THE CANADIAN **CYSTIC FIBROSIS REGISTRY**

2017 ANNUAL DATA REPORT

Cystic Fibrosis Canada™

CYSTIC FIBROSIS

Cystic fibrosis (CF) is a rare disease affecting over 4,300 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 $253 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 Alberta

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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.

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. These recalculations ensure 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 2017 were included in this report.

Individuals who are under 18 years of age 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, 2017.

When I joined Cystic Fibrosis Canada as President and CEO in June 2018, I was very impressed by the remarkable impact the organization has made in the understanding and treatment of CF. Data from the Canadian CF Registry has been invaluable in demonstrating the incredible progress of CF care and research in Canada. The pages of the 2017 Registry Annual Data Report demonstrate the contributions of dedicated healthcare teams, resilient patients, relentless advocates, and determined researchers. For their efforts and the resulting outcomes, we are so grateful.

In the 1960s, a child diagnosed with cystic fibrosis (CF) was not expected to survive past kindergarten. Today, the estimated median age of survival for a Canadian born with CF is more than 52 years of age – a number that has been stable for the past five years. That's almost a year of life for every year that Cystic Fibrosis Canada has operated. This continued achievement tells us that Cystic Fibrosis Canada is on the path to realizing our vision of ending CF. But there is still much work to do: far too many people still die far too young.

One way in which we hope to change the outcomes for people living with CF is through the new established Canadian Clinical Trials network, CF CanACT (Cystic Fibrosis Canada Accelerating Clinical Trials). The Canadian CF Registry is a well-recognized resource within our community, and it is our hope that it can be integrated with CF CanACT. This network will increase the capacity and enhance patient participation in clinical trials which will facilitate the development of new therapies and improved care to CF patients. We are excited to see the opportunities and outcomes of our programs that will help Canadians with CF.

On behalf of Cystic Fibrosis Canada, I want to extend my deepest gratitude to the clinic staff and patients who dedicate their time to input and share their data. This report would not be possible without your time and commitment.

Sincerely,

Kelly Grover
President and CEO, Cystic Fibrosis Canada

The Canadian CF Registry continues to be an invaluable resource of national CF data that is used to improve the quality of patient care, influence research, and bolster advocacy efforts across the country. These data are also leveraged to critically assess health outcomes of new therapies and identify potentially eligible patients for new and emerging treatments.

This year we saw the launch of the patient portal called *MyCFLifePortal* which is a secure, read-only website providing access for patients and their caregivers to view their own Registry data remotely. We are very excited for patients to be able to review their own data which we hope will increase engagement in their health and will stimulate discussions with their healthcare teams. In the future, we hope that *MyCFLifePortal* will also be a platform for educational material and enhance communication within the Canadian CF community. We express our sincerest gratitude to the entire CF community whose continued support and dedication made these incredible achievements possible.

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

2017 HIGHLIGHTS FROM THE CANADIAN CF REGISTRY

Cystic Fibrosis Canada

DEMOGRAPHICS

OVER 4,300 CANADIANS
WITH **CF** WITH **MEDIAN AGE**
OF **22.8** YEARS

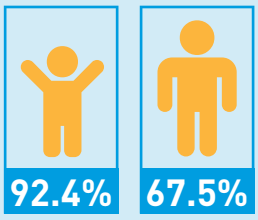
66 NEWBORN SCREENING
11 ADULT DIAGNOSIS
115 NEW CF **DIAGNOSES**

18.7% TRAVELLED
MORE THAN **250 KM**
TO RECEIVE **CF CARE**

60.9%
ARE ADULTS

HEALTH OUTCOMES

MEDIAN **FEV$_1$**
PERCENT PREDICTED



FOR CHILDREN FOR ADULTS

68.7% OF FEMALE ADULTS
63.5% OF MALE ADULTS
HAVE A NORMAL WEIGHT
(BMI BETWEEN 18.5 AND 24.9 KG/M^2)

48.7% OF **CHILDREN UNDER 2** YEARS
45.9% OF **CHILDREN BETWEEN 2-17** YEARS
ARE ABOVE THE NATIONAL GOAL OF **50TH** BMI PERCENTILE

CF CARE AND TREATMENTS

COLLECTIVELY MORE THAN
19,000 CLINIC VISITS
OVER
26,000 HOSPITAL DAYS
& ALMOST **1,000** COURSES OF HOME IV THERAPY

84.9%
TAKE PANCREATIC ENZYMES TO DIGEST FOOD & ABSORB NUTRIENTS

40.2% HAVE ***PSEUDOMONAS AERUGINOSA*** INFECTIONS

22.4%
HAVE CF-RELATED **DIABETES**

SURVIVAL

MEDIAN AGE OF SURVIVAL ESTIMATED TO BE **52.3** YEARS OF AGE

50% OF THOSE TRANSPLANTED TODAY EXPECTED TO **LIVE BEYOND** **10.3** YEARS

DEMOGRAPHICS

CANADIANS WITH CYSTIC FIBROSIS

In 2017, there were a total of 4,309 individuals with CF who attended one of the 42 accredited CF clinics across Canada (Figure 1) with 115 of those being newly diagnosed with CF. Overall, the total Canadian CF population has been steadily increasing and in the last two decades, has grown by 36.8% (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.

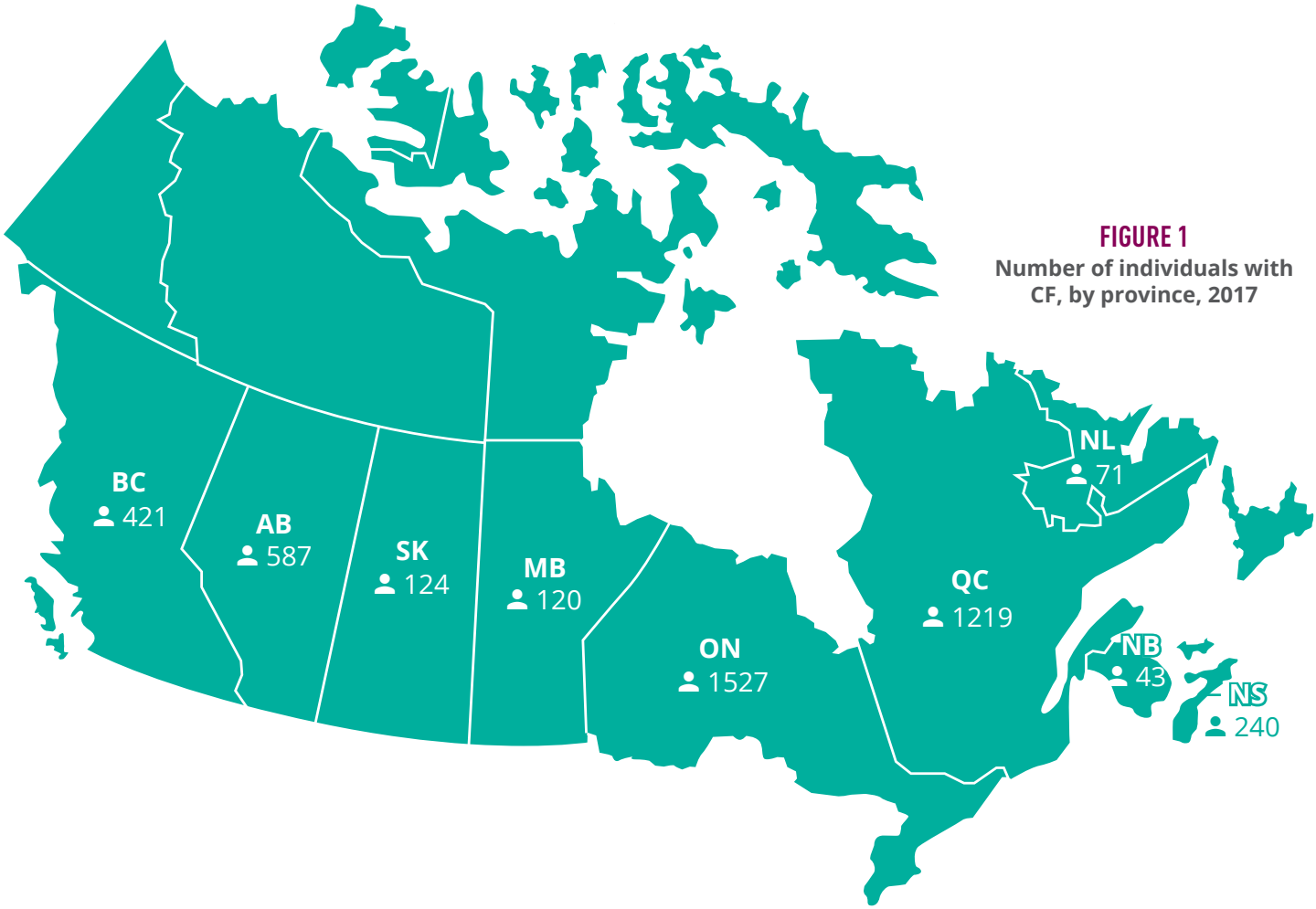


FIGURE 1
Number of individuals with CF, by province, 2017

PROVINCE*	NUMBER OF INDIVIDUALS WITH CF	FEMALE	MALE	ADULTS	CHILDREN
AB	587	287	300	322	265
BC	421	182	239	265	156
MB	120	50	70	64	56
NB	43	23	20	29	14
NL	71	28	43	51	20
NS	240	109	131	157	83
ON	1527	725	802	914	613
QC	1219	560	659	780	439
SK	124	48	76	63	61

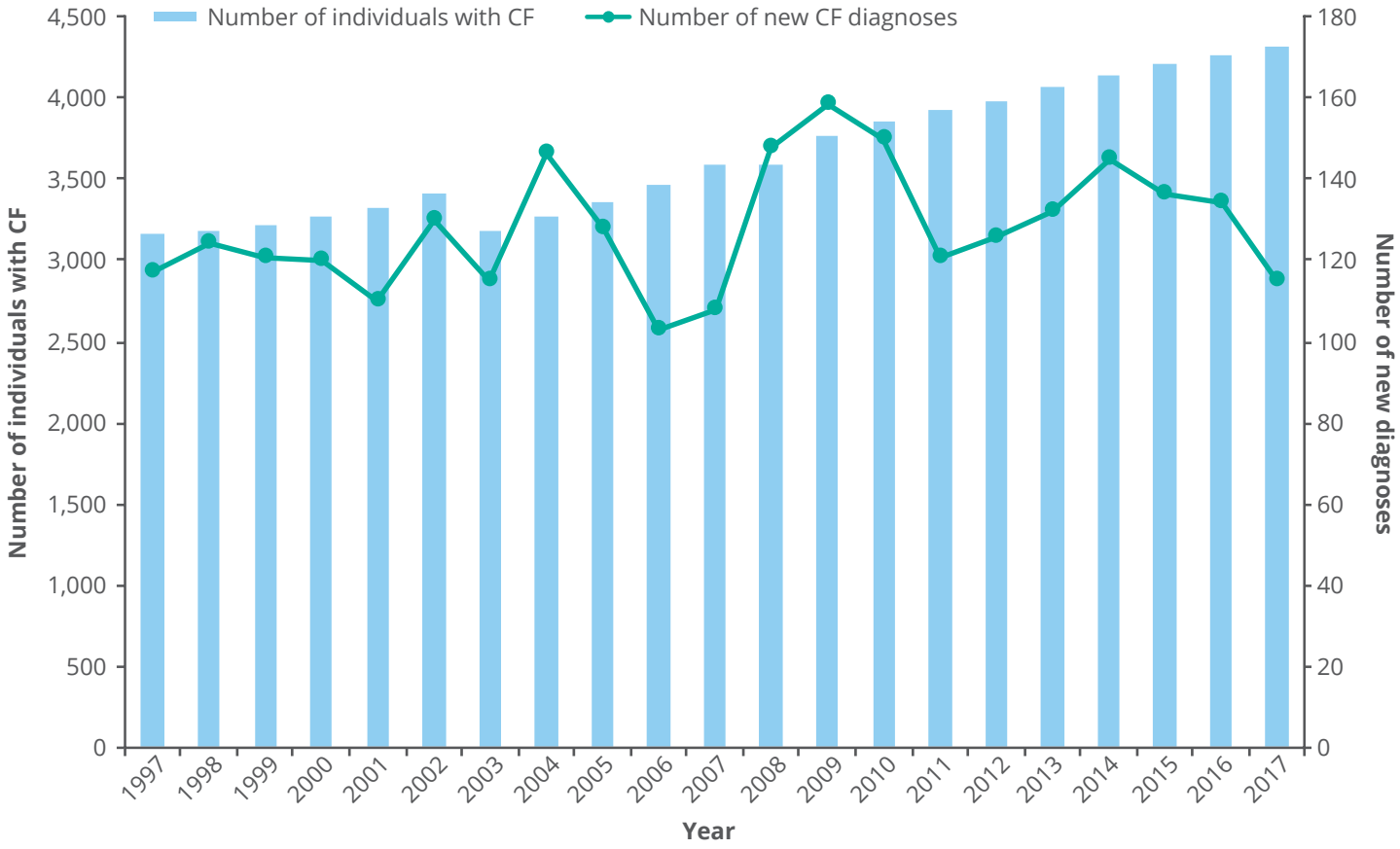
* individuals with CF living in provinces or territories not listed here are included if reported on by other CF clinics

DEMOGRAPHICS

NUMBER OF CANADIANS WITH CYSTIC FIBROSIS

FIGURE 2

Total number of individuals with CF and new CF diagnoses, 1997 to 2017



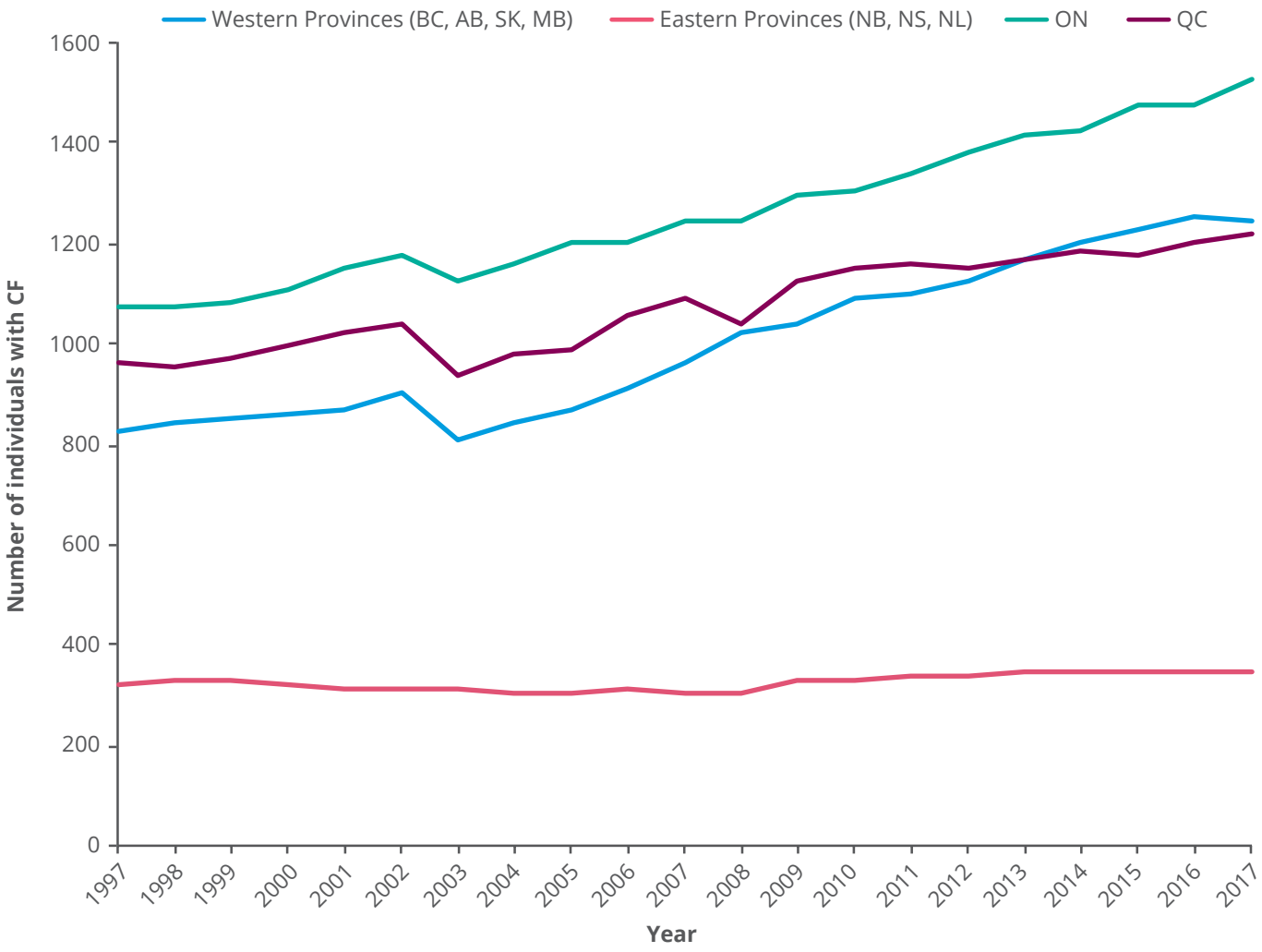
DEMOGRAPHICS

PROVINCIAL POPULATION CHANGE

Over the past two decades, the Canadian CF population has been growing with the largest increases seen in ON and the Western provinces (Figure 3). Comparing populations between 1997 and 2017, Alberta saw the largest percent growth of almost 80% (Figure 4).

FIGURE 3

CF population growth by region, 1997 to 2017



DEMOGRAPHICS

PROVINCIAL POPULATION CHANGE

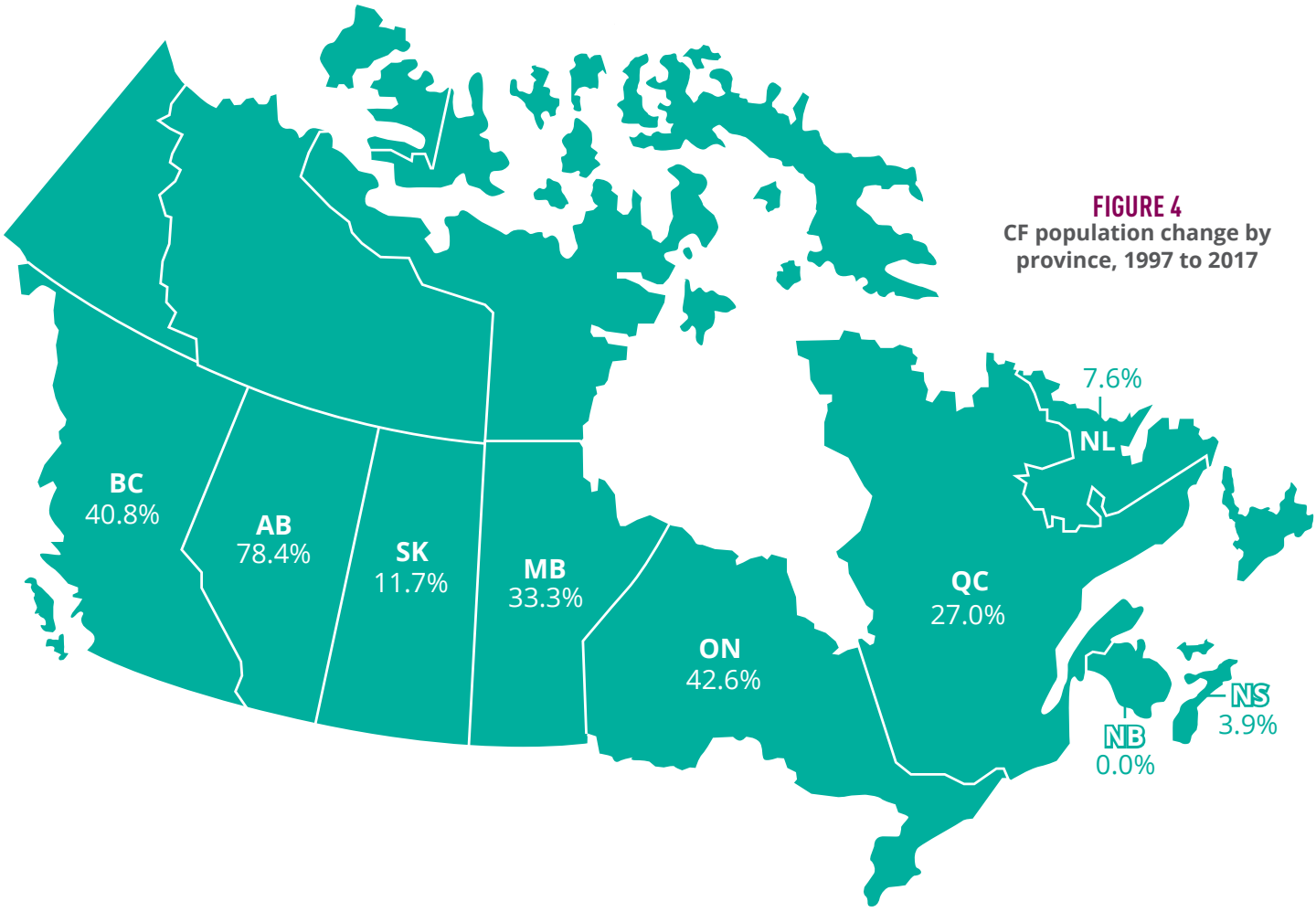


FIGURE 4
CF population change by province, 1997 to 2017

PROVINCE*	1997	2017	PERCENT CHANGE
AB	329	587	78.4%
BC	299	421	40.8%
MB	90	120	33.3%
NB	43	43	0.0%
NL	66	71	7.6%
NS	231	240	3.9%
ON	1071	1527	42.6%
QC	960	1219	27.0%
SK	111	124	11.7%

