Cystic Fibrosis
Fibrose kystique
Canada

2021 ANNUAL DATA REPORT

THE CANADIAN CYSTIC FIBROSIS REGISTRY

CYSTIC FIBROSIS

Cystic fibrosis (CF) is a rare disease affecting over 4,300 Canadians or roughly 1 in 3,850 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: February 2023

Scan the QR code below to access the online publication of the report, or please visit us at **www.cysticfibrosis.ca**.

Suggested citation (print): Cystic Fibrosis Canada. (2023). The Canadian Cystic Fibrosis Registry 2021 Annual Data Report. Toronto, Canada: Cystic Fibrosis Canada.

Suggested citation (online): Cystic Fibrosis Canada. (2023). The Canadian Cystic Fibrosis Registry 2021 Annual Data report. Retrieved from **https://www.cysticfibrosis.ca/registry/2021AnnualDataReport.pdf**.

Cover page: CF individuals from Nova Scotia

TABLE OF CONTENTS

OUR VISION IS A WORLD WITHOUT CYSTIC FIBROSIS

OUR MISSION IS TO END CYSTIC FIBROSIS

FOREWORD

With great pleasure, we present the 2021 Annual Data Report for the Canadian Cystic Fibrosis Registry.

The numbers you will see in this report represent thousands of Canadians who live with cystic fibrosis. Behind the charts and graphs are their stories of strength, struggle and triumph. The Canadian CF Registry, together with the scientists, clinicians and advocates who rely on it, owe a debt of gratitude to the Canadians living with CF who participate in this indispensable resource. Their generosity gives us an invaluable look at cystic fibrosis in Canada.

The data paint a picture of a disease in transition. This report shows that almost 25% of the Canadian CF population were treated with a highly effective modulator in 2021, with nearly 1,000 individuals on Trikafta. We know this number will continue to grow into 2022 and 2023, as access to these life-saving therapies expands and the Canadian CF Registry will enable us to track the effect of these new therapies on CF care. Will the number of hospitalizations change? Will new or different CF-related complications arise? This year's report continues to tell the story of a decline in lung transplants – falling to one-third of pre-pandemic levels in 2021.

We are encouraged to see a substantial increase in the median age of survival for a Canadian living with cystic fibrosis, increasing from 55.4 years in 2020 to 57.3 years in 2021. This means that 50% of children born with CF today are expected to live beyond 57.3 years. 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.

These facts, and the many others presented in our report, are not only a source of great interest for both people living with CF, clinicians and the scientific community, but they are also a valuable tool for Canadian health decision makers. Armed with detailed, real-world data, we can understand and advocate for our community's needs to those who make decisions about cystic fibrosis care and treatment. This past year, using data from the CF Registry, we advocated for expanded access to Trikafta for those aged six and up with at least one F508del mutation, and most importantly, we informed the decision to remove any upper limits on lung function.

Not only is the CF Registry instrumental in Cystic Fibrosis Canada's advocacy efforts, as one of the longest-running and most complete rare disease registries in the country - and the world, researchers in Canada and around the world rely on CF Registry data to enhance their understanding of the disease. As a member of the CF Registry Global Collaboration, a group comprising over 60 countries around the world, we continue to collaborate with international registries to advance health outcomes worldwide for people who live with cystic fibrosis.

We are endlessly grateful to those that make this invaluable tool possible: to the healthcare teams at the CF clinics who enter the data, to the people living with cystic fibrosis that participate in this program; to the families and caregivers who support them; and to the donors whose contributions make this work possible.

By supporting this tremendous resource, you are making a difference in many lives. Thank you.

Sincerely,

Kelly Grover
President and CEO
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

2021 HIGHLIGHTS FROM THE CANADIAN CF REGISTRY

Cystic Fibrosis Canada / Fibrose kystique Canada

DEMOGRAPHICS

4,338 CANADIANS WITH CYSTIC FIBROSIS

35% CHILDREN

65% ADULTS

98 NEW CF DIAGNOSIS

67 THROUGH NEWBORN SCREENING

35% TRAVELLED MORE THAN 100 KM TO RECEIVE CF CARE

CYSTIC FIBROSIS TREATMENT & CARE

17,485 CLINIC VISITS

15,961 HOSPITAL DAYS

10,735 HOME IV DAYS

16 LUNG TRANSPLANTS

38% HAD *PSEUDOMONAS AERUGINOSA* INFECTION

33% OF ADULTS HAVE CF-RELATED DIABETES

SURVIVAL

ESTIMATED MEDIAN POST-LUNG TRANSPLANT SURVIVAL IS 10.7 YEARS

ESTIMATED MEDIAN AGE OF SURVIVAL IS 57.3 YEARS OF AGE

HEALTH OUTCOMES

56% CHILDREN (<2 YEARS)

75% CHILDREN (2-17 YEARS)

62% ADULTS

HAVE AN ADEQUATE WEIGHT

MEDIAN LUNG FUNCTION

94.9% CHILDREN

67.7% ADULTS

INTRODUCTION

The Canadian Cystic Fibrosis Registry (CF Registry) is a collection of data from Canadians living with cystic fibrosis, that's 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 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 clinics on behalf of individuals living with CF. Given that most people living with CF attend one of these clinics, and nearly all provide permission to contributing 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 2021 Annual Data Report contains data from individuals diagnosed with CF who have consented to participate in the CF Registry and who were reported on by a Canadian CF clinic in calendar year 2021. This includes those who were diagnosed with CF or died in 2021. Data from individuals with a diagnosis of CF screen positive, inconclusive diagnosis (CFSPID) or CFTR-related disease are excluded from this report. Data from individuals who have received a lung transplant prior to 2021 were excluded from the following sections: Pulmonary Outcomes, Nutritional Outcomes, Microbiology, Therapies and Medications, Healthcare Encounters, and Complications. In previous years, data from these individuals were included in many of the figures and tables in these sections. Throughout the report, the population from which the percent or prevalence was calculated, is indicated in the title of each table or figure.

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, 2021. For the purposes of this report, sex refers to the biological sex of the individual. The year 2021 once again saw many disruptions to typical CF 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.

CF CARE IN CANADA IN 2021

The on-going COVID-19 pandemic continued to impact CF care delivery at CF clinics across Canada. CF Canada worked closely with CF clinics to complete data entry for 2021 despite the pandemic. However, changes in care delivery may be reflected in CF Registry data collection and reporting in 2021 due to disruptions in the CF care process and potentially incomplete data entry. Understanding the importance of capturing more information on CF care delivery, a "location" field was also added to the CF Registry at the end of 2020 and has been analyzed and presented for the first time in this report. While the COVID-19 pandemic certainly had a measurable impact on CF care, it is also important to note that 2021 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 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 effect is most noticeable in the section Healthcare Encounters.

SUMMARY OF THE CANADIAN CYSTIC FIBROSIS REGISTRY

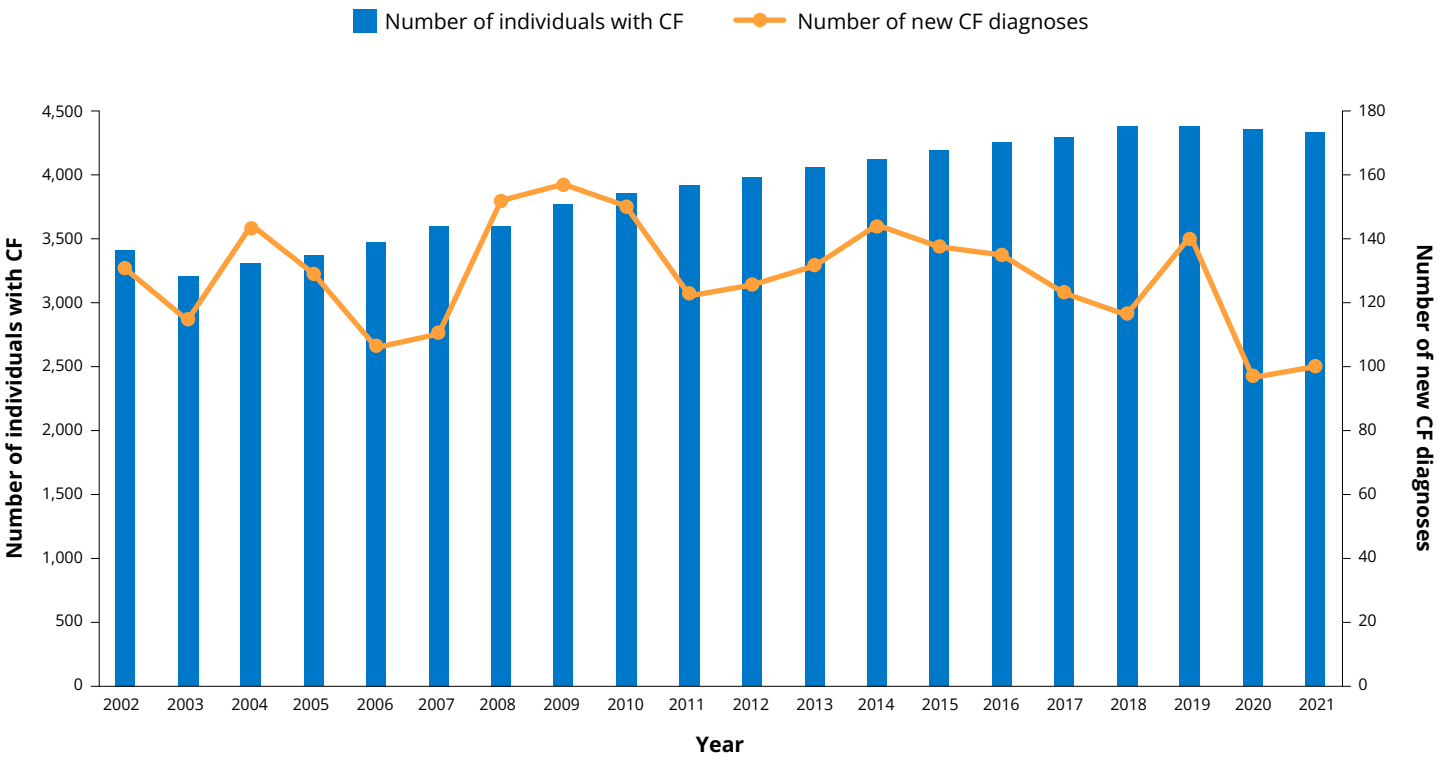
	2001	2006	2011	2016	2021
Number of individuals with CF reported on in the Canadian CF Registry	3,316	3,455	3,909	4,257	4,338
Adults (%)	47%	53%	58%	61%	65%
Females (%)	46%	47%	47%	46%	47%
Age (median, years)	16.8	18.9	20.6	22.8	25.3
Number of new diagnoses	111	104	121	134	98
Genotyped (%)	98.1%	98.8%	98.8%	99.0%	99.1%
Homozygous F508del (%)	52.1%	50.8%	49.2%	47.2%	45.7%
Heterozygous F508del (%)	36.9%	38.4%	39.1%	40.3%	41.1%
FEV_1 percent predicted (median)	72.3	72.4	73.8	76.5	77.9
BMI percentile (median)	43.0	43.6	45.8	45.3	49.1
BMI (median)	21.4	21.8	22.1	22.4	23.0
Number of transplants	33	53	49	50	22
Number of deaths	65	46	53	48	44
Estimated median age of survival (5-year)	35.9	44.3	47.9	53.3	57.3

DEMOGRAPHICS

OVERVIEW OF CANADIANS WITH CYSTIC FIBROSIS

In 2021, there were a total of 4,338 individuals with cystic fibrosis who attended one of the 41 accredited CF clinics across Canada (Figure 1). This included 98 individuals newly diagnosed with cystic fibrosis, 1,517 (35.0%) children and 2,821 (65.0%) adults, and 2,025 (46.7%) females and 2,313 (53.3%) males. Overall, the total Canadian CF population has been steadily increasing and has grown by 27.7% since 2002.

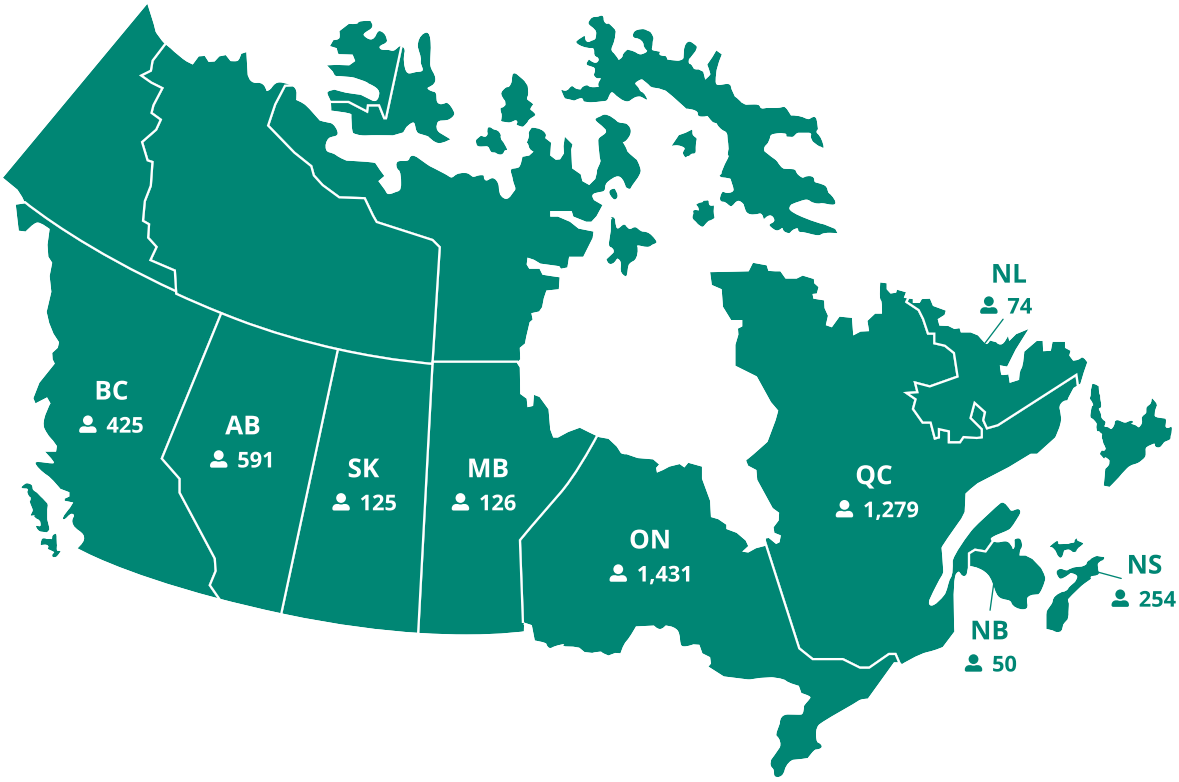
FIGURE 1: Total number of individuals with cystic fibrosis and new CF diagnoses, 2002 to 2021.



OVERVIEW OF CANADIANS WITH CYSTIC FIBROSIS

In Figures 2 to 4, individuals are reported based on their province of clinical care (the province in which they attended a CF 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 2021 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, 2021.



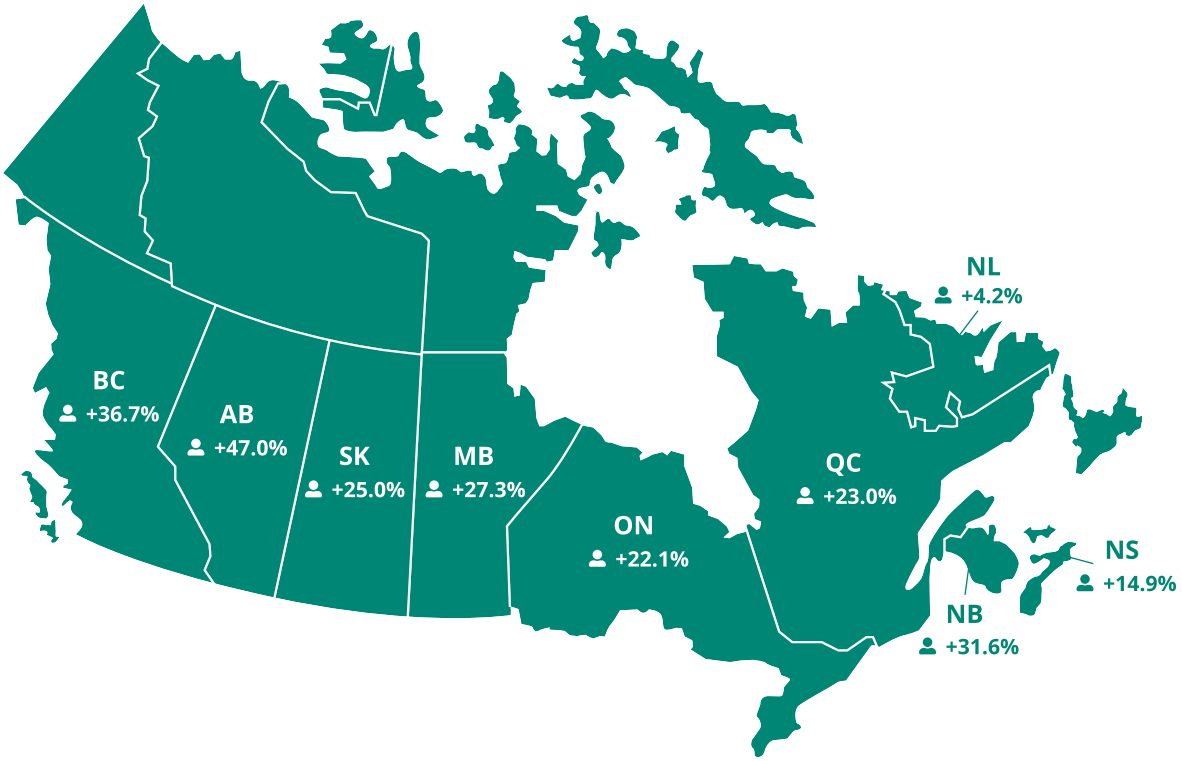
PROVINCE OF CLINICAL CARE*	NUMBER OF INDIVIDUALS WITH CF	FEMALE	MALE	ADULTS	CHILDREN
BC	425	188	237	276	149
AB	591	287	304	357	234
SK	125	50	75	74	51
MB	126	55	71	67	59
ON	1,431	685	746	970	461
QC	1,279	597	682	841	438
NB	50	25	25	36	14
NS	254	119	135	159	95
NL	74	29	45	49	25

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

OVERVIEW OF CANADIANS WITH CYSTIC FIBROSIS

Figure 3 shows the number of individuals with CF reported on by clinics within each province in 2002 and 2021, along with the percent change. It should be noted that during this period, provinces began including CF within their newborn screening (NBS) programs, beginning with Alberta in 2007. In addition, the number of CF clinics and availability of CF care in each province may have changed throughout this period. For comparison, the overall population change in each province is also included in the accompanying data table.

FIGURE 3: Change in cystic fibrosis population, by province of clinical care, 2002 to 2021.



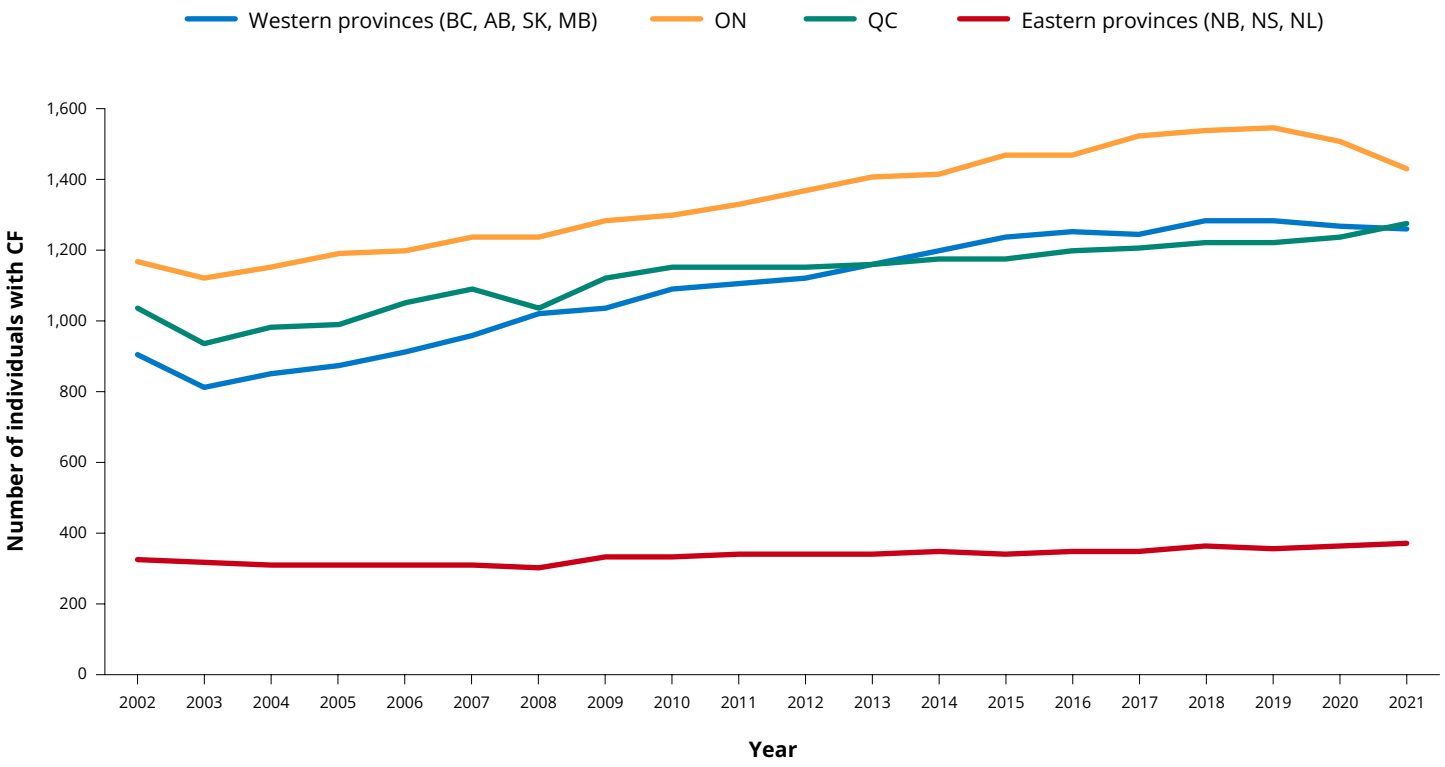
PROVINCE OF CLINICAL CARE*	INDIVIDUALS WITH CF			PROVINCIAL POPULATION†
	2002	2021	% CHANGE	% CHANGE
BC	311	425	36.7%	26.9%
AB	402	591	47.0%	42.0%
SK	100	125	25.0%	18.5%
MB	99	126	27.3%	20.3%
ON	1,172	1,431	22.1%	22.4%
QC	1,040	1,279	23.0%	15.6%
NB	38	50	31.6%	5.5%
NS	221	254	14.9%	6.0%
NL	71	74	4.2%	0.2%

** Individuals with cystic fibrosis living in provinces or territories not listed here are included, if reported on by CF clinics in other jurisdictions.*
† Provincial population obtained from Statistics Canada. Table 17-10-0005-01. Population estimates on July 1st, by age and sex.

OVERVIEW OF CANADIANS WITH CYSTIC FIBROSIS

Figure 4 shows the growth of the Canadian CF population in four regions across the country, over the past 20 years.

