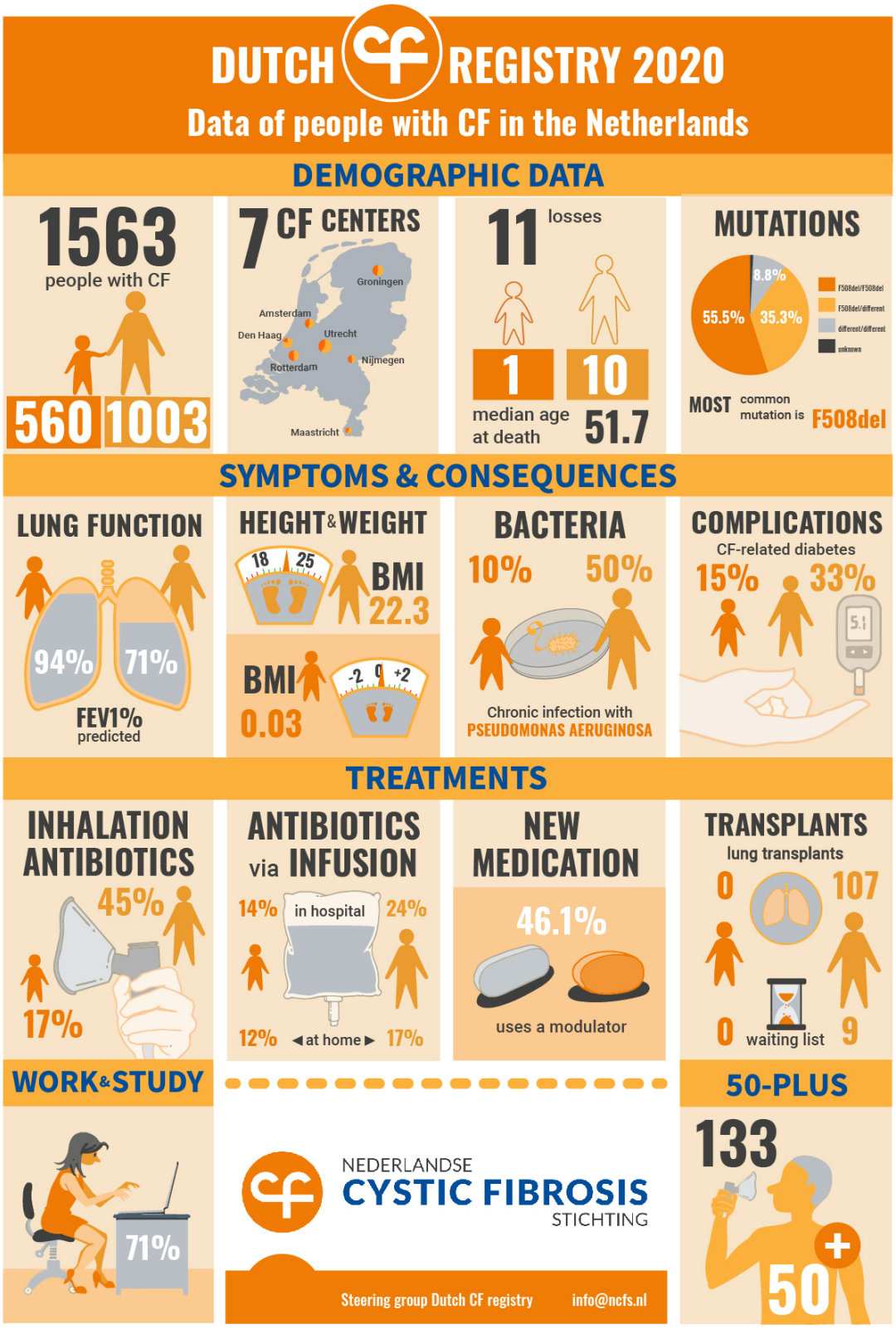
Dutch Cystic Fibrosis Registry

Data on people with cystic fibrosis in the Netherlands
Annual report for 2020

Published in 2021

NEDERLANDSE CYSTIC FIBROSIS STICHTING

Summary


DUTCH CF REGISTRY 2020
Data of people with CF in the Netherlands
DEMOGRAPHIC DATA
1563
people with CF
560
1003
7 CF CENTERS
Groningen
Amsterdam
Den Haag
Utrecht
Rotterdam
Nijmegen
Maastricht
11 losses
1
10
median age at death
51.7
MUTATIONS
8.8%
55.5%
35.3%
F508del/F508del
F508del/different
different/different
unknown
MOST common mutation is F508del
SYMPTOMS & CONSEQUENCES
LUNG FUNCTION
94%
71%
FEV1% predicted
HEIGHT & WEIGHT
18
25
BMI
22.3
BMI
0.03
-2
0
+2
BACTERIA
10%
50%
Chronic infection with PSEUDOMONAS AERUGINOSA
COMPLICATIONS
CF-related diabetes
15%
33%
5.1
TREATMENTS
INHALATION ANTIBIOTICS
45%
17%
ANTIBIOTICS via INFUSION
14%
in hospital
24%
12%
◄at home►
17%
NEW MEDICATION
46.1%
uses a modulator
TRANSPLANTS
lung transplants
0
107
0
waiting list
9
WORK & STUDY
71%
50-PLUS
133
50
NEDERLANDSE
CYSTIC FIBROSIS
STICHTING
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Foreword

The joint ambition of the Cystic Fibrosis (CF) centres and the Dutch CF Foundation (NCFS) has remained unchanged for quite some time: better care that results in a better and longer life for people with CF.

This online report of the Dutch CF Registry for 2020 has been realised with the cooperation of almost all people with CF, the efforts of many people working at the seven CF centres, and at the NCFS.

This report provides information and trends on many aspects of CF diagnostics and treatment, complications of CF and some aspects of living with CF. Data that is desperately needed to find out how all people with CF in the Netherlands are doing and where improvements can be made.

This report also presents the data for each centre separately and at a national level. It also includes information on the indicators that say something about the quality of CF care.

The CF centres have each received an overview of their own data in relation to the national averages. Every year, the NCFS organises meetings with the centres' paediatric pulmonologists, pulmonologists, paediatric gastro-enterologists and nutritionists. At these meetings, the treatments, results and differences between the centres are discussed in an open and positive atmosphere, and points for improvement are determined.

Of course, COVID-19 dominated the year 2020. What was very noticeable, was that fewer adults received IV treatment (both in hospital and at home), and fewer people with CF got the flue. However, the number of visits of people with CF to the CF centres only went down slightly, despite the pandemic. With the registry, we collected data about COVID-19 in people with CF for international publications.

It is also notable that most children with CF have a normal height and weight. At the same time, it turns out that almost 20% of adults are overweight, some even obese. Of course, more and more people with CF have the option of using a CFTR modulator. It is expected that we will start seeing the effects of that development in our reports.

For the first time, sufficient data was collected from the group of people with CF who underwent a lung transplant to conduct separate analyses. In the coming years, we will have to see what the long-term developments are for this group.

The Registry is also of increasing importance for the research and the development, reimbursement and evaluation of new drugs.

The summary is shown as an infographic, which is very suitable for use at symposia and conferences.

September 2021

Jacquelien Noordhoek, CEO of NCFS and chair of the Steering Group of the Dutch CF Registry

Table of contents

1. Demographic data

This chapter shows how many children and adults live with cystic fibrosis (CF) in the Netherlands. It also shows how many people with CF have died in recent years. In addition, the map of the Netherlands shows which hospitals provide specialist CF care to how many people.

a. Numbers

For the year 2020, the Dutch CF Registry contains data for 1,563 people with CF. Data was also collected for another 22 children with CFSPID: Screening Positive, Inconclusive Diagnosis; they tested positive for CF in the newborn screening, but the diagnosis was not confirmed with two CF-causing mutations and/or a sweat chloride value of 60 mmol/l or higher. It is possible that these children will develop CF when they are older, which is why they receive support from a CF centre. This means that the Registry contains data for a total of 1,585 people with CF or CFSPID.

There are also people receiving treatment at the CF centres without a confirmed CF diagnosis and without a (positive) newborn screening. They have CF-related symptoms and are therefore receiving treatment. Because it is highly unlikely that they will develop CF, the Registry Steering Group has decided not to include their data in the Registry. For the treatment of this group of people, of course, this makes no difference.

There are more and more adults with CF in the Netherlands (Figure 1). The number of children with CF or CFSPID is slowly decreasing.

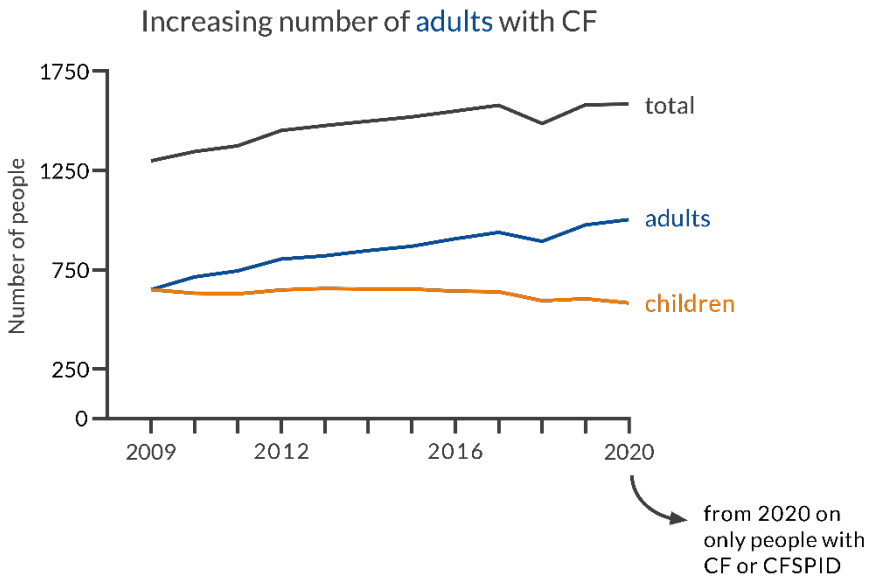

Figure 1. Number of people with CF, CFSPID or CF-related disease in the Dutch CF Registry, for the period 2009–2020.*
**CFSPID: positive newborn screening, no confirmed CF diagnosis.*

Not all people with CF or CFSPID gave permission for their data to be included in the Dutch Registry. We know that at least 100 more people are receiving treatment at the CF centres. We do not know if they have CF, CFSPID or no CF. It is estimated that, according to the data for 2020, there are about 1,650 people living with CF in the Netherlands.

b. Age

The average age of people with CF or a CF-related disease is going up (Figure 2). In 2020, the average age was 25.1. Half of them were older than 23.5 years of age; which is the median age.

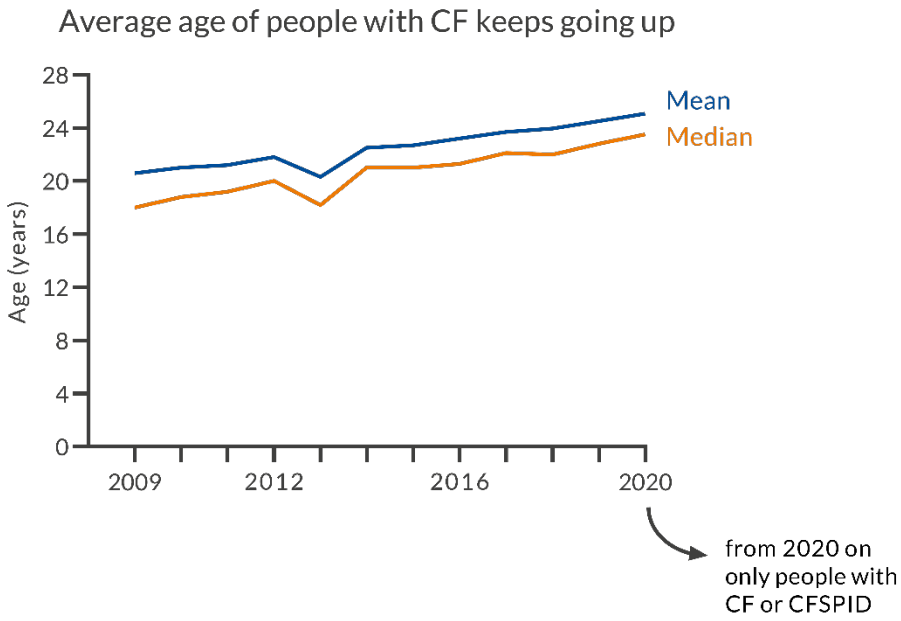

Figure 2. Average and median age of people with CF, CFSPID and/or CF-related disease for the period 2009–2020. *The median age is the midpoint of a distribution, with half the people being older and the other half younger. From 2020 onwards, the Registry only collects the data for people with CF and CFSPID.*

Figure 3 shows the ages of people with CF or CFSPID in 6-year age brackets. The diagram shows that most people are 18–29 years old, according to the data for 2020. It is also notable that 36 people are 60 years or older.

