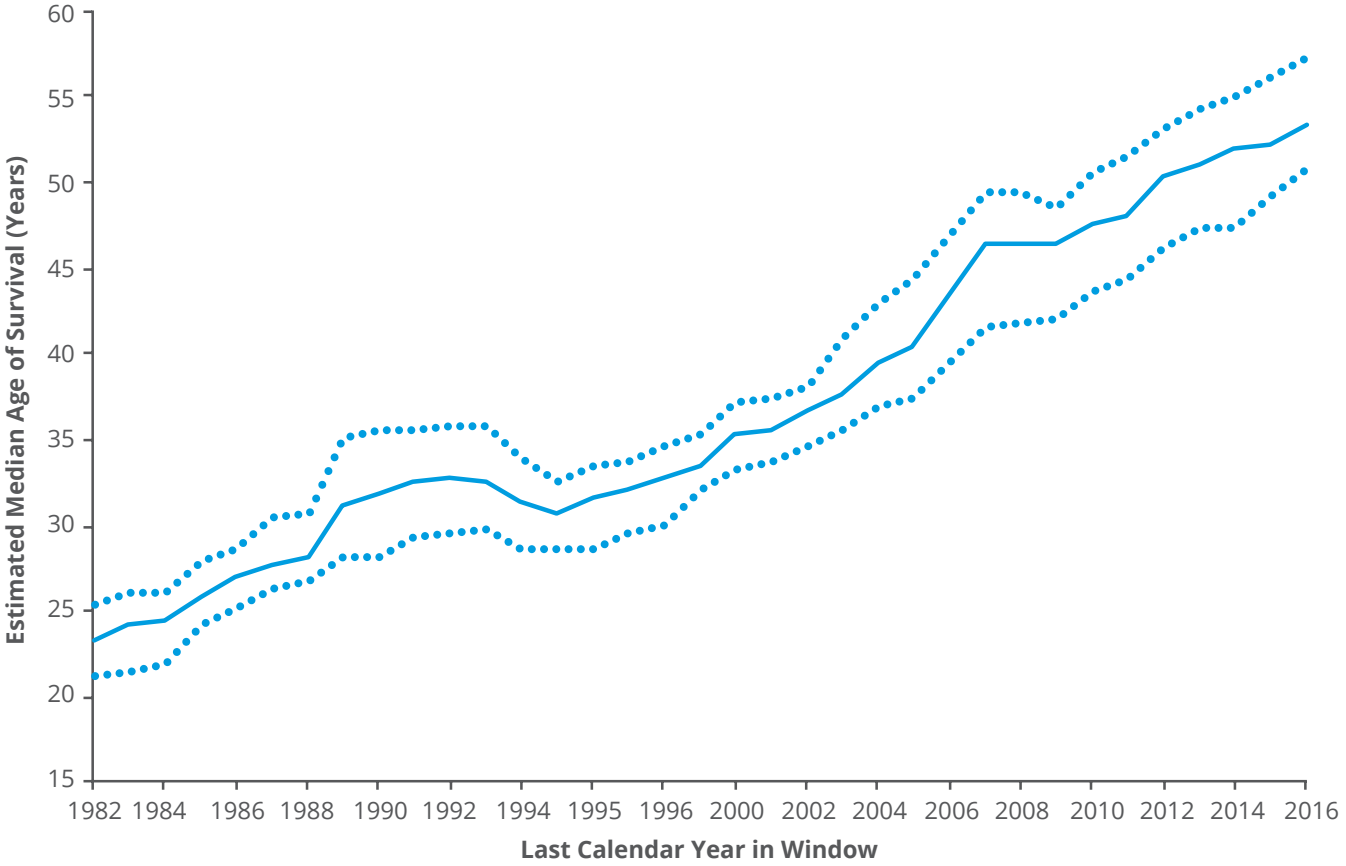
# SURVIVAL
## ESTIMATED MEDIAN AGE OF SURVIVAL

A 5-year rolling window was used to calculate the median age of survival to stabilize the estimates over time using the Cox proportional hazards model. The most recent 5-year window (2012-2016) included 4,877 people with CF and 232 deaths. The number of individuals with CF lost-to-follow-up was 213 (4.3%).