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

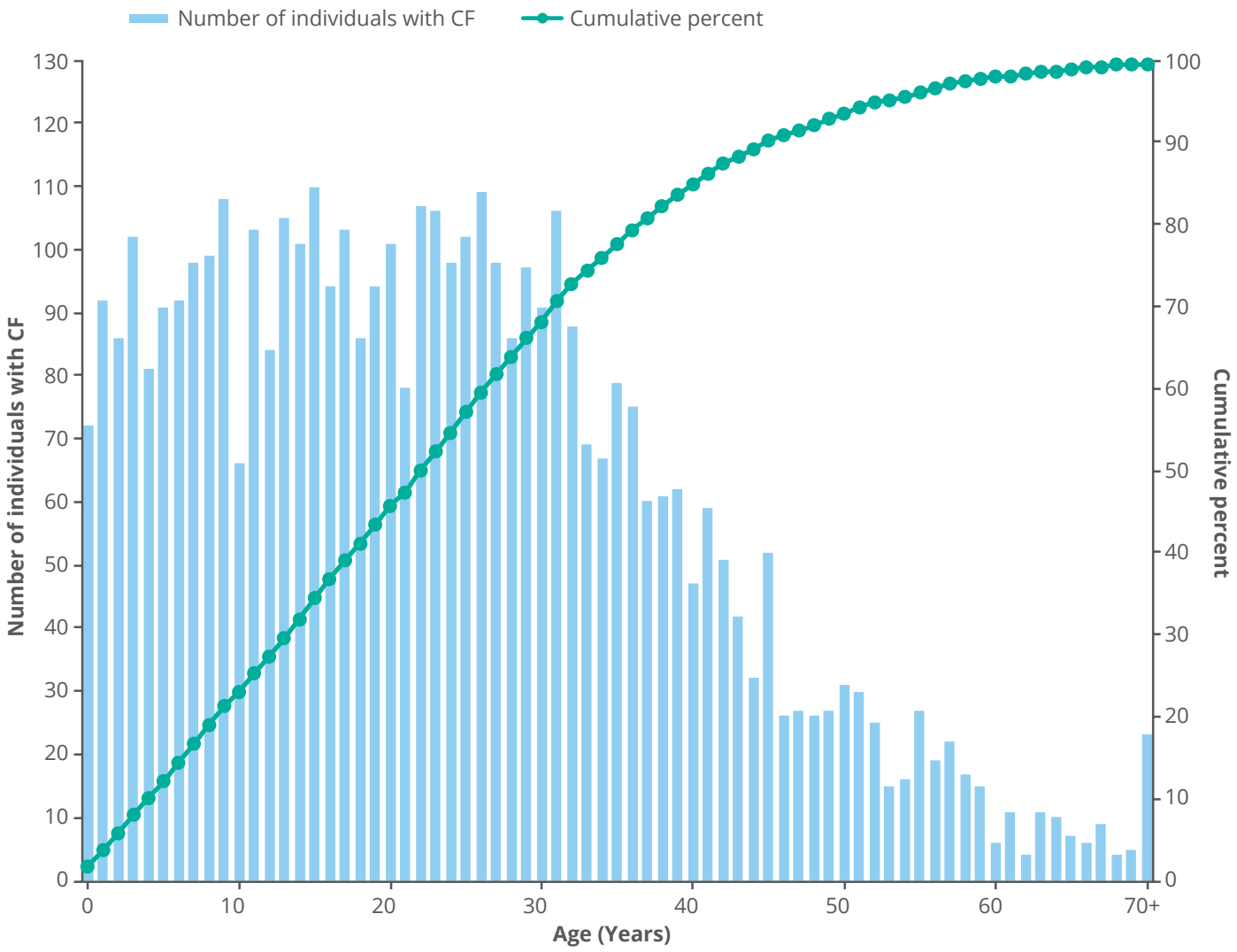
DEMOGRAPHICS

AGE DISTRIBUTION OF CANADIANS WITH CYSTIC FIBROSIS

Figure 5 shows the age distribution of the Canadian CF population in 2017. The median age of all individuals reported on in 2017 was 22.8 years with 60.9% of individuals over 18 years of age (Figure 8), 15.2% over 40 years of age and 0.5% over 70 years of age.

FIGURE 5

Age distribution of individuals with CF, as of December 31, 2017



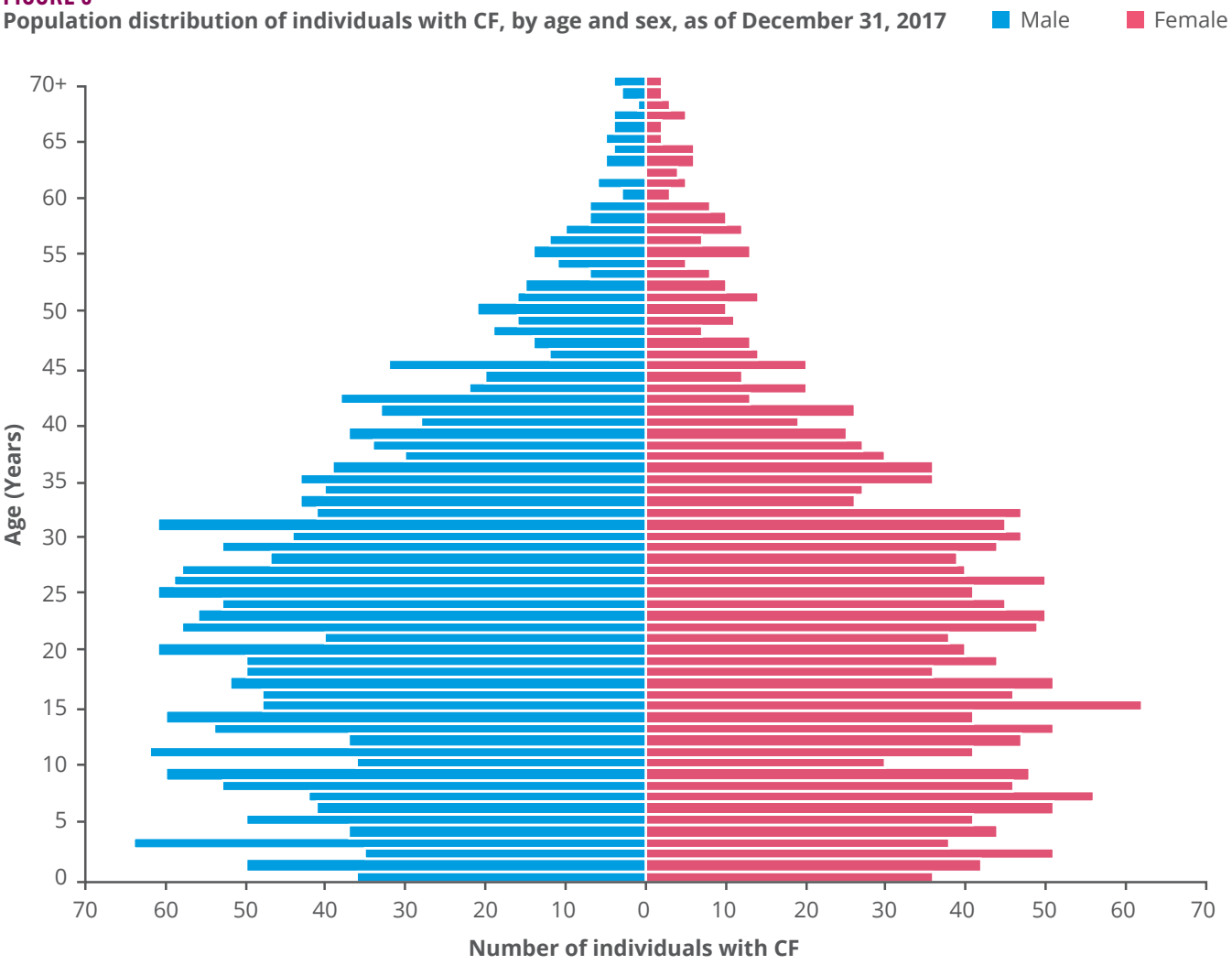
DEMOGRAPHICS

AGE AND SEX DISTRIBUTION OF CANADIANS WITH CYSTIC FIBROSIS

Males accounted for 53.9% of individuals reported on in 2017 with 9.2% of males and 7.2% of females over the age of 40 (Figure 6).

FIGURE 6

Population distribution of individuals with CF, by age and sex, as of December 31, 2017

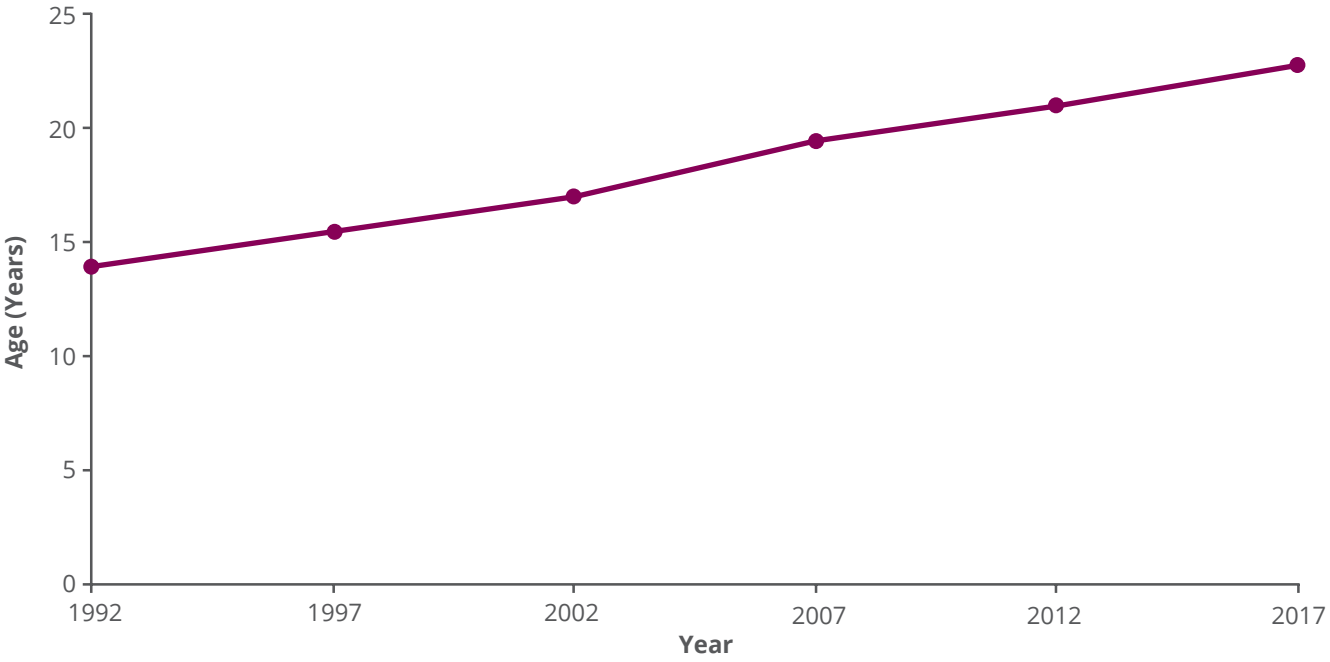


DEMOGRAPHICS

MEDIAN AGE OF CANADIANS WITH CYSTIC FIBROSIS

The current median age of individuals with CF reported on in 2017 was 22.8 years compared to 15.4 years over two decades ago (Figure 7).

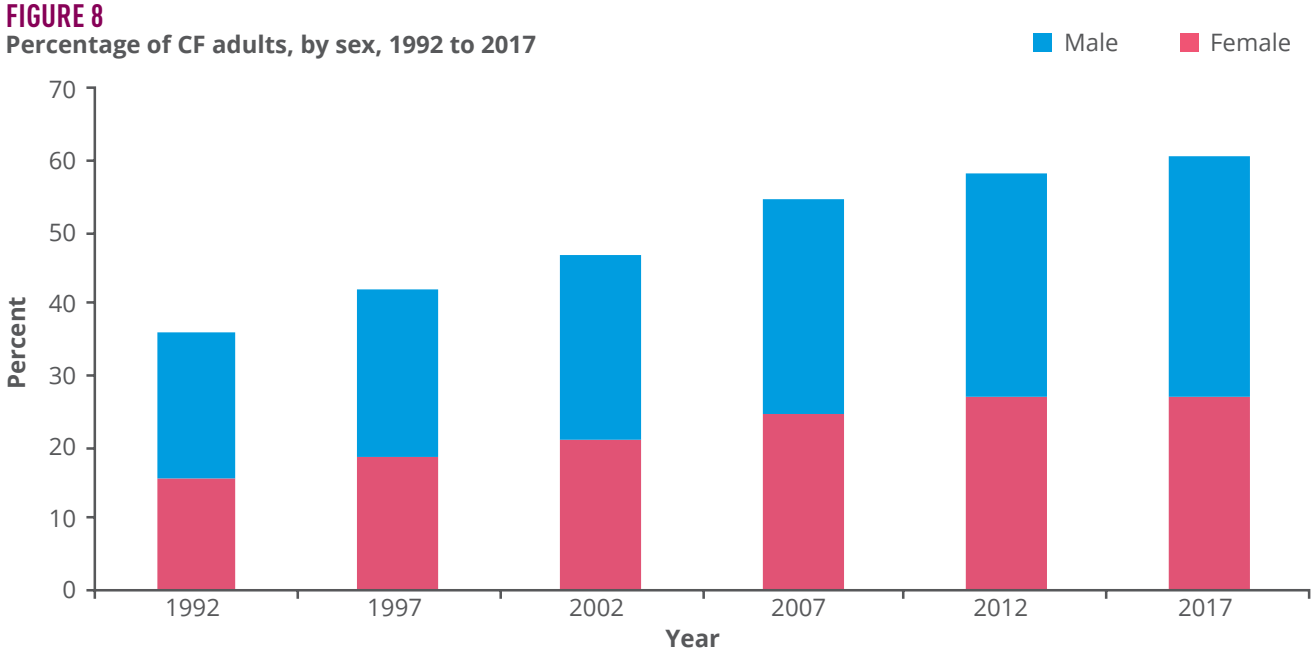
FIGURE 7
Median age of individuals with CF, 1992 to 2017



CANADIAN ADULTS WITH CYSTIC FIBROSIS

Adults (individuals aged 18 years or older) accounted for 60.9% of the 2017 Canadian CF population of which 44.6% were females.

FIGURE 8
Percentage of CF adults, by sex, 1992 to 2017



DIAGNOSIS
AGE AT DIAGNOSIS

The majority (59.9%) of individuals with CF reported on in 2017 were diagnosed before the age of one year, and over two thirds (67.5%) were diagnosed by the age of two years (Figure 9). By the age of 18 years, 92.6% of individuals had been diagnosed. Adults diagnosed later in life (18 years or older) account for only 7.4% of all diagnoses.

Figure 10 shows the percentage of newborns diagnosed through provincial newborn screening (NBS) programs since 2007 when NBS for CF started in Alberta. A decade ago, less than 10% of new CF diagnoses were identified through NBS. In 2017, over half of those newly diagnosed (57.4%) were made through NBS. As of September 2018, all provinces in Canada screen newborns for CF.

FIGURE 9
Age at diagnosis of CF individuals, as of December 31, 2017 (N = 4,240)

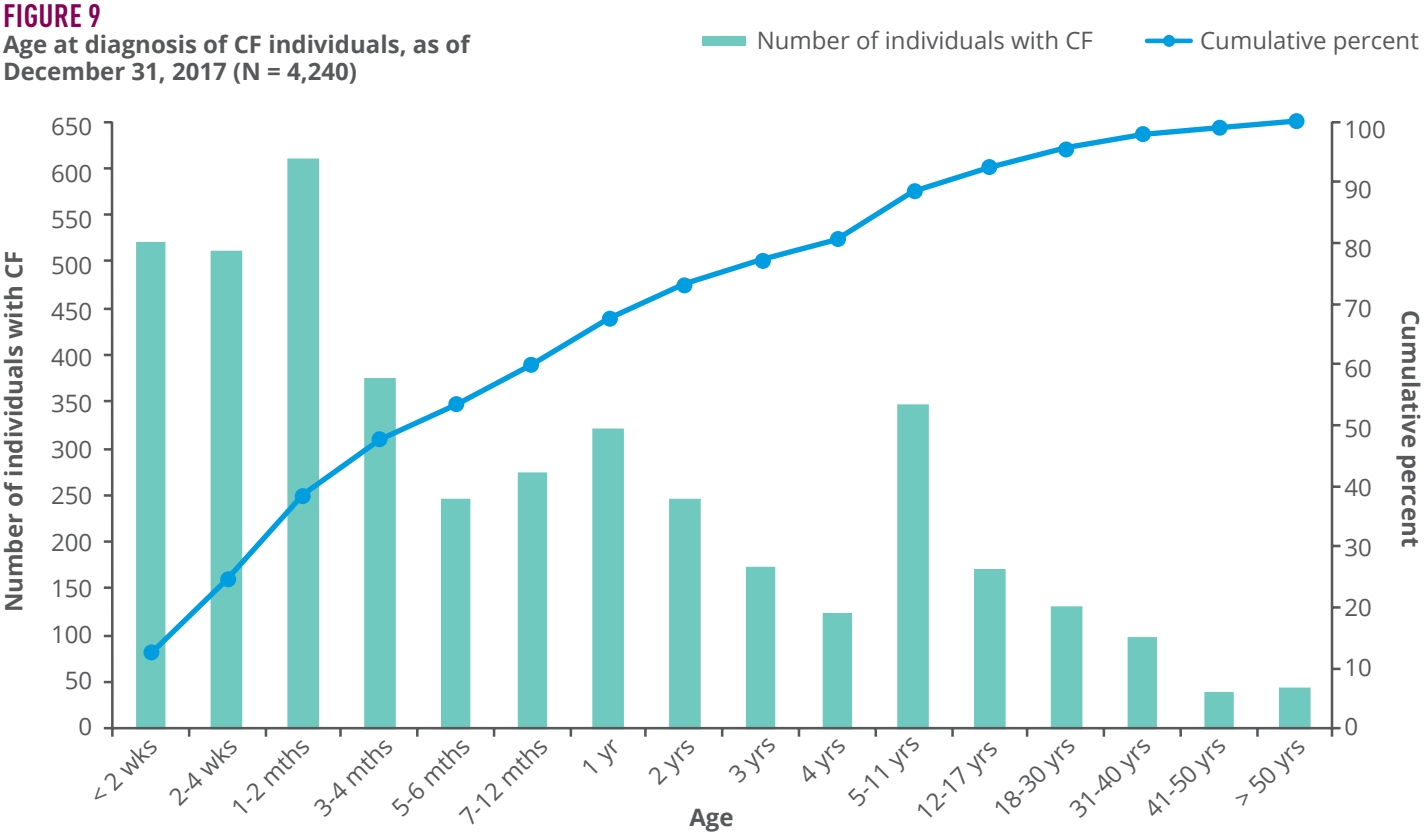
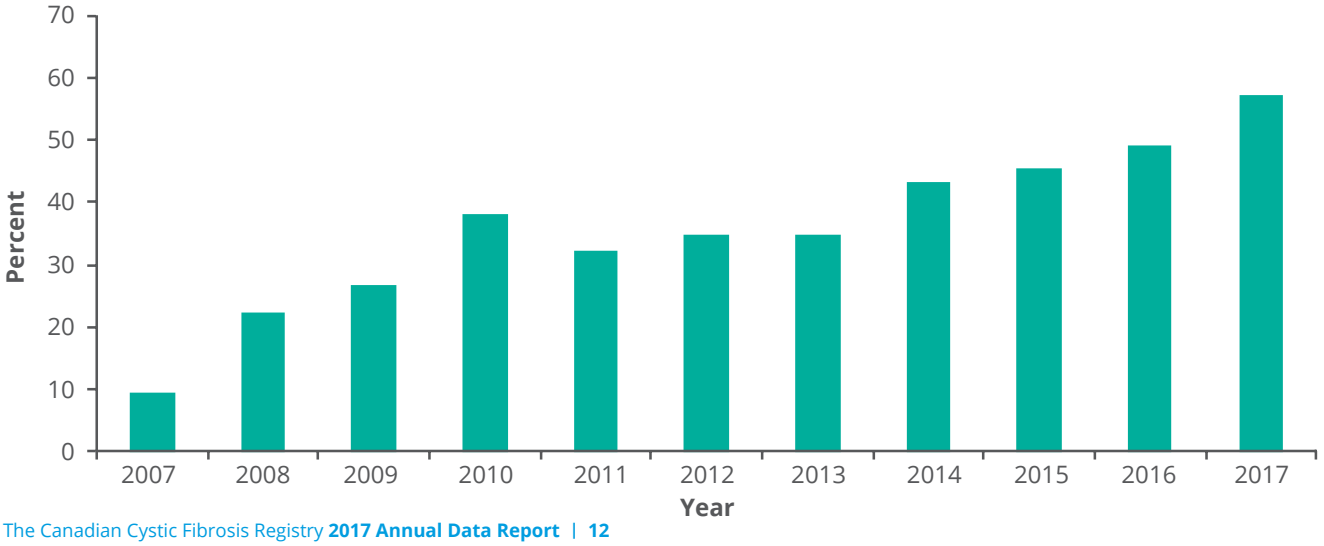


FIGURE 10
Percentage of all new CF diagnoses made through the NBS program, 2007 to 2017



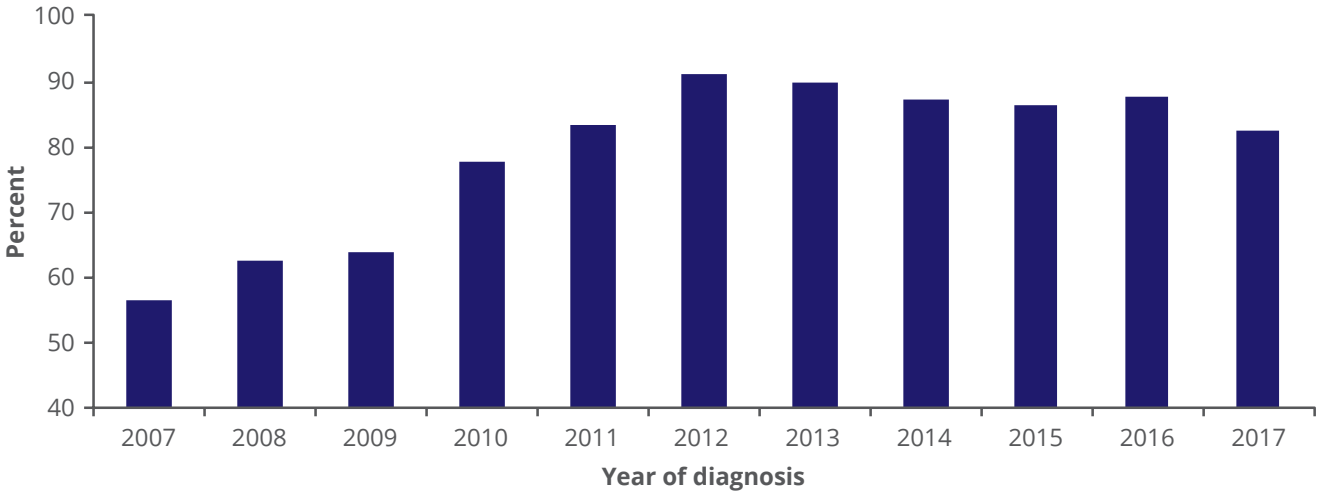
DIAGNOSIS

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 2017, there were 2,036 (47.3%) individuals with CF with at least one sweat chloride test result recorded. Since 2007, the number of newly diagnosed individuals with at least one sweat chloride test has been steadily increasing (Figure 11). In 2017, 95 of the 115 (82.6%) newly diagnosed individuals had at least one sweat chloride test result recorded which is over 25% more than in 2007.

