Cystic Fibrosis
Fibrose kystique
Canada

2022 ANNUAL DATA REPORT

THE CANADIAN CYSTIC FIBROSIS REGISTRY

CYSTIC FIBROSIS

Cystic fibrosis (CF) is a rare disease affecting over 4,400 Canadians or roughly 1 in 3,848 live births[1].

Cystic fibrosis 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; anxiety and depression are common among this population. Individuals with cystic fibrosis may reach the point where they require a lung transplant; most fatalities of people with cystic fibrosis are due to lung disease. There is no cure.

CYSTIC FIBROSIS CANADA

Since being founded by parents in 1960, Cystic Fibrosis Canada has grown into a leading organization with a central role engaging people living with cystic fibrosis, parents and caregivers, volunteers, researchers and healthcare professionals, industry, government, and donors.

We work together going further to change lives; advocating for access to therapy, supporting delivery of care, funding research, and providing information and support. We will not stop until all people with cystic fibrosis can and do experience everything life has to offer — and enjoy everything life has to offer.

For more information, visit **www.cysticfibrosis.ca**.

Published: December 2023

The information in this report is accurate to the time of publication.
For the most up-to-date version of the report, please visit us at **www.cysticfibrosis.ca**.

Suggested citation (print): Cystic Fibrosis Canada. (2023). *The Canadian Cystic Fibrosis Registry 2022 Annual Data Report. T*oronto, Canada: Cystic Fibrosis Canada.

Suggested citation (online): Cystic Fibrosis Canada. (2023). *The Canadian Cystic Fibrosis Registry 2022 Annual Data report.* Retrieved from **www.cysticfibrosis.ca**.

Cover page: Rianna, who lives with CF with her mom, Lina.

TABLE OF CONTENTS

OUR VISION IS A WORLD WITHOUT CYSTIC FIBROSIS

OUR MISSION IS TO END CYSTIC FIBROSIS

FOREWORD

We are immensely pleased to present the Canadian Cystic Fibrosis Registry 2022 Annual Data Report. The cystic fibrosis story is changing – and the data in this report demonstrate just how different a story it is becoming. In the 1960s, most children with CF weren't expected to live long enough to graduate high school. Today, more adults live with this disease than children. That is remarkable progress.

For the first time in our history, we can report that the estimated median age of survival for a Canadian with cystic fibrosis is 60 years of age - this means that half of the children born with CF today would be expected to live to be older than 60! Twenty years ago, that number was less than 37 years of age. This steady growth in the median age of survival is an indicator of the quality of CF care, research and treatments in Canada as well as the efforts that patients put into maintaining their health.

We believe that greater access to modulator therapies is just one contributor to this steady increase in the median age of survival. Our report finds that in 2022, there were 2,505 individuals being treated with CFTR modulator therapies, of those, 2,272 individuals were on Trikafta, more than twice that of the previous year. Cystic Fibrosis Canada is actively working to ensure more Canadians can access these potentially life-changing therapies, and data from our CF Registry will help us continue to build a case for wider access.

The data also reports a significant decrease in the total number of hospitalizations for individuals with CF. Since 2018, hospitalizations have dropped by 53%, and notably, the number of hospitalizations for pulmonary exacerbations, which typically would account for nearly all hospitalizations, decreased by over 63%. We are pleased to see these numbers, as fewer hospitalizations mean less severe disease and an increase in quality of life for our Canadian CF community.

Transplants, which were once the only option for end-stage care for a CF patient, are declining. Only seven transplants were performed in 2022, down nearly 90% from 2019. To date, 14 people have been removed from the active transplant waitlist, and almost all are on CFTR modulator therapy.

While we celebrate the changes the Canadian CF Registry has witnessed in the cystic fibrosis story, we remember those we have lost and recognize that while the data are pointing in the right direction, our community struggles daily with the burden of treatment and effects of this fatal disease.

We are incredibly grateful to the Canadians living with CF who actively participate in this indispensable resource, the healthcare teams at CF clinics who, without their collaboration there would be no CF Registry, supportive families and caregivers and the generous donors whose contributions make this work possible.

Dr. Paul Eckford PhD

Chief Scientific Officer
Cystic Fibrosis Canada

Dr. Anne Stephenson MD

Medical Director
Canadian Cystic Fibrosis Registry,
Cystic Fibrosis Canada

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

Cystic Fibrosis Canada
Fibrose kystique Canada

2022 HIGHLIGHTS FROM THE CANADIAN CF REGISTRY

DEMOGRAPHICS

4,445 CANADIANS WITH CYSTIC FIBROSIS

34% CHILDREN

66% ADULTS

80 NEW CF DIAGNOSIS

55 THROUGH NEWBORN SCREENING

35% TRAVELLED MORE THAN 100 KM TO RECEIVE CF CARE

CYSTIC FIBROSIS TREATMENT & CARE

16,750 CLINIC VISITS

10,478 HOSPITAL DAYS

5,964 HOME IV DAYS

7 ORGAN TRANSPLANTS

35% HAD PSEUDOMONAS AERUGINOSA INFECTION

33% OF ADULTS HAVE CF-RELATED DIABETES

SURVIVAL

HALF OF THE CANADIANS **BORN WITH CF TODAY** ARE EXPECTED TO LIVE BEYOND **60** YEARS OF AGE

HEALTH OUTCOMES

63% CHILDREN (<2 YEARS)

77% CHILDREN (2-17 YEARS)

61% ADULTS

HAVE AN ADEQUATE WEIGHT

97.1% CHILDREN

73.5% ADULTS

MEDIAN LUNG FUNCTION

INTRODUCTION

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

Participating individuals who attend any of the accredited 41 CF clinics across Canada, are represented in the Canadian Cystic Fibrosis Registry. With permission, clinical information is submitted by the CF cystic fibrosis clinics on behalf of individuals living with CF. Given that most people living with the disease attend one of these clinics, and nearly all provide permission to the utilization of their data, we are confident that the CF Registry includes data on virtually all Canadians diagnosed with cystic fibrosis — 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 those living with cystic fibrosis who consent to having their data submitted, and the exceptional effort and contribution from CF clinic team members who collect and enter the data.

INCLUSION AND EXCLUSION CRITERIA

This 2022 Annual Data Report contains data from individuals diagnosed with cystic fibrosis who have consented to participate in the CF Registry and who were reported on by a Canadian CF clinic in calendar year 2022. This includes those who were diagnosed with cystic fibrosis or died in 2022. Data from individuals with a diagnosis of CF screen positive, inconclusive diagnosis (CFSPID) or CFTR-related disease are excluded from this report. Throughout the report, the population from which the percent or prevalence was calculated, is indicated in the title of each table or figure.

Data from individuals who have received a lung transplant prior to 2022 were excluded from the following sections: Pulmonary Outcomes, Nutritional Outcomes, Microbiology, Therapies and Medications, and Healthcare Encounters.

HOW TO READ THIS REPORT

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

Individuals who are under 18 years of age are categorized as children and those 18 years of age or older are categorized as adults. Unless otherwise stated, age is calculated as of December 31, 2022. For the purposes of this report, sex refers to the biological sex of the individual which is not the same as gender identity or gender expression.

The last several years saw many disruptions to typical cystic fibrosis care and submission of data to the CF Registry, and some of these are reflected in the data presented in this report. The reader is encouraged to interpret any temporal trends with caution, and in the context of the information presented below.

CYSTIC FIBROSIS CARE IN CANADA IN 2022

Cystic Fibrosis Canada continues to work closely with CF clinics to complete data entry for 2022 despite on-going impacts of the COVID-19 pandemic and other possible extenuating circumstances.

While the COVID-19 pandemic certainly had a measurable impact on CF care, it is also important to note that 2021 and 2022 saw an unprecedented number of Canadians with CF become eligible for the triple combination CFTR modulator therapy elexacaftor/tezacaftor/ivacaftor, first through the Special Access Program starting in January 2020, then more broadly through commercial use when Health Canada approved the therapy in June 2021. The effects of COVID-19 are hard to disentangle from the impact of broad access to CFTR modulators. The combined effects of the on-going COVID-19 pandemic and the introduction of elexacaftor/tezacaftor/ivacaftor may be seen in some historical trends reported in this report and may be most noticeable in the Pulmonary Outcomes, Nutritional Outcomes and Healthcare Encounters sections.

SUMMARY OF THE CANADIAN CYSTIC FIBROSIS REGISTRY

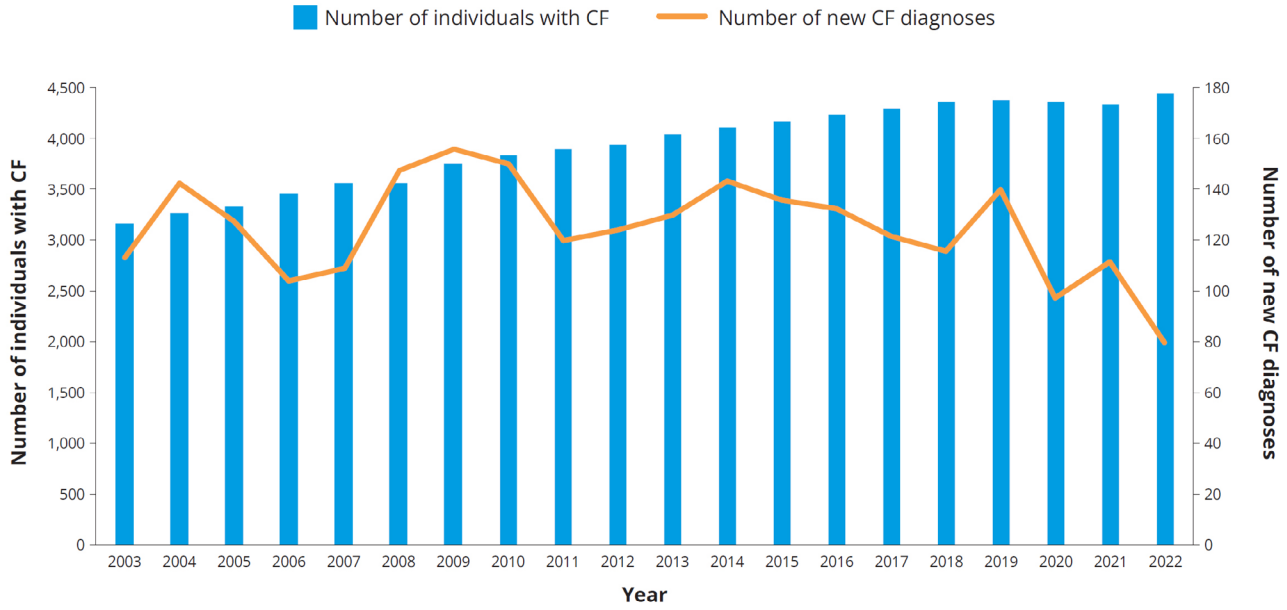
Detail	2002	2007	2012	2017	2022
Number of individuals with CF reported on in the Canadian CF Registry	3,396	3,574	3,960	4,298	4,445
Adults (%)	47%	55%	59%	61%	66%
Females (%)	46%	47%	47%	46%	46%
Age (median, years)	17.2	19.5	21.1	23.0	25.8
Number of new diagnoses	128	109	124	122	80
Genotyped (%)	98.3%	98.6%	98.9%	99.2%	99.1%
Homozygous F508del (%)	52.0%	50.5%	49.1%	47.2%	45.5%
Heterozygous F508del (%)	36.9%	38.2%	38.9%	40.5%	41.4%
FEV_1 percent predicted (median)	73.3	71.9	74.8	76.7	82.5
BMI percentile (median)	43.0	44.3	44.8	46.3	46.8
BMI (median)	21.7	21.8	22.1	22.5	23.4
Number of transplants	33	40	38	50	7
Number of deaths	57	49	43	66	40
Estimated median age of survival (5-year)	36.7	46.4	49.0	51.9	59.9

DEMOGRAPHICS

OVERVIEW OF CANADIANS WITH CYSTIC FIBROSIS

In 2022, there were a total of 4,445 individuals with cystic fibrosis who attended one of the 41 accredited CF clinics across Canada (Figure 1). This included 80 individuals newly diagnosed with cystic fibrosis, 1,496 (33.7%) children and 2,949 (66.3%) adults, and 2,034 (45.8%) females and 2,411 (54.2%) males.

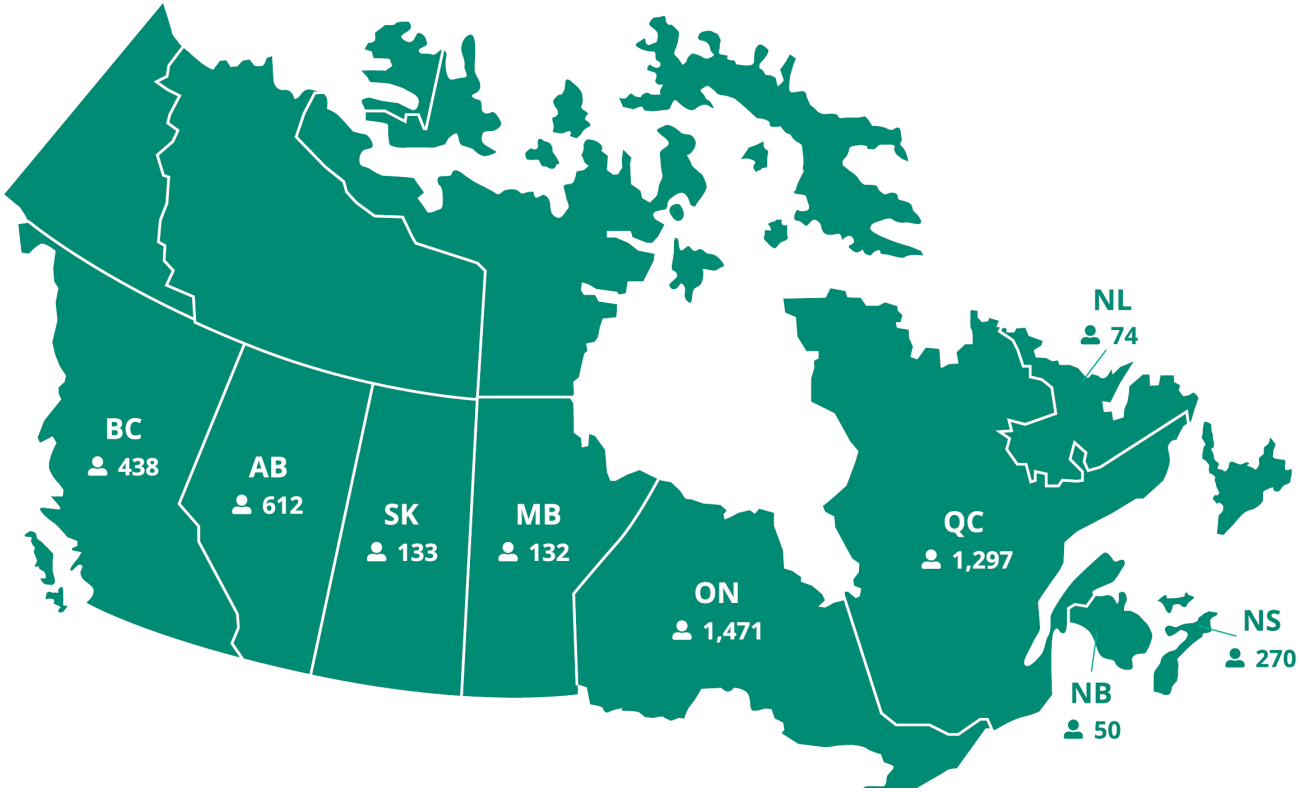
Figure 1 Total number of individuals with cystic fibrosis and new CF diagnoses, 2003 to 2022.



OVERVIEW OF CANADIANS WITH CYSTIC FIBROSIS

In Figure 2, individuals are reported based on their province of clinical care (the province in which they attended a cystic fibrosis clinic that reported their data to the CF Registry). Some individuals attend clinics in a province that is not their province of residence. Those who attended CF clinics in multiple provinces in 2022 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. Individuals are only counted once (i.e. unique individuals) in the national reported numbers.

Figure 2 Number of individuals with cystic fibrosis, by province of clinical care, 2022.



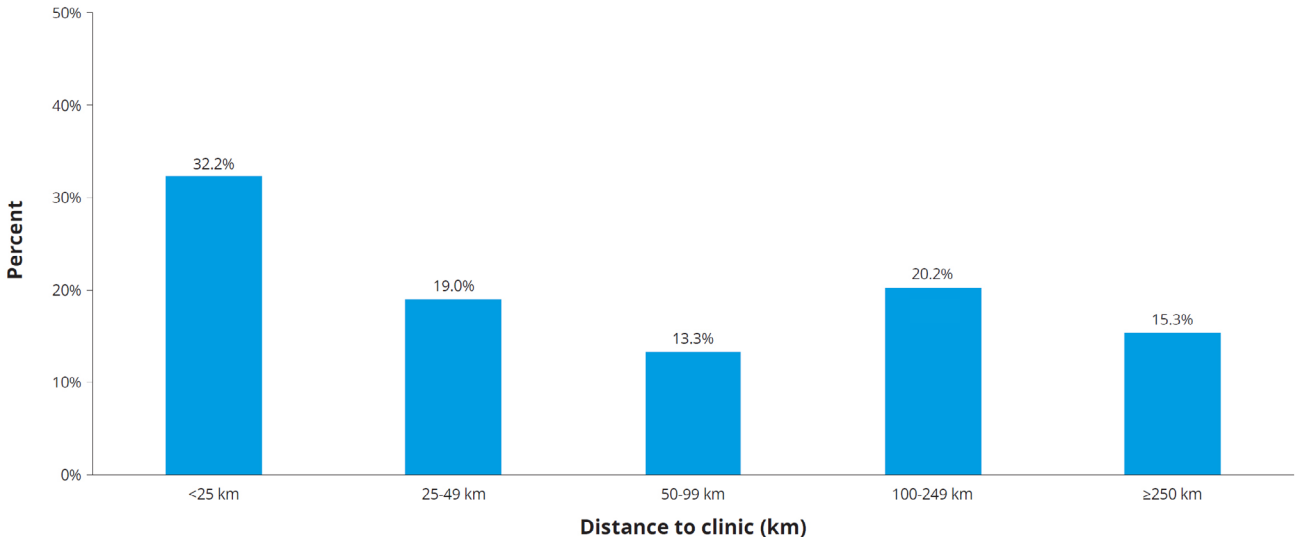
PROVINCE OF CLINICAL CARE*	NUMBER OF INDIVIDUALS WITH CF	FEMALE	MALE	ADULTS	CHILDREN
BC	438	185	253	291	147
AB	612	286	326	379	233
SK	133	56	77	79	54
MB	132	58	74	72	60
ON	1,471	689	782	1,025	446
QC	1,297	596	701	862	435
NB	50	25	25	34	16
NS	270	125	145	174	96
NL	74	29	45	50	24

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

DISTANCE TO CLINICS

The CF Registry began collecting the location of residence of those living with cystic fibrosis in 2015, through the first three digits of their postal code, or the forward sortation area (FSA). Distance to the reporting clinic were calculated in kilometers (km) using the fastest driving route. In 2022, there were 3,931 (88.4%) individuals with cystic fibrosis with at least one valid location recorded. While 2,013 (51.2%) of those with a reported location attended a CF clinic within 50 km of where they live, 1,395 (35.5%) travelled more than 100 km and 602 (15.3%) travelled more than 250 km for their CF care (Figure 3).

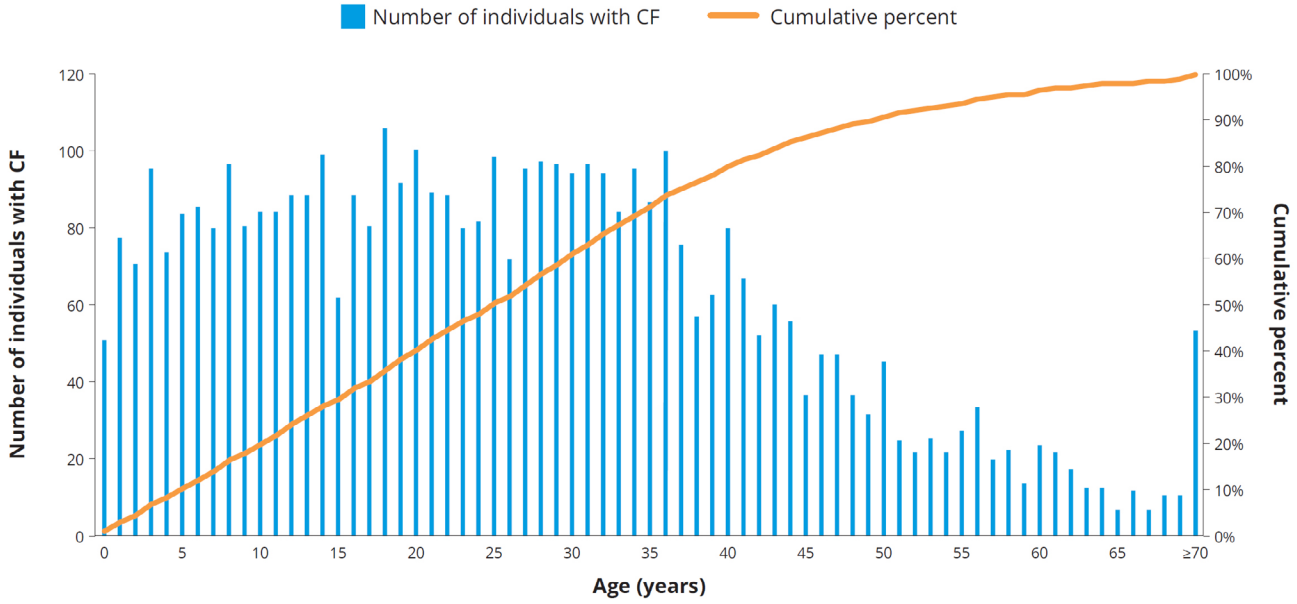
Figure 3 Distance travelled to clinic, 2022. [N = 3,931].



AGE DISTRIBUTION

Figure 4 shows the age distribution of the 4,445 Canadians living with cystic fibrosis in 2022.