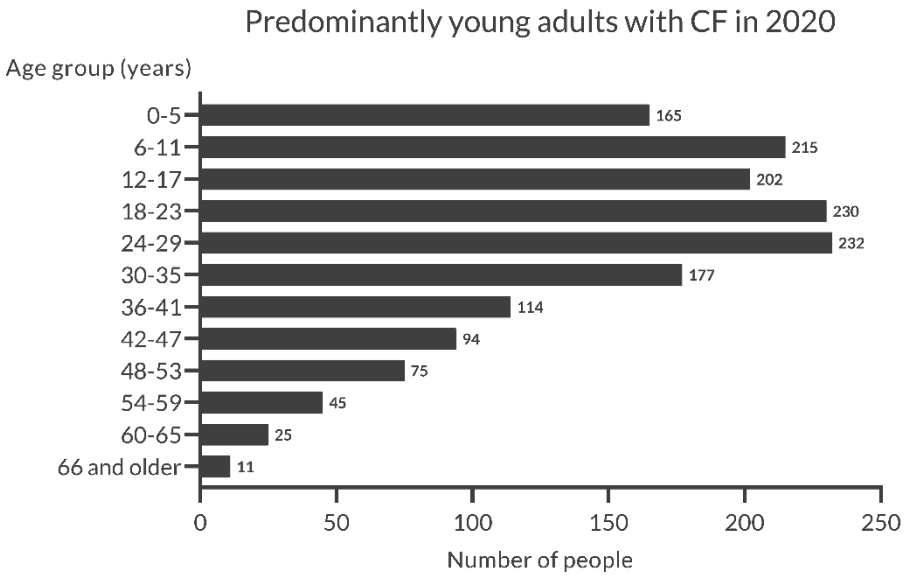

Figure 3. Median age by 6-year age brackets. The median age is the midpoint of a distribution, with half the people being older and the other half younger. The numbers behind each bar indicate how many people were in that age bracket in 2020.

c. Deaths of people with CF

Unfortunately, more people with CF died in 2020 than in the previous three years (Figure 4). A total of 11 people died. Six of them have had a lung transplant in the past.

Half of those who died in 2020, were older than 51.7 years, which means the other half were younger. We call this the median age of death. This age fluctuates over the years. This is because the age is calculated with relatively small numbers. The number has never been higher than in 2020. This means that, looking at the whole group, people with CF are dying at increasingly older ages.

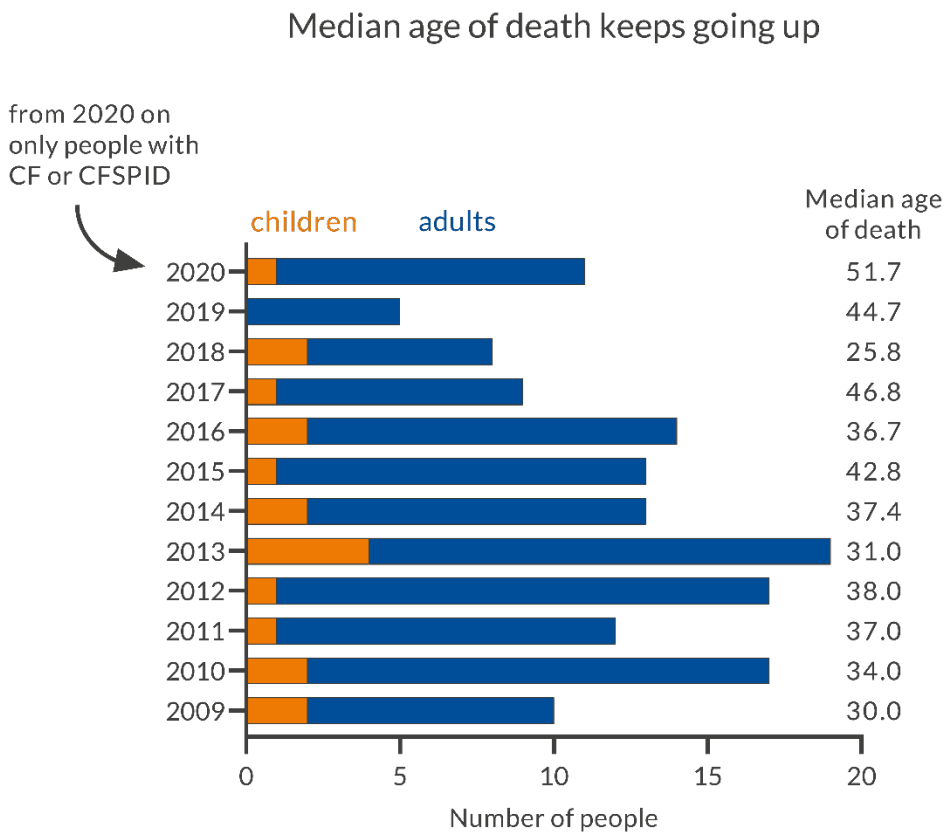

Figure 4. Number of deceased children and adults with CF, CFSPID or CF-related disease. From 2020 onwards, the Registry only contains data on people with CF and CFSPID. The median age shows that half the people who died were older than that age and the other half were younger.

d. CF care in the Netherlands

Seven hospitals in the Netherlands provide specialist CF care to children and adults. The map (Figure 5) shows where these hospitals are located. The numbers indicate how many children and adults with CF or CFSPID are being treated there, according to the data for 2020. Table 1 shows the numbers of people per centre in recent years.

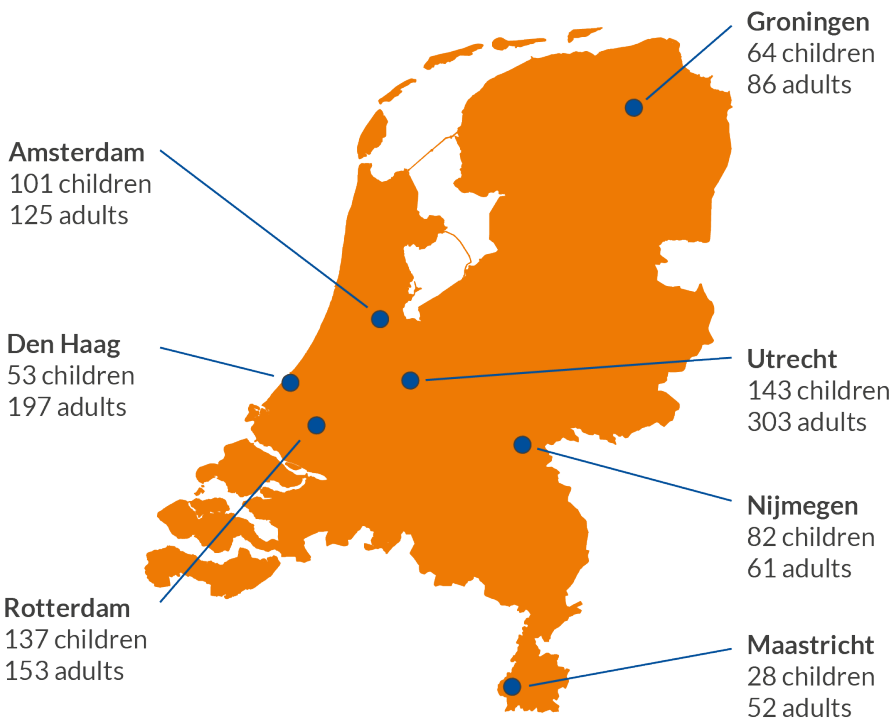

Figure 5. Map of the Netherlands showing where the CF centres are located. For each CF centre, it shows how many adults and children with CF or CFSPID are being treated there in 2020. CFSPID: positive newborn screening, no confirmed CF diagnosis.

Table 1. Number of people with CF, CFSPID or CF-related disease per CF centre, for the period from 2014 onward. ***From 2020 onwards****, the Registry will only contain the data for people with CF and CFSPID. It is estimated that about 100 people with CF are not included. *In 2018, the number of participants in the CF Registry was temporarily lower due to unsigned consent forms.*

	2014	*2015*	*2016*	*2017*	*2018*	*2019*	***2020***
UMC Utrecht							
Children	206	196	190	191	158	146	**143**
Adults	231	245	260	281	251	308	**303**
Erasmus MC Rotterdam							
Children	149	143	140	149	135	141	**137**
Adults	121	120	139	138	122	134	**153**
HagaZiekenhuis							
Children	55	63	59	55	55	52	**53**
Adults	210	210	217	215	200	204	**197**
Amsterdam UMC							
Children	102	105	104	100	104	102	**101**
Adults	100	106	109	116	118	121	**125**
UMC Groningen							
Children	69	73	74	72	65	67	**64**
Adults	88	84	83	80	83	90	**86**
Radboud UMC Nijmegen							
Children	47	49	52	58	67	73	**82**
Adults	50	57	56	56	57	64	**61**
Maastricht UMC							
Children	34	28	26	27	29	28	**28**
Adults	37	42	40	40	43	51	**52**
TOTAL	**1,499**	**1,521**	**1,549**	**1,578**	**1,487***	**1,581**	**1,585**

2. CF diagnosis

In this chapter, you can read more about the age at which CF is diagnosed and the characteristics of CF. The data includes people who had a lung transplant. The chapter also gives more information about CF as part of the newborn screening and how many children were born with CF in recent years.

a. Children born since 2016

Since 2016, at least 129 children were born with CF or CFSPID (Figure 6), an average of 29 children per year. This average excludes the year 2020, as registration is always a bit later. Each year, the most recent year is incomplete. This can be because for some children, the test to confirm the diagnosis has not yet been completed, the parents have not yet given their consent for the Registry, or the child was born in the last months of the year. In the next report, for the year 2021, the 2020 data will be more complete.

Of the 22 children with CFSPID (positive newborn screening result, but no confirmed CF diagnosis) in the Registry, three of them were born in the period 2016–2020 (Figure 6).

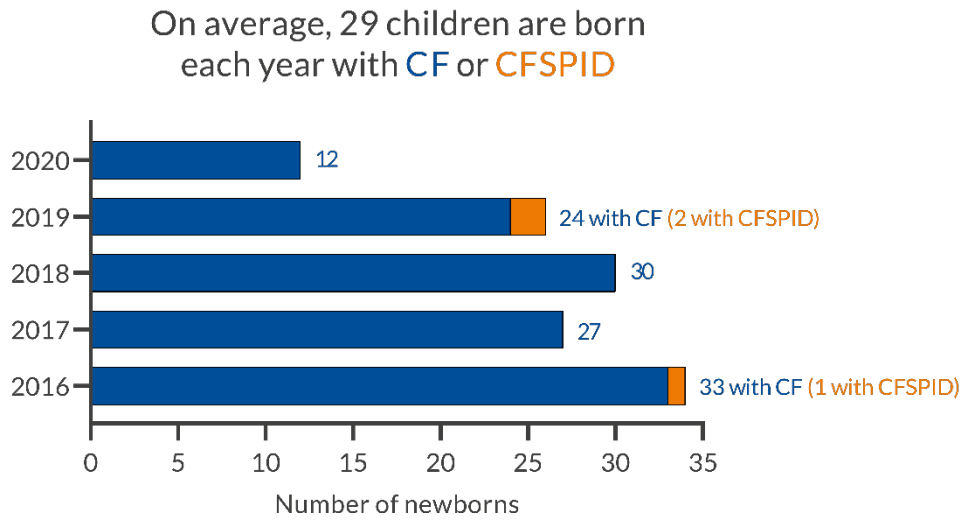

Figure 6. Children born with CF or CFSPID since 2016. CFSPID stands for a positive newborn screening result for CF, but no confirmed diagnosis.

b. Results of the newborn screening from 2016 onwards

Of all the 126 children in the Registry born with CF since 2016, the vast majority were diagnosed with CF through a positive newborn screening result (Figure 7). The remaining children with CF did not have a positive newborn screening:

- Five children did have CF, but initially had a negative newborn screening result. This is called a false negative
- Six children were not given a newborn screening (for CF) and were later found to have CF
- Another possibility is that a baby has constipated bowels (meconium ileus) at birth, causing further CF testing to be done immediately. The newborn screening then does not test for CF. This was the case for two children
- For three children, it is not known whether the screening was done or the results are unknown

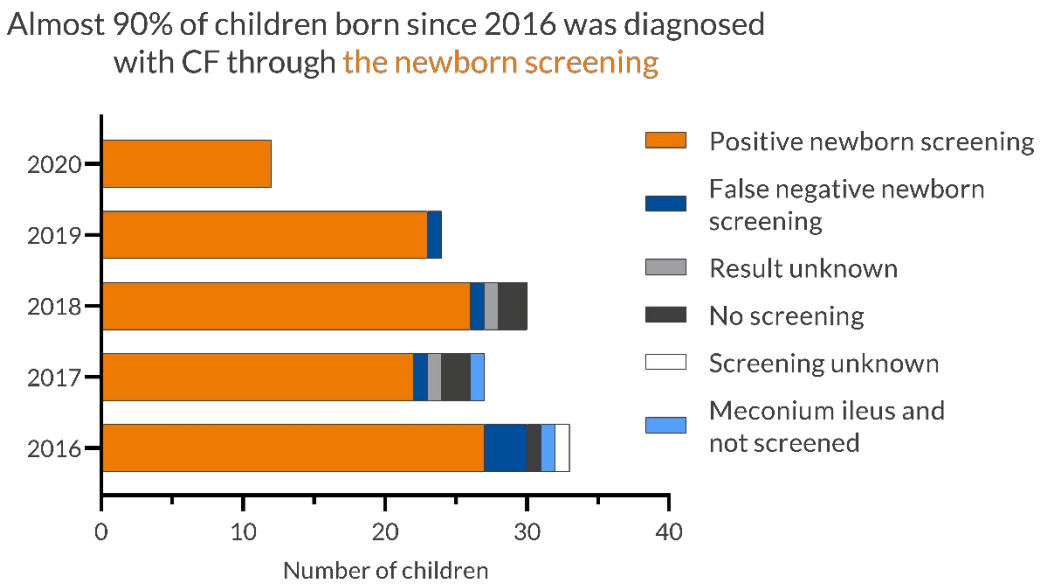

Figure 7. Results of the newborn screening for CF for children born with CF since 2016. Children with CFSPID, i.e., no confirmed CF diagnosis, were not included in this analysis.

c. Symptoms in children leading to a CF diagnosis

The paediatric centres treated a total of 586 children with CF, according to the data for 2020. 276 children with CF were diagnosed through a positive newborn screening result. For one child, it is not known whether a newborn screening for CF was done.

The other 309 children did not receive the CF diagnosis after the newborn screening. In 282 cases, screening was not done or CF was not yet included in the newborn screening. A study on CF in the screening started in 2008, and CF has been officially included in the newborn screening since 2011. Furthermore, 22 children got a negative result, but still had CF. For five children with CF, the results of screening are unknown.

Without an early test for CF, such as the newborn screening which is performed on new-born babies, the diagnosis is usually based on symptoms or other characteristics (symptoms). Figure 8 clearly shows that the children without a (positive) newborn screening more frequently had symptoms in the lead-up to the CF diagnosis than children with a positive screening result.

About 20% of children had constipated bowels at birth (meconium ileus, Figure 8). Almost 90% of children without a (positive) newborn screening for CF also had other symptoms. The most common ones were respiratory problems and growth and nutritional problems.

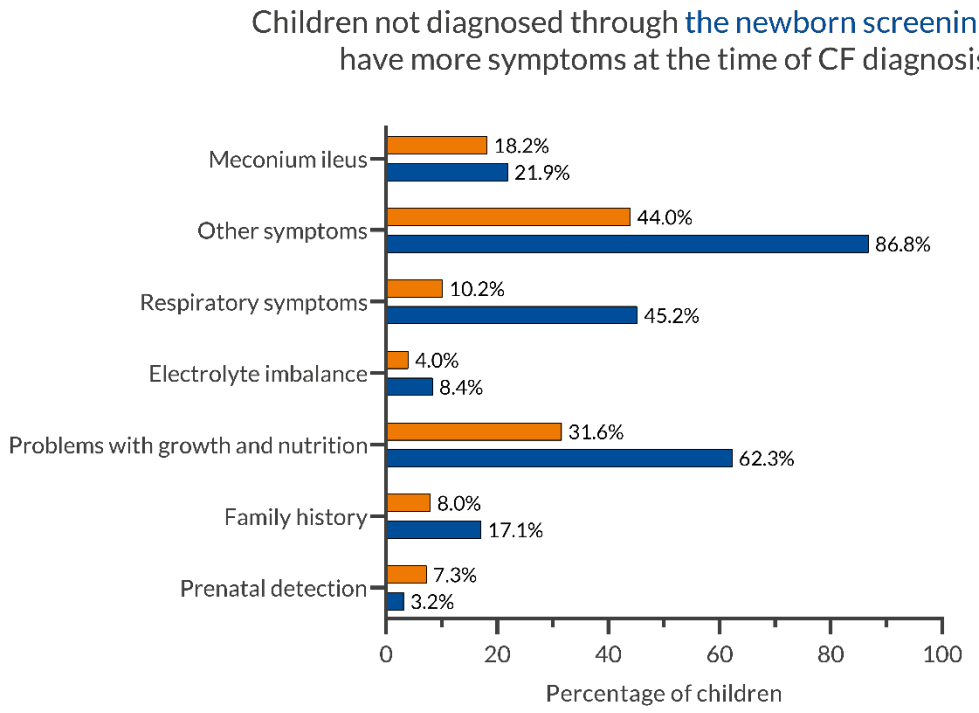

Figure 8. Symptoms children with CF have in the lead-up to the diagnosis. Percentages with a specific symptom were broken down into two groups. The group of children who were diagnosed with CF through newborn screening and the group of children who were not diagnosed through newborn screening.

Some symptoms/characteristics are infrequent and are not given in Figure 8. Of the group of children diagnosed with CF through newborn screening, 2.5% had liver problems, 0.4% had nasal problems, and 1.1% had rectal problems. In the other group of children, who were not diagnosed with CF through newborn screening, 6.1% had liver problems, 5.5% had nasal problems and 1.9% had rectal problems.

d. Age at CF diagnosis

The age at which CF was diagnosed is known for 1,478 people with CF. The average age is 3.9 years. The median age is much lower: 0.3 years. This means that half of the people with CF were younger than 0.3 years old at the time of diagnosis and the other half were older.

Figure 9 shows at what age children were diagnosed with CF. It also shows the ages of people with CF who are now adults, but who got their CF diagnosis as a child. The last group is the group of adults who discovered they have CF in adulthood.

The average age at which CF is diagnosed, is 0.85 years for the 560 children and 2.7 years for the 813 adults diagnosed with CF as children (Figure 9). Half of the children got their CF diagnosis before they were two months old. For half of the adults (with a childhood diagnosis), this was the case before the age of 8 months.

105 adults with CF (11.4% of adults) were diagnosed in adulthood. The average age at diagnosis is 34 years. Half of them were older than 32 years of age; the other half were between the ages of 18 and 32.

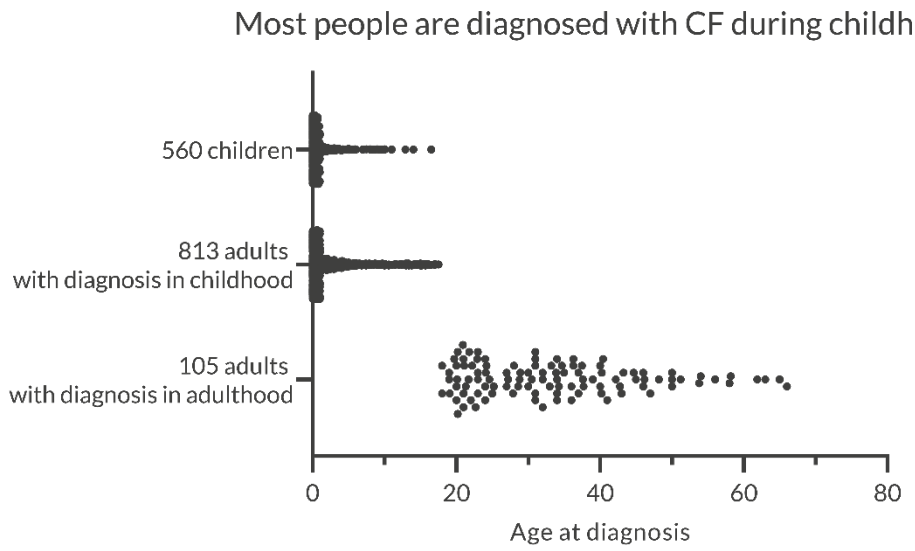

Figure 9. Age at the time of CF diagnosis for all people with CF for whom this is known. By 2020, the age at diagnosis was known for 1,478 people with CF.

3. CF and mutations

A person has CF if there are two mutations in the DNA that cause CF. A person inherits these mutations from his/her father and mother. Almost all people with CF in the Netherlands have had their mutations tested. This is also known for the children with CFSPID. This chapter shows which mutations are most common. It makes use of data for all people with CF or CFSPID, whether they have had a lung transplant or not. It concerns a total of 1,585 people.

a. Distribution of mutations in people with CF

Most people with CF in the Netherlands have two F508del mutations (Figure 10). Overall, 90.8% have at least one F508del mutation. A handful of people never had their mutations analysed.

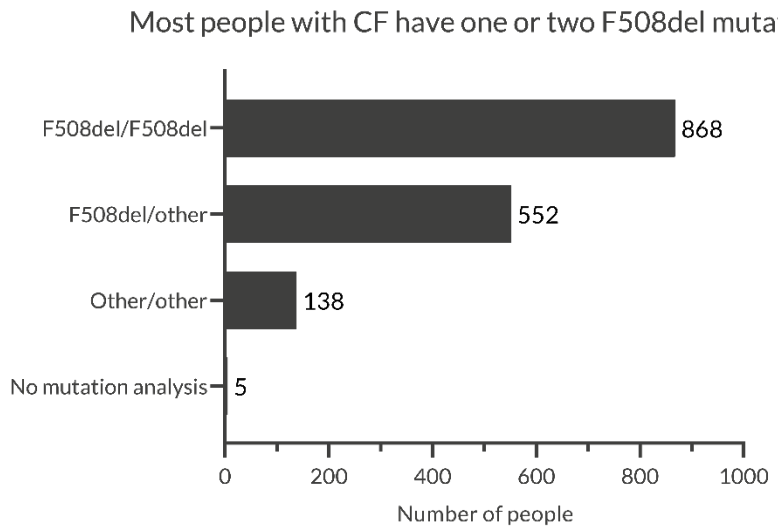

Figure 10. Combination of CF mutations divided into 4 groups. All people with CF in the Registry for 2020, whether they have had a lung transplant or not, were included in this analysis.

Figure 11 shows how common each mutation type is for each age bracket. It is quite clear to see that in each age bracket, the vast majority of people with CF have at least one F508del mutation. It is also notable that two F508del mutations are less common in those who were 48 years of age or older in 2020. For more information on people over 50, see Chapter 13, Over-50s and CF, page 50.

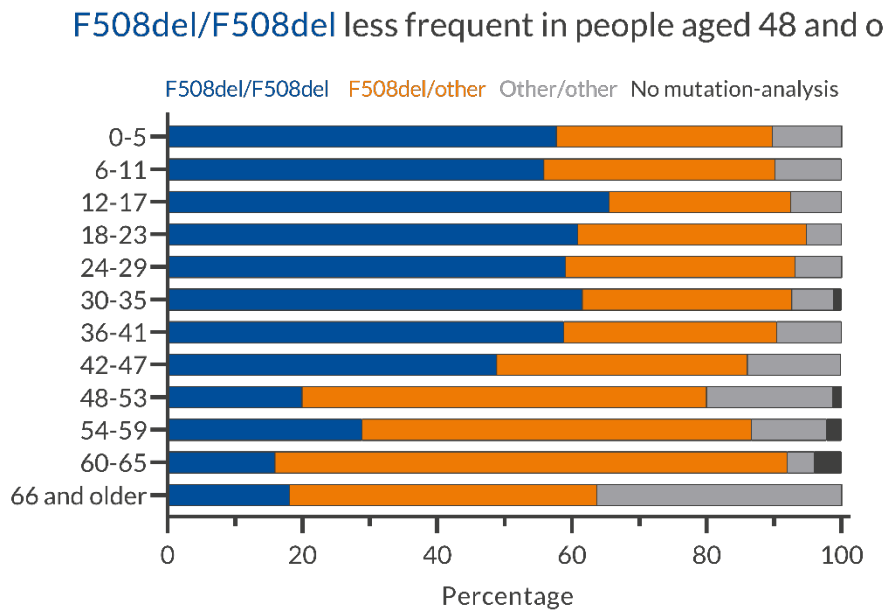

Figure 11. Distribution of mutations in people with CF in 2020, given in 6-year age brackets.

b. Mutations in children with CFSPID

Of the 22 children with CFSPID, 18 have one F508del mutation combined with another mutation, and four of them have no F508del mutations.