FIGURE 11

Percentage of newly diagnosed individuals with at least one sweat chloride test, 2007 to 2017

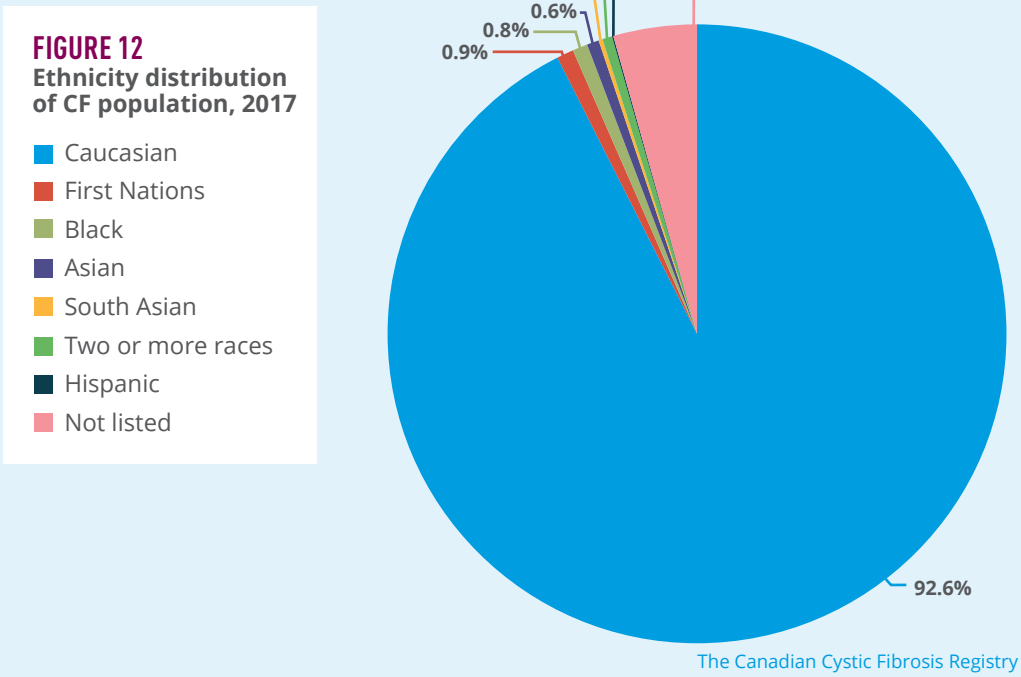


ETHNICITY

Caucasians account for the majority (92.6%) of the Canadian CF population. Of those remaining who have an identified ethnicity (Figure 12), they are divided among five other ethnic groups (First Nations, Black, Asian, South Asian and Hispanic). Ethnicity is captured through self-report.

FIGURE 12

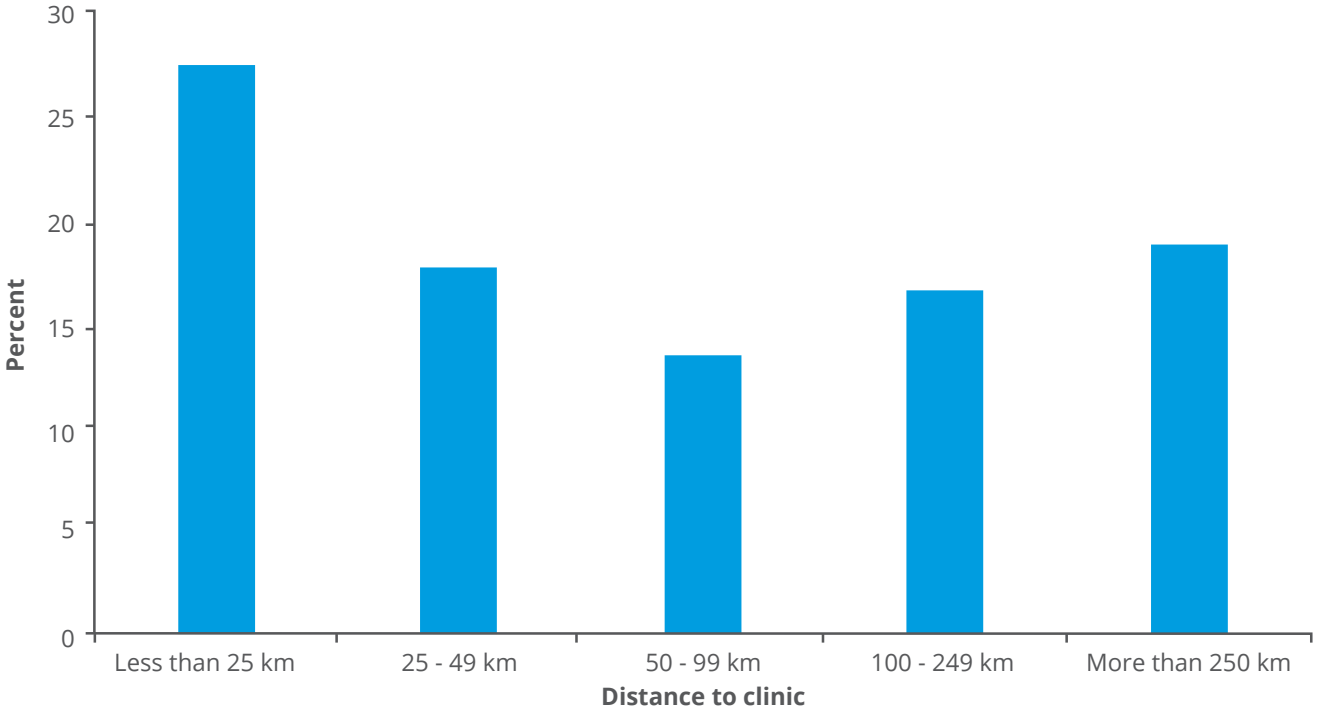
Ethnicity distribution of CF population, 2017



DISTANCE TO CLINICS

The CCFR began collecting the general location (first three letters of the postal code) of individuals with CF in 2015. Distances to the reporting clinic were calculated in kilometers (km) using the fastest driving route. In 2017, there were 1,484 (34.4%) CF individuals with at least one valid location recorded (Figure 13). The majority (58.4%) of those with a reported location attend a CF clinic within 100 km of where they live while 18.7% travel more than 250 km for their CF care.

FIGURE 13
Distance travelled to clinic for individuals with CF (N = 1,484), 2017

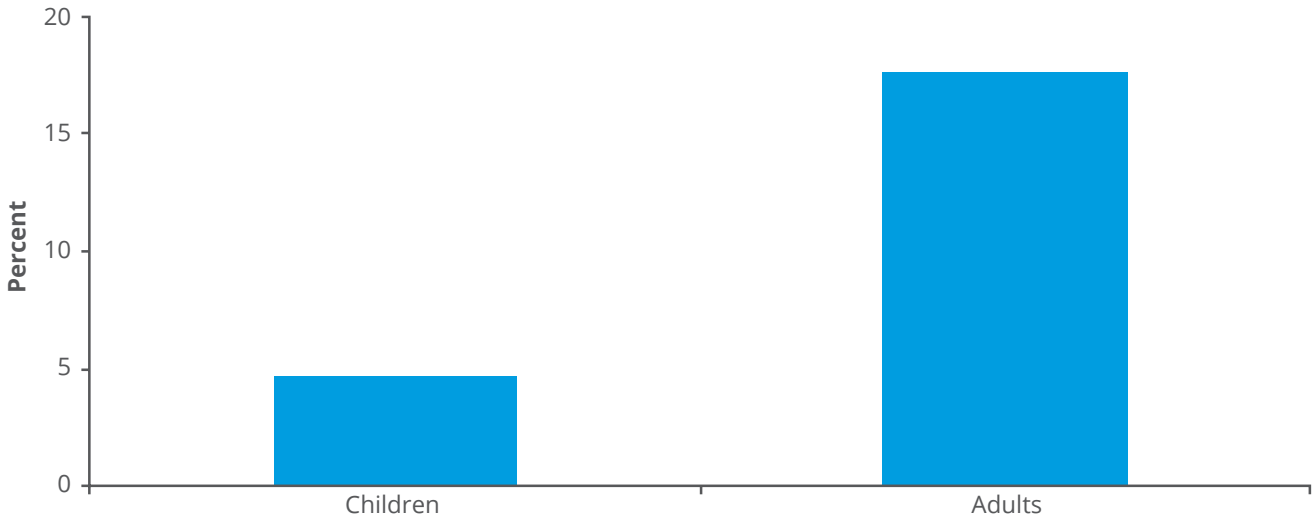


MENTAL HEALTH

In 2017, there were 542 (12.6%) individuals with CF reported with clinically diagnosed depression or anxiety. 80 (4.7%) were children and 462 (17.6%) were adults (Figure 14).

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 definitions of depression and anxiety can vary greatly.

FIGURE 14
Percentage of children and adults diagnosed with depression or anxiety, 2017



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.

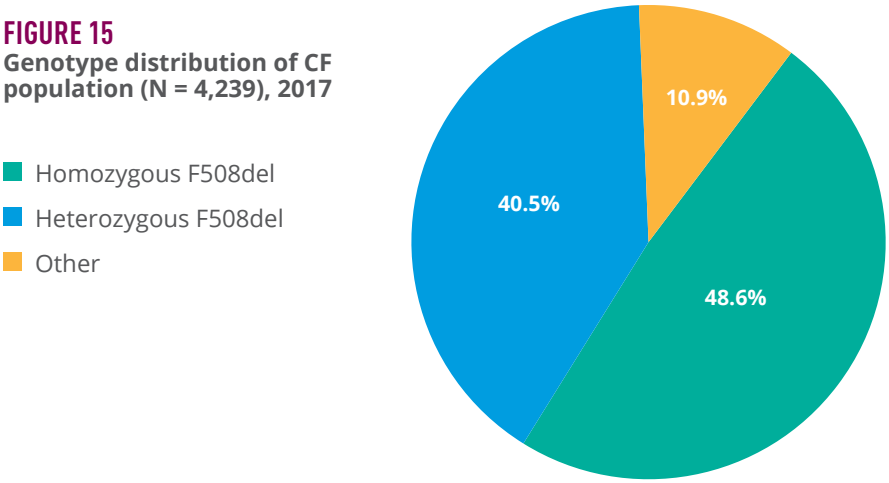
The most common CF mutation worldwide is a three base-pair deletion in the *CFTR* gene resulting in the deletion of the phenylalanine (F) residue at position 508 in the CFTR protein, commonly referred to as **F508del**. CF disease-causing mutations can be classified into five major categories depending 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 (4,239, 98.3%) individuals with CF reported in 2017 had at least one CF mutation recorded. Almost half (2,059, 48.6%) have two copies of the F508del mutation and almost 90% carry at least one copy of the F508del mutation (Figure 15). Those diagnosed as a child (under 18 years) were more likely to have two copies of the F508del mutation (52.0%) while those diagnosed as an adult (18 years or older) were more likely to have one copy of the F508del mutation (66.9%) (Figure 16). In the entire CCFR, 91.9% of all individuals with CF reported as being alive have at least one CF mutation recorded. The majority (85.3%) of those individuals with no mutations reported are adults and 1.6% are under one year of age.

FIGURE 15
Genotype distribution of CF population (N = 4,239), 2017



GENOTYPE

FIGURE 16
Genotype distribution of individuals with CF, by diagnosis age group (N = 4,178), 2017

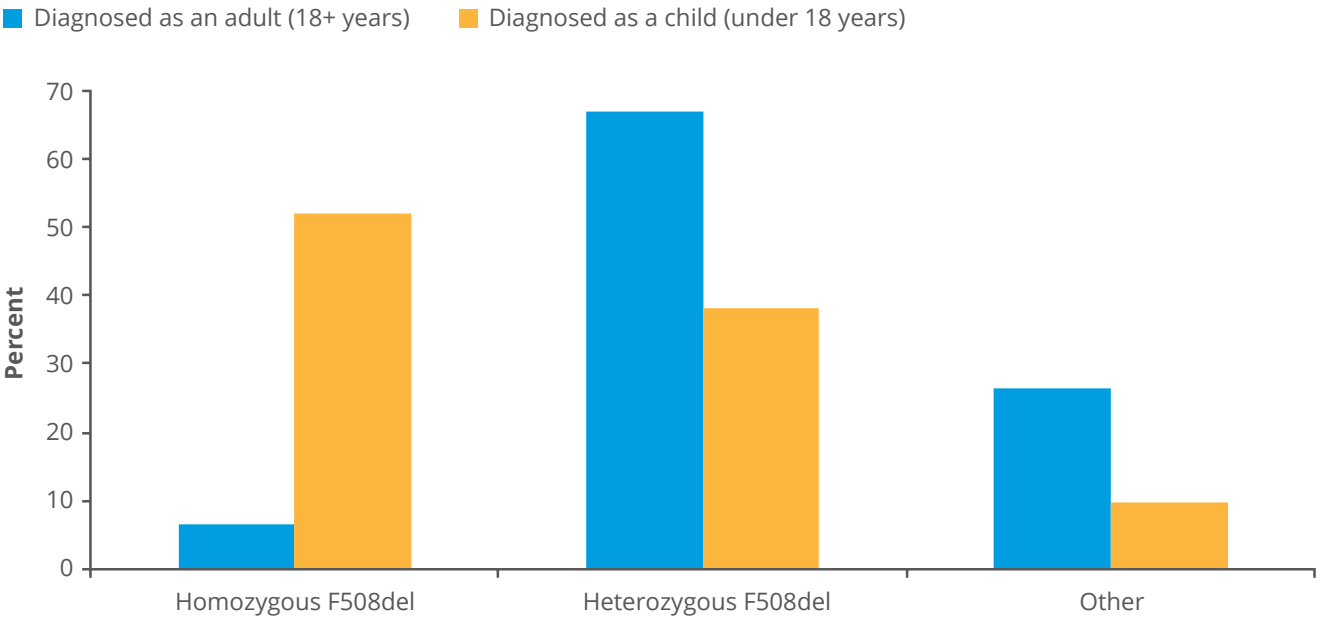


Table 2 lists the most common mutations for individuals with CF reported in 2017. After F508del, 621+1G->T is the next most frequent mutation identified in 5.8% of the population

TABLE 2
Frequency of the top 10 most common CF mutations on one or both alleles of CF individuals (N = 4,239), 2017

MUTATION	NUMBER	PERCENTAGE
F508del	3,776	89.1%
621+1G->T	246	5.8%
G542X	149	3.5%
G551D	132	3.1%
711+1G->T	112	2.6%
A455E	110	2.6%
L206W	98	2.3%
N1303K	85	2.0%
R117H	80	1.9%
G85E	66	1.6%

RESPIRATORY

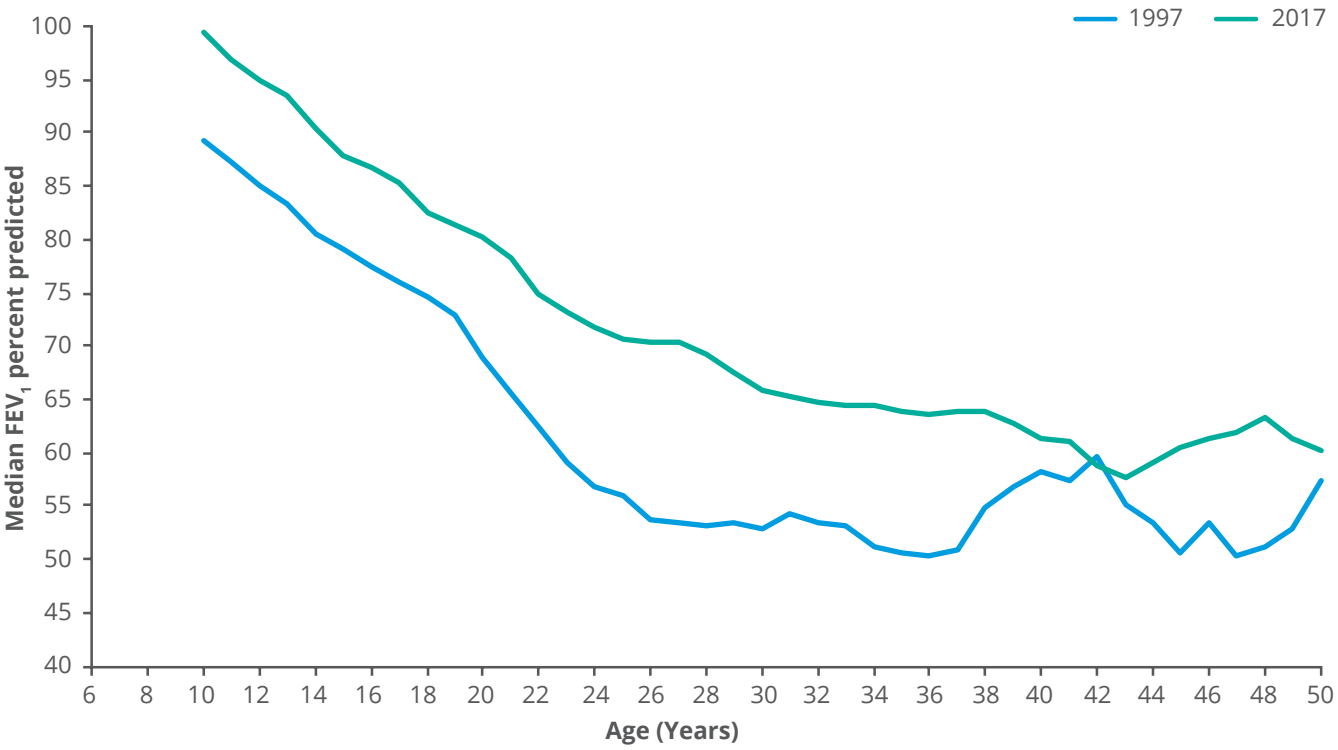
MEDIAN FEV_1 PERCENT PREDICTED

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 17 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. The median FEV_1 at 30 years of age was 63.8% in 2017 compared to 53.1% in 1997 marking an improvement of nearly 11% over the last two decades. Interestingly, the trends between these two time periods are similar. Individuals born recently have a higher median FEV_1 percent predicted at age 6 years and have a slower rate of decline than those born earlier (Figure 18). The upticks seen in some of the birth cohort lines for the later ages are due to the small sample sizes resulting from the method used to group ages in the calculations.

FIGURE 17

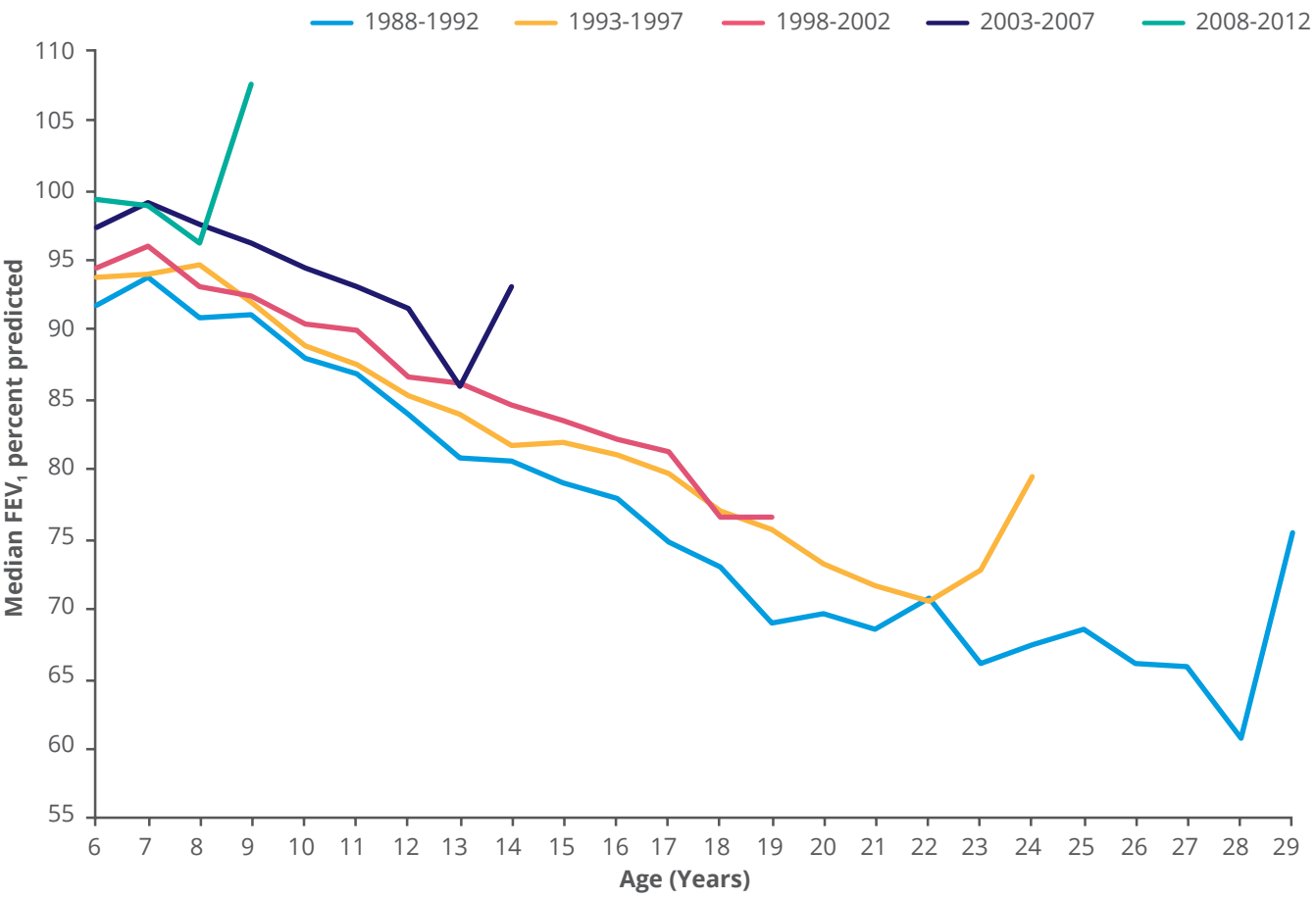
Median FEV_1 percent predicted vs. age of CF individuals (5-year moving window), 1997 and 2017*



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

FIGURE 18

Median FEV_1 percent predicted of individuals with CF, by birth cohort, 2017*



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

RESPIRATORY

RESPIRATORY STATUS

The majority (55.7%) of children, aged 6 to 17 years in 2017, have normal lung function while the majority (37.2%) of adults have moderate lung function, as shown in Figure 19. Over time, the median FEV_1 percent predicted has been steadily increasing for both age groups, and in 2017 these values were 67.5% for adults and 92.4% for children (6-17 years of age), as shown in Figure 20. Both figures display data from individuals reported on in 2017, including those who are post-transplant. Table 3 defines severity of lung disease using FEV_1 categories.