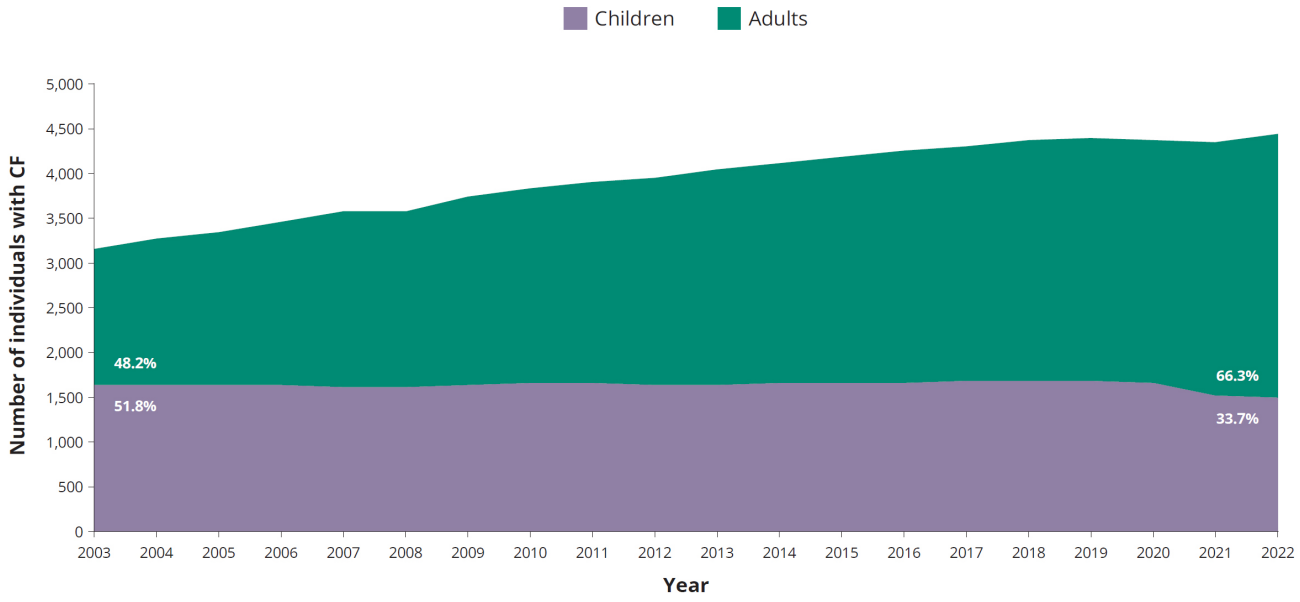
Figure 4 Age distribution, 2022. [N = 4,445].



AGE DISTRIBUTION

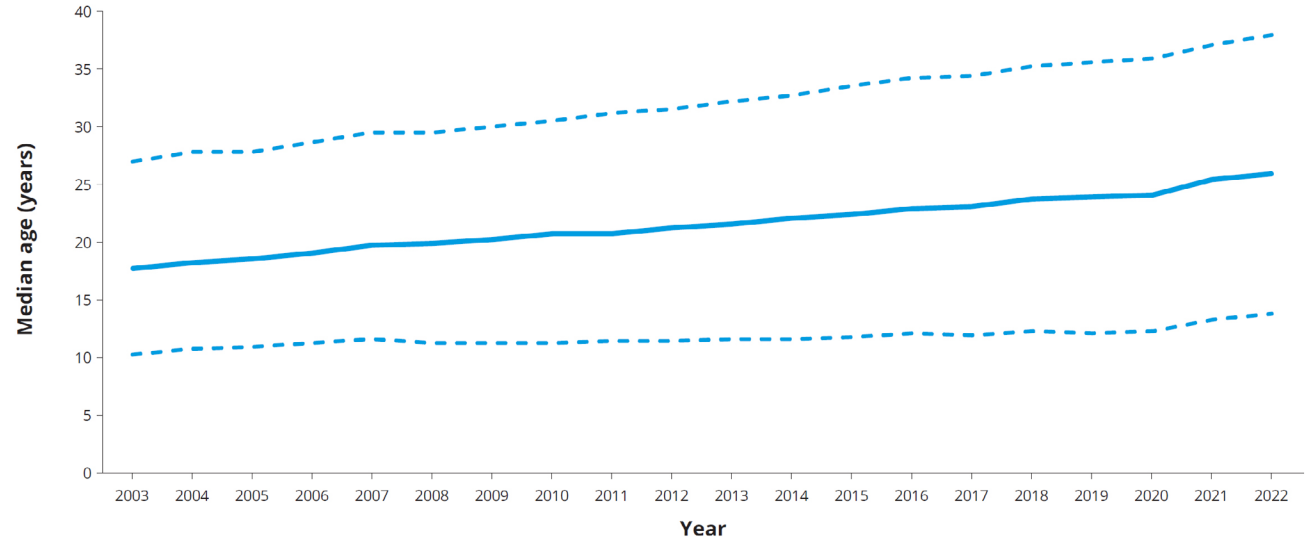
Improvements in treatment and care in the last few decades have led to an increase in the number of Canadian adults living with cystic fibrosis. Twenty years ago in 2003, less than half of all Canadians living with cystic fibrosis were adults (individuals aged 18 years and older) (Figure 5). In 2022, there were 2,949 adults living with CF, accounting for 66.3% of the Canadian CF population, and 974 (21.9%) adults aged 40 years and over.

Figure 5 Number of children and adult, 2003 to 2022.



It follows that the median age of individuals with cystic fibrosis has increased steadily over the past 20 years. From 17.5 years in 2003, to 25.8 years among those reported on in 2022 (shown in Figure 6, along with the 25th and 75th percentile of ages).

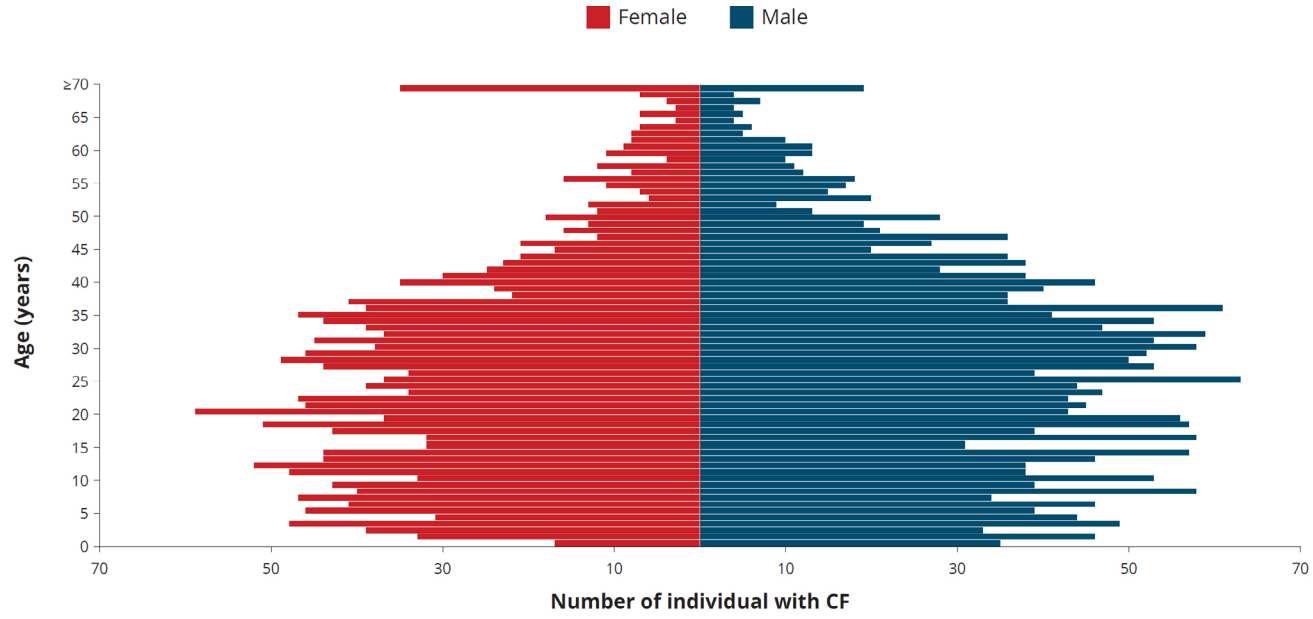
Figure 6 Median age, 2003 to 2022.



AGE-SEX DISTRIBUTION

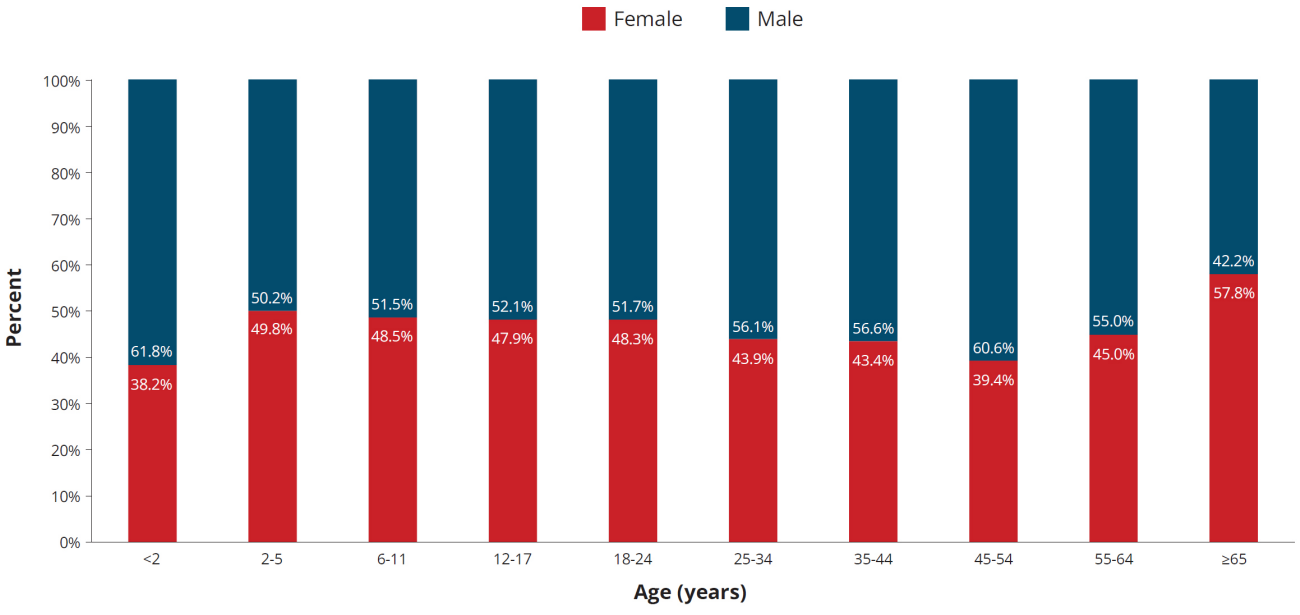
Figure 7 shows the age-sex distribution for all individuals reported on in 2022.

Figure 7 Age-sex distribution, 2022. [N = 4,445].



The sex distribution of those living with CF differed by age group. As seen in Figure 8, children under age 18 years (with the exception of the youngest age group) were fairly evenly distributed between the sexes, with the proportion of males increasing into adulthood before reaching a peak of 60.6% male for those aged 45-54 years. After age 55, the proportion of females begins to increase, to 57.8% female for those age ≥65 year.

Figure 8 Sex distribution, by age, 2022. [N = 4,445].



DIAGNOSIS

There were 80 new diagnoses of cystic fibrosis in 2022 that were recorded in the CF Registry. Of these, 55 (68.8%) were made through provincial newborn screening (NBS) programs.

AGE AT DIAGNOSIS

In total, 4,354 (98.0%) of individuals with cystic fibrosis reported on in 2022, had a recorded diagnosis date, and of those, 2,659 (61.1%) were diagnosed before the age of one year, and 3,196 (73.4%) were diagnosed by the age of two years (Figure 9). Adult diagnoses, those diagnosed at 18 years and older, accounted for only 355 (8.2%) of all individuals reported on in 2022.

Figure 9 Age at diagnosis of cystic fibrosis individuals, 2022. [N = 4,354].

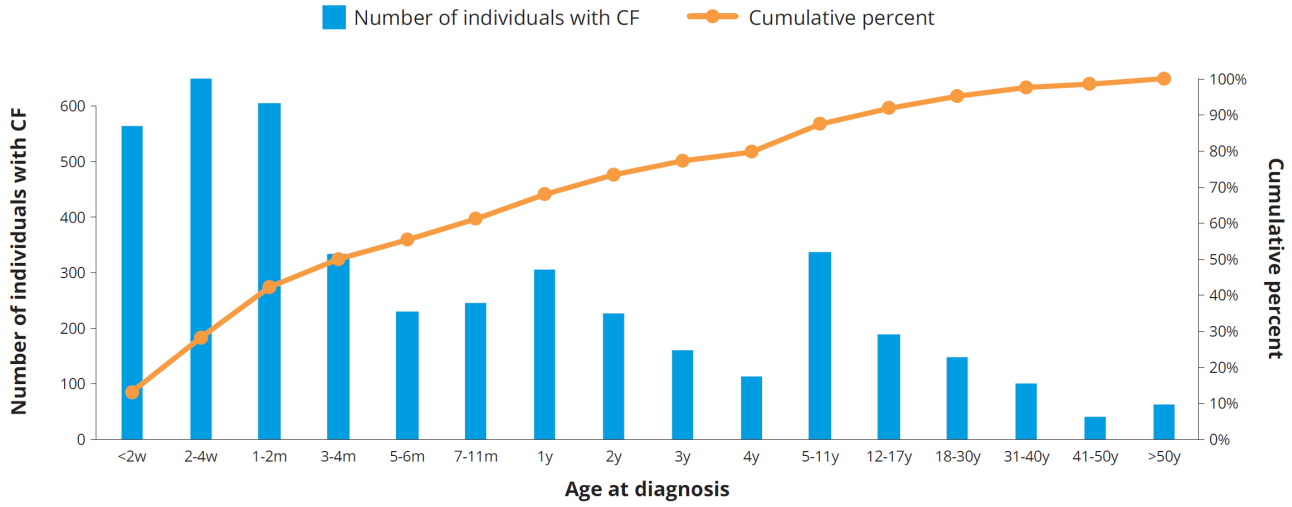
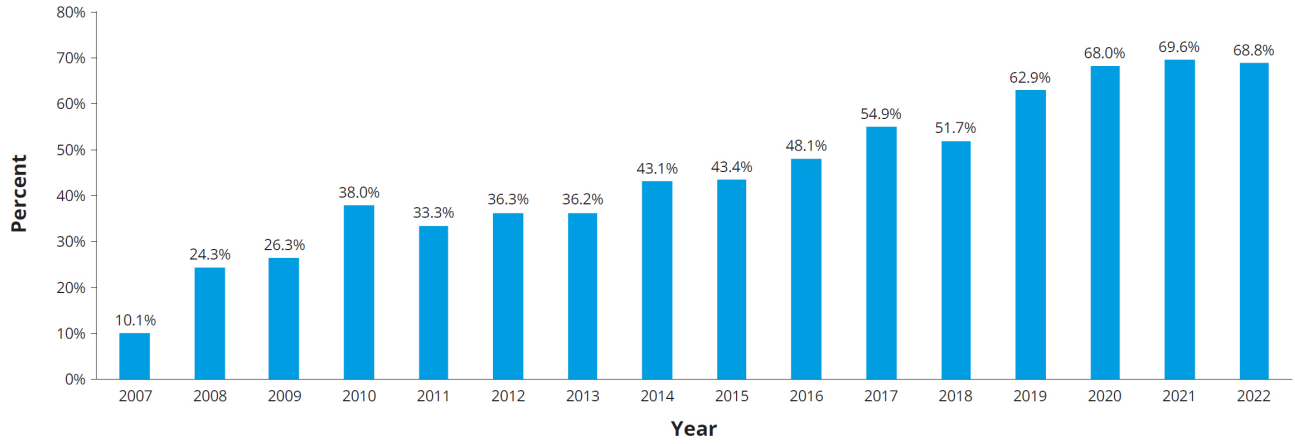


Figure 10 shows the percentage of newborns diagnosed through provincial NBS programs since 2007, when NBS for CF started in Alberta. At that time, only 10.1% of new CF diagnoses were identified through NBS. In the spring of 2018, Quebec became the last jurisdiction to start screening newborns for cystic fibrosis. Newborn screening is now in practice for all provinces across Canada and remains essential for early diagnosis and intervention. Out of 375 individuals reported on in 2022 who were under 5 years of age at the end of 2022, 50 (13.3%) did not have a reported record of NBS.

Figure 10 Percentage of all new CF diagnoses made through the NBS program, 2007 to 2022.



GENOTYPE

Cystic fibrosis 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[2].

By far, the most common CF mutation in Canada 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. F508del is also the most common mutation worldwide, however, the distributions of mutations can vary widely from country to country, depending on a number of factors, such as the geographical ancestry of the individuals being reported on.

CF disease-causing mutations can be classified into six major categories depending on how the mutation impacts the production and function of the CFTR protein and are summarized in Table 1. Mutations where the impact on the CFTR protein is unknown cannot be classified. CFTR protein modulator medications target specific classes of mutations.

It should be noted that not everyone with the same class of mutation or the same mutation will have the same clinical manifestations of cystic fibrosis.

Table 1 Classification of CFTR gene 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, N1303K
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
VI	The CFTR protein is made and works properly but the stability of the protein at the cell surface is reduced.	Q1412X

GENOTYPE

Nearly all individuals with cystic fibrosis reported on in 2022 (4,404 out of 4,445; 99.1%) had at least one CFTR gene mutation recorded. 2,021 (45.5%) have two copies of the F508del mutation (referred to as homozygous F508del) and 1,842 (41.4%) carry a single copy of the F508del mutation (referred to as heterozygous F508del). In total, almost 87% carry at least one copy of the F508del mutation (Figure 11).

Figure 11 Distribution of genotypes, 2022. [N = 4,445].

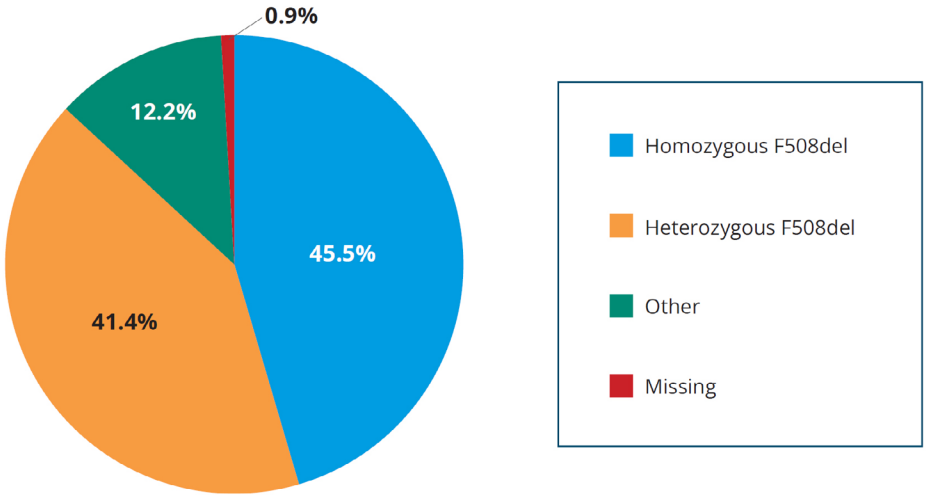
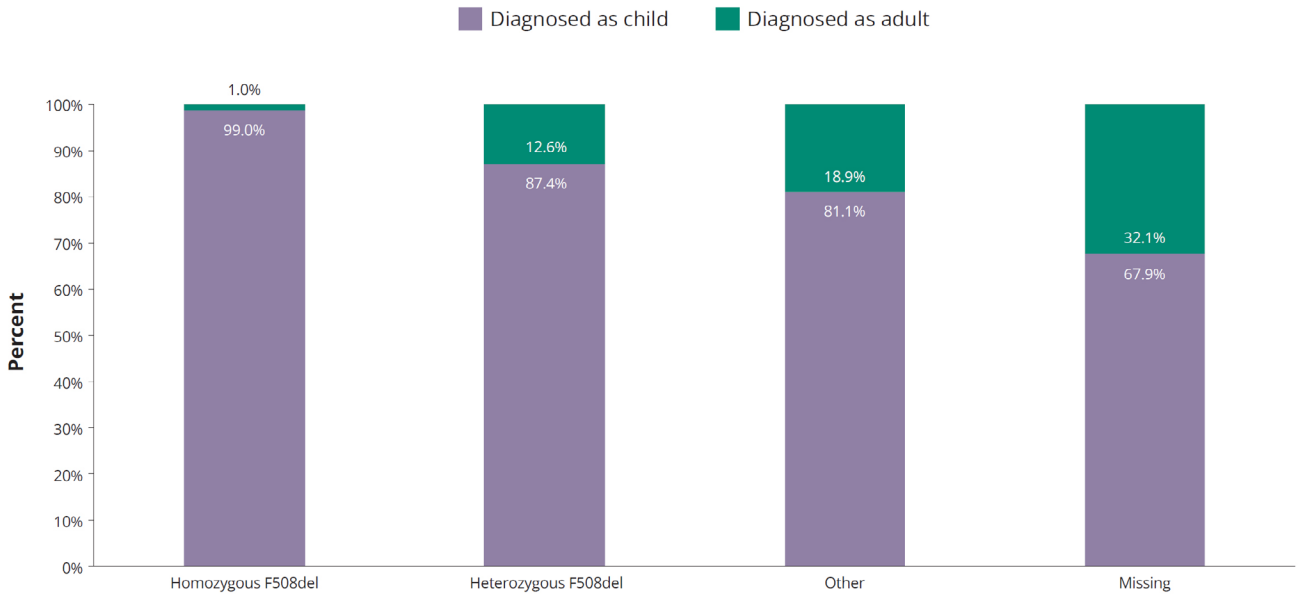


Figure 12 shows the genotype distribution of the CF population by the age of diagnosis. Individuals with more severe disease symptoms are generally diagnosed earlier; milder forms of cystic fibrosis may only be diagnosed in adulthood. Nearly all individuals (99.0%) who were homozygous F508del were diagnosed as a child (under 18 years).

Figure 12 Distribution of genotypes, by age at diagnosis, 2022. [N = 4,354].



GENOTYPE

Table 2 shows the number of people with cystic fibrosis who carry at least one of each mutation, and the proportion among those individuals with recorded mutations. Only mutations found in at least 5 individuals with CF are included in Table 2.

Note that individuals in the table are not mutually exclusive. For example, if an individual has mutations F508del and G551D, they would be included in both counts.

Table 2 Frequency of CFTR gene mutations, 2022. [N = 4,404].