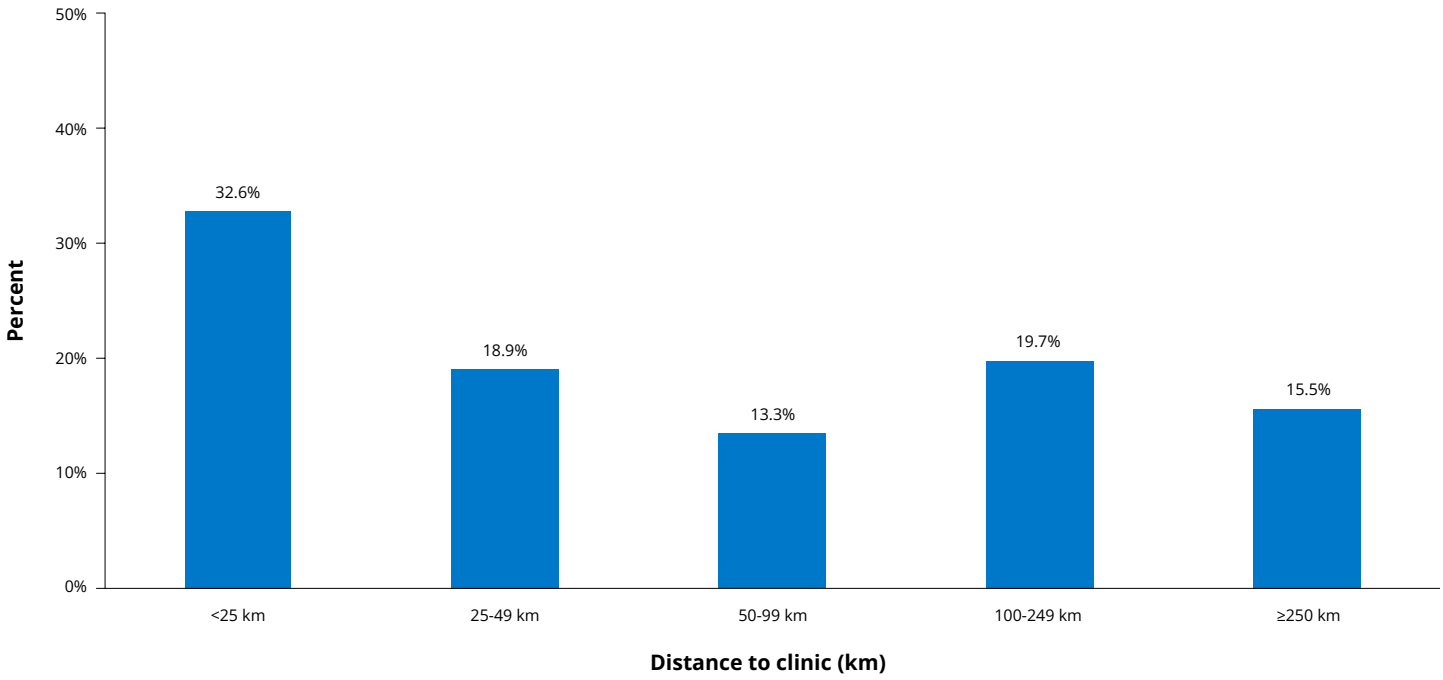
FIGURE 4: Change in cystic fibrosis population, by region of clinical care, 2002 to 2021.



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 2021, there were 2,393 (55.2%) individuals with cystic fibrosis with at least one valid location recorded. While 1,233 (51.5%) of those with a reported location attended a CF clinic within 50 km of where they live, 842 (35.2%) travelled more than 100 km and 371 (15.5%) travelled more than 250 km for their CF care (Figure 5).

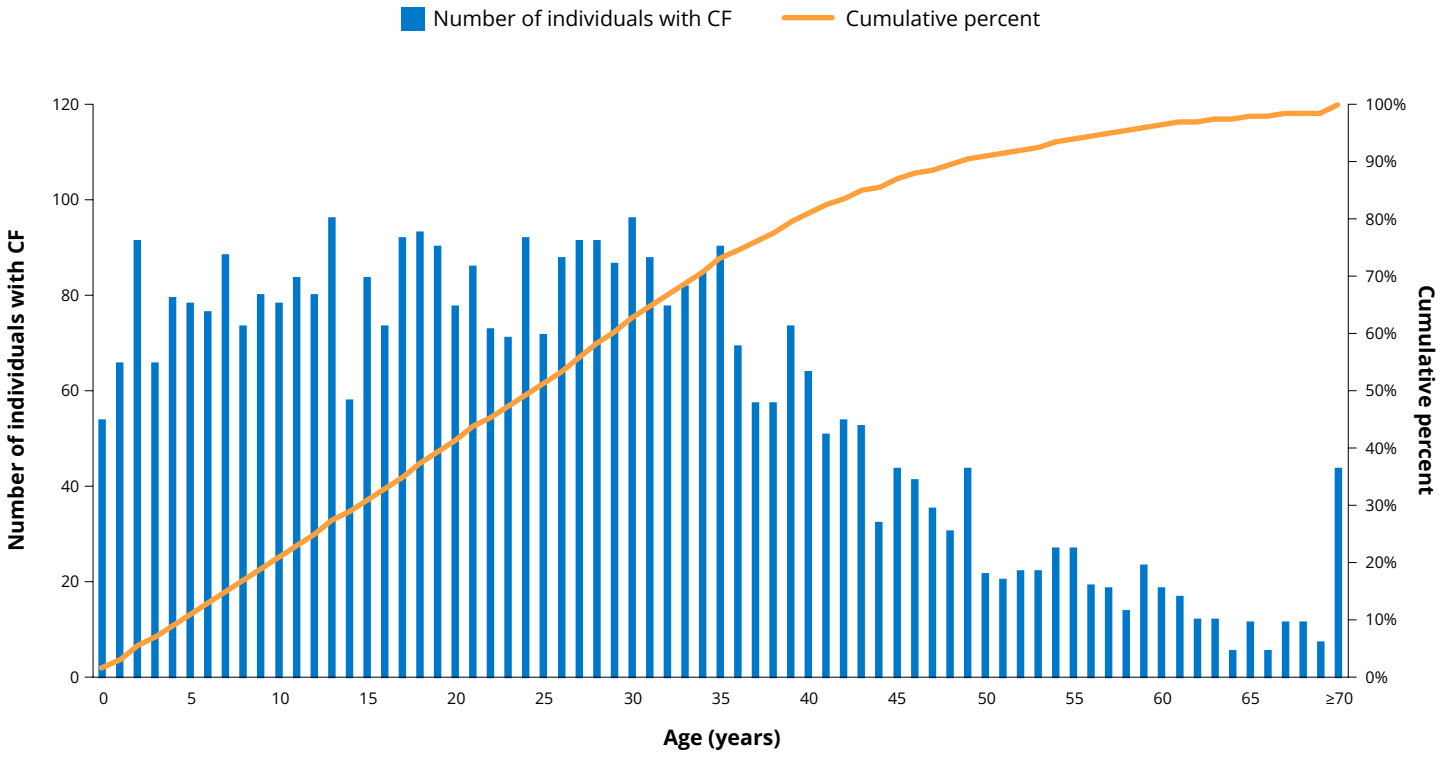
FIGURE 5: Distance travelled to clinic, 2021. [N = 2,393].



AGE DISTRIBUTION

Figure 6 shows the age distribution of the 4,338 Canadians living with cystic fibrosis in 2021.

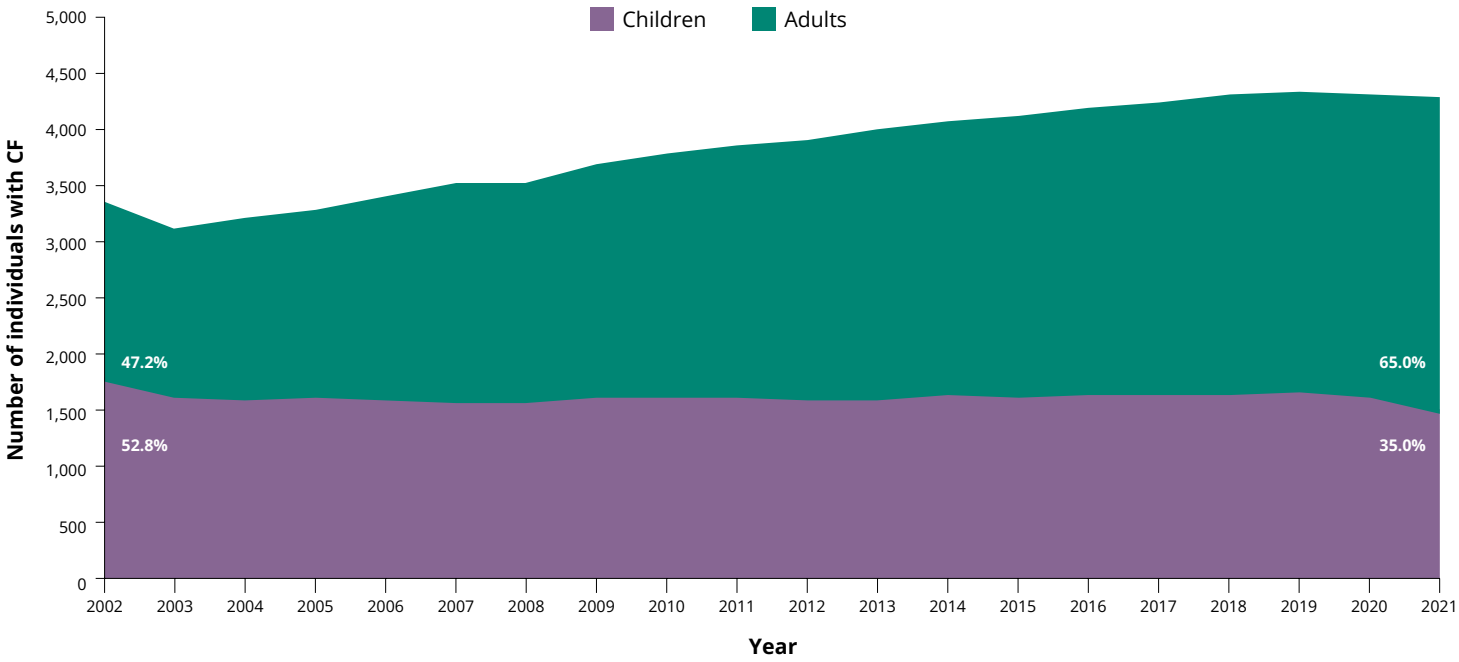
FIGURE 6: Age distribution, 2021. [N = 4,338].



AGE DISTRIBUTION

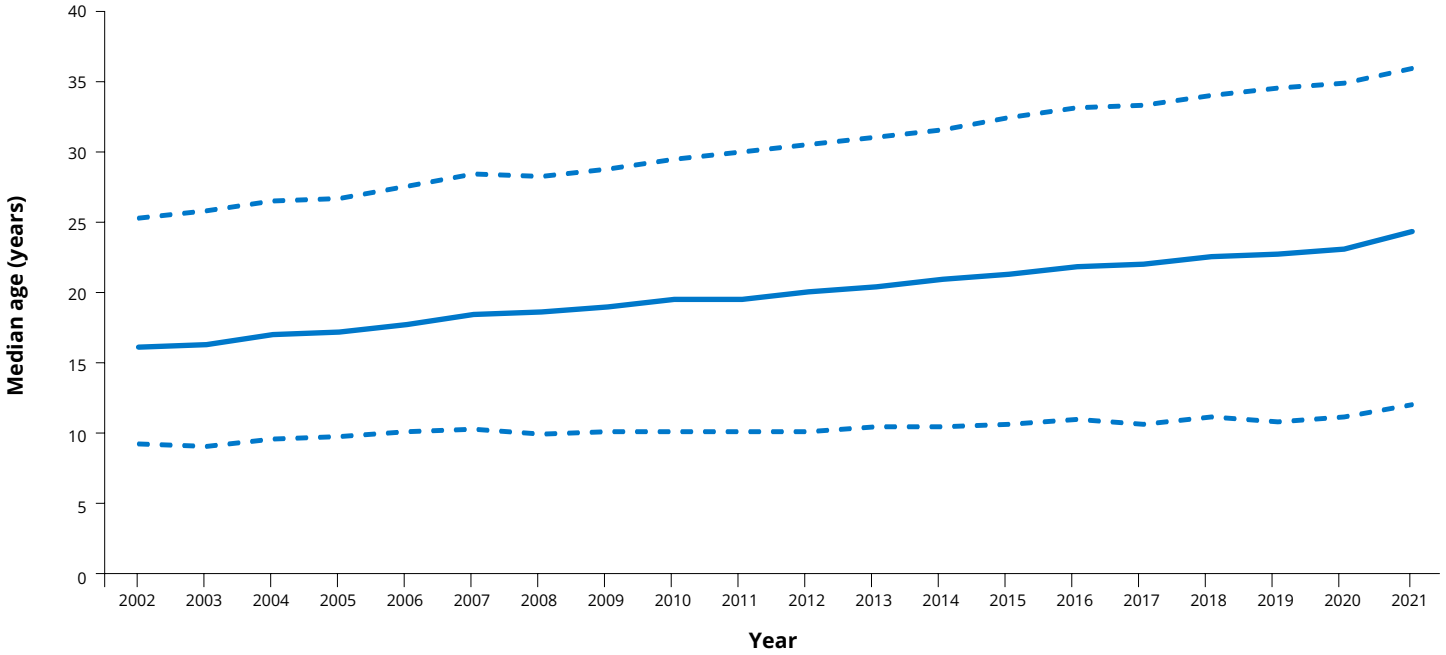
Improvements in treatment and care in the last few decades have led to an increase in the number of Canadian adults living with cystic fibrosis. Twenty years ago in 2002, less than half of all Canadians living with cystic fibrosis were adults (individuals aged 18 years and older) (Figure 7). In 2021, there were 2,821 adults living with CF, accounting for 65.0% of the Canadian CF population, and 883 (20.4%) adults aged 40 years and over.

FIGURE 7: Number of children and adult, 2002 to 2021.



It follows that the median age of individuals with cystic fibrosis has increased steadily over the past 20 years. From 17.2 years in 2002, to 25.3 years among those reported on in 2021 (shown in Figure 8, along with the 25th and 75th percentile of ages).

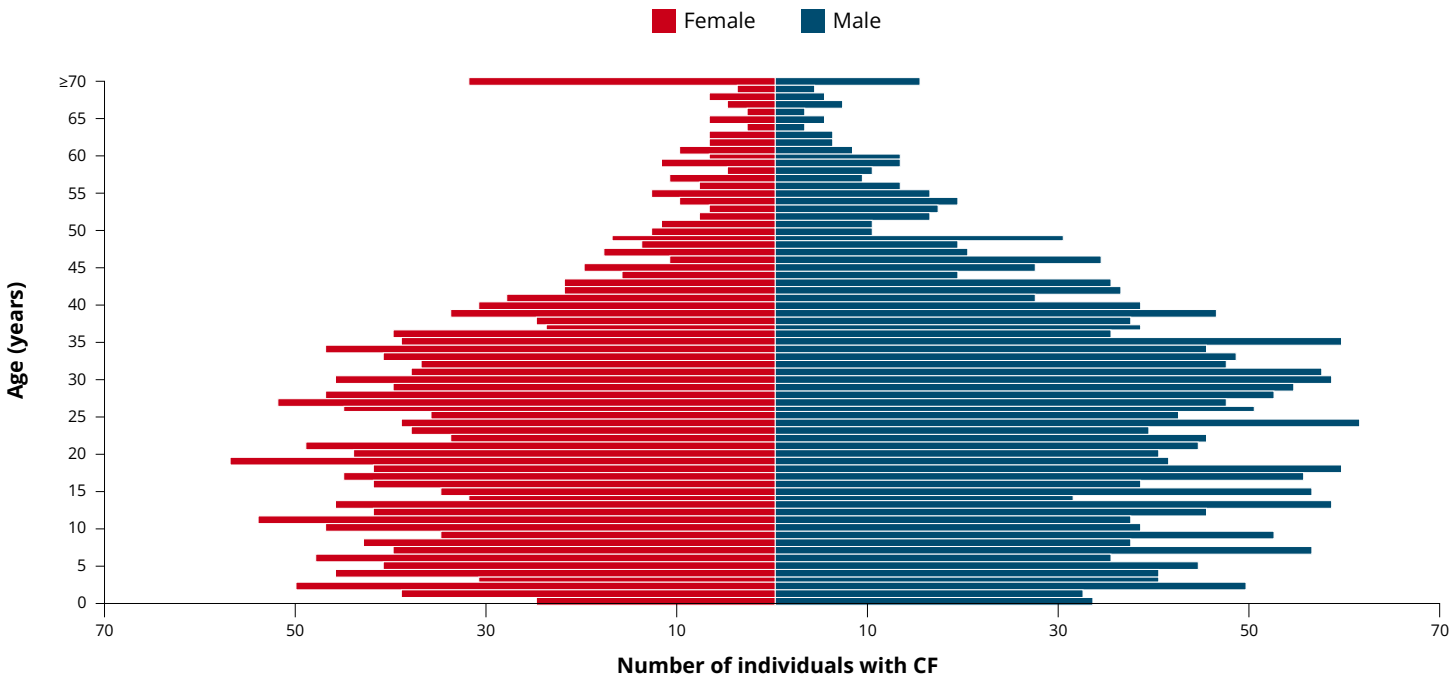
FIGURE 8: Median age, 2002 to 2021.



AGE-SEX DISTRIBUTION

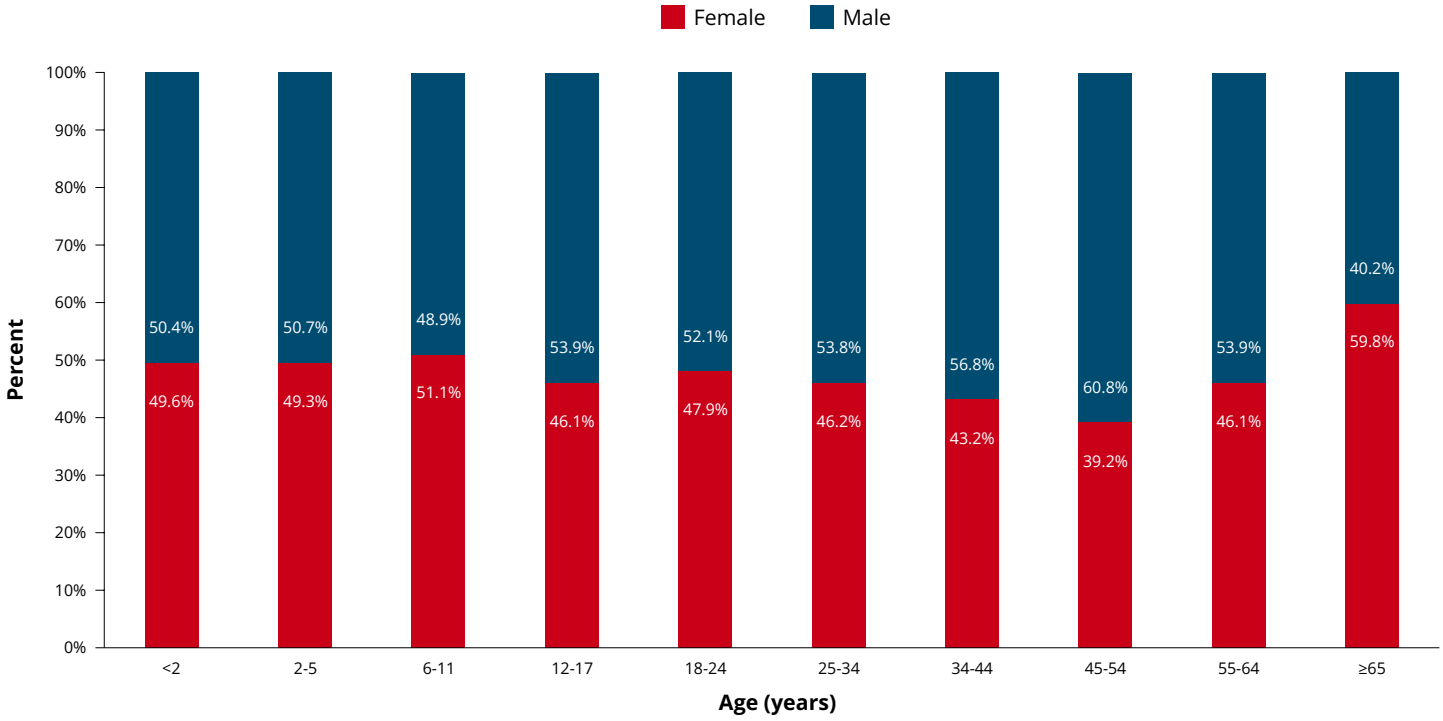
Figure 9 shows the age-sex distribution for all individuals reported on in 2021.

FIGURE 9: Age-sex distribution, 2021. [N = 4,338].



The sex distribution of those living with CF differed by age group. As seen in Figure 10, 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 60.8% male for those aged 45-54 years. After age 55, the proportion of females begins to increase to 59.8% female for those age ≥65 year.

FIGURE 10: Sex distribution, by age, 2021. [N = 4,338].



DIAGNOSIS

There were 98 new diagnoses of CF in 2021 that were recorded in the CF Registry. Of these, 67 (68.4%) were made through provincial newborn screening (NBS) programs.

AGE AT DIAGNOSIS

In total, 4,254 (98.1%) of individuals with cystic fibrosis reported on in 2021, had a recorded diagnosis date, and of those, 2,574 (60.5%) were diagnosed before the age of one year, and 3,109 (73.1%) were diagnosed by the age of two years (Figure 11). Adult diagnoses, those diagnosed at 18 years and older, accounted for only 346 (8.1%) of all individuals reported on in 2021.

FIGURE 11: Age at diagnosis of cystic fibrosis individuals, 2021. [N = 4,254].

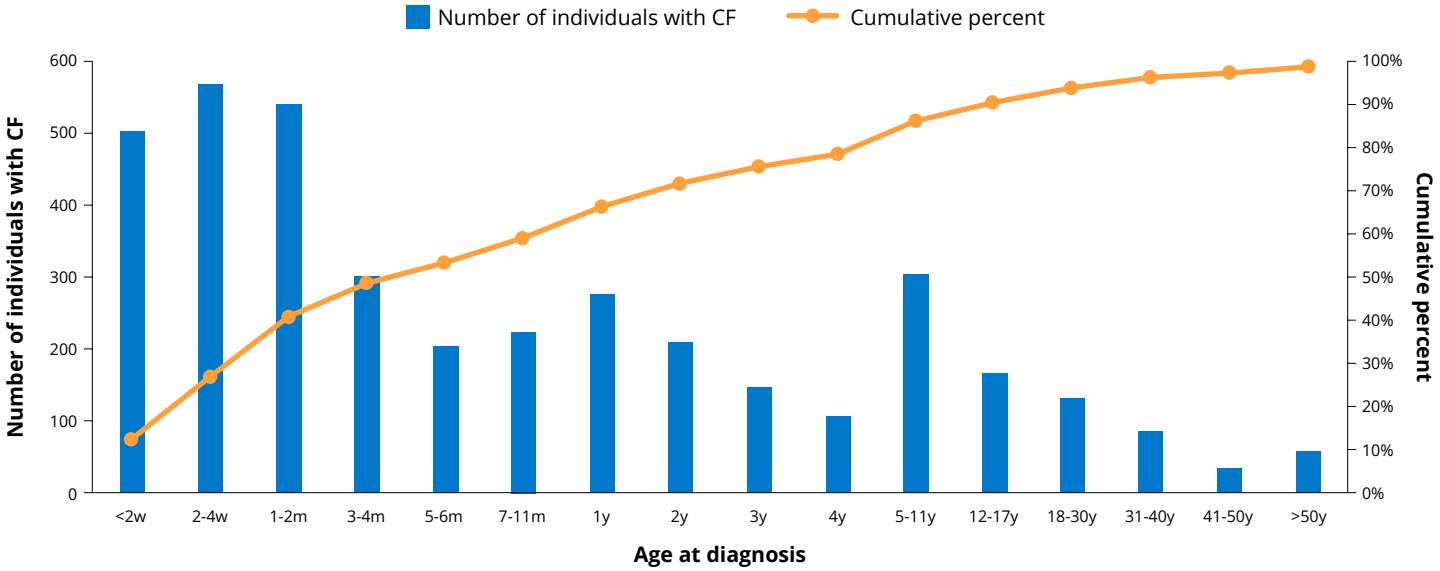
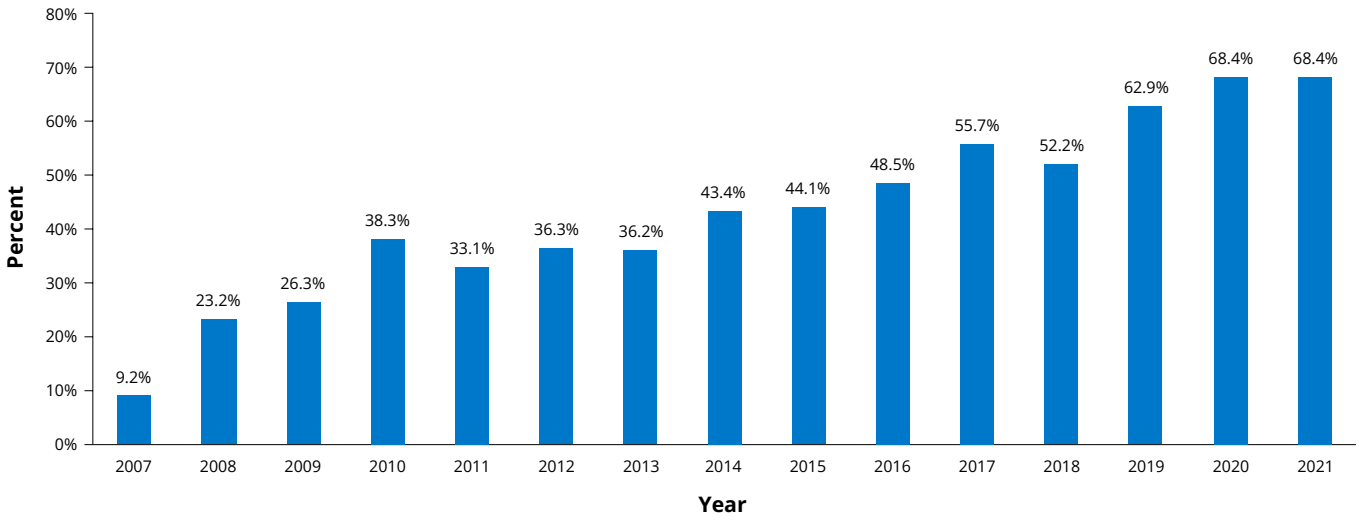


Figure 12 shows the percentage of newborns diagnosed through provincial NBS programs since 2007, when NBS for CF started in Alberta. At that time, only 9.2% of new CF diagnoses were identified through NBS. In the spring of 2018, Quebec became the last jurisdiction to start screening newborns for cystic fibrosis. Newborn screening is now in practice for all provinces across Canada and remains essential for early diagnosis and intervention.