Most children with CFSPID have an R117H mutation. This mutation was first assessed as a cause of CF. However, most people with this mutation have a sweat chloride value that is not indicative of CF. Additional testing and studies found that only a few people with this mutation actually develop CF; and if so, they only develop it later in life. For that reason, the R117H mutation is no longer considered as a cause of CF. Since 2016, the R117H mutation is no longer included in the newborn screening panel.

c. Most common mutations

Table 2 shows the fifteen most common mutations in people with CF and CFSPID in the Netherlands, according to the data for 2020. Everyone has two mutations, bringing the total number of mutations to 3,170. The order of the mutations and the percentages on the list change little over the years.

Table 2. The fifteen most common mutations in people with CF and CFSPID in the Netherlands in 2020. Together, 1,585 people have 3,170 mutations.

Mutation	Number of people	Percentage (%)
F508del	2,306	72.7
A455E	123	3.9
R117H	59	1.9
G542X	57	1.8
1717-1G->A	43	1.4
3272-26A->G	39	1.2
S1251N	38	1.2
N1303K	36	1.1
R553X	31	1.0
R1162X	30	0.9
2789+5G->A	24	0.8
3849+10kbC->T	18	0.6
E60X	18	0.6
711+1G->T	16	0.5
W1282X	13	0.4
Unknown	23	0.7
Mutations not analysed	10	0.3
Other	286	9.0
Total number of mutations	**3,170**	**100.0**

4. Treatment of CF: CFTR modulators

Several drugs have been developed in recent years to help people with CF alleviate their physical symptoms as much as possible. For several years now, drugs are available that address the basic problem of CF: the tough mucus throughout the body, which is caused by an abnormal sweat duct (CFTR) that causes mucus to become tough in various organs. These drugs, called CFTR modulators, have a major impact on the people who take them.

This chapter explains more about how often which types of CFTR modulators are prescribed. The information here is based on data for people with CFSPID, whether they have had a lung transplant or not. People who had a lung transplant, cannot yet use a CFTR modulator, as studies regarding their safety in these patients have not yet been completed.

a. People taking a CFTR modulator

Not all people with CF are eligible for a CFTR modulator. The drugs that are available at the moment, have been developed for specific mutations. People who do not have the "right" mutations, cannot take these drugs. However, exceptions are made if a patient is in distress due to very poor pulmonary function, for example. Also, most CFTR modulators are not yet suitable for children under the age of 12. Studies in young children are still ongoing. In addition, people who have had a transplant, cannot use a CFTR modulator. This has to do with the medications they are already taking to prevent rejection of the new organ. However, studies are currently under way to see if the modulator is safe for use for this group. In addition, new CFTR modulators are constantly being developed, that may be even more effective.

In 2020, about half of all the people with CF were eligible for a CFTR modulator. Not all of them used one of the available CFTR modulators. Figure 12 shows the percentage of people, by CFTR modulator and/or subgroup, who were prescribed a drug in 2020. 86.5% of those with a gating mutation (e.g., G551D, G178R, and S1251N) and 25% of those with an R117H mutation are taking ivacaftor (Kalydeco). 88.8% of children with two F508del mutations are taking lumacaftor/ivacaftor (Orkambi). Of the children over 12 years of age and adults with two F508del mutations, 27.3% were prescribed lumacaftor/ivacaftor (Orkambi) and 56.4% tezacaftor/ivacaftor (Symkevi) in 2020.

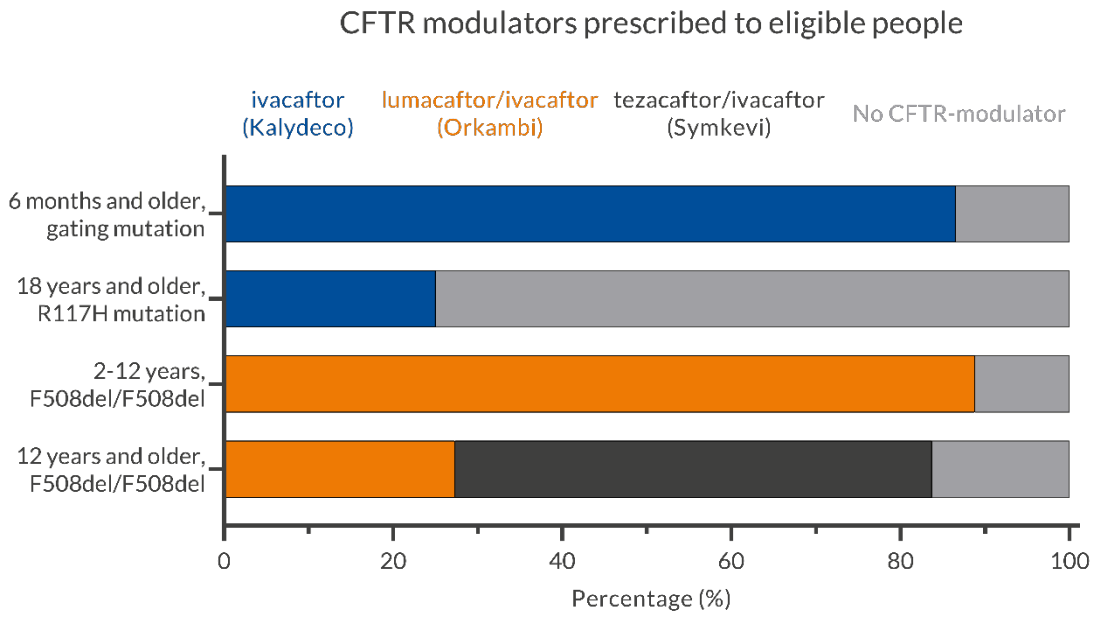

Figure 12. People who are eligible for one of the CFTR modulators covered by health insurance in the Netherlands in 2020. The percentages are broken down for whether or not a CFTR modulator was prescribed.

b. Users by modulator

In 2020, ivacaftor (Kalydeco) was prescribed to 53 people. Three of them switched to another CFTR modulator in 2020. A total of 50 people were using ivacaftor (Kalydeco) on 31 December 2020 (Figure 13). No distinction was made between the people who were officially eligible for this drug and those who received it in the context of compassionate use or a study.

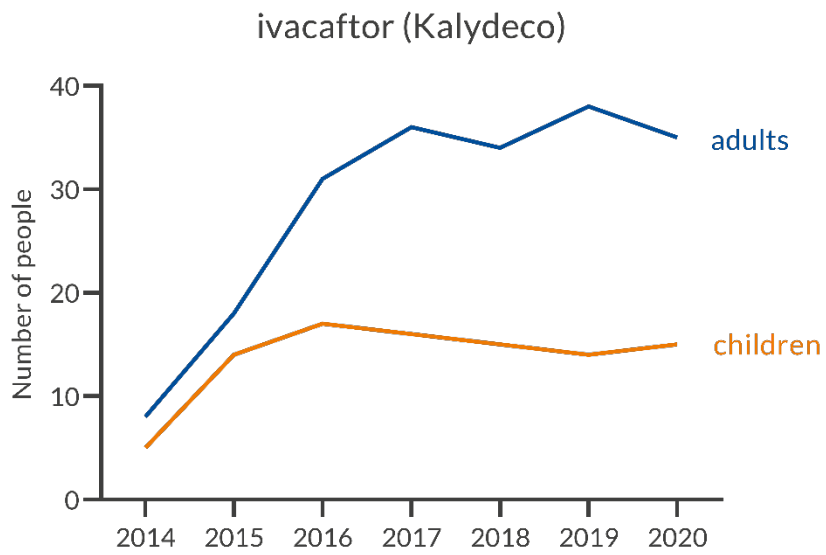

Figure 13. Number of children and adults with CF who were prescribed ivacaftor (Kalydeco) on 31 December 2020.

Lumacaftor/ivacaftor (Orkambi) is a combination of two CFTR modulators. In 2020, the drug was prescribed to 317 people with CF on 31 December 2020 (Figure 14). No distinction was made between people who were officially eligible for this drug and those who were not.

In 2019, we saw a sharp drop in the number of users, as a new CFTR modulator became available: tezacaftor/ivacaftor (Symkevi), and many people who were aged 12 years and older switched to that type of medication. In 2020, the drug was also deemed suitable for children as young as 6 years old. A total of 44 children and adults switched to another CFTR modulator, and 6 people stopped using it without switching. 26 people switched from tezacaftor/ivacaftor (Symkevi) to lumacaftor/ivacaftor (Orkambi) in 2020. For more information on tezacaftor/ivacaftor (Symkevi), see Figure 15.

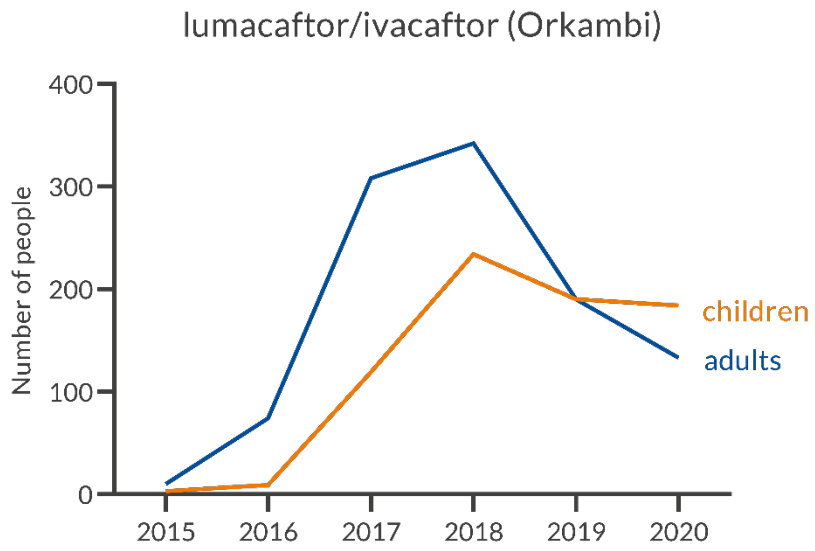

Figure 14. Number of children and adults with CF who were prescribed lumacaftor/ivacaftor (Orkambi) on 31 December 2020.

314 people with CF were prescribed tezacaftor/ivacaftor (Symkevi) on 31 December 2020 (Figure 15). 63 people stopped using it early; 48 of them switched to another CFTR modulator and 15 stopped without switching.

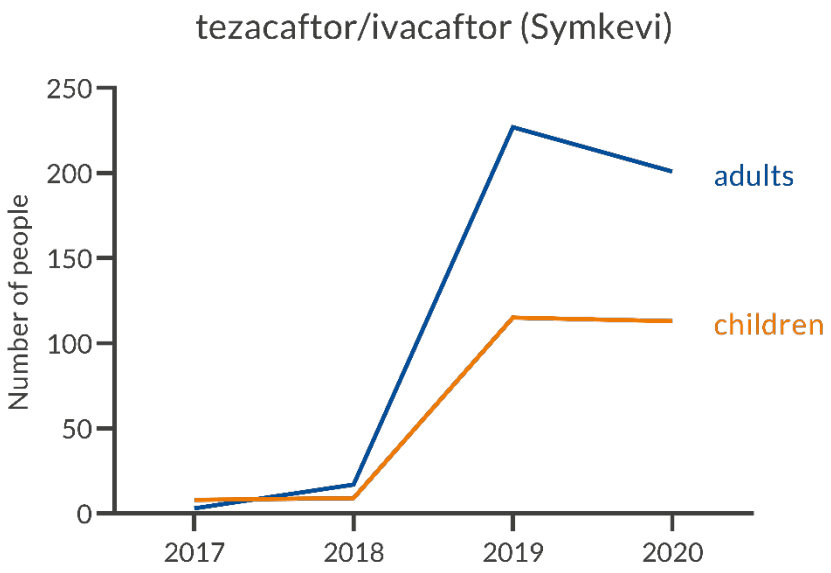

Figure 15. Number of children and adults with CF who were prescribed tezacaftor/ivacaftor (Symkevi) on 31 December 2020.