In 2016, the median age of survival is currently estimated to be **53.3 years of age** (Figure 46). In 2012, the estimated median age of survival passed 50 years of age for the first time and it has remained steady since. The median age of survival is the estimated age to which 50% of the CF population would be expected to survive assuming that current treatments, therapies and mortality rates remain constant. Transplanted individuals are included in the survival analysis because transplant is considered a form of therapy for end-stage CF. Excluding deaths post-transplant would overestimate the median age of survival[7].

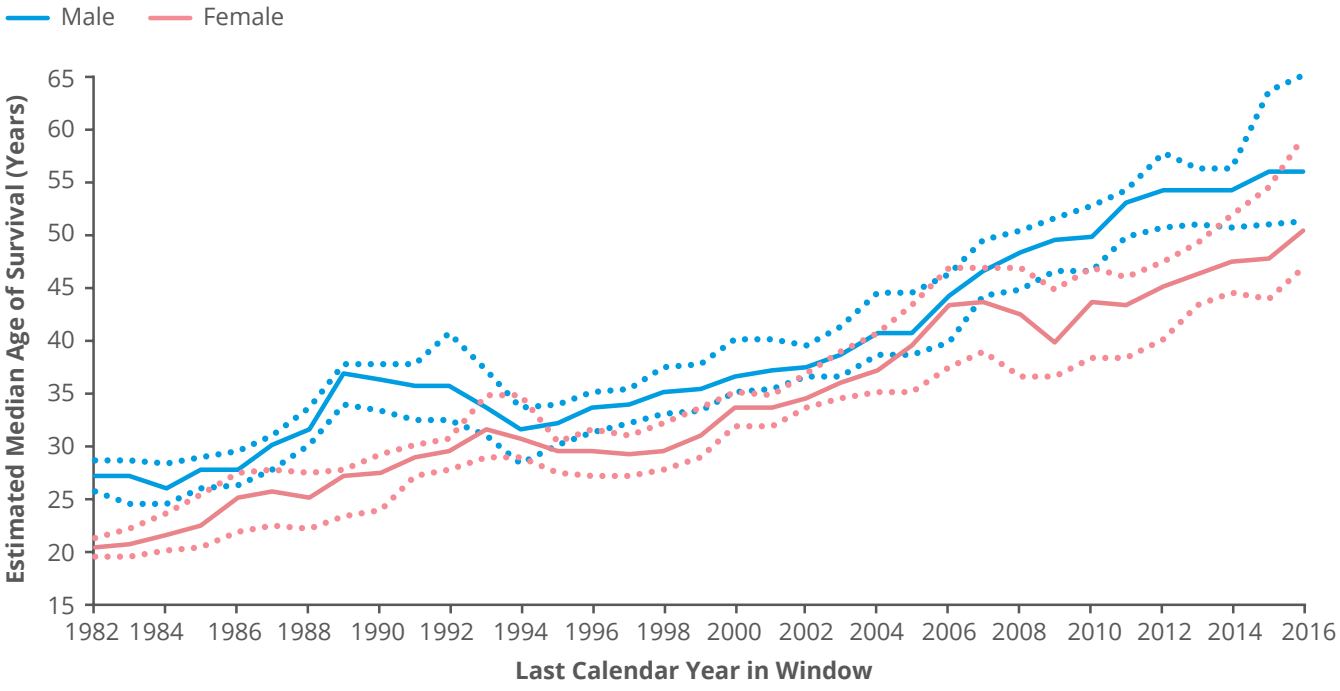
Males continue to have a higher median age of survival compared to females however, the female cohort surpassed 50 years of age for the first time (Figure 47). While the cause of lower survival in females is not well understood, it has been documented in published CF literature. Survival by birth cohort is presented in Figure 48 and indicates that survival is higher for those born more recently. The probability of surviving beyond age 20 years is 62.1% for those born before 1975 compared to 91.6% for those born in 1985 and later.