FIGURE 12: Percentage of all new CF diagnoses made through the NBS program, 2007 to 2021.



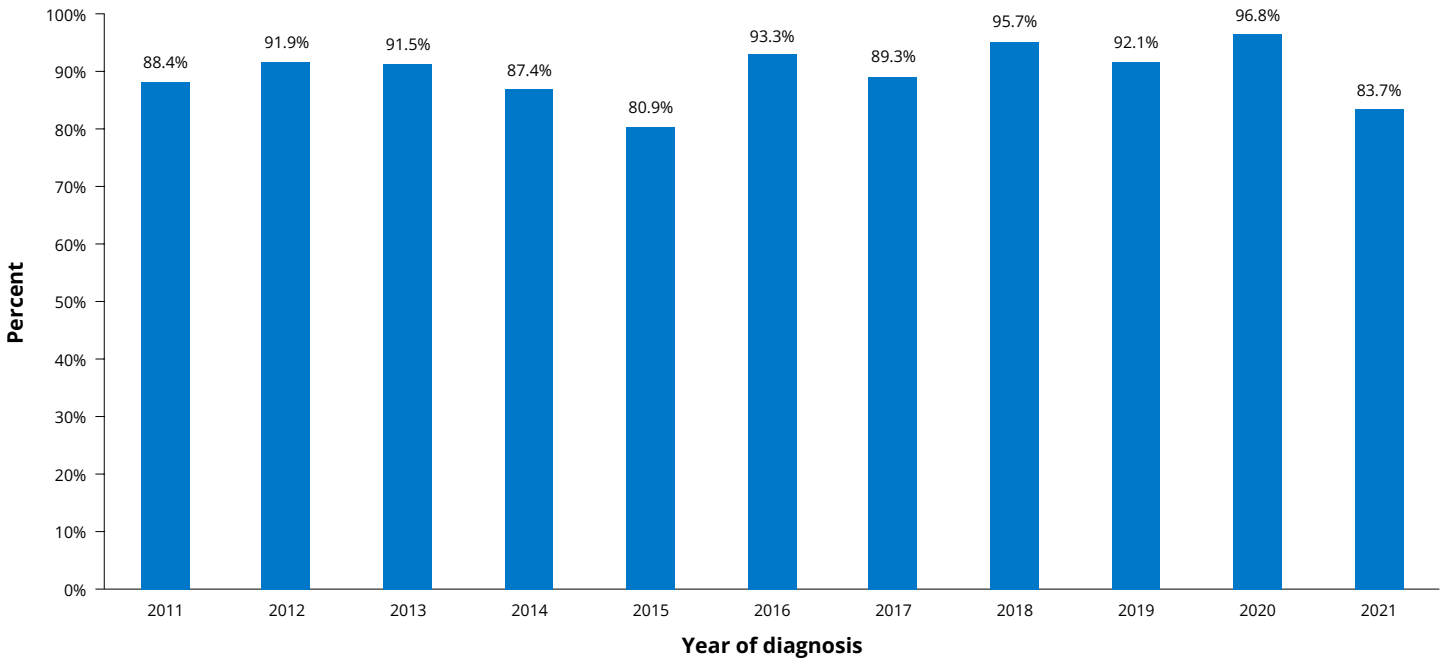
SWEAT CHLORIDE TESTING

Sweat chloride testing is used in the diagnosis of CF, by measuring the concentration of salt in a person's sweat. Sweat chloride testing is ordered for individuals with positive newborn screen for cystic fibrosis, a family history of cystic fibrosis, or symptoms of the disorder. It is also routinely used as part of CFTR modulator initiation and monitoring.

Individuals with cystic fibrosis 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 CF Registry 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 13). In 2021, 82 (83.7%) of the 98 newly diagnosed individuals had at least one sweat chloride test result recorded in the year. The proportion among newly diagnosed individuals is expected to increase, as sweat chloride testing data after 2021 is captured.

FIGURE 13: Percentage of newly diagnosed individuals with at least one sweat chloride test, 2011 to 2021.



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[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 five 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.

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
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

GENOTYPE

Nearly all individuals with cystic fibrosis reported on in 2021 (4,297 out of 4,338; 99.1%) had at least one CFTR gene mutation recorded. 1,983 (45.7%) have two copies of the F508del mutation (referred to as homozygous F508del) and 1,781 (41.1%) 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 14).

Note that the mutation I507del is reported separately from the mutation F508del in this report. In previous reports, these two mutations were grouped together. As a result, the proportion of individuals with at least one F508del mutation may be lower compared to previous reports.

FIGURE 14: Distribution of genotypes, 2021. [N = 4,338].

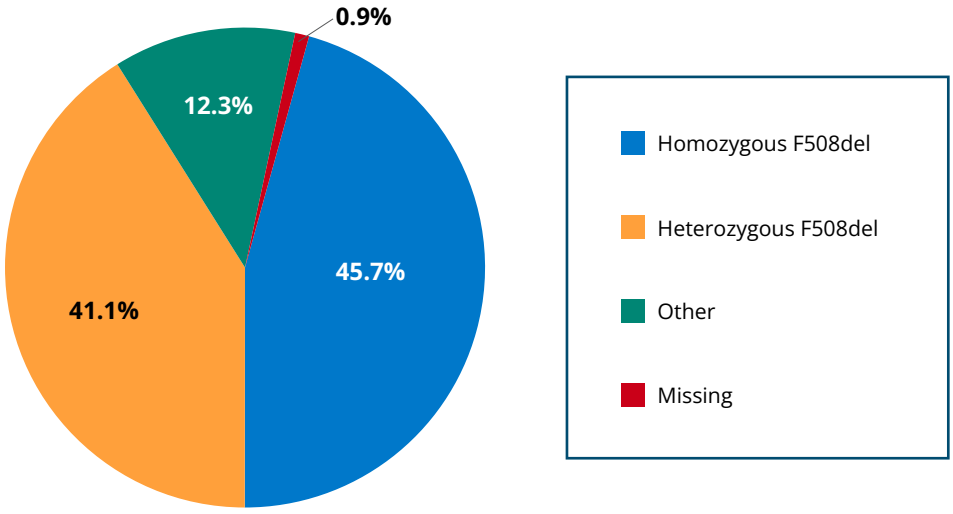
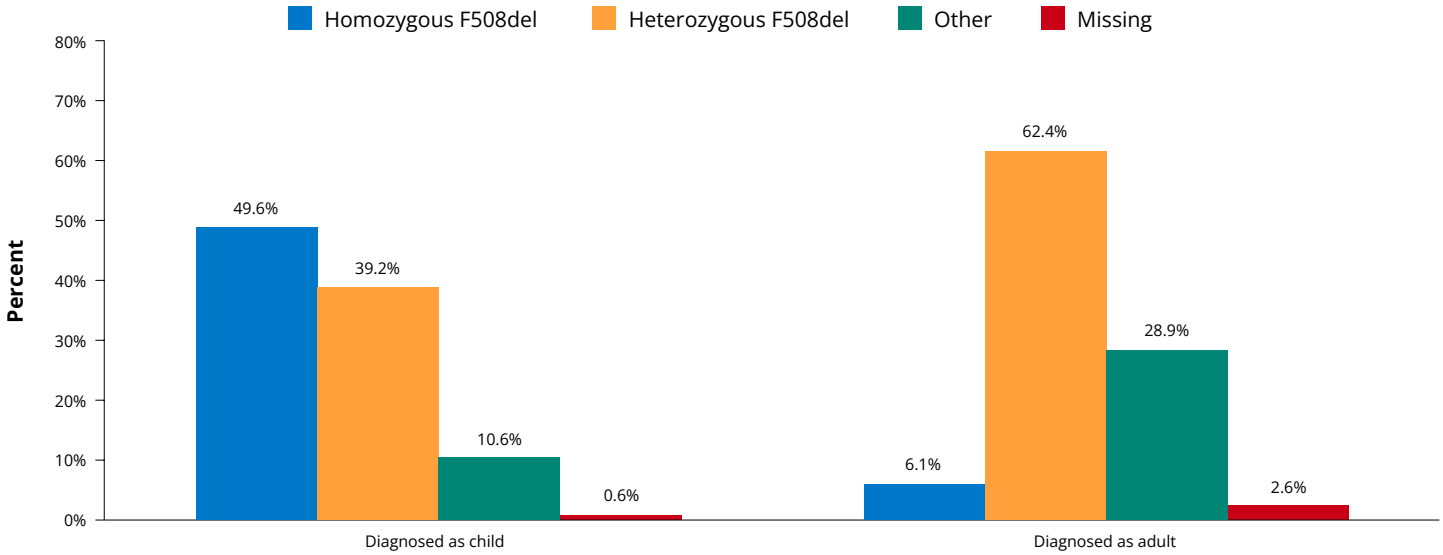


Figure 15 shows the genotype distribution of the CF population by the age of diagnosis. Individuals with more severe disease symptoms are generally diagnosed earlier; milder forms of cystic fibrosis may only be diagnosed in adulthood. Those diagnosed as a child (under 18 years) were more likely to be homozygous F508del (49.6%) while those diagnosed as an adult (18 years and older) were more likely to be heterozygous F508del (62.4%).

FIGURE 15: Distribution of genotypes, by age at diagnosis, 2021. [N = 4,254].



GENOTYPE

Table 2 shows the number of people with CF 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 the table is 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, 2021. [N = 4,297].

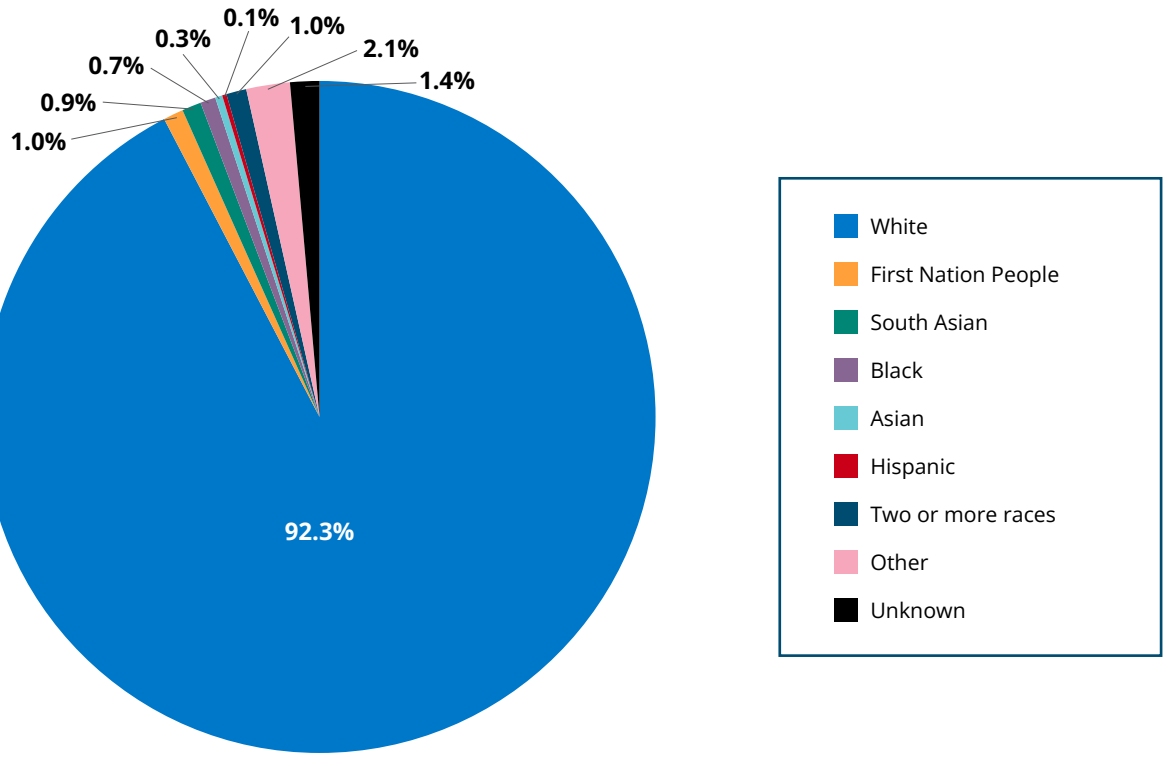
MUTATION	NUMBER*	PERCENT*	MUTATION	NUMBER*	PERCENT*
F508del	3,766	87.6%	R117C	14	0.3%
621+1G->T	262	6.1%	1154insTC	13	0.3%
G542X	141	3.3%	3905insT	13	0.3%
G551D	133	3.1%	TG12	13	0.3%
L206W	120	2.8%	P574H	11	0.3%
A455E	114	2.7%	2183AA->G	10	0.2%
711+1G->T	112	2.6%	394delTT	10	0.2%
N1303K	85	2.0%	R347H	10	0.2%
M1101K	71	1.7%	S549N	10	0.2%
R117H	70	1.6%	2622+1G->A	9	0.2%
G85E	64	1.5%	4016insT	9	0.2%
I507del	60	1.4%	D110H	9	0.2%
5T	58	1.3%	R1066C	9	0.2%
3849+10kbC->T	54	1.3%	R75X	9	0.2%
2789+5G->A	49	1.1%	V520F	9	0.2%
P67L	38	0.9%	L558S	8	0.2%
W1282X	37	0.9%	Q1313X	8	0.2%
1717-1G->A	36	0.8%	2789+2insA	7	0.2%
R553X	35	0.8%	711+3A->G	7	0.2%
S489X	31	0.7%	L1254X	7	0.2%
3199del6	28	0.7%	L218X	7	0.2%
R334W	28	0.7%	V456A	7	0.2%
D1152H	27	0.6%	1078delT	6	0.1%
1898+1G->A	25	0.6%	3876delA	6	0.1%
CFTRdele2,3	24	0.6%	A559T	6	0.1%
Y1092X	24	0.6%	S466X	6	0.1%
3659delC	23	0.5%	TG11	6	0.1%
I148T	22	0.5%	1461ins4	5	0.1%
R1162X	21	0.5%	2184delA	5	0.1%
R560T	21	0.5%	D579G	5	0.1%
2184insA	20	0.5%	G178R	5	0.1%
R347P	18	0.4%	M470V	5	0.1%
Q493X	17	0.4%	Q220X	5	0.1%
E60X	16	0.4%	R75Q	5	0.1%
3120+1G->A	15	0.3%	S4X	5	0.1%
R1158X	15	0.3%	T854T	5	0.1%
1525-1G->A	14	0.3%	Y569D	5	0.1%
3272-26A->G	14	0.3%			

** 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 (92.3%) of the Canadian CF population is White. Of those remaining who have an identified ancestry (Figure 16), 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 16: Distribution of ethnicity, 2021. [N = 4,338].



PULMONARY OUTCOMES

Lung function measurements are critical for evaluating and monitoring lung health in individuals living with CF. Although measures of lung function are made in children as young as 3 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.

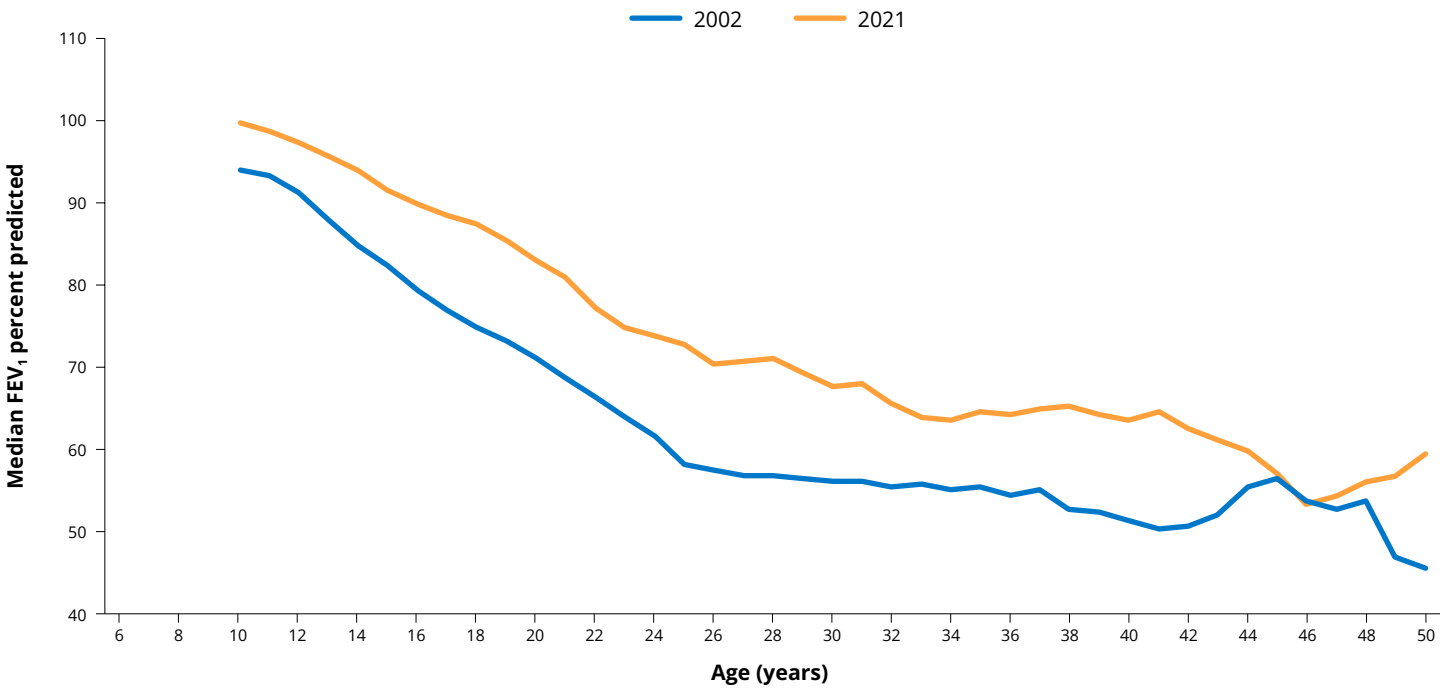
In this section, the first stable (i.e. not measured during a pulmonary exacerbation or other destabilizing event) FEV_1 percent predicted measurement of the year was used for each individual age 6 and older at the time of measurement, to summarize pulmonary function. If no clinically stable measurements 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 2021, and any FEV_1 percent predicted measurements taken after lung transplant in 2021, were excluded from this section of the report.

MEDIAN FEV_1 PERCENT PREDICTED

Figure 17 shows the median FEV_1 percent predicted from age 6 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 2002. The median FEV_1 at 25 years of age (the median age of an individual living with cystic fibrosis in 2021) was 71.3% predicted in 2021 compared to 51.6% predicted in 2002, marking an improvement of 19.7% over the last two decades.

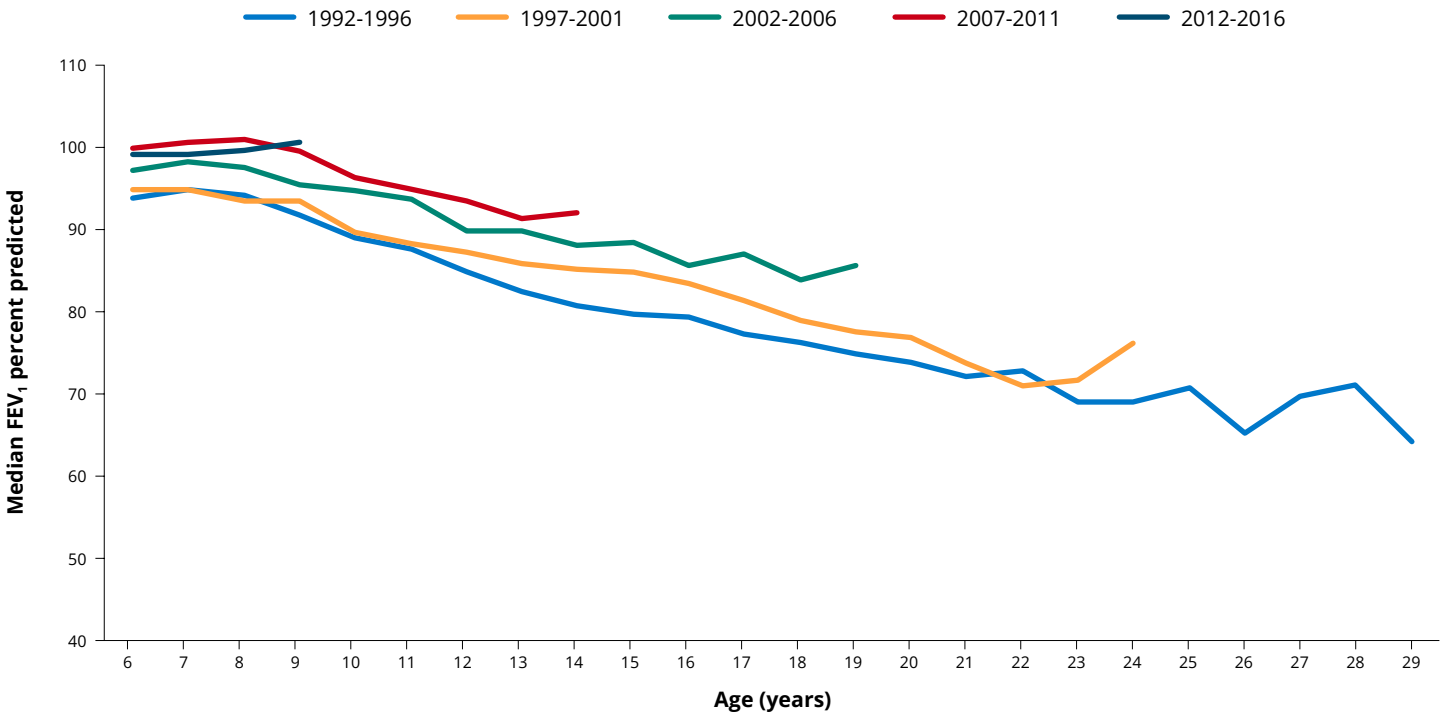
FIGURE 17: Median FEV_1 percent predicted, by age (5-year moving window), 2002 and 2021.



MEDIAN FEV_1 PERCENT PREDICTED

Individuals born more recently had a higher median FEV_1 percent predicted at age 6 years and had a slower rate of decline than those born earlier (Figure 18). 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.