TABLE 3
Lung function classification by FEV_1 percent predicted

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

FIGURE 19
Respiratory status of children and adults with CF, 2017

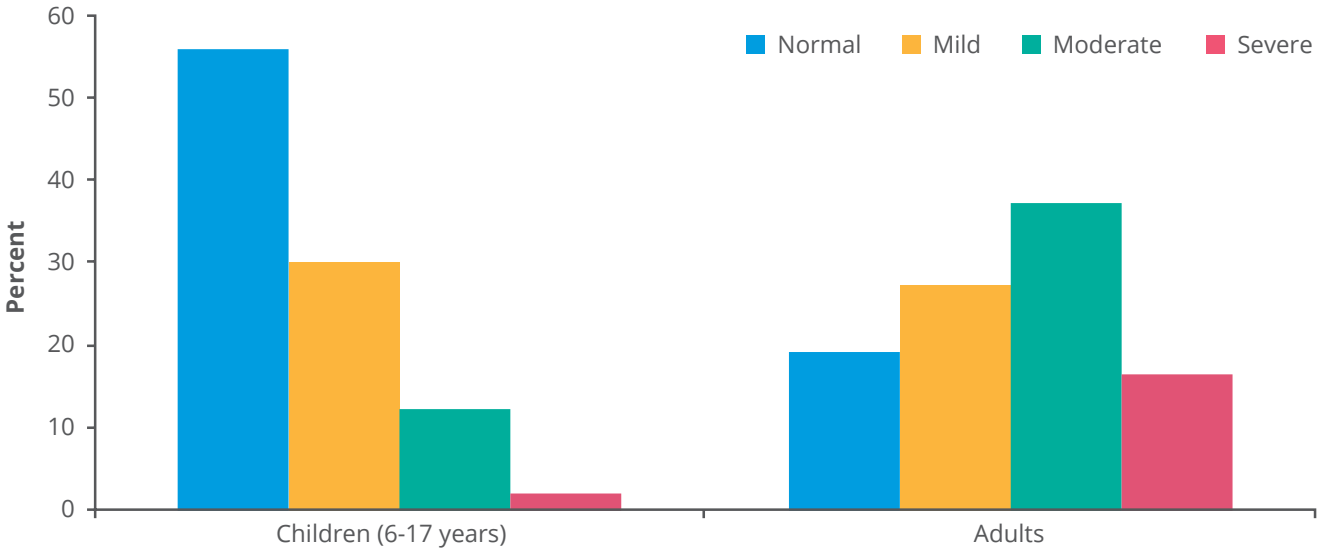
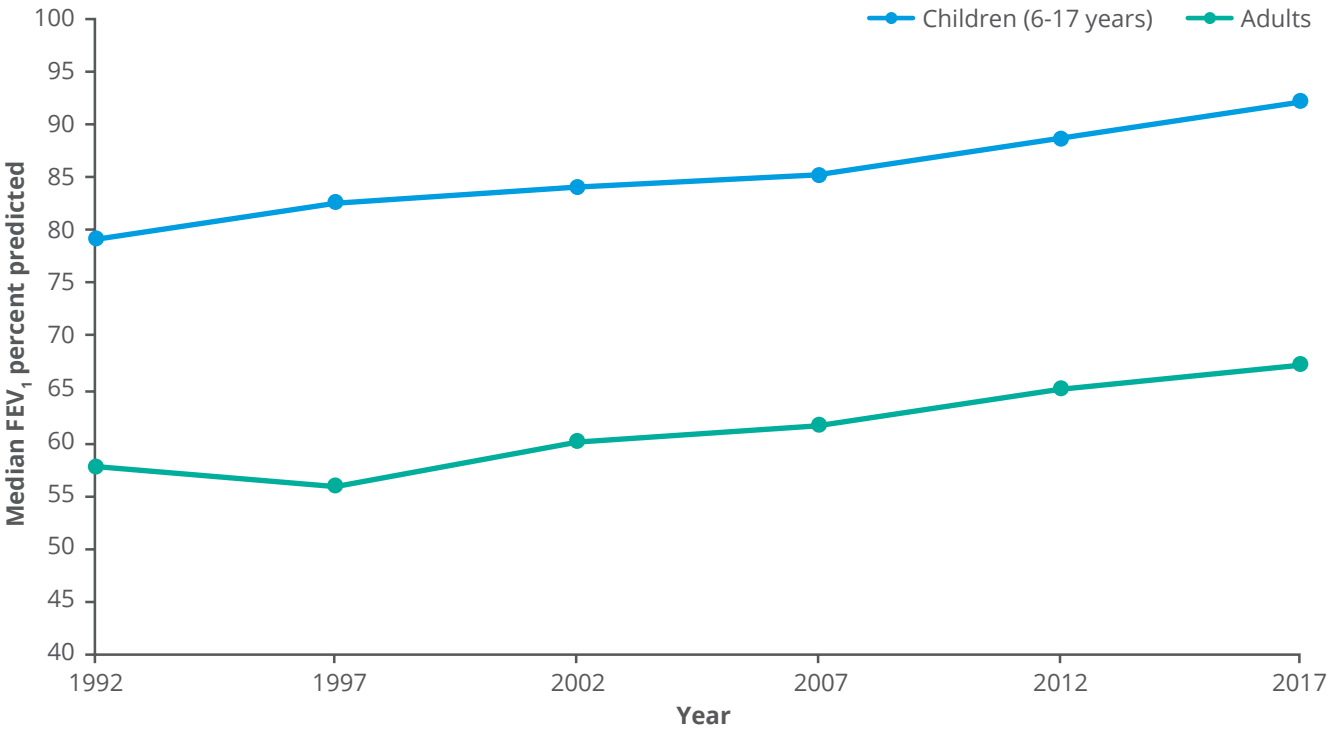


FIGURE 20
Median FEV_1 percent predicted values for children and adults with CF, 1992 to 2017



RESPIRATORY

RESPIRATORY STATUS BY SEX

Figures 21 and 22 show that between males and females for both age groups (children aged 6-17 years and adults), the distribution of lung function severity is similar across each category.

FIGURE 21

Respiratory status of children (6 to 17 years) with CF, by sex, 2017

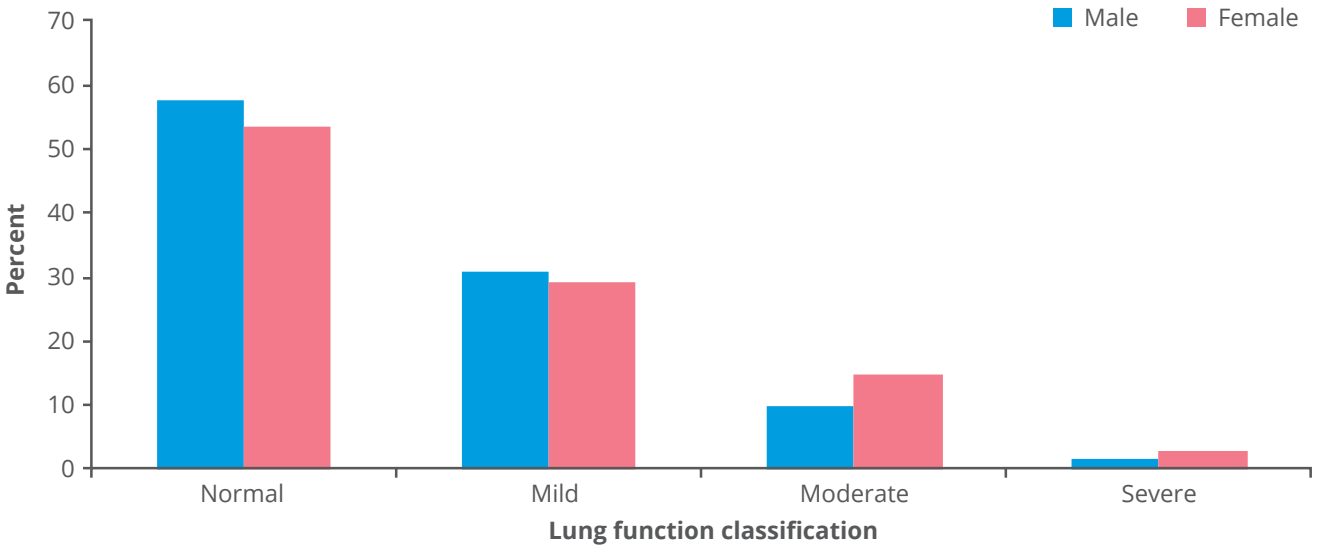
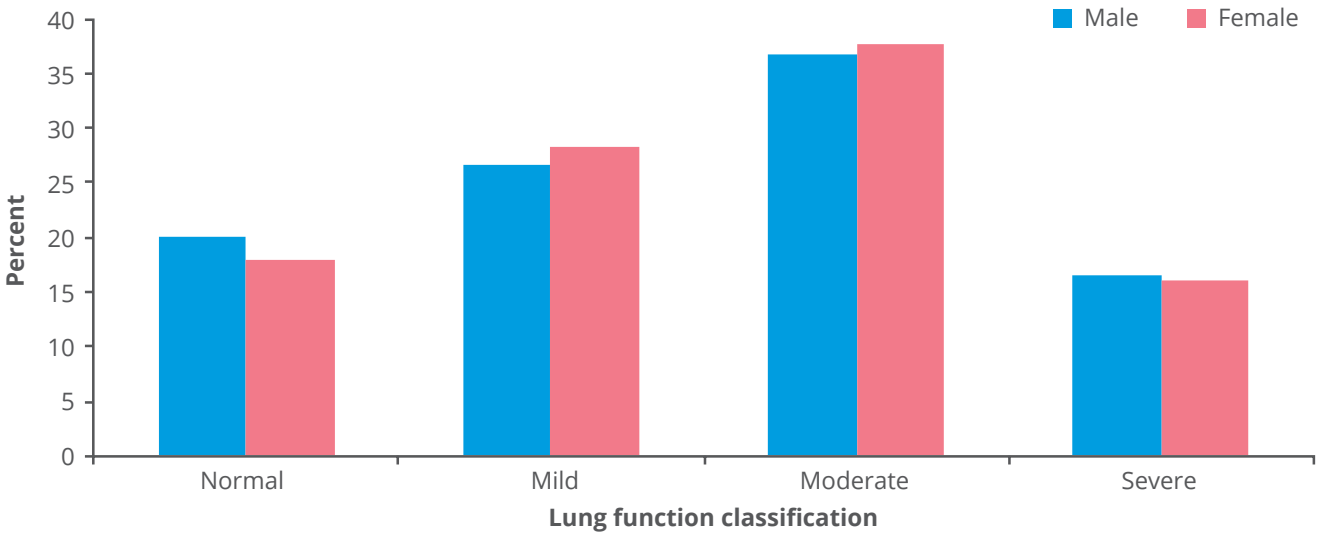


FIGURE 22

Respiratory status of adults (18 years of age and older) with CF, by sex, 2017



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 2017, the majority (84.9%) of individuals with CF were taking supplemental pancreatic enzymes (pancreatic insufficient) compared to 15.1% who were not (pancreatic sufficient), as shown in Figure 23.

For individuals currently 40 years of age or older, 29.7% were pancreatic sufficient (Figure 24). 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 being pancreatic sufficient.

FIGURE 23
Pancreatic status of individuals with CF, 2017

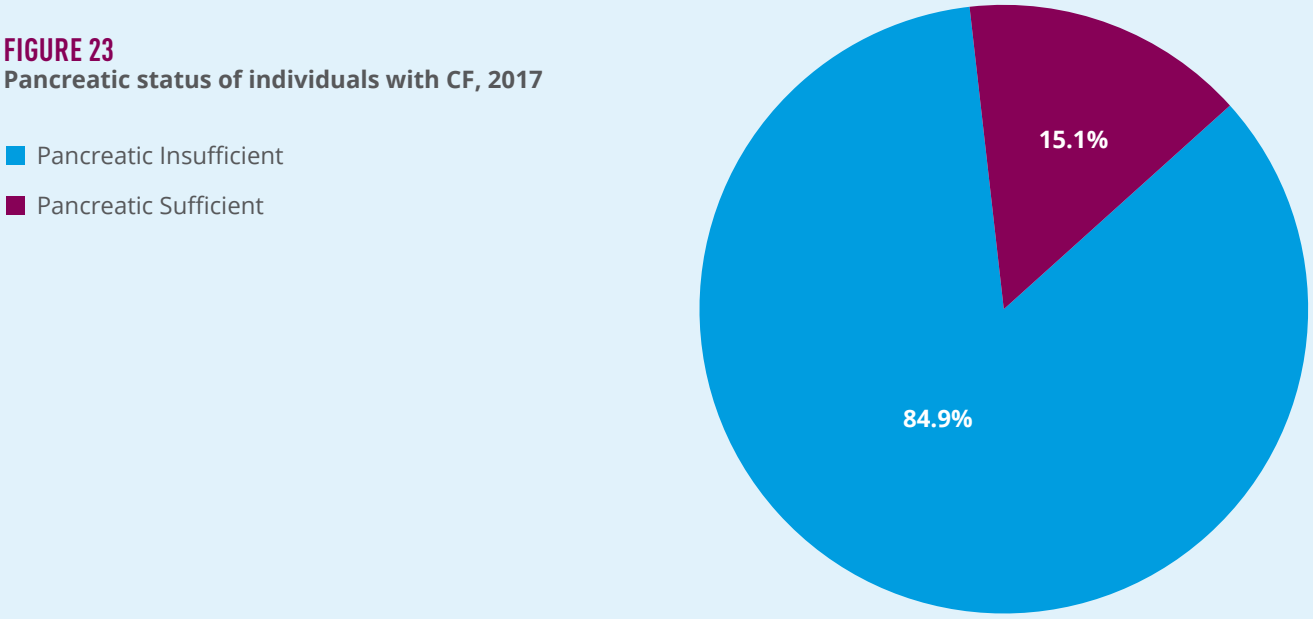
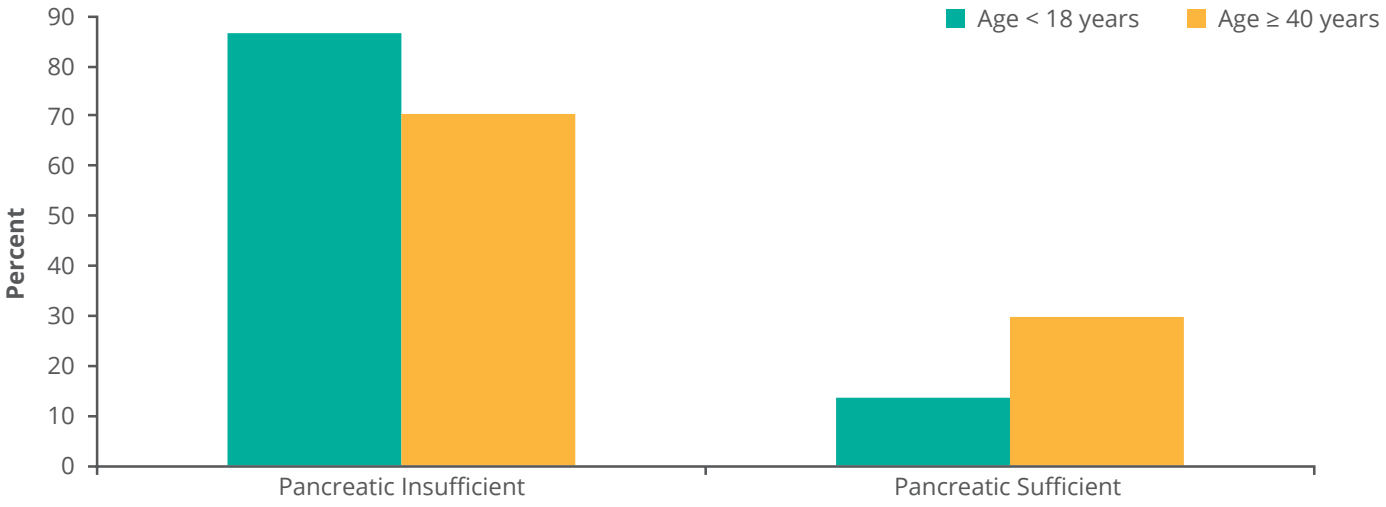


FIGURE 24
Pancreatic status of individuals with CF, by age group, 2017



NUTRITION
BMI PERCENTILE

BMI percentiles[4] are calculated following the World Health Organization (WHO) guidelines for children under 2 years of age, and the Centers for Disease Control and Prevention (CDC) guidelines for children ages 2 to 17 years. 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 details the BMI percentile classification categories following the respective WHO or CDC guidelines[5]. The ranges of BMI percentile classifications were updated in 2016 and as such will be different from those described in reports prior to 2016.

The national median BMI percentile for children under 2 and between 2 and 17 years of age are 47.2 and 46.3, respectively. The majority of children with CF (61.0% of children under 2 years and 76.7% of children 2-17 years) have an adequate weight (Figure 25). The 50th BMI percentile is the national goal for children with CF and in 2017, 48.7% of children under 2 years and 45.9% of children 2-17 years exceeded this goal.

FIGURE 25
BMI percentile status for children with CF, 2017

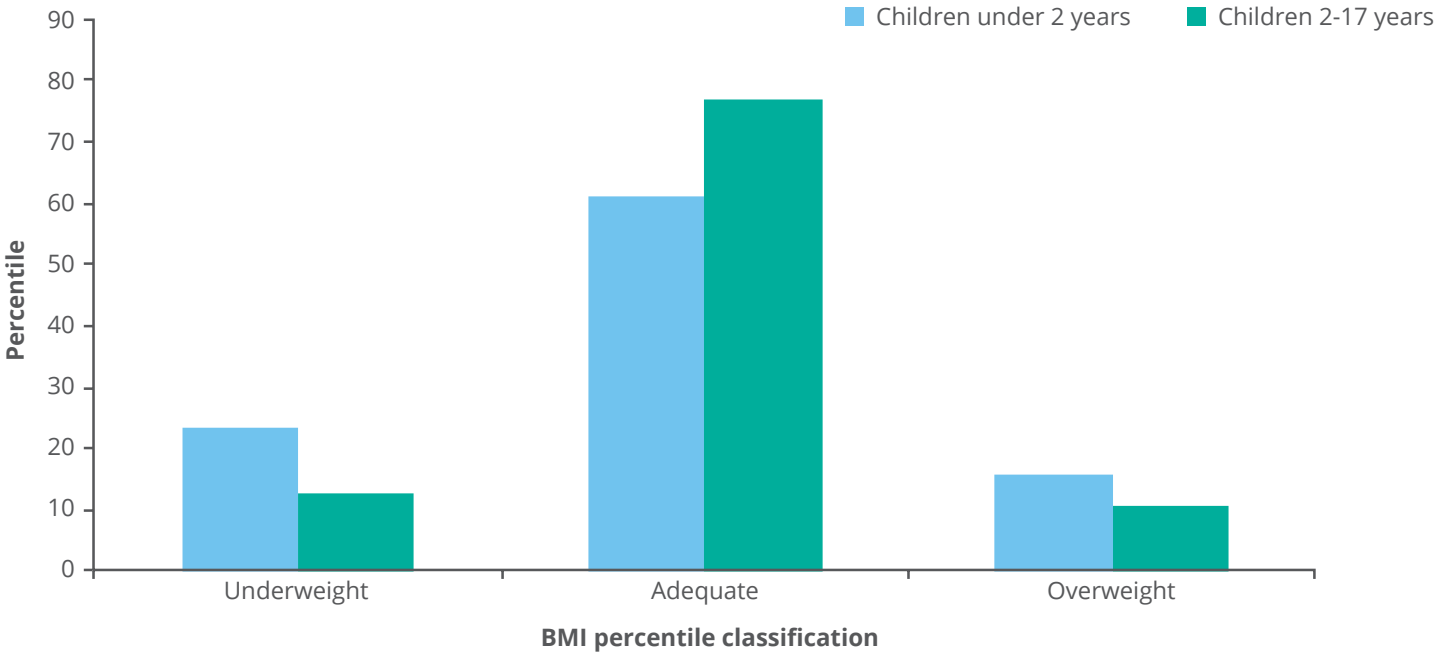


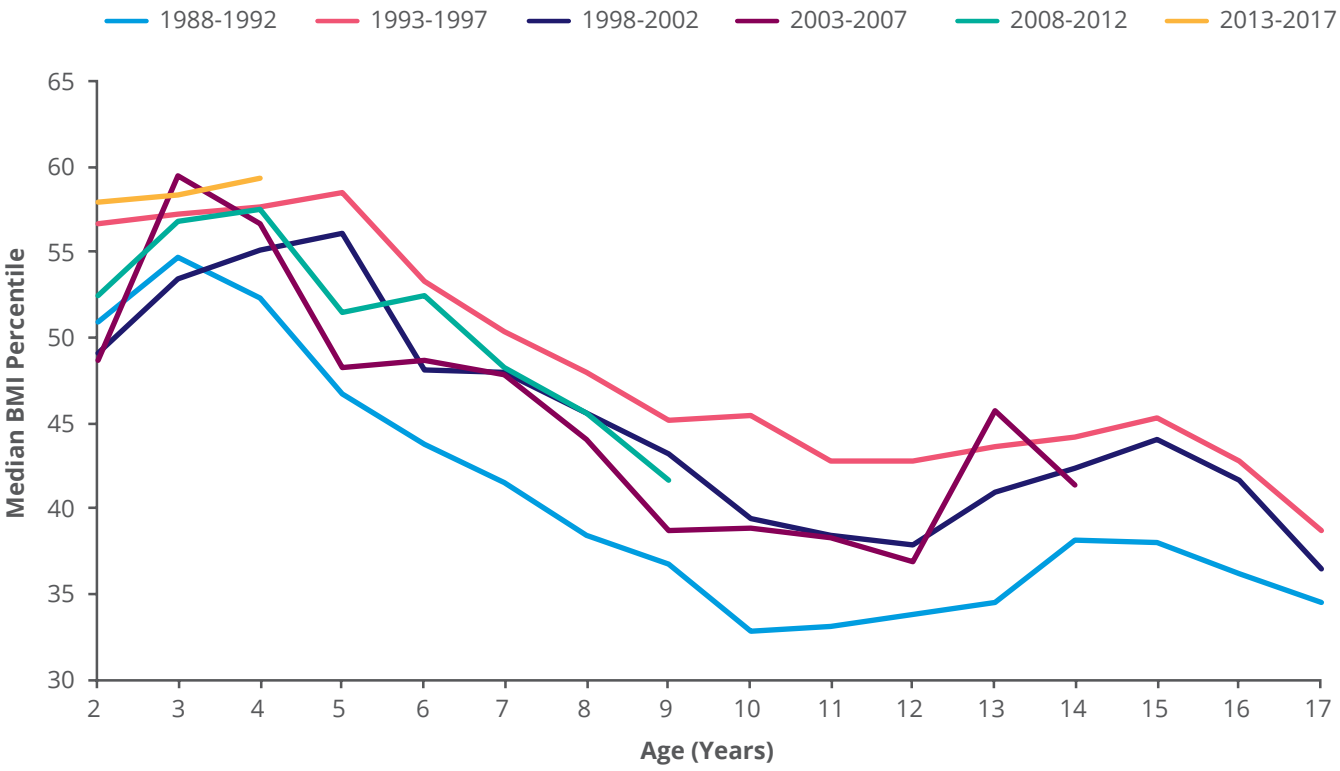
TABLE 4
BMI percentile classification

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

NUTRITION

Figure 26 below shows the median BMI percentile for children between 2 and 17 years of age by birth cohort. As the birth cohorts become more recent, the median BMI percentile at age 2 increases for the most part. The nutritional status is relatively stable in the early ages (2-4 years) followed by a gradual decline in BMI percentiles over the ages until approximately age 10 years. Median BMI percentile seems to stabilize after 10 years of age.