**FIGURE 46**
**Estimated median age of survival of CF individuals (moving 5 year window with 95% confidence intervals), 1982 to 2016**



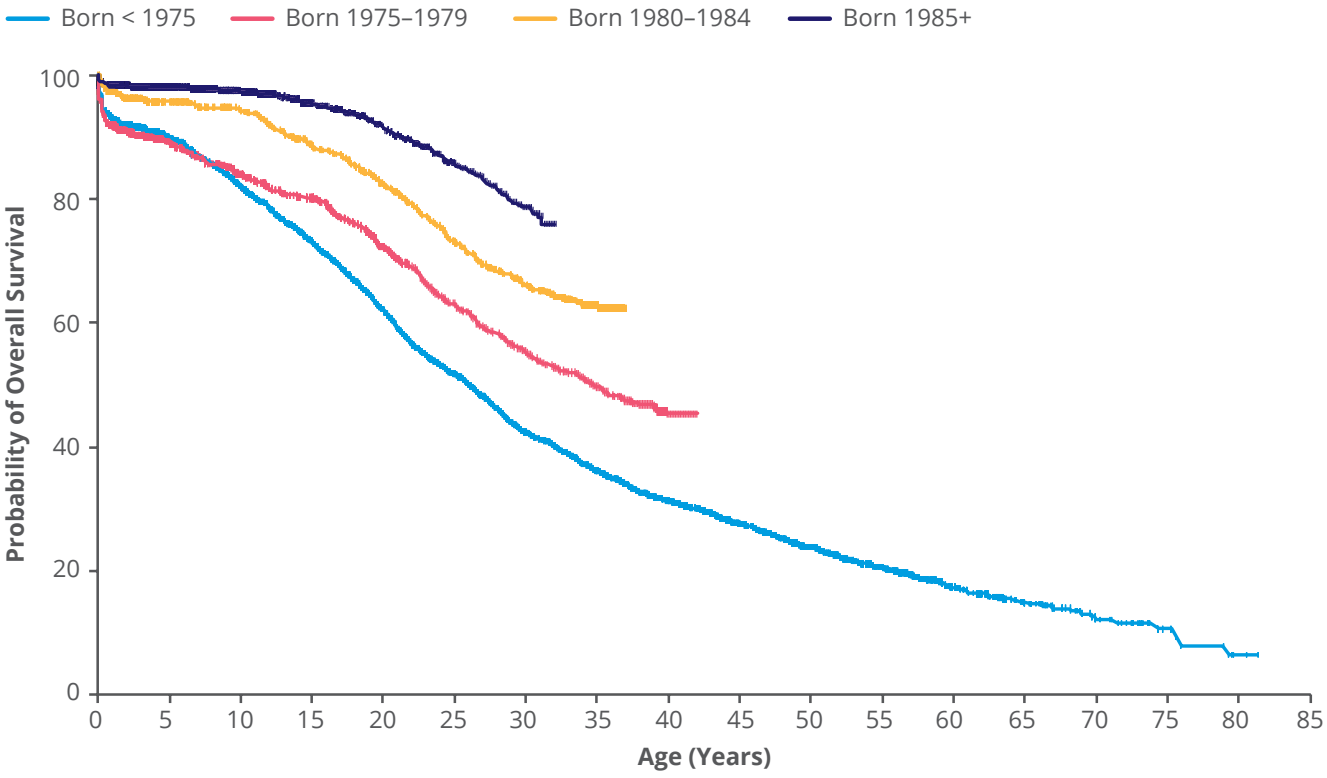
## FIGURE 47

**Estimated median age of survival of CF individuals (moving 5 year window with 95% confidence intervals), by sex, 1982 to 2016**