The latest CFTR modulator consists of a combination of three drugs. It is called Kaftrio and contains the drugs ivacaftor, tezacaftor and elexacaftor. In 2020, this drug was not covered by health insurance in the Netherlands. Still, 94 children and adults were prescribed the drug; either because they were participating in a study or because their health was so poor that they could not wait any longer.

Another CFTR modulator combination of three drugs is currently in development. We know that in 2020, 6 adults were prescribed this drug through participation in a study.

c. Effect of CFTR modulators on sweat chloride

A CFTR modulator almost always has an effect on the sweat chloride value. In a number of people with CF, this value was measured just before starting a CFTR modulator and also during use. Data is included here for 259 people who used a modulator in 2020.

Figure 16 shows the change in sweat chloride for all 259 people, broken down by CFTR modulator. It is notable that ivacaftor (Kalydeco) and the triple combinations gave the greatest decrease in the sweat chloride value. At group level, the sweat chloride value for people taking lumacaftor/ivacaftor (Orkambi) or tezacaftor/ivacaftor (Symkevi) also decreased, but in some people it actually increased.

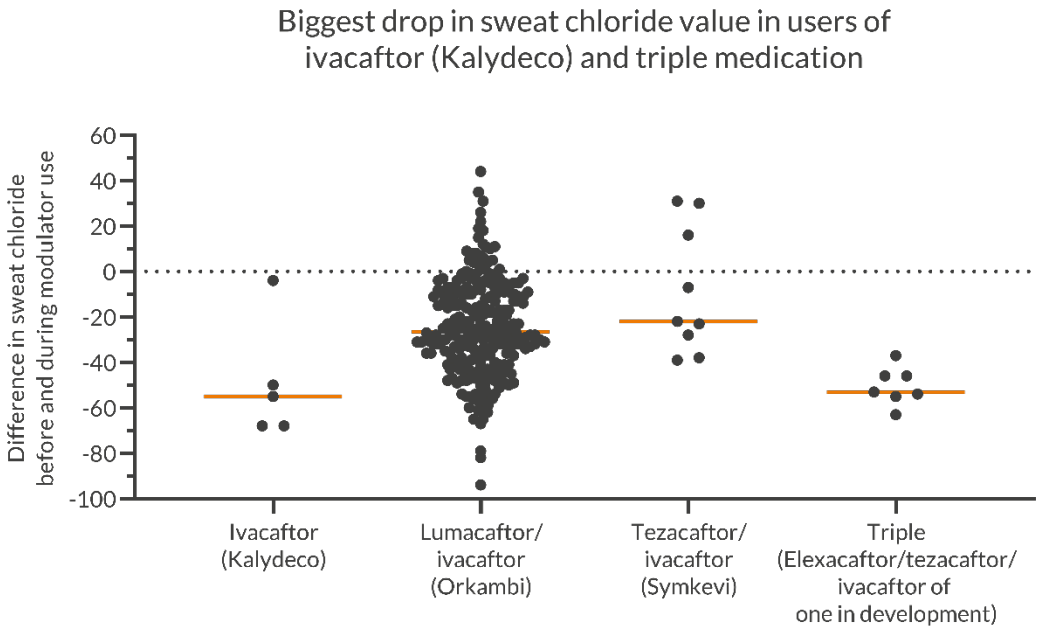

Figure 16. Change in sweat chloride value due to CFTR modulator use. Data for people with CF who have not had a lung transplant and who used a modulator in 2020. The orange line indicates the median value: half of the people experienced a larger drop in their sweat chloride value, the other half a smaller drop.

5. Treatment of CF: other types of medication

People with CF suffer from various symptoms and physical problems, and therefore take many types of drugs and follow different therapies. This chapter gives more information on the treatment of respiratory, gastrointestinal and liver problems. Figures are also given on hospitalisations and transplants.

The information on treatments in this chapter is based on data for people with a confirmed diagnosis of CF who have not had a lung transplant. They must also have been seen by a CF centre in 2020. In total, data for 1,439 people (577 children and 862 adults) was used to create the following diagrams. The information on people who had a lung transplant is listed separately.

a. Respiratory problems and treatment

Many people with CF have respiratory problems (nose and mouth, throat, lungs). Various types of drugs are available to alleviate the symptoms. Figure 17 shows how many children and adults received medication for respiratory symptoms. Almost all drugs were prescribed more often to adults than to children. This makes sense, because CF affects the lungs, and adults usually have poorer pulmonary function as a result. For more information on CF and pulmonary function, see Chapter 6 Pulmonary function, page 29.

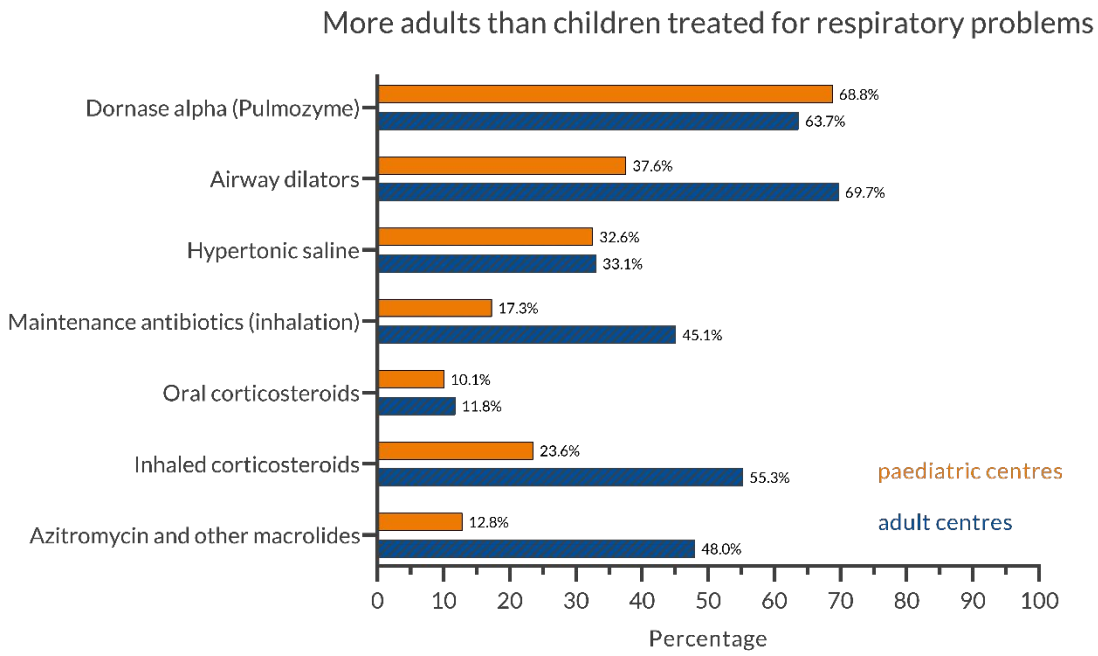

Figure 17. Treatment of respiratory problems in people with CF in 2020 who have not had a lung transplant. Percentages of symptoms are broken down by paediatric and adult centre. rhDNase stands for mucolytic dornase alfa.

Some people have such poor pulmonary function that they require extra oxygen. In 2020, 0.3% of children and 0.6% of adults received oxygen therapy through a nasal cannula or mask. Oxygen via a mask was given to 0.5% of children and 3.2% of adults.

Figure 17 shows the inhalation antibiotics used as maintenance treatment (continuous). Maintenance means that inhalation antibiotics are given for a period of at least three months. Figure 18 shows this information again, but then broken down by types of antibiotics. For each separate drug (e.g. tobramycin), the percentage of people who received at least one course of the drug is given. Figure 18 clearly shows that almost all inhalation antibiotics, except tobramycin, are most commonly prescribed to those persons with CF who visit the adult centres.

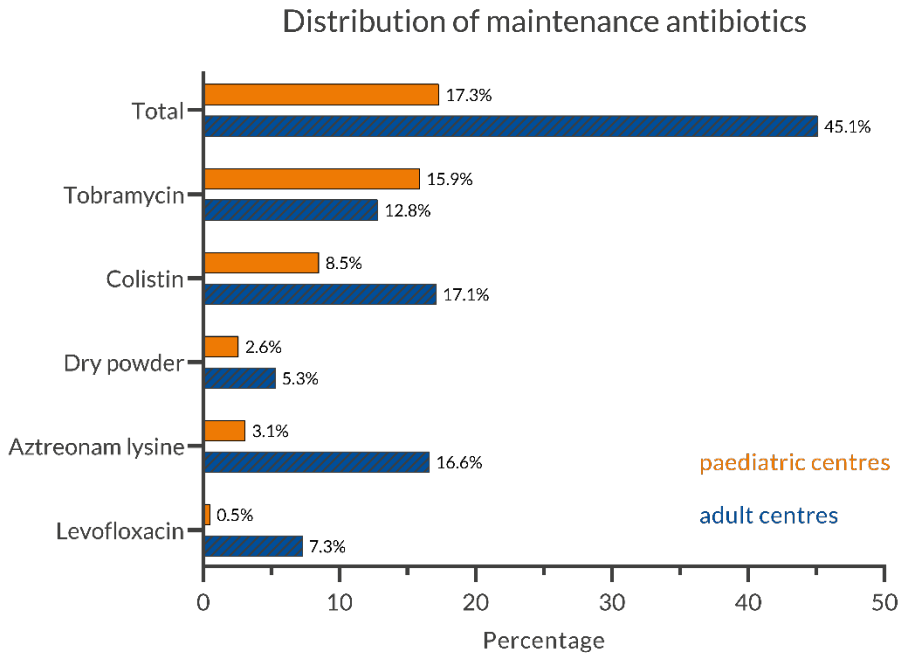

Figure 18. Percentage of children and adults on a specific type of maintenance antibiotics (inhalation) in 2020.

If a person has a pulmonary infection with the *Pseudomonas aeruginosa* bacterium, they are usually treated with inhalation antibiotics. Figure 65 shows the percentage of people with such an infection who received at least one course of inhalation antibiotics in 2020. This figure uses data for all people with CF who have not had a lung transplant. They were also seen at a centre in 2020 and had a persistent Pseudomonas infection. In total, the Registry contains data for 461 people. 379 of them received at least one course of inhalation antibiotics, which is 82.2%.

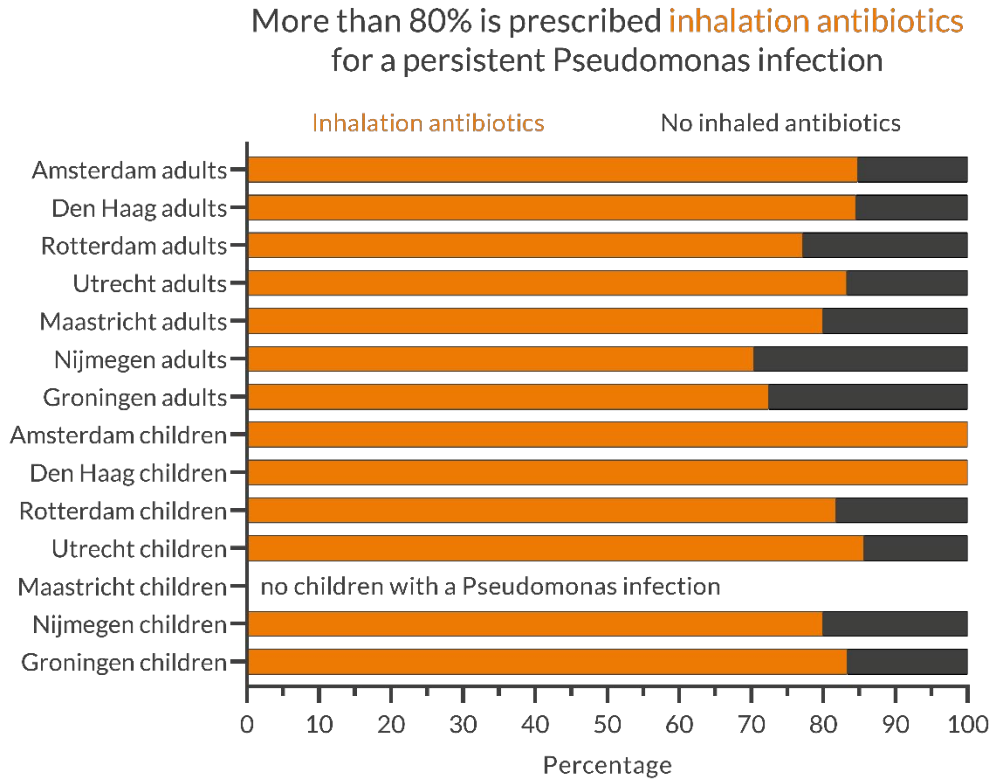

Figure 19. Percentage of people who received at least one course of inhalation antibiotics for a persistent Pseudomonas aeruginosa infection in the lungs. Data are shown by centre.

b. IV antibiotics

Sometimes, antibiotics in pill form or via inhalation are not enough to treat someone with CF if they have a bacterial or fungal infection. Antibiotics can then be introduced directly into the blood stream by means of an IV drip. This is called intravenous antibiotic treatment, or IV for short. This treatment takes place in hospital and/or at home.

