THE CANADIAN CYSTIC FIBROSIS REGISTRY

2018 ANNUAL DATA REPORT

Cystic Fibrosis Canada
Fibrose kystique Canada

CYSTIC FIBROSIS

Cystic fibrosis (CF) is a rare disease affecting over 4,370 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 mucus causes severe respiratory problems. Mucus 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 $261 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.

Suggested citation (print): Cystic Fibrosis Canada. (2018). *The Canadian Cystic Fibrosis Registry 2018 Annual Data Report.* Toronto, Canada: Cystic Fibrosis Canada.

Suggested citation (online): Cystic Fibrosis Canada. (2018). *The Canadian Cystic Fibrosis Registry 2018 Annual Data Report.* Retrieved from https://www.cysticfibrosis.ca/uploads/RegistryReport2018/2018RegistryAnnualDataReport.pdf

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Cover page: CF individual from Saskatchewan

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Published: December 2019

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THE CANADIAN CYSTIC FIBROSIS REGISTRY

The *Canadian Cystic Fibrosis Registry* (CCFR) is a collection of national CF patient 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 2018 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, 2018.

I am pleased to share the 2018 Annual Data Report for the Canadian Cystic Fibrosis Registry (CCFR) and to announce that numbers have remained stable over the last year, including the estimated median age of survival for a Canadian born with cystic fibrosis (CF). These steady health outcomes are a result of the contributions of dedicated healthcare teams, resilient patients, advocates, and researchers; we thank you for your commitment to advancing knowledge and helping people with CF.

In the 1970s, Cystic Fibrosis Canada founded, and has since managed, the Canadian CF Registry. The CCFR is Canada's only and the world's longest-running comprehensive CF database. With the goal of monitoring clinical trends in Canadian CF patients, the Canadian Cystic Fibrosis Registry has made a remarkable impact on our understanding and treatment of the disease, and has been invaluable in demonstrating the incredible progress of CF care and research in Canada and beyond.

Cystic Fibrosis Canada continues to prioritize the CCFR, expanding its use into new programs, including enhancing patient experiences by providing patients access to their data stored in the CCFR through the *MyCFLifePortal* and facilitating clinical trials through the Cystic Fibrosis Canada Accelerating Clinical Trial Network (CFCanACT). In addition, this year, the Registry was expanded to capture more medical testing data and in an effort to assist clinics in their practice, reporting features have also been enhanced.

While data from the CCFR has become the foundation for new programs, it continues to be a valuable resource for Canadian and global researchers alike. Over the last several years, the Registry has had nearly 50 requests for data from CF researchers across Canada and around the world, on topics related to survival, CF-related diabetes, epidemiology of CF, therapies and more. We are proud to be able to support researchers advance knowledge on the disease through the high quality data captured in the CCFR.

On behalf of Cystic Fibrosis Canada, I would like to extend my sincere gratitude to the clinic staff and patients who make this report possible. This incredible resource would not be possible without you.

Sincerely,

Kelly Grover
President and CEO
Cystic Fibrosis Canada

I would like to take this opportunity to thank all the individuals living with CF and their families for allowing their data to be included in The Canadian CF Registry. I would also like to acknowledge all the clinic staff for their continued support of the Registry. Without all of you, the Registry would not be possible.

The Canadian CF Registry is an extremely valuable resource of national CF data that is used to improve the quality of patient care, influence research, and bolster advocacy efforts across the country. Canadian researchers and those worldwide, continue to use registry data to answer important clinical questions which will further our understanding of issues facing Canadians with CF.

These data are also leveraged to critically assess health outcomes of new therapies and identify potentially eligible patients for new and emerging treatments. The Registry team has worked hard this year to improve the functionality of Ad-hoc Reporting that is available within the Registry platform. Having the ability to quickly and efficiently identify potentially eligible subjects for clinical trials of new therapies is a priority for CF Canada. This feature will streamline this process so that more patients may have the opportunity to be part of this pivotal process to identify life-saving medications to treat CF.

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, Unity Health Toronto, St. Michael's site, Toronto

Cystic Fibrosis Canada
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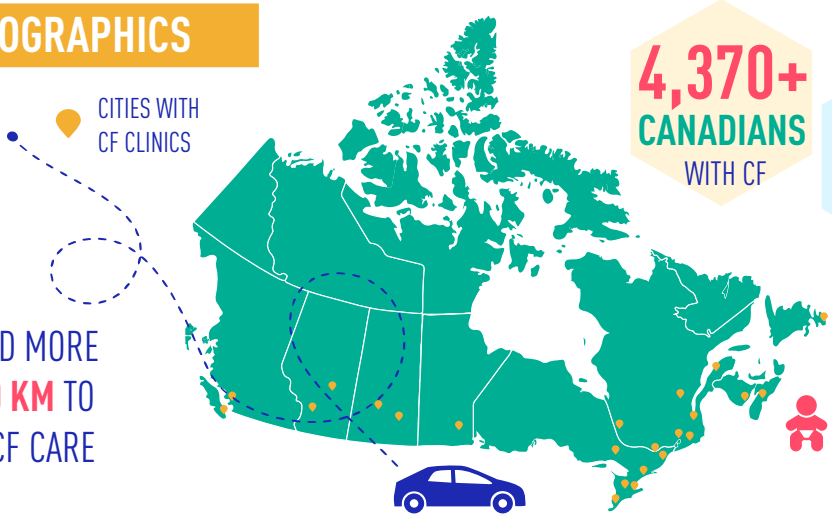
2018 HIGHLIGHTS FROM THE CANADIAN CF REGISTRY

DEMOGRAPHICS



4,370+ CANADIANS WITH CF

16% ARE ADULTS OVER 40

MEDIAN AGE **23.5** YEARS

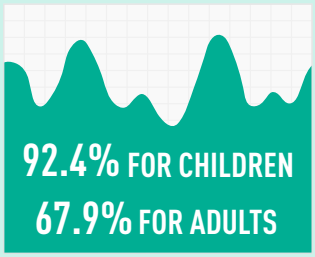
18% TRAVELLED MORE THAN **250 KM** TO RECEIVE CF CARE

111 NEW CF DIAGNOSES

59 NEWBORN SCREENING

HEALTH OUTCOMES

MEDIAN FEV_1% PREDICTED



64% ADULTS **75%** CHILDREN HAVE AN ADEQUATE WEIGHT

CYSTIC FIBROSIS TREATMENT & CARE

58 PEOPLE RECEIVED A **LUNG TRANSPLANT**

39% HAVE ***PSEUDOMONAS AERUGINOSA*** INFECTIONS

50% OF **PEOPLE OVER 35** HAVE **CF-RELATED DIABETES**

COLLECTIVELY

18,900+ CLINIC VISITS

26,500+ HOSPITAL DAYS

17,700+ HOME IV THERAPY DAYS

SURVIVAL

ESTIMATED **MEDIAN AGE OF SURVIVAL** IS **52.1** YEARS OF AGE

ESTIMATED **MEDIAN POST-LUNG TRANSPLANT SURVIVAL** IS **10.5** YEARS

DEMOGRAPHICS

CANADIANS WITH CYSTIC FIBROSIS

In 2018, there were a total of 4,371 individuals with CF who attended one of the 42 accredited CF clinics across Canada (Figure 1), with 111 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 37.5% (Figure 2). Individuals are associated with the province in which they attended a CF clinic. Those who attended CF clinics in multiple provinces in 2018 will be counted in each of those provinces for provincial-level statistics, and therefore these figures should not be summed to obtain a national total. However, individuals are only counted once (*i.e.* unique individuals) in the national reported numbers.

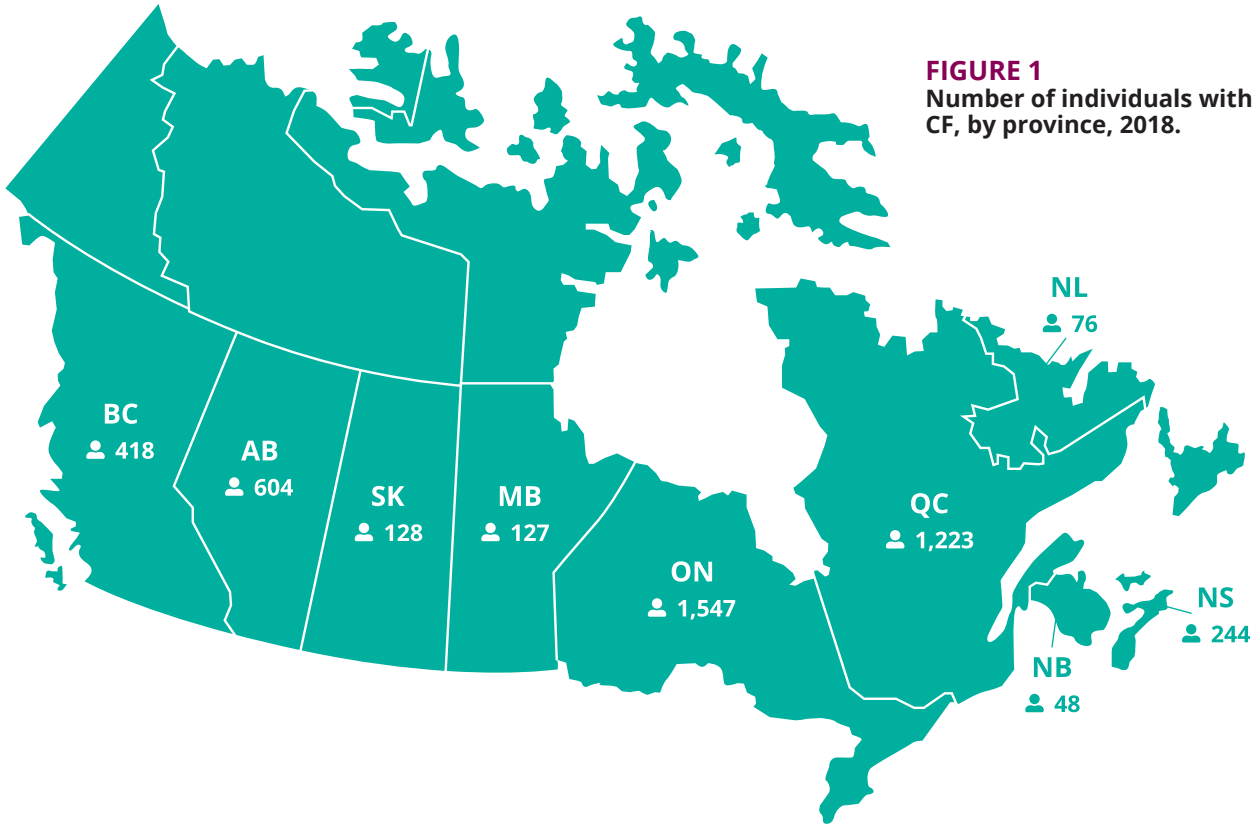


FIGURE 1
Number of individuals with CF, by province, 2018.

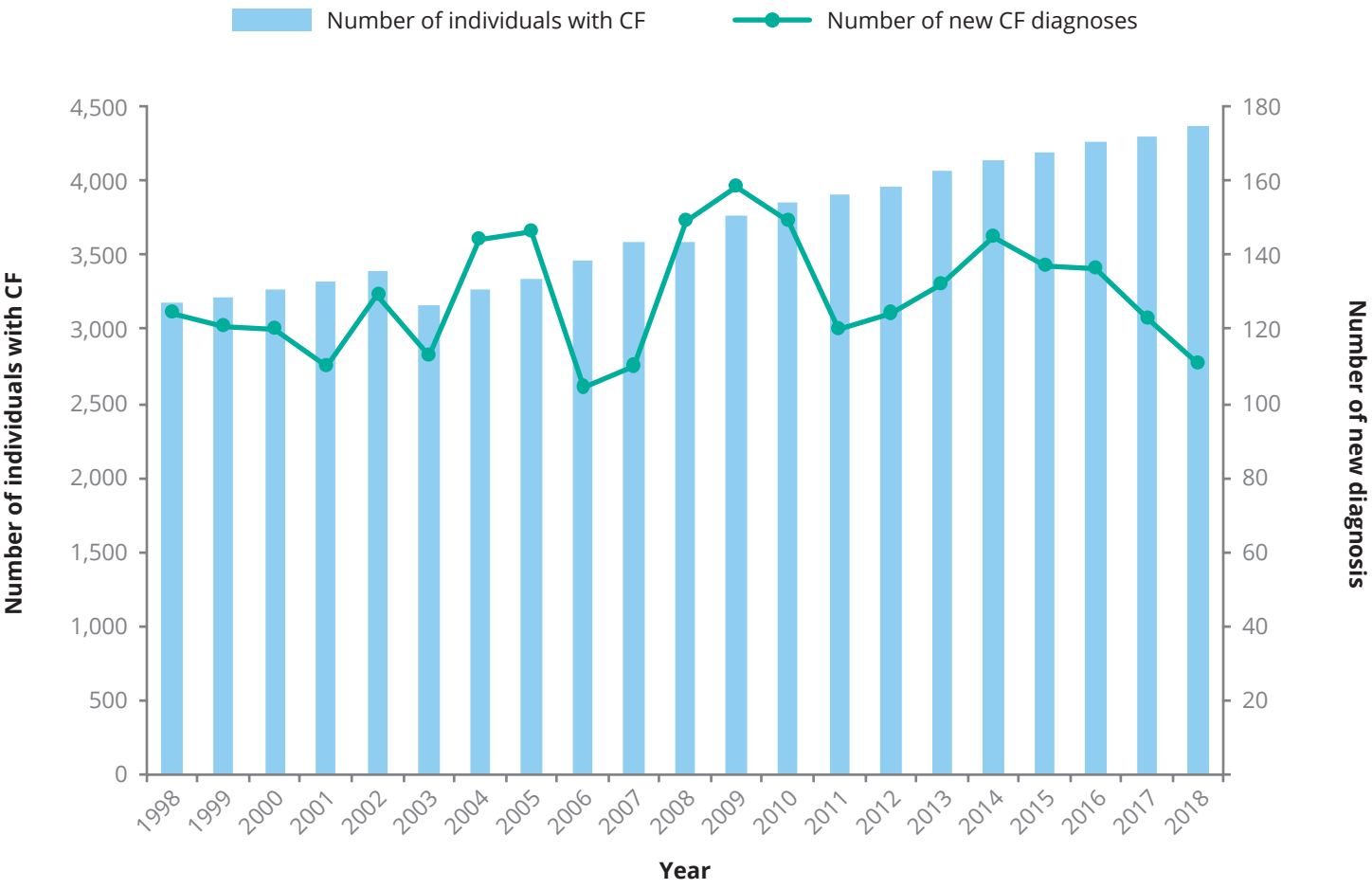
PROVINCE *	NUMBER OF INDIVIDUALS WITH CF	FEMALE	MALE	ADULTS	CHILDREN
BC	418	182	236	259	159
AB	604	289	315	342	262
SK	128	52	76	67	61
MB	127	54	73	68	59
ON	1,547	742	805	948	599
QC	1,223	568	655	787	436
NB	48	26	22	34	14
NS	244	111	133	156	88
NL	76	30	46	55	21

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

DEMOGRAPHICS

CANADIANS WITH CYSTIC FIBROSIS

FIGURE 2
Total number of individuals with CF and new CF diagnoses, 1998 to 2018.

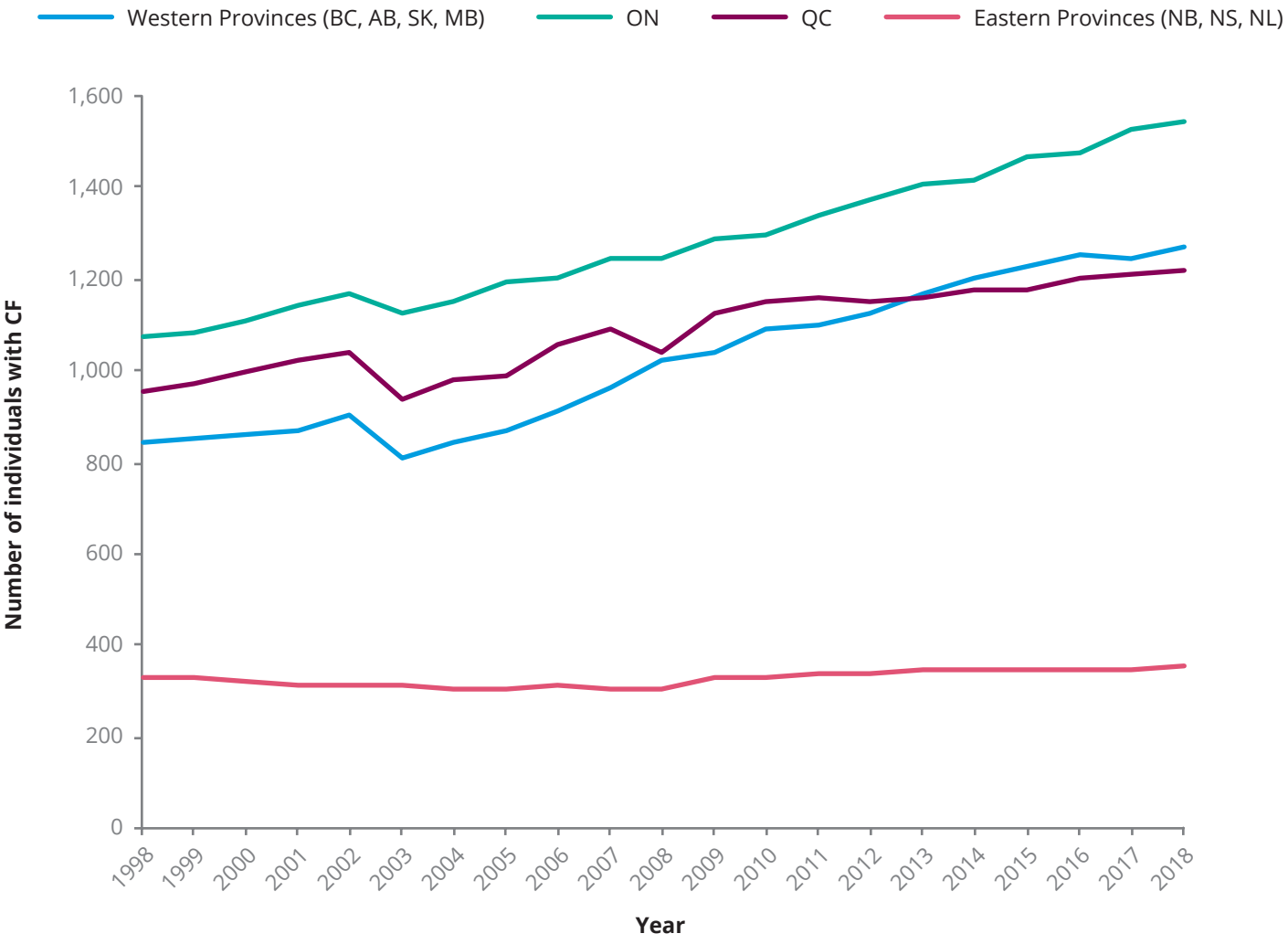


DEMOGRAPHICS

PROVINCIAL POPULATION CHANGE

Over the past two decades, the Canadian CF population has grown, with the largest increases seen in clinic visits in Ontario and the western provinces of British Columbia, Alberta, Saskatchewan and Manitoba (Figure 3). Comparing populations between 1998 and 2018, Alberta saw the largest percent growth of almost 80% (Figure 4).

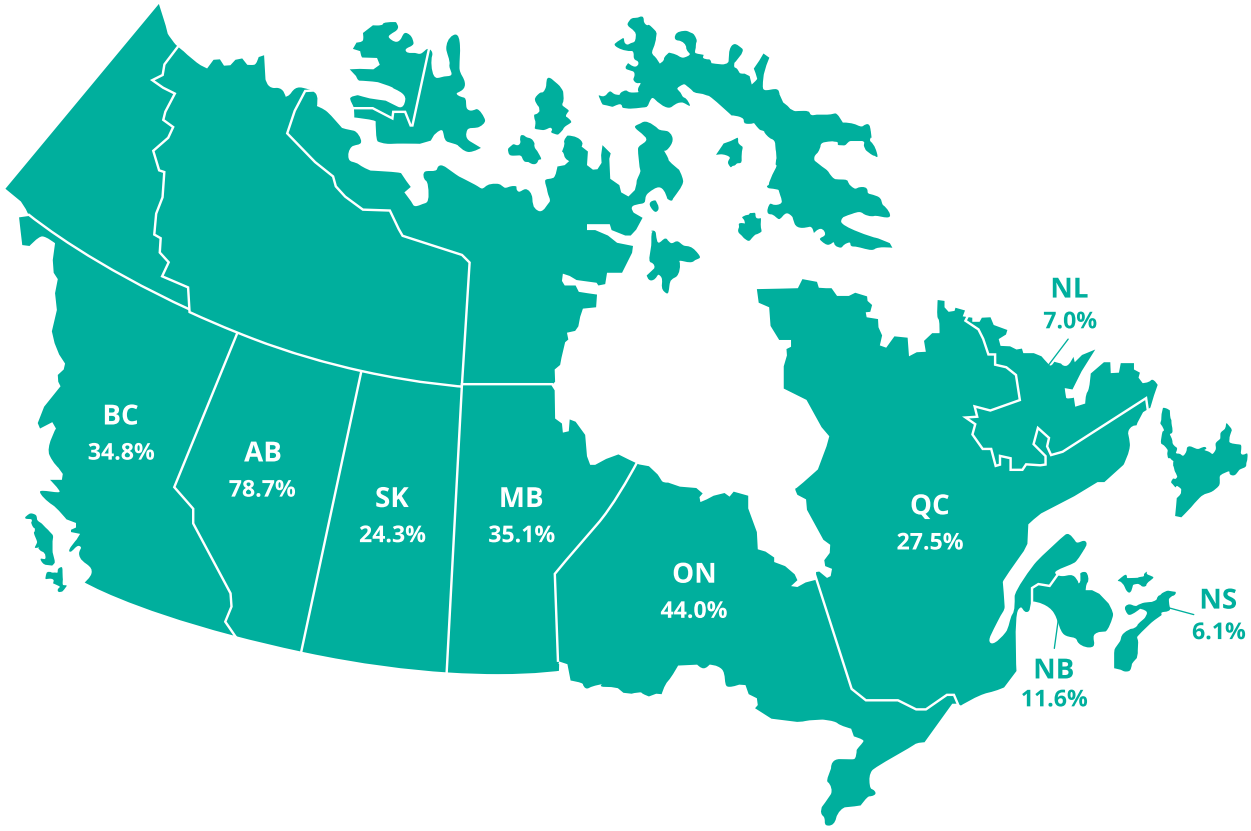
FIGURE 3
CF population growth by region, 1998 to 2018.