MUTATION	NUMBER*	PERCENT*
F508del	3,861	87.7%
621+1G->T	262	5.9%
G542X	147	3.3%
G551D	132	3.0%
L206W	121	2.7%
A455E	120	2.7%
711+1G->T	110	2.5%
N1303K	88	2.0%
M1101K	74	1.7%
R117H	72	1.6%
G85E	68	1.5%
I507del	64	1.5%
5T	61	1.4%
3849+10kbC->T	59	1.3%
2789+5G->A	51	1.2%
P67L	40	0.9%
1717-1G->A	38	0.9%
W1282X	38	0.9%
R553X	37	0.8%
S489X	36	0.8%
D1152H	29	0.7%
3199del6	28	0.6%
R334W	28	0.6%
1898+1G->A	26	0.6%
CFTRdele2,3	25	0.6%
Y1092X	25	0.6%
3659delC	23	0.5%
2184insA	21	0.5%
R1162X	21	0.5%
R347P	20	0.5%
R1158X	19	0.4%
R560T	19	0.4%
Q493X	18	0.4%
3272-26A->G	16	0.4%
3120+1G->A	15	0.3%
R117C	15	0.3%
TG12	15	0.3%

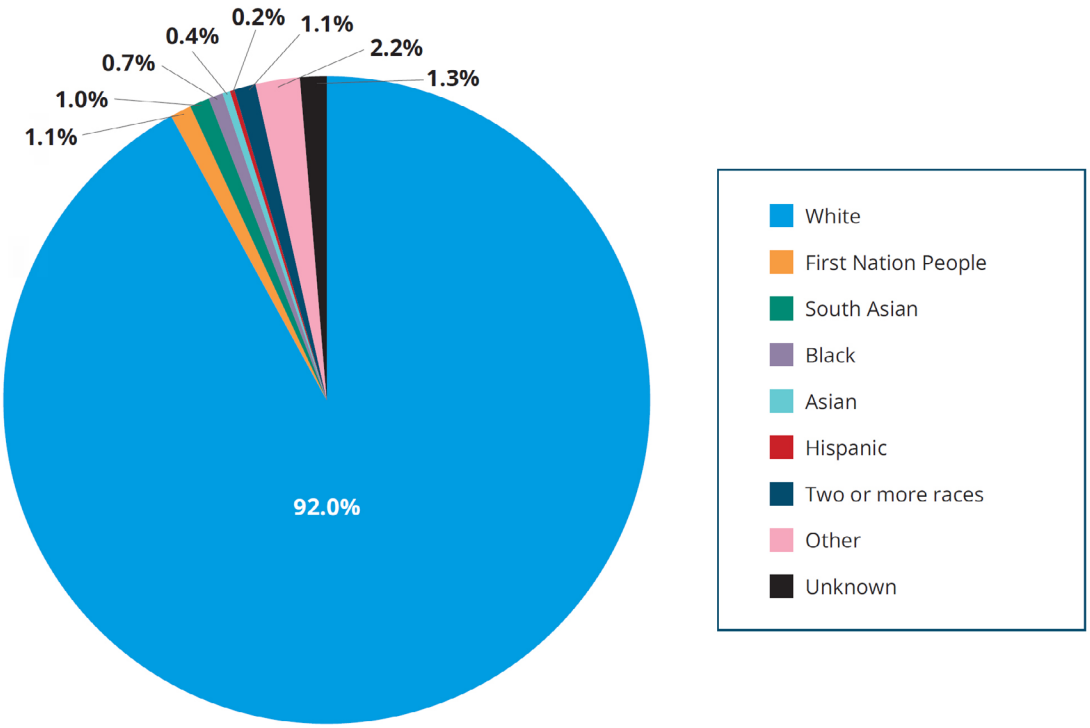
MUTATION	NUMBER*	PERCENT*
1525-1G->A	14	0.3%
E60X	14	0.3%
1154insTC	13	0.3%
2789+2insA	13	0.3%
3905insT	13	0.3%
2183AA->G	12	0.3%
P574H	12	0.3%
R347H	11	0.2%
394delTT	10	0.2%
4016insT	10	0.2%
Q1313X	10	0.2%
R1066C	10	0.2%
S466X	10	0.2%
S549N	10	0.2%
2622+1G->A	9	0.2%
L558S	9	0.2%
R75X	9	0.2%
1078delT	8	0.2%
711+3A->G	8	0.2%
L1254X	8	0.2%
V456A	8	0.2%
V520F	8	0.2%
3876delA	7	0.2%
L218X	7	0.2%
2184delA	6	0.1%
A559T	6	0.1%
D110H	6	0.1%
R1070Q	6	0.1%
1461ins4	5	0.1%
D579G	5	0.1%
L1077P	5	0.1%
Q220X	5	0.1%
T1299I	5	0.1%
TG11	5	0.1%
TG13	5	0.1%
Y569D	5	0.1%

** The number and percentage of individuals with a given mutation includes those with one or two copies of the mutation.*

ETHNICITY

Cystic fibrosis can affect anyone anywhere in the world. The majority (92.0%) of the currently identified Canadian CF population is White. Of those remaining who have an identified ancestry (Figure 13), they are divided among five groups (First Nations, Black, Asian, South Asian, and Hispanic). Ethnicity is captured and reported by the CF clinic entering the data.

Figure 13 Distribution of ethnicity, 2022. [N = 4,445].



PULMONARY OUTCOMES

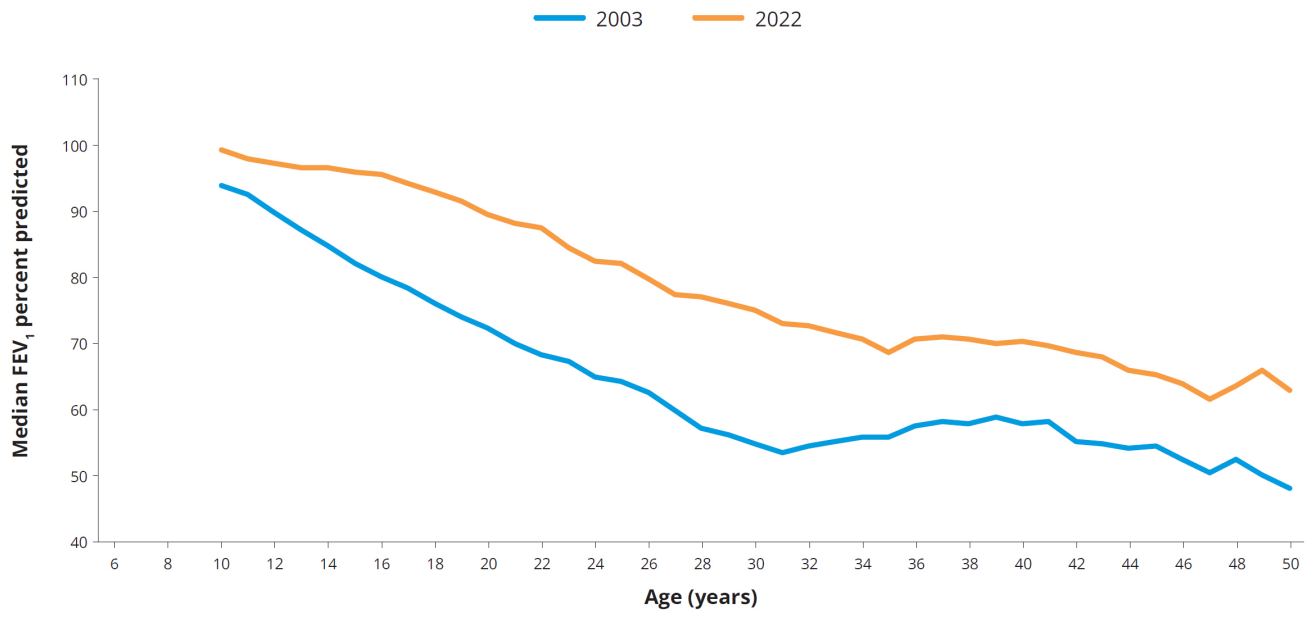
Lung function measurements are critical for evaluating and monitoring lung health in individuals living with cystic fibrosis. Although measures of lung function are made in children as young as three years of age, they are generally more reliable starting at six years of age. FEV_1 (forced expiratory 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 the measured FEV_1 to the average FEV_1 of a healthy population of similar age, height, ethnicity, and sex. Global Lung Initiative (GLI) equations are used to calculate the FEV_1 percent predicted values[3]. Although FEV_1 percent predicted is a commonly used measure of lung function in the CF population, it may not be sensitive enough to detect mild changes in the airways or early lung disease.

In this section, the first stable (i.e. not measured during a pulmonary exacerbation or other destabilizing event) FEV_1 percent predicted measurement of the year was used for each individual age six and older at the time of measurement, to summarize pulmonary function. If no clinically stable measurements were available, the first measurement regardless of the indicated status was used. Individuals were grouped by the age at which the FEV_1 percent predicted was measured, and any age-specific distributions were calculated among all those with a measurement in that age group.

Individuals who received a lung transplant prior to 2022, and any FEV_1 percent predicted measurements taken after lung transplant in 2022, were excluded from this section of the report.

Figure 14 shows the median FEV_1 percent predicted from age six to 50 years using a 5-year moving average window. At an individual level, lung function declined with age as lung disease progressed, whereas the median FEV_1 percent predicted of the entire population has increased since 2003. The median FEV_1 at 26 years of age (the median age of an individual living with cystic fibrosis in 2022) was 76.7% predicted in 2022 compared with 57.1% predicted in 2003, marking an improvement of 19.6% over the last two decades.

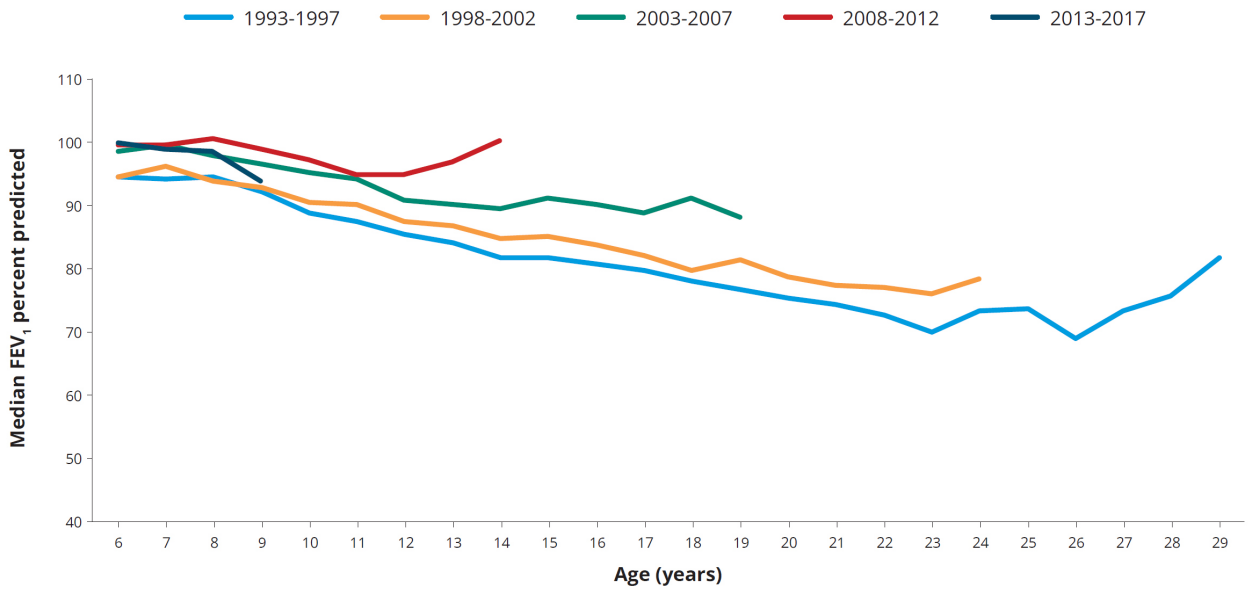
Figure 14 Median FEV_1 percent predicted, by age (5-year moving window), 2003 and 2022.



PULMONARY OUTCOMES

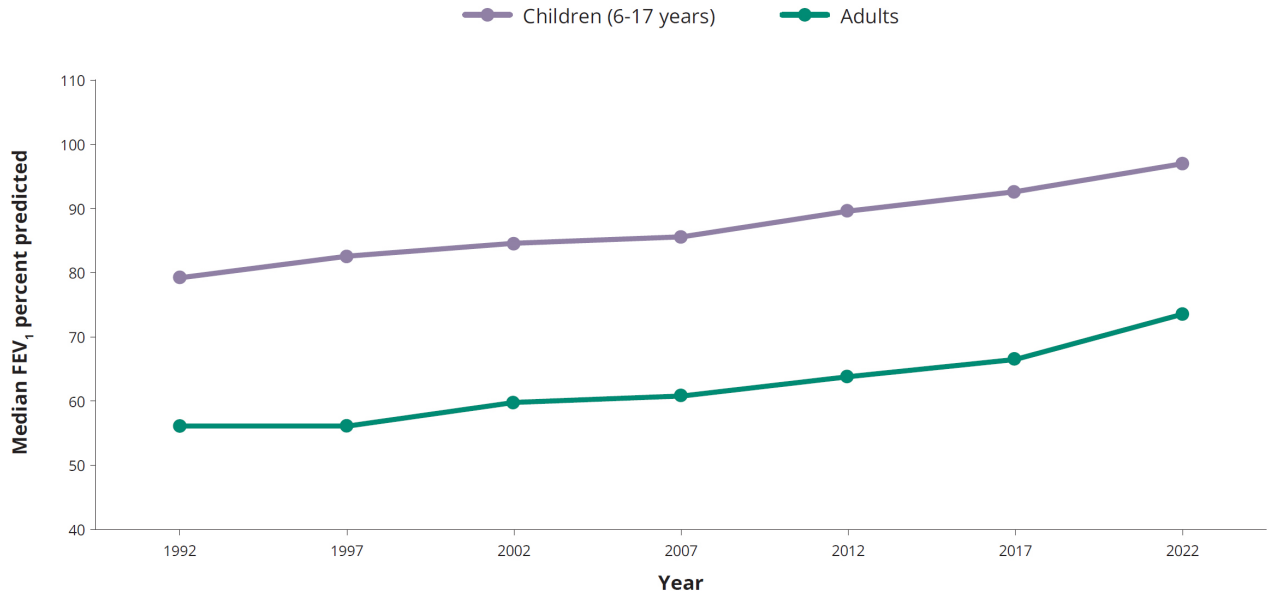
Individuals born more recently had a higher median FEV_1 percent predicted at age six years than those born earlier (Figure 15). The deviations in trends present in some of the birth cohort lines for the later ages are due to the small sample sizes resulting from the method used to group ages in the calculations.

Figure 15 Median FEV_1 percent predicted, by birth cohort, 2022.



Over time, the median FEV_1 percent predicted has increased steadily in both age groups, and in 2022 the median FEV_1 percent predicted was 73.5% in adults and 97.1% in children (6-17 years of age) (Figure 16).

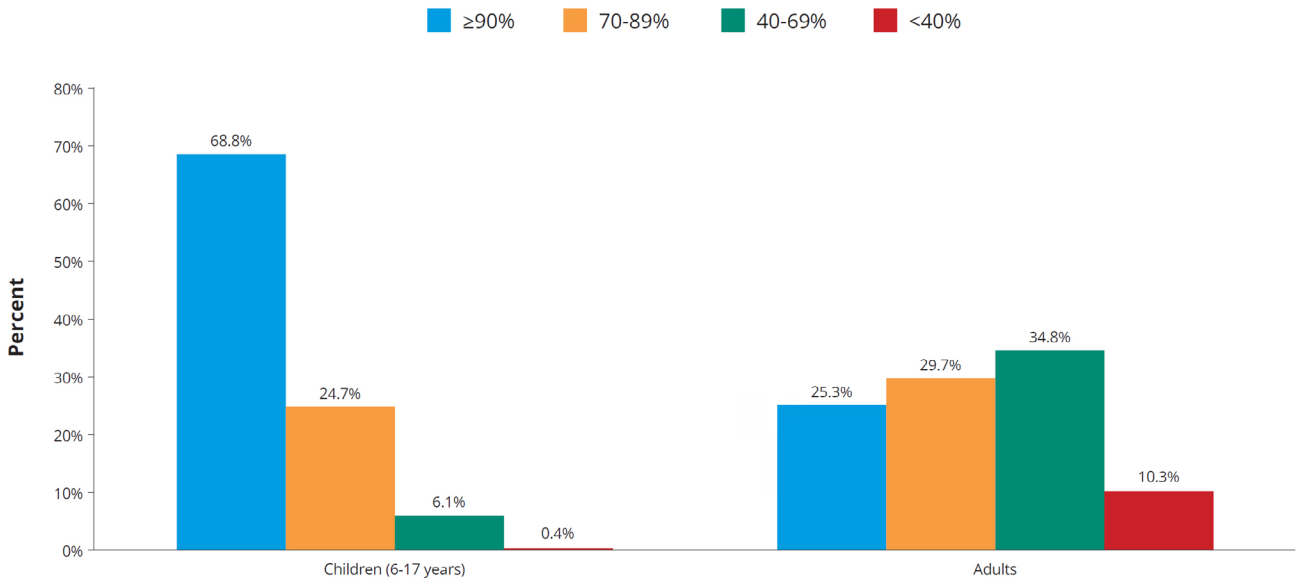
Figure 16 Median FEV_1 percent predicted, by age, 1992 to 2022.



PULMONARY OUTCOMES

In 2022, 1,071 children 6-17 years and 2,543 adults had a recorded FEV_1 percent predicted measurement. Of those, 737 (68.8%) children 6-17 years had pulmonary function ≥90% predicted, while only 643 (25.3%) adults had pulmonary function in this range (Figure 17).

Figure 17 Pulmonary function, by age, 2022. [N = 1,071 children (6-17 years); N = 2,543 adults].



PULMONARY OUTCOMES

Figure 18 and Figure 19 show the distribution of pulmonary function between females and males, and among children and adults, respectively. Among children, more males had FEV_1 percent predicted at or above 90% predicted, compared with females. Among adults, more males had FEV_1 percent predicted less than 40% predicted, compared with females.

Figure 18 Pulmonary function in children (6 to 17 years), by sex, 2022. [N = 518 females; N = 553 males].

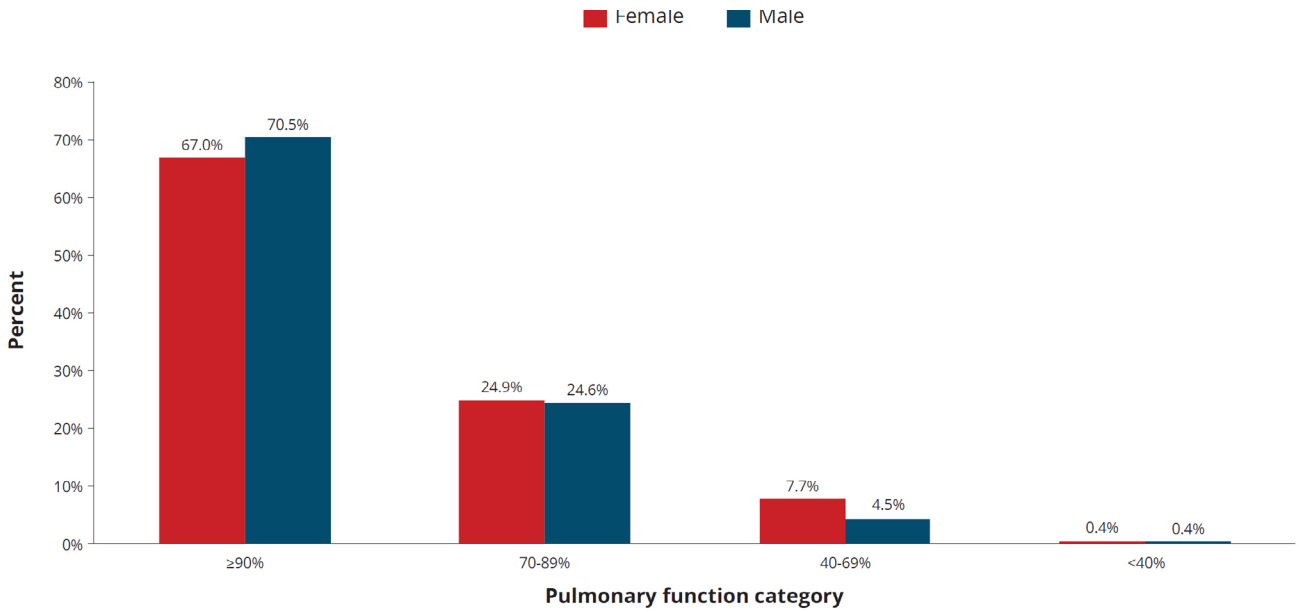
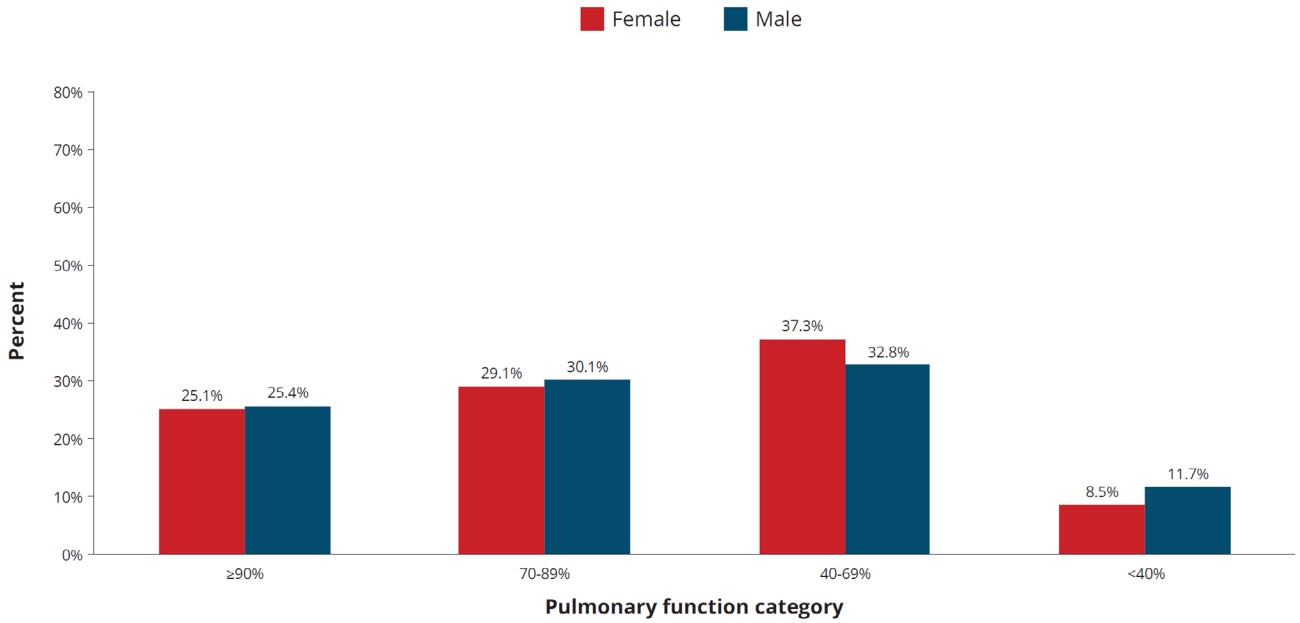


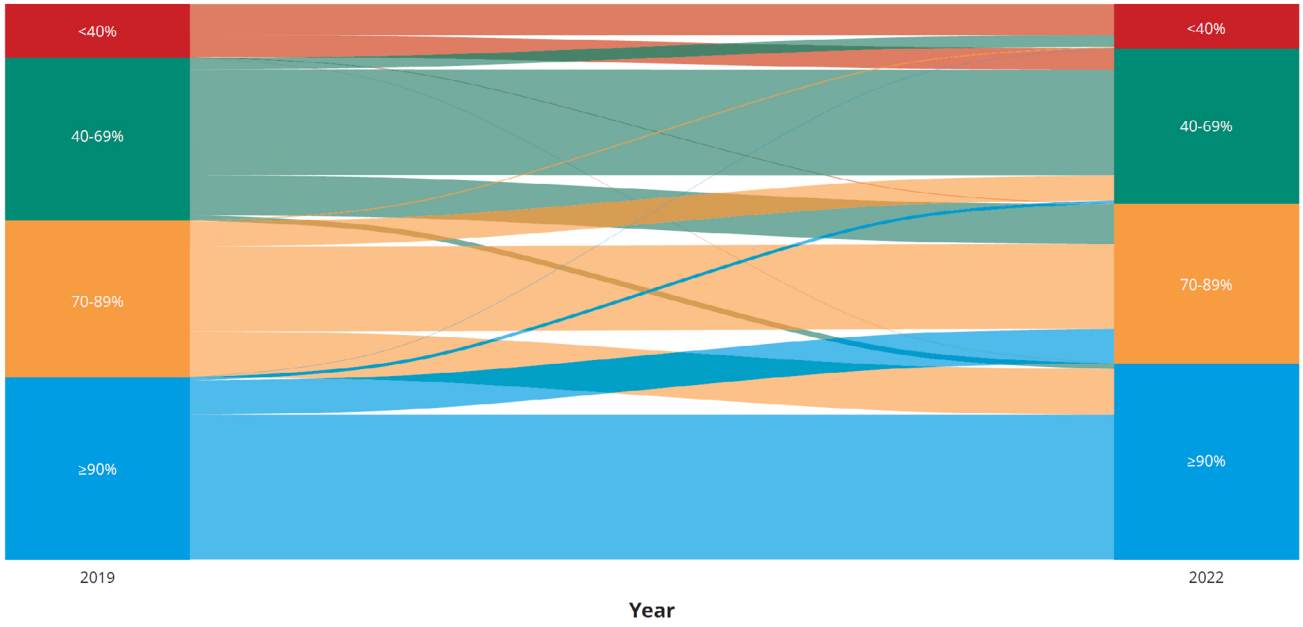
Figure 19 Pulmonary function in adults, by sex, 2022. [N = 1,130 females; N = 1,413 males].