FIGURE 26
Median BMI percentile for children (2-17 years) with CF, by birth cohort, 2017



NUTRITION

BMI PERCENTILE BY SEX

Figures 27 and 28 show the BMI percentile status for males and females in children under 2 years (N = 228) and children 2-17 years (N = 1,522). For both males and females, the median BMI percentiles have been increasing over time. While males show a slightly higher median BMI percentile in earlier years, by 2017, there is no difference between the sexes (Figure 29).

FIGURE 27

BMI percentile status for children (under 2 years) with CF, by sex, 2017

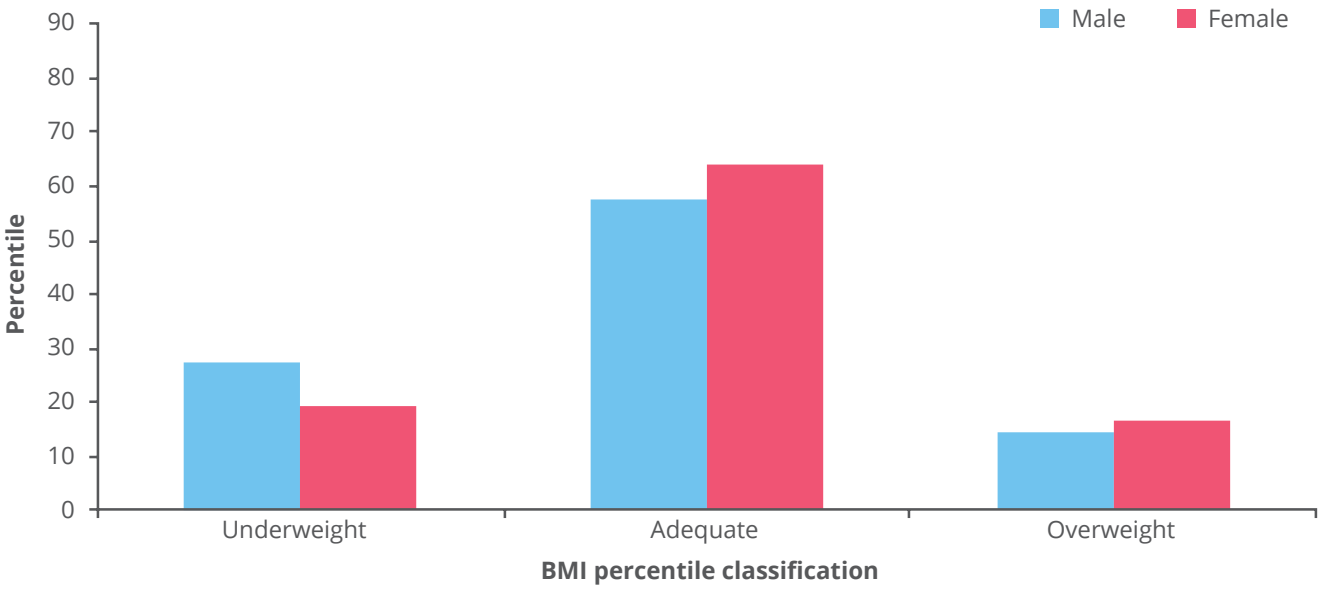


FIGURE 28

BMI percentile status for children (2-17 years) with CF, by sex, 2017

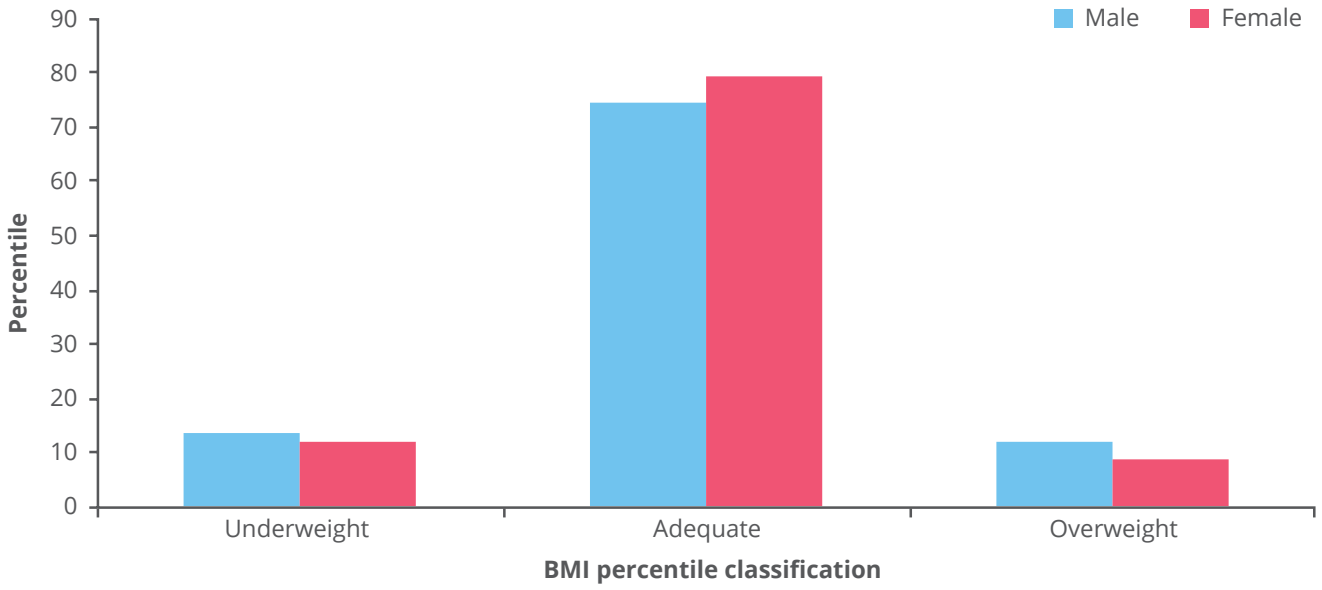
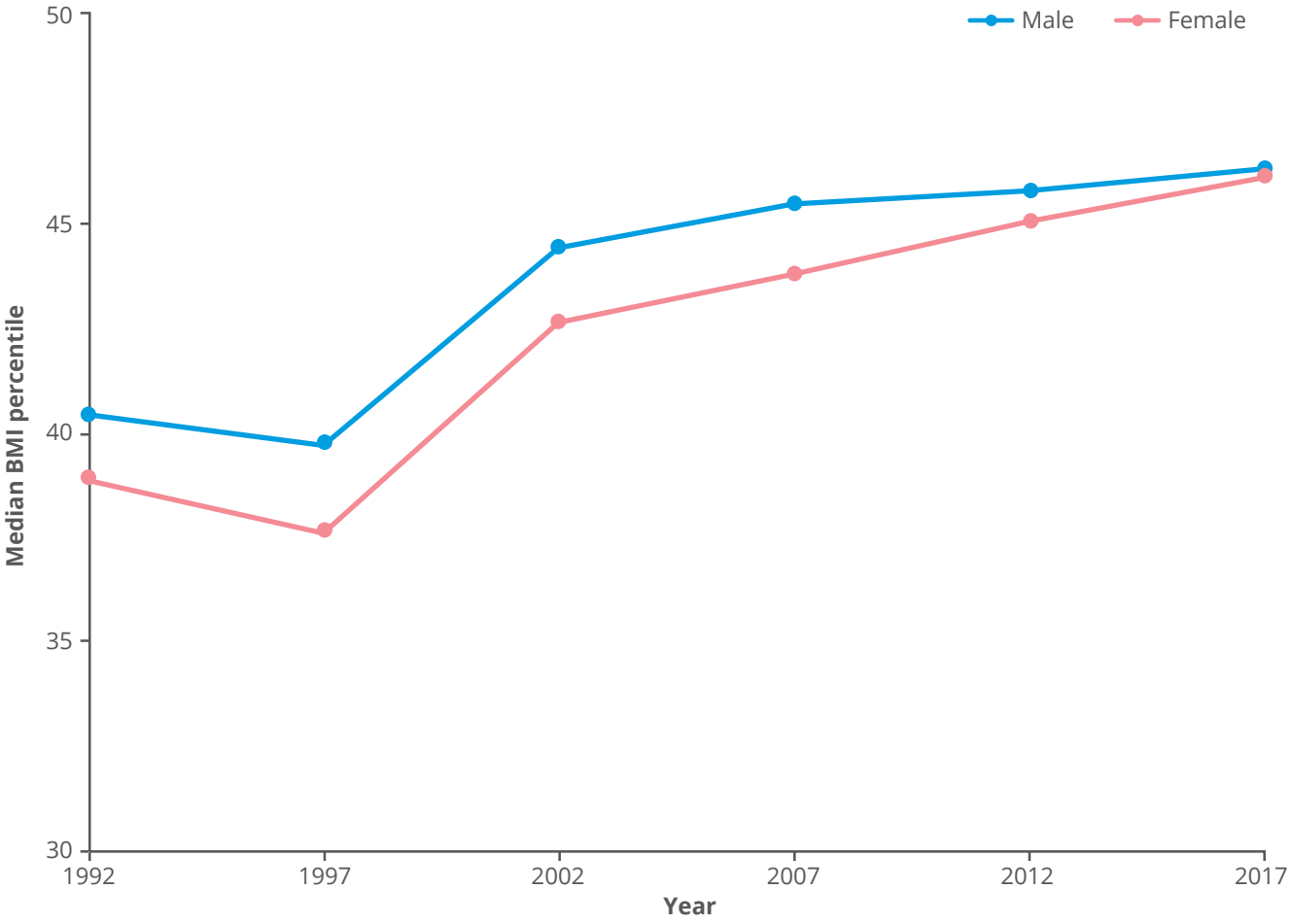


FIGURE 29
Median BMI percentile for children (2-17 years) with CF, by sex, 1992 to 2017



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 were updated in 2016 to follow the WHO guidelines[6]. As such, the proportions of BMI classifications will be different from those described in reports prior to 2016. In 2017, the national median BMI for adults (aged 18 or older) was 22.5 kg/m^2. The majority (65.8%) of the adult CF population had a normal weight while 9.0% were considered underweight and 5.7% were considered obese (Figure 30).

FIGURE 30
BMI status for adults with CF, 2017

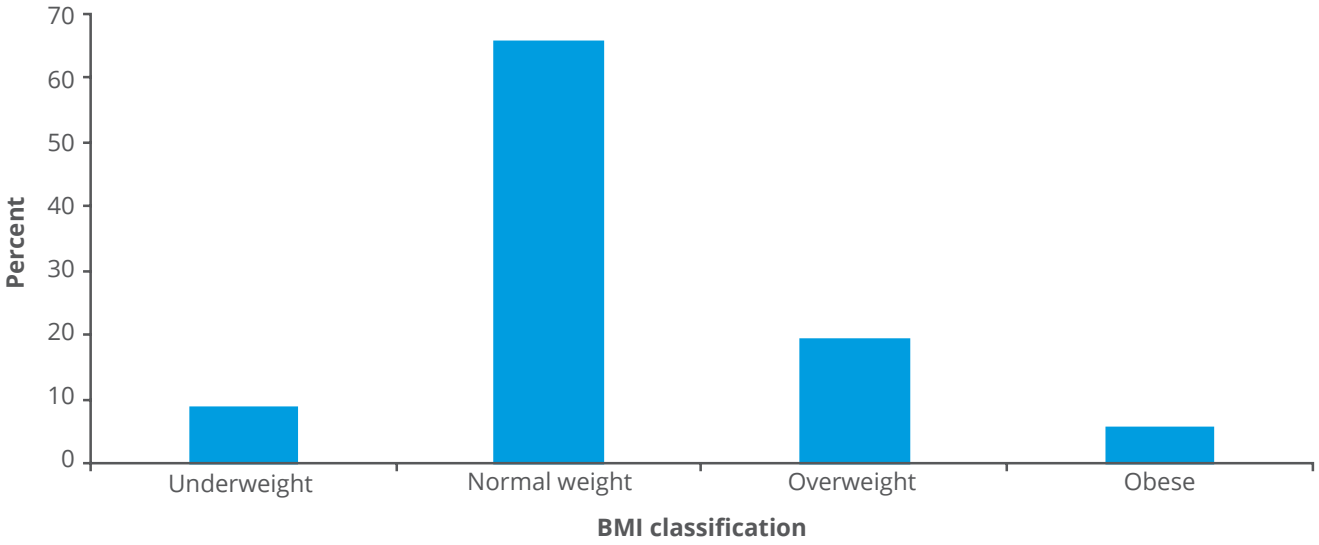


TABLE 5
BMI classification

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 31 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 2017, while more females (12.1%) were considered underweight compared to males (6.5%), the median BMI over the past 25 years has been steadily rising within the CF adult population for both sexes (Figure 32) and can be attributed to fewer individuals who are underweight and more adults classified as either overweight or obese (Figures 33 and 34).