DEMOGRAPHICS

PROVINCIAL POPULATION CHANGE

FIGURE 4
CF population change by province, 1998 to 2018.



PROVINCE *	1998	2018	PERCENT CHANGE
BC	310	418	34.8%
AB	338	604	78.7%
SK	103	128	24.3%
MB	94	127	35.1%
ON	1,074	1,547	44.0%
QC	959	1,223	27.5%
NB	43	48	11.6%
NS	230	244	6.1%
NL	71	76	7.0%

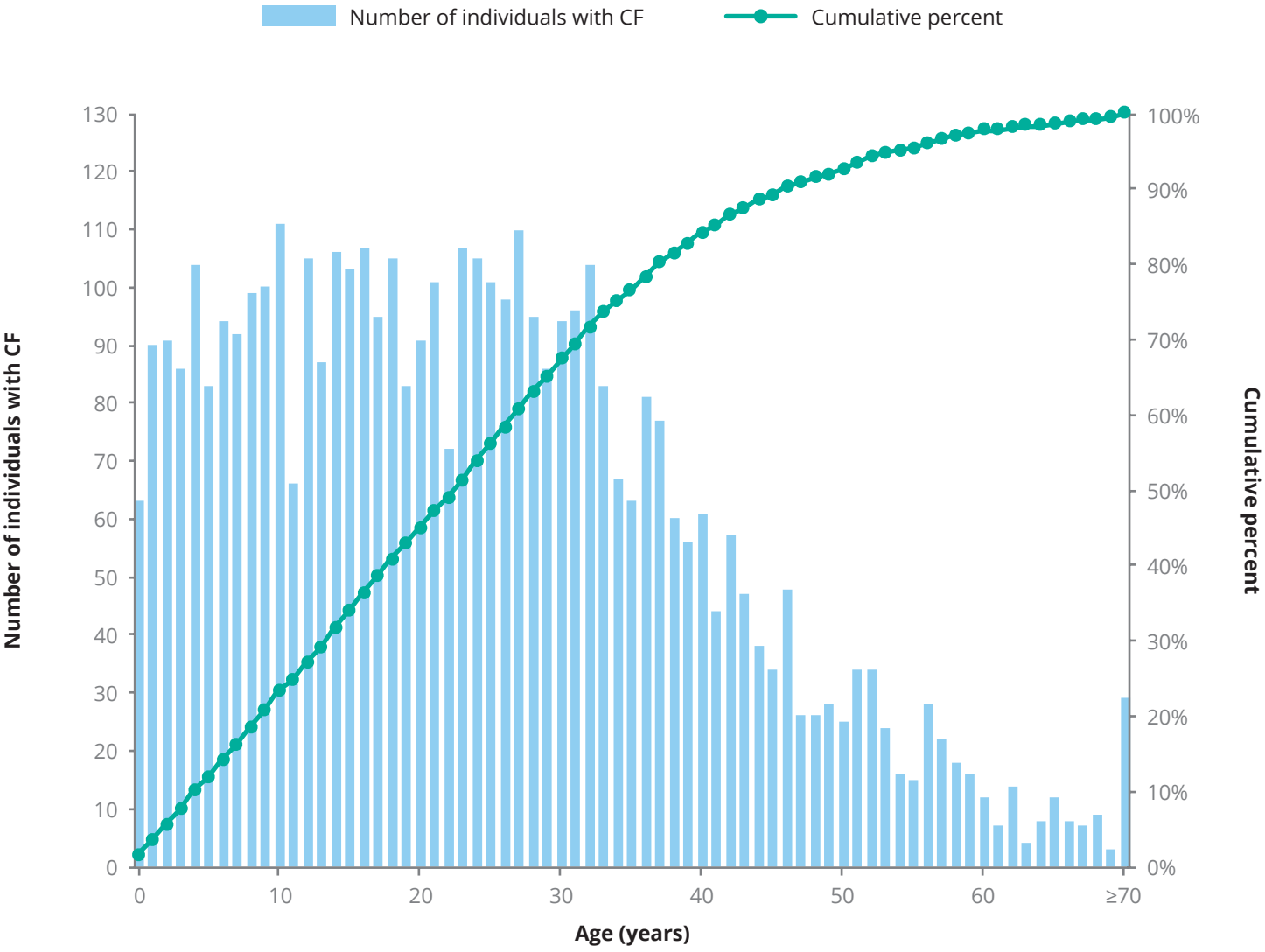
** Individuals with CF living in provinces or territories not listed here are included, if reported on by CF clinics in other jurisdictions.*

DEMOGRAPHICS

AGE DISTRIBUTION OF CANADIANS WITH CYSTIC FIBROSIS

Figure 5 shows the age distribution of the 4,371 Canadians living with CF in 2018. The median age of all individuals reported on in 2018 was 23.5 years. 61.5% of these individuals were adults (over 18 years of age) (see Figure 9 for more details), 15.9% were over 40 years of age, and 0.5% were over 70 years of age.

FIGURE 5
Age distribution of individuals with CF, as of December 31, 2018.

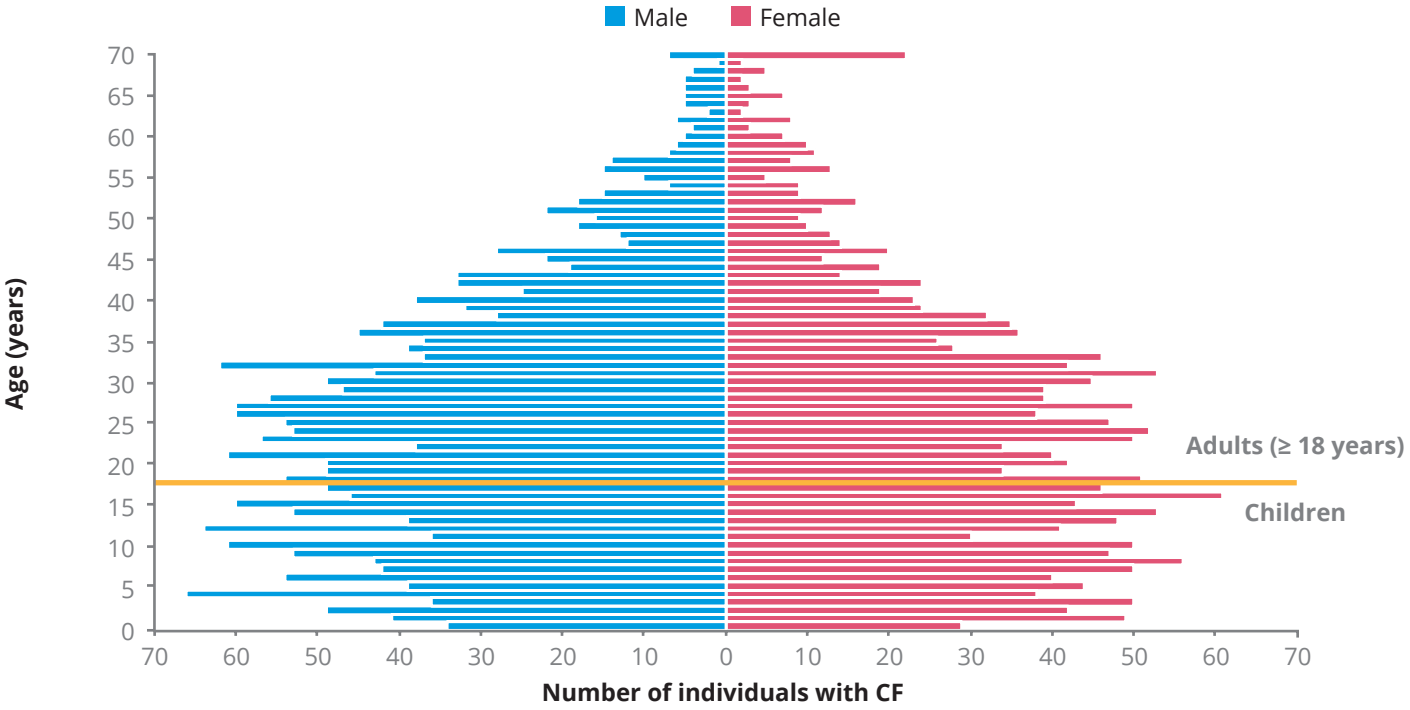


DEMOGRAPHICS

AGE AND SEX DISTRIBUTION OF CANADIANS WITH CYSTIC FIBROSIS

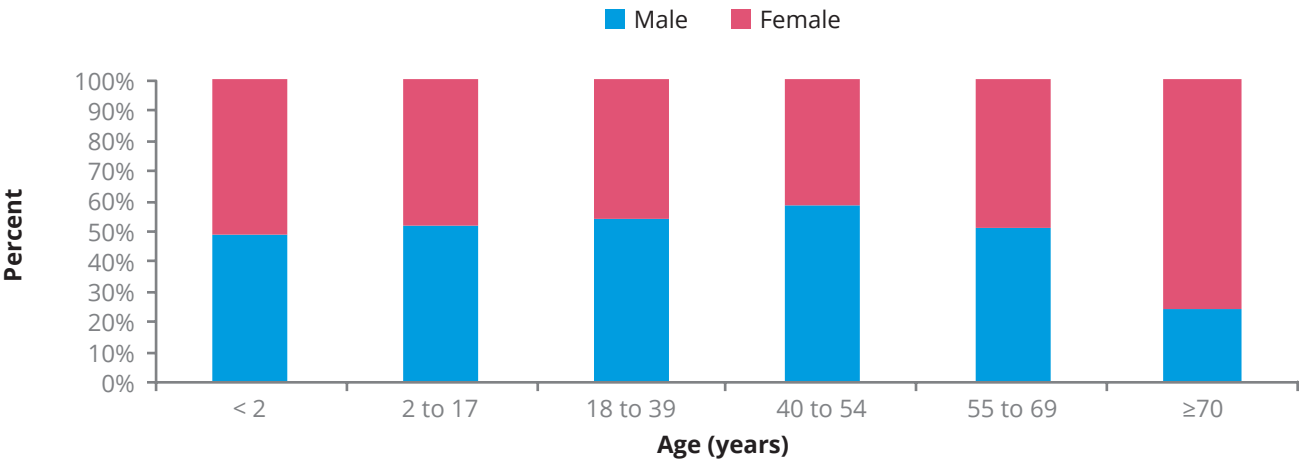
Figure 6 shows the age-sex distribution (referring to biological sex) for all individuals reported on in 2018. Overall, males accounted for 53.5% of individuals living with CF, however the proportion of males varied by age group.

FIGURE 6
Population distribution of individuals with CF, by age and sex, as of December 31, 2018.



As seen in Figure 7, children under age 18 years were fairly evenly distributed between the sexes, with the proportion of males increasing into adulthood before reaching a peak of 58.9% male for those aged 40 to 54 years. After age 55, the proportion of females begins to increase to 75.9% female for those aged 70+. The sex-distribution across all adults with CF (age 18 years and older) is relatively even at just over half being male (Figure 9).

FIGURE 7
Sex-distribution of individuals with CF, by age group, as of December 31, 2018.

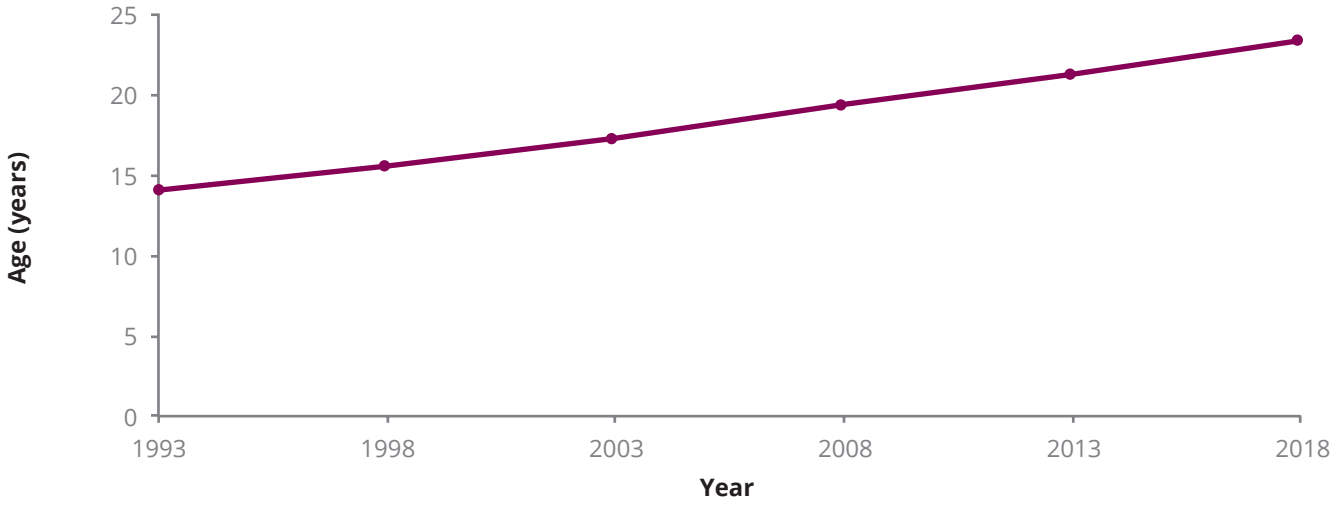


DEMOGRAPHICS

MEDIAN AGE OF CANADIANS WITH CYSTIC FIBROSIS

The current median age of individuals with CF reported on in 2018 was 23.5 years compared to 22.8 years in 2017. Twenty-five years ago, the median age of individuals with CF was just 14.1 years. (Figure 8)

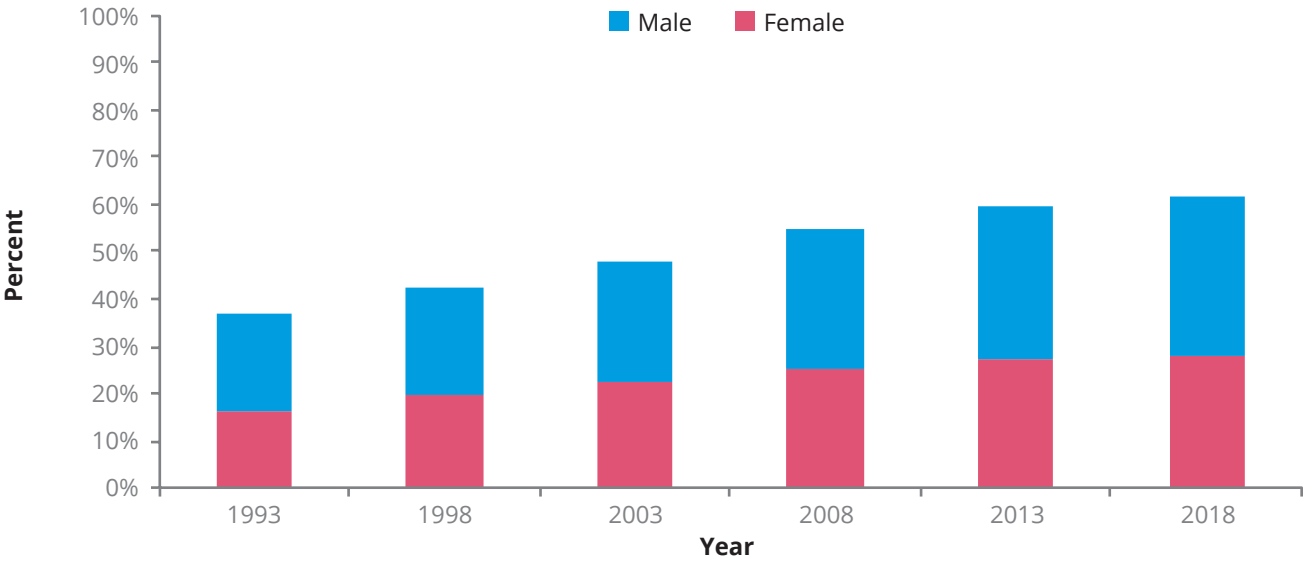
FIGURE 8
Median age of individuals with CF, 1993 to 2018.



CANADIAN ADULTS WITH CYSTIC FIBROSIS

Improvements in treatment and care in the last few decades has led to an increase in the number of Canadian adults living with cystic fibrosis. Adults (individuals aged 18 years or older) accounted for 61.5% of the 2018 Canadian CF population of which 54.7% are male and 45.3% are females. The sex-distribution of adults with CF has remained constant over time.

FIGURE 9
Percentage of CF adults, by sex, 1993 to 2018.



DIAGNOSIS

AGE AT DIAGNOSIS

The majority (60.0%) of individuals with CF reported on in 2018 were diagnosed before the age of one year, and nearly three quarters (73.4%) were diagnosed by the age of two years (Figure 10), compared to 67.5% in 2017. Adults diagnosed later in life (18 years or older) accounted for only 7.7% of all individuals diagnosed in 2018.

Figure 11 shows the percentage of newborns diagnosed through provincial newborn screening (NBS) programs since 2007, when NBS for CF started in Alberta. A decade ago, 22.1% of new CF diagnoses were identified through NBS, with Quebec being the last province to start screening newborns. In 2018, over half of new diagnoses (59; 53.2%) were made through NBS. NBS is now in practice in all provinces across Canada and remains essential for early diagnosis and intervention.

FIGURE 10
Age at diagnosis of CF individuals, as of December 31, 2018 (N = 4,294).

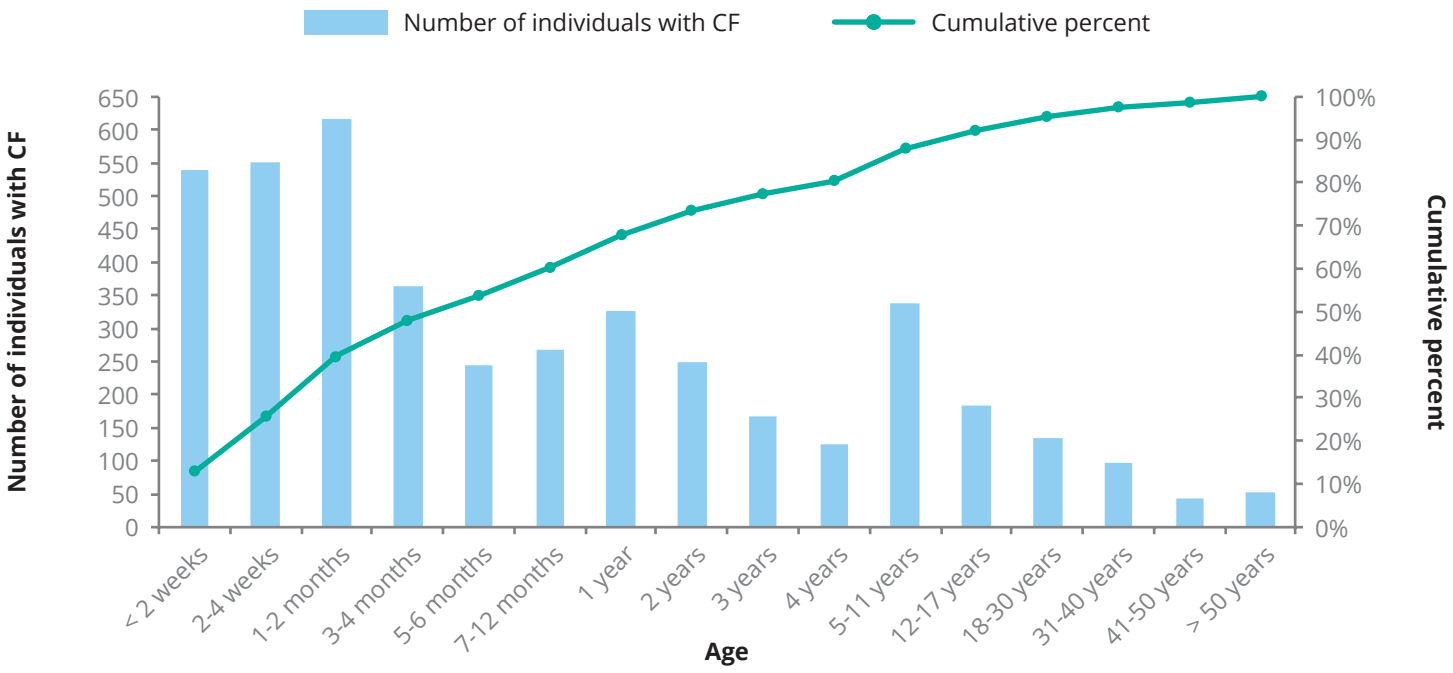
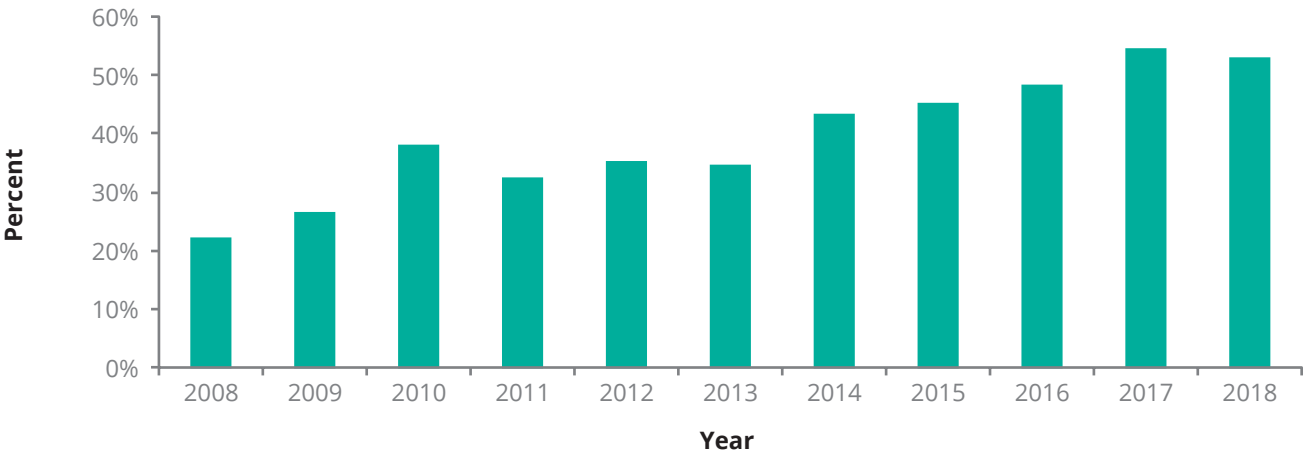


FIGURE 11
Percentage of all new CF diagnoses made through the NBS program, 2008 to 2018.