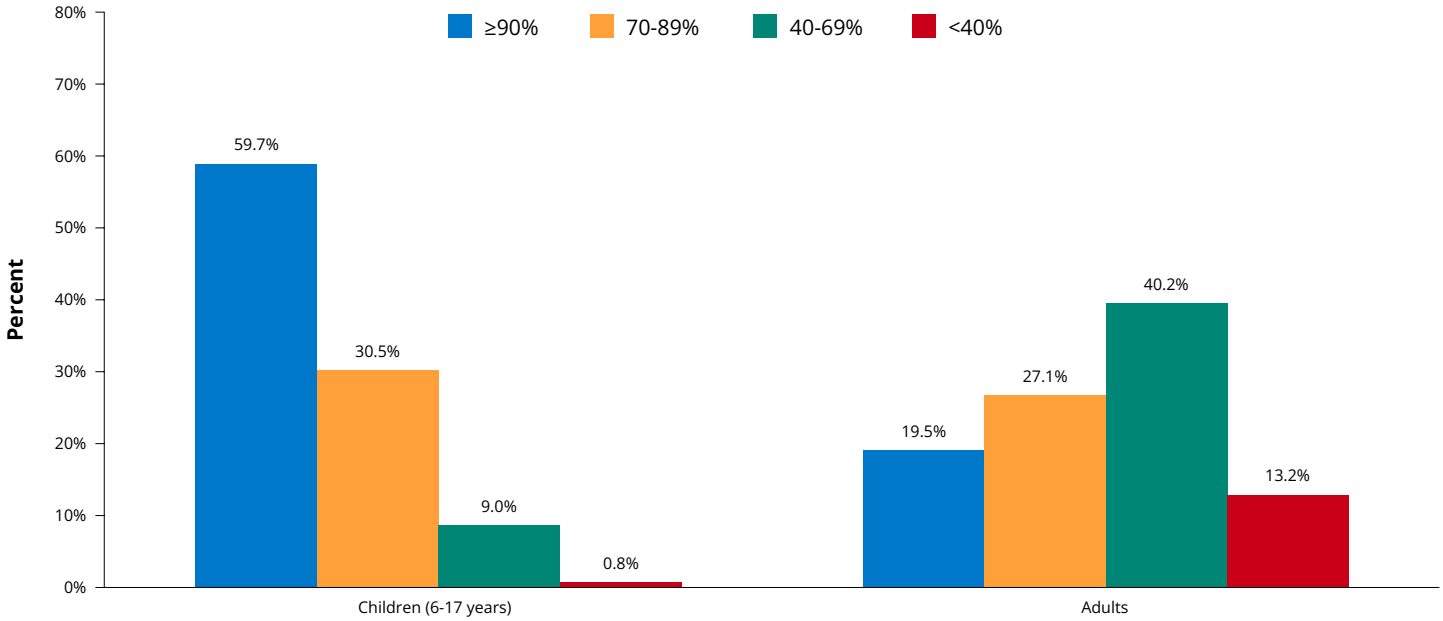
FIGURE 18: Median FEV_1 percent predicted, by birth cohort, 2021.



PULMONARY FUNCTION BY AGE

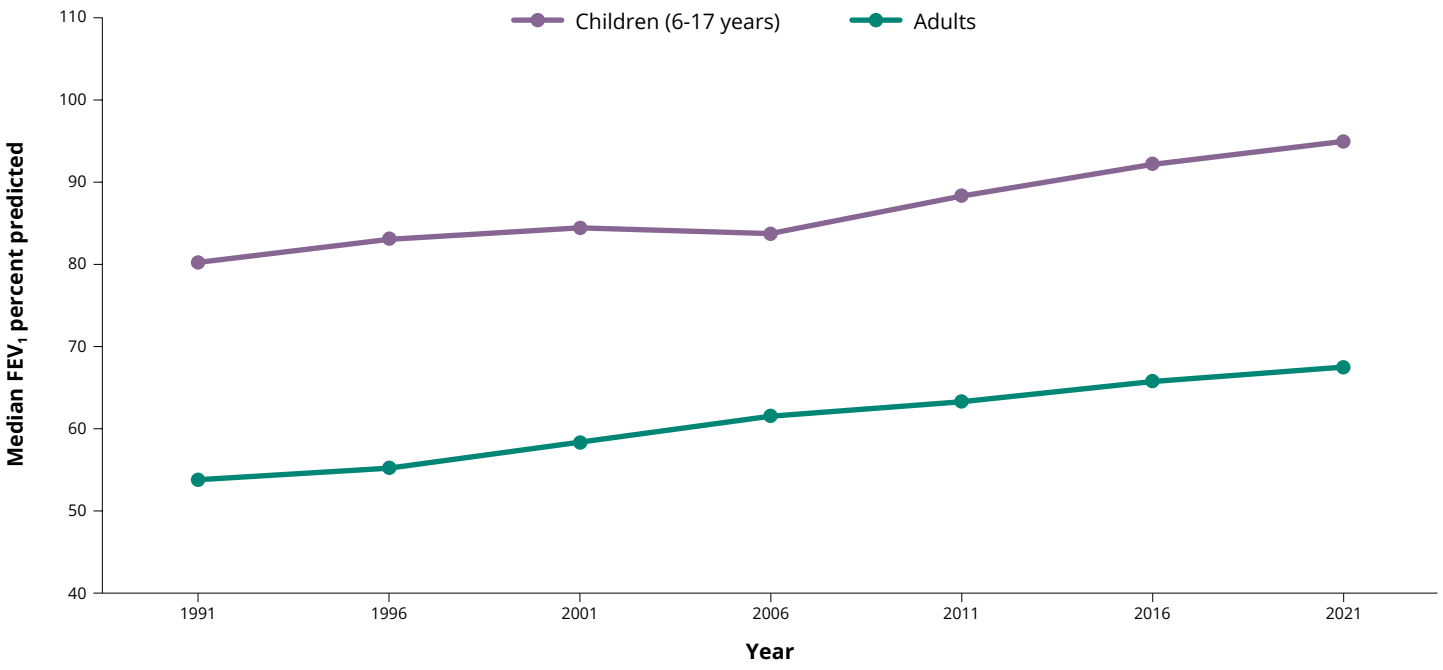
In 2021, 1,065 children 6-17 years and 2,390 adults had a recorded FEV_1 percent predicted measurement. Of those, 636 (59.7%) children 6-17 years had pulmonary function ≥90% predicted, while only 467 (19.5%) adults had pulmonary function in this range (Figure 19).

FIGURE 19: Pulmonary function, by age, 2021. [N = 1,065 children (6-17 years); N = 2,390 adults].



Over time, the median FEV_1 percent predicted has increased steadily in both age groups, and in 2021 the median FEV_1 percent predicted was 67.7% in adults and 94.9% in children (6-17 years of age) (Figure 20).

FIGURE 20: Median FEV_1 percent predicted, by age, 1991 to 2021.



PULMONARY FUNCTION BY SEX

Figure 21 and Figure 22 show the distribution of pulmonary function between females and males, among children and adults, respectively. Among children, more males had FEV_1 percent predicted at or above 90% predicted, compared to females. Among adults, more males had FEV_1 percent predicted less than 40% predicted, compared to females.

FIGURE 21: Pulmonary function in children (6 to 17 years), by sex, 2021. [N = 517 females; N = 548 males].

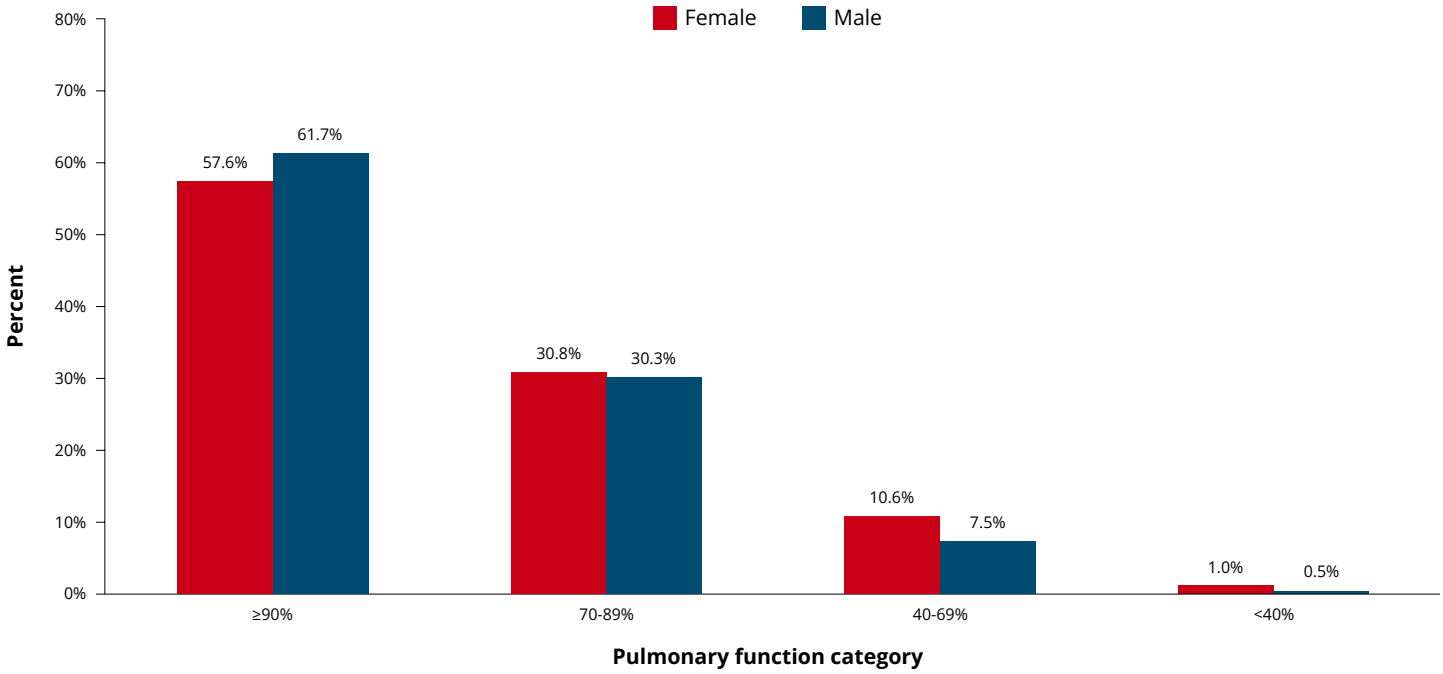
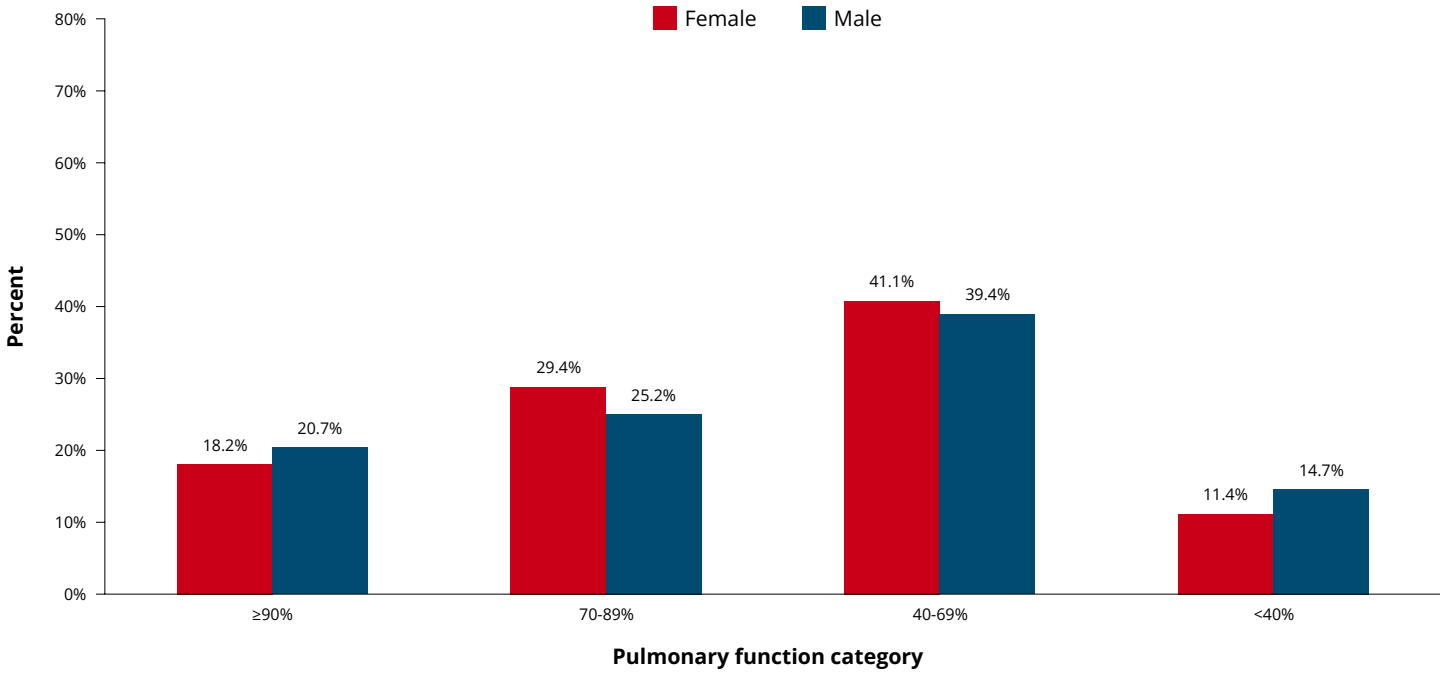


FIGURE 22: Pulmonary function in adults, by sex, 2021. [N = 1,090 females; N = 1,300 males].



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 2021, 3,610 (83.6%) individuals with cystic fibrosis were identified as pancreatic insufficient, compared to 707 (16.4%) who were not (identified as pancreatic sufficient), as shown in Figure 23. For individuals 40 years of age or older, 247 (28.1%) were pancreatic sufficient (Figure 24).

FIGURE 23: Pancreatic status, 2021. [N = 4,317].

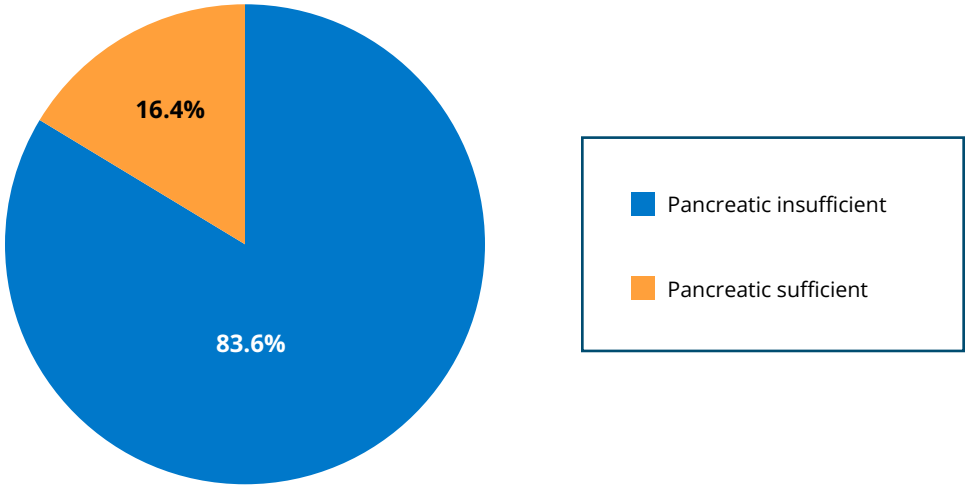
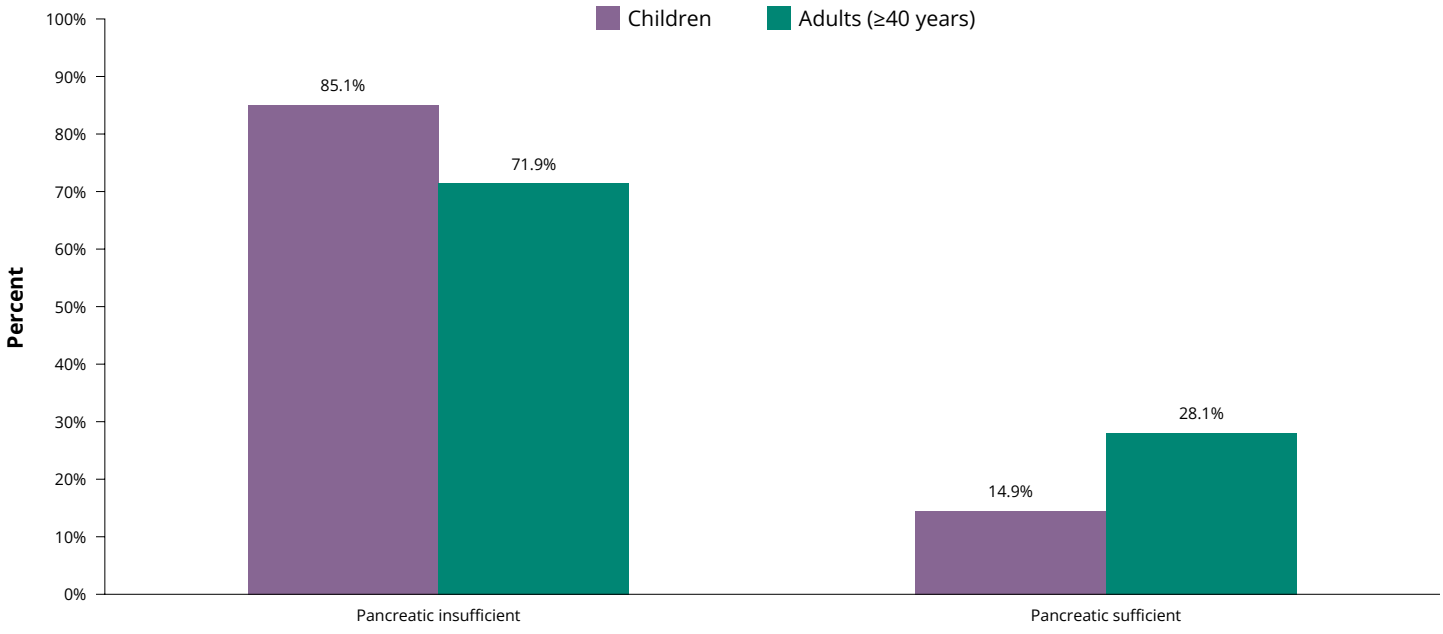


FIGURE 24: Pancreatic status, by age, 2021. [N = 1,505 children; N = 878 adults (≥40 years)].



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 BMI percentiles are 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 exist, 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 2021, and any BMI percentile measurements taken after lung transplant in 2021, 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].

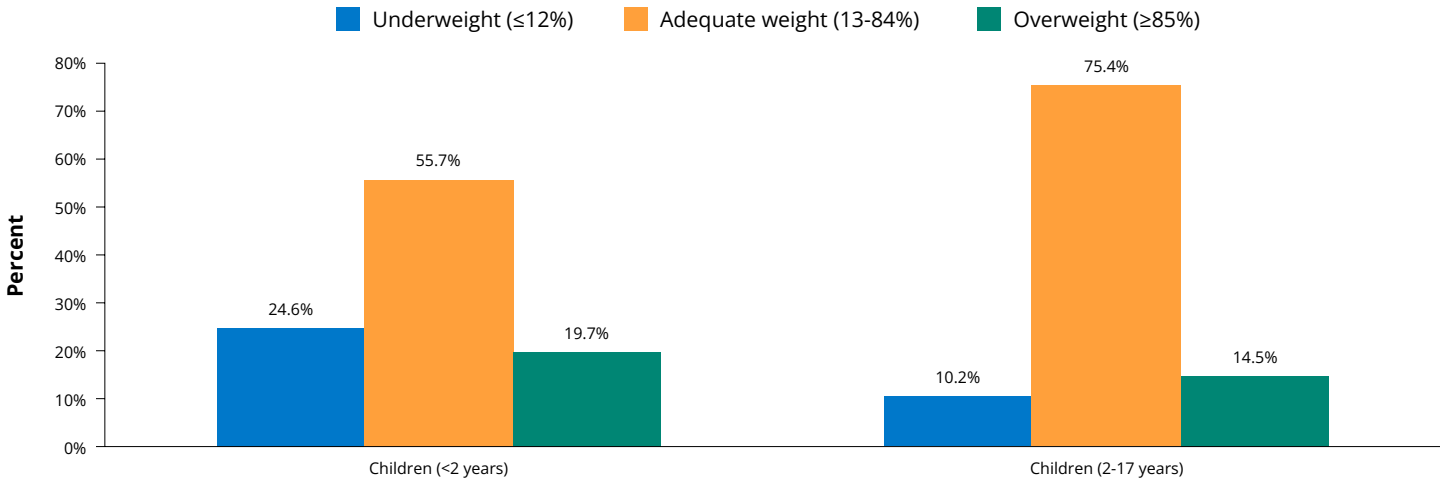
TABLE 3: BMI percentile classification.

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

In 2021, 203 under 2 years and 1,369 2-17 years had a recorded BMI percentile measurement. The national median BMI percentile in children under 2 was 44.7 and in children 2-17 years was 49.8. The 50th BMI percentile is the national goal for children with cystic fibrosis and in 2021, 44.8% of children under 2 years and 49.6% of children 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, 113 (55.7%) children under 2 and 1,032 (75.4%) children 6-17 years had an adequate weight (i.e. neither underweight nor overweight) (Figure 25).

FIGURE 25: BMI percentile in children, 2021. [N = 203 children (<2 years); N = 1,369 children (2-17 years)].



BMI PERCENTILE

For both males and females, the median BMI percentiles have been increasing over time (Figure 26). While males showed a slightly higher median BMI percentile in earlier years, the gap between sexes has diminished over time.

FIGURE 26: Median BMI percentiles in children (2-17 years), by sex, 1991 to 2021.