FIGURE 31

BMI status for adults with CF, by sex, 2017

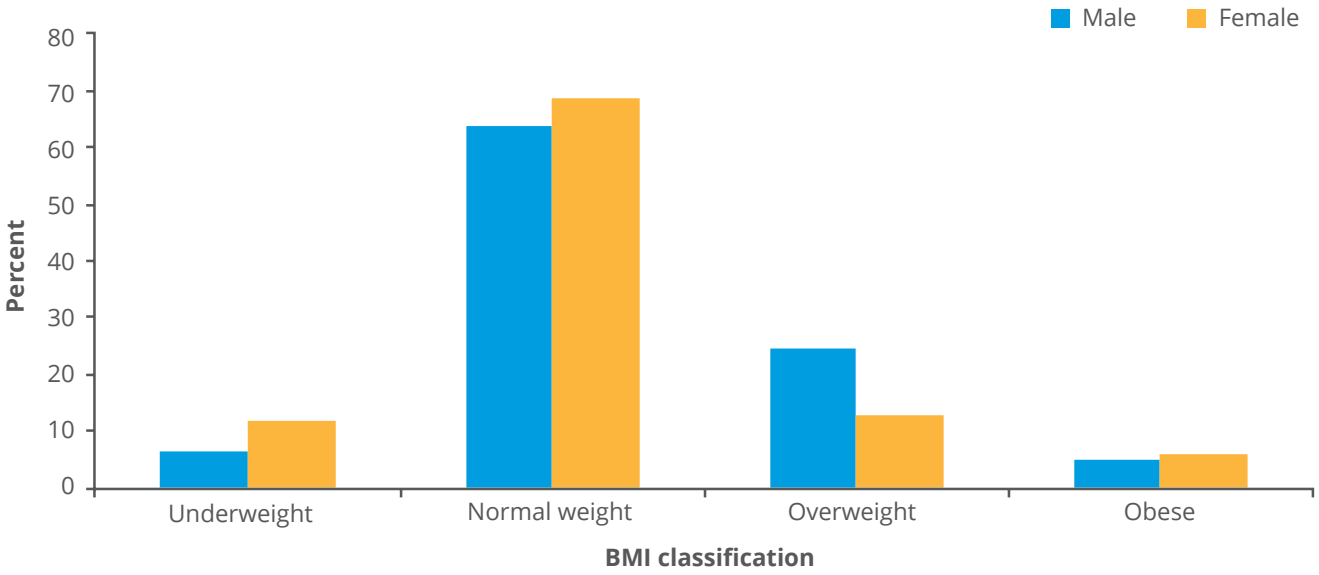


FIGURE 32

Median BMI value for adults with CF, by sex, 1992 to 2017

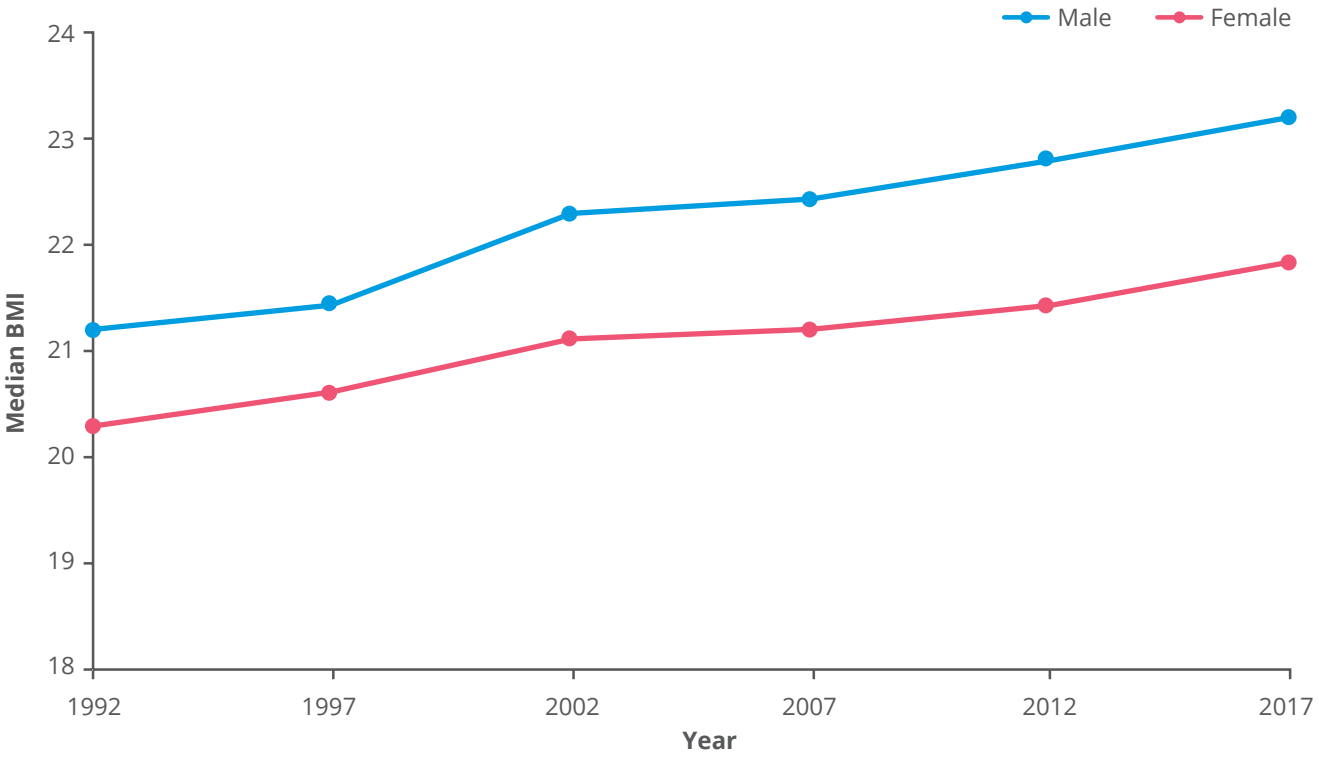


FIGURE 33
Percentage of male adults with CF, by BMI status, 1992 to 2017

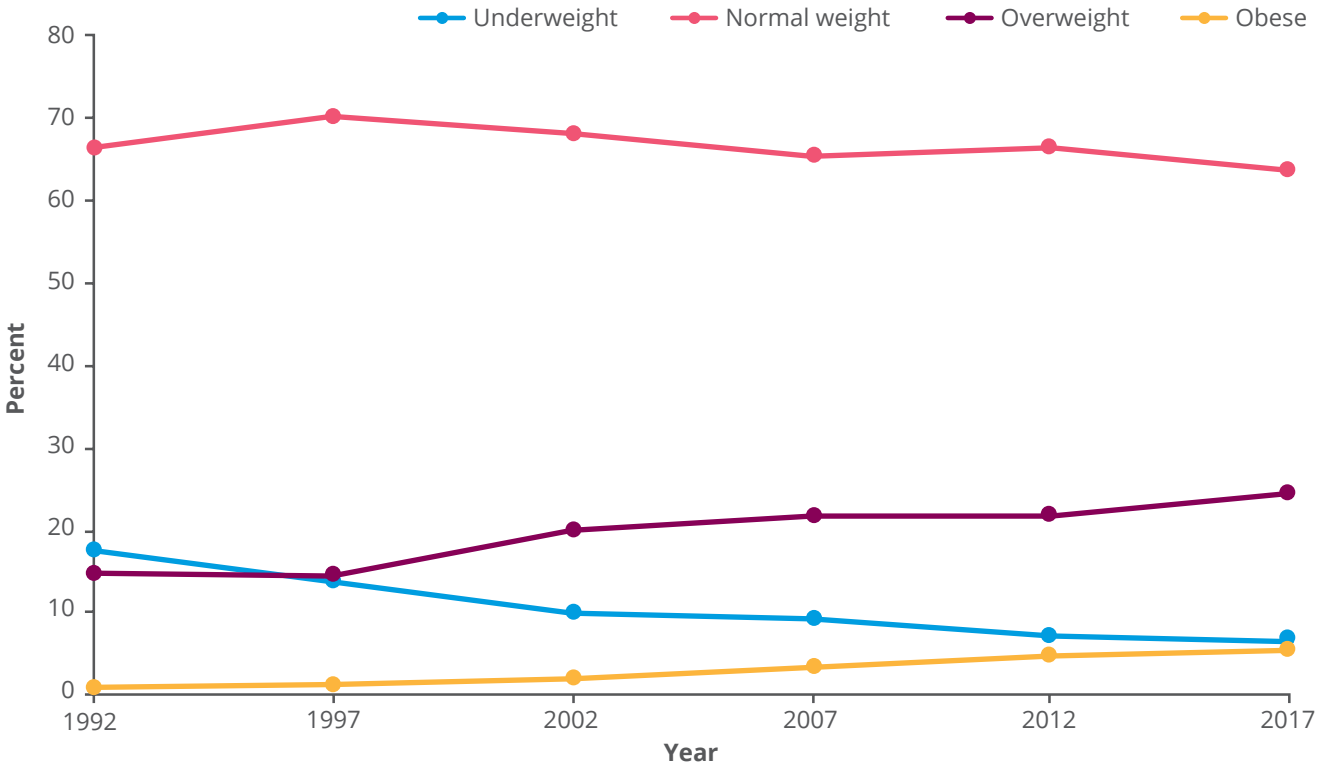
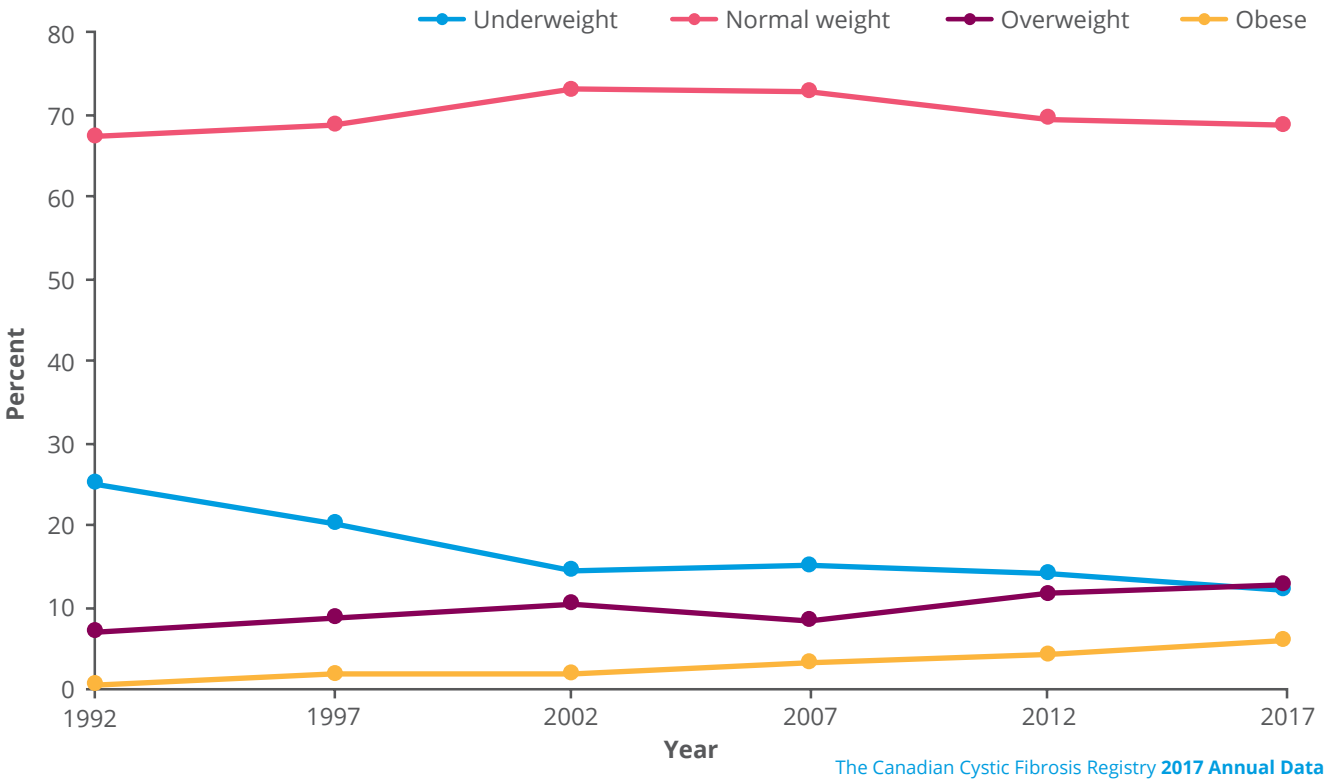


FIGURE 34
Percentage of female adults with CF, by BMI status, 1992 to 2017



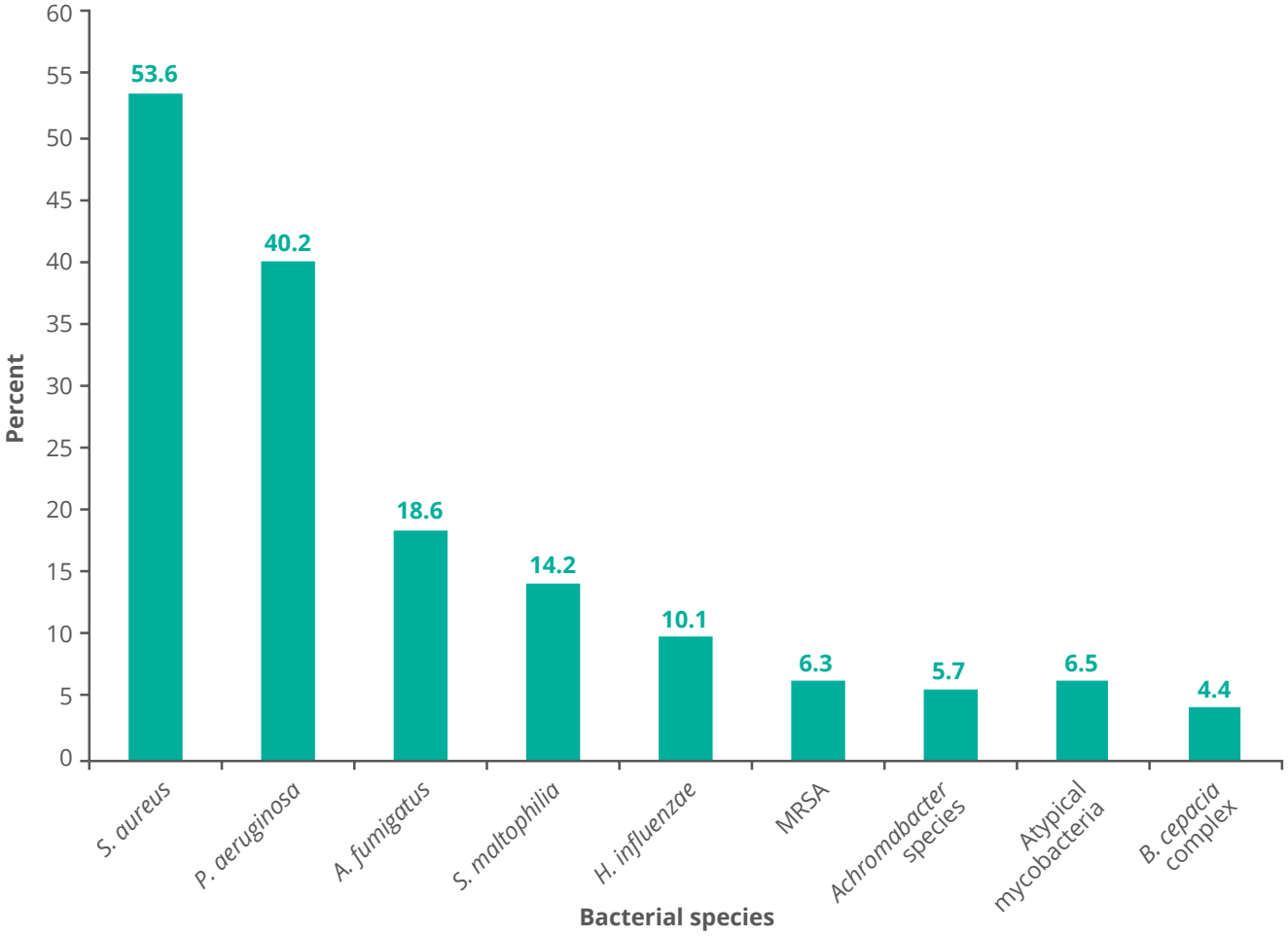
MICROBIOLOGY

BACTERIAL SPECIES AND RESPIRATORY INFECTIONS

Staphylococcus aureus (53.6%) and *Pseudomonas aeruginosa* (40.2%) are the most common pulmonary pathogens in Canadians with CF (Figure 35). The CCFR aims to track relevant bacterial species for the CF population and several have been added in recent years including MRSA (Methicillin-resistant *Staphylococcus aureus*) (2003), *Achromabacter* species (formally called *Alcaligenes* species) (2011) and Atypical mycobacteria (2011).

FIGURE 35

Prevalence of bacterial species cultured from airways of individuals with CF (all ages), 2017



MICROBIOLOGY

Figure 36 shows that over the past several years, there has been a slight decline in prevalence for some of the more common pulmonary pathogens but a slight increase in the less frequently found pathogens such as *Achromabacter* species (formerly *Alcaligenes* species) and Atypical mycobacteria. This may be due, in part, to an increase in reporting of these organisms rather than a true increase in prevalence. When examining the prevalence of pathogens by age (Figure 37), 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 (4.4%). New acquisition of BCC is infrequent and typically, the *Burkholderia* species that is reported is an environmental strain rather than the epidemic cenocepacia strain.

FIGURE 36
Prevalence of respiratory infections of individuals with CF, 2013 to 2017

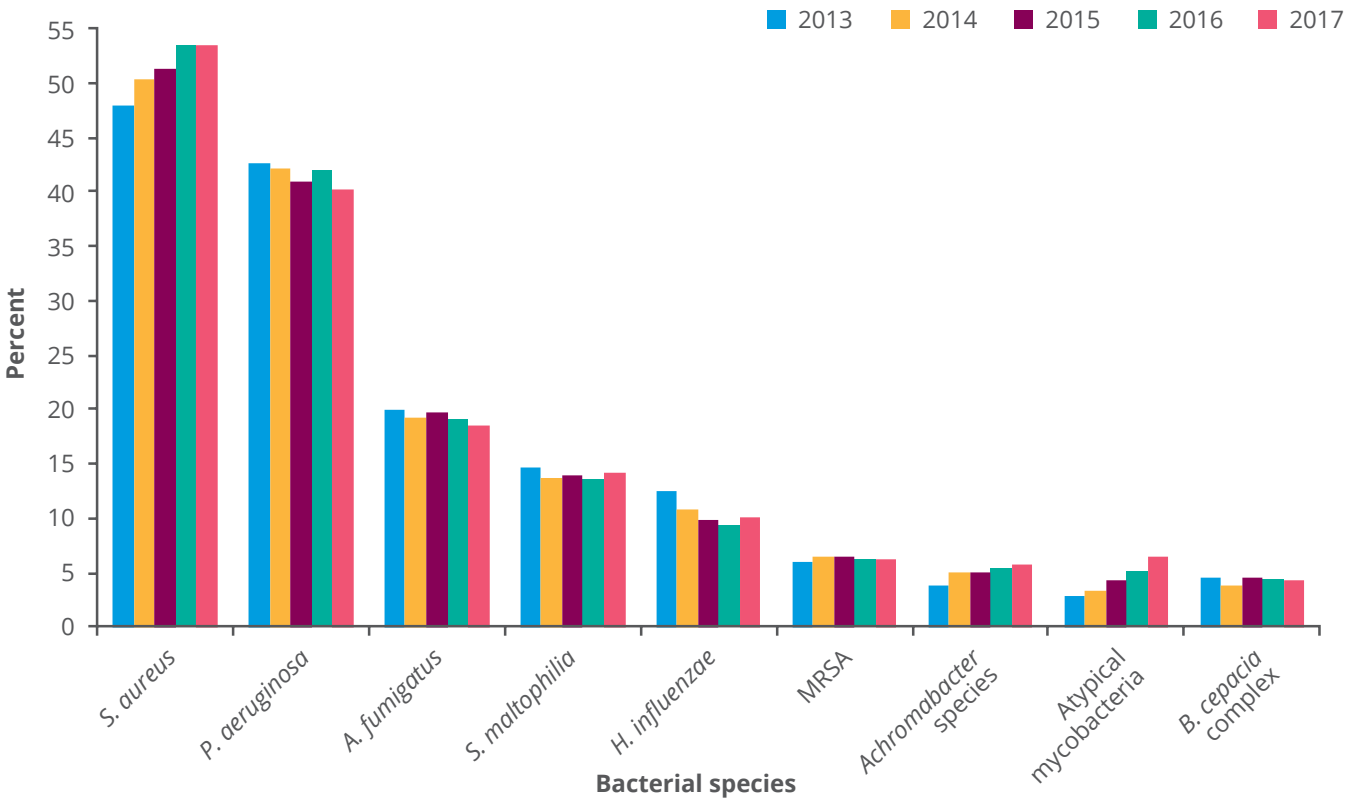
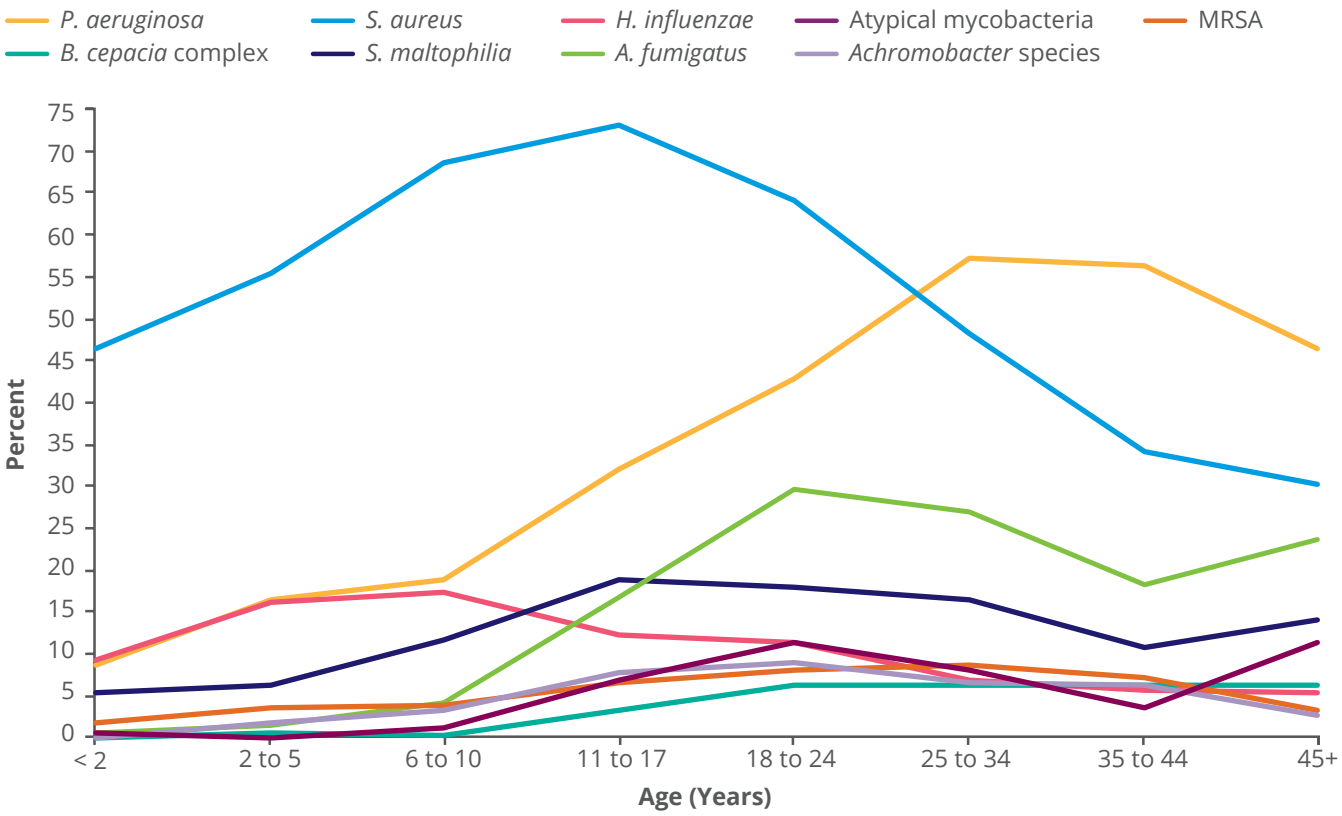


FIGURE 37
Age-specific prevalence of respiratory infections in individuals with CF, 2017



MICROBIOLOGY

BURKHOLDERIA CEPACIA COMPLEX (BCC)

In 2017, there were 191 (4.4%) unique individuals with CF who grew at least one *Burkholderia cepacia* complex (BCC) species. *B. cenocepacia* (32.8%) and *B. multivorans* (25.9%) were the two most common types of BCC species (Figure 38). Of the unique individuals who had BCC in 2017 (N = 191), 163 (85.3%) were adults and 47 (24.6%) adults were over the age of 40 (Figure 39). Not all BCC bacteria have been speciated as 4.9% 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 9.3%, though it was not included in Figure 38 because it is not officially recognized as part of the BCC.

FIGURE 38
***Burkholderia cepacia* complex species prevalence in individuals with CF (N = 191), 2017**

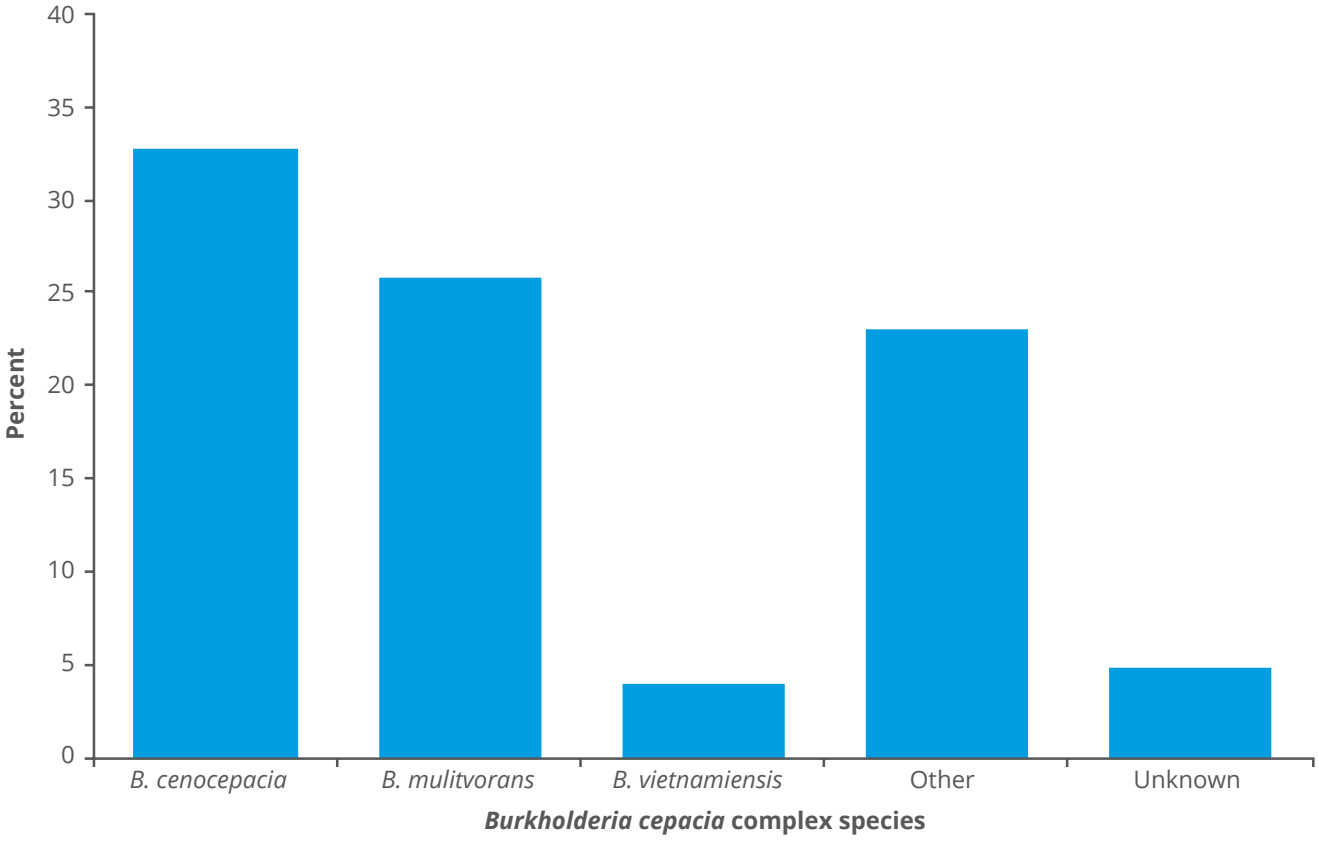
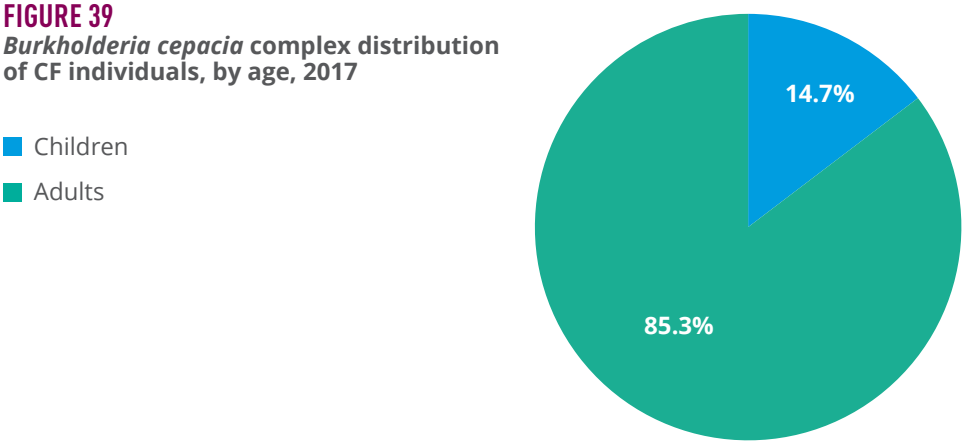


FIGURE 39
***Burkholderia cepacia* complex distribution of CF individuals, by age, 2017**



CF-RELATED DIABETES (CFRD)

In 2017, CFRD was reported in 965 (22.4%) individuals with CF affecting 53 (3.1%) children and 912 (34.8%) adults (Figure 40). Of those individuals with CFRD, 0.3% were under 11 years of age, 48.8% were female, 21.7% have received a transplant, and 47.7% were 35 years of age or older. No children under 6 years of age were reported as having CFRD, however, there is an increasing prevalance of CFRD in the adult population (Figure 41).