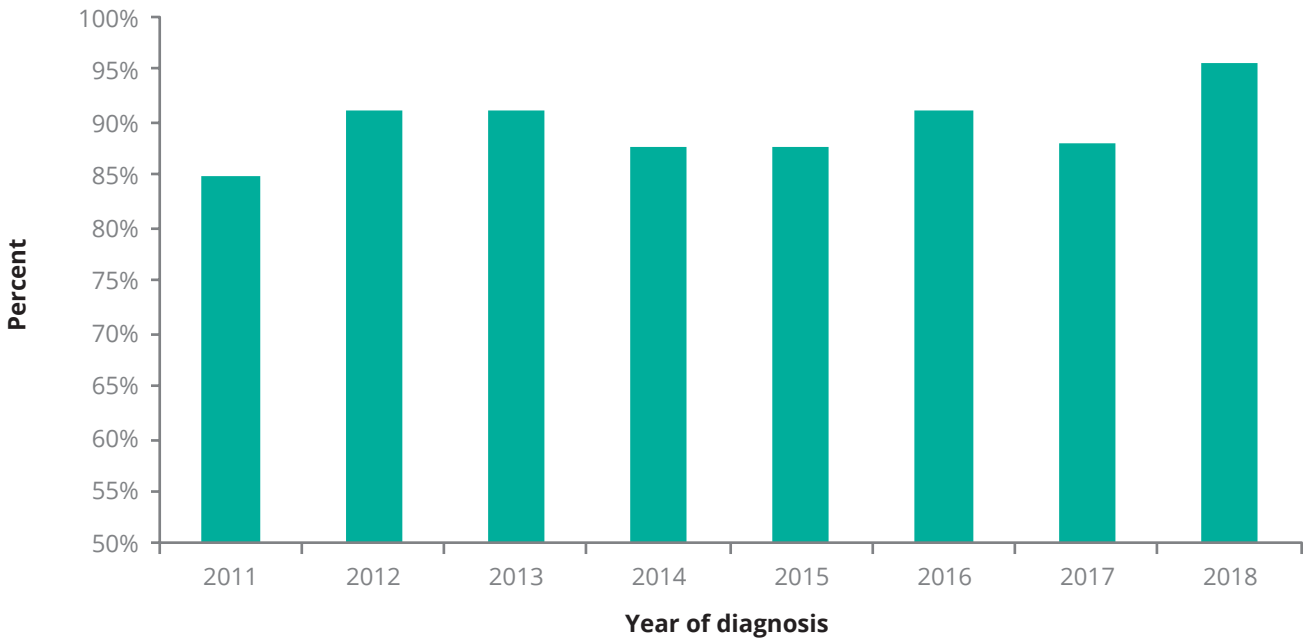


DIAGNOSIS

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. Since 2011, the number of newly diagnosed individuals with at least one sweat chloride test has remained fairly stable (Figure 12). In 2018, 106 of the 111 (95.5%) newly diagnosed individuals had at least one sweat chloride test result recorded.

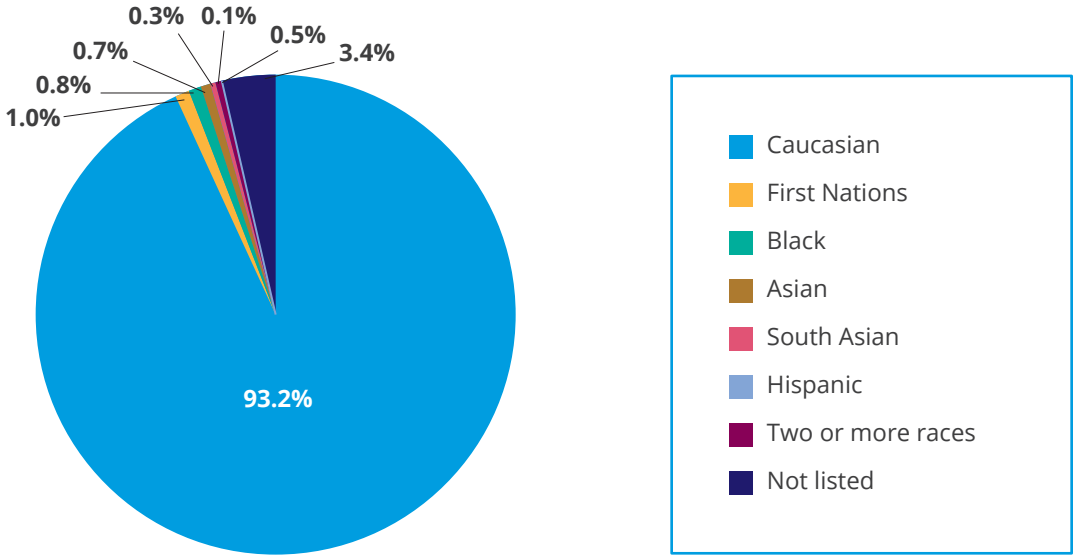
FIGURE 12
Percentage of newly diagnosed individuals with at least one sweat chloride test, 2011 to 2018.



ETHNICITY

Caucasians account for the majority (93.2%) of the Canadian CF population. Of those remaining who have an identified ethnicity (Figure 13), they are divided among five other ethnic groups (First Nations, Black, Asian, South Asian and Hispanic). Ethnicity is captured through self-report.

FIGURE 13
Ethnicity distribution of CF population, 2018.



DISTANCE TO CLINICS

The CCFR began collecting the location of residence of those living with CF in 2015, through the first three digits of their postal code, or the forward sortation area (FSA). Distances to the reporting clinic were calculated in kilometers (km) using the fastest driving route. In 2018, there were 1,661 (38.0%) CF individuals with at least one valid location recorded (Figure 14). While the majority (64.8%) of those with a reported location attends a CF clinic within 100 km of where they live, 17.8% travel more than 250 km for their CF care.

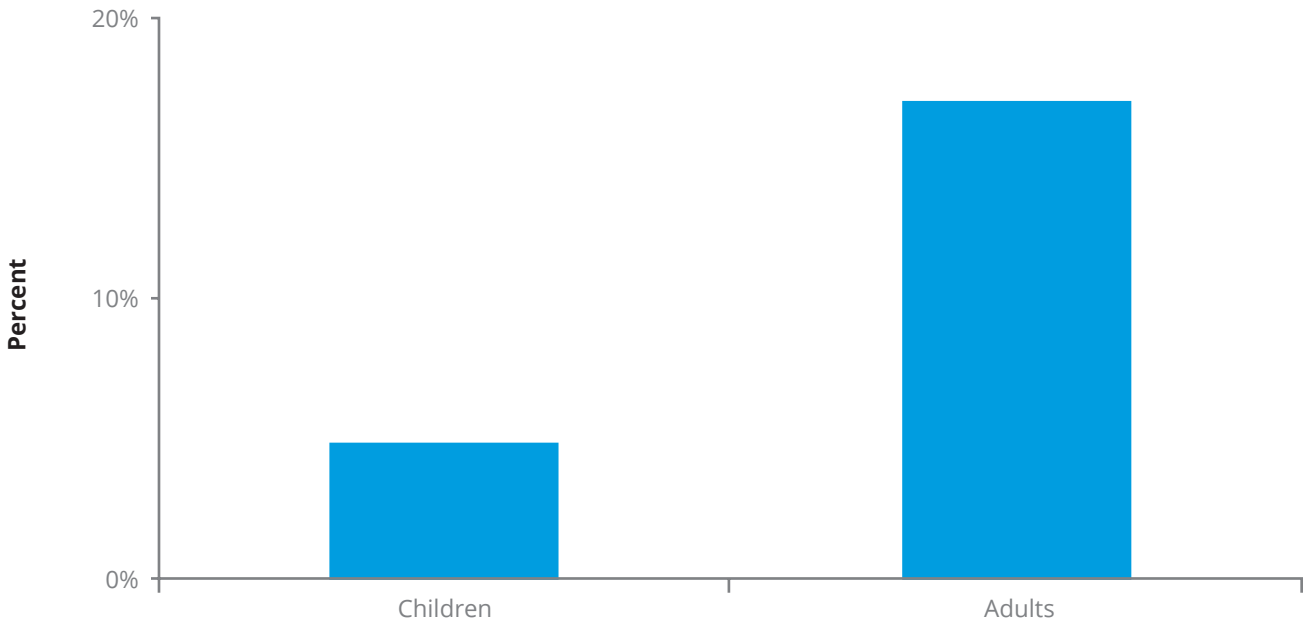
FIGURE 14
Distance travelled to clinic for individuals with CF (N =1,661), 2018.

MENTAL HEALTH

In 2018, there were 538 individuals with CF (12.3% of all individuals) with reported clinically diagnosed depression or anxiety. 81 of these diagnoses were children and 457 were adults, representing 4.8% of all children and 17.0% of all adults living with CF (Figure 15).

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 15
Percentage of children and adults diagnosed with depression or anxiety, 2018.



GENOTYPE

CF is caused by mutations in one or more alleles in a single gene located on chromosome 7, called the cystic fibrosis transmembrane conductance 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.

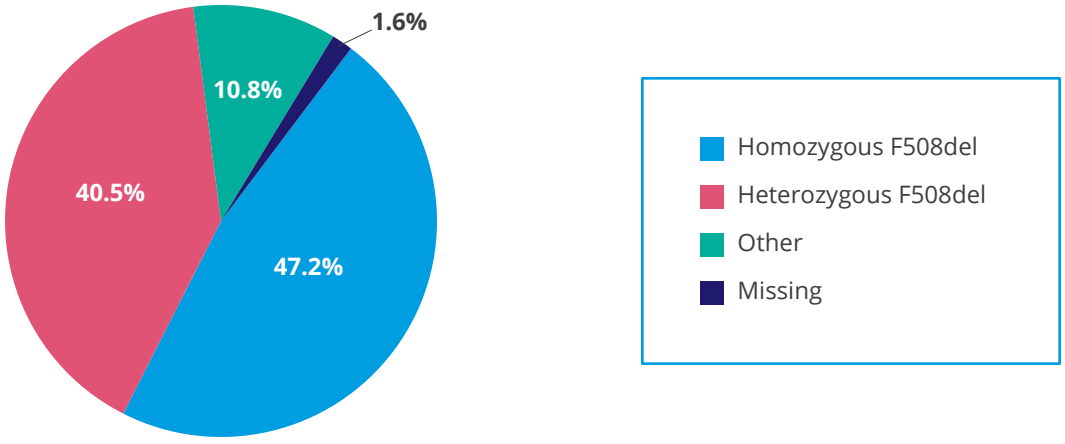
The most common CF mutation worldwide is a three base-pair deletion in the CFTR gene resulting in the deletion of the phenylalanine (F) residue at position 508 in the CFTR protein, commonly referred to as **F508del**. CF disease-causing mutations can be classified into five major categories depending 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 individuals with CF reported on in 2018 (4,302; 98.4%) had at least one CF mutation recorded. Almost half (2,063; 47.2%) have two copies of the F508del mutation (referred to as homozygous F508del) and 40.5% carry a single copy of the F508del mutation (referred to as heterozygous F508del). In total, almost 90% carry at least one copy of the F508del mutation (Figure 16). Individuals with more severe disease symptoms are generally diagnosed earlier, milder forms of cystic fibrosis may only be diagnosed in adulthood. Figure 17 shows the genotype distribution of the CF population by the age of diagnosis. Those diagnosed as a child (under 18 years) were more likely to be homozygous F508del (51.5%) while those diagnosed as an adult (18 years or older) were more likely to be heterozygous F508del (67.3%). Of all the individuals with CF recorded in the CCFR and alive as of 2018, 98.4% have at least one CF mutation recorded. Out of the 397 people in the entire CCFR with no mutations recorded, the majority (88.4%) are adults, 11.6% are under 18 years of age, and 0.8% are under 1 year of age.

FIGURE 16
Genotype distribution of CF population (N = 4,371), 2018.



GENOTYPE

FIGURE 17
Genotype distribution of individuals with CF, by diagnosis age group (N = 4,371), 2018.

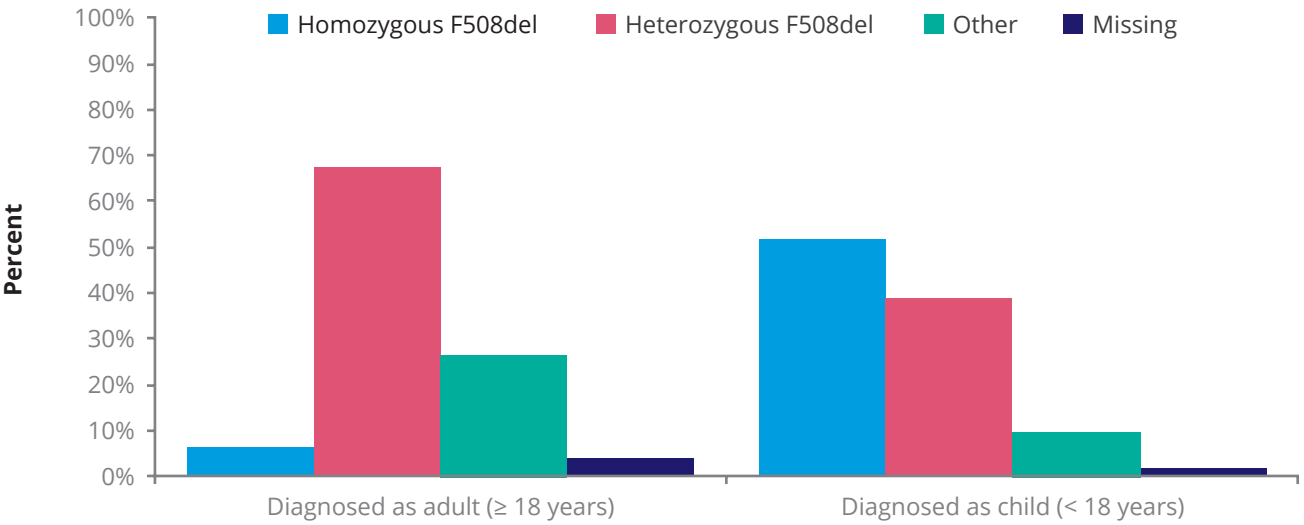


Table 2 lists the most common mutations for individuals with CF reported in 2018. After F508del, 621+1G->T is the next most frequent mutation identified in 5.7% of the population.

TABLE 2
Frequency of the top 10 most common CF mutations on one or both alleles of CF individuals (N = 4,302), 2018.

MUTATION	NUMBER	PERCENTAGE
F508del	3,832	89.1%
621+1G->T	245	5.7%
G542X	145	3.4%
G551D	136	3.2%
711+1G->T	114	2.6%
A455E	106	2.5%
L206W	100	2.3%
N1303K	86	2.0%
R117H	79	1.8%
G85E	68	1.6%

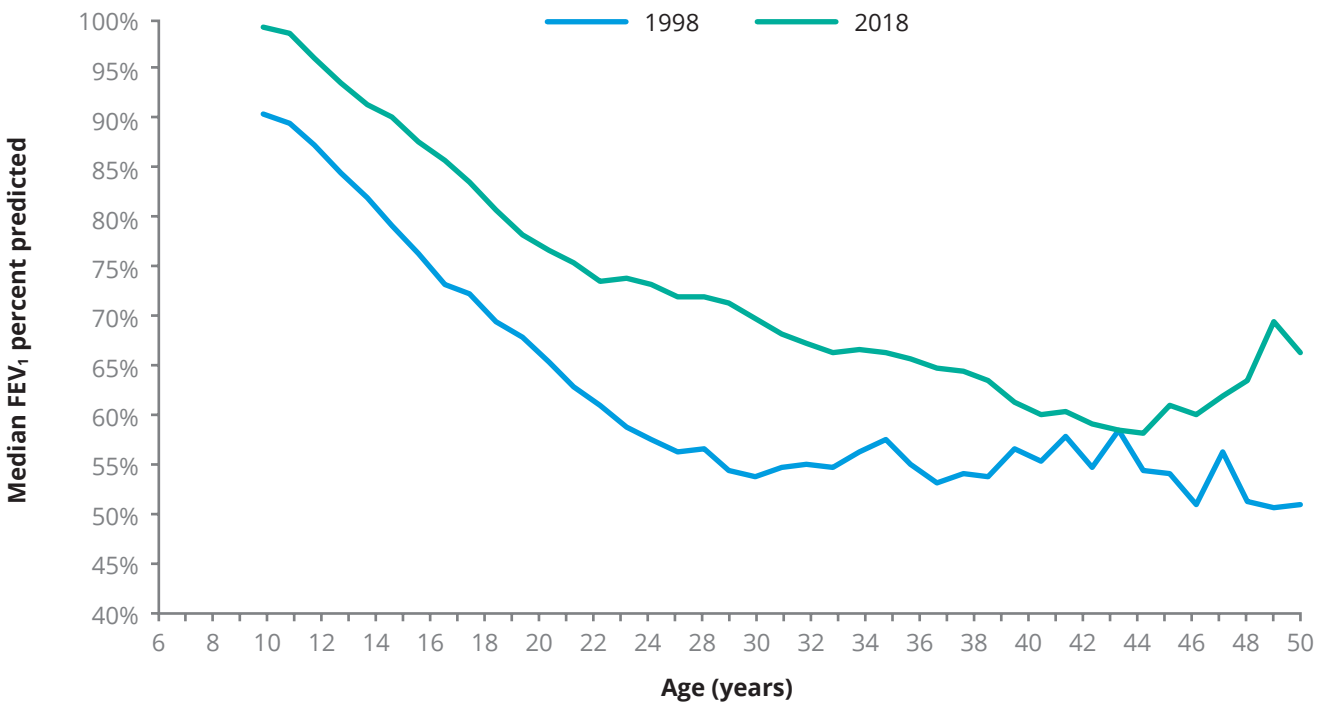
MEDIAN FEV_1 PERCENT PREDICTED

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, ethnicity, and sex. Global Lung Initiative (GLI) equations[3] are used to calculate the percent predicted FEV_1 values.

In this report, the first complete and stable lung measurement of the year was used per individual with CF to summarize lung function. If none exist, the first complete measurement regardless of the lung status was used. Figure 18 shows the median FEV_1 percent predicted from ages 6 to 50 years using 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 since 1998. The median FEV_1 at 23 years of age (the median age of an individual living with CF) was 69.5% predicted in 2018 compared to 58.6% predicted in 1998, marking an improvement of nearly 11% over the last two decades.

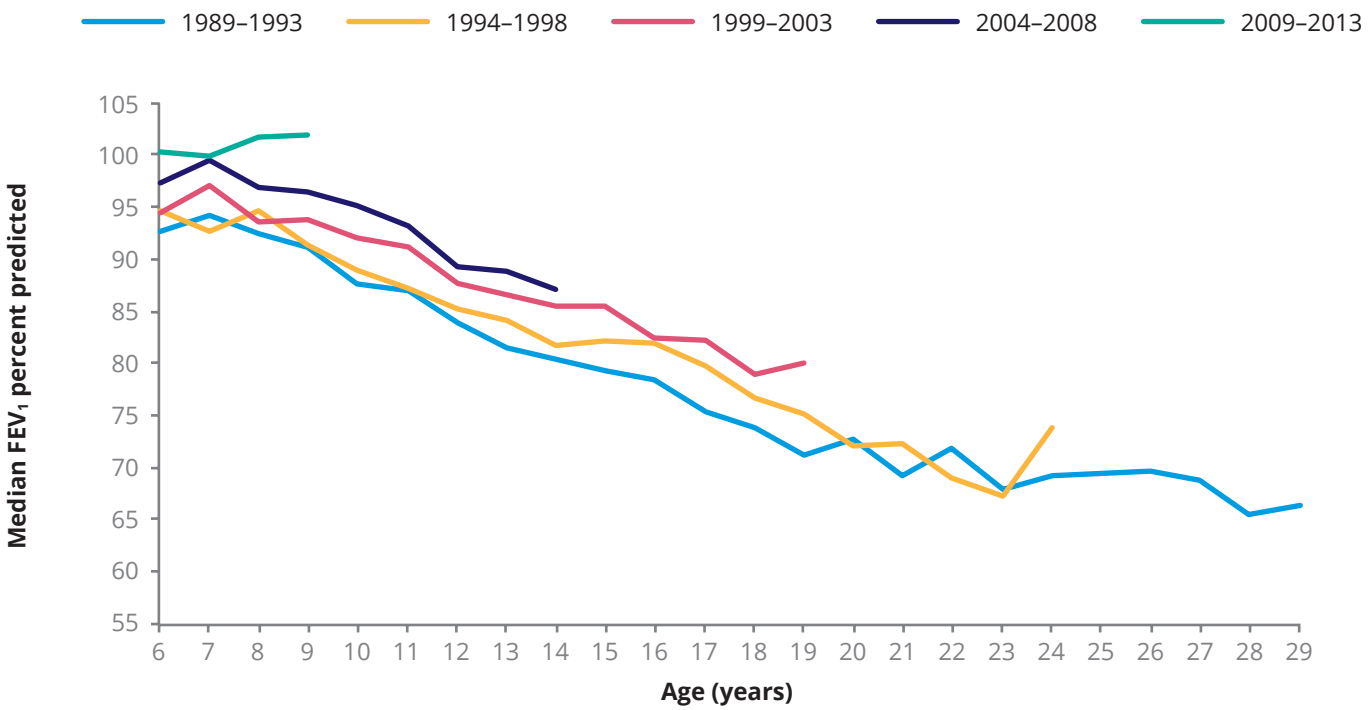
Individuals born recently have a higher median FEV_1 percent predicted at age 6 years and have a slower rate of decline than those born earlier (Figure 19). The upticks seen in some of the birth cohort lines for the later ages are due to the small sample sizes resulting from the method used to group ages in the calculations.