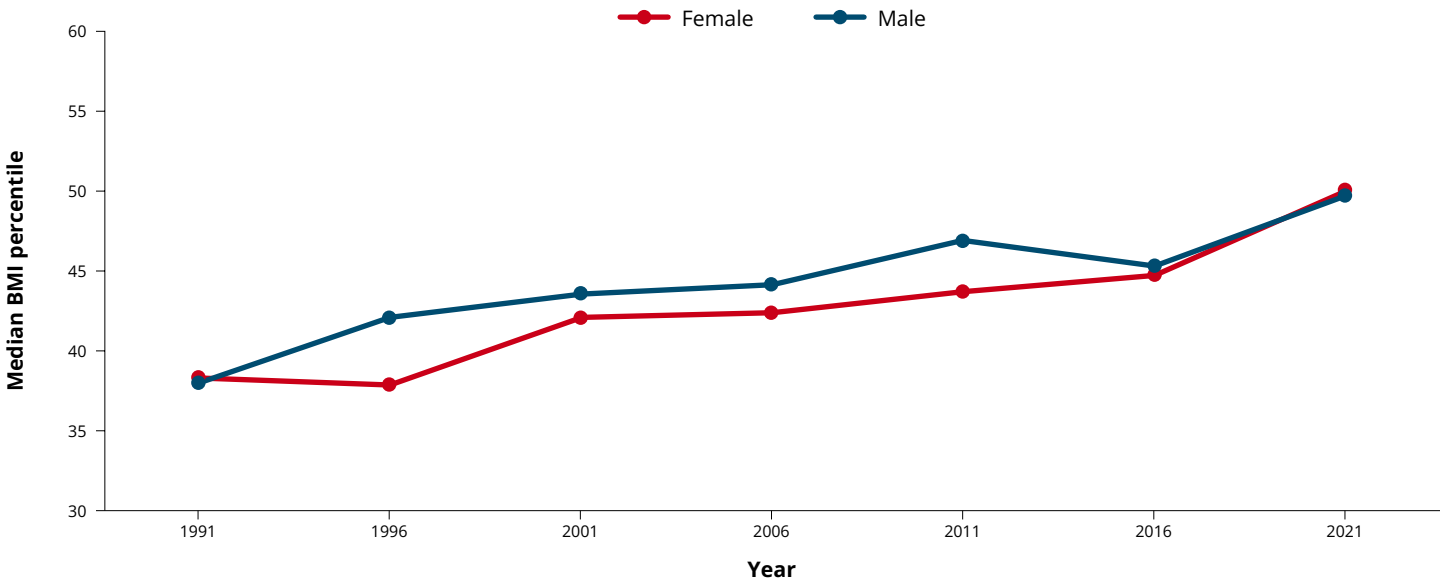
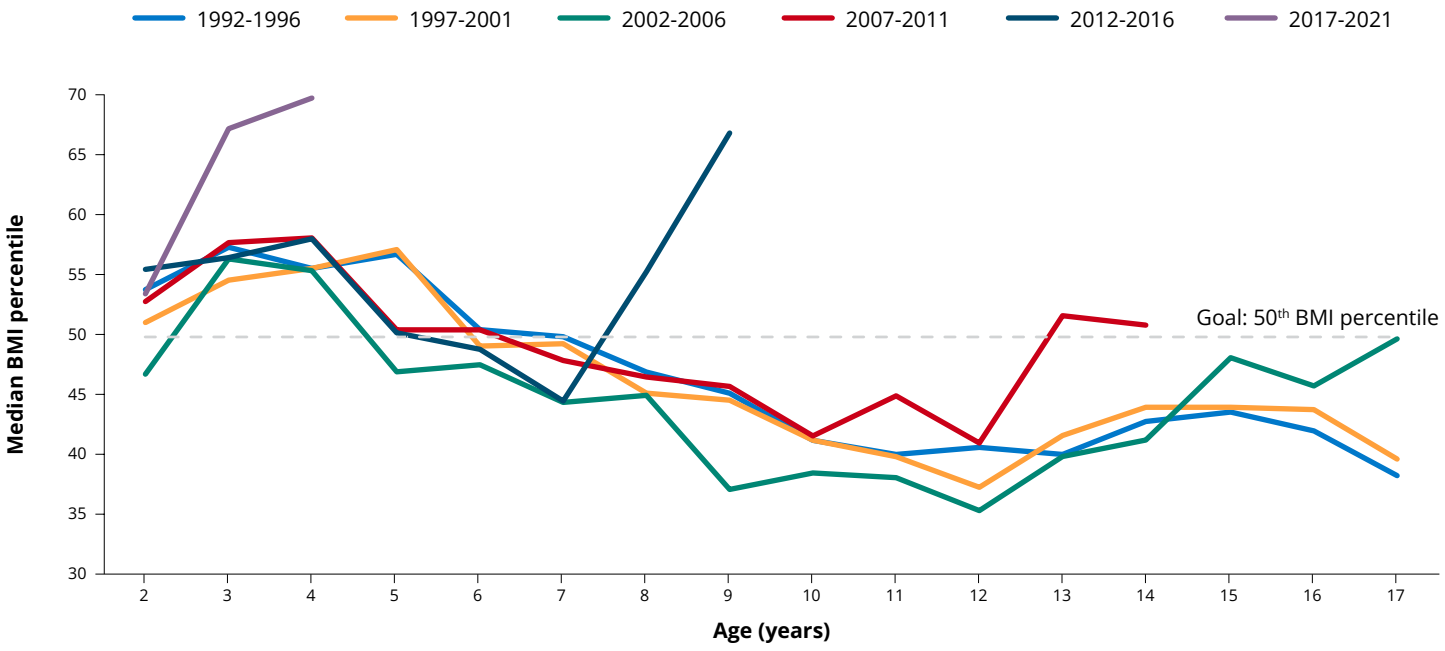


Figure 27 below shows the median BMI percentile for children 2-17 years, by birth cohort. In more recent birth cohorts, the median BMI percentile at age 2 years increased for the most part. The nutritional status was relatively stable in the early ages (2 to 4 years) followed by a gradual decline in 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 27: Median BMI percentile in children (2-17 years), by birth cohort, 2021.



BMI PERCENTILE

Figure 28 and Figure 29 show the distribution of BMI percentile for females and males in children under 2 years and children 2-17 years.

FIGURE 28: BMI percentile classification in children (<2 years), by sex, 2021. [N = 101 females; N = 102 males].

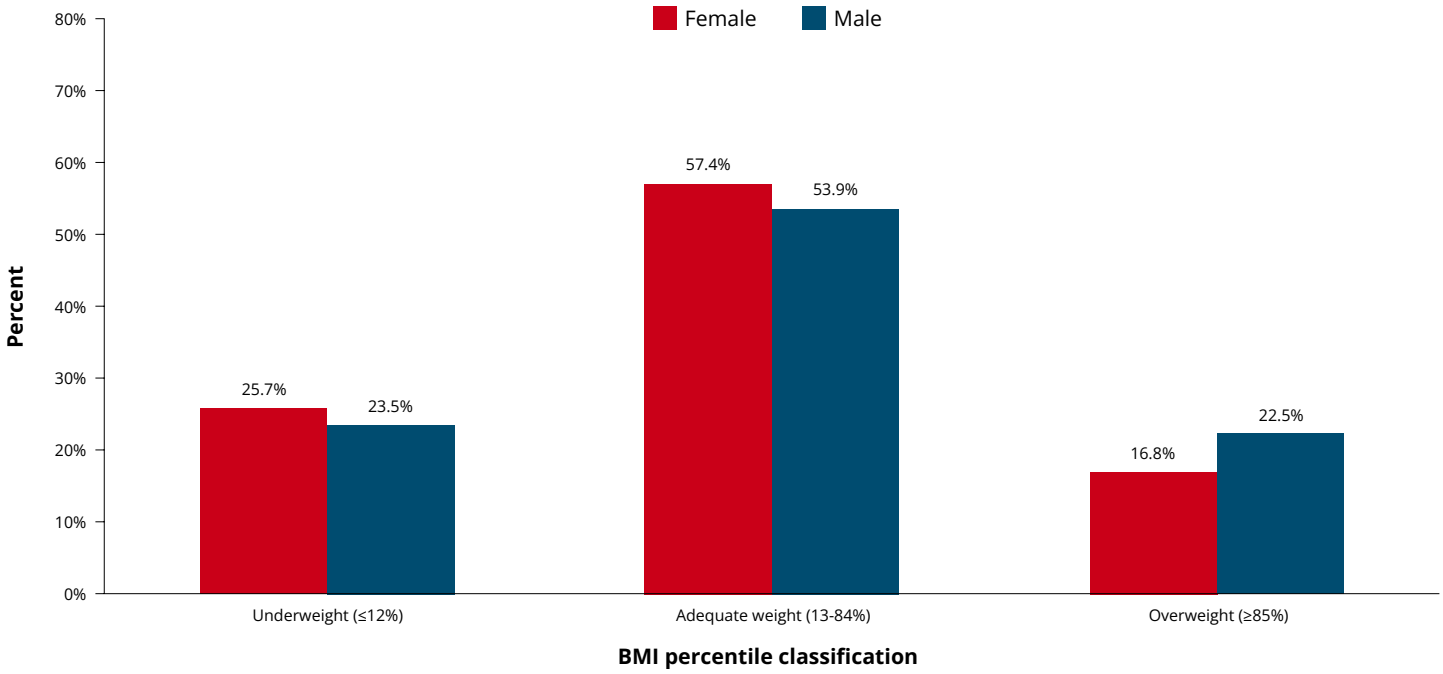
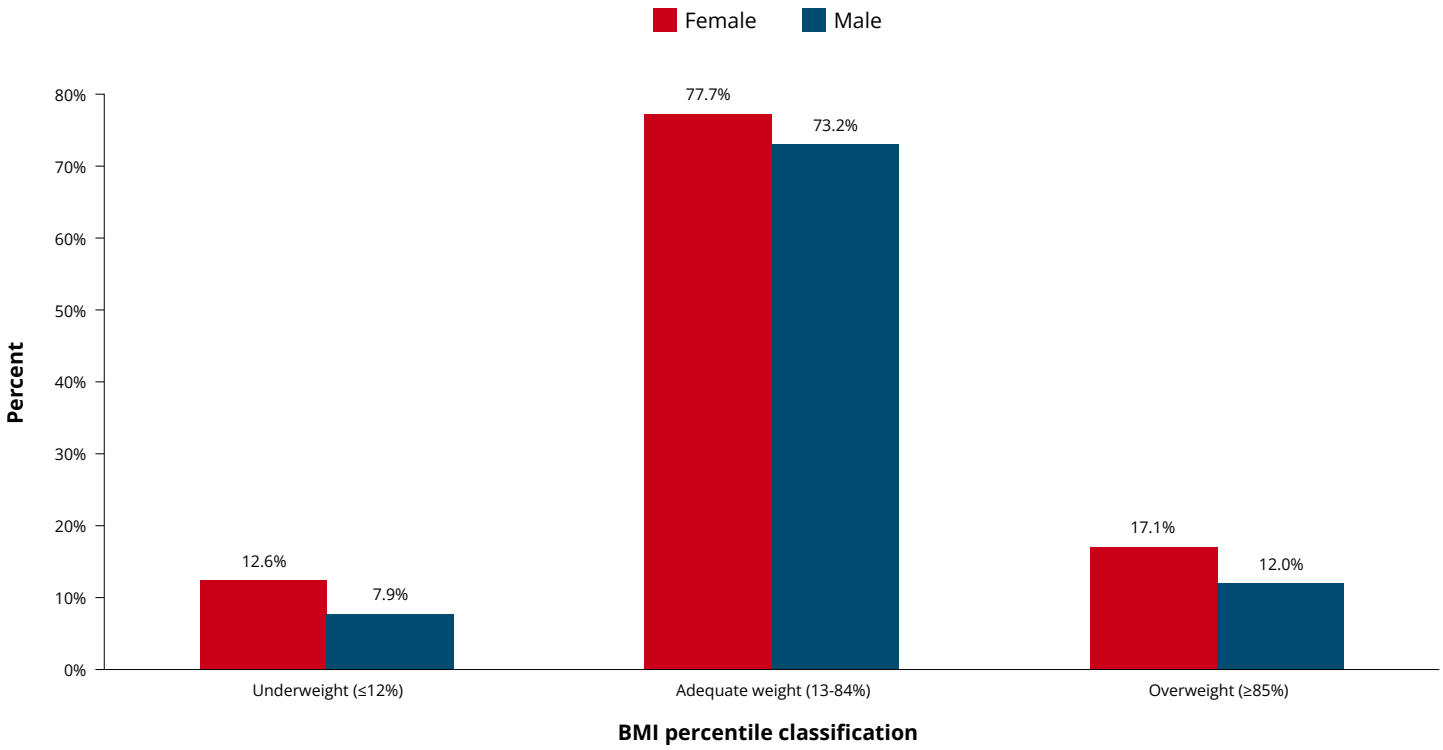


FIGURE 29: BMI percentile classification in children (2-17 years), by sex, 2021. [N = 660 females; N = 709 males].



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 2021, and any BMI measurements taken after lung transplant in 2021, were excluded from this section of the report.

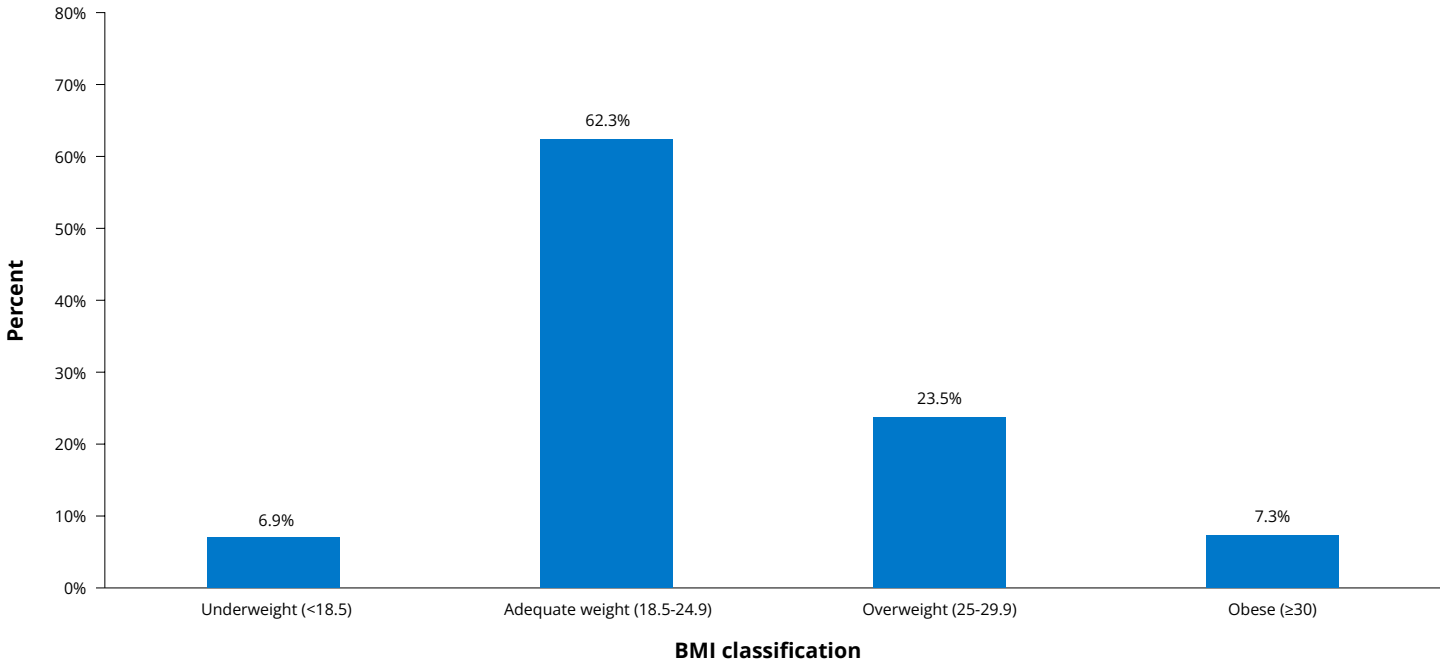
Table 4 below describes the BMI classifications and their BMI ranges according to the WHO guidelines[6]. These guidelines were updated in 2016 and as such, the proportions of BMI classifications will be different from those described in reports prior to 2016.

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 2021, 2,384 adults (age 18 years and older) had a recorded BMI measurement. Among those with a recorded BMI, 1,485 (62.3%) adults with cystic fibrosis had an adequate weight, while 164 (6.9%) were considered underweight and 735 (30.8%) were considered overweight or obese (Figure 30).

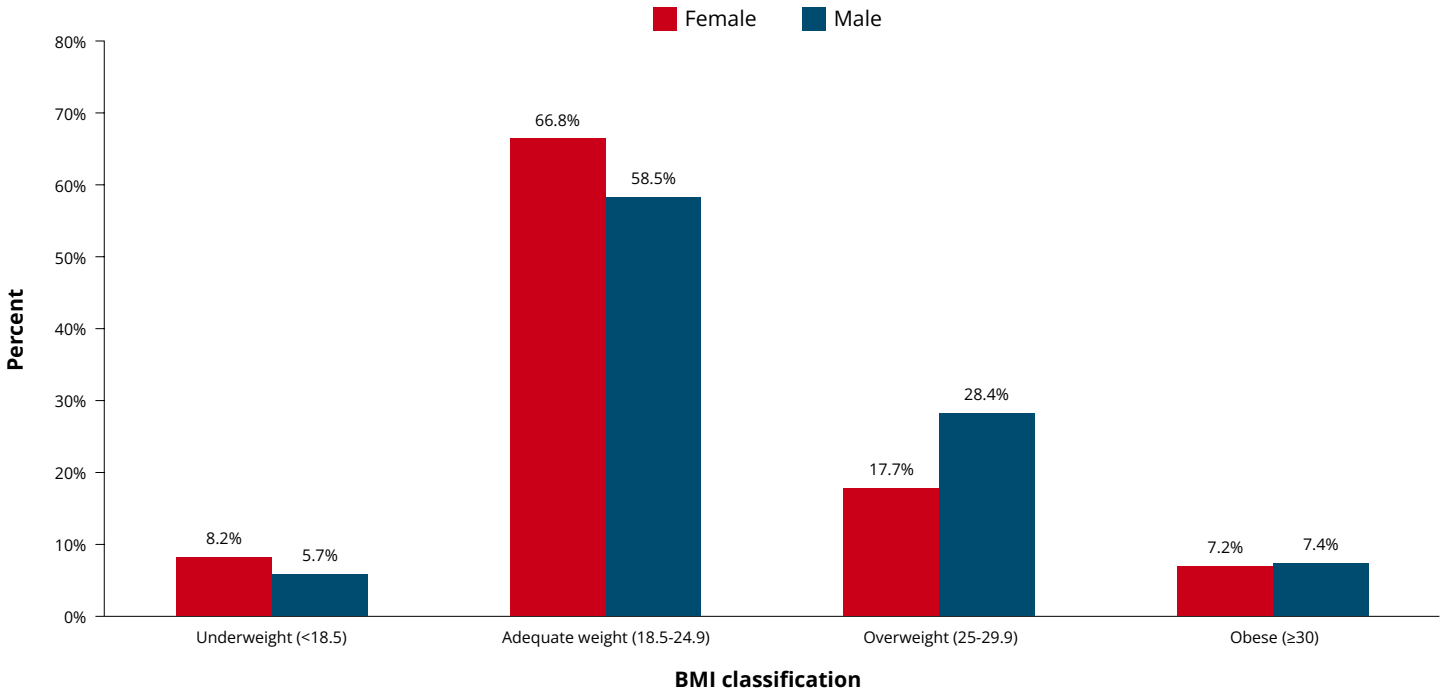
FIGURE 30: BMI classification in adults, 2021. [N = 2,384].



BMI

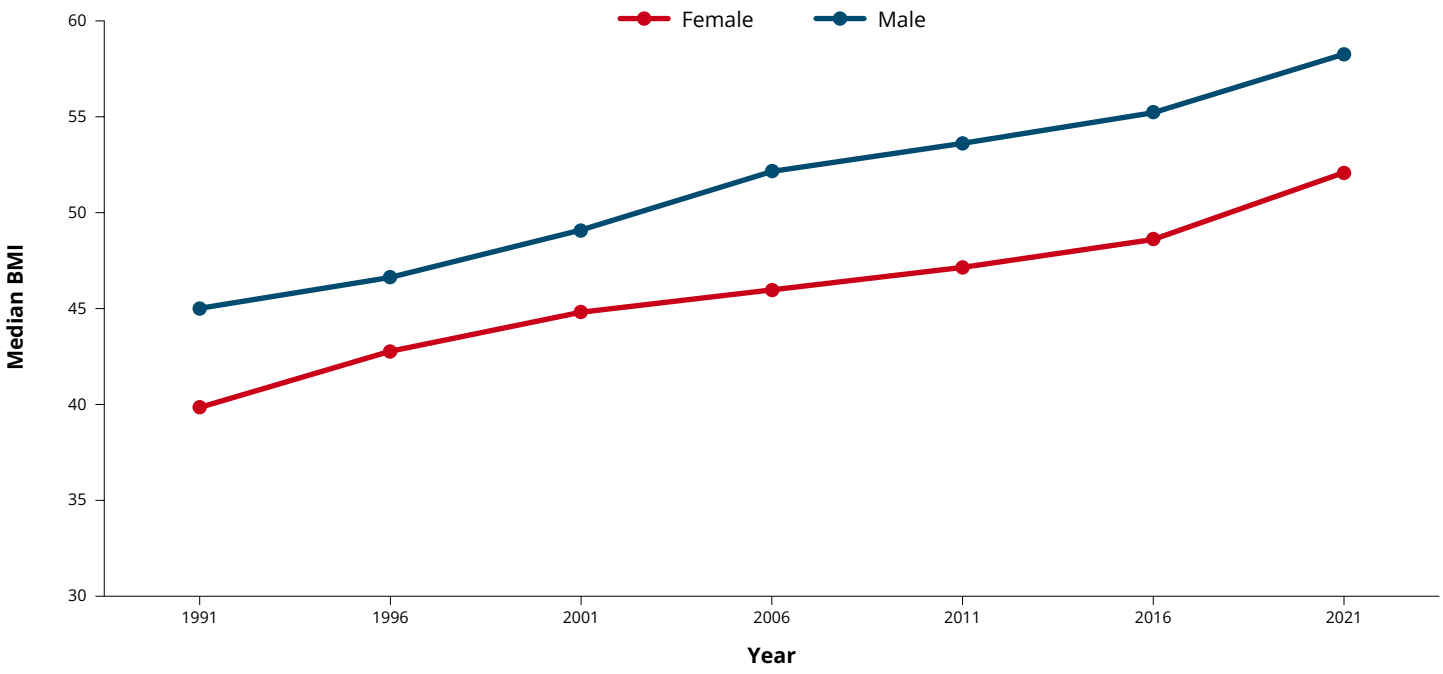
Figure 31 shows the distribution of BMI for adult females and males. Individuals who were muscular may have a higher BMI due to increased weight from larger amounts of muscle mass. In 2021, 89 (8.2%) females were considered underweight compared to 75 (5.7%) males, and 269 (24.9%) females were considered overweight or obese compared to 466 (35.7%) males.

FIGURE 31: BMI classification in adults, by sex, 2021. [1,079 females, N = 1,305 males].



The median BMI has risen steadily over the past 25 years within the cystic fibrosis adult population in both sexes (Figure 32).

FIGURE 32: Median BMI in adults, by sex, 1991 to 2021.



BMI

Figure 33 and Figure 34 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 males, the proportion of individuals classified as obese has surpassed the proportion of those classified as underweight.

FIGURE 33: BMI classification in adult males, 1991 to 2021.