FIGURE 40

Percentage of children and adults reported to have CFRD, 2017

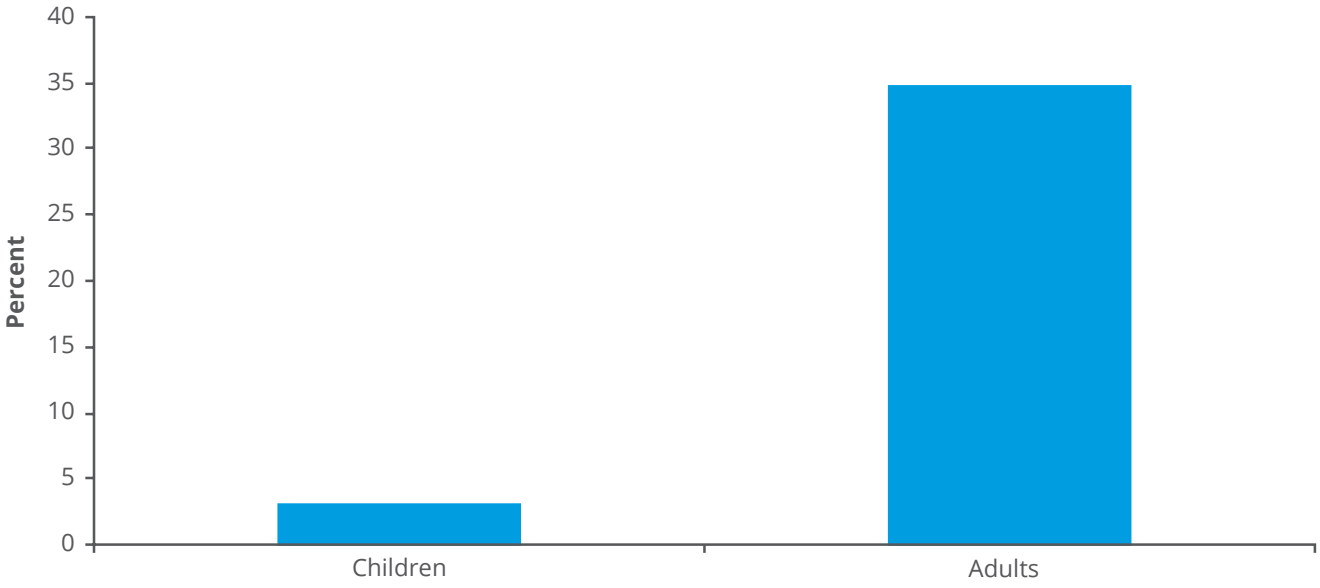
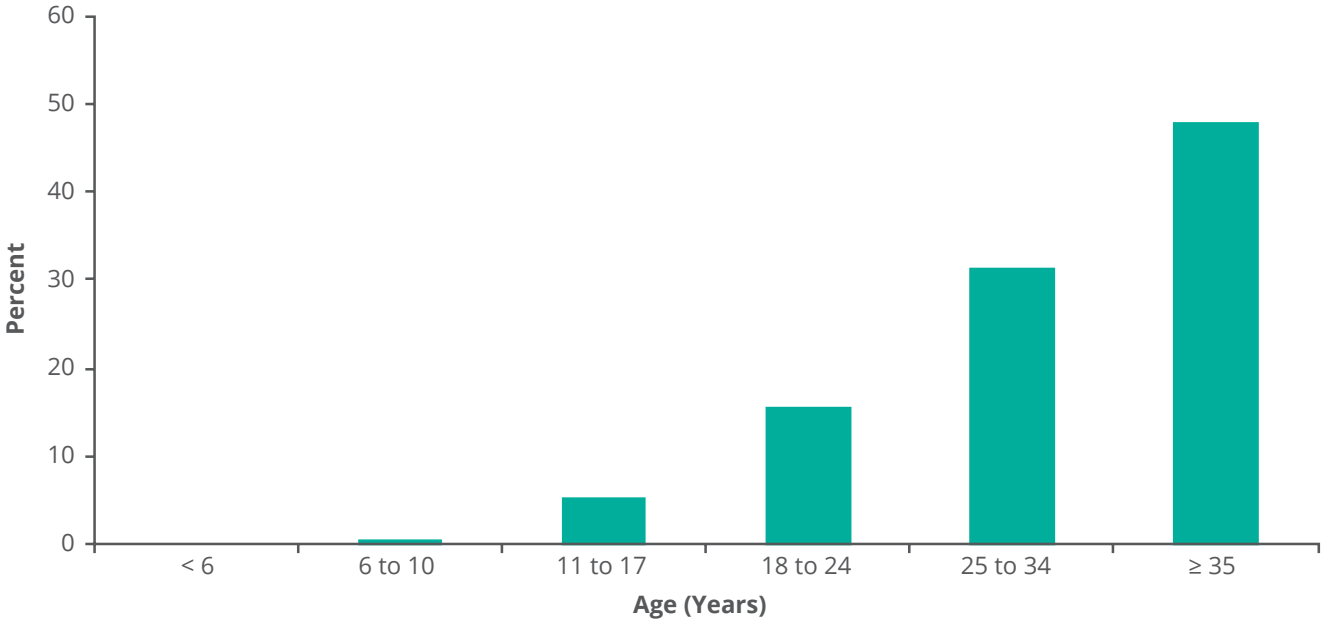


FIGURE 41

Percentage of CF individuals with CFRD by age (N = 965), 2017

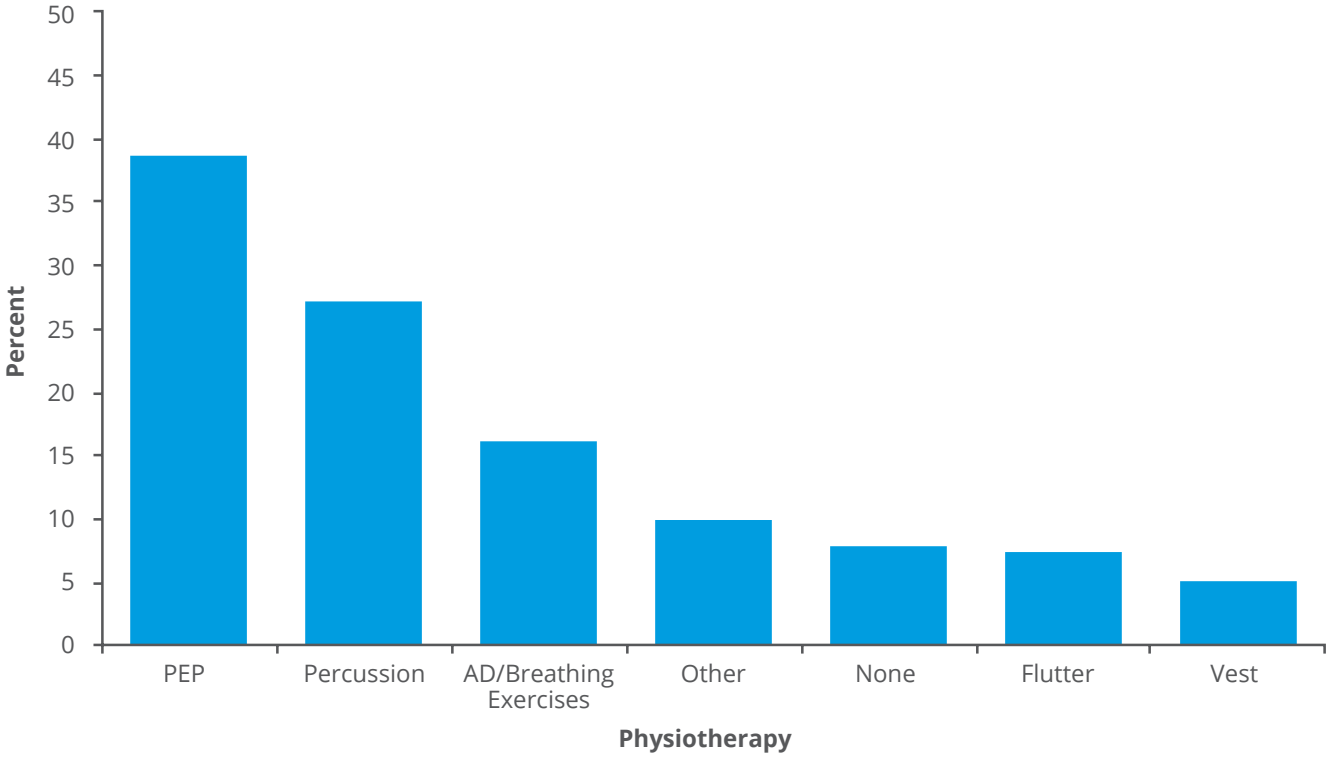


PHYSIOTHERAPY

Physiotherapy is done to help clear mucous from airways using a variety of methods. Figure 42 shows the multiple forms of physiotherapy that are tracked in the CCFR. The most commonly used form of therapy are positive expiratory pressure (PEP) (38.8%) and percussion (27.1%) while 7.9% were reported as not doing any form of physiotherapy.

Note: Individuals who have ever received a lung transplant (7.3% of the 2017 reported CF population) were excluded from these calculations because, typically, chest phyisotherapy is not part of routine post-transplant treatment.

FIGURE 42
Physiotherapy usage of CF individuals (N = 3,994), 2017



MEDICATIONS

In 2017, there were a total of 3,470 individuals over the age of 6 years and have never received a transplant (1,160 children 6-17 years and 2,310 adults). Figure 43 shows that of those individuals, 2,241 (64.6%) were prescribed mucolytic therapy during the calendar year (hypertonic saline and/or Dornase alfa).

Note: Individuals who have undergone lung transplantation previously were excluded from these calculations because, typically, the medications listed are not typically part of routine post-transplant treatment.

There were 1,565 individuals over the age of 6 years who have never received a transplant and were reported to have *Pseudomonas aeruginosa* in 2017 which include 312 children (6-17 years) (19.9%) and 1,253 adults (80.1%). There were 228 children (6-17 years) (73.1%) and 975 adults (78.8%) who were prescribed inhaled antibiotic treatment, and 71 children (6-17 years) (22.7%) and 744 adults (59.4%) who were prescribed macrolide therapy (azithromycin) (Figure 44).

Of the 426 CF patients on cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapy in 2017, 281 (66.0%) are taking Lumacaftor/Ivacaftor, 123 (28.6%) are taking Ivacaftor and the remaining 23 (5.4%) on other CFTR modulator therapies.

MEDICATIONS

FIGURE 43
Percentage of CF individuals on mucolytics, by age group, 2017

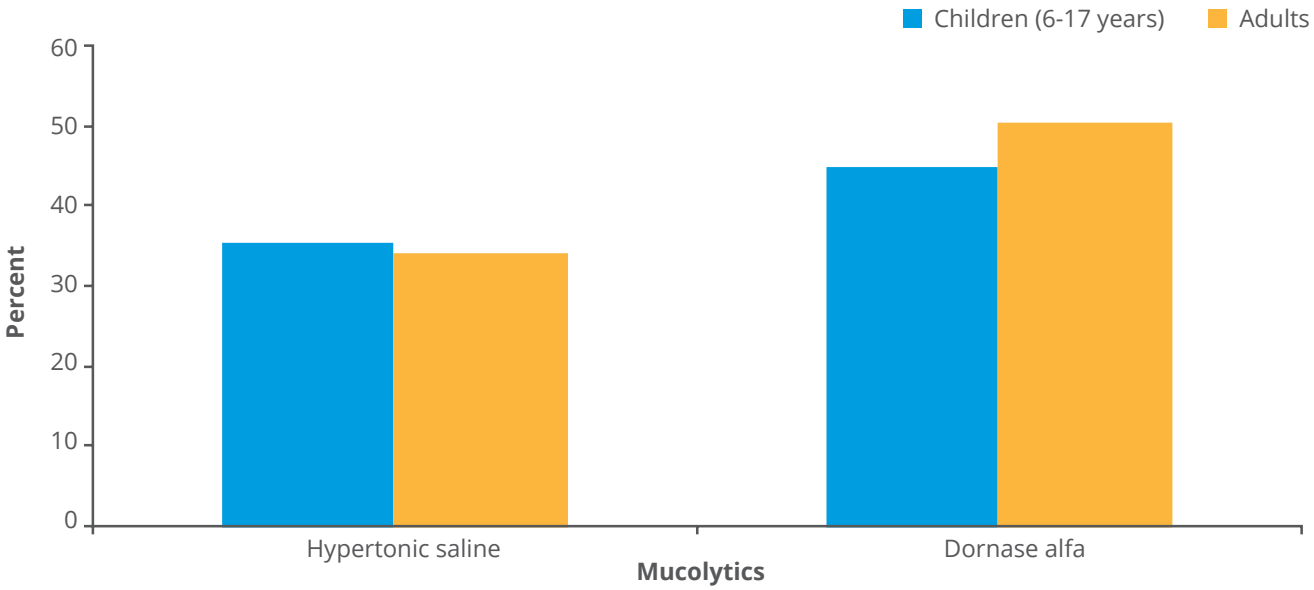
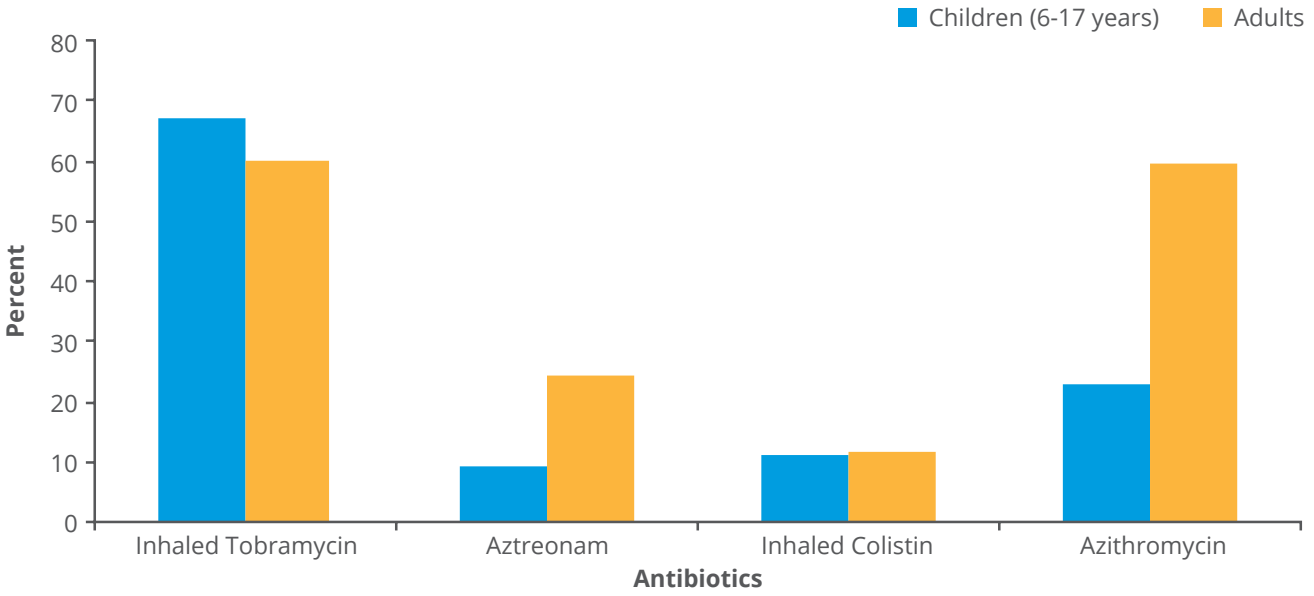


FIGURE 44
Percentage of CF individuals on antibiotics, by age group, 2017



HOSPITALIZATION AND HOME IV

In 2017, there were 1,180 (27.4%) individuals with CF who spent over 26,000 days in hospital from a total of 2,113 hospitalizations recorded which do not include visits to the out-patient CF clinics (Table 6). A total of 4,255 (98.7%) individuals with CF visited a CF clinic at least once with 3,387 (78.6%) having three or more clinic visits. Out of all individuals with CF reported on in 2017, there were more children (91.8%) than adults (70.1%) belonging to the latter group. At home, individuals with CF had over 18,000 days on IV antibiotics from a total of 972 courses.

TABLE 6
Total number of hospital days and home IV courses recorded for individuals with CF, 2017

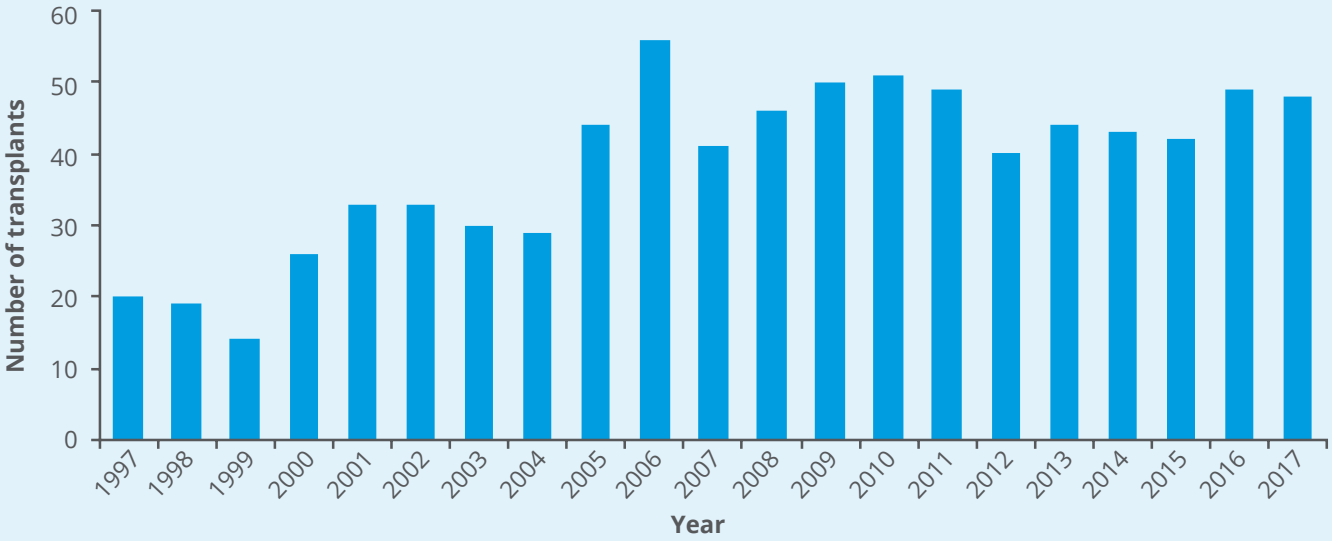
	TOTAL NUMBER
Hospital Days	26,365
Hospitalizations	2,113
Clinic Visits	19,419
Home IV Courses	972
Home IV Days	18,108

TRANSPLANTS

Figure 45 shows the number of transplants carried out per year as reported in the CCFR. In 2017, 46 individuals with CF received a transplant with a median age at the time of transplant of 28.1 years. Although the numbers provided represent primarily lung transplants, individuals who received other combinations or organs (e.g. lung and liver, liver, heart andlung, heart etc.) are also included in the total.

As of December 31, 2017, there were 815 individuals with CF reported as having received one or more transplants with a median age at the time of transplant of 28.5 years. Of these patients, 54 (6.6%) have received at least two lung transplants, 466 (57.2%) were reported as being alive and 258 (55.4%) of those living patients were male.

FIGURE 45
Number of transplants per year of CF individuals, 1997 to 2017



SURVIVAL

In 2017, there were 60 deaths recorded in the CCFR. Figure 46 shows the cumulative number of deaths and the age range from 2013 to 2017. Over the past two decades, a gradual increase in the median age of death can be seen. The median age of death was 33.6 years in 2017 compared to 26.2 years in 1997 (Figure 47). This number tells us that half of those who died were younger than 33.6 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. 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 1997 (Figure 48). In 2017, this value was 1.4%. The most common cause of death was related to pulmonary complications and 28 (46.7%) individuals with CF who passed away in 2017 were post-transplant.