FIGURE 18
Median FEV_1 percent predicted vs. age of CF individuals (5-year moving window), 1998 and 2018*.



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

FIGURE 19
Median FEV_1 percent predicted of individuals with CF, by birth cohort, 2018*.



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

RESPIRATORY STATUS

The majority (55.7%) of children, aged 6 to 17 years in 2018, have normal lung function (defined as >90% predicted) while only 19.1% of adults have normal lung function, as shown in Figure 20. Over time, the median FEV_1 percent predicted has been steadily increasing for both age groups, and in 2018 these values were 67.9% for adults and 92.4% for children (6-17 years of age), as shown in Figure 21. Both figures display data from individuals reported on in 2018, 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 20
Respiratory status of children and adults with CF, 2018.

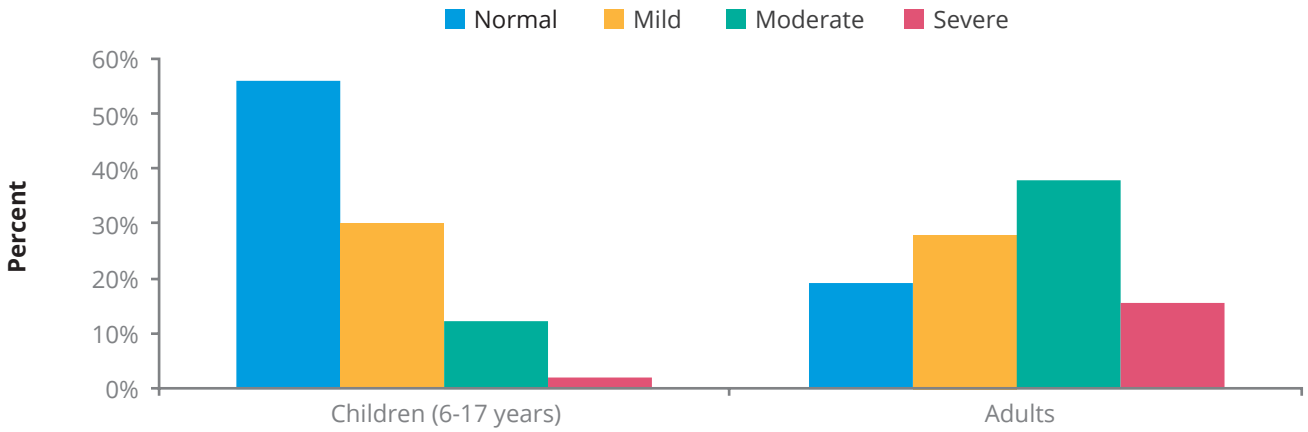
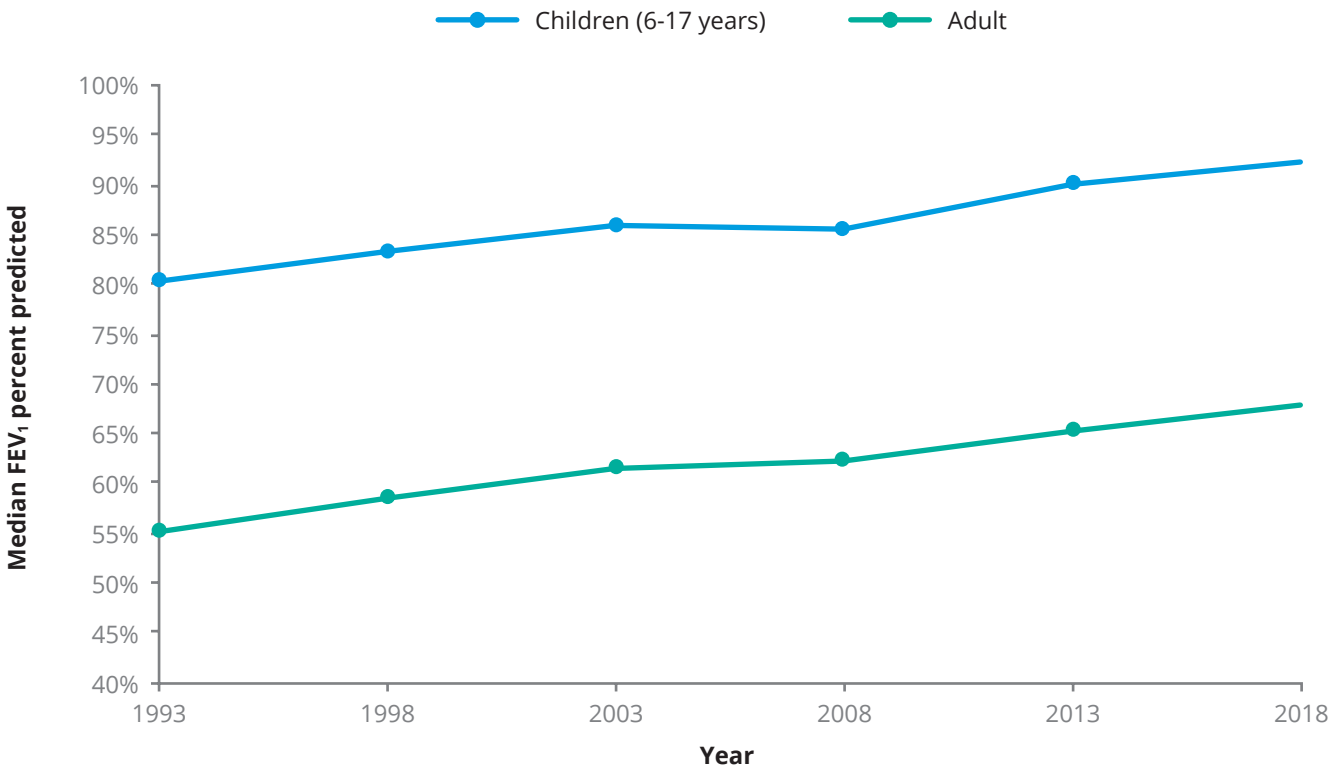


FIGURE 21
Median FEV_1 percent predicted values for children and adults with CF, 1993 to 2018.



RESPIRATORY STATUS BY SEX

Figure 22 and Figure 23 show that between males and females for both children and adults, the distribution of lung function severity is fairly similar across each category.

FIGURE 22
Respiratory status of children (6 to 17 years) with CF, by sex, 2018.

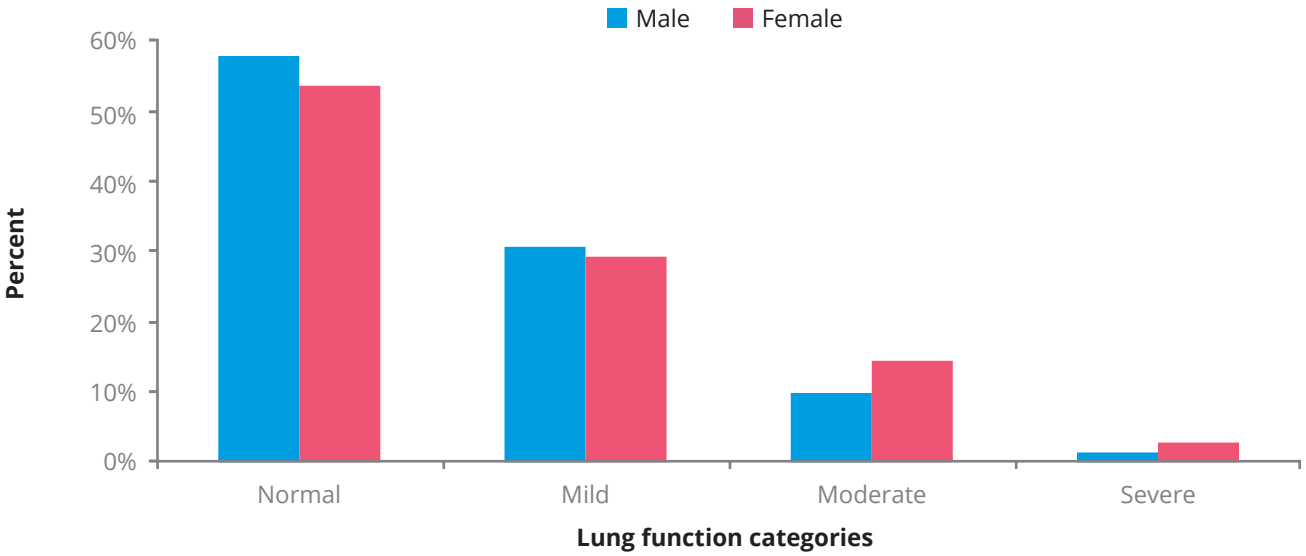
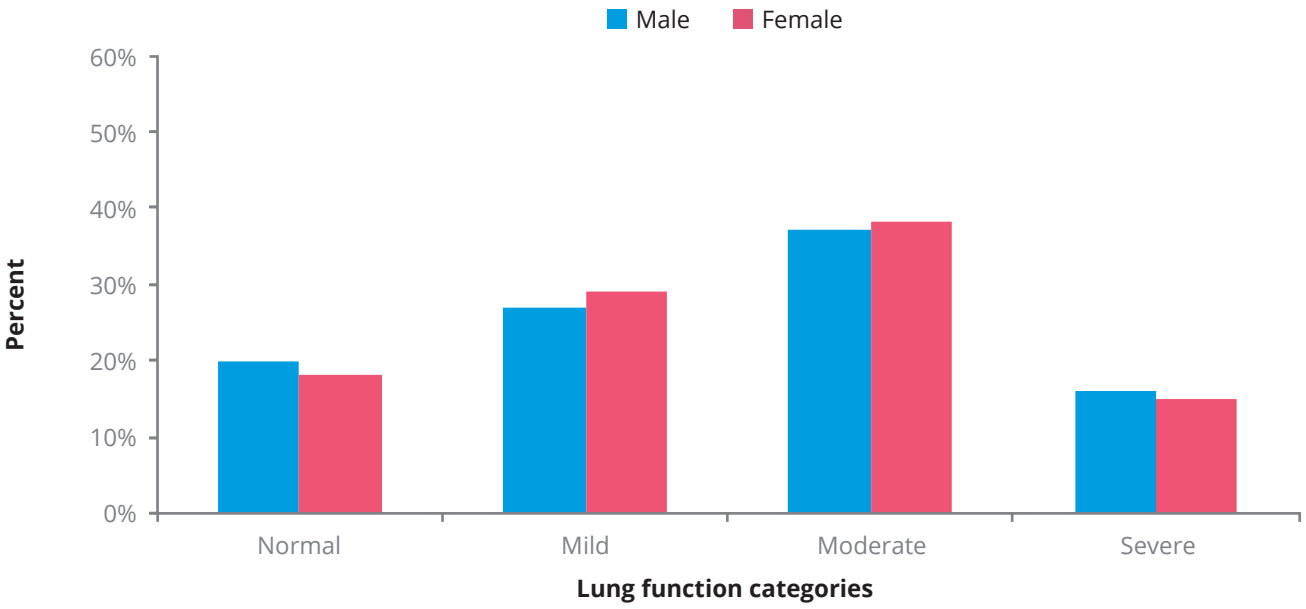


FIGURE 23
Respiratory status of adults (18 years of age and older) with CF, by sex, 2018.



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 2018, the majority (84.4%) of individuals with CF were taking supplemental pancreatic enzymes (and identified as pancreatic insufficient) compared to 15.6% who were not (identified as pancreatic sufficient), as shown in Figure 24.

For individuals 40 years of age or older, 29.7% were pancreatic sufficient (Figure 25). 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 24
Pancreatic status of individuals with CF, 2018.

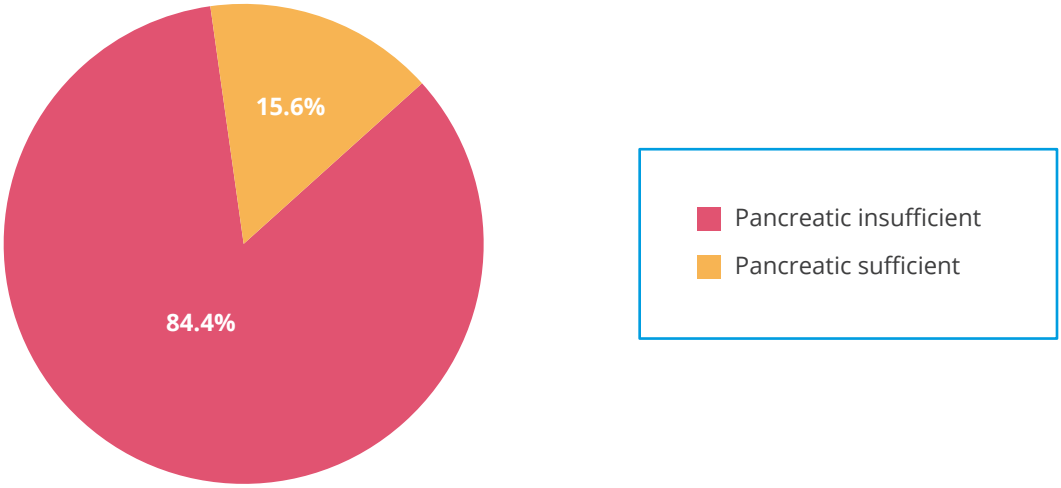
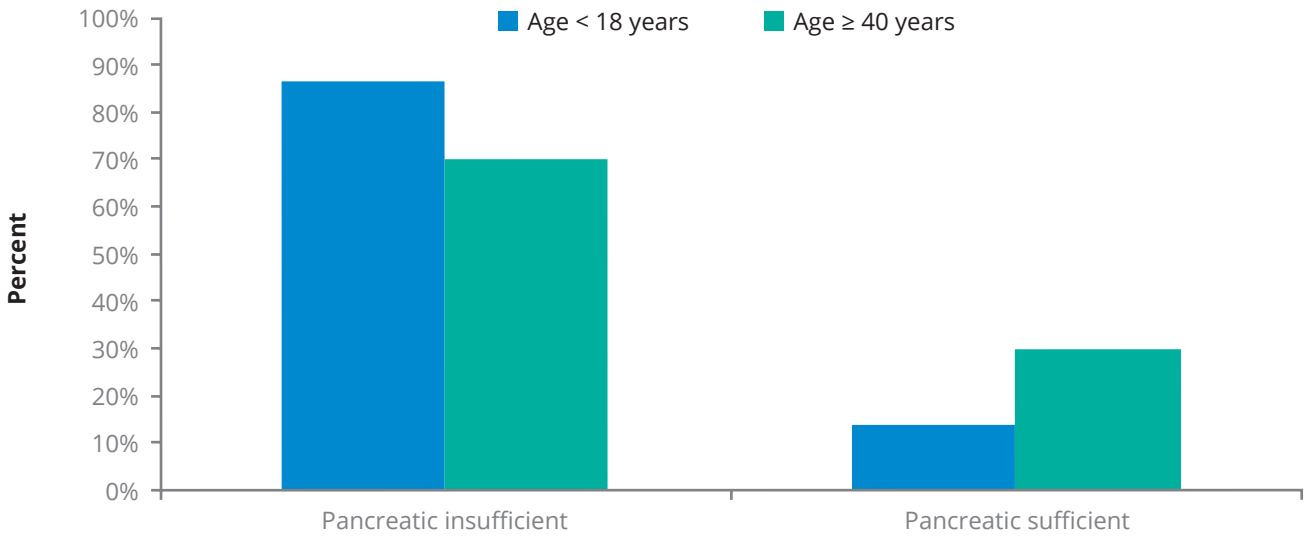


FIGURE 25
Pancreatic status of individuals with CF, by age group, 2018.



NUTRITION

BODY MASS INDEX (BMI) PERCENTILE

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 only calculated for adults 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, therefore using BMI percentiles are a more appropriate measure.

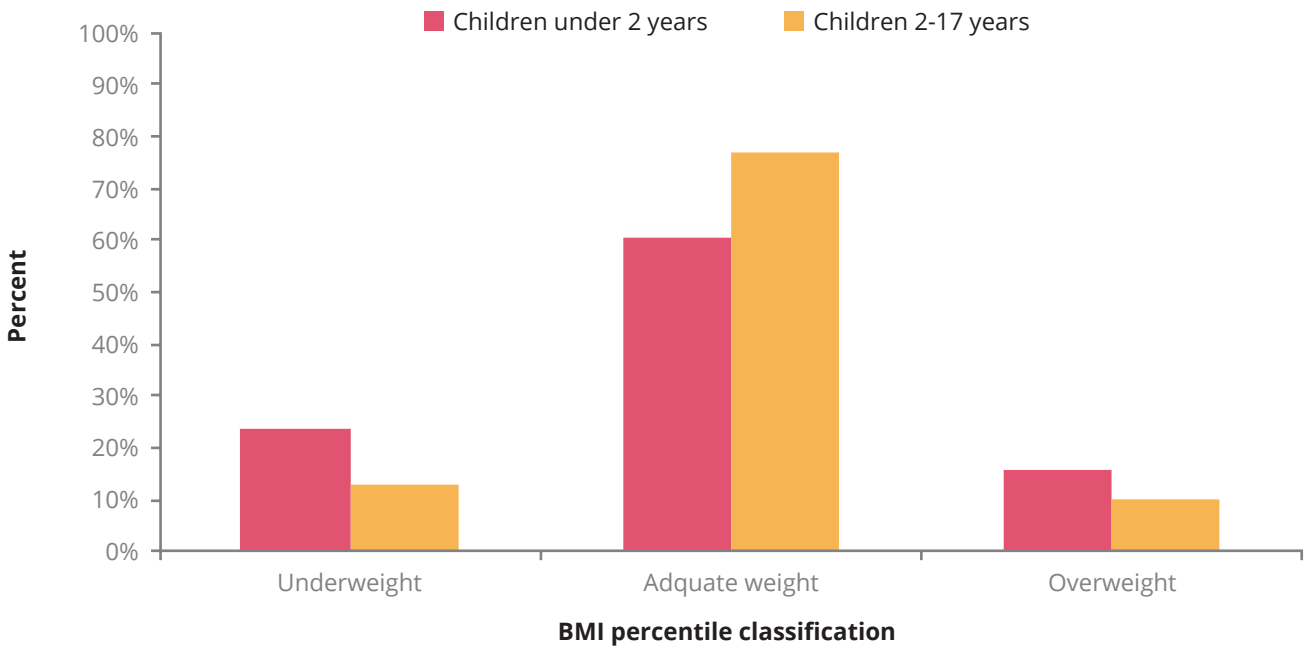
BMI percentiles[4] are calculated following the World Health Organization (WHO) guidelines for children under 2 years of age, and the Centers for Disease Control and Prevention (CDC) guidelines for children ages 2 to 17 years. BMI percentiles allow comparisons to be made between the individual's height 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 national median BMI percentile for children under 2 and children between 2 and 17 years of age are 46.1 and 46.6, respectively. The majority of children with CF (60.4% of children under 2 years and 76.8% of children 2-17 years) have an adequate weight (Figure 26). The 50th BMI percentile is the national goal for children with CF and in 2018, 48.0% of children under 2 years and 46.0% of children 2-17 years exceeded this goal.

TABLE 4
BMI percentile classification.

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

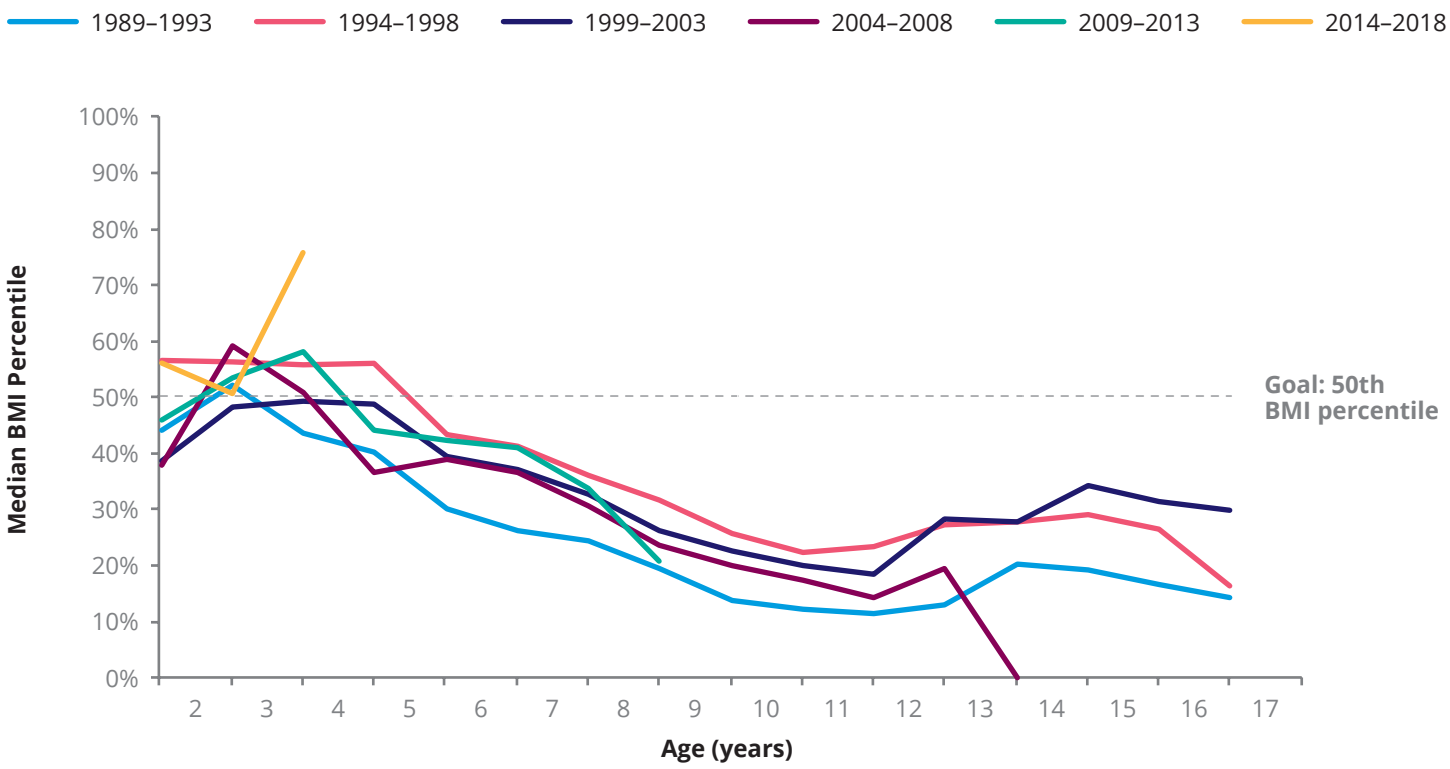
FIGURE 26
BMI percentile status for children with CF, 2018.