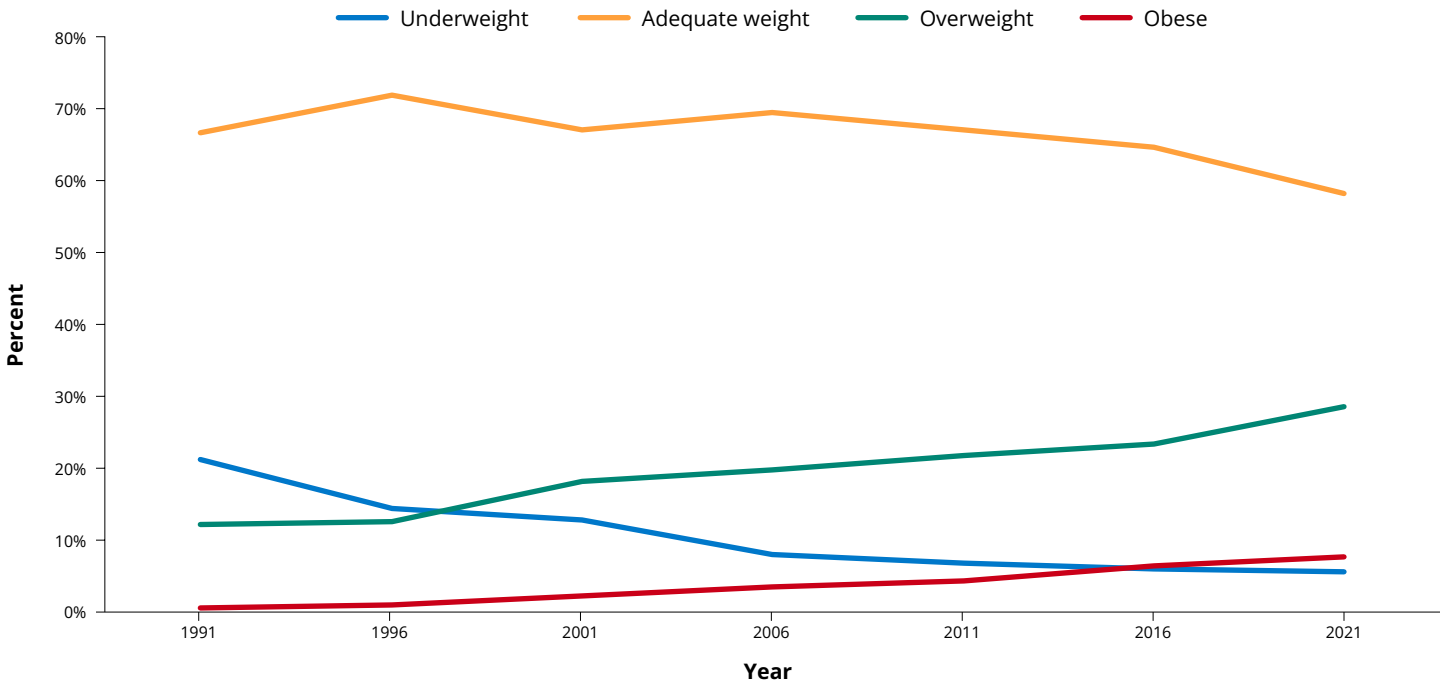
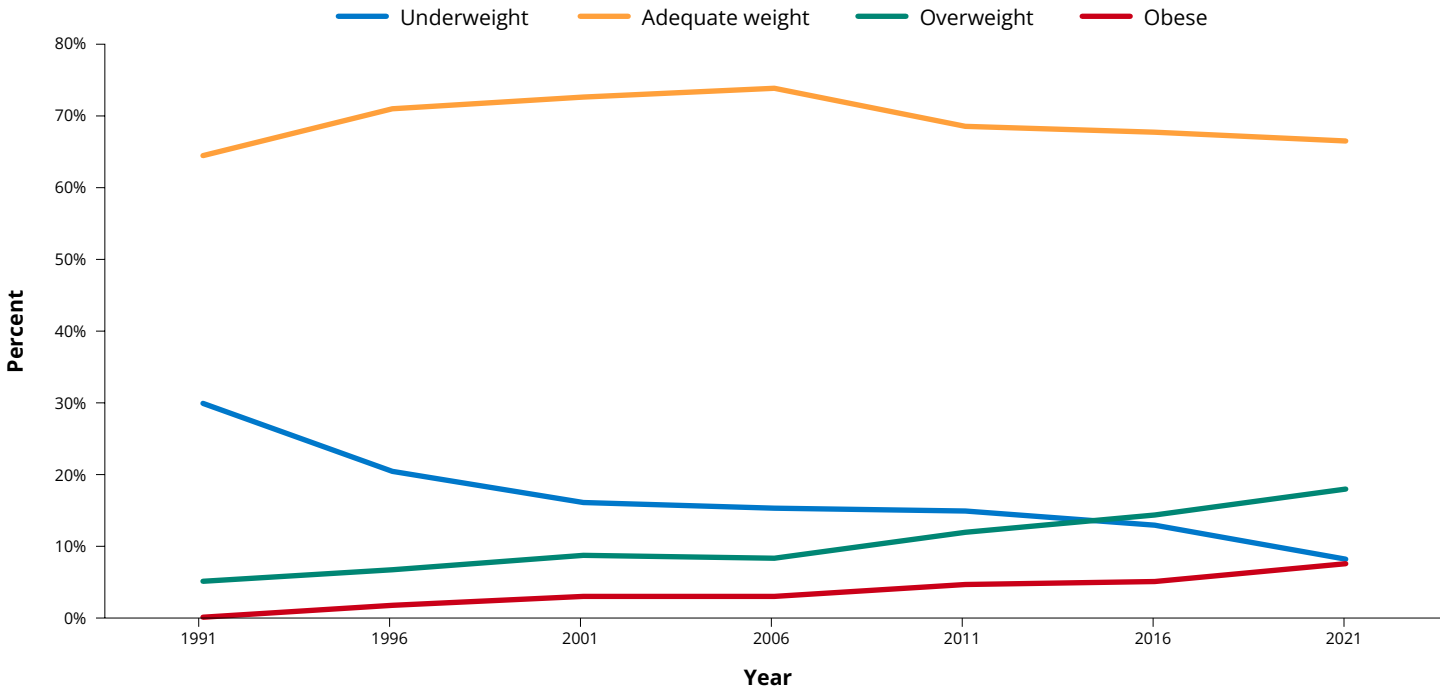


FIGURE 34: BMI classification in adult females, 1991 to 2021.



RESPIRATORY INFECTIONS

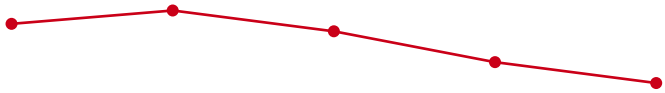
In this section, individuals were grouped by the age at which the culture was taken. Prevalence was defined as having at least one culture positive for each bacterial species, and was calculated among those who had at least one microbiology or mycobacteria sample in 2021. In previous years, the prevalence was calculated among all individuals with cystic fibrosis reported on in the year. As a result, the prevalence of bacterial infections reported in this year's report, may be higher compared to previous years.

Individuals who received a lung transplant prior to 2021, and any cultures taken after lung transplant in 2021, 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 2021, 3,756 (86.6%) 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 2,226 (59.3%) individuals, and *Pseudomonas aeruginosa* (*P. aeruginosa*) which was found in 1,437 (38.3%) individuals (Table 5). Further details on the trends in prevalence of respiratory infections are presented in Figure 35.

TABLE 5: Trends in prevalence of respiratory infections, 2017 to 2021. [N = 3,756].

BACTERIA	PERCENT WITH INFECTION IN 2021	TREND IN INFECTION PREVALENCE OVER TIME 2017 2018 2019 2020 2021
S. aureus	59.3%	
P. aeruginosa	38.3%	
A. fumigatus	15.8%	
S. maltophilia	13.7%	
H. influenza	5.5%	
MRSA	5.6%	
Achromobacter species	5.6%	
B. cepacia complex	3.9%	
Atypical mycobacteria	7.9%	

COMMON BACTERIAL SPECIES

While decreasing, Figure 35 shows that over the past several years, *S. aureus* and *P. aeruginosa* remained the two most prevalent pulmonary pathogens among individuals with cystic fibrosis. There appears to be a slight increase in the prevalence of less frequently found pathogens like MRSA and atypical mycobacteria. However, this may be due to increased reporting of these organisms rather than a true increase in prevalence.

FIGURE 35: Prevalence of respiratory infections, 2017 to 2021.

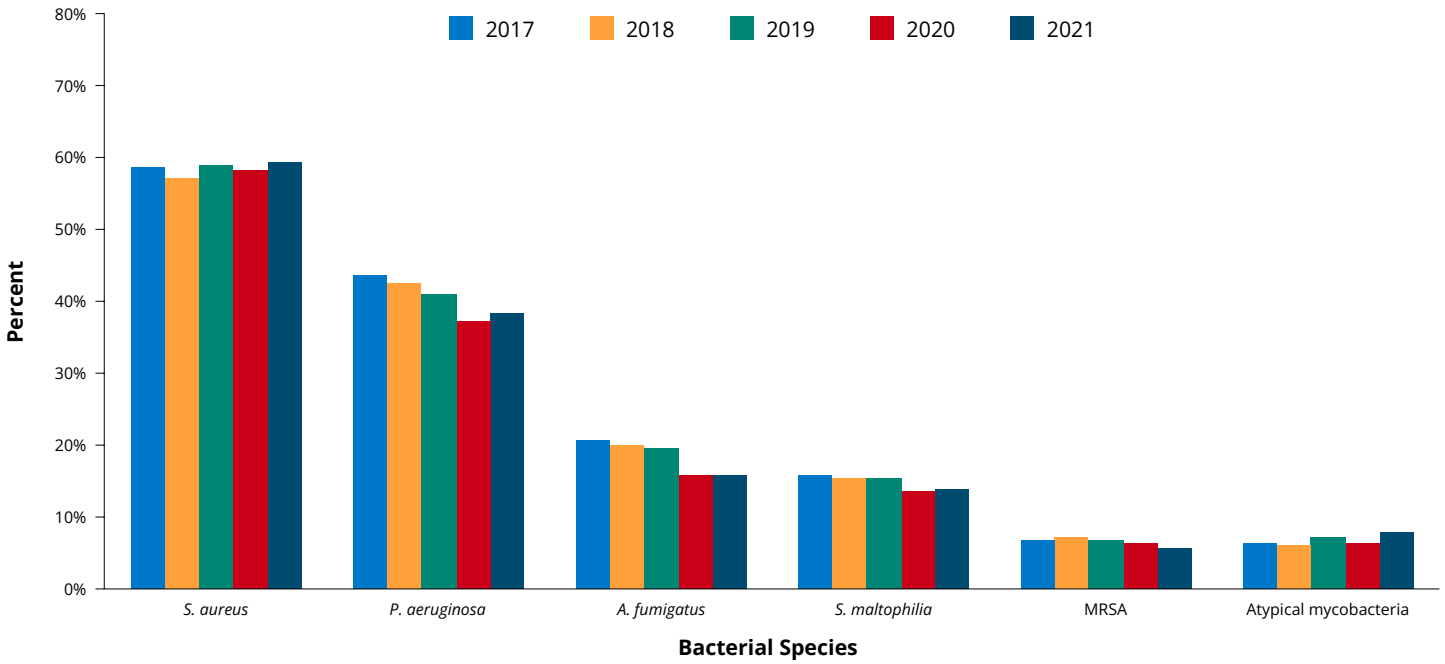
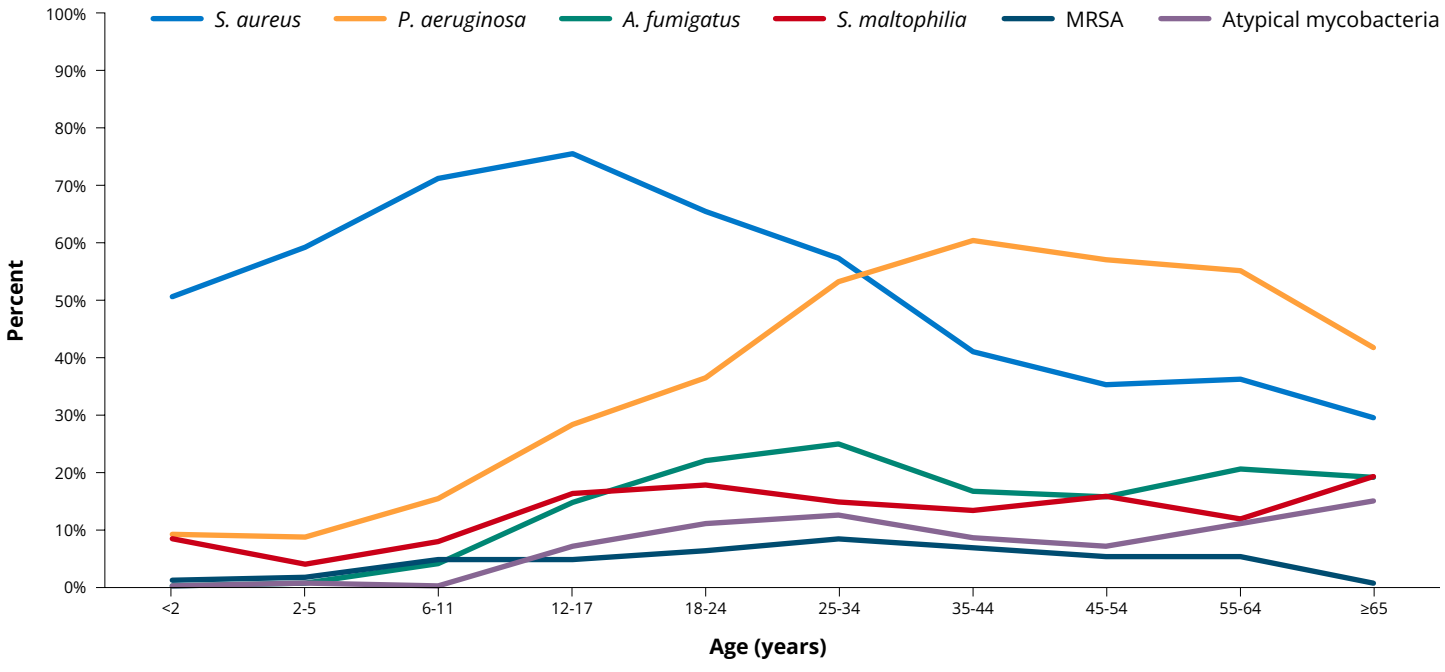


Figure 36 shows the prevalence of pulmonary pathogens by age at culture. *S. aureus* is more common in children with cystic fibrosis and *P. aeruginosa* is more common in the adult CF population.

FIGURE 36: Prevalence of respiratory infections, by age, 2021.

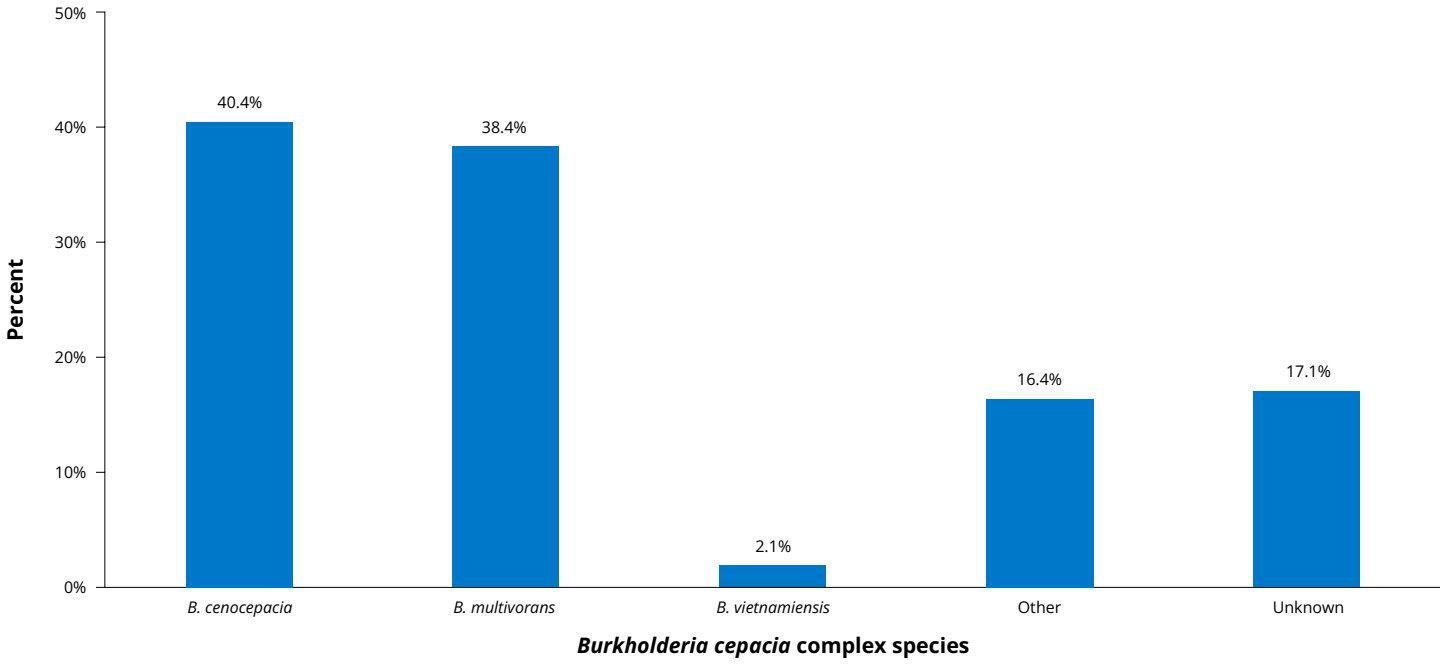


BURKHOLDERIA CEPACIA COMPLEX

The prevalence of *Burkholderia cepacia* complex (BCC) species is low, with only 146 (3.9%) individuals who grew at least one BCC species in 2021. 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* (40.4%) and *B. multivorans* (38.4%) (Figure 37). Not all BCC bacteria have been speciated, as 25 (17.1%) 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.

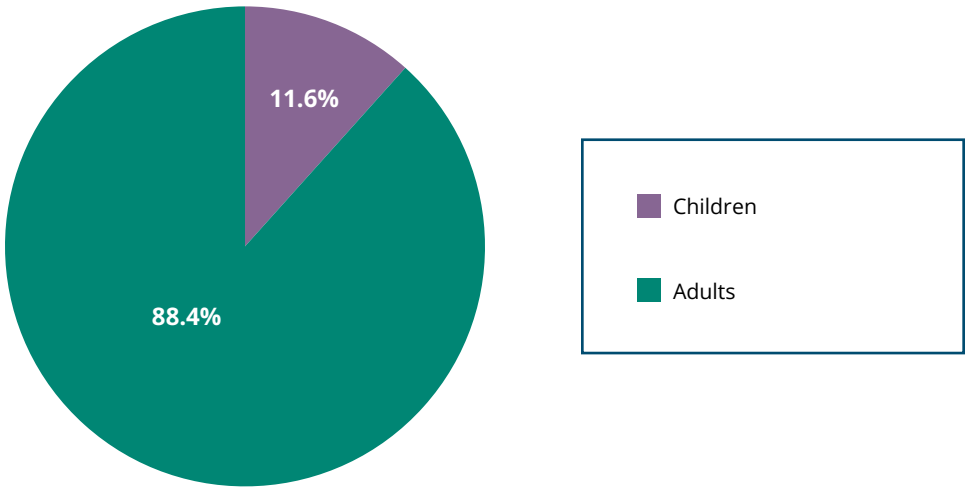
Note that 20 individuals grew *B. gladioli*, however they are not included in Figure 37, because it is not officially recognized as a BCC species.

FIGURE 37: Prevalence of *Burkholderia cepacia* complex species, 2021. [N = 146].



Of the individuals who had BCC in 2021, 17 (11.6%) were children and 129 (88.4%) adults at the time of culture (Figure 38).

FIGURE 38: Prevalence of *Burkholderia cepacia* complex, by age, 2021. [N = 146].



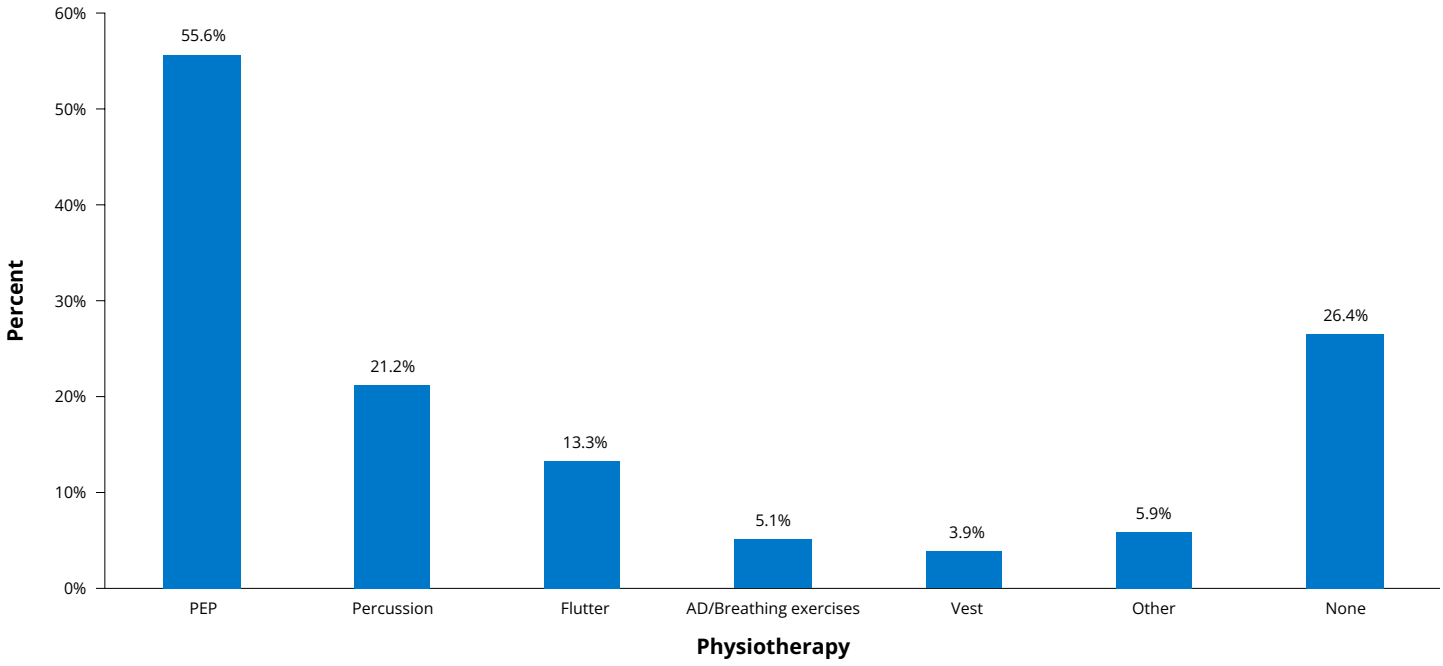
THERAPIES AND MEDICATIONS

PHYSIOTHERAPY

Physiotherapy is done to help 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 2021. The most commonly used forms of therapy were positive expiratory pressure (PEP) (55.6%) and percussion (21.2%).

Individuals who received a lung transplant prior to 2021 are excluded from this section of the report. Typically, chest physiotherapy is not part of routine post-transplant treatment.

FIGURE 39: Physiotherapy usage, 2021. [N = 4,078].



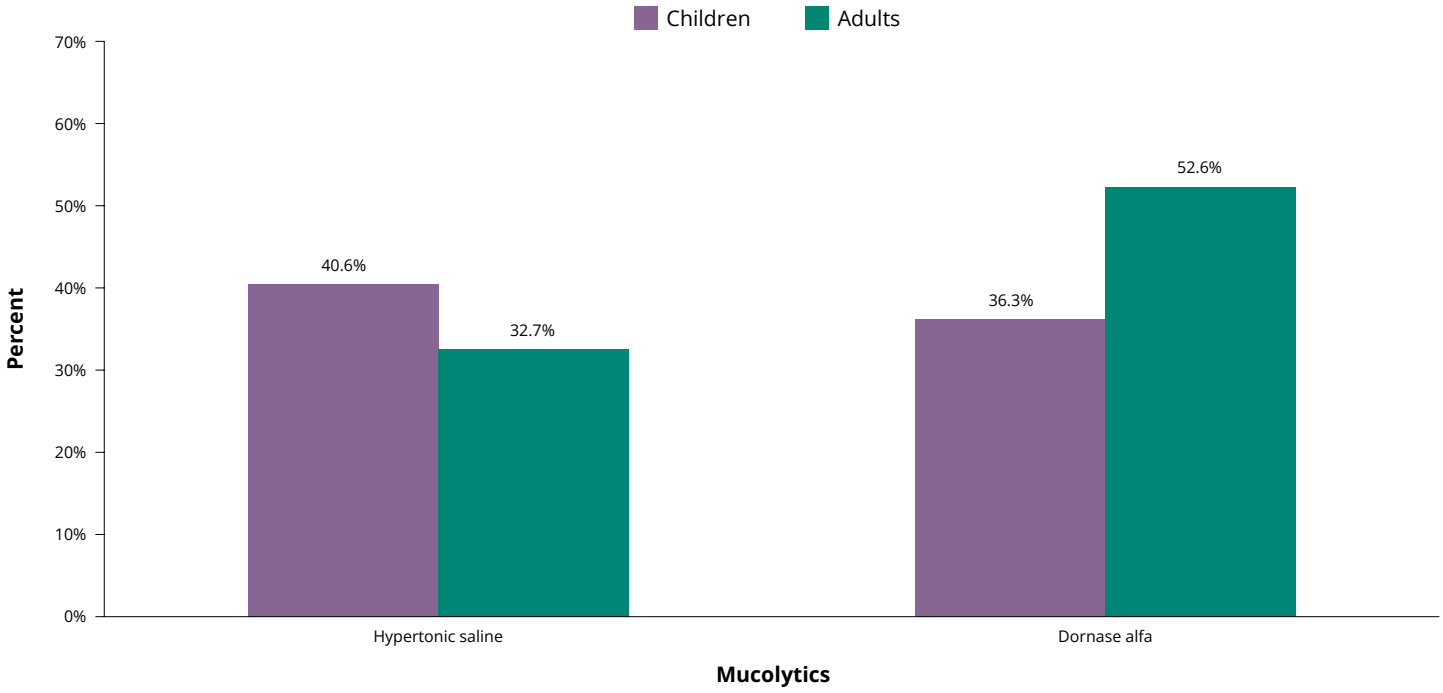
MUCOLYTICS

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 (40.6%) than adults (32.7%), while use of dornase alfa was more common among adults (52.6%) than children (36.3%).

Individuals who received a lung transplant prior to 2021 are excluded from this section of the report.

FIGURE 40: Mucolytics usage, by age, 2021. [N = 1,516 children; N = 2,562 adults].