## FIGURE 48

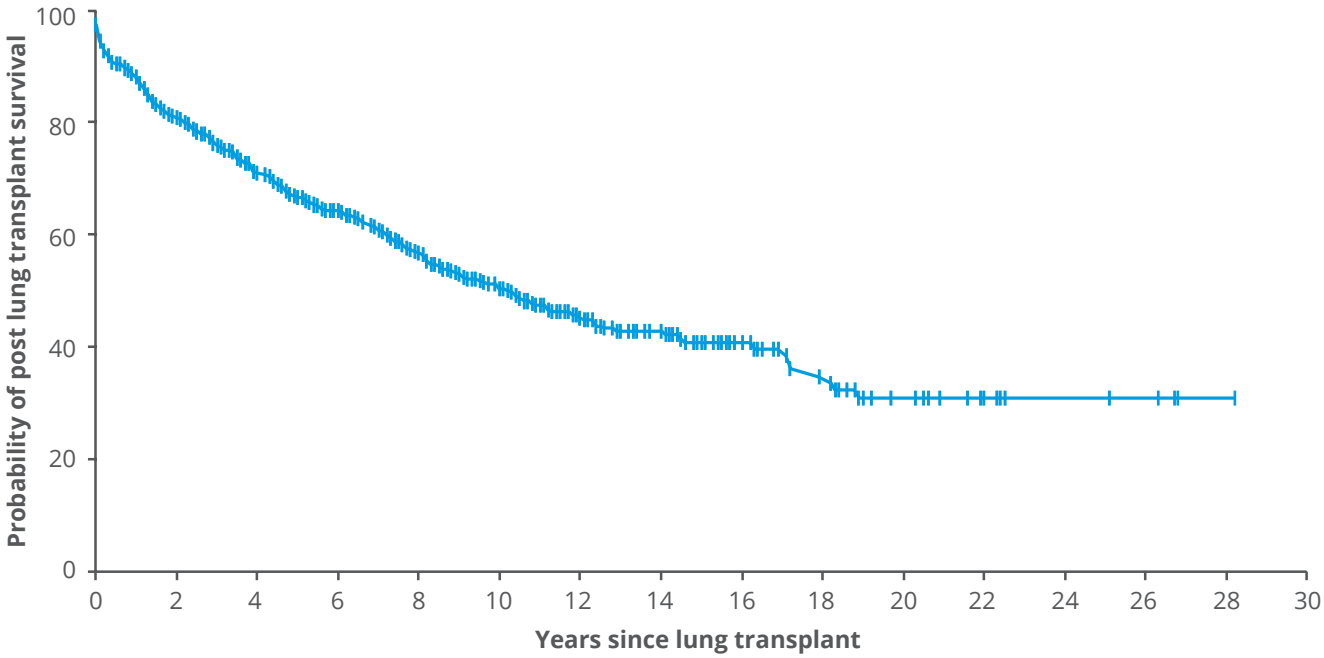
**Overall survival of individuals with CF, by birth cohort, 2016**



# SURVIVAL
## POST LUNG TRANSPLANT SURVIVAL

Between 1988 and 2016, there were 694 lung transplants that took place and 302 deaths post lung transplant. Figure 49 shows the probability of survival post lung transplant which is 88.0% at one year, 75.8% at three years and 66.7% at five years. Overall, the median post lung transplant survival is 10.2 years which means that 50% of patients lived beyond 10 years following transplantation.

**FIGURE 49**
**Post lung transplant survival of individuals with CF, 2016**



# 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 the World Health Organization[8]. 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. Life expectancy is not the same as median age of survival.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.

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 whfo 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* above). 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 survival in 2016 is 53.3 years, we are saying that if a child with CF is born in Canada in 2016, they have a 50% chance of living beyond 53.3 years of age based on current mortality rates. In other words, half of the CF population would be expected live to an age older than 53.3 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 in 2016.

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

# REFERENCES


1. Quittner, A. L. *et al.* Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers: results of The International Depression Epidemiological Study across nine countries. *Thorax* **69**, 1090–1097 (2014).

2. Quittner, A. L. *et al.* International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety. *Thorax* **0**, 1–9 (2015).

3. Stanojevic, S. *et al.* Reference ranges for spirometry across all ages: a new approach. *Am. J. Respir. Crit. Care Med.* **177**, 253–60 (2008).

4. Grummer-Strawn, L. M., Reinold, C. & Krebs, N. F. Use of World Health Organization and CDC growth charts for children aged 0-59 months in the United States. *MMWR. Recomm. reports* **59**, 1–15 (2010).

5. Cole, T. J., Bellizzi, M. C., Flegal, K. M. & Dietz, W. H. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* **320**, (2000).

6. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Heal. Organ. - Tech. Rep. Ser.* **894**, i–xii, 1-253 (2000).

7. Sykes, J. *et al.* A standardized approach to estimating survival statistics for population-based cystic fibrosis registry cohorts. *J. Clin. Epidemiol.* **70**, 206–13 (2016).