NUTRITION

Figure 27 below shows the median BMI percentile for children between 2 and 17 years of age by birth cohort. In more recent birth cohorts, the median BMI percentile at age 2 years increases for the most part. The nutritional status is relatively stable in the early ages (2 to 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 27
Median BMI percentile for children (2-17 years) with CF, by birth cohort, 2018.



BMI PERCENTILE BY SEX

Figure 28 and Figure 29 show the BMI percentile status for males and females in children under 2 years (N = 225) and children 2-17 years (N = 1,503).

FIGURE 28
BMI percentile status for children (under 2 years) with CF, by sex, 2018.

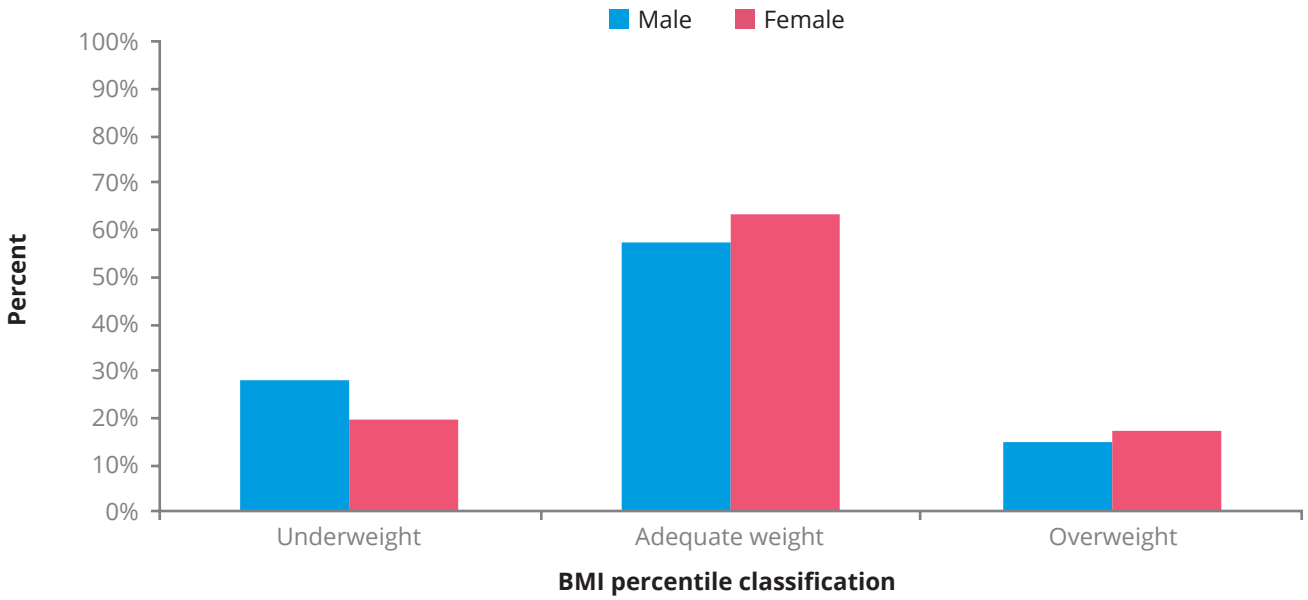
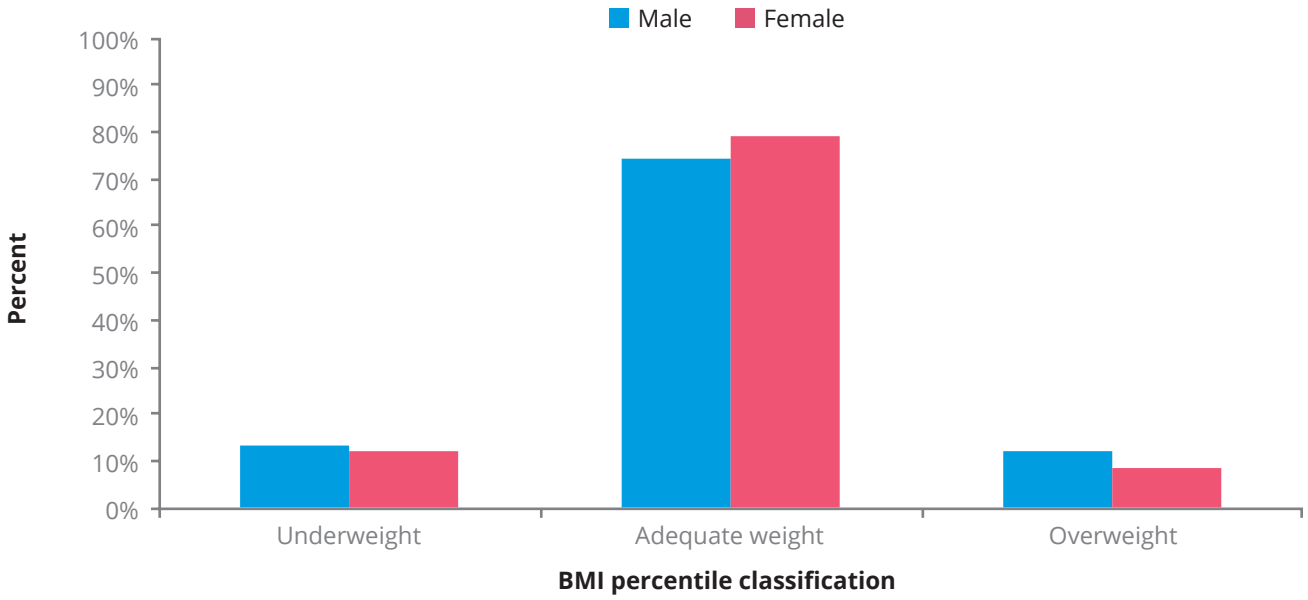


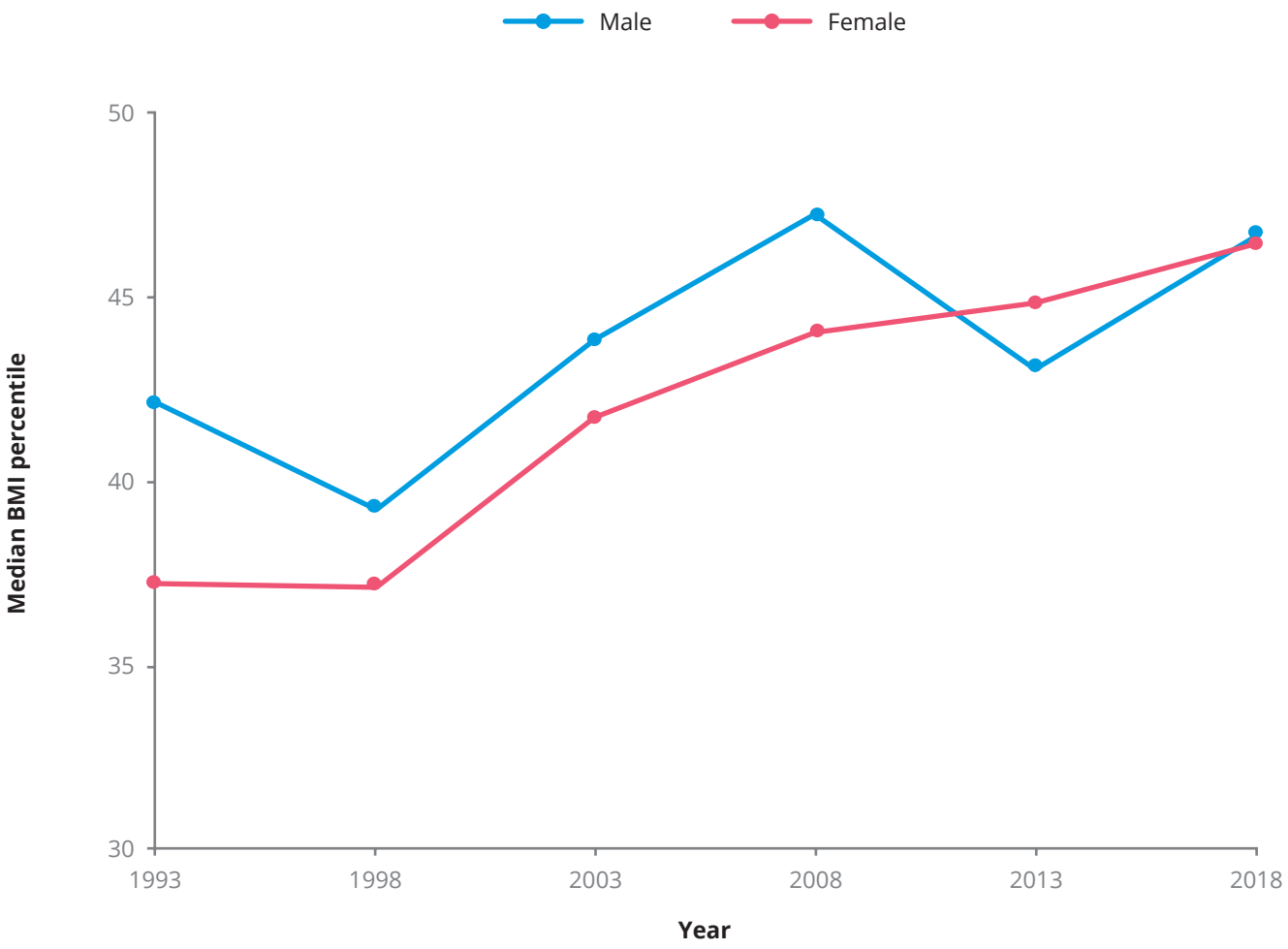
FIGURE 29
BMI percentile status for children (2-17 years) with CF, by sex, 2018.



NUTRITION

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 2018, there is no difference between the sexes (Figure 30).

FIGURE 30
Median BMI percentiles for children (2-17 years) with CF, by sex, 1993 to 2018.



NUTRITION

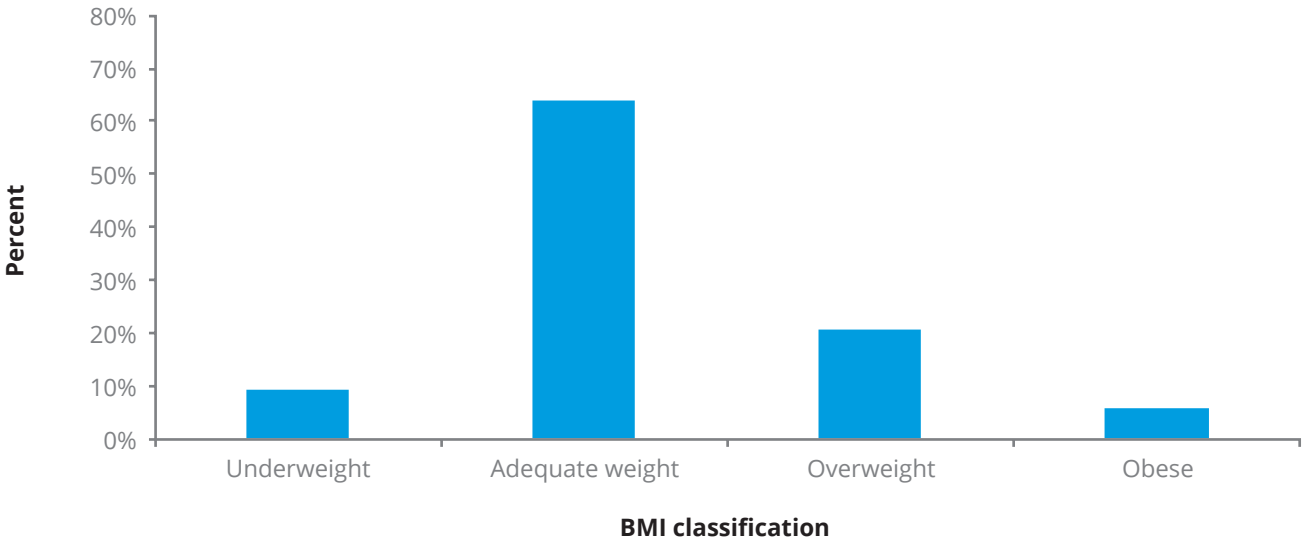
BMI

Table 5 below describes the BMI classifications and their BMI ranges according to the WHO guidelines[6]. These guidelines were updated in 2016 and as such, the proportions of BMI classifications will be different from those described in reports prior to 2016. Also note that "adequate weight" was referred to as "normal weight" in prior reports. In 2018, the national median BMI for adults (aged 18 or older) was 22.5 kg/m^2. The majority (64.0%) of the adult CF population had an adequate weight, while 9.4% were considered underweight and 5.8% were considered obese (Figure 31).

TABLE 5
BMI classification.

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

FIGURE 31
BMI status for adults with CF, 2018.



NUTRITION

BMI BY SEX

Figure 32 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 2018, while more females (11.7%) were considered underweight compared to males (7.5%), the median BMI over the past 25 years has been steadily rising within the CF adult population for both sexes (Figure 33) and can be attributed to fewer individuals who are underweight and more adults classified as either overweight or obese (Figure 34 and Figure 35).

FIGURE 32
BMI status for adults with CF, by sex, 2018.

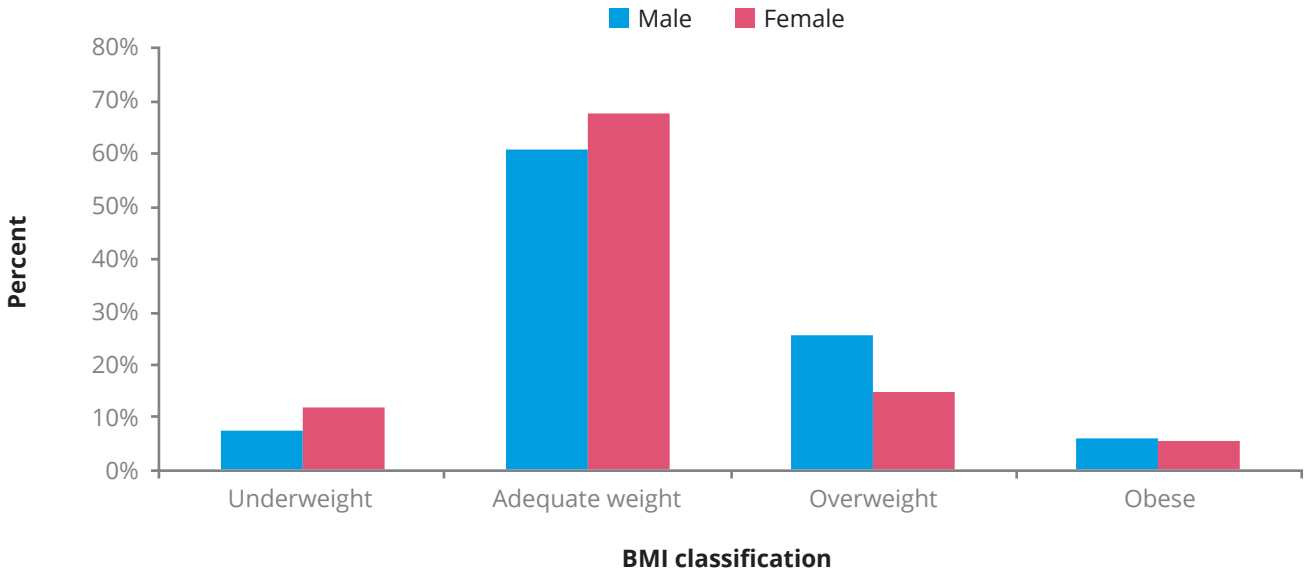


FIGURE 33
Median BMI values for adults with CF, by sex, 1993 to 2018.

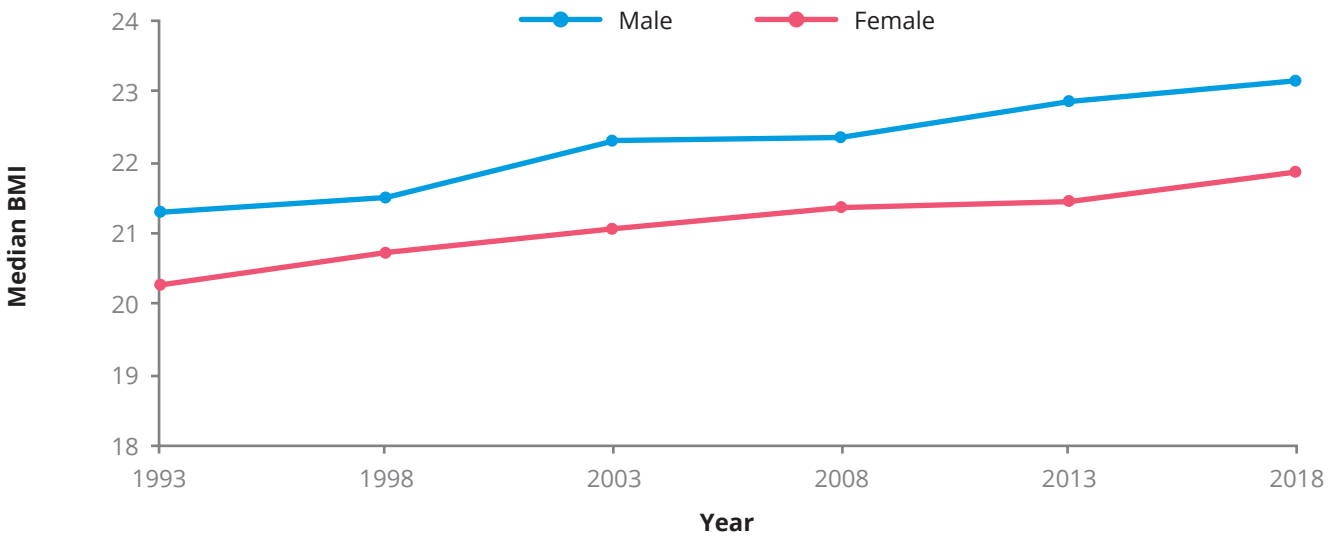


FIGURE 34
Percentage of male adults with CF, by BMI status, 1993 to 2018.