PULMONARY OUTCOMES

Figure 20 shows the movement between pulmonary function categories from 2019 to 2022. Of the 3,133 individuals who had a reported FEV_1 percent predicted in both years, the vast majority (65.9%) had no change in pulmonary function category, while 642 (20.5%) improved their pulmonary function by at least one category. However, 425 (13.6%) individuals experienced pulmonary function decline by at least one category. It is important to note that widespread initiation of highly effective modulator therapy occurred during this time.

Figure 20 Movement between pulmonary function categories, 2019 to 2022. [N = 3,133].



NUTRITIONAL OUTCOMES

PANCREATIC STATUS

Pancreatic insufficiency causes malnutrition in individuals with cystic fibrosis. Pancreatic enzymes are given as supplements to help with digestion and absorption of nutrients.

In 2022, 3,671 (83.4%) individuals with cystic fibrosis were identified as pancreatic insufficient, compared with 731 (16.6%) who were not identified as pancreatic sufficient, as shown in Figure 21. For individuals 40 years of age or older, 262 (27.2%) were pancreatic sufficient (Figure 22).

Figure 21 Pancreatic status, 2022. [N = 4,402].

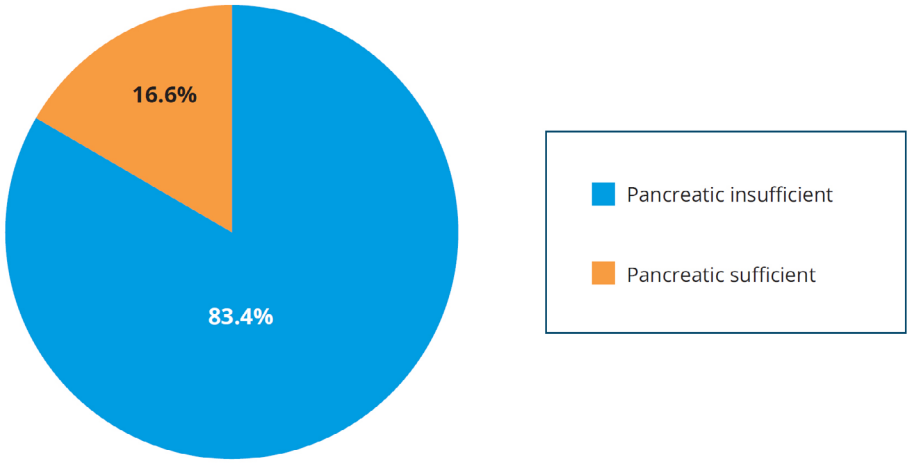
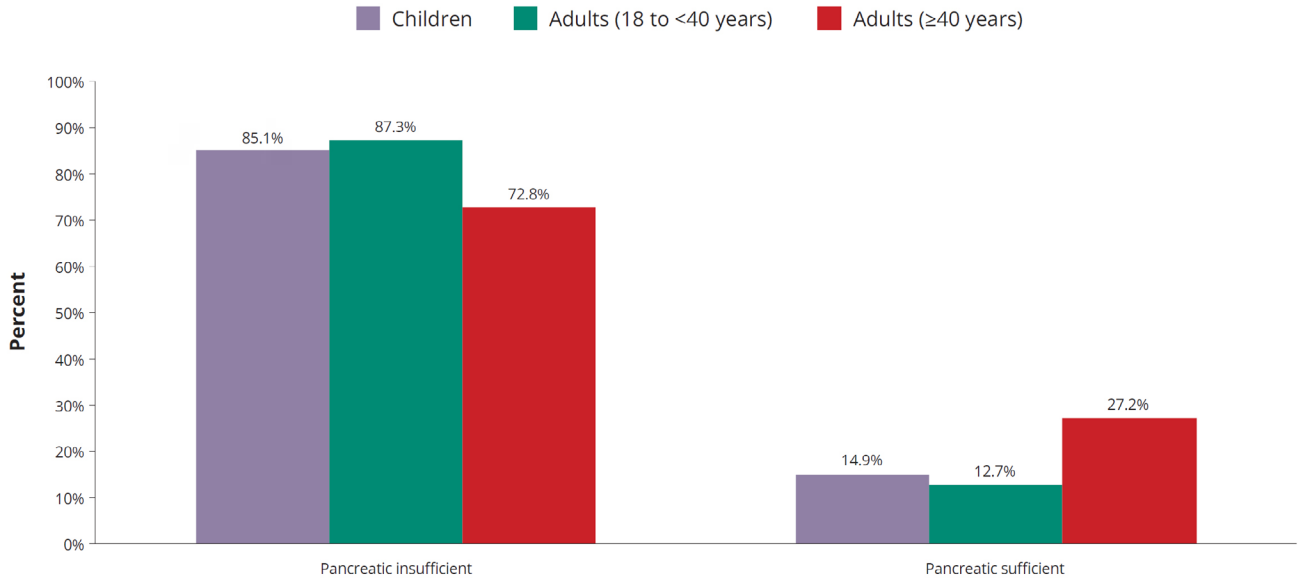


Figure 22 Pancreatic status, by age, 2022. [N = 1,472 children; N = 1,966 adults (18-39 years); N = 964 adults (≥40 years)].



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, measured BMI is only reported for adults because they have attained their maximal height. As children are rapidly growing, one must consider the child's age when assessing their nutritional status, thus using growth charts to calculate BMI percentiles is a more appropriate measure.

In this section, the BMI percentile obtained at the time of the individual's first stable FEV_1 percent predicted measurement of the year was used to summarize their nutritional outcome. If there was no FEV_1 percent predicted measured (for example, in children <6 years), the first stable BMI percentile measurement was used. If none existed, the first complete BMI percentile regardless of the indicated status was used. Individuals were grouped by the age at which the BMI percentile was measured, and any age-specific distributions were calculated among all those with a measurement in that age group.

Individuals who received a lung transplant prior to 2022, and any BMI percentile measurements taken after lung transplant in 2022, were excluded from this section of the report.

BMI percentiles were 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[4]. BMI percentiles allow comparisons to be made between children who are the same age and sex. Table 3 details the BMI percentile classification categories following the respective WHO or CDC guidelines[5].

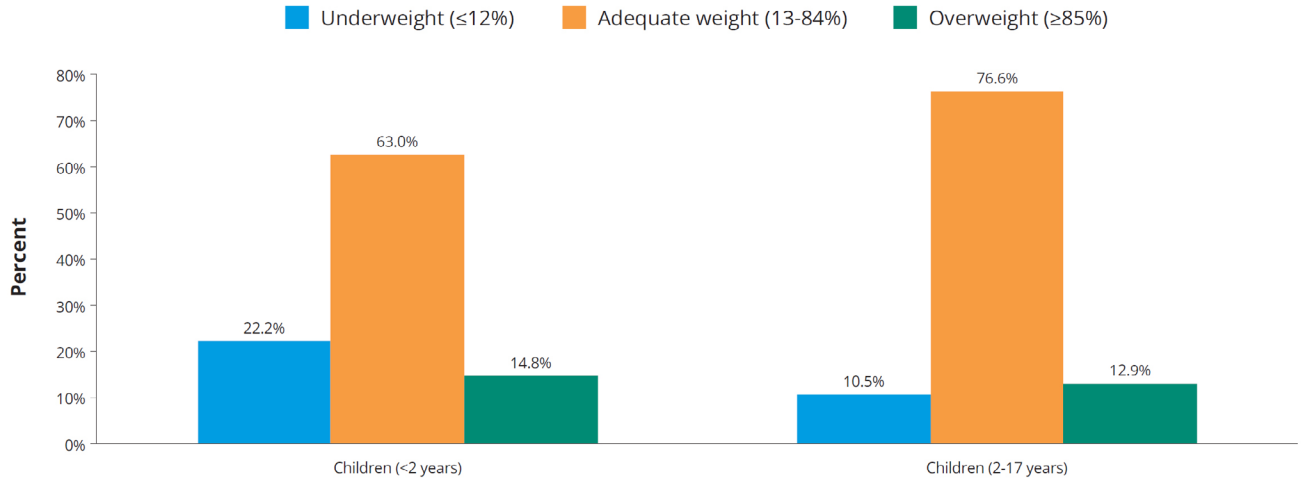
Table 3 BMI percentile classification.

CLASSIFICATION	RANGE
Underweight	≤ 12th percentile
Adequate weight	> 12th percentile to < 85th percentile
Overweight	≥ 85th percentile

In 2022, 189 children under 2 years of age and 1,380 children aged 2-17 years had a recorded BMI percentile measurement. The national median BMI percentile in children under 2 years of age was 38.2 and in children aged 2-17 years was 48.1. The 50th BMI percentile is the national goal for children with cystic fibrosis and in 2022, 38.1% of children under 2 years and 47.5% of children aged 2-17 years exceeded this goal. It is important to note that different guidelines were used to calculate BMI percentile in these two pediatric age groups, which may result in some underlying differences.

Of those with a recorded BMI percentile, 119 (63.0%) children under 2 and 1,057 (76.6%) children 6-17 years had an adequate weight (i.e. neither underweight nor overweight) (Figure 23).

Figure 23 BMI percentile in children, 2022. [N = 189 children (<2 years); N = 1,380 children (2-17 years)].



BMI PERCENTILE

For both males and females, the median BMI percentiles have been increasing over time (Figure 24). While males showed a slightly higher median BMI percentile in earlier years, the gap between sexes has diminished over time.

Figure 24 Median BMI percentiles in children (2-17 years), by sex, 1992 to 2022.

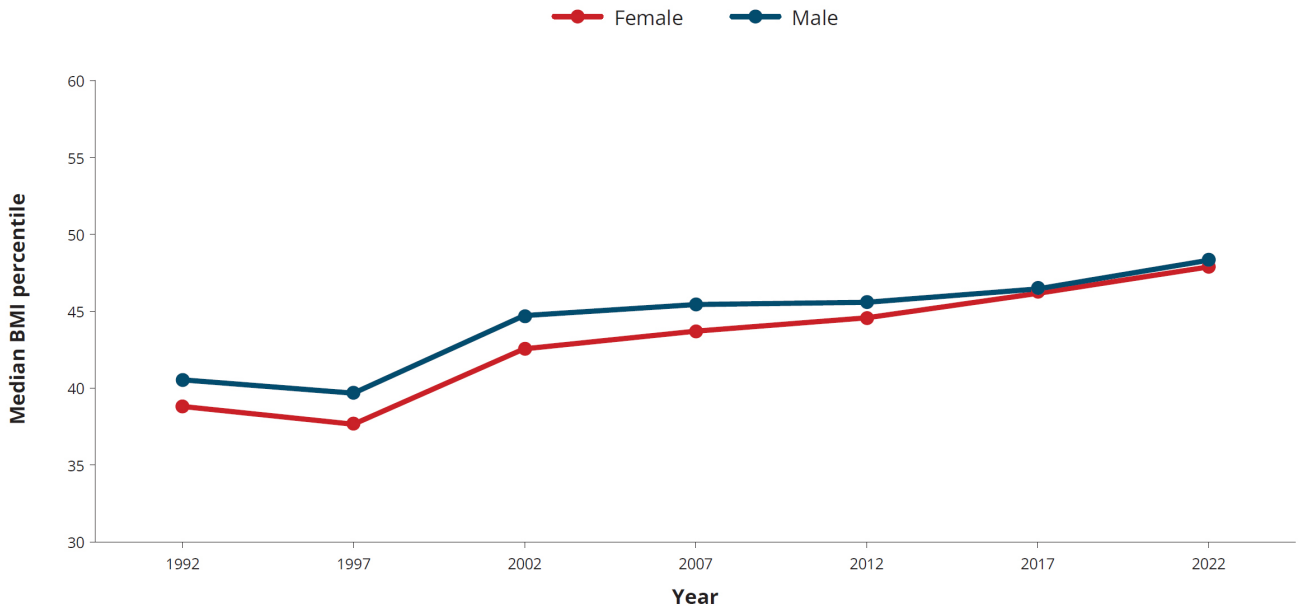
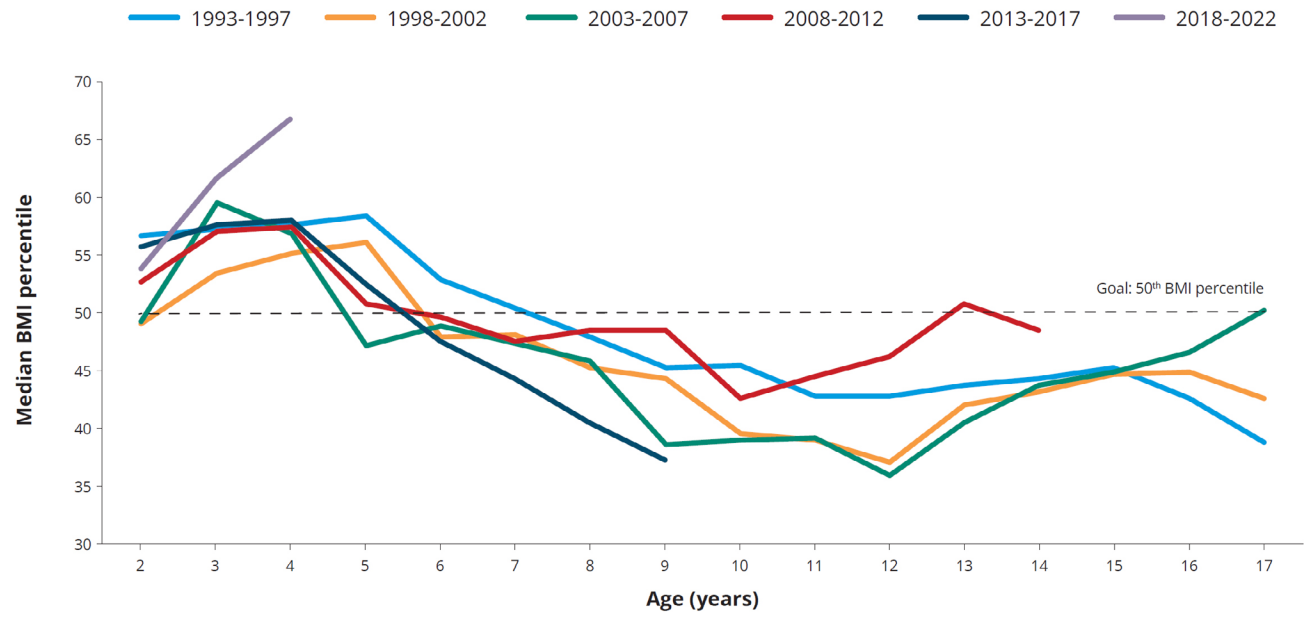


Figure 25 below shows the median BMI percentile for children 2-17 years, by birth cohort. In more recent birth cohorts, the median BMI percentile at age 2 years increased for the most part. The nutritional status was relatively stable in the early ages (2 to 4 years) followed by a gradual decline in BMI percentiles over the ages until approximately age 10 years. Median BMI percentile stabilized after 10 years of age. The deviations in trends present 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 25 Median BMI percentile in children (2-17 years), by birth cohort, 2022.



BMI PERCENTILE

Figure 26 and Figure 27 show the distribution of BMI percentile for females and males in children under 2 years and children 2-17 years.

Figure 26 BMI percentile classification in children (<2 years), by sex, 2022. [N = 79 females; N = 110 males].

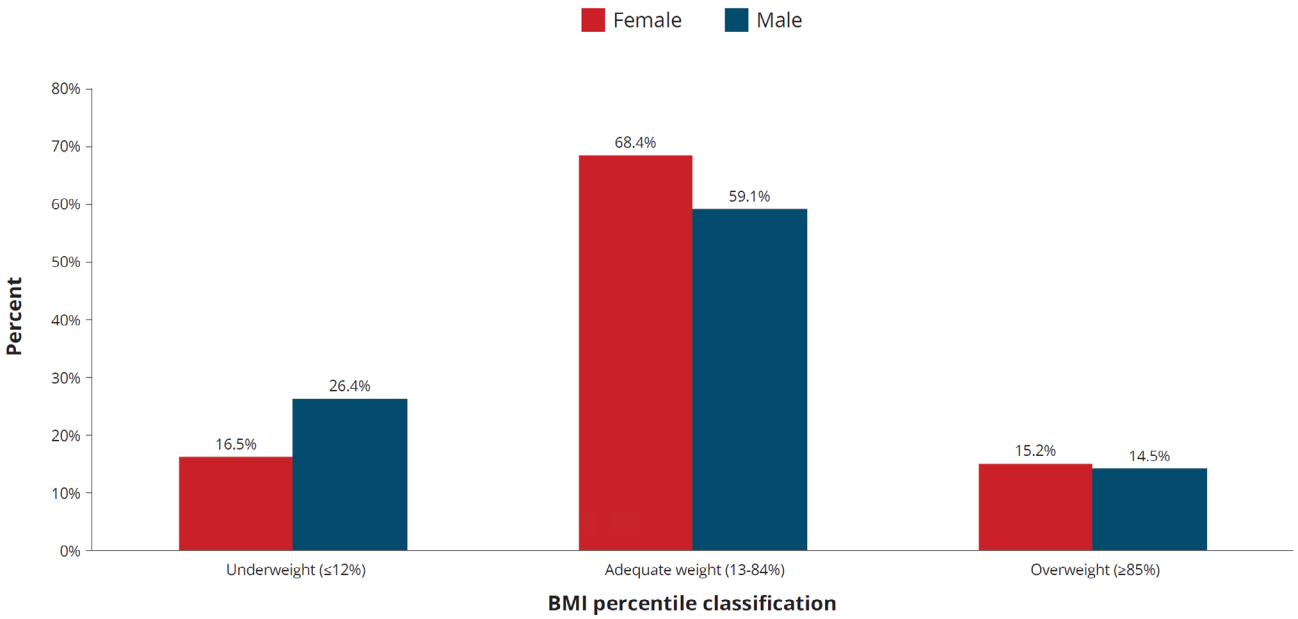
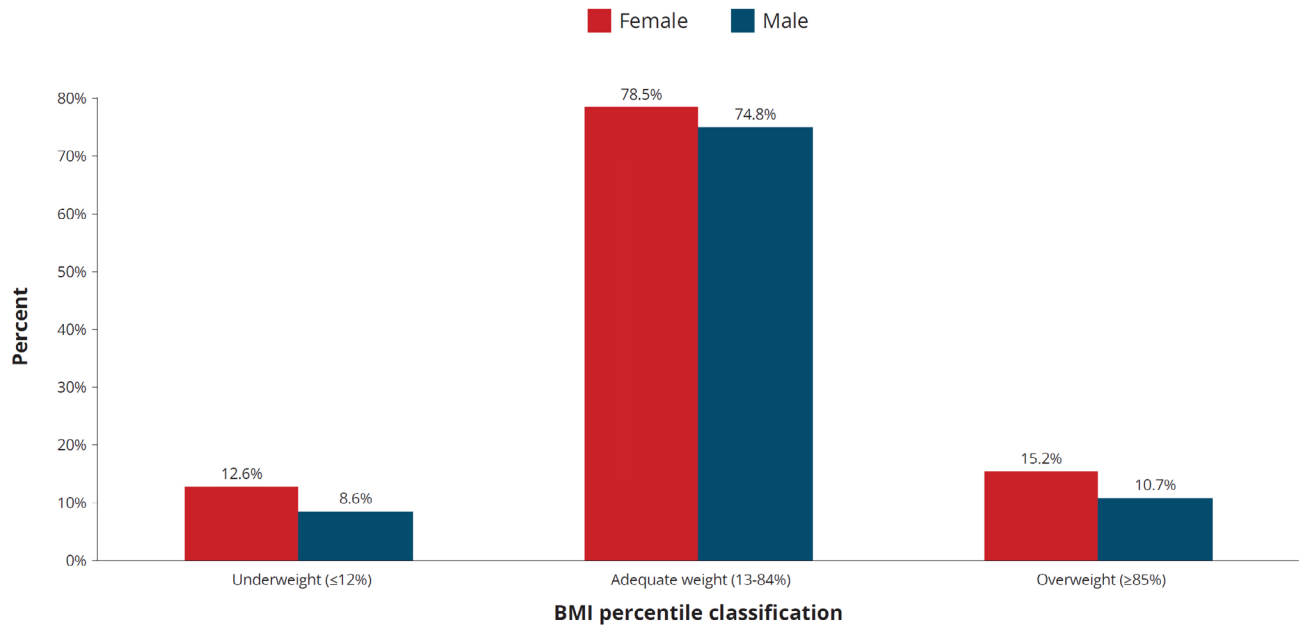


Figure 27 BMI percentile classification in children (2-17 years), by sex, 2022. [N = 669 females; N = 771 males].



BMI

In this section, the BMI obtained at the time of the individual's first stable FEV_1 percent predicted measurement of the year was used to summarize their nutritional outcome. If there was no FEV_1 percent predicted measured, the first stable BMI measurement was used. If none exist, the first complete BMI regardless of the indicated status was used. Individuals were grouped by the age at which the BMI was measured, and any age-specific distributions were calculated among all those with a measurement in that age group.

Individuals who received a lung transplant prior to 2022, and any BMI measurements taken after lung transplant in 2022, were excluded from this section of the report.