8. World Health Organization. World Health Statistics: Life expectancy, Data by country. (2016). Available at: http://apps.who.int/gho/data/node.main.SDG2016LEX?lang=en. (Accessed: 1st September 2016)

# ACKNOWLEDGMENTS

Thank you to the following groups and people who made outstanding contributions to the *Canadian Cystic Fibrosis Registry* and this 2016 Registry Annual Report.

**Dr. Anne Stephenson**, Medical Director, Registry, Cystic Fibrosis Canada and CF Physician, St. Michael's Hospital, Toronto

**Dr. Denise Mak**, Director, Data & Analytics, Registry, Cystic Fibrosis Canada

**Ali Mahmood**, Data Analyst, Registry, Cystic Fibrosis Canada

**Jenna Sykes**, Research Biostatistician, St. Michael's Hospital, Toronto

**Dr. Sanja Stanojevic**, Biostatistician, The Hospital for Sick Children, Toronto

## CANADIAN CF REGISTRY REVIEW PANEL

**Dr. Mark Chilvers** (BC Children's Hospital, Vancouver)

**Dr. Larry Lands** (Montreal Children's Hospital, Montreal)

**Dr. Nancy Porhownik** (Winnipeg Health Sciences Centre, Winnipeg)

**Dr. Bradley Quon** (St. Paul's Hospital, Vancouver)

**Dr. Anne Stephenson** (Cystic Fibrosis Canada and St. Michael's Hospital, Toronto)

**Dr. Lisa Strug** (The Hospital for Sick Children, Toronto)

**Dr. Ian Waters** (Royal Jubilee Hospital, Victoria)

## CANADIAN CF CLINICS

| | |
|---|---|
| Victoria General Hospital, Victoria | St. Michael's Hospital, Toronto |
| Royal Jubilee Hospital, Victoria | Kingston Health Sciences Centre, Kingston |
| BC Children's Hospital, Vancouver | Children's Hospital of Eastern Ontario, Ottawa |
| St. Paul's Hospital, Vancouver | Ottawa General Hospital, Ottawa |
| Alberta Children's Hospital, Calgary | *Centre de santé et de services sociaux de Gatineau, Hull* |
| Foothills Hospital, Calgary | Montreal Children's Hospital, Montreal |
| University of Alberta Hospitals, Edmonton | Montreal Chest Institute, Montreal |
| Royal University Hospital, Saskatoon | *Hôpital Ste-Justine, Montréal* |
| Regina General Hospital, Regina | *Hôtel-Dieu de Montréal, Montréal* |
| Winnipeg Children's Hospital, Winnipeg | *Centre Universitaire de Santé de l'Estrie, Sherbrooke* |
| Health Sciences Centre, Winnipeg | *Centre hospitalier de l'Université Laval, Québec* |
| Health Sciences North/*Horizon Santé-Nord*, Sudbury | *Institut universitaire de cardiologie et de pneumologie de Québec, Québec* |
| Windsor Regional Hospital, Windsor | *Hôpital de Chicoutimi, Chicoutimi* |
| London Health Sciences Centre, London | *Centre hospitalier régional de Rimouski, Rimouski* |
| Children's Hospital, London Health Sciences Centre, London | *Centre de santé et des services sociaux de Rouyn-Noranda, Rouyn-Noranda* |
| Grand River Hospital, Kitchener | IWK Health Centre, Halifax |
| St. Mary's Hospital, Kitchener | QEII Health Sciences Centre, Halifax |
| Hamilton Health Sciences Corporation, Hamilton | Saint John Regional Hospital, Saint John |
| McMaster Children's Hospital, Hamilton | Janeway Children's Health Centre, St. John's |
| The Hospital for Sick Children, Toronto | Health Sciences Centre, St. John's |

**Funding for the design and distribution of this report was generously supported by an unrestricted grant from Merck Canada, manufacturer of COTAZYM®**


This report was managed and created exclusively by Cystic Fibrosis Canada.
No external groups or organizations had any contribution or influence into the content of this report.


**www.cysticfibrosis.ca**

2323 Yonge Street, Suite 800 | Toronto, ON M4P 2C9
2017-11 | Cette publication est aussi disponible en français
Charitable registration: 10684 5100 RR0001