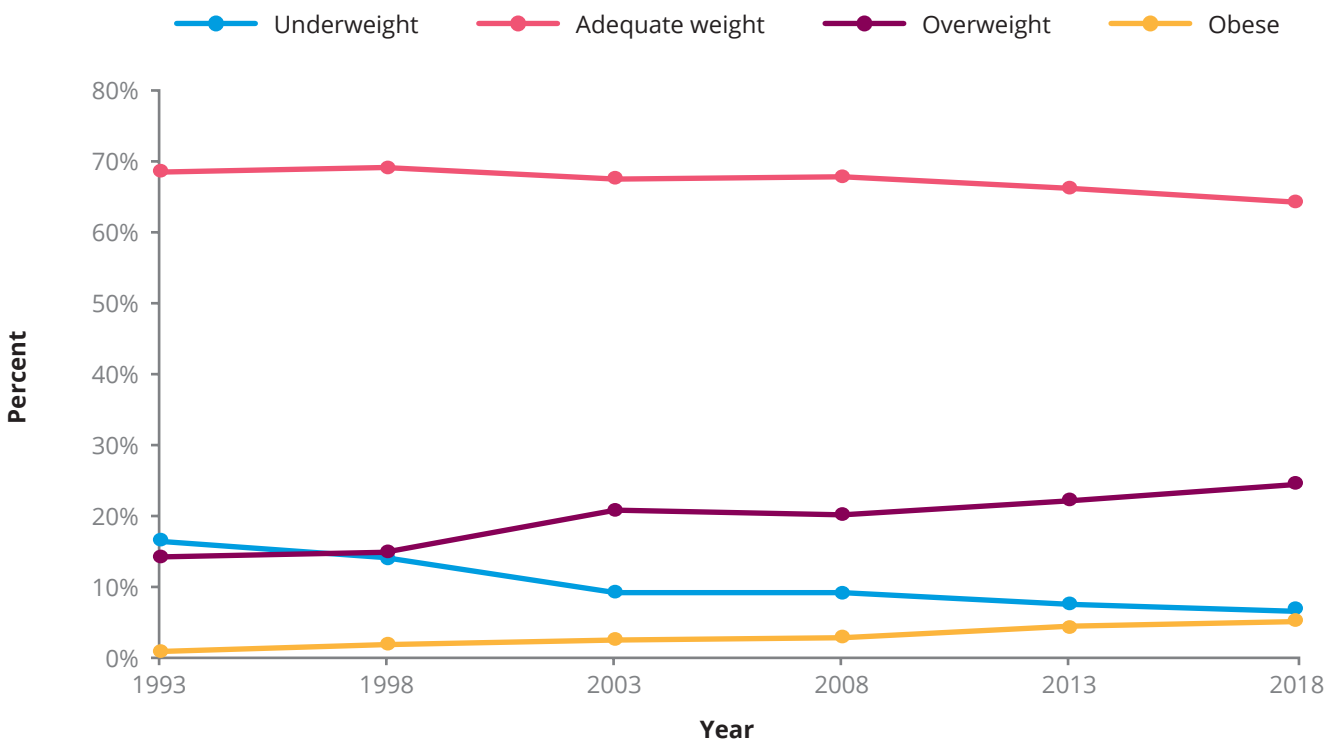
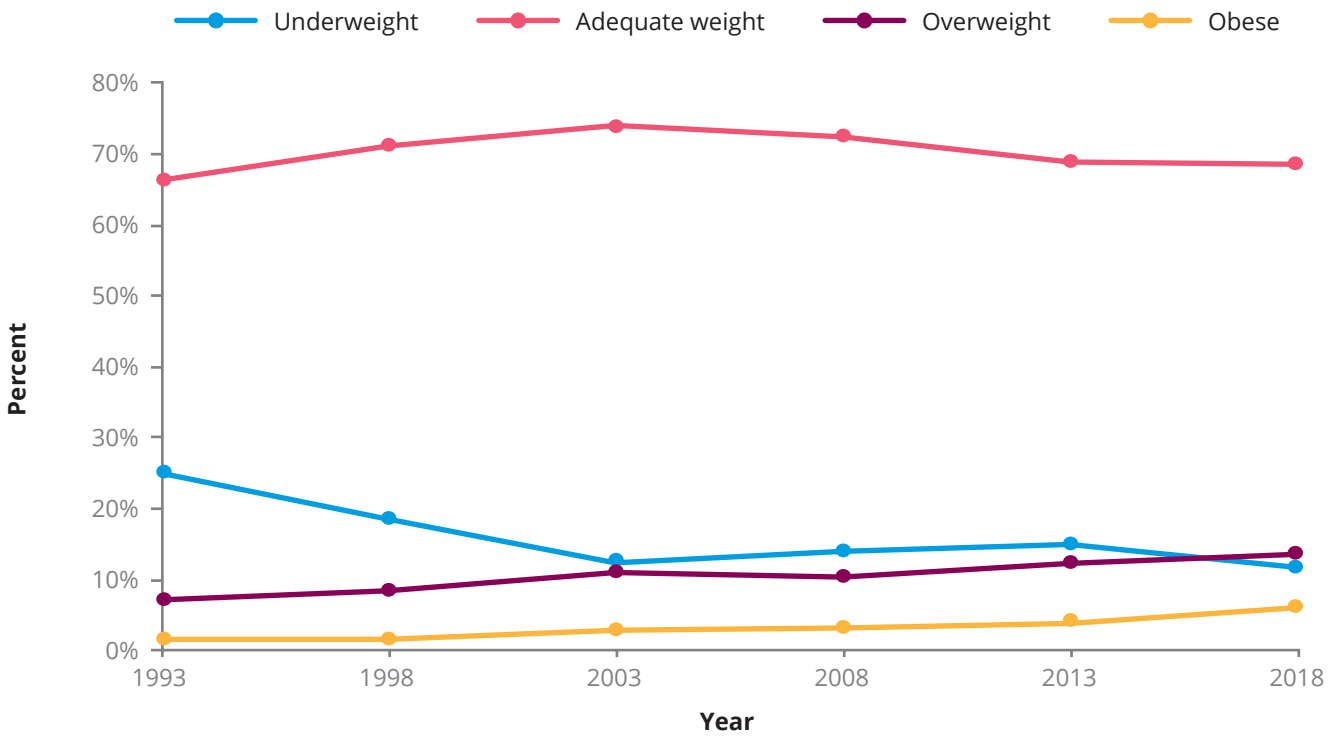


FIGURE 35
Percentage of female adults with CF, by BMI status, 1993 to 2018.

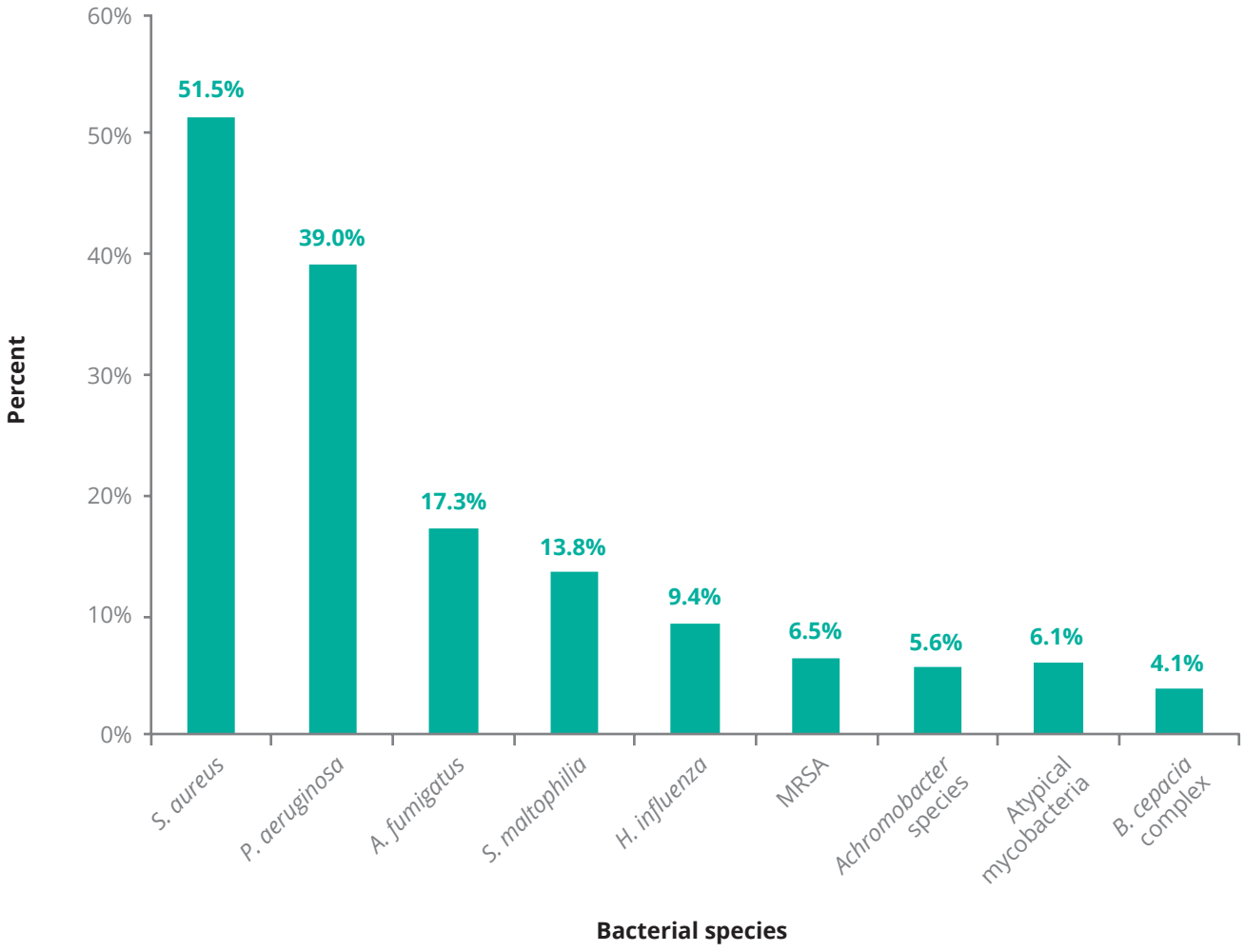


MICROBIOLOGY

BACTERIAL SPECIES AND RESPIRATORY INFECTIONS

Staphylococcus aureus (S. aureus) and *Pseudomonas aeruginosa (P. aeruginosa)* are the most common pulmonary pathogens in Canadians with CF (Figure 36), found to be prevalent in 51.5% and 39.0% of all individuals, respectively. The CCFR aims to track relevant bacterial species for the CF population and several have been added in recent years including MSRA (2003), Achromobacter species (formally called Alcaligenes species) (2011), and Atypical mycobacteria (2011).

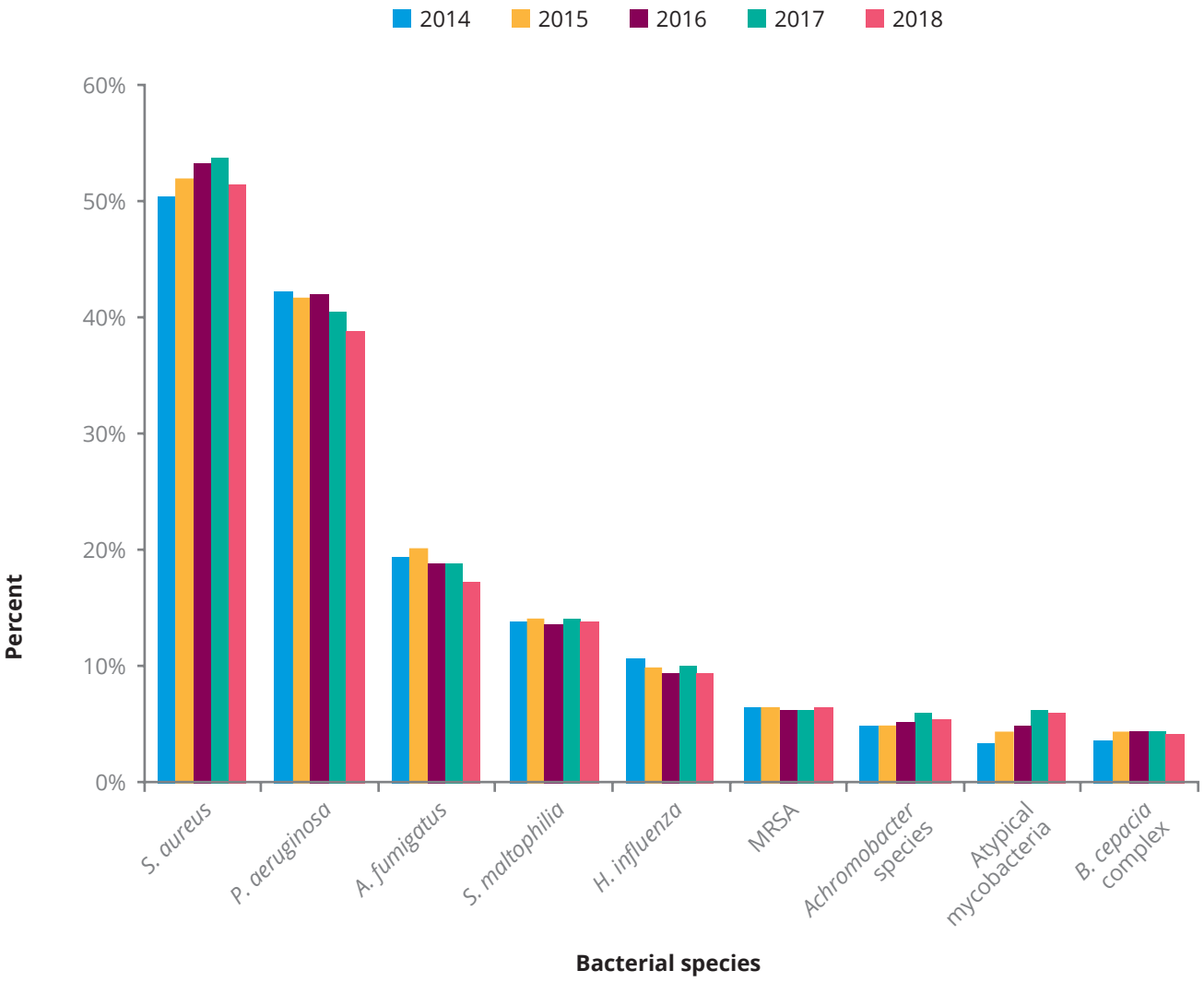
FIGURE 36
Prevalence of bacterial species cultured from airways of individuals with CF (all ages), 2018.



MICROBIOLOGY

Figure 37 shows that over the past several years, *Staphylococcus aureus (S. aureus)* and *Pseudomonas aeruginosa (P. aeruginosa)* remain the two most prevalent pulmonary pathogens among individuals with CF. And though there has been a slight decrease in prevalence for some of the more common pulmonary pathogens, there has also been a slight increase in the less frequently found pathogens such as *Achromobacter* 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.

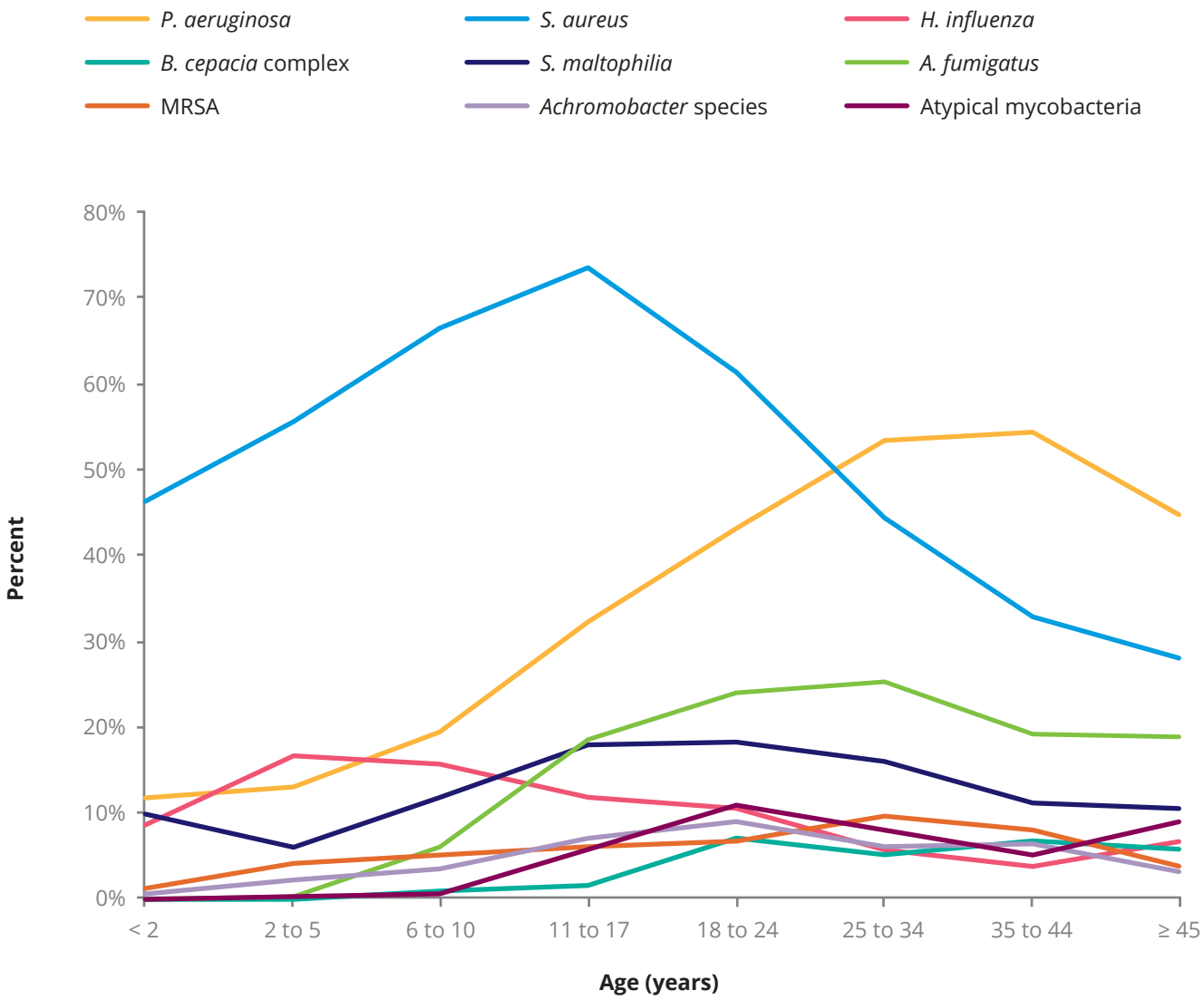
FIGURE 37
Prevalence of respiratory infections of individuals with CF, 2014 to 2018.



MICROBIOLOGY

When examining the prevalence of pathogens by age (Figure 38), it appears that *Staphylococcus aureus (S. aureus)* is more common in children with CF and *Pseudomonas aeruginosa (P. aeruginosa)* is more common in the adult CF population. *Burkholderia cepacia* complex (*B. cepacia* complex or BCC) is more commonly seen in older individuals with CF, but the prevalence is low for the entire CF population (4.1%). Furthermore, new acquisition of BCC is infrequent and typically, the *Burkholderia* species that is reported is an environmental strain rather than the epidemic *cenocepacia* strain (for more details see Figure 39 and Figure 40).

FIGURE 38
Age-specific prevalence of respiratory infections in individuals with CF, 2018.



MICROBIOLOGY

BURKHOLDERIA CEPACIA COMPLEX (BCC)

Out of all individuals with CF with bacterial species recorded in 2018, 178 (4.1%) unique individuals grew at least one *Burkholderia cepacia* complex (BCC) species. The two most common types of BCC species are *B. cenocepacia* (42.3%) and *B. multivorans* (26.5%) (Figure 39). Of the unique individuals who had BCC in 2018, 162 (91.0%) were adults and 49 (27.5%) were over the age of 40 (Figure 40). Not all BCC bacteria have been speciated, as 1.7% 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 9.8%, though it was not included in Figure 39 because it is not officially recognized as part of the BCC.

FIGURE 39
***Burkholderia cepacia* complex species prevalence in individuals with CF (N = 178), 2018.**

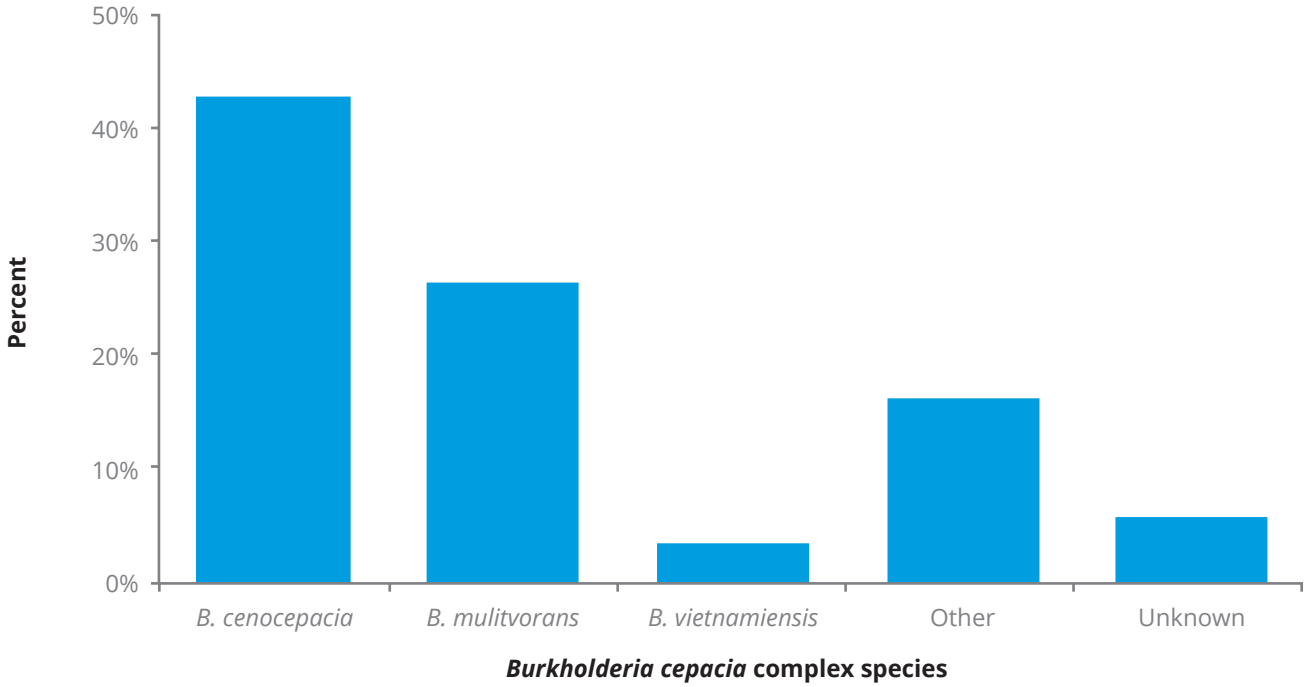
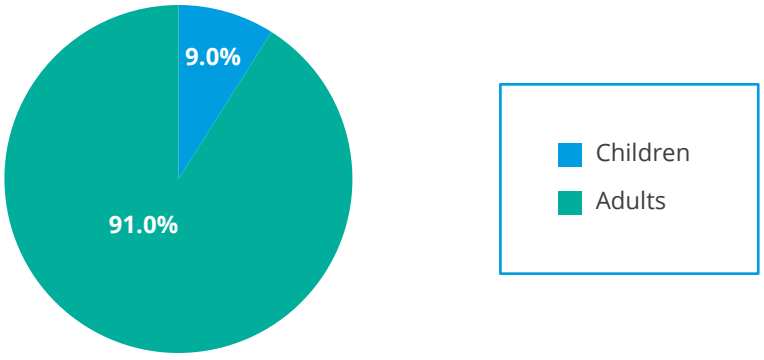


FIGURE 40
***Burkholderia cepacia* complex distribution of CF individuals, by age, 2018.**



CF-RELATED DIABETES (CFRD)

CFRD is a unique type of diabetes common in individuals living with CF. CFRD is often associated with weight-loss and lung function decline, but with early dianosis and proper treatment, CFRD can be managed successfully. In 2018, CFRD was reported in 957 (21.9%) individuals with CF, affecting 55 (3.3%) children and 902 (33.5%) adults (Figure 41). Of those individuals with CFRD, 49.1% were female, 23.5% have received a transplant, and 49.8% were 35 years of age or older. While there are very few children reported as having CFRD, there is an increasing prevalance of CFRD in the adult population (Figure 42).