In 2020, 85.6% of children did not spend any days in hospital for IV antibiotic treatment. For the adult group, this was 75.9%. 88.4% of children did not receive IV antibiotic treatment at home in 2020. For adults, this was 82.6%.

Figure 19 shows what these percentages are for 2020 and the previous years. The percentage of adults receiving IV antibiotic treatment is decreasing for the second year in a row. Still, proportionately, more adults than children receive such treatment.

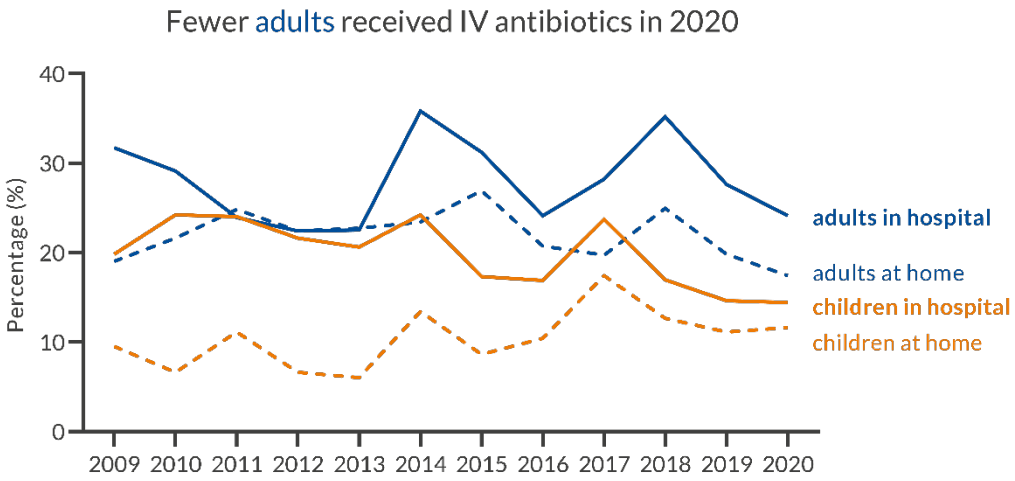

Figure 20. Children and adults who received at least one day of IV antibiotic treatment in the given year (2009–2020). Data for people with CF who have not had a lung transplant. The percentages are broken down into home treatment and hospital treatment.

Figure 20 shows the average number of days of IV antibiotic treatment in 2020 broken down by age bracket. Overall, all people who received at least one day of IV treatment, received an average of 34.5 days of IV antibiotic treatment in one given year. The median value is 21 days, meaning that half of the people received fewer than 21 days of treatment and the other half more than 21 days.

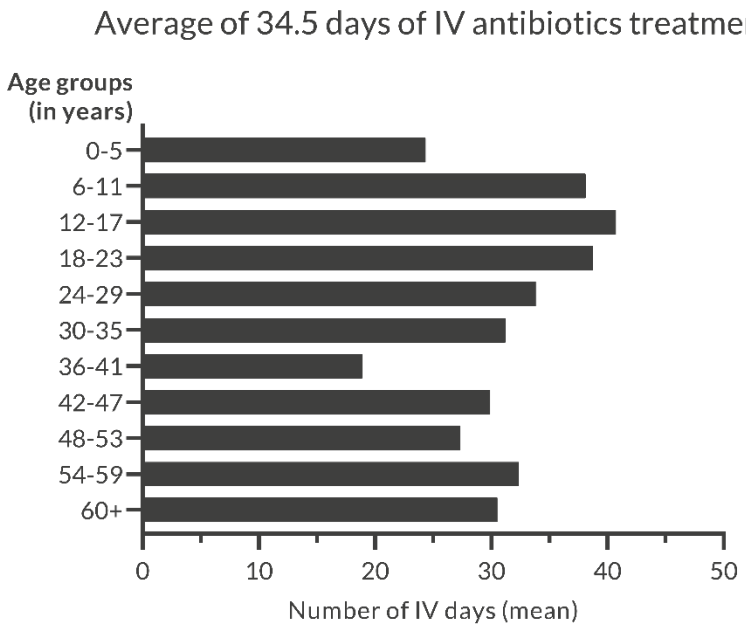

Figure 21. Average number of days of IV antibiotic treatment per year for people who received IV treatment. IV = intravenously, through an infusion directly into the blood stream.

Figure 64 shows the averages of all CF centres in the Netherlands. Most averages were between 20 and 40 days.

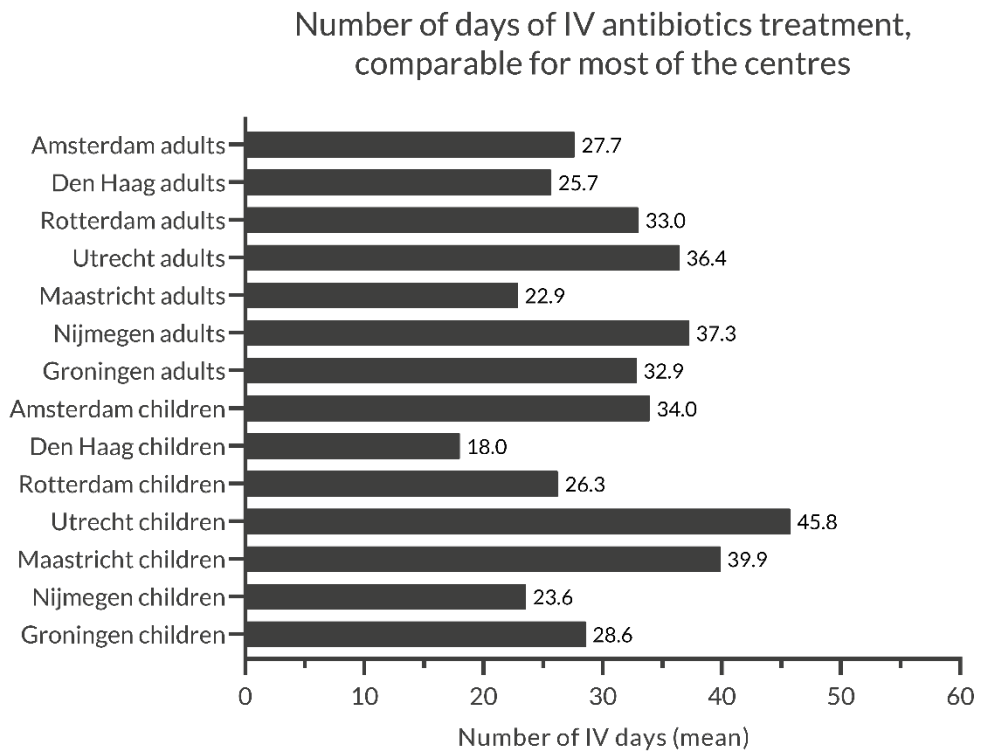

Figure 22. Average number of IV antibiotic treatments per centre in 2020. Calculated for all people with CF who received at least one day of IV treatment.

c. Gastrointestinal and liver problems and treatment

Many people with CF also have problems with their gastrointestinal tract, the organs that digest food so that nutrition is absorbed into the body. Consequently, they are often seeing a dietitian. In 2020, 94.3% of children have seen a dietitian at least once. For the adults, the percentage is lower, 62.0%.

There are various drugs available to alleviate gastrointestinal problems. Figure 21 shows how many children and adults use medication to alleviate symptoms, according to the data for 2020. Pancreatic enzymes are most commonly used.

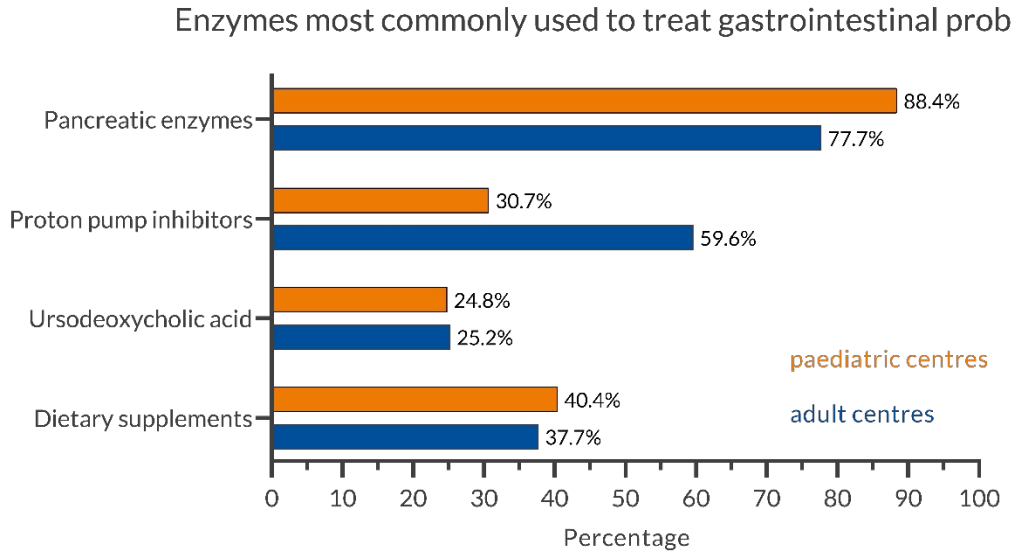

Figure 23. Treatment of gastrointestinal and liver problems in people with CF in 2020 who have not had a lung transplant. The percentages are broken down for children and adults. Pancreatic enzymes digest the food, so that it can be better absorbed by the body; proton pump inhibitors help against heartburn. Dietary supplements help gain or maintain weight. Ursodeoxycholic acid can improve bile function.

Figure 21 shows that approx. 40% of all the people with CF use nutritional supplements. Figure 22 shows how often each type of nutritional supplement was prescribed. Most children and adults of that 40% take supplemental nutritional drinks. A small number of people receive supplemental nutrition via a tube or gastric stoma.

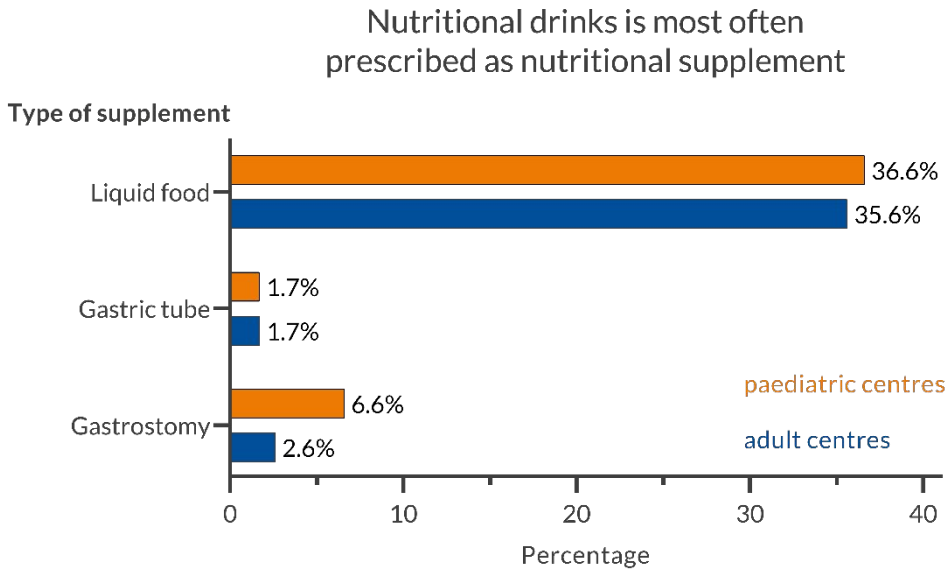

Figure 24. Supplemental nutrition prescribed in 2020, broken down for children and adults with CF, who have not had a lung transplant.

d. Transplants

According to the data for 2020, of all the 1,563 people with CF, 107 have had a lung transplant. In 2020, four people received a transplant. For more information on CF and the group who had a lung transplant, see Chapter 12 People who had a lung transplant, page 45.

