



2020 TRENDS REPORT:
A DISEASE IN TRANSITION

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The year 2020 was one for the history books in so many ways. For those who monitor the state of cystic fibrosis (CF) in Canada, it will be remembered as a year filled with uncertainty, optimism, and change.

Cystic Fibrosis Canada's **Canadian Cystic Fibrosis Registry 2020 Annual Data Report** sheds light on how the events of this unusual year as well as advancements in treatments and access to new drugs over the last decade have impacted people who live with cystic fibrosis.

Here, we explore three trends that emerge from the data in 2020 and ask what they might mean for the Canadian CF community. While we didn't conduct scientific studies and aren't able to draw any specific conclusions, we can ask some intriguing questions given the observed data.

For context, the impact of COVID-19 on the CF community in 2020 was significant - fear of contracting the virus kept many people at home and we saw a shift from inpatient care to outpatient. At the same time, some people began Trikafta, a life-changing CF drug, either through compassionate use or via clinical trials. The 2020 data shows a decrease in hospitalizations for Canadians with cystic fibrosis, which, no doubt, the pandemic played a role in, but also could be an indication of what is to come as more individuals access modulator therapies. Those with severe lung disease may not have needed IV antibiotics and therefore, were able to avoid hospital stays. As such, the data in this year's annual report paints a picture of both a community and a disease in transition.

BODY WEIGHT IS CHANGING. IS THIS THE FIRST OF MANY NEW REALITIES FOR AN AGING CF POPULATION?

Historically, children with cystic fibrosis suffered from malnutrition. Despite the identification of the disease in 1938, increasing research and improved treatments, the struggle to keep weight on remained a familiar part of the disease for many people living with cystic fibrosis. However, recent data from the Canadian Cystic Fibrosis Registry demonstrates this trend is changing.

Over the past 25 years, the proportion of adults with cystic fibrosis who are underweight, as determined by their body mass index (BMI), has decreased (Figure 1 and Figure 2). Over the same period, a growing proportion of the Canadian CF population has become overweight or obese. The trend is more pronounced in men, who are more likely to be overweight or obese than women regardless of whether or not they require enzymes to digest and absorb their food, CF mutations or whether or not they are taking a modulator medication.



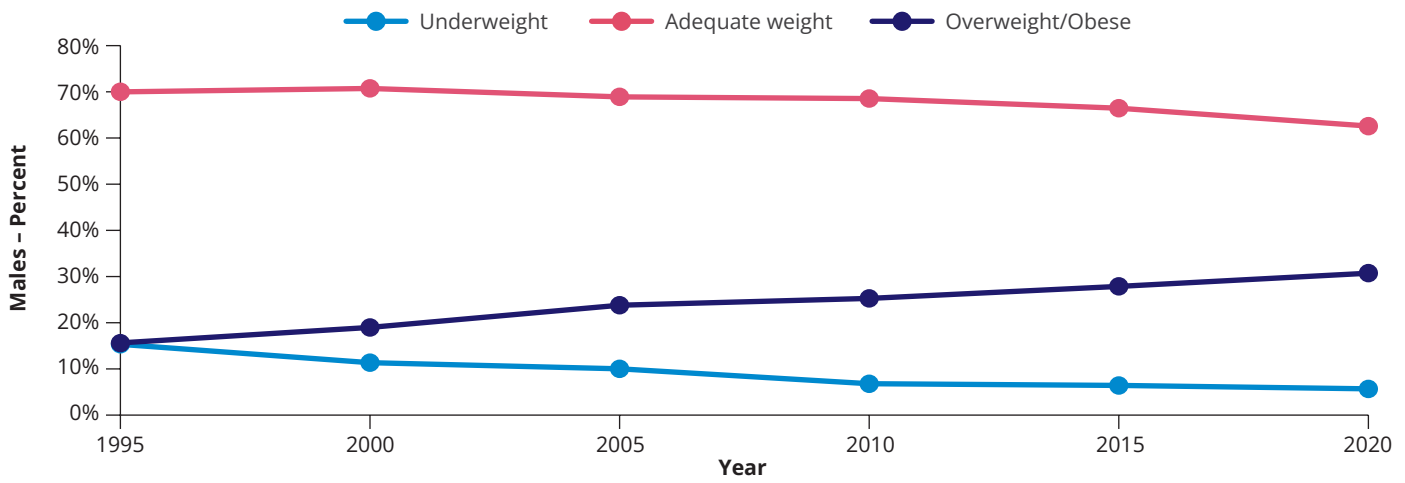


Figure 1. The percentage of Canadian males with cystic fibrosis with a body mass index (BMI) status of Underweight, Adequate weight or Overweight/Obese over the past 25 years.