FIGURE 41
Percentage of children and adults reported to have CFRD, 2018.

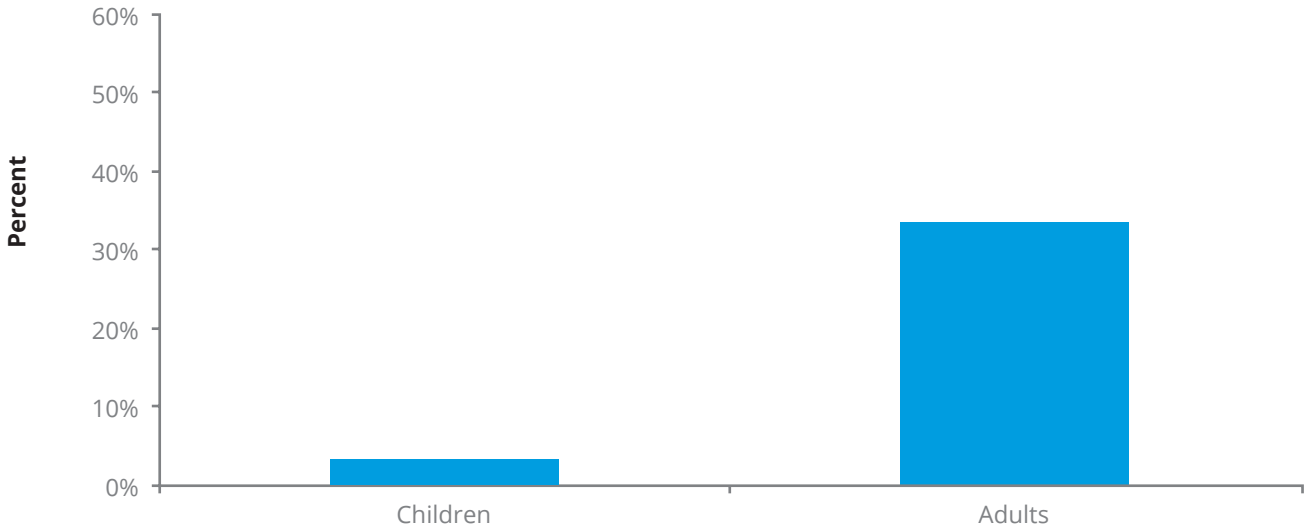
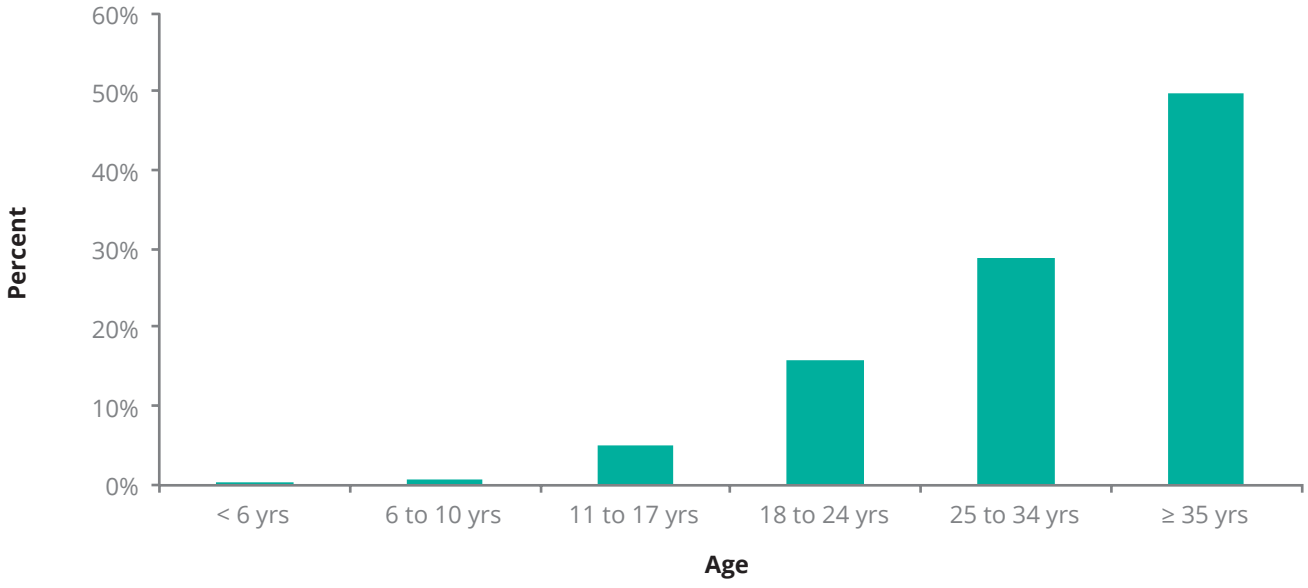


FIGURE 42
Percentage of CF individuals with CFRD by age, 2018.

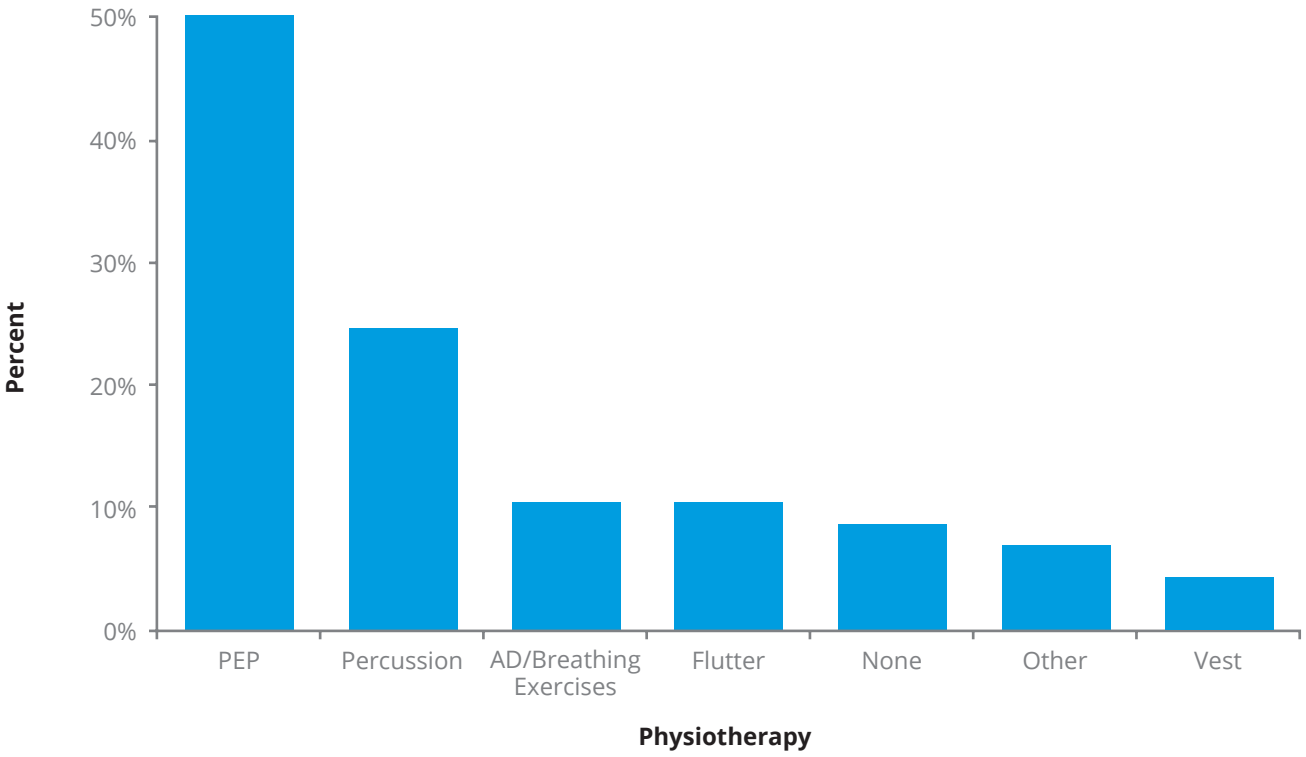


PHYSIOTHERAPY

Physiotherapy is done to help clear mucus from airways using a variety of methods. Figure 43 shows the multiple forms of physiotherapy that are tracked in the CCFR. The most commonly used form of therapy are positive expiratory pressure (PEP) (50.2%) and percussion (24.6%), while 8.7% were reported as not doing any form of physiotherapy.

Note: Individuals who have ever received a lung transplant (7.7% of the 2018 reported CF population) were excluded from these calculations because, typically, chest phyisotherapy is not part of routine post-transplant treatment.

FIGURE 43
Physiotherapy usage of CF individuals (N = 4,034), 2018.



MEDICATIONS

In 2018, there were a total of 3,517 individuals over the age of 6 years (1,160 children aged 6-17 years and 2,357 adults) who never received a transplant. Individuals who ever received a transplant (any organ) were excluded from the following figures, because the medications listed are not typically part of routine post-transplant treatment. Figure 44 shows that of individuals who never received a transplant, 2,241 (63.7%) were prescribed mucolytic therapy during the calendar year (hypertonic saline and/or dornase alfa).

There were 1,528 individuals over the age of 6 years who have never received a transplant and were reported to have *Pseudomonas aeruginosa* in 2018, which include 310 children (6-17 years) (20.3%) and 1,218 adults (79.7%). Of those, there were 203 children (65.5%) and 701 adults (57.6%) who were prescribed inhaled antibiotic treatment, and 79 children (25.5%) and 714 adults (58.6%) who were prescribed macrolide therapy (Azithromycin) (Figure 45).

Of the 496 individuals with CF who are on cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapy in 2018, lumacaftor/ivacaftor was recorded for 317 (64.7%), ivacaftor was recorded for 131 (26.4%) and other CFTR modulator therapies (tezacaftor/izacaftor or other modulators) was recorded for 69 (13.9%).

FIGURE 44
Percentage of CF individuals on mucolytics, by age group, 2018.

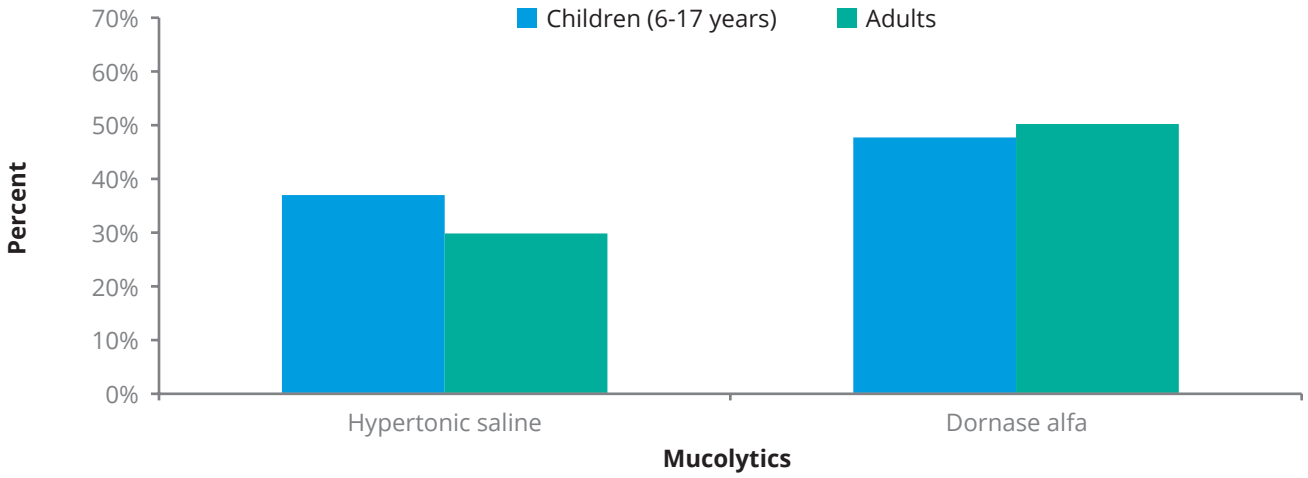
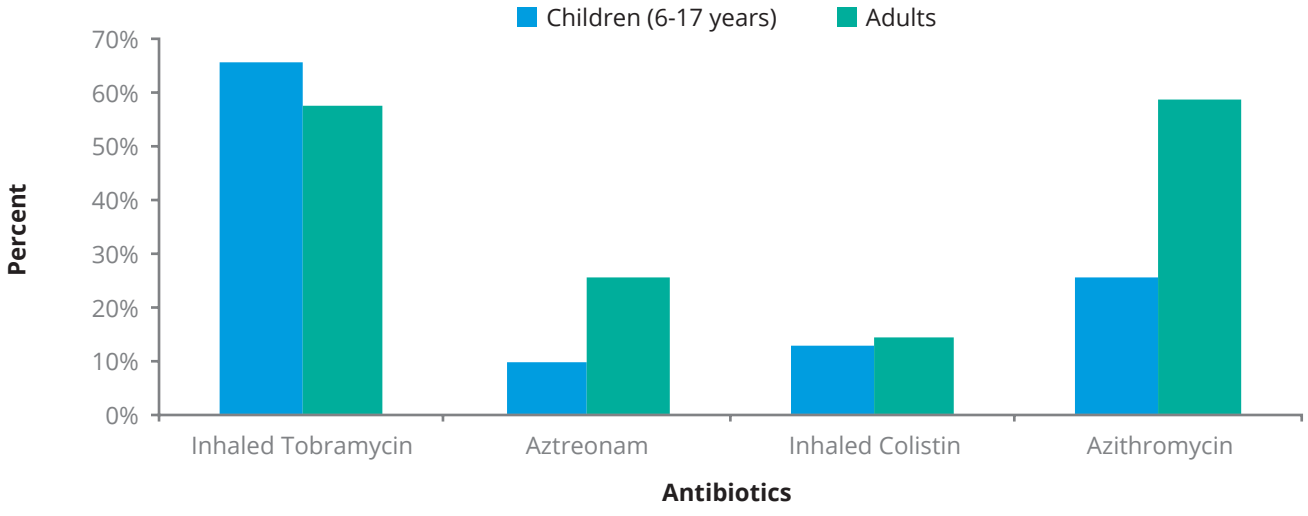


FIGURE 45
Percentage of CF individuals on antibiotics, by age group, 2018.



HOSPITALIZATION AND HOME IV

The CCFR captures the date of admission and discharge from hospital. From these data, the total number of hospitalizations per patient are calculated. In 2018, there were 1,209 (27.7%) individuals with CF who altogether spent over 26,500 days in hospital from a total of 2,138 hospitalizations recorded, which do not include visits to the out-patient CF clinics (Table 6). At home, individuals with CF had over 17,700 days on IV antibiotics from a total of 941 courses. A total of 4,334 (99.2%) individuals with CF visited a CF clinic at least once with 3,331 (76.2%) having three or more clinic visits. These clinic visits can include telemedicine appointments, during which patients receive medical education, or health advice and information via telecommunication technologies. Of the people having 3 or more clinic visits, 1,490 (88.6%) were children and 1,841 (68.5%) were adults.

TABLE 6
Total number of hospital days and home IV courses recorded for individuals with CF, 2018.

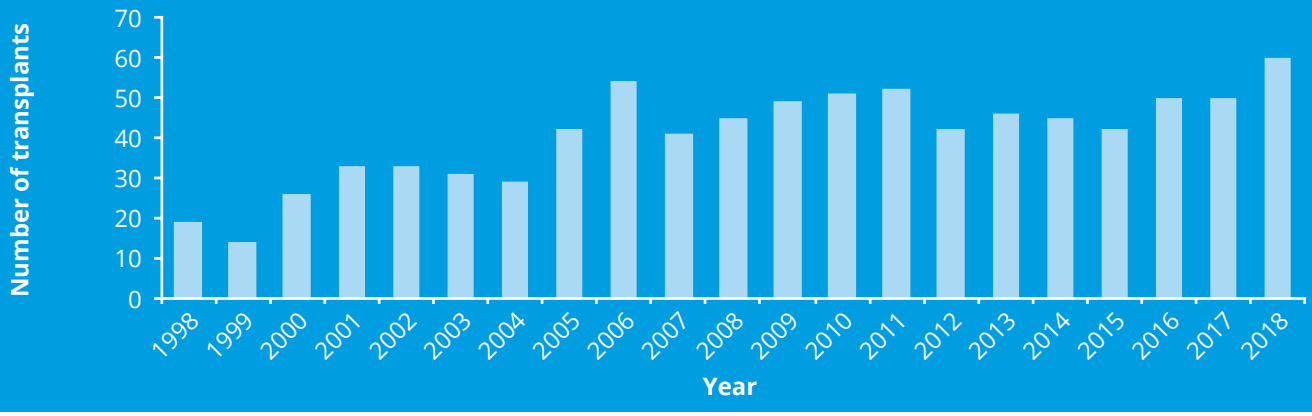
	TOTAL NUMBER
Hospital Days	26,573
Hospitalizations	2,138
Clinic Visits	18,916
Home IV Courses	941
Home IV Days	17,730

TRANSPLANTS

For some individuals with advanced disease, transplantation may be the next step to help regain health. Figure 46 shows the number of transplants carried out per year as reported in the CCFR. In 2018, 60 individuals with CF received a transplant with a median age at the time of transplant of 29.8 years. Although the numbers provided represent primarily lung transplants (58 lung transplants in 2018), individuals who received other combinations or organs (e.g. lung and liver, liver, heart and lung, heart) are also included in the total.

The first transplant recorded in the CCFR was performed in 1988, and as of December 31, 2018, there were 873 unique 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, 62 (6.4%) have received at least two lung transplants, 488 (50.7%) were reported as being alive, and 274 (54.7%) of those living patients were male.

FIGURE 46
Number of transplants per year of CF individuals, 1998 to 2018.

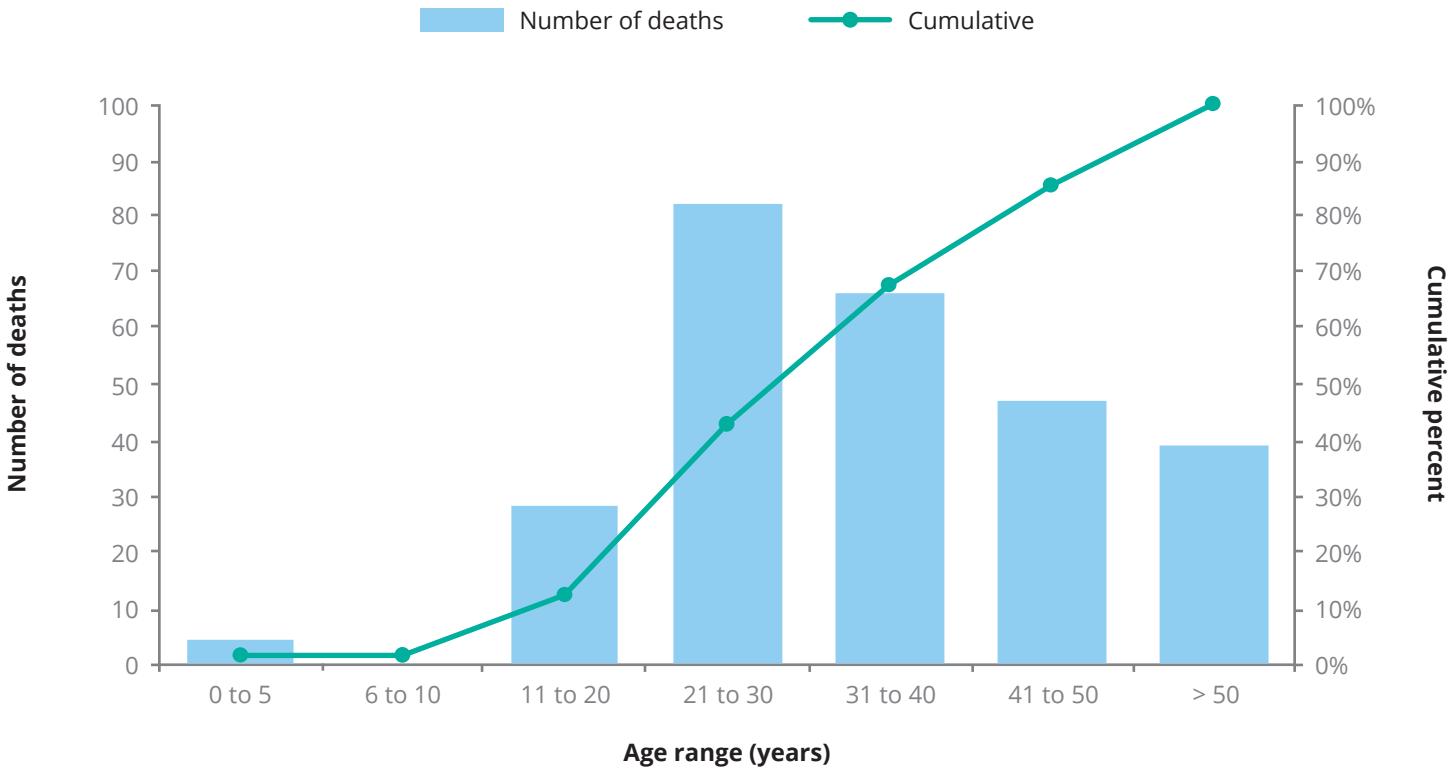


SURVIVAL

The survival and health outcomes in Canadians living with CF continues to improve over time. In 2018, there were 51 deaths recorded in the CCFR, compared to 63 deaths in 2017. Figure 47 shows the cumulative number of deaths and the age at death from 2014 to 2018. Over the past two decades, a gradual increase in the median age of death can be seen. The median age of death was 33.0 years in 2018 compared to 33.6 years in 2017 and 25.0 years in 1998 (Figure 48). The median age of death tells us that half of those who died were younger than 33.0 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 1998 (Figure 49). In 2018, this value was 1.2%.