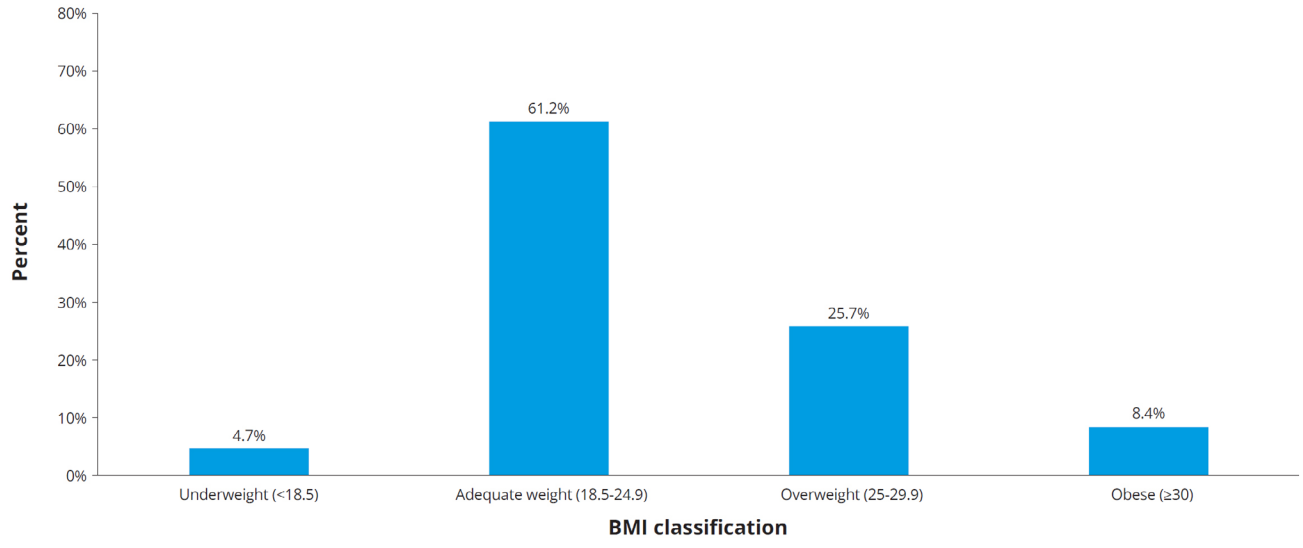
Table 4 below describes the BMI classifications and their BMI ranges according to the WHO guidelines[6]. These guidelines were updated in 2016 and as such, the proportions of BMI classifications will be different from those described in reports prior to 2016.

Table 4 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

In 2022, 2,537 adults (age 18 years and older) had a recorded BMI measurement. Among those with a recorded BMI, 1,553 (61.2 %) adults had an adequate weight, while 120 (4.7%) were considered underweight and 864 (34.1%) were considered overweight or obese (Figure 28).

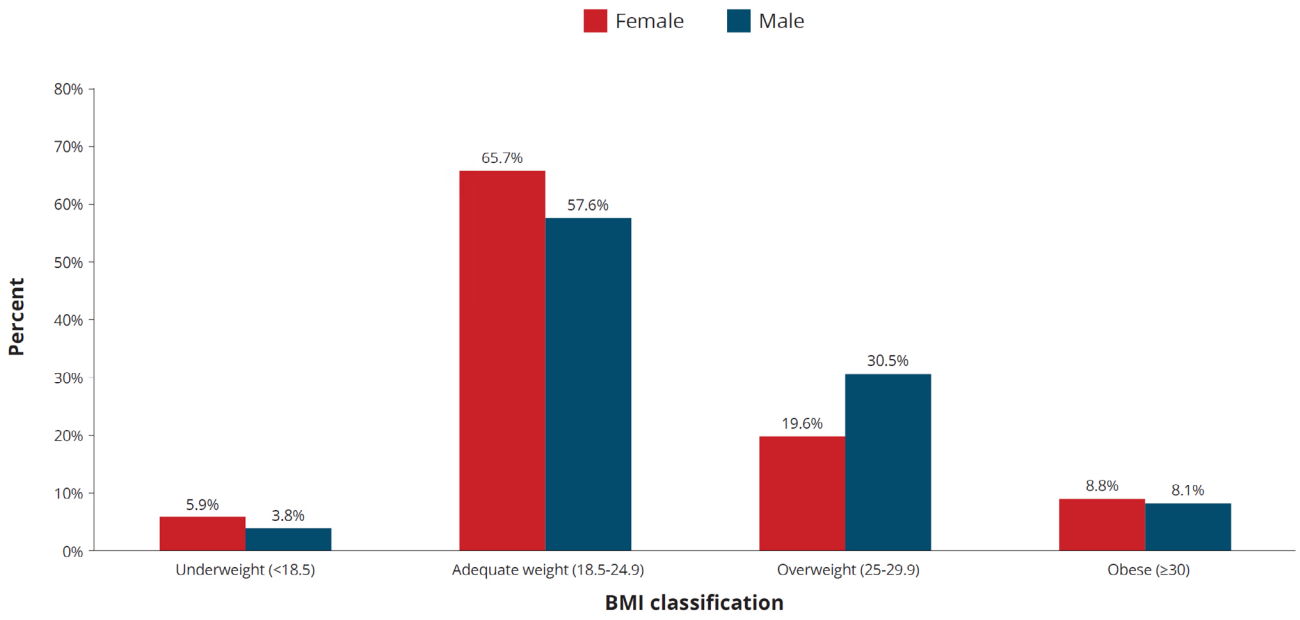
Figure 28 BMI classification in adults, 2022. [N = 2,537].



BMI

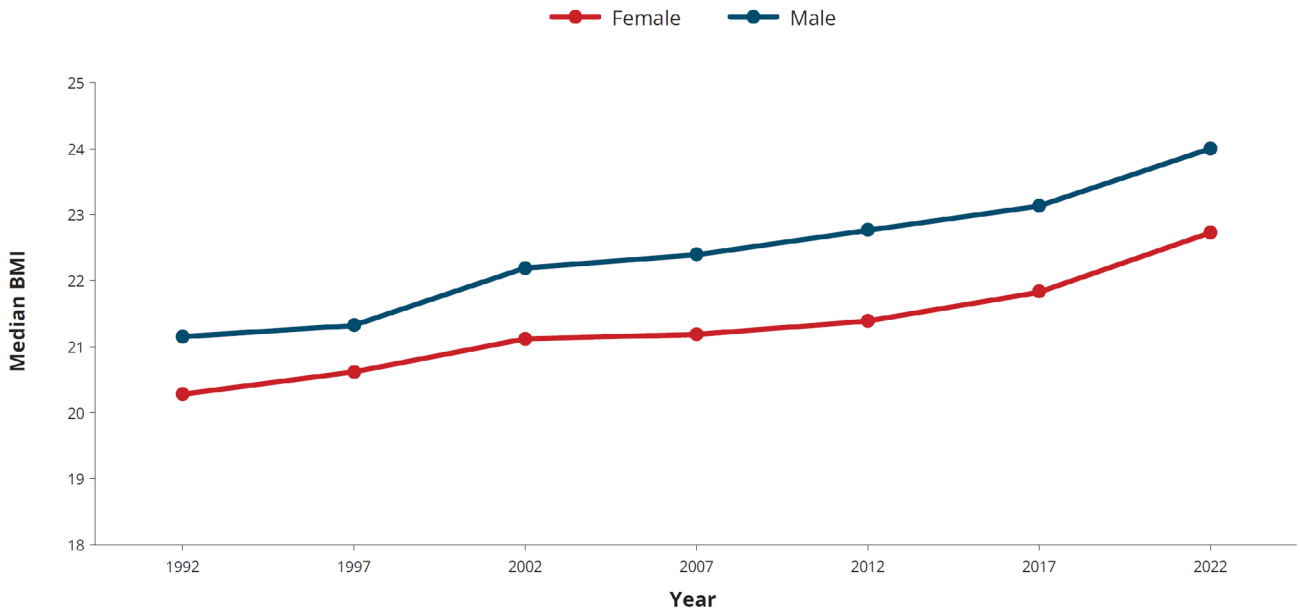
Figure 29 shows the distribution of BMI for adult females and males. Individuals who were muscular may have a higher BMI due to increased weight from larger amounts of muscle mass. In 2022, 67 (5.9%) females were considered underweight compared with 53 (3.8%) males, and 321 (28.4%) females were considered overweight or obese compared with 543 (38.6%) males.

Figure 29 BMI classification in adults, by sex, 2022. [1,131 females; N = 1,406 males].



The median BMI has risen steadily over the past 30 years within the cystic fibrosis adult population in both sexes, with a more notable increase the last five years. (Figure 30).

Figure 30 Median BMI in adults, by sex, 1992 to 2022.



BMI

Figure 31 and Figure 32 show the decreasing trend in proportion of adults classified as underweight, and the increasing trend in proportion of adults classified as overweight or obese. Most notably in both females and males, the proportion of individuals classified as obese has surpassed the proportion of those classified as underweight.

Figure 31 BMI classification in adult males, 1992 to 2022.

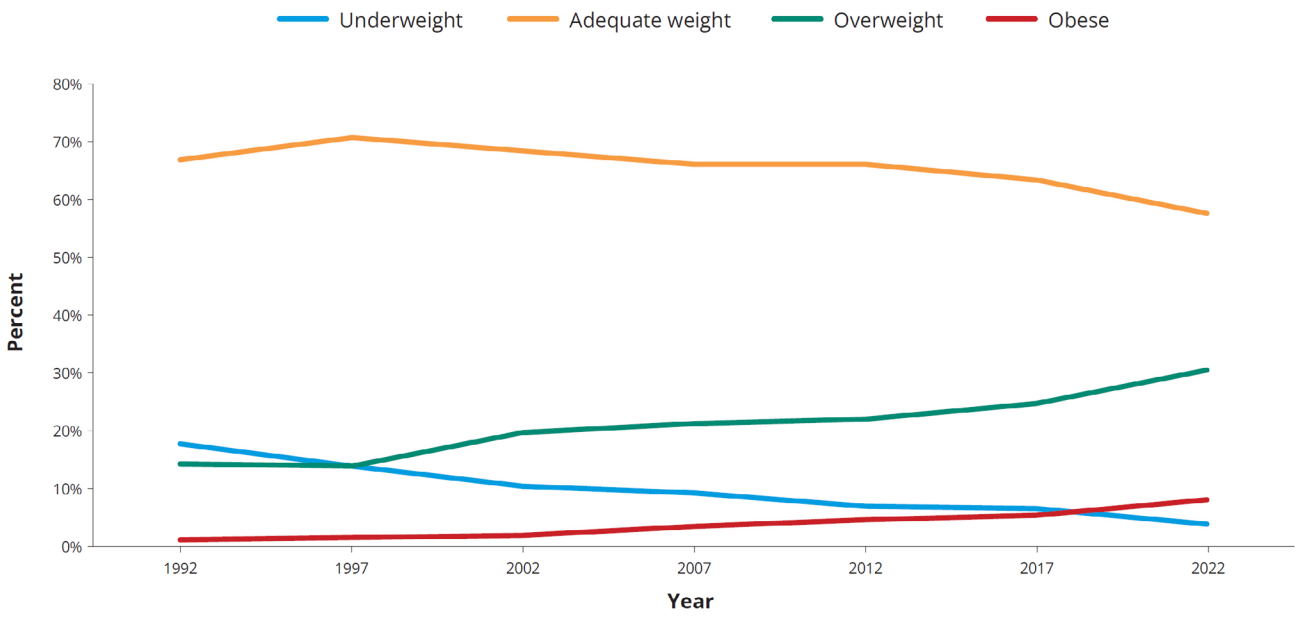
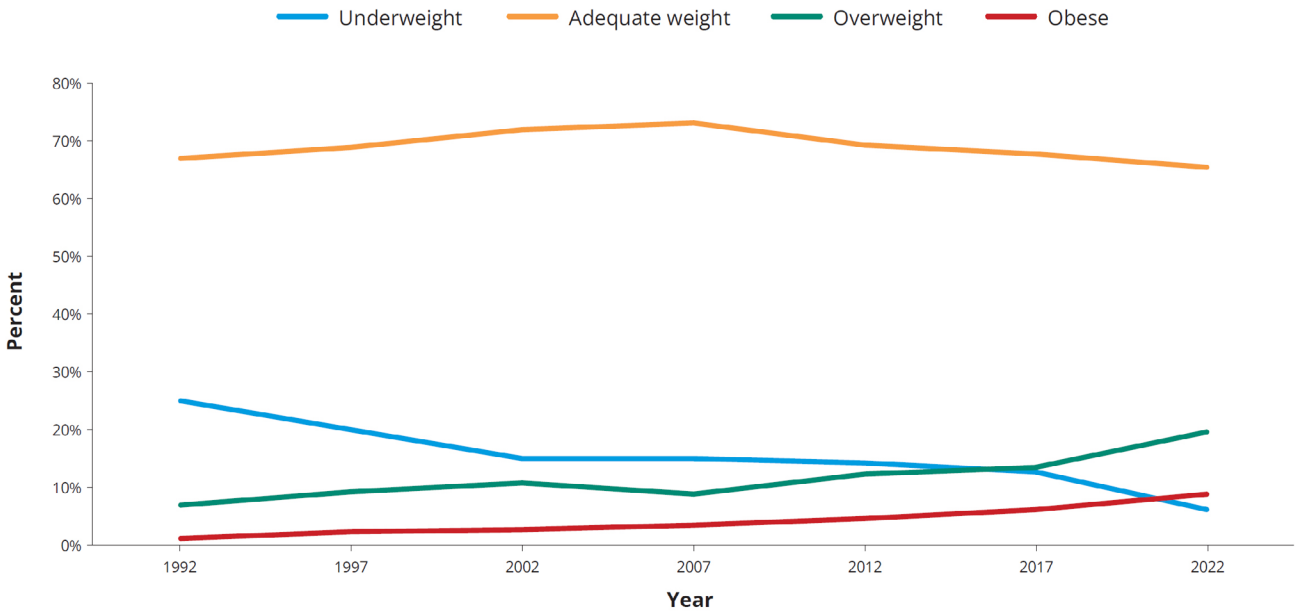


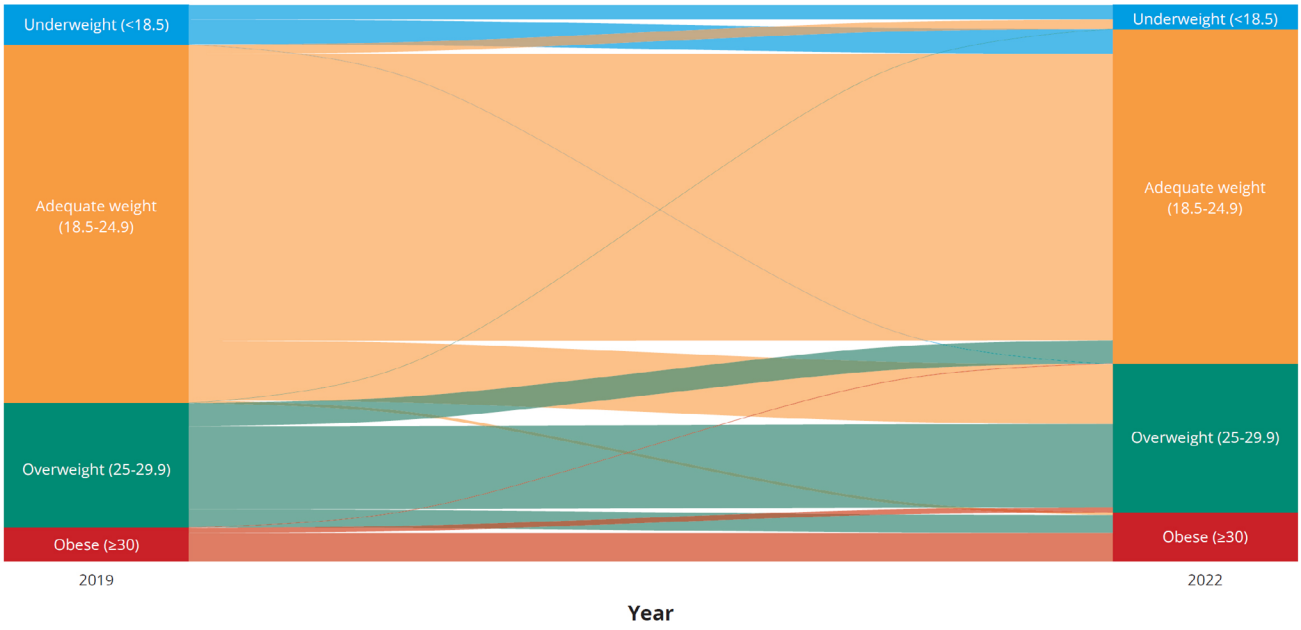
Figure 32 BMI classification in adult females, 1992 to 2022.



BMI

Figure 33 shows the movement between BMI classification in from 2019 to 2022. Of the 2,071 adults with a recorded BMI measurement in both years, the vast majority (74.1%) had no change in nutritional category. 143 (6.9%) individuals went down by at least one nutritional category, and 393 (19.0%) individuals went up by at least one nutritional category. Notably, 232 (11.2%) individuals who were previously classified as having an adequate weight in 2019, were classified as either overweight or obese in 2022. It is important to note that widespread initiation of highly effective modulator therapy occurred during this time.

Figure 33 Movement between BMI classification in adults, 2019 to 2022. [N = 2,071].



RESPIRATORY INFECTIONS

In this section, individuals were grouped by the age at which the culture was taken. Prevalence was defined as having at least one culture positive for each bacterial species and was calculated among those who had at least one microbiology or mycobacteria sample in 2022.

Individuals who received a lung transplant prior to 2022, and any cultures taken after lung transplant in 2022, were excluded from this section of the report.

COMMON BACTERIAL SPECIES

Chronic and recurrent infection of the airways is one of the most severe consequences of cystic fibrosis. In 2022, 3,745 (84.3%) individuals had at least one microbiology or mycobacteria sample recorded in the CF Registry. The most common pulmonary pathogens were *Staphyloccocus aureus* (*S. aureus*) which was found in 2,131 (56.9%) individuals, and *Pseudomonas aeruginosa* (*P. aeruginosa*) which was found in 1,297 (34.6%) individuals (Table 5). Further details on the trends in prevalence of respiratory infections are presented in Figure 34.

Table 5 Trends in prevalence of respiratory infections, 2018 to 2022. [N = 3,745].

BACTERIAL SPECIES	PERCENT WITH INFECTION IN 2022	TREND IN INFECTION PREVALENCE OVER TIME 2018 2019 2020 2021 2022
S. aureus	56.9%	
P. aeruginosa	34.6%	
S. maltophilia	11.2%	
Aspergillus species	9.5%	
H. influenza	8.4%	
MRSA	4.6%	
Achromobacter species	4.1%	
B. cepacia complex	3.5%	
Atypical mycobacteria	5.4%	

COMMON BACTERIAL SPECIES

While decreasing, Figure 34 shows that over the past several years, *S. aureus* and *P. aeruginosa* remained the two most prevalent pulmonary pathogens among individuals with cystic fibrosis. In 2022, *Stenotrophomonas maltophilia* (*S. maltophilia*) surpassed *Aspergillus* species as the third most prevalent bacterial species.

Figure 34 Prevalence of respiratory infections, 2018 to 2022.

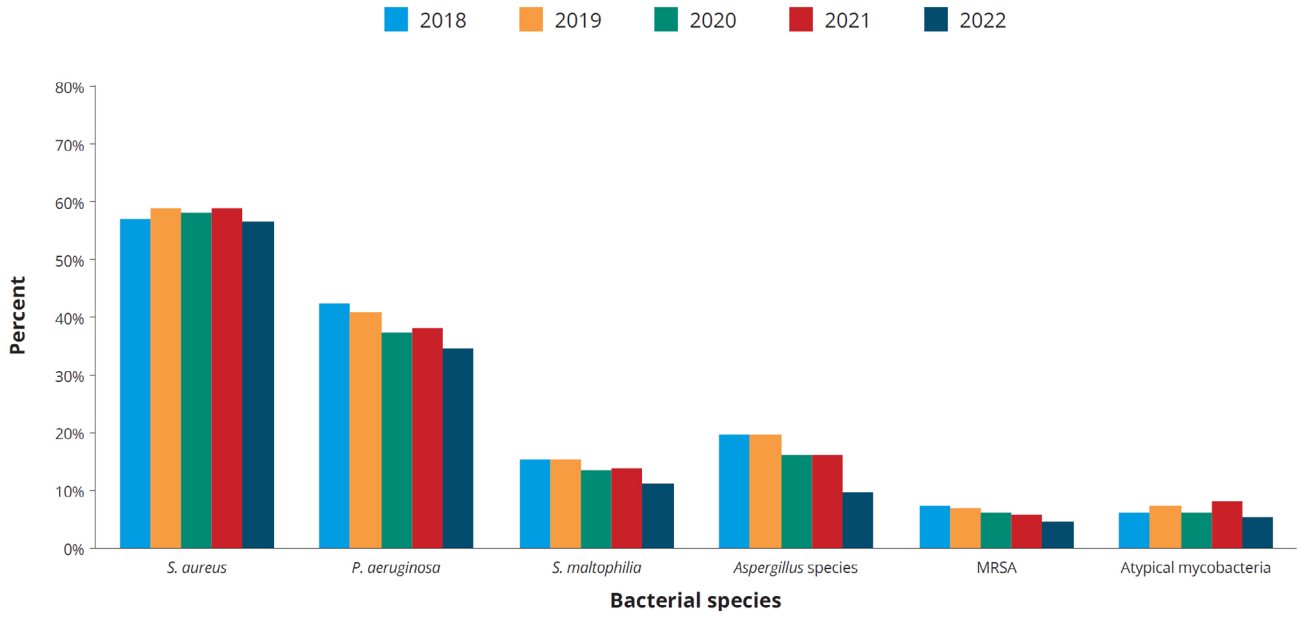
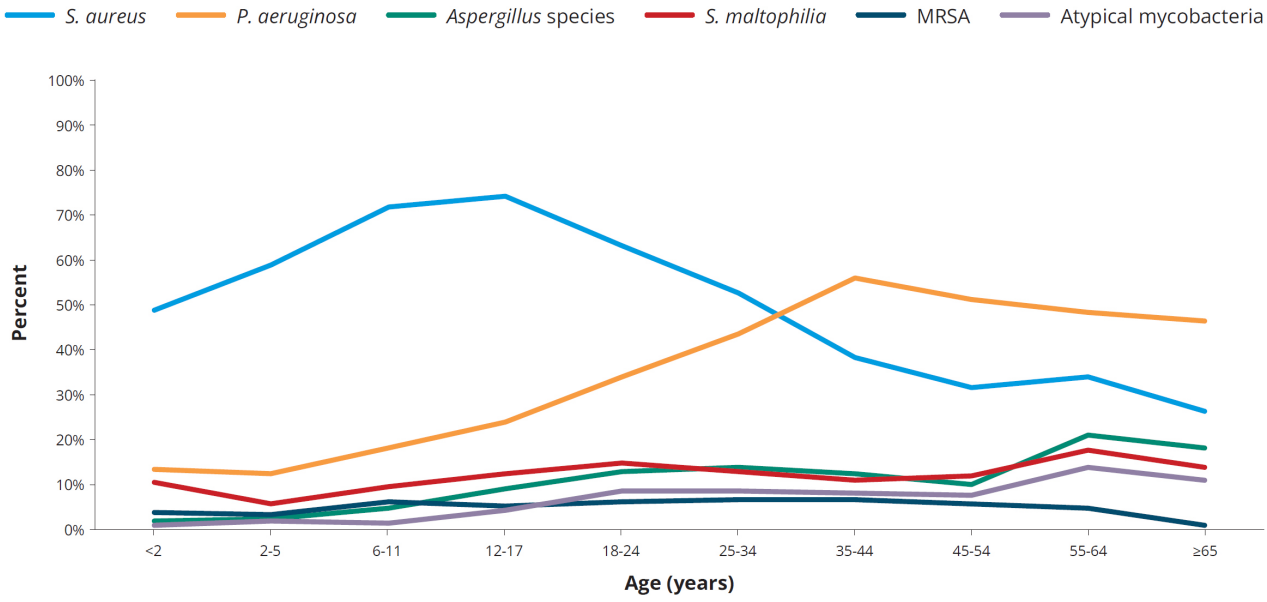


Figure 35 shows the prevalence of pulmonary pathogens by age at culture. *S. aureus* is more common in children with cystic fibrosis and *P. aeruginosa* is more common in the adult CF population. There also appears to be a trend towards older colonization of *P. aeruginosa*, from late adolescent in previous years, to early adulthood in 2022.