Seven people had a liver transplant, eight people had a kidney transplant. Some people received multiple donor organs.

On 31 December 2020, there were still nine people on the waiting list for a lung transplant, and three people were waiting for a new liver.

6. Pulmonary function

This chapter discusses the pulmonary function of people with CF in the Netherlands, which is measured from the age of six. The Registry for 2020 contains data for 1,282 people with a confirmed CF diagnosis who are six years of age or older and who have not had a lung transplant. 1,231 people had at least one pulmonary function test.

Because the mucus in the lungs is thick and tough in people with CF, they often suffer from infections and inflammation. These cause a drop in pulmonary function. How well the lungs work, can be measured in several ways, for instance by a pulmonary function test, with the FEV1 method giving the most important value. The FEV1 measures how much air a person can expel in a second, which says something about the air flow in the airways. This test is done in patients from the age of six. The air volume is compared to a person of the same age, height and gender who does not have CF and reflected as a percentage. A FEV1% of 90% or higher is considered a healthy pulmonary function.

a. Pulmonary function by age group

In 2020, half of children had a pulmonary function above 94.3%, and the other half a function that was below that value. This percentage was the median pulmonary function for children; for adults, the median pulmonary function was 70.5%.

Figure 23 shows the pulmonary function by age group. Half of the teenagers (age bracket 12–17 years) had a pulmonary function below 90%, which, in other words, is no longer a healthy, normal pulmonary function. The median pulmonary function deteriorates for the older age groups. From the age bracket 36–41 years and up, the percentage remains stable. This is because patients with very poor pulmonary function die and those with better pulmonary function stay alive.

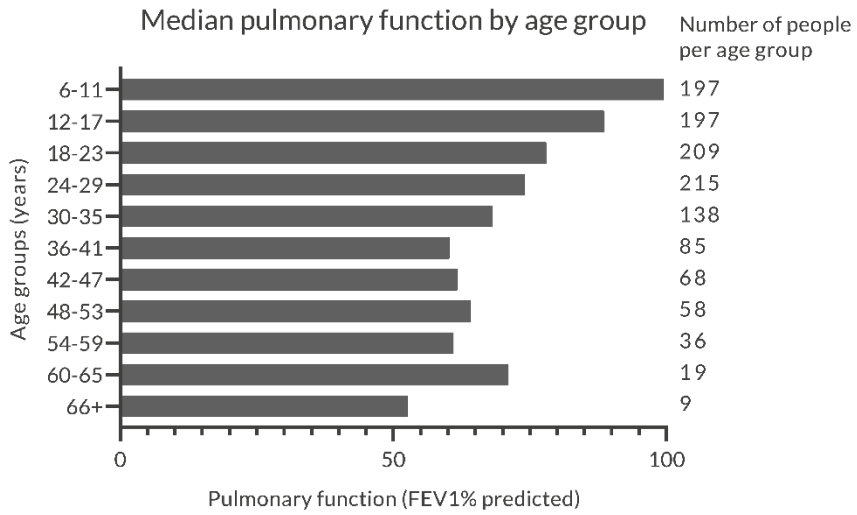

Figure 25. Median pulmonary function FEV1% predicted in 2020, Based on data for people with CF who were six years of age or older and who have not had a lung transplant.

The FEV1% can also be classified into groups. This classification is also used internationally: below 40%, 40–70%, 70–90% or a healthy pulmonary function of 90% and higher. At the paediatric centres, 58.6% of the children had a normal pulmonary function of 90% or higher. 32.2% had a pulmonary function of 70–90% and 9.2% had a pulmonary function of 40–70%. At the adult centres, 20.8% of adults still had a

normal pulmonary function. 30.1% fell in the category 70–90%, most (39.3%) had a pulmonary function of 40-70%, and 9.7% had a pulmonary function below 40%.

Figure 24 shows all pulmonary function measurements by age group for the listed categories. As indicated and visible in this figure, there were no children with a pulmonary function below 40% in 2020. The percentage of people with a pulmonary function of 70% or higher continues to go down until the age of 42 years.

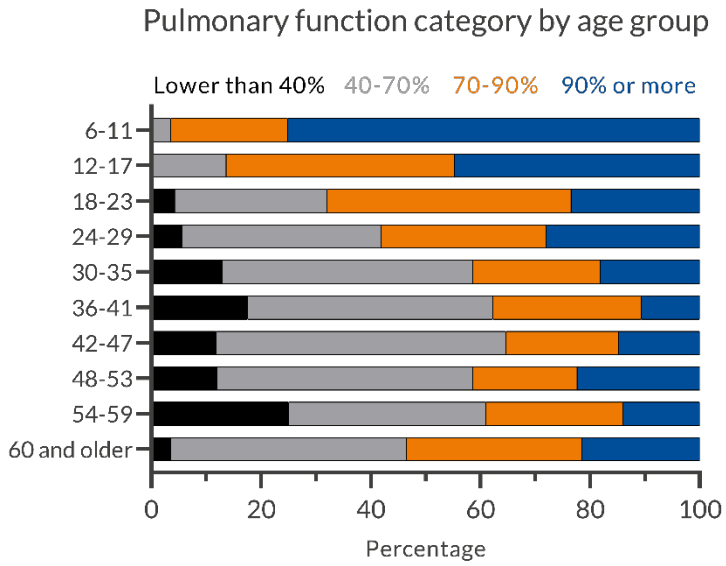

Figure 26. Distribution of pulmonary function groups in people with CF who have not had a lung transplant, broken down by age groups.

b. Pulmonary function in children

Figure 25 zooms in on the pulmonary function (FEV1) of the children, by paediatric centre, using the data of a total of 415 children who were at least six years old and who received treatment at one and the same centre during the year. This figure also shows that there were no children with a pulmonary function below 40% in 2020. In fact, at almost all the centres, at least half of the children had a healthy, normal pulmonary function of 90% or higher.

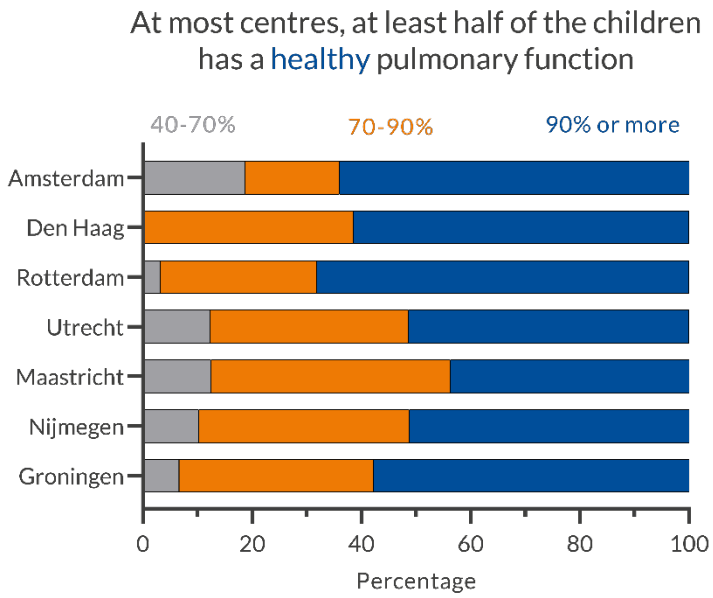

Figure 27. Distribution of pulmonary function in children with CF by CF centre.

The pulmonary function of the children is gradually improving. In 2015, the median pulmonary function of children up to the age of 18 years was 92.4%. In 2020, this had gone up to 95.0%.

Looking at it by age group, the pulmonary function in 2020 is notably higher for the group 15–17 years (Figure 26).

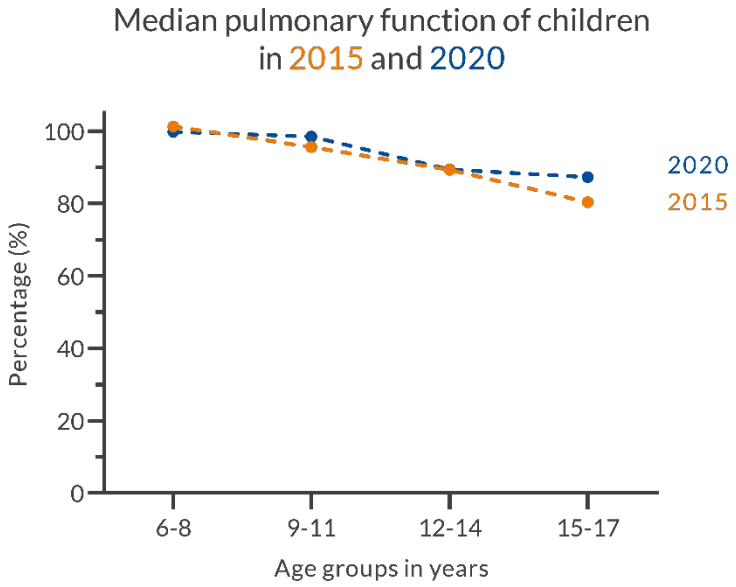

Figure 28. Median pulmonary function by age group for children in 2015 and 2020.

c. Pulmonary function in adults

Figure 27 shows the distribution in pulmonary function groups by centre. This figure shows, for example, that in 2020 Nijmegen and Groningen had the most adults with a pulmonary function below 40%. The hospital in Amsterdam treated the most people with a healthy pulmonary function of 90% or higher. The figure is based on data for a total of 816 adults.

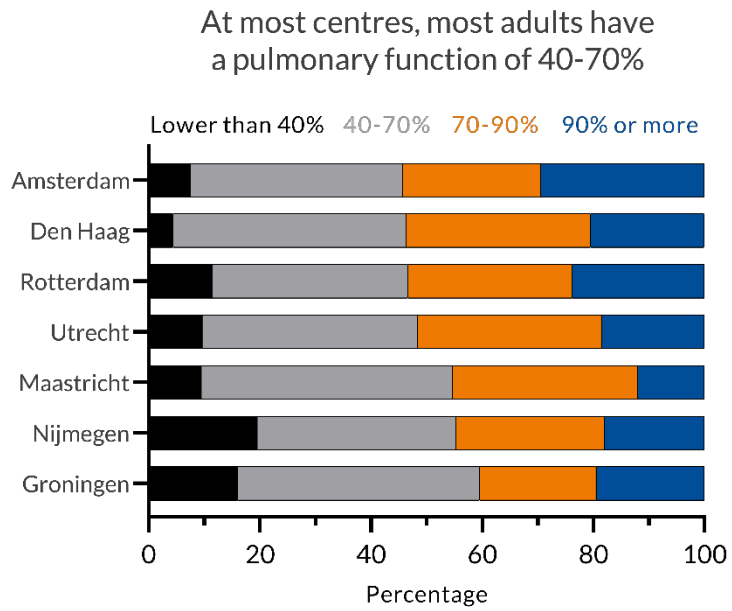

Figure 29. Distribution of pulmonary function in adults with CF by CF centre.

In 2015, the median pulmonary function of adults was 66.3%. In 2020, this value had gone up to 70.5%. Figure 28 shows that this improvement is not visible in all age groups.

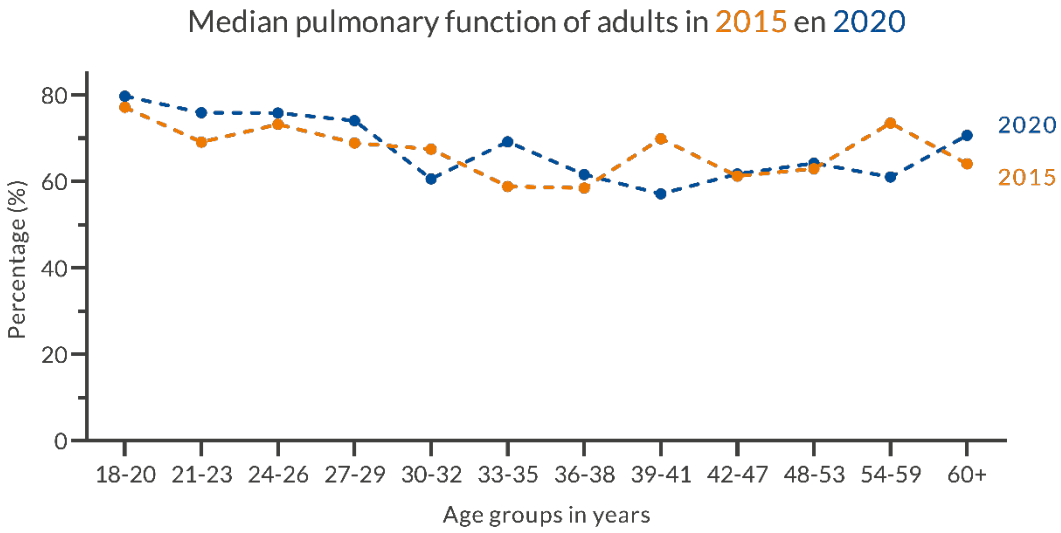

Figure 30. Median pulmonary function by adult age group in 2015 and 2020.