Risk factors such as pulmonary exacerbations and malnutrition are often associated with increased risk of death. In 2018, the most common cause of death was related to pulmonary complications (49%). 30 (58.8%) individuals with CF who died in 2018 never received a transplant (any organ).

FIGURE 47
Age at death, 2014 to 2018.



SURVIVAL

FIGURE 48
Median age at death per year, 1998 to 2018.

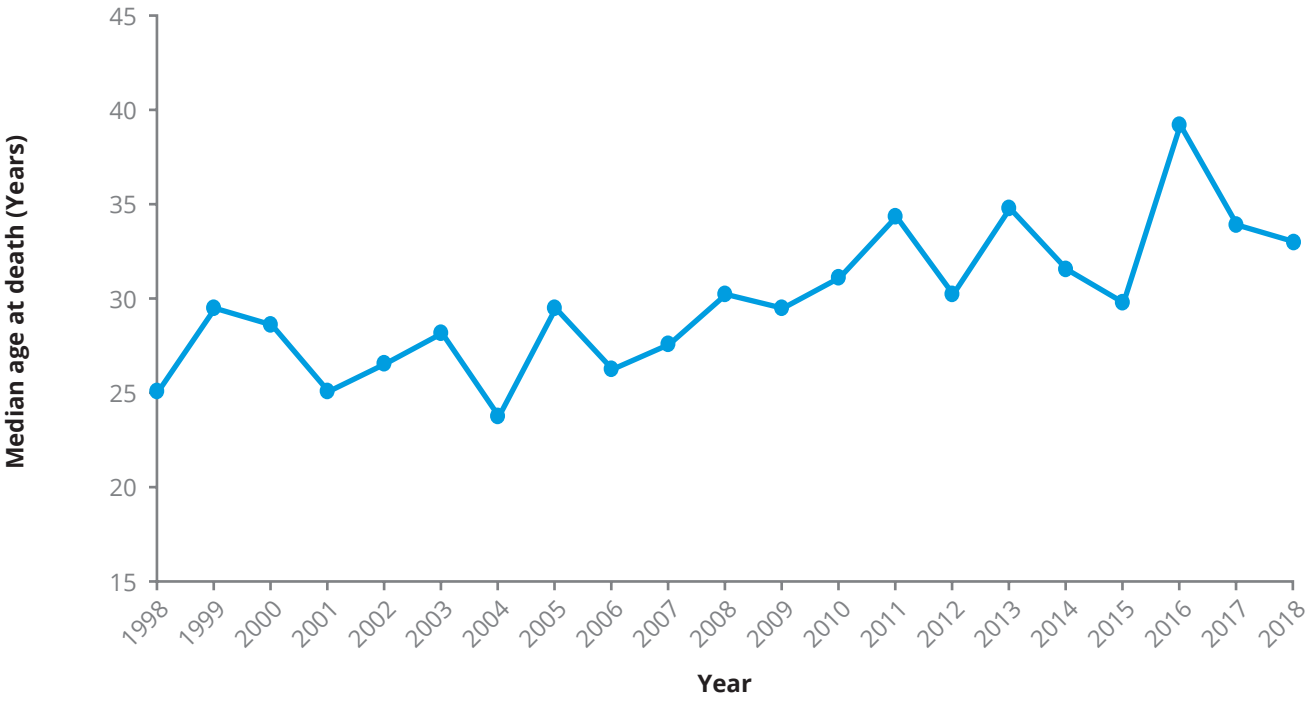
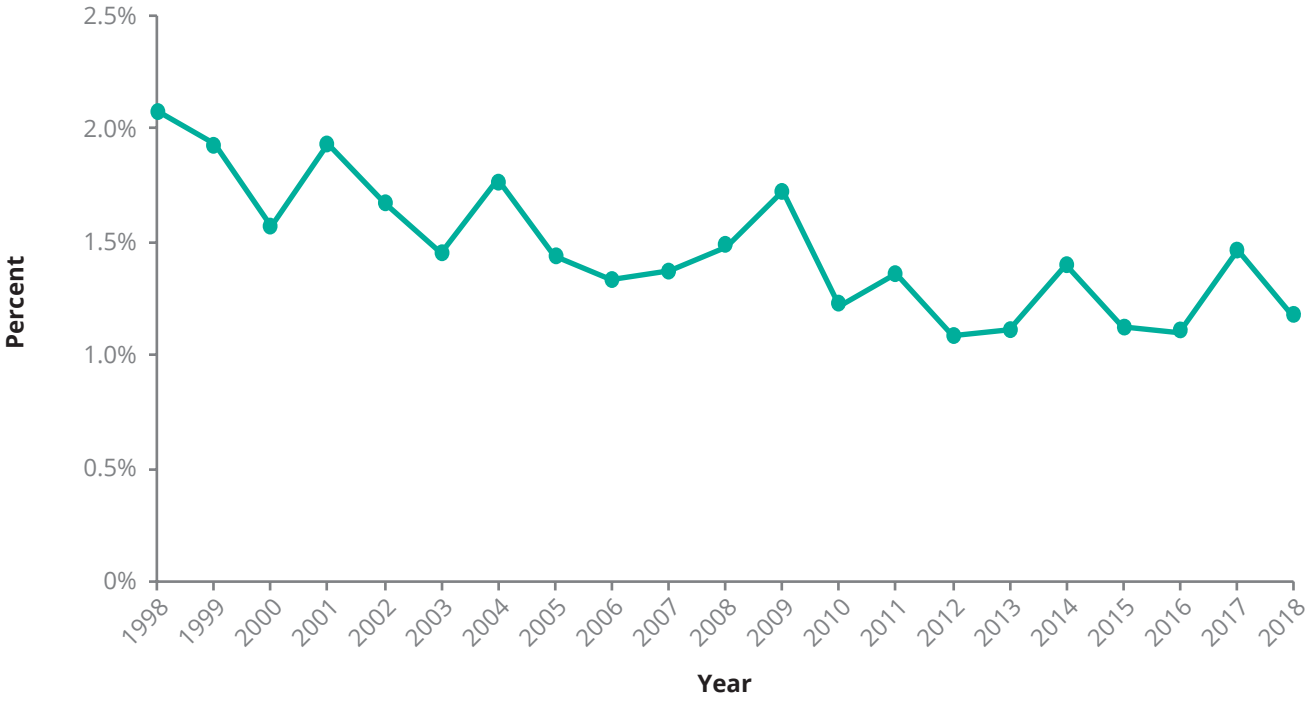


FIGURE 49
Death rate per year, 1998 to 2018.



SURVIVAL

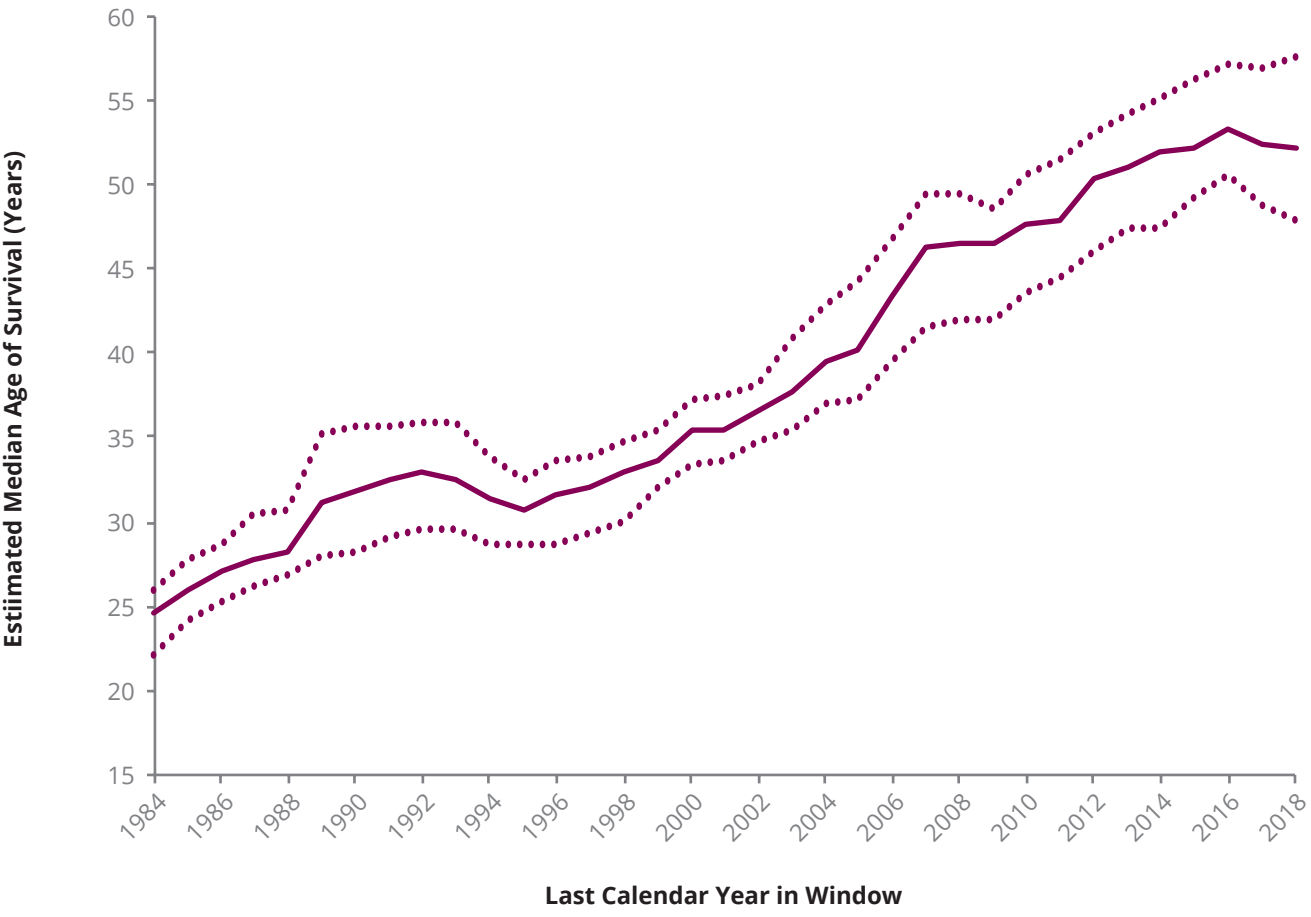
ESTIMATED MEDIAN AGE OF SURVIVAL

A 5-year rolling window, to stabilize the estimates over time, was used to calculate the median age of survival using the Cox proportional hazards model. The most recent 5-year window (2014 - 2018) included 5,029 people with CF and 266 deaths. The number of individuals with CF lost-to-follow-up (defined as individuals with CF who are alive, but haven't been reported on in the past 2 years) was 169 (3.4%).

In 2018, the median age of survival is currently estimated to be **52.1 years of age** (Figure 50). 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 current age-specific mortality rates will remain stable. 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 51). 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 52 and indicates that the expected median age of survival is higher when considering more recent cohorts. The probability of surviving beyond age 20 years is 91.4% for those born in 1985 or later compared to 62.1% for those born before 1975.

FIGURE 50
Estimated median age of survival for a moving 5-year window with 95% confidence intervals, 1984 to 2018.



SURVIVAL

FIGURE 51
Estimated median age of survival for a moving 5-year window with 95% confidence intervals, by sex, 1984 to 2018.

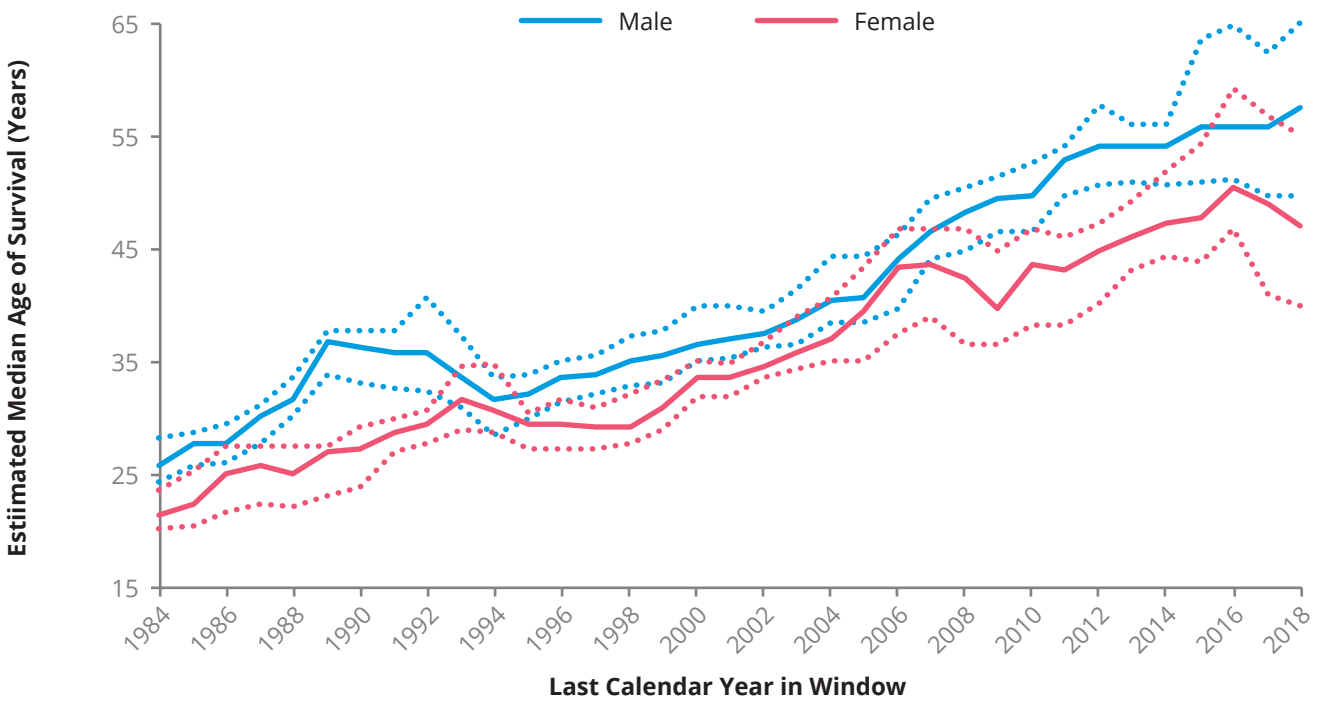
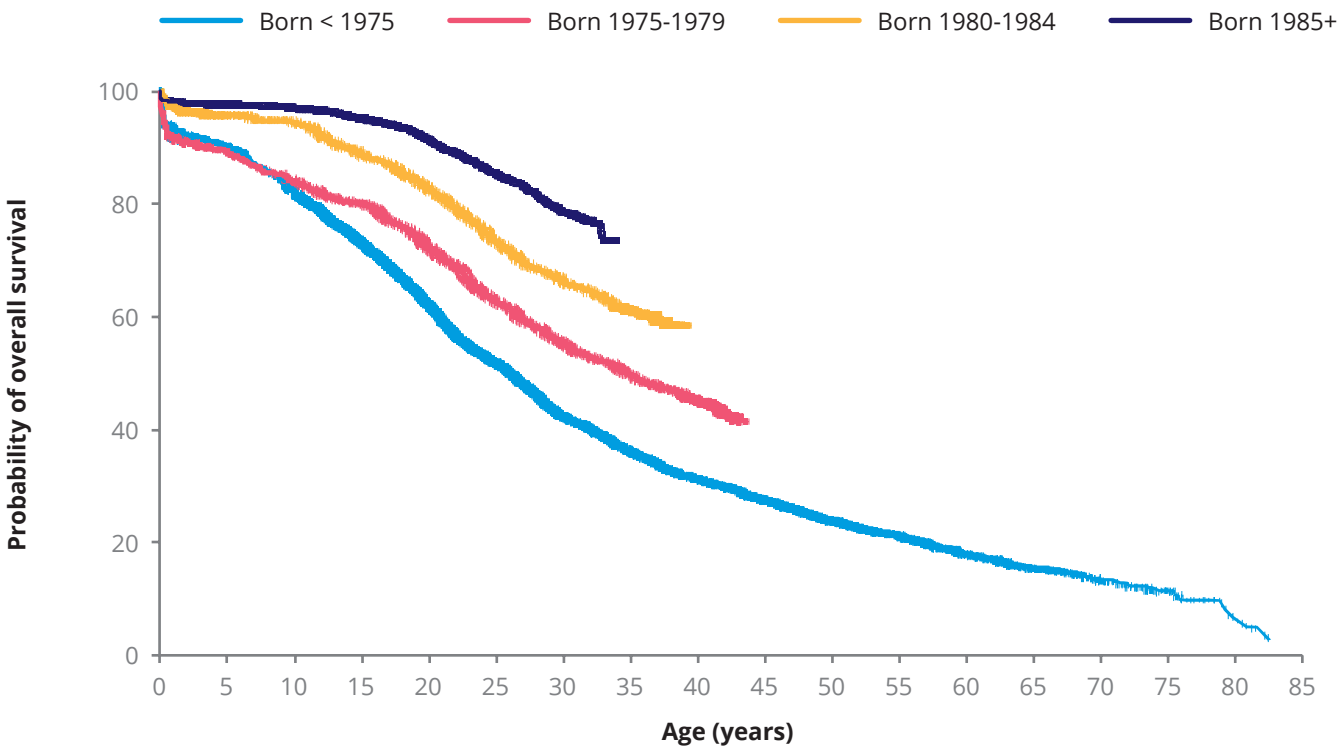


FIGURE 52
Overall survival of individuals with CF, by birth cohorts, 2018.

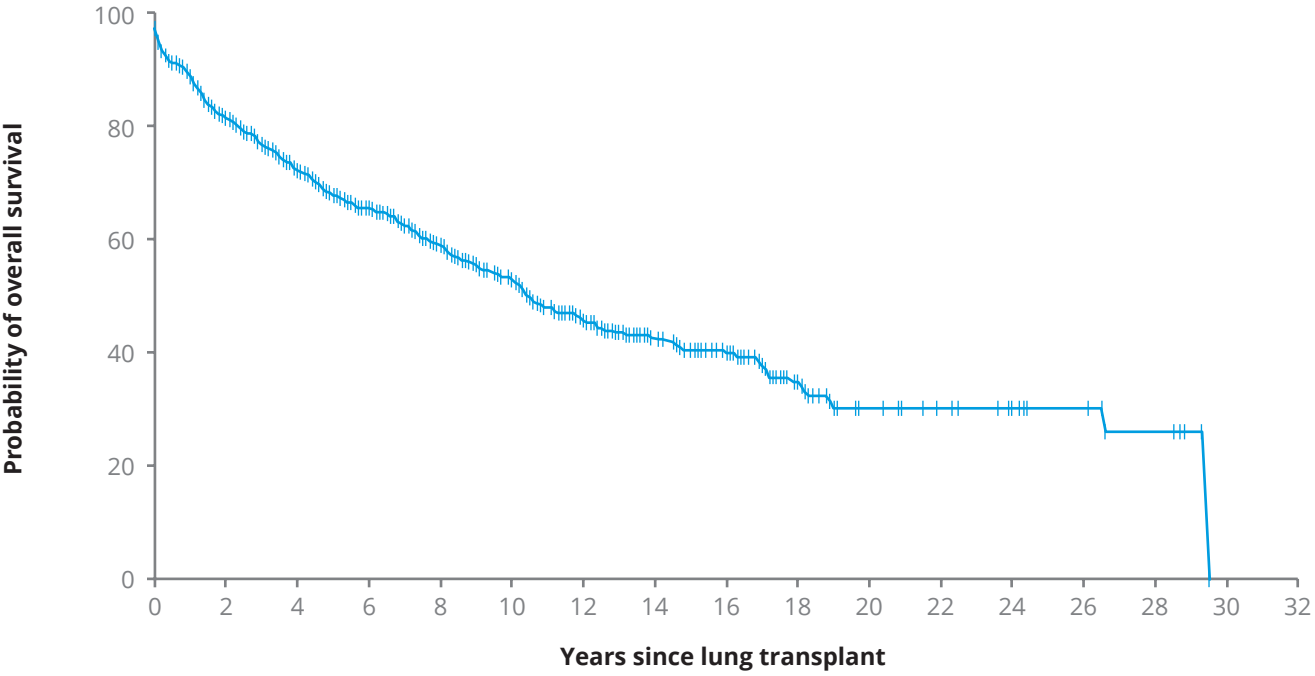


SURVIVAL

POST LUNG TRANSPLANT SURVIVAL

Between 1988 and 2018, there were 842 lung transplants that took place and 365 deaths post lung transplant. Figure 53 shows the probability of survival post lung transplant which is 88.7% at one year, 76.7% at three years and 67.7% at five years. Overall, 50% of those patients transplanted today would be expected to live beyond 10.5 years following lung transplantation.

FIGURE 53
Post lung transplant survival, 2018.



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 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 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 2018 is 52.1 years, we are saying that if a child with CF is born in Canada in 2018, they have a 50% chance of living beyond 52.1 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 52.1 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 2018.

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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ACKNOWLEDGMENTS

Thank you to the following groups and people who made outstanding contributions to the *Canadian Cystic Fibrosis Registry* and this 2018 Annual Data Report.

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

Dr. John Wallenburg, Chief Scientific Officer, Cystic Fibrosis Canada

Stephanie Cheng, Director, Registry, Cystic Fibrosis Canada

Theresa Le, Data Analyst, Registry, Cystic Fibrosis Canada

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

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FUNDING FOR THE DESIGN AND DISTRIBUTION OF THIS REPORT WAS GENEROUSLY SUPPORTED BY AN UNRESTRICTED GRANT FROM

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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.

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2019–12 | Cette publication est aussi disponible en français
Charitable registration: 10684 5100 RR0001