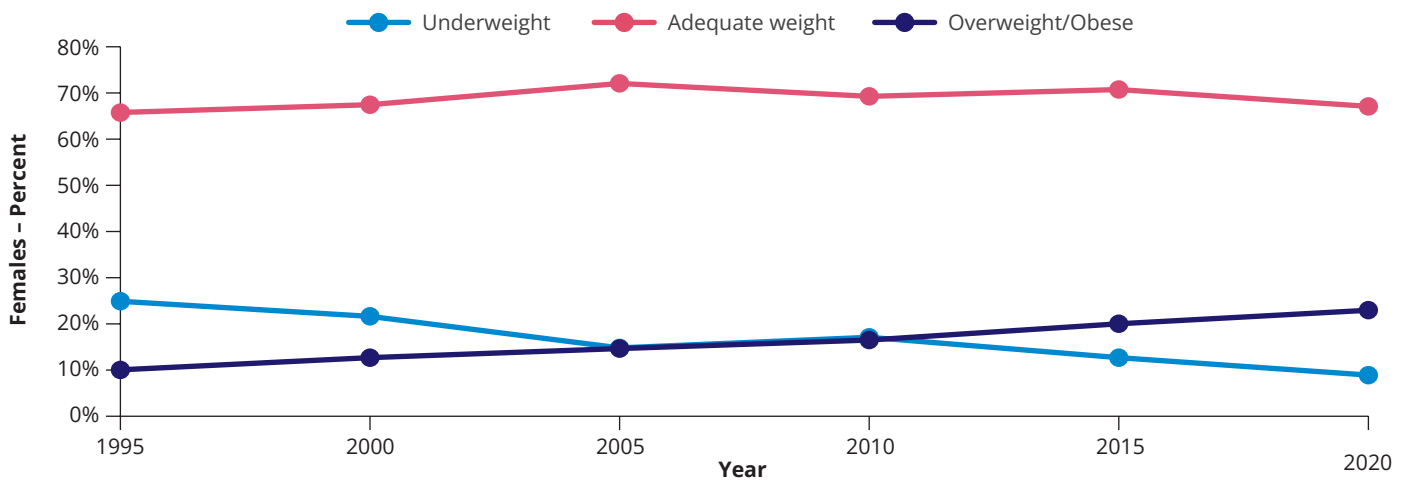


Figure 2. The percentage of Canadian females with cystic fibrosis with a body mass index (BMI) status of Underweight, Adequate weight or Overweight/Obese over the past 25 years.

As people with cystic fibrosis live longer, healthier lives thanks to advances in treatment and improved standards of care, we will be watching the trends in nutrition closely. Increases in weight is a known side effect of some of the new modulator therapies therefore, as more Canadians with CF gain access to these therapies, we anticipate the trends in weight that we have seen will be accentuated. We will also monitor what impact, if any, this trend might have on the mental and physical health of Canadians with cystic fibrosis. For some, weight gain will feel like positive progress, for others, a challenging change to what they are used to. We also need to be aware of the fact that weight gain in combination with prolonged survival may bring about new complications that have previously been rare in individuals with CF such as vascular or heart disease. We will work with experts in the field to ensure that treatment plans and nutritional recommendations reflect the current needs of Canadians with cystic fibrosis.



As adults with cystic fibrosis live longer than ever before, the face of the disease is changing. We are starting to see new realities, like a different weight trajectory for some patients. It makes us wonder what other affects will emerge with an aging population. We will watch this trend and if needed, modify treatment plans accordingly.



Dr. Anne Stephenson

Medical Director, Registry, Cystic Fibrosis Canada
CF Physician, Unity Health Toronto, St. Michael's site, Toronto

WHAT CHANGES WILL TRIKAFTA HAVE ON THE FUTURE OF THE DISEASE?

While Trikafta was not approved for use in Canada in 2020, some Canadians gained access through clinical trials or Special Access Programs, which provide compassionate access to those who meet eligibility criteria. In total, 28 children and 169 adults were recorded to be on the medication in 2020. As many of these people started the drug part-way through the year, it is too soon to see any real trends in the data. However, an early look at lung function reinforces that cystic fibrosis is a heterogenous disease and individual responses to Trikafta will vary. Many of those who began Trikafta saw a dramatic increase in lung function and others showed a more moderate increase or no significant change in lung function. We know that as a heterogenous disease, the response to Trikafta will be individual and as such, those who demonstrated a more muted improvement in lung function may have seen improvements in other areas that are equally as important to consider, such as in BMI or overall quality of life.