FIGURE 46
Age at death, 2013 to 2017

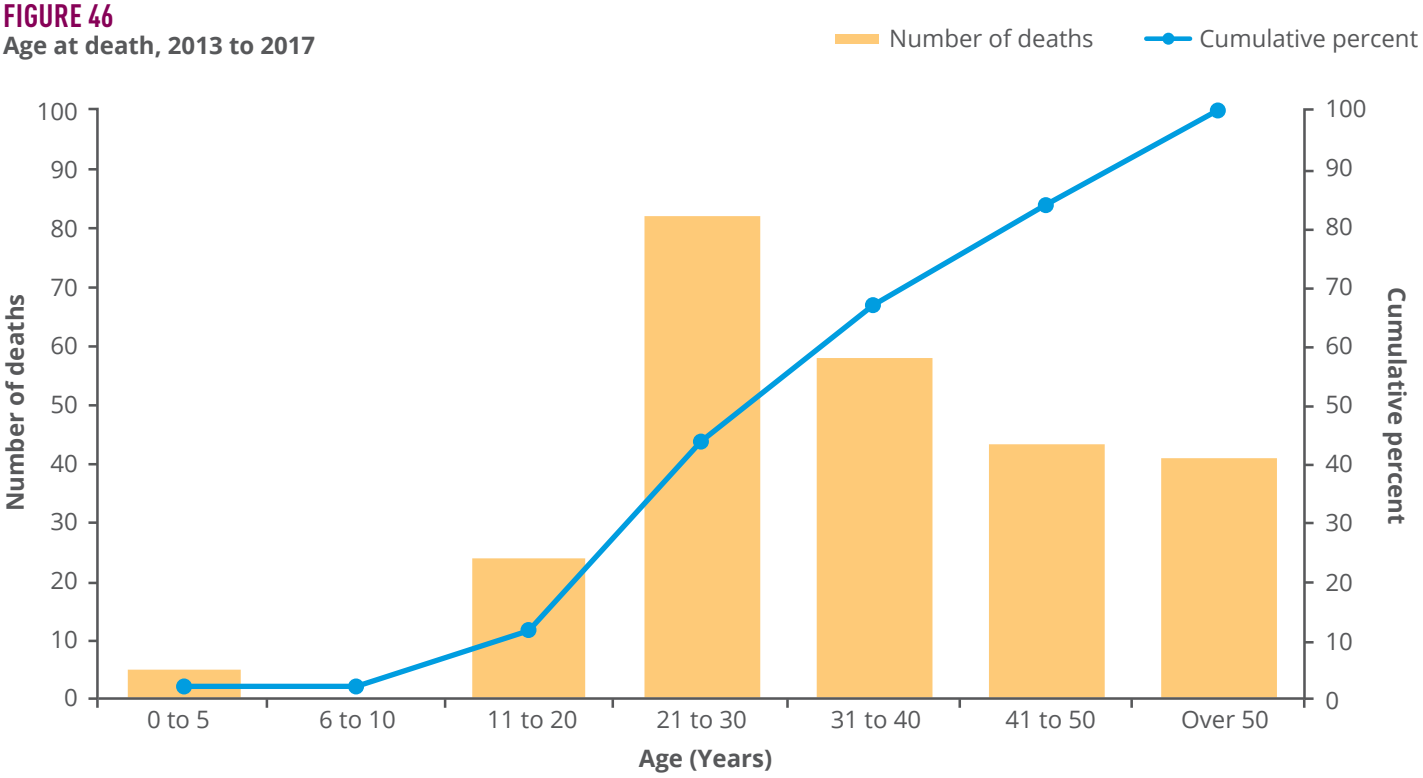


FIGURE 47
Median age at death per year, 1997 to 2017

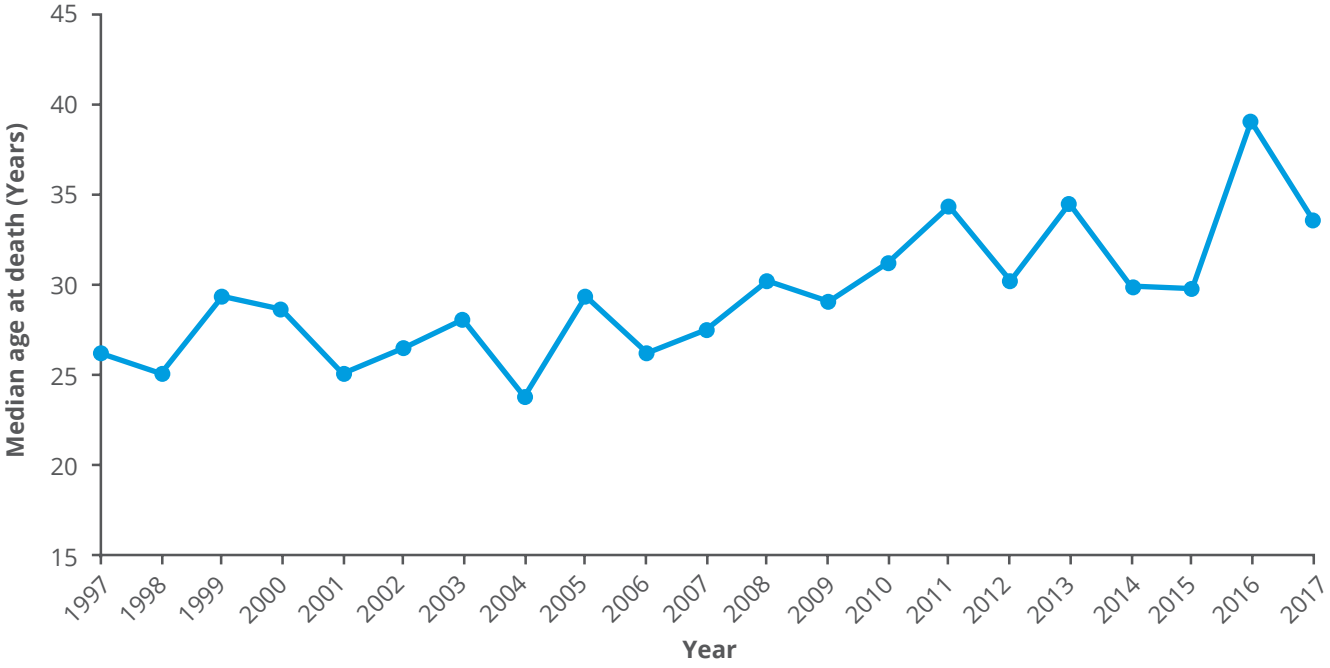
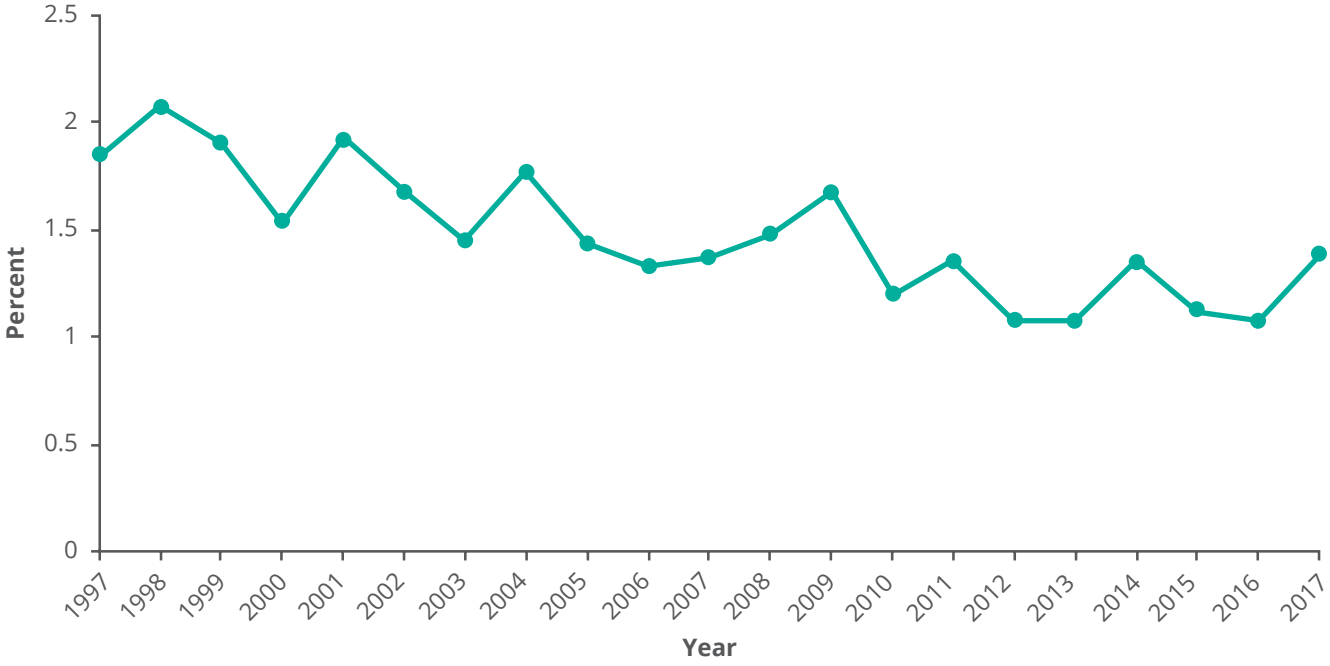


FIGURE 48
Death rate per year, 1997 to 2017



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 (2013-2017) included 4,927 people with CF and 253 deaths. The number of individuals with CF lost-to-follow-up was 156 (3.2%).

In 2017, the median age of survival is currently estimated to be **52.3 years of age** (Figure 49). In 2012, the estimated median age of survival passed 50 years of age for the first time and it has remained steady since. The estimated median age of survival is the age beyond which we expect 50% of babies with CF born today to live, under the assumption that recent age-specific mortality rates will hold for the rest of their lives. 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].

The median age of survival remains stable for both males and females with males continuing to have a higher median age of survival compared to females (Figure 50). 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 51 and indicates that survival is higher for those born more recently. The probability of surviving beyond age 20 years is 91.3% for those born in 1985 or later compared to 62.1% for those born before 1975.

FIGURE 49

Estimated median age of survival for a moving 5-year window with 95% confidence intervals, 1983 to 2017

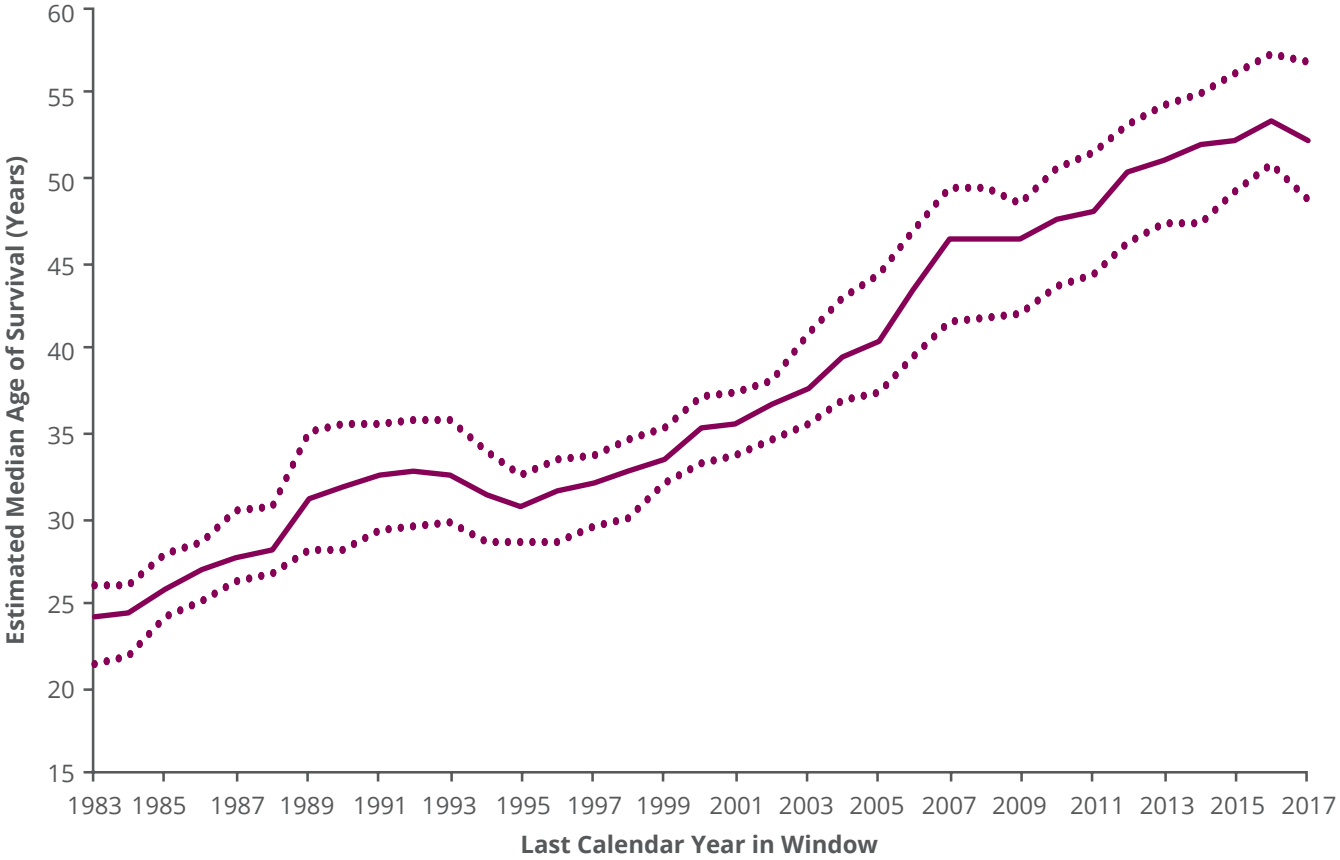


FIGURE 50
Estimated median age of survival for a moving 5-year window with 95% confidence intervals, by sex, 1983 to 2017

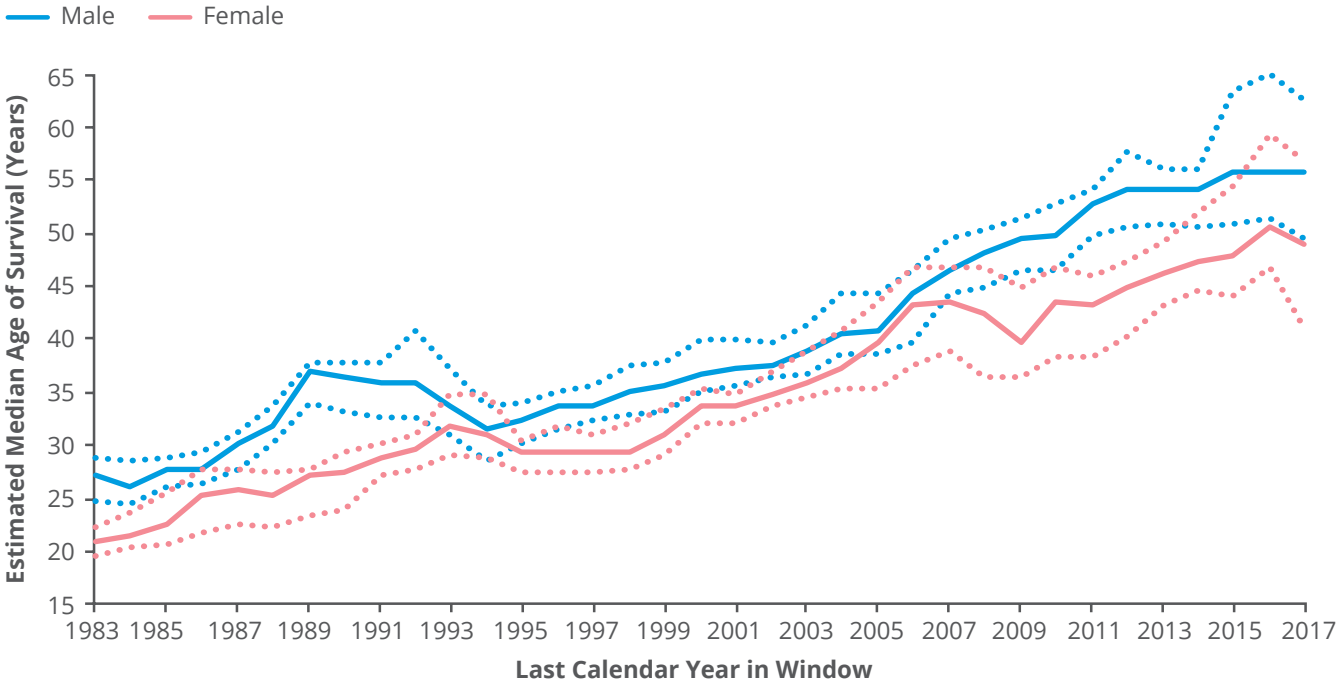
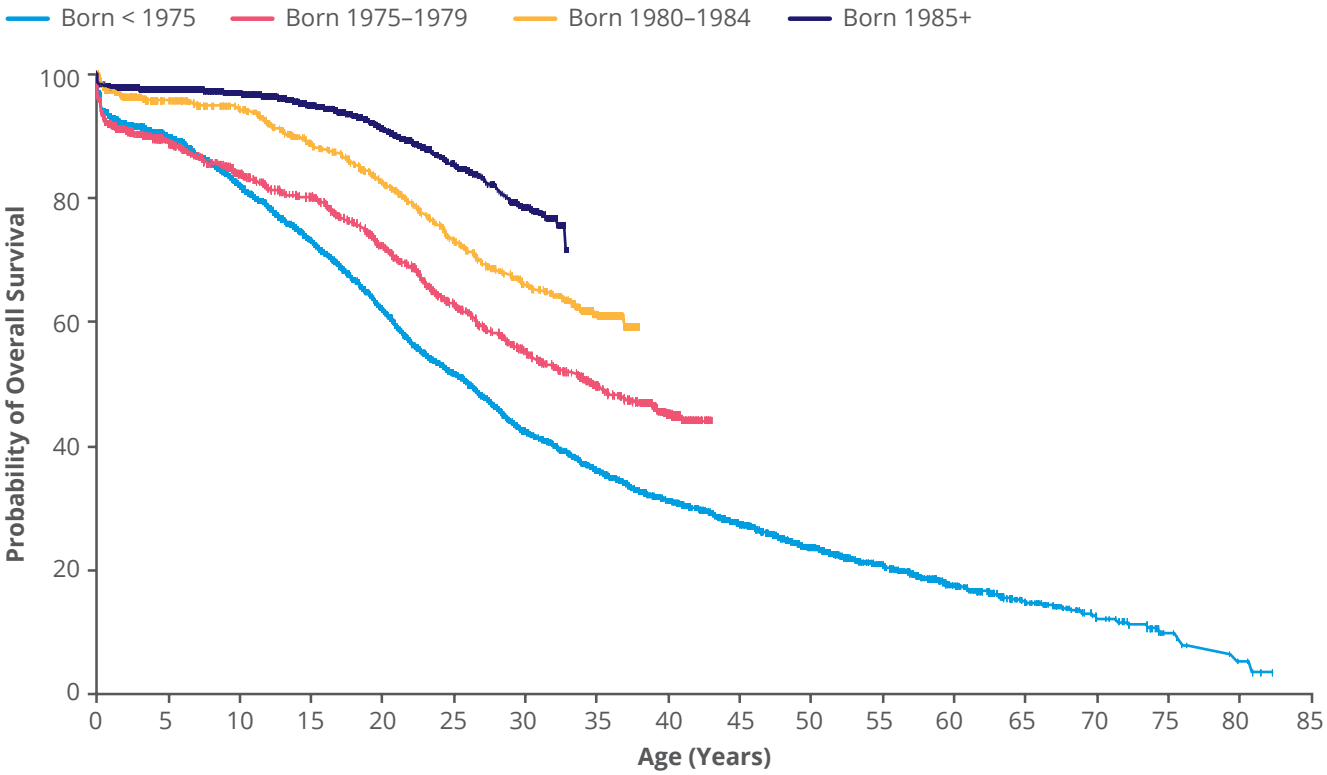


FIGURE 51
Overall survival of individuals with CF, by birth cohorts, 2017

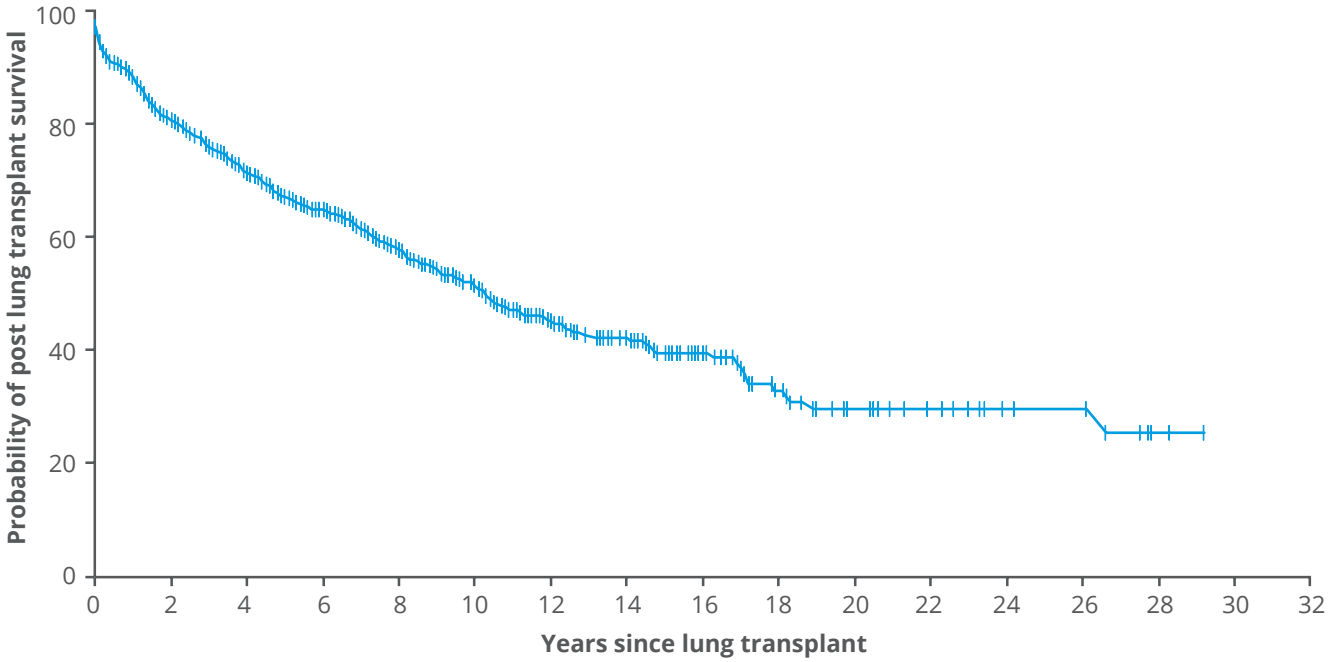


SURVIVAL

POST LUNG TRANSPLANT SURVIVAL

Between 1988 and 2017, there were 788 lung transplants that took place and 341 deaths post lung transplant. Figure 52 shows the probability of survival post lung transplant which is 88.2% at one year, 75.9% at three years and 67.0% at five years. Overall, 50% of those patients transplanted today would be expected to live beyond 10.3 years following lung transplantation.

FIGURE 52
Post lung transplant survival, 2017



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 born today 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 who have died AND those who are still alive. It is the **age beyond which we expect 50% of babies with CF born today to live, under the assumption that recent age-specific mortality rates will hold for the rest of their lives**[9]. This is NOT the age at which people born today 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 2017 is 52.3 years, we are saying that if a child with CF is born in Canada in 2017, they have a 50% chance of living beyond 52.3 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 52.3 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 2017.

It is important to note that these survival estimates apply to a population of individuals and do not necessarily apply to any one individual.

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