Figure 35 Prevalence of respiratory infections, by age, 2022.

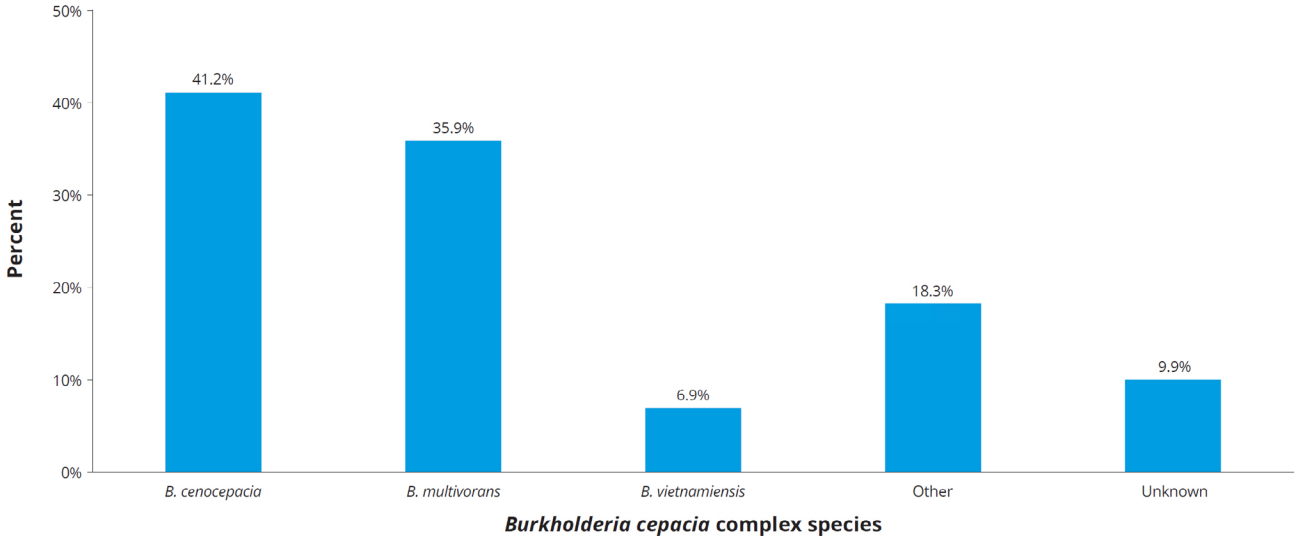


BURKHOLDERIA CEPACIA COMPLEX

The prevalence of *Burkholderia cepacia* complex (BCC) species is low, with only 131 (3.5%) individuals who grew at least one BCC species in 2022. 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. The two most prevalent types of BCC species were *B. cenocepacia* (41.2%) and *B. multivorans* (35.9%) (Figure 36). Not all BCC bacteria have been speciated, as 13 (9.9%) of the individuals grew BCC species that 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 CF Registry in 2011.

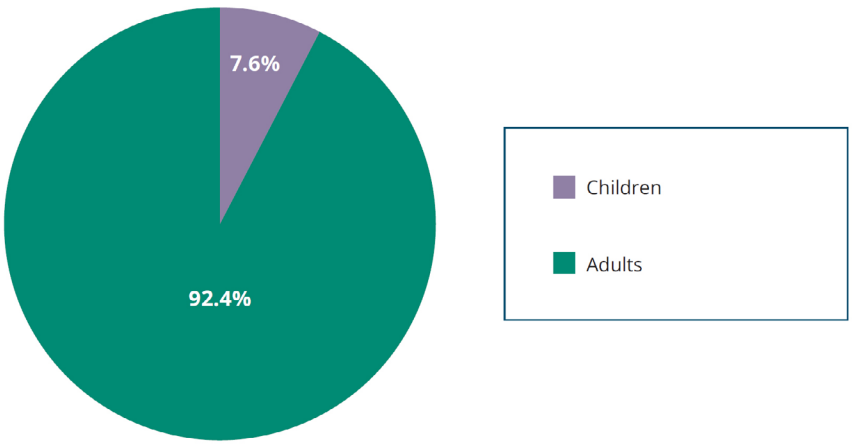
Note that 14 individuals grew *B. gladioli*, however they are not included in Figure 36, because it is not officially recognized as a BCC species.

Figure 36 Prevalence of *Burkholderia cepacia* complex species, 2022. [N = 131].



Of the individuals who had BCC in 2022, 10 (7.6%) were children and 121 (92.4%) adults at the time of culture (Figure 37).

Figure 37 Prevalence of *Burkholderia cepacia* complex, by age, 2022. [N = 131].



RESPIRATORY CULTURES

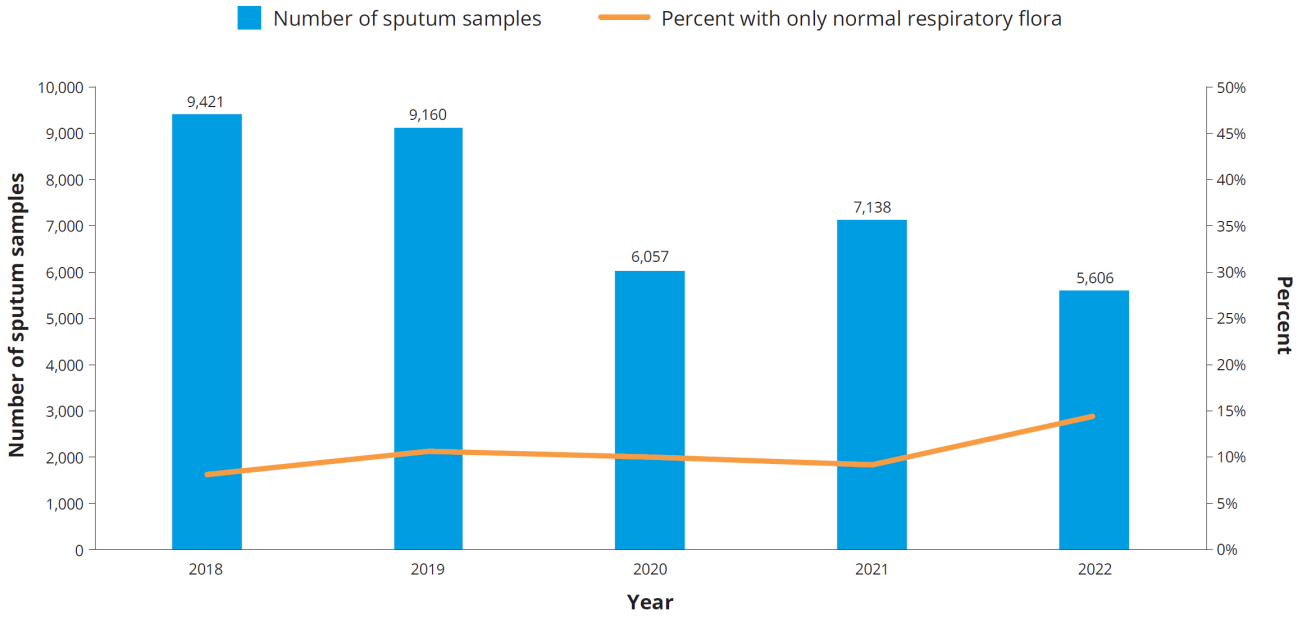
Table 6 shows the trend in the respiratory cultures (both microbiology and mycobacteria samples) from 2018 to 2022. In 2022, 89.9% of individuals had at least one microbiology or mycobacteria sample, and 53.2% of had at least one sputum sample. This represents a 5.5% and 15.9% decrease, respectively, from 2018.

Table 6 Respiratory cultures, 2018 to 2022.

Details	2018	2019	2020	2021	2022	PERCENT CHANGE (2018 TO 2022)
Individuals with at least one microbiology or mycobacteria sample	95.0%	94.7%	88.2%	92.1%	89.8%	-5.5%
Individuals with at least one microbiology or mycobacteria sputum sample	63.3%	62.9%	55.0%	59.2%	53.2%	-15.9%

Figure 38 shows the number of reported sputum samples over the past several years, and the proportion of those samples that had only the presence of normal respiratory flora (and no pulmonary pathogens). Normal respiratory flora may be found in healthy individuals in the general population. From 2018 to 2021, while the number of collected sputum samples decreased, the percentage of samples with only normal respiratory flora remained stable. In 2022, the number of samples was relatively stable, but the percentage of samples with only normal respiratory flora increased from 9.2% in 2021 to 14.4% in 2022 which may be due to the evolving microbiome in the era of highly effective modulator therapy.

Figure 38 Number of sputum samples and percent of sputum samples with only normal respiratory flora, 2018 to 2022.



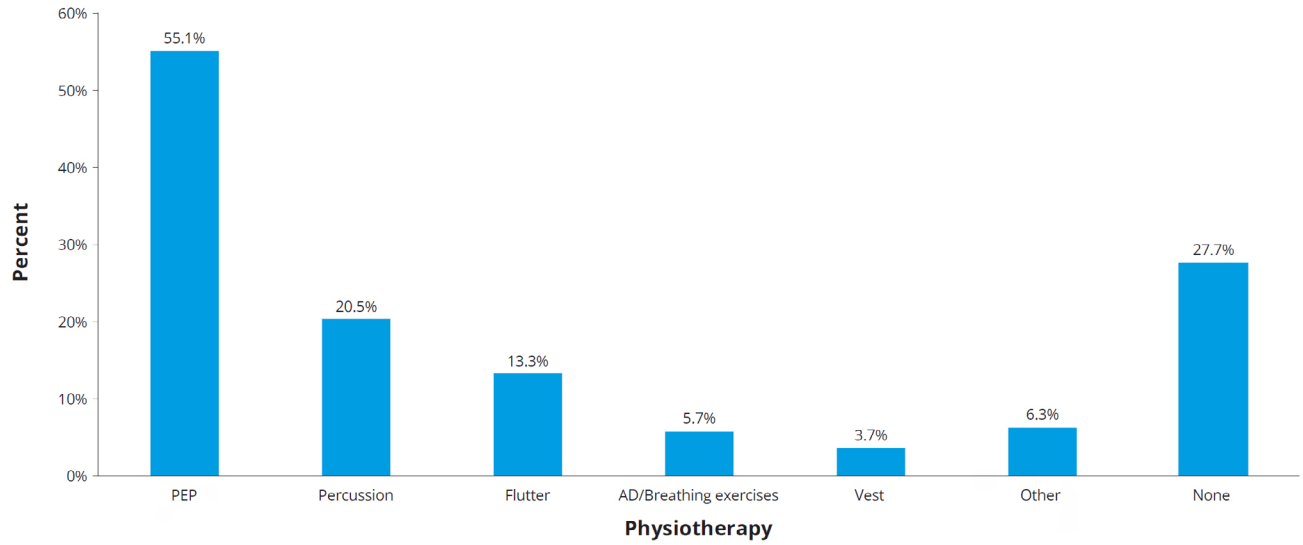
THERAPIES AND MEDICATIONS

PHYSIOTHERAPY

Physiotherapy helps to clear mucus from airways using a variety of methods. Figure 39 shows the distribution of physiotherapy recorded in the CF Registry. The category of "None" includes those with indication of no physiotherapy regimen and also those for whom no information on physiotherapy was recorded in 2022. The most commonly used forms of therapy were positive expiratory pressure (PEP) (55.1%) and percussion (20.5%).

Individuals who received a lung transplant prior to 2022 are excluded from this section of the report. Typically, chest physiotherapy is not part of routine post-transplant treatment.

Figure 39 Physiotherapy usage, 2022. [N = 4,169].



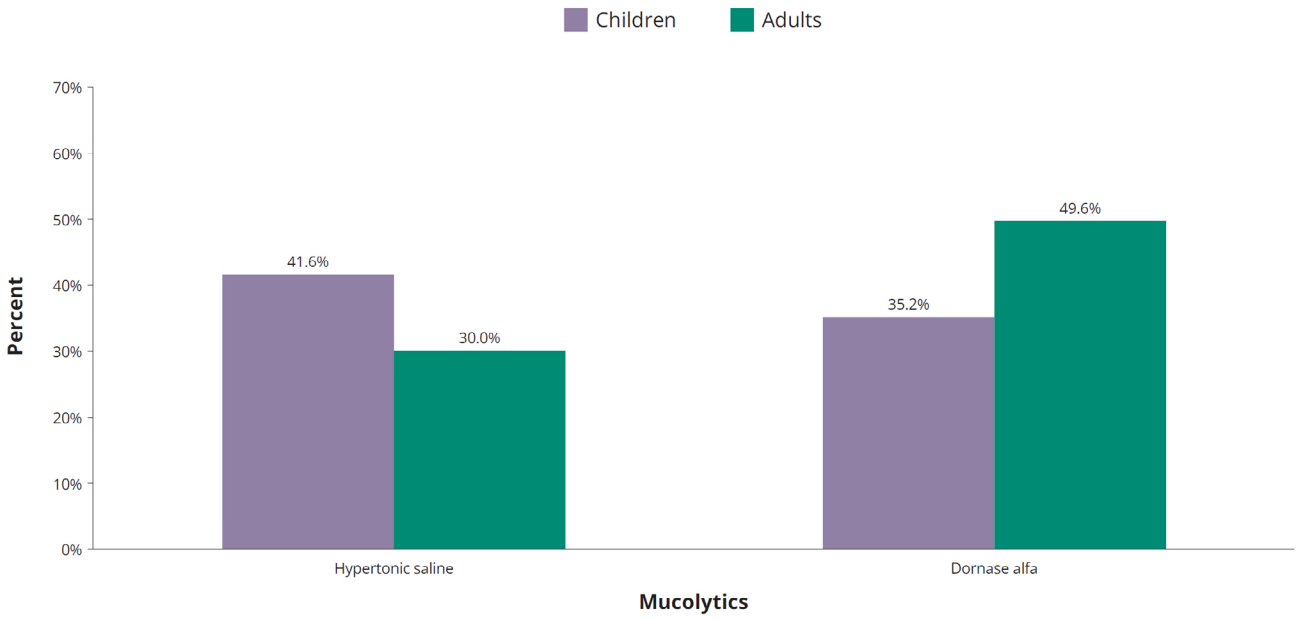
MUCOLYTICS

Mucolytics, including hypertonic saline and dornase alfa, are medications that thin the mucus and help with airway clearance.

Figure 40 shows chronic use of hypertonic saline is more common among children (41.6%) than adults (30.0%), while use of dornase alfa was more common among adults (49.6%) than children (35.2%). Overall, the use of mucolytics in 2022 is less than what was reported in 2021.

Individuals who received a lung transplant prior to 2022 are excluded from this section of the report.

Figure 40 Mucolytics usage, by age, 2022. [N = 1,496 children; N = 2,673 adults].



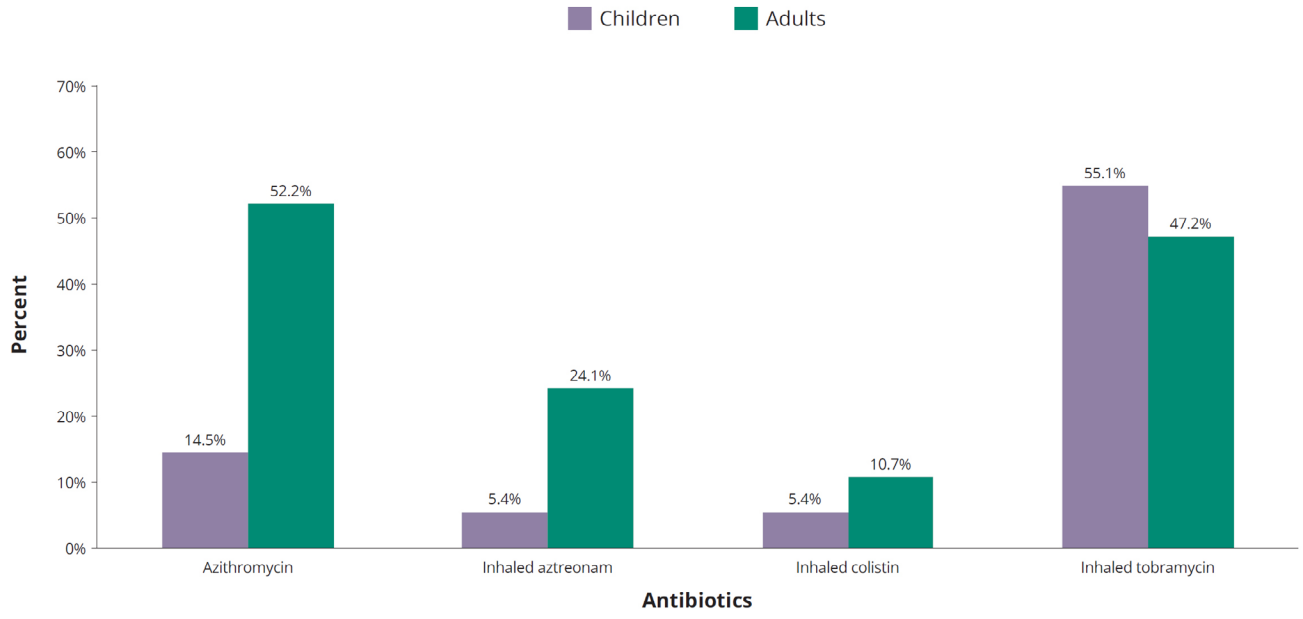
INHALED ANTIBIOTICS AND AZITHROMYCIN

Inhaled antibiotics, including inhaled aztreonam, inhaled colistin and inhaled tobramycin, target *Pseudomonas aeruginosa*, one of the most prevalent respiratory infections in individuals with CF. Azithromycin is an oral antibiotic also used for chronic *Pseudomonas aeruginosa* for its anti-inflammatory and anti-biofilm properties.

In 2022, there were 1,297 (276 children and 1,021 adults) individuals who were reported to have *Pseudomonas aeruginosa* and have never received a lung transplant prior to 2022. Of those, 152 (55.1%) children and 482 (47.2%) adults were prescribed inhaled tobramycin treatment, and 40 (14.5%) children and 533 (52.2%) adults were prescribed azithromycin (Figure 41).

Individuals who received a lung transplant prior to 2022 are excluded from this section of the report.

Figure 41 Inhaled antibiotics and azithromycin usage, by age, 2022. [N = 276 children; N = 1,021 adults].



CFTR MODULATORS

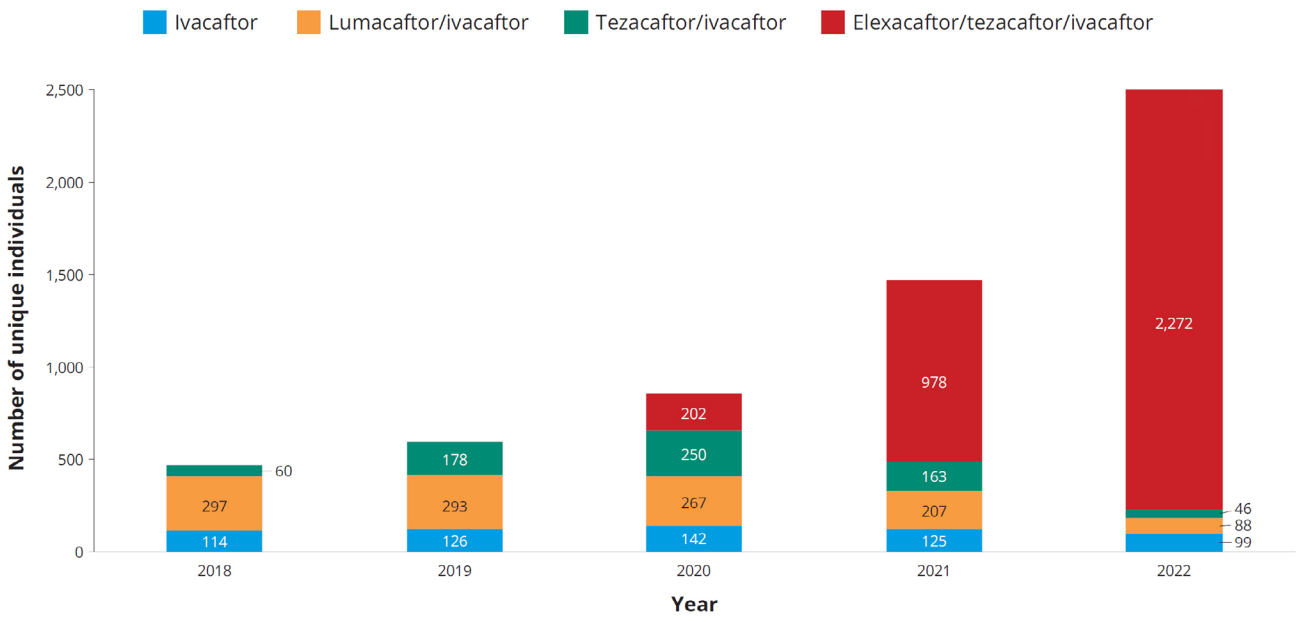
CFTR modulator therapies are designed to improve the production, intracellular processing, and function of the malfunctioning protein made by the CFTR gene. These drugs are an important advance in managing cystic fibrosis, however their efficacy depends on the specific mutations in an individual with CF since different mutations result in different CFTR protein changes.

Single agent ivacaftor was approved by Health Canada on November 26, 2012, for people with the G551D mutation. Ivacaftor approval for an additional 9 mutations was received in June 2014, followed by the approval for the R117H mutation in March 2015. Lumacaftor/ivacaftor was approved in January 2016 and tezacaftor/ivacaftor in January 2018. In June 2021, Health Canada approved the triple combination therapy elexacaftor/ivacaftor/tezacaftor for sale in Canada for individuals 12 years of age and older, with at least one F508del mutation. By the end of 2021, all jurisdictions in Canada had added this therapy onto their public drug program formularies. In April 2022, Health Canada approved the therapy to include individuals who are 6-11 years old with at least one copy of the F508del mutation.

Individuals who have received a lung transplant are not indicated for modulator therapy. Individuals who received a lung transplant prior to 2022 are therefore excluded from this section of the report.

The total number of individuals on CFTR modulator therapy increased from 471 in 2018 to 2,505 in 2022 (Figure 42).

Figure 42 CFTR modulator usage, 2018 to 2022.



CFTR MODULATORS

Eligibility for CFTR modulator therapy was determined by age and genotype outlined by Health Canada for each modulator as of December 31, 2022. An individual was considered eligible for CFTR modulators as follows:

- Ivacaftor: 4 months of age and older and had one of the following mutations: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, R117H.
- Lumacaftor/ivacaftor: 12 months of age and older and had two copies of the F508del mutation.
- Tezacaftor/ivacaftor: 12 years of age and older and had one of the following mutations: P67L, D110H, R117C, L206W, R352Q, A455E, D579G, 711+3A->G, S945L, S977F, R1070W, D1152H, 2789+5G->A, 3272-26A->G, 3849+10kbC->T.
- Elexacaftor/tezacaftor/ivacaftor: 6 years of age and older and had at least one copy of the F508del mutation.

In 2022, there were 2,505 unique individuals (675 children and 1,830 adults) on CFTR modulator therapies (Table 7). There were 997 unique individuals (456 children and 541 adults) eligible for at least one CFTR modulator but with no record of CFTR modulator usage in 2022. 15.7% of individuals were not considered currently eligible by age and genotype, for any CFTR modulator therapies.