Given the varied and individualized responses, it would be incorrect to rely on any single parameter to evaluate an individual's response to the drug. It is our CF physicians and care teams, familiar with the clinical history of their patients, who are best positioned to determine if a patient is showing improvement. Furthermore, CF care teams and patients recognize that symptoms beyond lung function must be considered when evaluating benefit while also weighing any potential risks of new therapies. The potential benefit from Trikafta is so significant^{1 2} that everyone who has the potential to benefit from Trikafta should be able to access the drug, and their physicians should be provided with the tools to track their responses and report on the impact, both medically and psychosocially. This is in part why some Canadian CF clinics are participating in a study to do just that. The Can-Impact-CF study is a Canadian observational study being led by Dr. Bilodeau, Dr. Quon, Dr. Ratjen and Dr. Rayment that will evaluate the long-term impact of CFTR modulators on people with cystic fibrosis. We can begin to pose some questions on how these different experiences will affect those with cystic fibrosis.

- Will there be changes in the mental health of individuals with cystic fibrosis?
- How will quality of life, number of transplants, clinic visits and hospital admissions change as more people begin to access Trikafta?
- Will our community become even more heterogenous, as some people gain access to Trikafta and have changing realities and needs? While others don't and continue to suffer with a heavy burden?

It could mean more diversity of experiences across the community, and therefore new approaches to treatment and care will be needed so no one is left behind. What is certain, is that as Trikafta becomes available for more people in Canada, cystic fibrosis will continue to be a disease in transition.

“For many Canadians with CF, Trikafta is transformative, and every patient with an F508del mutation should be given the opportunity to find out if it works for them.”



Dr. John Wallenburg
Chief Scientific Officer,
Cystic Fibrosis Canada

DO FEWER LUNG TRANSPLANTS IN 2020 SIGNAL EARLY PROMISE FOR THE FUTURE?

In 2020, only 21 people with cystic fibrosis received a lung transplant, compared to 59 and 53 in 2018 and 2019, respectively.

	# OF LUNG TRANSPLANTS	AT LEAST ONE COPY OF F508del
2018	59	57 (96.0%)
2019	53	46 (86.8%)
2020	21	17 (85.0%)

The dramatic drop might partly be explained by the COVID-19 pandemic, during which organ donations decreased and some transplant programs were temporarily suspended.

However, another factor was access to Trikafta. The Canadian CF Registry data shows that many individuals who were on the transplant list were removed from the list after starting this medication. We are starting to see the changes that Trikafta will have on the CF community in Canada. Though the medication remained out of reach for most of the community in 2020, anecdotally it 'rescued' people from needing lung transplants, and the majority of people whose names were removed from the transplant waitlist in 2020 were on CFTR modulators.

The mutation profile of people who received lung transplants in 2020 remained about the same as in previous years – about 85% of these individuals have at least one copy of F508del. As the community gains access to Trikafta, we expect to see a shift in this distribution in the coming years.

This is a hopeful signal about the impact of CFTR modulator treatments. We'll be watching eagerly with the expectation that more people will be removed from the transplant list in 2021 as they gain access to Trikafta and other modulators.

The decrease in lung transplants for people who were on modulator therapies is an early sign of hope for our community. For many, a diagnosis of cystic fibrosis would almost certainly mean a lung transplant in the future, but this is changing. We will continue to watch this trend as more of our community receives access to Trikafta and other modulators, and we will continue to invest in research and clinical care to ensure that those who are not eligible to access Trikafta, will have more treatment options in the future.



Kelly Grover
President and CEO,
Cystic Fibrosis Canada

LIVES ARE CHANGING, LEADING TO NEW QUESTIONS

Cystic fibrosis is a disease in transition. We are seeing people living longer, healthier lives. These changes raise many questions. In the years to come, will we stray from the high-fat diet? Will lung transplants continue to decrease as predicted³ as more people receive access to modulators? What will the long-term effects of the COVID-19 pandemic be on individuals with cystic fibrosis? These are questions and themes that we will continue to ask, and monitor.

We sincerely thank the individuals who consent to participate in the CF Registry and share their information, the CF clinic team members who collect and enter the data, the researchers who interpret and leverage the data, and the donors whose generosity has supported this invaluable resource since 1970s.

THANK YOU



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