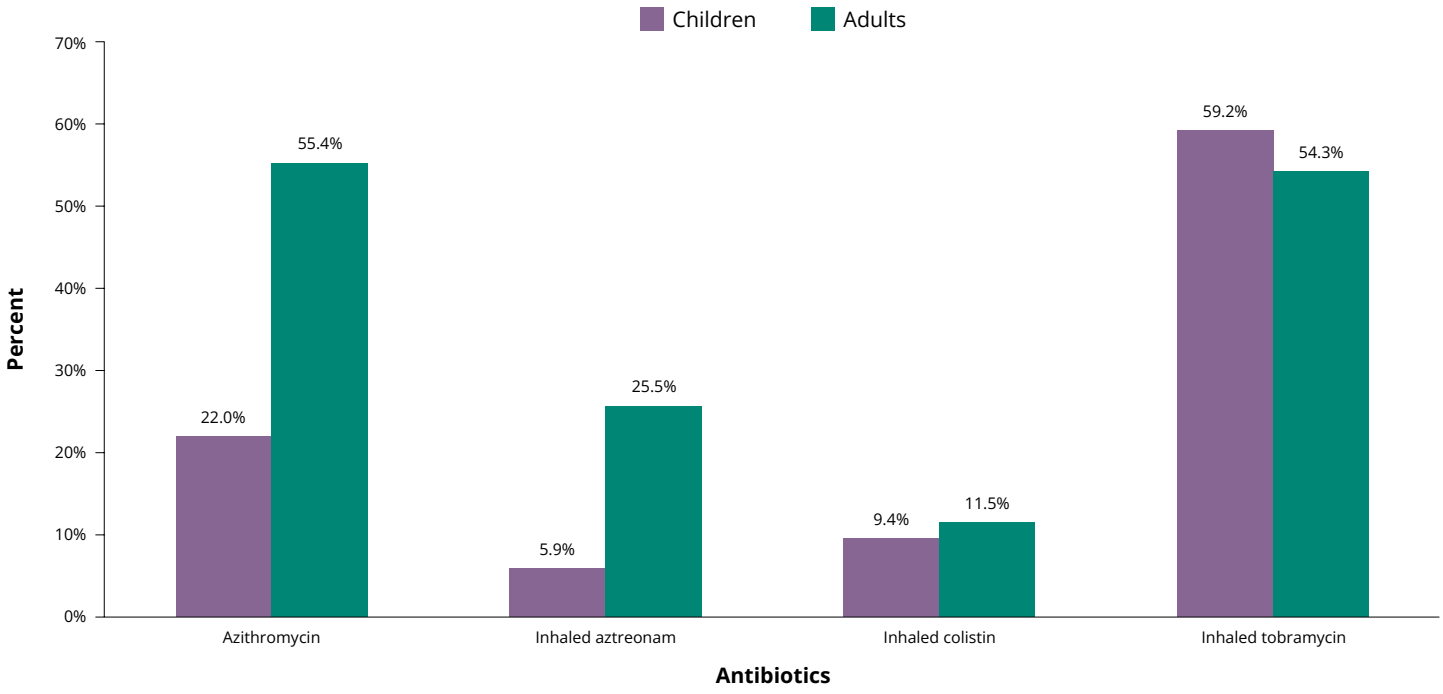
INHALED ANTIBIOTICS AND AZITHROMYCIN

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 2021, there were 1,437 (287 children and 1,150 adults) individuals who were reported to have *Pseudomonas aeruginosa* and have never received a lung transplant prior to 2021. Of those, 170 (59.2%) children and 624 (54.3%) adults were prescribed inhaled tobramycin treatment, and 63 (22.0%) children and 637 (55.4%) adults were prescribed azithromycin (Figure 41).

Individuals who received a lung transplant prior to 2021 are excluded from this section of the report.

FIGURE 41: Inhaled antibiotics and azithromycin usage, by age, 2021. [N = 287 children; N = 1,150 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 CF, 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 ivacaftor/tezacaftor 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 December 2021, Health Canada commenced a subsequent review for the therapy to include individuals who are 6-11 years old with at least one copy of the F508del mutation.

Individuals who received a lung transplant prior to 2021 are excluded from this section of the report.

In 2021, there were 1,455 unique individuals (345 children and 1,110 adults) on CFTR modulator therapies (Table 6).

TABLE 6: CFTR modulator usage, by age, 2021.

CFTR MODULATOR	CHILDREN	ADULTS	TOTAL
ivacaftor	52	81	133
lumacaftor/ivacaftor	134	79	213
tezacaftor/ivacaftor	26	139	165
elexacaftor/tezacaftor/ivacaftor	133	811	944

** For more information about CFTR modulators, please visit **https://www.cysticfibrosis.ca/our-programs/advocacy/access-to-medicines***

HEALTHCARE ENCOUNTERS

Table 7 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 4,061 (99.6%) individuals with cystic fibrosis visited a CF clinic (had a recorded clinic visit date and/or clinical measurement) at least once in 2021 with 3,318 (81.4%) having three 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 three or more clinic visits, 1,362 were children and 1,956 were adults, making up 89.8% and 76.3% of all children and adults, respectively. In 2021, there were a total of 17,485 clinic visits. Though the number of unique individuals with a clinic visit hasn't changed dramatically, there was a noticeable decrease in total number of clinic visits between 2019 and 2020, which was sustained in 2021. This is presumably due to the COVID-19 pandemic.

In 2020, like clinic visits, there was also a reduction in the number of individuals with a recorded clinical measurement (-8.1% with a FEV_1 percent predicted recorded and -6.8% with a BMI recorded) or microbiology culture (-5.9%), likely due to an increase in virtual clinic visits. These figures have increased in 2021, but not back to pre-pandemic levels.

In 2021, there were 832 (20.4%) unique individuals with cystic fibrosis who altogether spent 15,961 days in hospital from a total of 1,305 recorded hospitalizations, which do not include visits to the out-patient CF clinics. This included 913 hospitalizations for pulmonary exacerbations and 1,083 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 2017, there's been a sizable decrease in hospitalizations among individuals with CF. The number of individuals hospitalized each year decreased by 26.4%. The number of hospitalizations decreased by 34.1%, and most notably, the number of hospitalizations for pulmonary exacerbation, the most common reason for hospitalization, decreased by 41.6%, going from 78.9% of all hospitalizations in 2017 to 70.0% in 2021.

At home, 401 (9.8%) unique individuals with cystic fibrosis had 10,735 days on IV antibiotics from a total of 589 courses. Similar to the trends in hospitalizations, the number of individuals on home IV decreased by 31.8% since 2017, and the number of home IV courses and home IV days decreased by 37.3% and 42.1%, 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

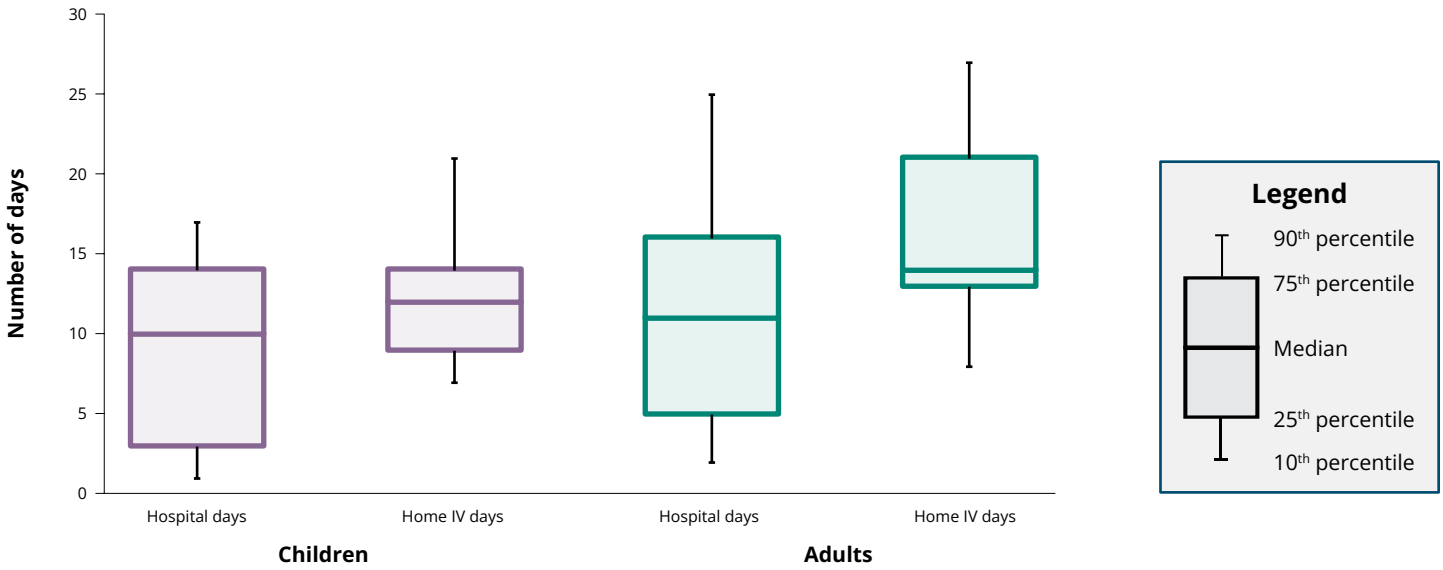
TABLE 7: Healthcare encounters, 2017 to 2021.

HEALTHCARE ENCOUNTER	2017	2018	2019	2020	2021	PERCENT CHANGE (2017 TO 2021)
Clinic visits						
Total clinic visits	18,782	18,346	18,477	17,284	17,485	-6.9%
Unique individuals with a clinic visit	4,028	4,107	4,107	4,079	4,061	0.8%
Unique individuals with ≥3 clinic visits	3,282	3,251	3,302	3,249	3,318	1.1%
Clinical measurement						
Unique individuals with a FEV_1 percent predicted recorded	3,431	3,506	3,508	3,223	3,455	0.7%
Unique individuals with a BMI recorded	4,001	4,074	4,081	3,802	3,956	-1.1%
Unique individuals with a microbacterial culture	3,882	3,924	3,900	3,668	3,799	-2.1%
Hospitalizations						
Unique individuals hospitalized	1,131	1,152	1,078	866	832	-26.4%
Hospitalizations	1,981	1,989	1,864	1,389	1,305	-34.1%
Hospital days	24,546	24,503	23,790	15,830	15,961	-35.0%
Hospitalizations for pulmonary exacerbation	1,563	1,551	1,338	962	913	-41.6%
Percent of all hospitalizations that were for pulmonary exacerbations	78.9%	78.0%	71.8%	69.3%	70.0%	-11.3%
Hospitalizations in individuals with at least 1 F508del mutation	1,742	1,773	1,682	1,205	1,083	-37.8%
Percent of all hospitalizations that were in individuals with at least 1 F508del mutation	87.9%	89.1%	90.2%	86.8%	83.0%	-5.6%
Home IV						
Unique individuals on home IV	588	565	513	470	401	-31.8%
Home IV courses	940	914	841	746	589	-37.3%
Home IV days	18,541	16,739	15,813	13,570	10,735	-42.1%

HEALTHCARE ENCOUNTERS

Figure 42 shows the distribution of days hospitalized and days on home IV by age group. In 2021, the distribution of hospital days is relatively similar between age groups, where children were hospitalized for an average of 10 days and adults for 11 days. However, the number of days on home IV varied more among adults compared to children. Though the median number days spent on home IV was similar between children and adults (12 days vs. 14 days), a quarter of all adults spent over 21 days on home IV in 2021.

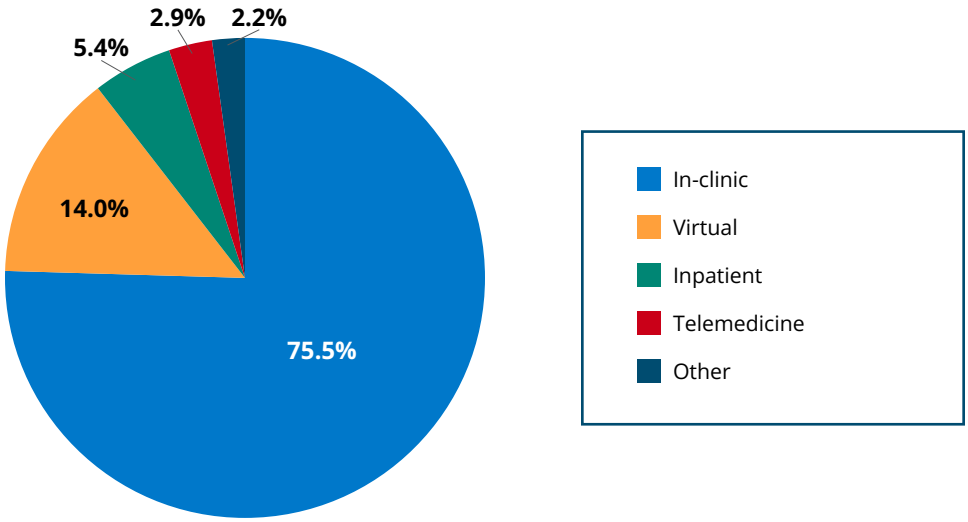
FIGURE 42: Distribution of hospital and home IV days, by age, 2021.



2021 marked the first year where the location in which the clinical measurements were taken, was captured completely in the CF Registry. Introduced at the end of 2020, this new 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, despite the on-going COVID-19 pandemic, of the 17,625 clinical measurement and/or clinic visit records with known location, 13,301 (75.5%) were taken in-clinic.

FIGURE 43: Distribution of location of clinical measurement and/or clinic visit, 2021.



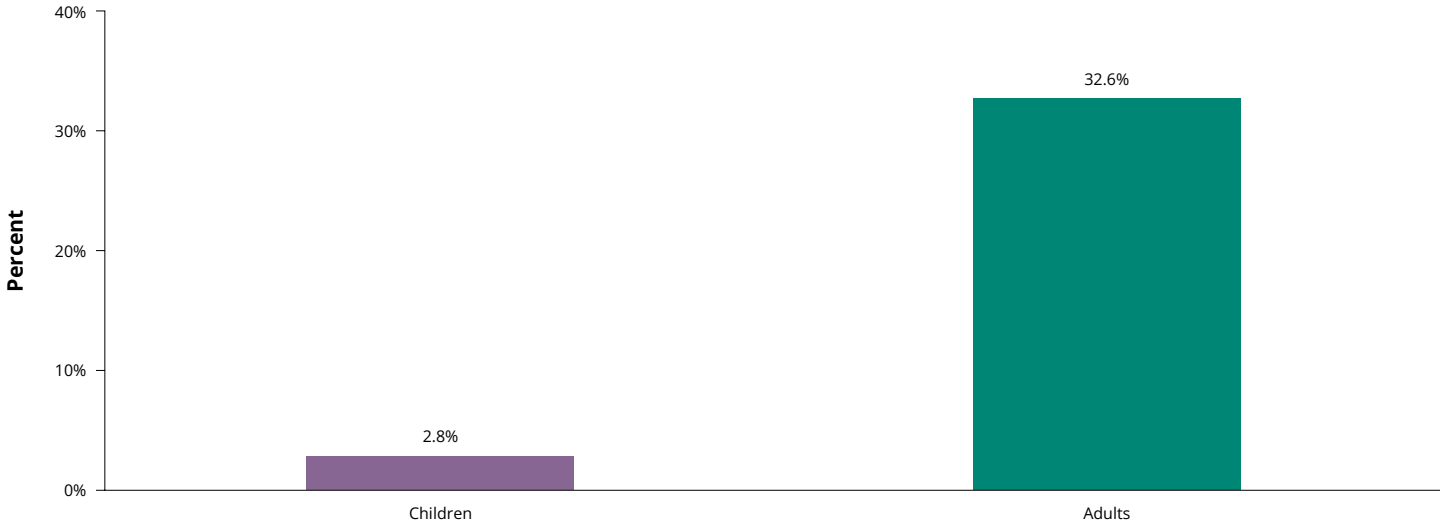
COMPLICATIONS

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.

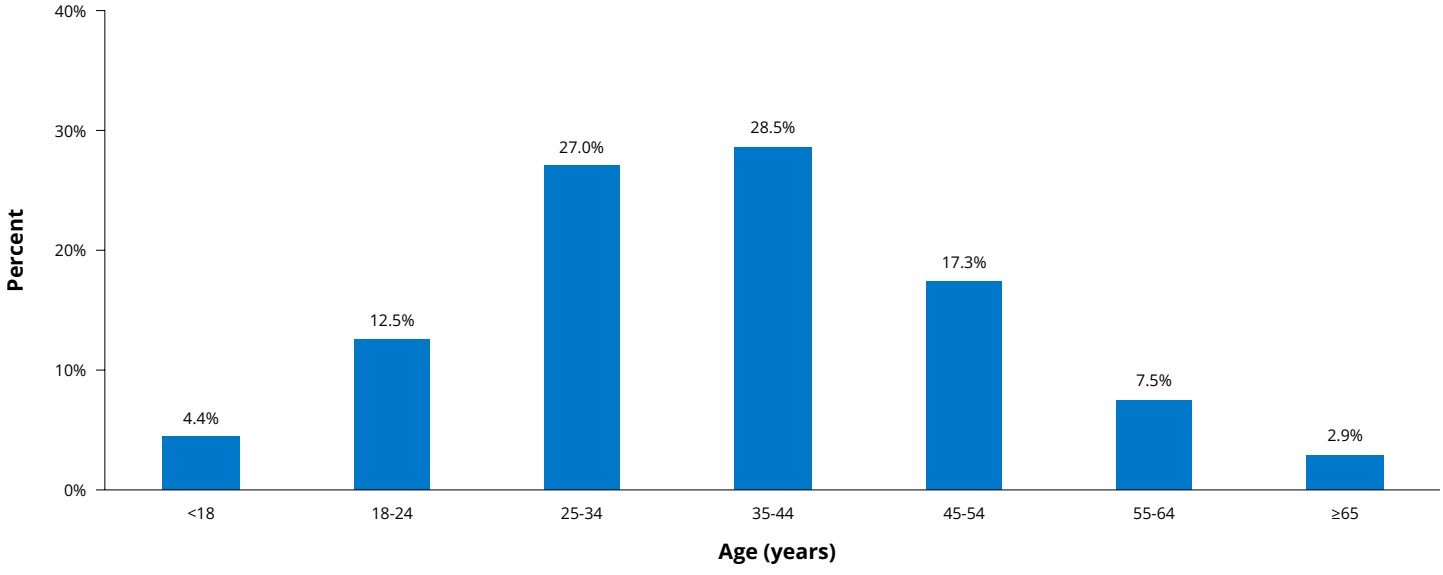
In 2021, CFRD was reported in 963 (22.2%) individuals with cystic fibrosis. While CFRD is not routinely screen in children younger than 10 years of age, 42 (2.8%) children and 921 (32.6%) adults (Figure 44) were recorded as having CFRD in 2021.

FIGURE 44: CF-related diabetes in children and adults, 2021. [N = 1,517 children; N = 2,821 adults].



Of those individuals with CFRD, only 42 (4.4%) were in children, 541 (56.2%) were in those age 35 and older, and 28 (2.9%) were in those age 65 and older (Figure 45).

FIGURE 45: Distribution of age of individuals diagnosed with CF-related diabetes, 2021. [N = 963].

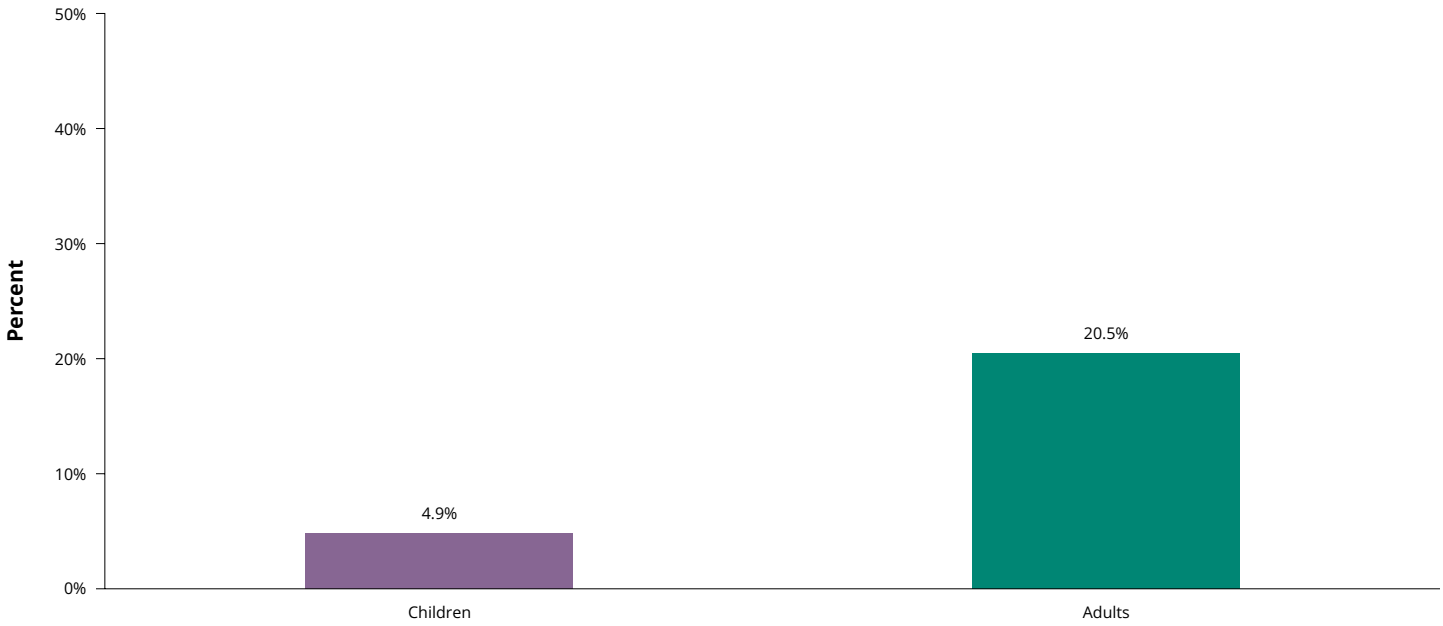


MENTAL HEALTH

In 2021, there were 654 (15.1%) individuals with cystic fibrosis with a recorded complication depression or anxiety in the CF Registry. 75 of these diagnoses were children and 579 were adults, representing 4.9% of all children and 20.5% 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, 2021. [N = 1,517 children; N = 2,821 adults].

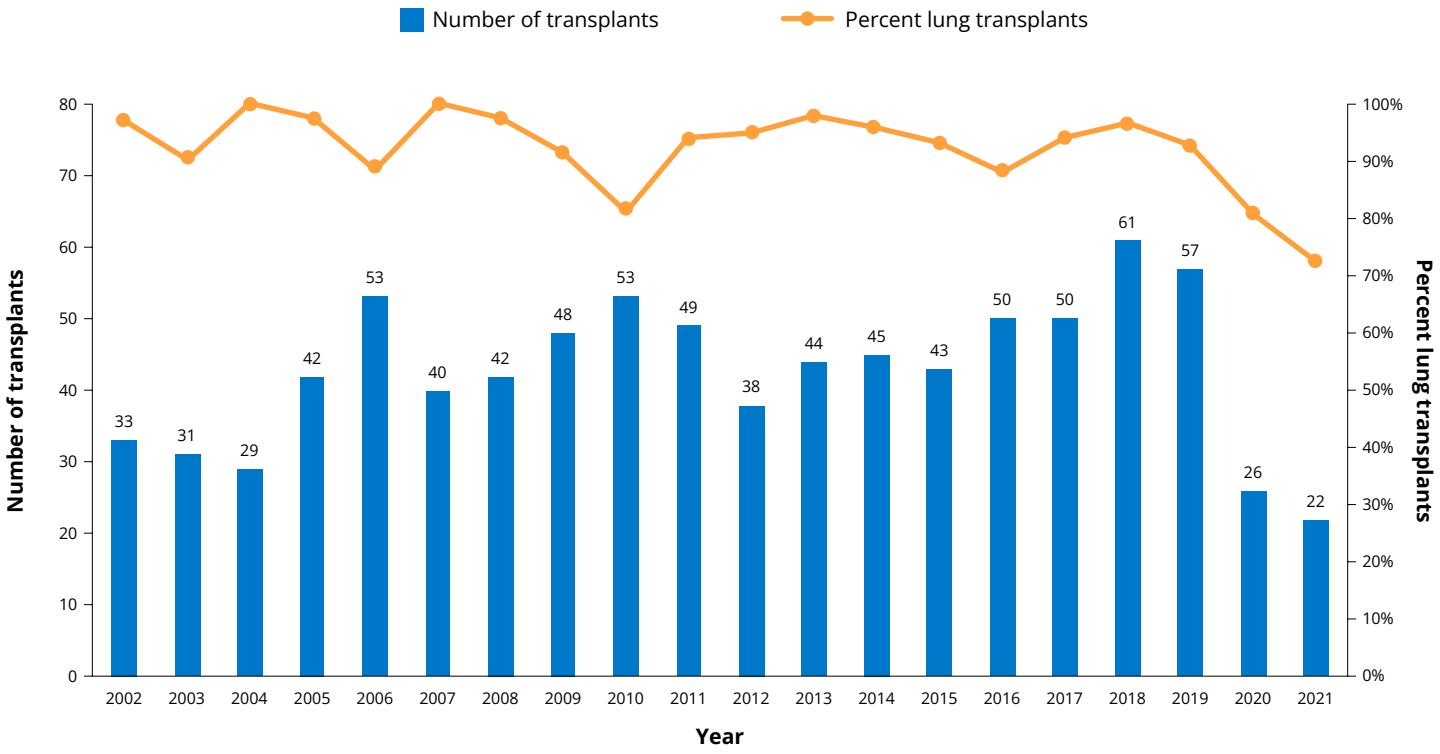


TRANSPLANTS

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 CF Registry. In 2021, there were 22 transplants among individuals with cystic fibrosis, and the median age at transplant was 29.1 years. Although the numbers provided represent primarily lung transplants (16 lung transplants in 2021), 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 to 57 transplants conducted in 2019, and has continued to fall in 2021 (down 61.4% since 2019). Notably, the proportion of lung transplants among all transplants in people with CF, also fell from 93.0% in 2019 to 80.8% in 2020 and 72.7% in 2021.