Table 7 CFTR modulator usage, by age, 2022.

CFTR MODULATOR*	CHILDREN	ADULTS	TOTAL
Ivacaftor	46	53	99
Lumacaftor/ivacaftor	73	15	88
Tezacaftor/ivacaftor	13	33	46
Elexacaftor/tezacaftor/ivacaftor	543	1,729	2,272
Not currently on a modulator but deemed eligible†	456	541	997

** For more information about CFTR modulators, please visit **https://www.cysticfibrosis.ca/our-programs/advocacy/access-to-medicines**.*
† Not currently on a modulator but deemed eligible by age and genotype at the end of 2022.

HEALTHCARE ENCOUNTERS

Table 8 summarizes healthcare encounters, including: clinic visits, clinical measurements, hospitalizations and home IV courses for individuals with cystic fibrosis. Individuals who received a lung transplant prior to the specified year, and any hospitalizations or home IV courses that ended after lung transplant in that year, are excluded from this section of the report. For each individual, the number of clinic visits was determined by either the total number of clinical measurements, or the total number of recorded clinic visits, whichever is larger.

A total of 4,154 (99.6%) individuals with cystic fibrosis visited a CF clinic (had a recorded clinic visit date and/or clinical measurement) at least once in 2022 with 2,455 (58.9%) having four or more clinic visits. These clinic visits included telemedicine or virtual appointments, during which patients received medical education, or health advice and information via telecommunication technologies. Of the people having four or more clinic visits, 1,043 were children and 1,412 were adults, making up 69.7% and 52.8% of all children and adults, respectively. In 2022, there was a total of 16,750 clinic visits. Though the number and proportion of individuals with at least one clinic visit hasn't changed dramatically, there was a noticeable decrease in the total number of clinic visits in 2020 and 2021, compared with 2019, likely due to the COVID-19 pandemic. The total number of clinic visits decreased further in 2022.

In 2020, there was also a reduction in the number of individuals with a recorded clinical measurement (FEV1 percent predicted or BMI), likely due to an increase in virtual clinic visits. These figures have increased, and in 2022, were back to pre-pandemic levels.

In 2022, there were 624 (15.0%) unique individuals with cystic fibrosis who altogether spent 10,478 days in hospital from a total of 935 recorded hospitalizations, which do not include visits to the out-patient CF clinics. This included 569 hospitalizations for pulmonary exacerbations. This also includes 710 hospitalizations among individuals with at least one F508del mutation (who are currently or will be eligible for the triple combination therapy elexacaftor/ivacaftor/tezacaftor). Since 2018, there's been a large decrease in hospitalizations among individuals with CF. The number of individuals hospitalized each year decreased by 45.8%. The number of hospitalizations decreased by 53.0%, and most notably, the number of hospitalizations for pulmonary exacerbation, the most common reason for hospitalization, decreased by 63.4%, going from 1,553 (78.0% of all hospitalizations) in 2018 to 569 (60.9% of all hospitalizations) in 2022.

At home, 234 (5.7%) unique individuals had 5,964 days on IV antibiotics from a total of 315 courses. Even more pronounced than the trends in hospitalizations, the number of individuals on home IV decreased by 58.6% since 2018, and the number of home IV courses and home IV days decreased by 65.5% and 64.4%, respectively. Note that home IV may be used as part of treatment prior to, or following hospitalization, and as such, may not represent unique episodes of care.

HEALTHCARE ENCOUNTERS

Table 8 Healthcare encounters, 2018 to 2022.

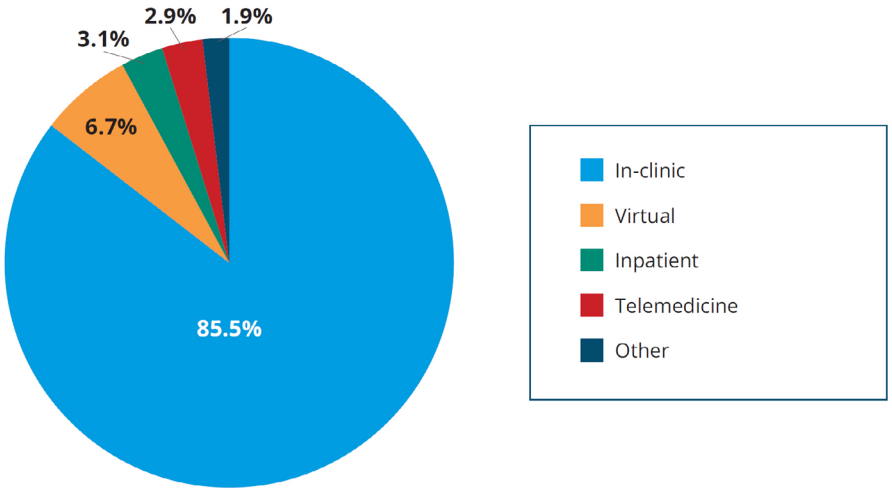
HEALTHCARE ENCOUNTER	2018	2019	2020	2021	2022	PERCENT CHANGE (2018 TO 2022)
Clinic visits						
Total clinic visits	18,355	18,473	17,456	17,800	16,750	-8.7%
Unique individuals with a clinic visit	4,099	4,097	4,069	4,071	4,154	1.3%
Unique individuals with ≥4 clinic visits	2,462	2,517	2,372	2,484	2,455	-0.3%
Clinical measurement						
Unique individuals with a FEV_1 percent predicted recorded	3,509	3,510	3,225	3,464	3,614	3.0%
Unique individuals with a BMI recorded	4,074	4,080	3,805	3,974	4,105	0.8%
Unique individuals with a microbacterial culture	3,925	3,899	3,623	3,773	3,745	-4.6%
Hospitalizations						
Unique individuals hospitalized	1,152	1,077	869	836	624	-45.8%
Hospitalizations	1,990	1,863	1,392	1,311	935	-53.0%
Hospital days	24,540	23,789	15,881	16,600	10,478	-57.3%
Hospitalizations for pulmonary exacerbation	1,553	1,337	964	915	569	-63.4%
Percent of all hospitalizations that were for pulmonary exacerbations	78.0%	71.8%	69.3%	69.8%	60.9%	-22.0%
Hospitalizations in individuals with at least 1 F508del mutation	1,772	1,681	1,208	1,092	710	-59.9%
Percent of all hospitalizations that were in individuals with at least 1 F508del mutation	89.0%	90.2%	86.8%	83.4%	75.9%	-14.7%
Home IV						
Unique individuals on home IV	565	513	470	401	234	-58.6%
Home IV courses	914	841	746	589	315	-65.5%
Home IV days	16,739	15,813	13,570	10,756	5,964	-64.4%

HEALTHCARE ENCOUNTERS

The location in which the clinical measurements were taken, was first introduced at the end of 2020. This variable aimed to identify and distinguish the different settings in which clinical measurements were taken and/or the method by which clinic visits were conducted.

As seen in Figure 43, of the 17,054 clinical measurement and/or clinic visit records with known location, 14,574 (85.5%) were taken in-clinic.

Figure 43 Distribution of location of clinical measurement and/or clinic visit, 2022.



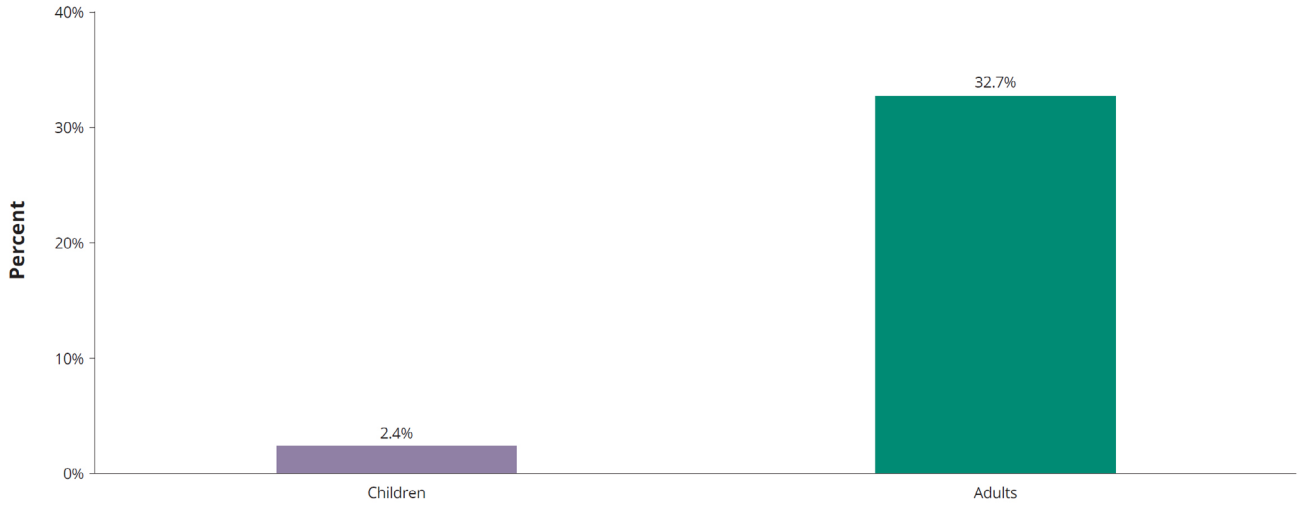
COMPLICATIONS

CYSTIC FIBROSIS-RELATED DIABETES

Cystic fibrosis-related diabetes (CFRD) is a unique type of diabetes common in individuals living with cystic fibrosis. CFRD is often associated with weight loss and lung function decline, but with early diagnosis and proper treatment, CFRD can be managed successfully.

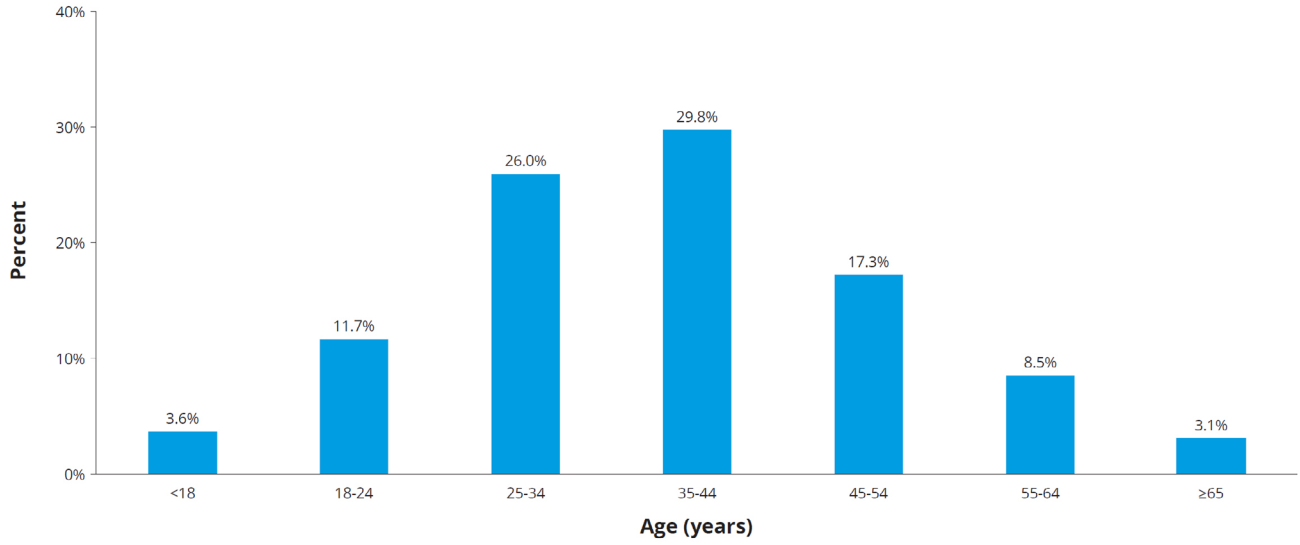
In 2022, CFRD was reported in 1,000 (22.5%) individuals with cystic fibrosis. While CFRD is not routinely screened in children younger than 10 years of age, 36 (2.4%) children and 964 (32.7%) adults (Figure 44) were recorded as having CFRD in 2022.

Figure 44 CF-related diabetes in children and adults, 2022. [N = 1,496 children; N = 2,949 adults].



Of those individuals with CFRD, 587 (58.7%) were age 35 and older, and 31 (3.1%) were age 65 and older (Figure 45).

Figure 45 Distribution of age of individuals diagnosed with CF-related diabetes, 2022. [N = 1,000].

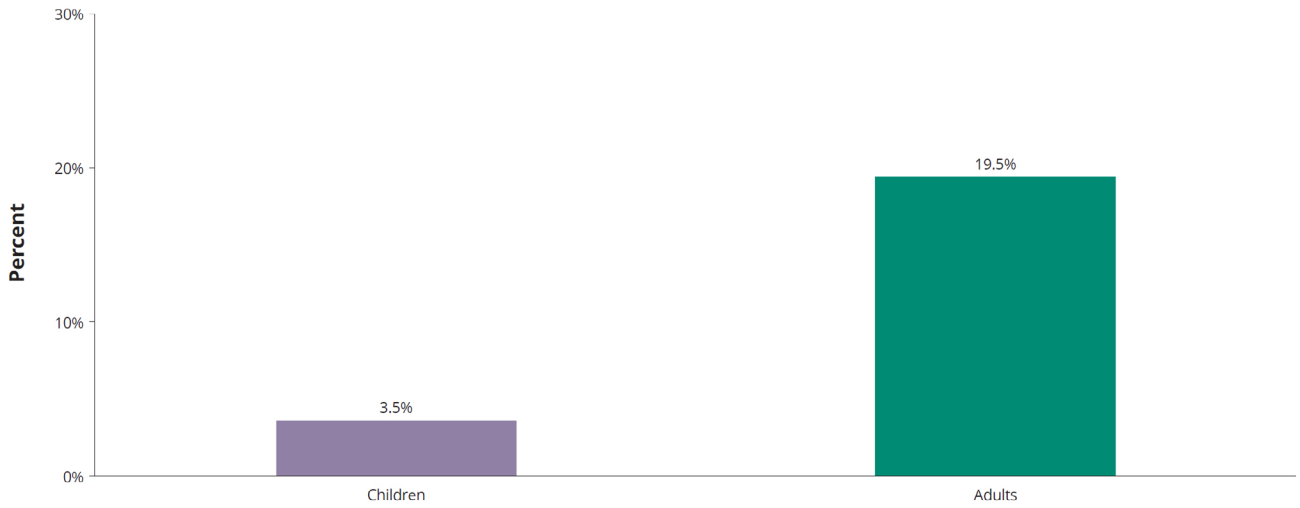


MENTAL HEALTH

In 2022, there were 628 (14.1%) individuals with cystic fibrosis with a recorded complication of depression or anxiety in the CF Registry. Fifty-three (53) of these diagnoses were children and 575 were adults, representing 3.5% of all children and 19.5% of all adults living with cystic fibrosis (Figure 46).

These prevalence rates are in line with findings from The International Depression/Anxiety Epidemiology Study (TIDES) which showed elevated rates of depression and anxiety among individuals with cystic fibrosis and their parents/caregivers[7,8].

Figure 46 Depression or anxiety in children and adults, 2022. [N = 1,496 children; N = 2,949 adults].



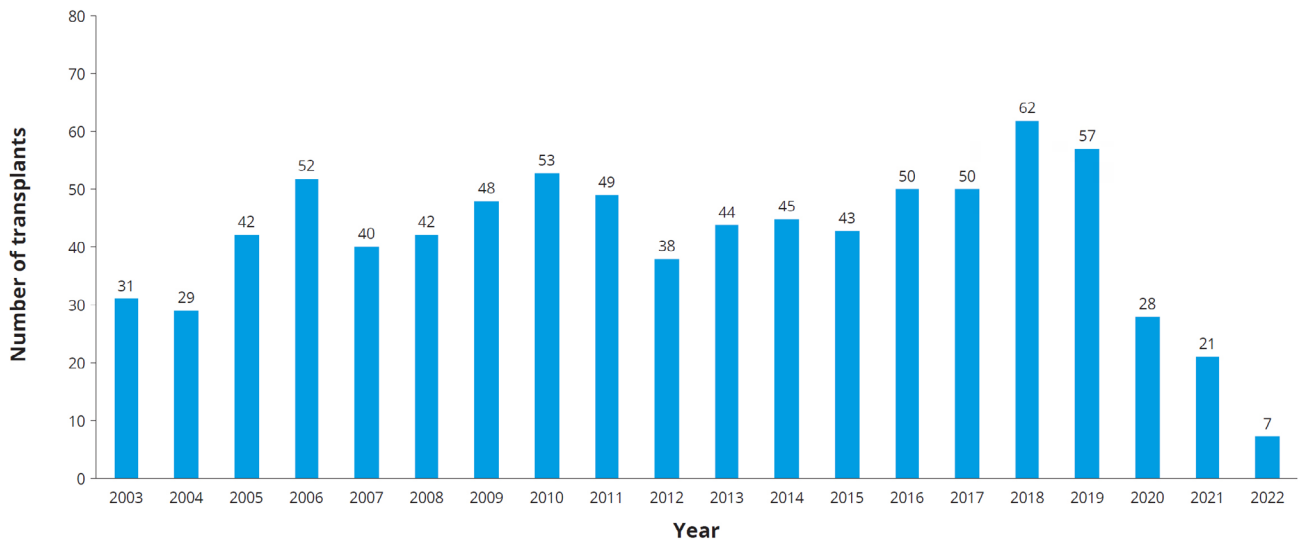
TRANSPLANTS

For some individuals with advanced disease, transplantation may be the next step to help regain health. Figure 47 shows the number of transplants carried out per year as reported in the CF Registry. In 2022, there were 7 transplants among individuals with cystic fibrosis, and the median age at transplant was 28.5 years. Although the numbers provided represent primarily lung transplants, individuals who received other combinations or organs (e.g. lung and liver, liver, heart and lung, heart) are also included in the total. The total number of transplants dropped over 50% in 2020, compared with 57 transplants conducted in 2019, and has continued to fall in 2021 (down 63.2% from 2019) and 2022 (down 87.7% from 2019).

The first transplant recorded in the CF Registry was performed in 1988. As of December 31, 2022, there were 1,067 organ transplants among 961 individuals with cystic fibrosis, reported in the CF Registry. Among these individuals, 497 (51.7%) were alive as of December 31, 2022. The vast majority of all organ transplants recorded in the CF Registry were lung transplants, with 996 lung transplants among 924 unique individuals. Of these patients, 70 (7.6%) individuals have received more than one lung transplant.

A new transplant status was added in 2020 to capture information on individuals who have been removed from the active transplant waitlist. To date, 14 people have been removed from the active transplant waitlist, and almost all are were on CFTR modulator therapy.

Figure 47 Number of transplants (any organ), 2003 to 2022.



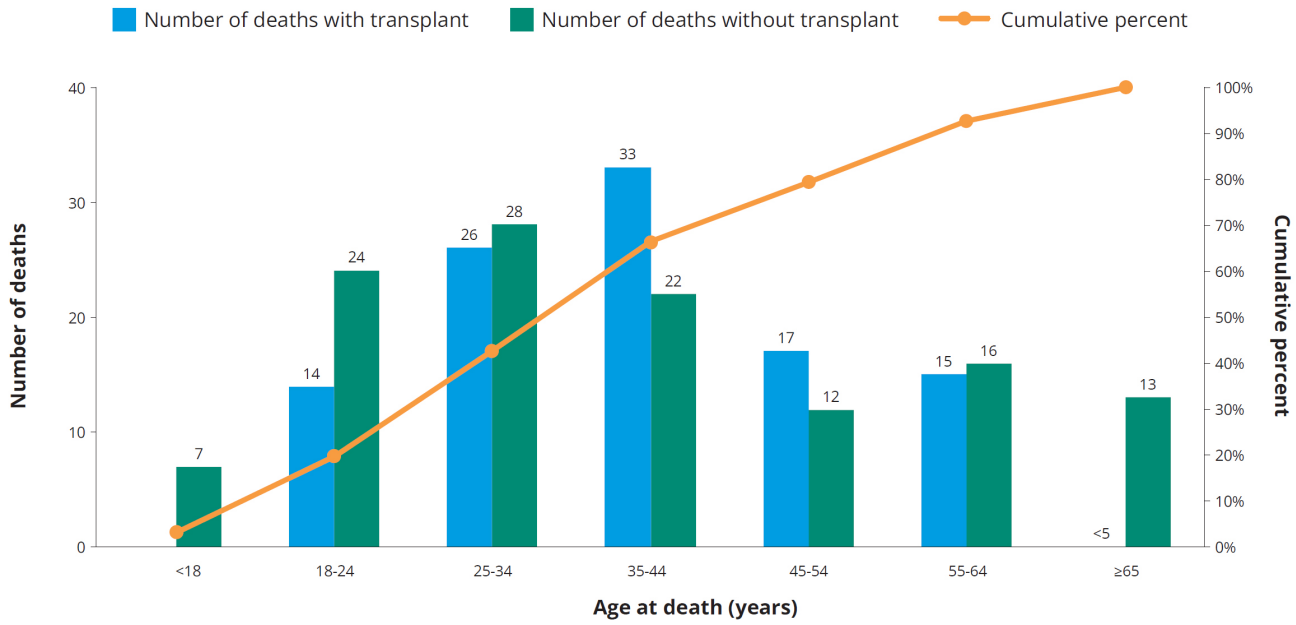
SURVIVAL

The survival and health outcomes in Canadians living with cystic fibrosis continues to improve over time. In 2022, there were 40 deaths recorded in the CF Registry, and 15 (37.5%) individuals with cystic fibrosis who died in 2022 had never received an organ transplant.

Risk factors such as pulmonary exacerbations and malnutrition are often associated with increased risk of death. In 2022, 34 (85.0%) of the 40 deaths had a recorded cause of death, with 20 (58.8%) indicating cause of death relating to pulmonary/infection/cardiovascular complications.

Figure 48 shows the cumulative number of deaths between 2018 and 2022, as well as the transplant status and age at death.

Figure 48 Cumulative number of deaths and age at death, 2018 to 2022. [N = 231].



SURVIVAL

Over the past two decades, a gradual increase in the median age of death can be seen (Figure 49). The median age of death was 38.4 years in 2022, compared with 28.1 years in 2003. The median age of death tells us that half of those who died in 2022 were younger than 38.4 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.

Figure 49 Median age at death, 2003 to 2022.

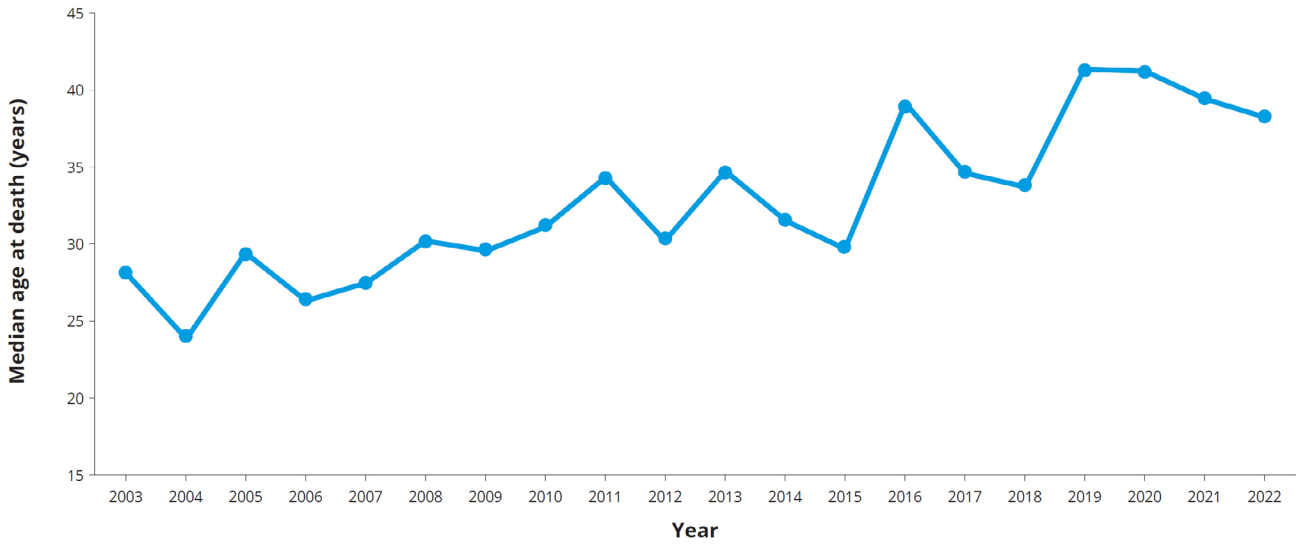
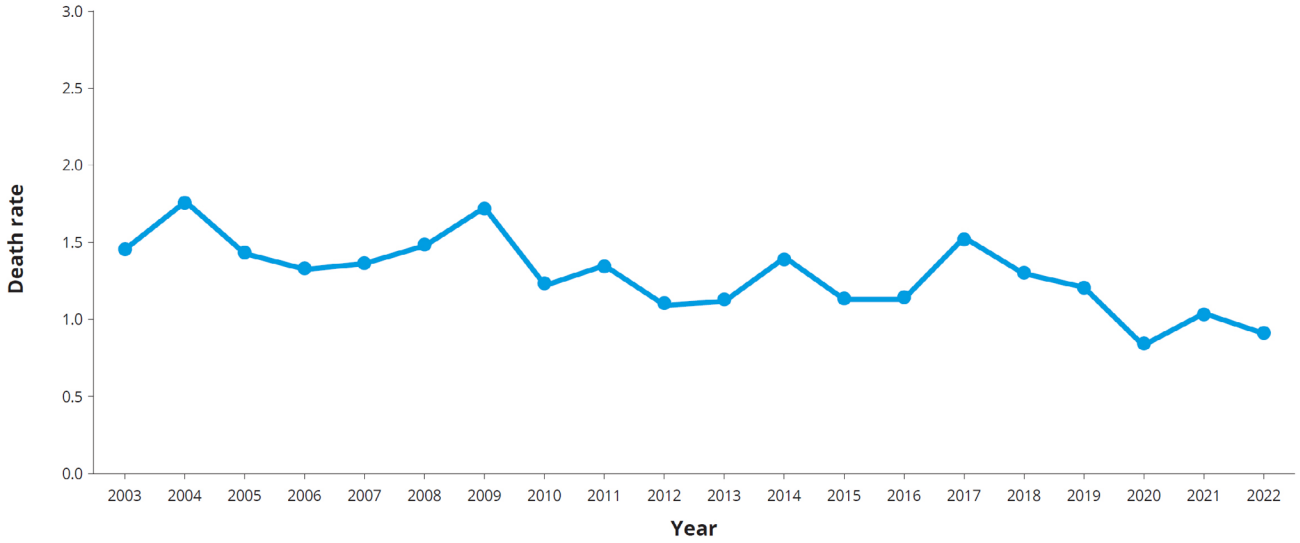


Figure 50 shows the annual death rate, calculated as the number of deaths among the total number of individuals were reported on in the year. The death rate has decreased steadily since 2003, and has appeared to stabilize in recent years. It was 0.9 in 2022.

Figure 50 Death rate, 2003 to 2022.



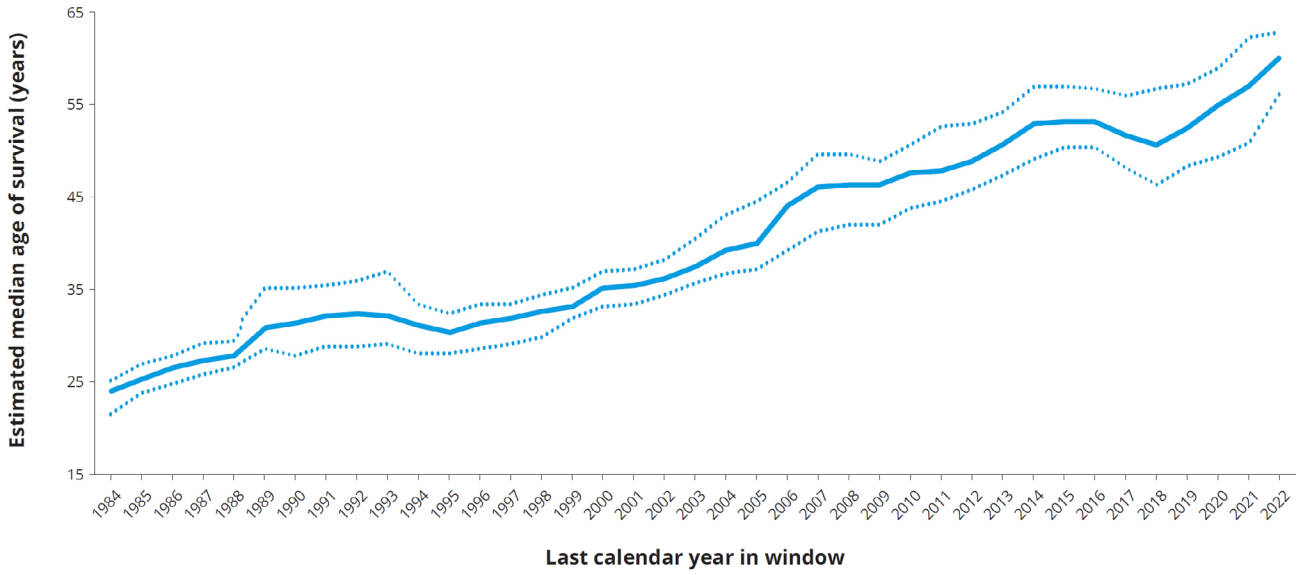
ESTIMATED MEDIAN AGE OF SURVIVAL

A 5-year rolling window, to stabilize the estimates over time, was used to calculate the median age of survival using a Cox proportional hazards model. In other words, we look at the cumulative number of deaths in a 5-year window, rather than reporting for each calendar year. The estimated median age of survival is the age beyond which we expect 50% of babies with cystic fibrosis 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[9].

The most recent 5-year window (2018 to 2022) included 5,150 people with cystic fibrosis and 231 deaths. Out of these people, the number of individuals with cystic fibrosis lost-to-follow-up (defined as individuals with cystic fibrosis we assume are alive but haven't been reported on in the past 2 years) was 213 (4.1%). In 2022, the median age of survival was estimated to be 59.9 years of age (Figure 51).

The estimated median age of survival surpassed 30 years of age for the first time in 1989, and 40 years of age, 16 years later, in 2005. The pace at which survival improved in the CF community coincided with advances in care, and the estimated median age of survival passed 50 years of age for the first time, 7 years later in 2012. It has remained relatively steady for most of the next decade, with a notable increase the last several years, reaching 59.9 years in 2022.

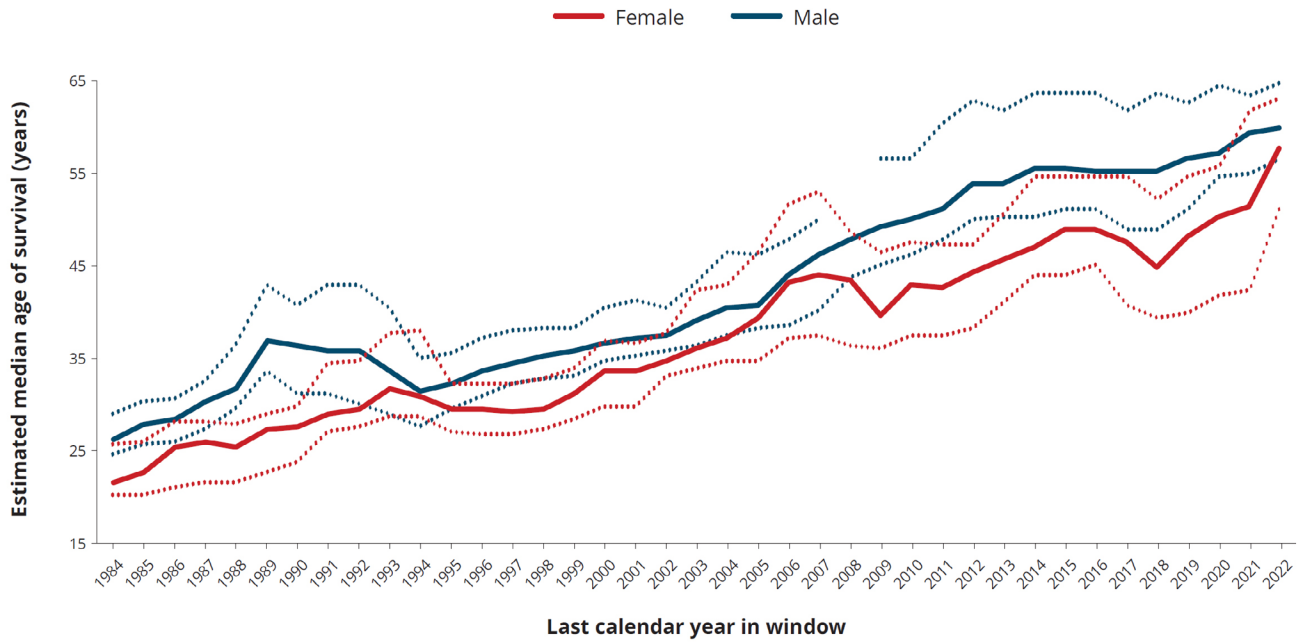
Figure 51 Estimated median age of survival for a moving 5-year window with 95% confidence intervals, 1984 to 2022.



ESTIMATED MEDIAN AGE OF SURVIVAL

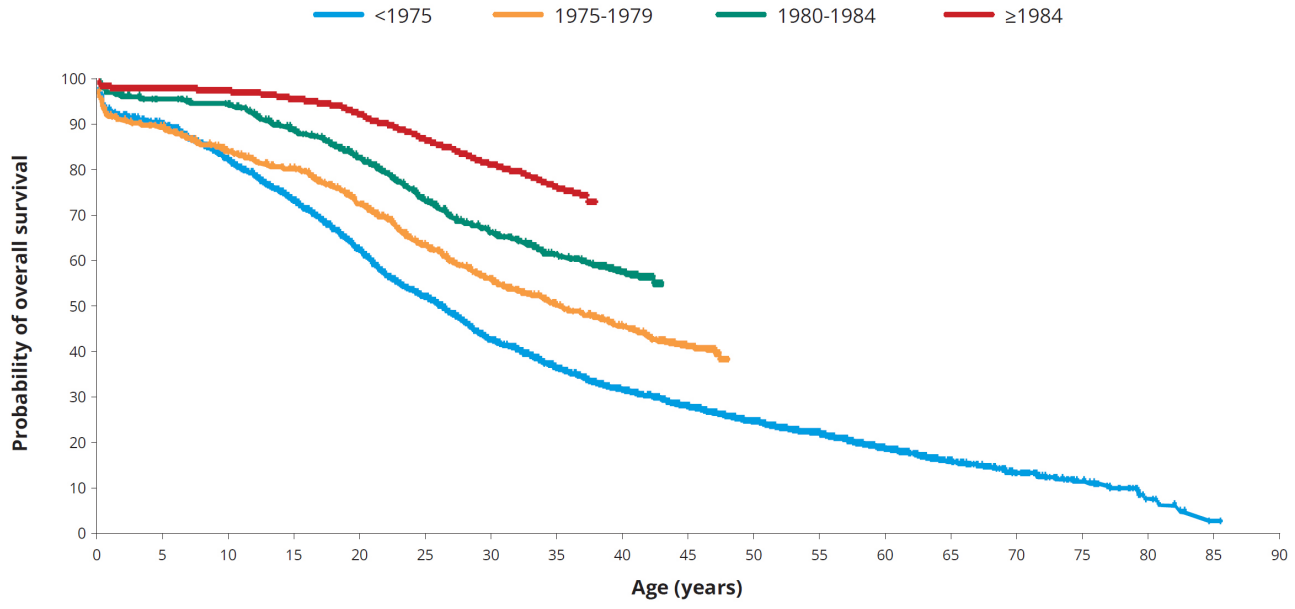
The median age of survival remained stable among males, with a nominal increase the last 3 years. In contrast, the median age of survival among females shows a marked improvement, quickly closing the gap between males and females (Figure 52). While the cause of lower survival in females is not well understood, it has been documented in published CF literature [10, 11, 12]. The upper confidence interval could not be estimated in 2008 for males, as there were not enough individuals to obtain an estimate.

Figure 52 Estimated median age of survival for a moving 5-year window with 95% confidence intervals, by sex, 1984 to 2022.



Survival by birth cohort is presented in Figure 53 and indicates that the overall probability of survival was higher in the more recent birth cohorts. The probability of surviving beyond age 20 years was 92.2% for those born in 1985 or later, compared with 62.2% for those born before 1975.

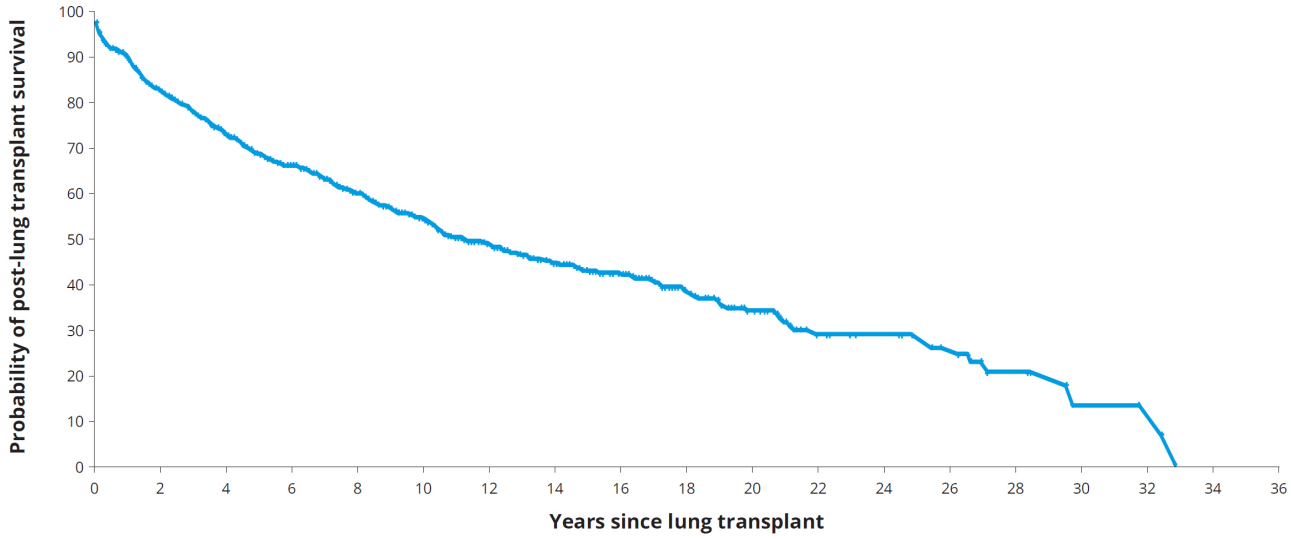
Figure 53 Overall survival, by birth cohorts, 2022.



POST-LUNG TRANSPLANT SURVIVAL

Between 1988 and 2022, there were 924 lung transplant recipients and 454 deaths post-lung transplant. Figure 54 shows the probability of survival post-lung transplant which was 89.1% at one year, 77.4% at three years and 68.1% at five years. Overall, 50% of those patients transplanted today would be expected to live beyond 10.9 years following lung transplantation.

Figure 54 Post-lung transplant survival, 2022.



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[13]. 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 from 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 cystic fibrosis born today to live, under the assumption that recent age-specific mortality rates will hold for the rest of their lives[14]. This is NOT the age at which people with cystic fibrosis 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 cystic fibrosis are living (for example, median age at death and annual death rate).

When we say that the median age of survival in 2022 is 59.9 years, we are saying that if a child with cystic fibrosis is born in Canada in 2022, they have a 50% chance of living beyond 59.9 years of age based on current mortality rates. In other words, half of the CF population would be expected to live to an age older than 59.9 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 2022.

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

REFERENCES

1. Stephenson AL, Swaleh S, Sykes J, Stanojevic S, Ma X, Quon BS, Faro A, Marshall B, Ramos KJ, Ostrenga J, Elbert A, Desai S, Cromwell E, Goss CH Contemporary cystic fibrosis incidence rates in Canada and the United States. J Cyst Fibros. Advanced online publication.
2. Cystic Fibrosis Mutation Database, "CFMD Statistics," 15 November 2022. [Online]. Available: http://genet.sickkids.on.ca/StatisticsPage.html.
3. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BC, Enright PL, Hankinson JL, Ip MSM, Zheng J, Stocks J. Multi-ethnic reference values for spirometry for the 3-95-yr age range: The global lung function 2012 equations. Eur Respir J 2012; 40; 6: 1324-1343.
4. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. Acta Paediatr Suppl 2006; 450: 76-85.
5. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: International survey. BMJ 2000; 320(7244): 1240-1243.
6. World Health Organization. Obesity: preventing and managing the global epidemic: report of a WHO consultation. WHO Technical Report Series, Geneva, 1999.
7. Quittner AL, Abbott J, Georgiopoulos AM, Goldbeck L, Smith B, Hempstead SE, Marshall B, Sabadosa KA, Elborn S. International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety. Thorax 2016; 71(1): 26-34.
8. Quittner AL, Goldbeck L, Abbott J, Duff A, Lambrecht P, Solé A, Tibosch MM, Brucefors AB, Yüksel H, Catastini P, Blackwell L, Barker D. Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers: results of The International Depression Epidemiological Study across nine countries. Thorax 2014; 69(12): 1090-1097.
9. Sykes J, Stanojevic S, Goss CH, Quon BS, Marshall BC, Petren K, Ostrenga J, Fink A, Elbert A, Stephenson AL. A standardized approach to estimating survival statistics for population-based cystic fibrosis registry cohorts. J Clin Epidemiol 2016; 70:206-213.
10. Harness-Brumley CL, Elliott AC, Rosenbluth DB, Raghavan D, Jain Raksha. Gender differences in outcomes of patients with cystic fibrosis. J Womens Health 2014; 23(12): 1012-020.
11. McIntyre K. Gender and survival in cystic fibrosis. Curr Opin Pulm Med 2013; 19(6): 692-697.
12. Keogh RH, Szczesniak R, Taylor-Robinson D, Bilton D. Up-to-date and projected estimates of survival for people with cystic fibrosis using baseline characteristics: A longitudinal study using UK patient registry data. J Cyst Fibros 2018; 17(2): 218-227.
13. World Health Organization, "The Global Health Observatory: Life expectancy at birth (years)" 15 November 2022. [Online]. Available: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/life-expectancy-at-birth-(years).
14. Keogh RH, Stanojevic S. A guide to interpreting estimated median age of survival in cystic fibrosis patient registry reports. J Cyst Fibros 2018; 17(2): 213-217.

ACKNOWLEDGMENTS

Thank you to the following groups and people who made outstanding contributions to the Canadian Cystic Fibrosis Registry and this 2022 Registry Annual Data Report.

REPORT PREPARED BY

Noma Abdulrahem, Data Analyst, Registry, Cystic Fibrosis Canada

Stephanie Cheng, Director, Registry, Cystic Fibrosis Canada

Dr. Paul Eckford, Chief Scientific Officer, Cystic Fibrosis Canada

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

Dr. Sanja Stanojevic, Biostatistician, Dalhousie University

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

CANADIAN CYSTIC FIBROSIS REGISTRY REVIEW PANEL

Dr. Mark Chilvers (BC Children's Hospital)	Dr. Anne Stephenson (Cystic Fibrosis Canada and St. Michael's Hospital)
Dr. Sophie Corriveau (McMaster University)	Dr. Lisa Strug (The Hospital for Sick Children)
Dr. Larry Lands (Montreal Children's Hospital)	Dr. Julian Tam (Royal University Hospital)
Dr. Bradley Quon (St. Paul's Hospital)	Dr. Ian Waters (Royal Jubilee Hospital)
Dr. Ranjani Somayaji (Foothills Medical Centre)	Dr. Valerie Waters (The Hospital for Sick Children)
Dr. Sanja Stanojevic (Dalhousie University)	

CANADIAN CYSTIC FIBROSIS CLINICS

Victoria General Hospital, Victoria	The Hospital for Sick Children, Toronto
Royal Jubilee Hospital, Victoria	St. Michael's Hospital, Toronto
BC Children's Hospital, Vancouver	Kingston Health Sciences Centre, Kingston
St. Paul's Hospital, Vancouver	Children's Hospital of Eastern Ontario, Ottawa
Alberta Children's Hospital, Calgary	Ottawa General Hospital, Ottawa
Foothills Hospital, Calgary	Hôpital de Rouyn-Noranda, Rouyn-Noranda
Stollery Children's Hospital, Edmonton	Montreal Children's Hospital, Montreal
University of Alberta Hospital, Edmonton	Centre hospitalier universitaire mère-enfant (CHU Sainte-Justine), Montréal
Jim Pattison Children's Hospital, Saskatoon	Montreal Chest Institute, Montreal
Royal University Hospital, Saskatoon	Centre hospitalier de l'Université de Montréal (CHUM), Montréal
Regina General Hospital, Regina	Centre hospitalier universitaire de Sherbrooke (CHUS), Sherbrooke
Winnipeg Children's Hospital, Winnipeg	Centre hospitalier universitaire de Québec - Université Laval (CHUL) - Centre mère-enfant Soleil, Québec
Health Sciences Centre, Winnipeg	Institut universitaire de cardiologie et de pneumologie de Québec, Québec
Health Sciences North/Horizon Santé-Nord, Sudbury	Hôpital de Chicoutimi, Chicoutimi
Windsor Regional Hospital, Windsor	Hôpital régional de Rimouski, Rimouski
Children's Hospital, London Health Sciences Centre, London	Saint John Regional Hospital, Saint John
London Health Sciences Centre, London	IWK Health Centre, Halifax
Grand River Hospital, Kitchener	QEII Health Sciences Centre, Halifax
St. Mary's Hospital, Kitchener	Janeway Children's Health Centre, St. John's
McMaster Children's Hospital, Hamilton	Health Sciences Centre, St. John's
Hamilton Health Sciences Corporation, Hamilton	

Matthew, who lives with CF, at his home in Ontario.

Cystic Fibrosis
Fibrose kystique
Canada

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

Cette publication est aussi disponible en français.

Charitable registration : 10684 5100 RR0001

WWW.CYSTICFIBROSIS.CA