The first transplant recorded in the CF Registry was performed in 1988. As of December 31, 2021, there were 1,059 organ transplants among 953 individuals with cystic fibrosis, reported in the CF Registry. Among them, 519 (54.5%) were alive as of December 31, 2021. The vast majority of all organ transplants recorded in the CF Registry were lung transplants, with 988 lung transplants among 917 unique individuals. Of these patients, 69 (7.5%) individuals have received more than one lung transplants A new transplant status was added in 2020 to capture information on individuals who have been removed from the active transplant waitlist. To date, 12 people have been removed from the active transplant waitlist.

FIGURE 47: Number of transplants (any organ), 2002 to 2021.



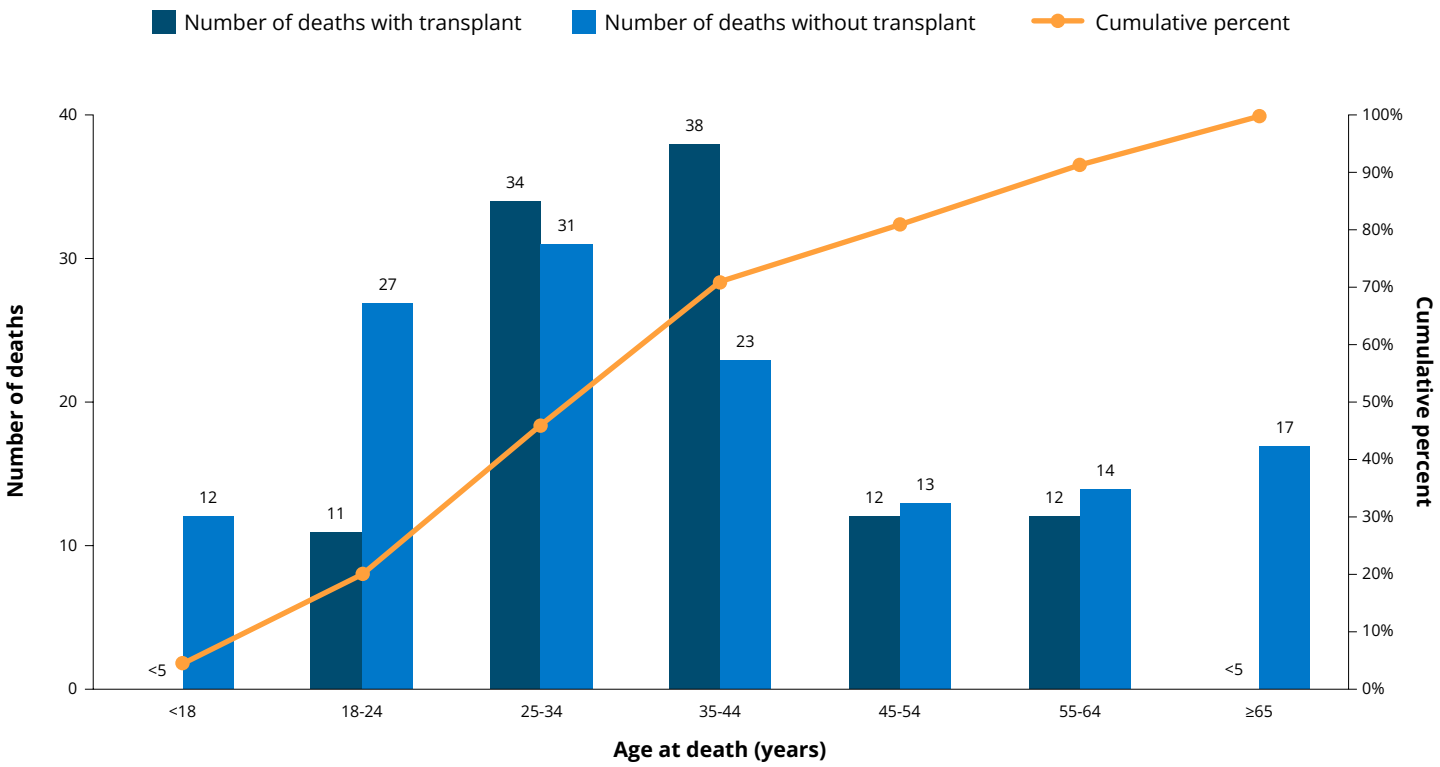
SURVIVAL

The survival and health outcomes in Canadians living with cystic fibrosis continues to improve over time. In 2021, there were 44 deaths recorded in the CF Registry, and 24 (54.5%) individuals with cystic fibrosis who died in 2021 had never received an organ transplant.

Risk factors such as pulmonary exacerbations and malnutrition are often associated with increased risk of death. In 2021, 39 (88.6%) of the 44 deaths had a recorded cause of death, with 17 (43.6%) indicating cause of death relating to pulmonary/ infection/cardiovascular complications.

Figure 48 shows the cumulative number of deaths between 2017 and 2021, as well as the transplant status and age at death.

FIGURE 48: Cumulative number of deaths and age at death, 2017 to 2021. [N = 248].



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 38.7 years in 2021, compared to 26.6 years in 2002. The median age of death tells us that half of those who died in 2021 were younger than 38.7 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, 2002 to 2021.

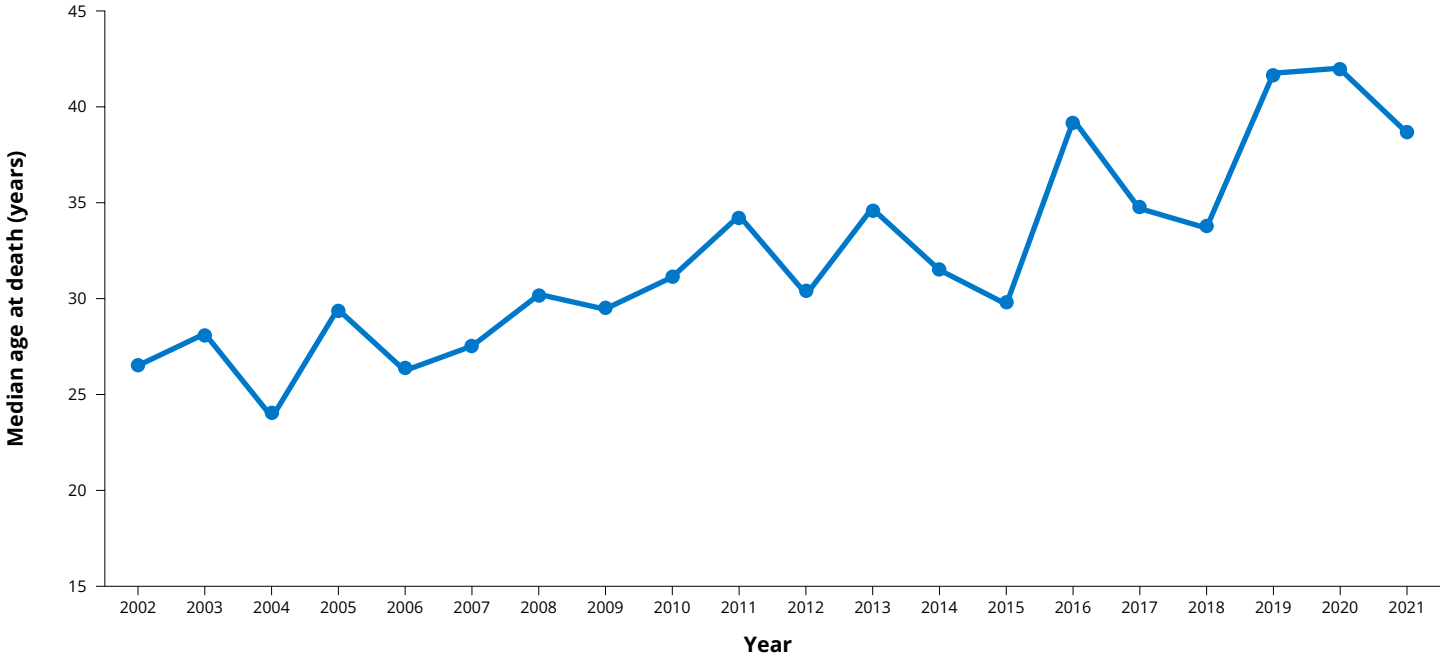
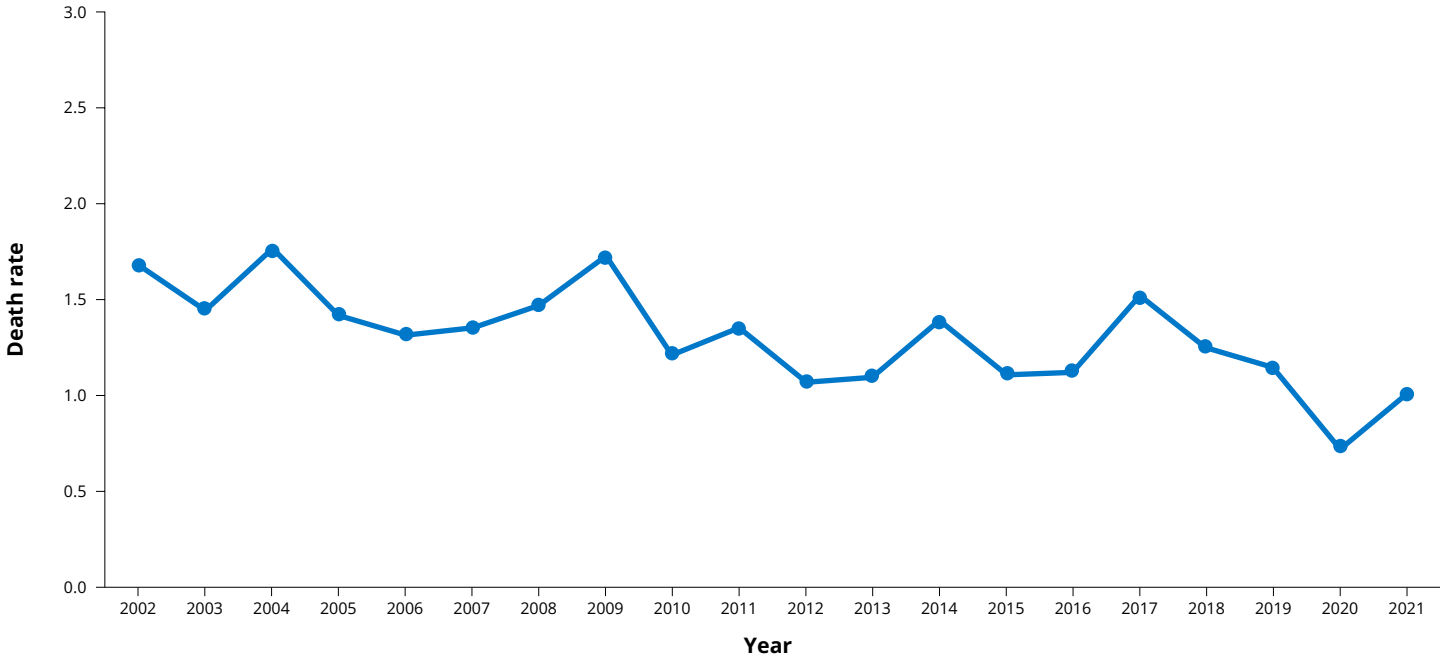


Figure 50 shows the annual death rate, calculated as the number of deaths among the total number of individuals were reported on in the year. The death rate has decreased steadily since 2000 and was 1.0 in 2021.

FIGURE 50: Death rate, 2002 to 2021.

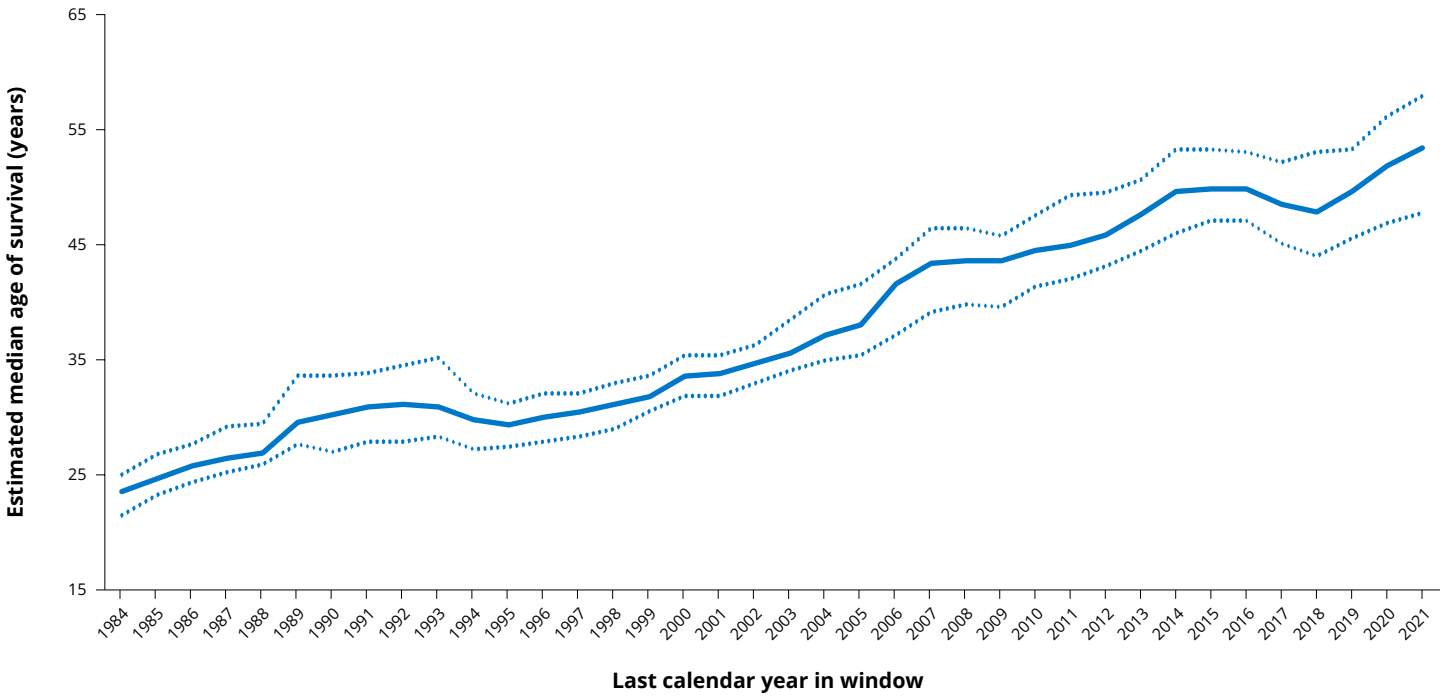


ESTIMATED MEDIAN AGE OF SURVIVAL

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. 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 (2017 to 2021) included 5,142 people with cystic fibrosis and 248 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 239 (4.6%). In 2021, the median age of survival was estimated to be 57.3 years of age (Figure 51). In 2012, the estimated median age of survival passed 50 years of age for the first time, and it has remained steady since.

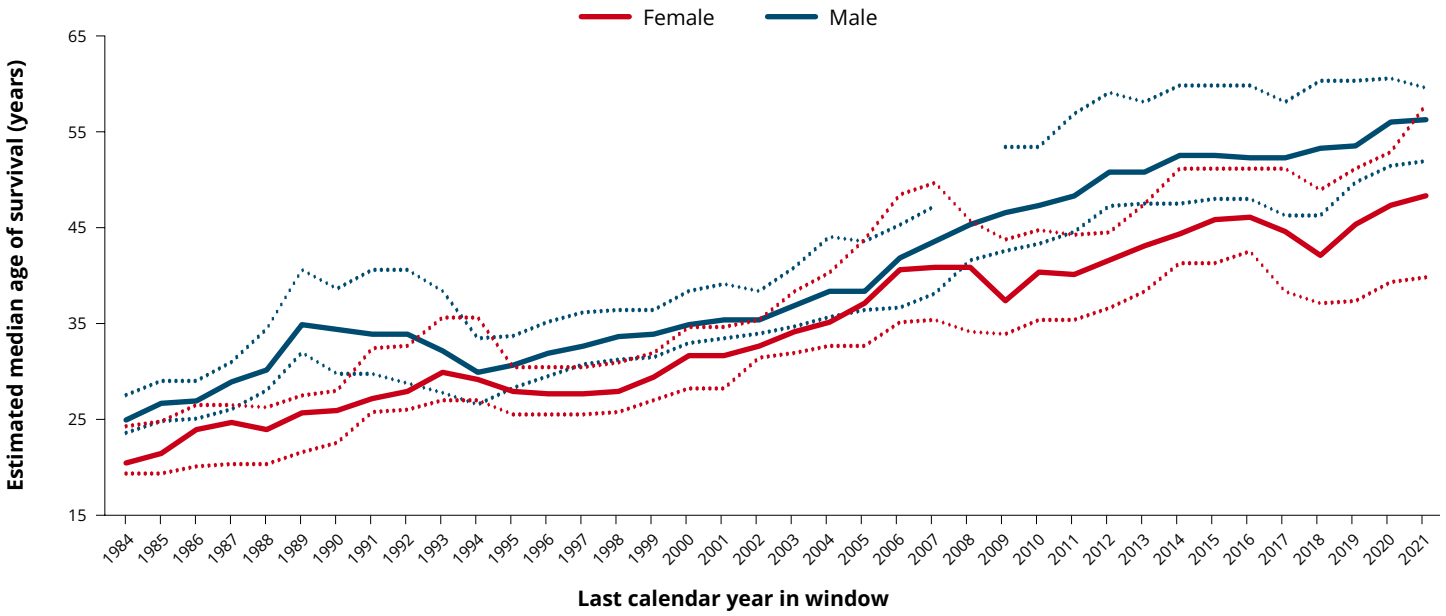
FIGURE 51: Estimated median age of survival for a moving 5-year window with 95% confidence intervals, 1984 to 2021.



ESTIMATED MEDIAN AGE OF SURVIVAL

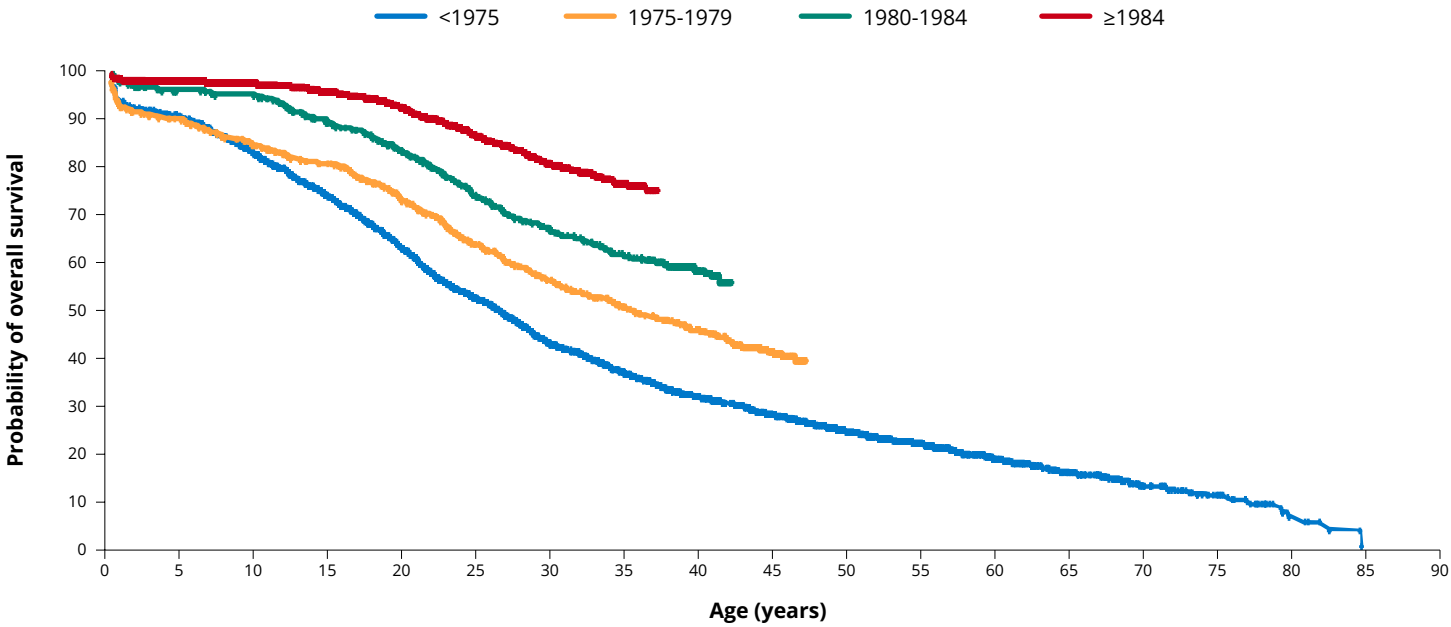
The median age of survival remained stable for both males and females, and males continued to have a higher median age of survival compared to females (Figure 52). While the cause of lower survival in females is not well understood, it has been documented in published CF literature[10, 11, 12]. The upper confidence interval could not be estimated in one time period, as there weren't 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 2021.



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 92.0% for those born in 1985 or later, compared to 62.2% for those born before 1975.

FIGURE 53: Overall survival, by birth cohorts, 2021.



POST-LUNG TRANSPLANT SURVIVAL

Between 1988 and 2021, there were 917 lung transplant recipients and 425 deaths post-lung transplant. Figure 54 shows the probability of survival post lung transplant which was 89.1% at one year, 77.3% at three years and 68.2% at five years. Overall, 50% of those patients transplanted today would be expected to live beyond 10.7 years following lung transplantation.

FIGURE 54: Post-lung transplant survival, 2021.

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 2021 is 57.3 years, we are saying that if a child with cystic fibrosis is born in Canada in 2021, they have a 50% chance of living beyond 57.3 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 57.3 years. Of course, mortality rates are not static and are constantly changing as new therapies and medicines for CF become available. Thus, this estimate is a reflection of the most accurate data that is available in 2021.

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 2021 Registry Annual Data Report.

REPORT PREPARED BY

Stephanie Cheng, Director, Registry, Cystic Fibrosis Canada

Theresa Le, Data Analyst, Registry, Cystic Fibrosis Canada

Noma Abdulrahem, Data Analyst, Registry, Cystic Fibrosis Canada

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

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

Dr. Sanja Stanojevic, Biostatistician, Dalhousie University, Halifax

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	

Cystic Fibrosis
Fibrose kystique
Canada

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.

2323 Yonge Street, Suite 800 | Toronto, ON M4P 2C9
2023–02 | Cette publication est aussi disponsible en français
Charitable registration: 10684 5100 RR0001

www.cysticfibrosis.ca