7. Height and weight of children with CF

This chapter describes the characteristics of height and weight in children. The information here is based on data for children with a confirmed CF diagnosis who have not had a lung transplant.

a. Measure for the height and weight of children

The body mass index (BMI) is one way to express the relationship between height and weight. However, for children, this measure is not quite appropriate. A child continues to grow and also puts on weight throughout childhood. The height and weight can also be converted to different Z-scores.

The Z-score is a value that is corrected for age and gender (and ethnic background). A Z-score between -2 and 2 is normal: 95% of children in the Netherlands have a Z-score in this bracket, and a Z-score of 0 is average.

Figure 29 shows the Z-scores for three methods to measure and express the relationship between height and weight: height-for-age, weight-for-age, and BMI. The median Z-score for each three-year age bracket is shown. This means that half of the children in that age group are below the median value and the other half are above it.

The Z-scores for the BMI fluctuate around the mean value of 0 (Figure 29). The values for weight-for-age are also close to 0. This is not true for height-for-age: in all the age groups, the Z-score is quite low. The median values still fall within the normal range of -2 to 2, however. In general, children with CF are slightly smaller than average, but not extremely so.

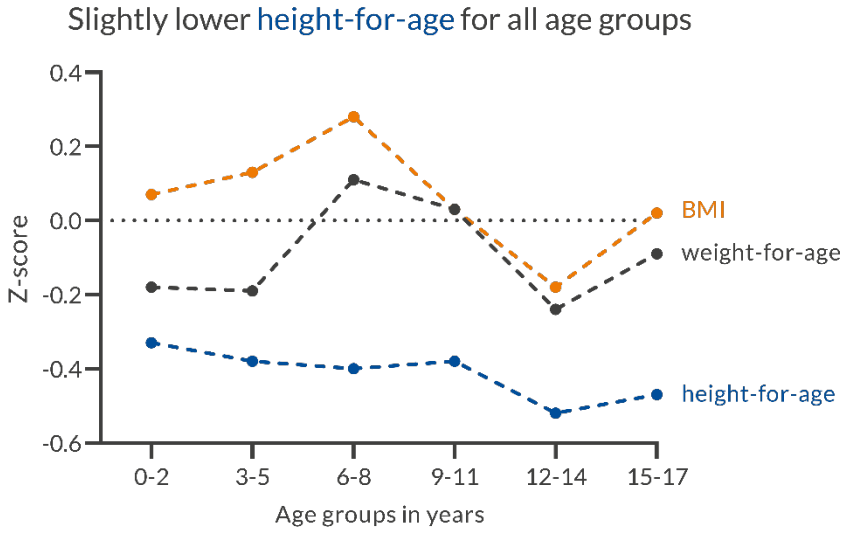

Figure 31. Different measures for the height and weight of children with CF in 2020. The Z-score is a value that is corrected for age and gender (and ethnic background). A Z-score between -2 and 2 is normal: 95% of children in the Netherlands have a Z-score in this bracket, and a Z-score of 0 is average.

b. Height and weight in groups

Another way to look at height and weight is to divide the BMI, weight-for-age and height-for-age into groups. A Z-score lower than -2 means that a child has a lower weight or BMI or is smaller than most children. A Z-score higher than 2 means that a child has a higher weight or BMI or is taller than most children. 95% of all children with CF had a normal BMI in 2020 (Figure 30). The differences between the paediatric CF centres are small.

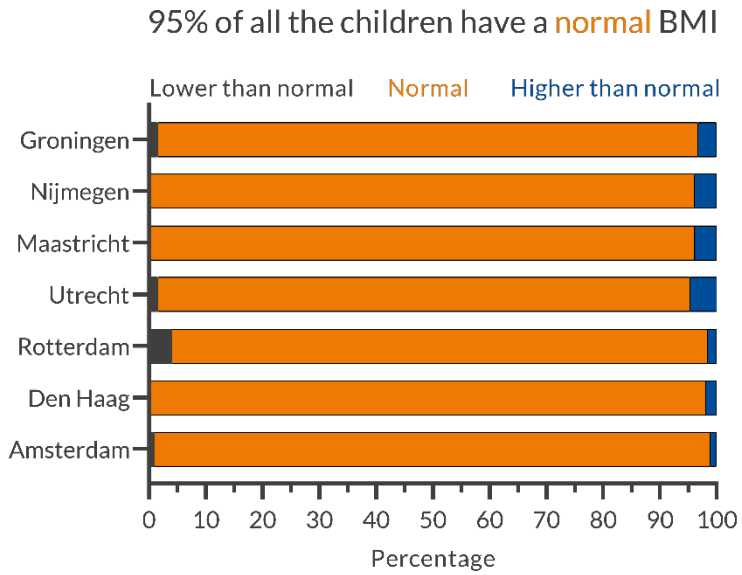

Figure 32. BMI distribution of children with CF in 2020. A normal Z-score for the BMI is between -2 and 2. A value lower than -2 is a lower than normal MBI, and a value higher than 2 is higher than normal. The Z-score is a value that is corrected for age and gender (and ethnic background). A Z-score between -2 and 2 is normal: 95% of children in the Netherlands have a Z-score in this bracket, and a Z-score of 0 is average.

The weight is age-appropriate for 94.3% of all children with CF in 2020. Figure 31 shows the distribution by paediatric CF centre in 2020.

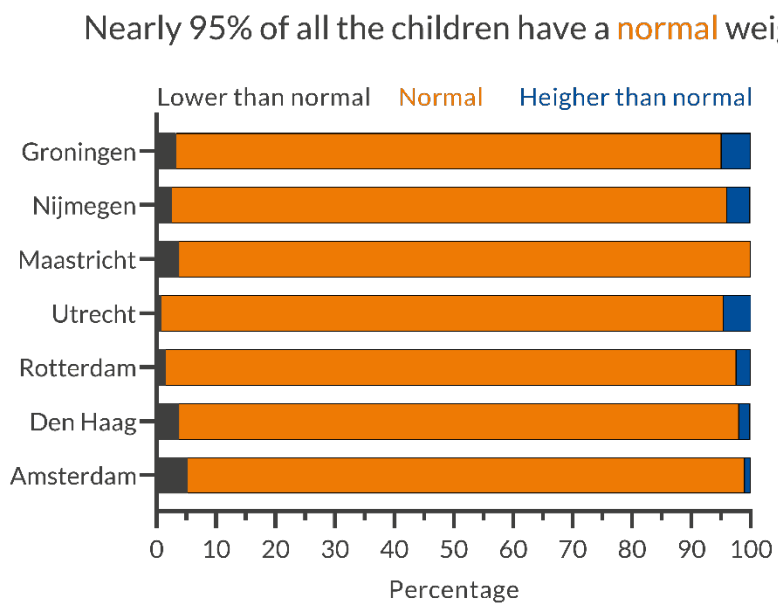

Figure 33. Weight-for-age of children with CF in 2020. A normal Z-score for weight-for-age is between -2 and 2. A value lower than -2 is a lower than normal weight-for-age, and a value higher than 2 is higher than normal. The Z-score is a value that is corrected for age and gender (and ethnic background). A Z-score between -2 and 2 is normal: 95% of children in the Netherlands have a Z-score in this bracket, and a Z-score of 0 is average.

Most children with CF are slightly smaller than average. However, 92.7% have a normal height (Figure 32). In Maastricht, a lot of children are smaller than normal. This is not because they get a different treatment, but because there are large regional differences in how tall people (and children) are within the Netherlands. In general, children in the South (Limburg) are smaller than e.g. children in the North (Groningen).

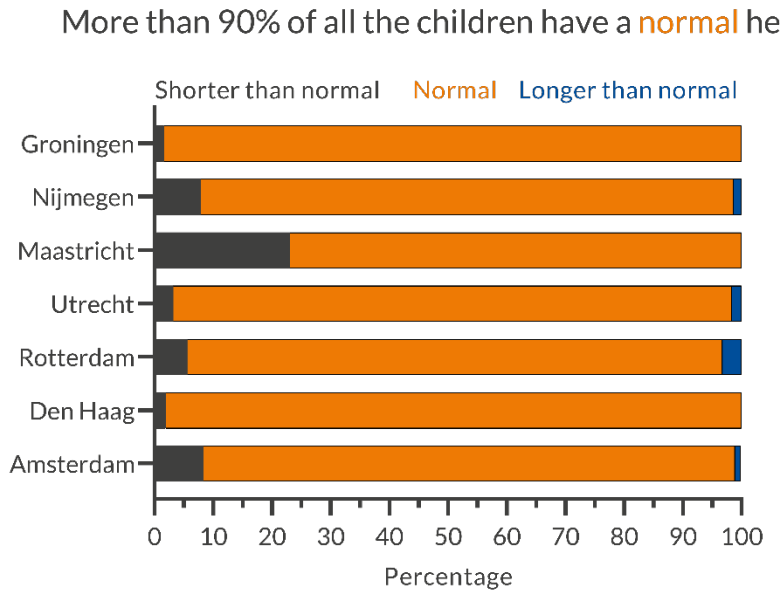

Figure 34. Height for-age of children with CF in 2020. A normal Z-score for height-for-age is between -2 and 2. A value lower than -2 is a lower than normal height-for-age, and a value higher than 2 is higher than normal. The Z-score is a value that is corrected for age and gender (and ethnic background). A Z-score between -2 and 2 is normal: 95% of children in the Netherlands have a Z-score in this bracket, and a Z-score of 0 is average.

8. Height and weight of adults

This chapter describes the characteristics of height and weight in adults. The information here is based on data for adults with a confirmed CF diagnosis who have not had a lung transplant.

a. Age and BMI in adults

The median BMI of adults is within the healthy range of 18.5–25, which applies to almost all age groups (Figure 33). In the group of people aged 66 and older, half have a BMI higher than 25.6. In general, the BMI is higher in older adults than it is in young adults.

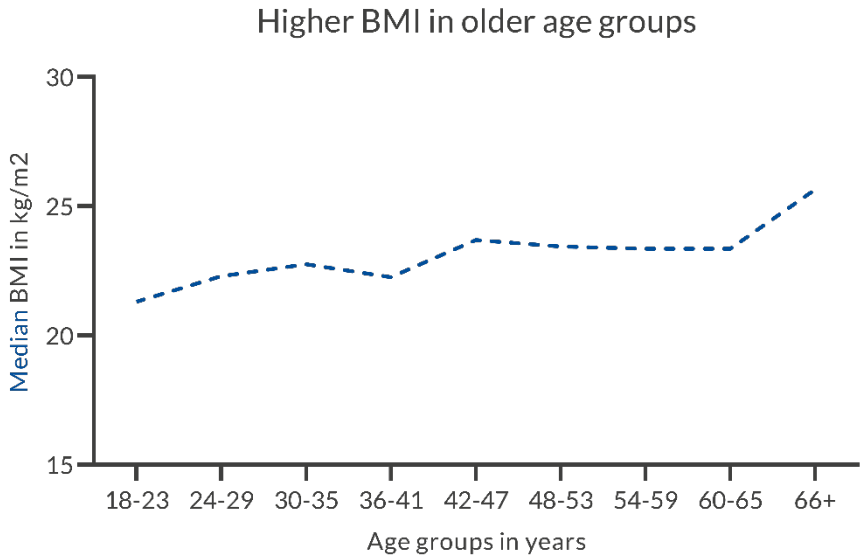

Figure 35. Median BMI of adults with CF in 2020.

b. BMI by adult centre

The BMI values can also be grouped together. A BMI lower than 18.5 is considered lower than normal. A normal BMI falls in the range 18.5–25. A BMI that is higher than normal has a value of 25 or higher.

Figure 34 shows all the BMI values of adults with CF divided into three groups. Overall, 7.2% of adults have a BMI that is lower than normal and 18.9% have a BMI that is higher than normal. This means that nearly three-quarters of adults have a normal BMI.

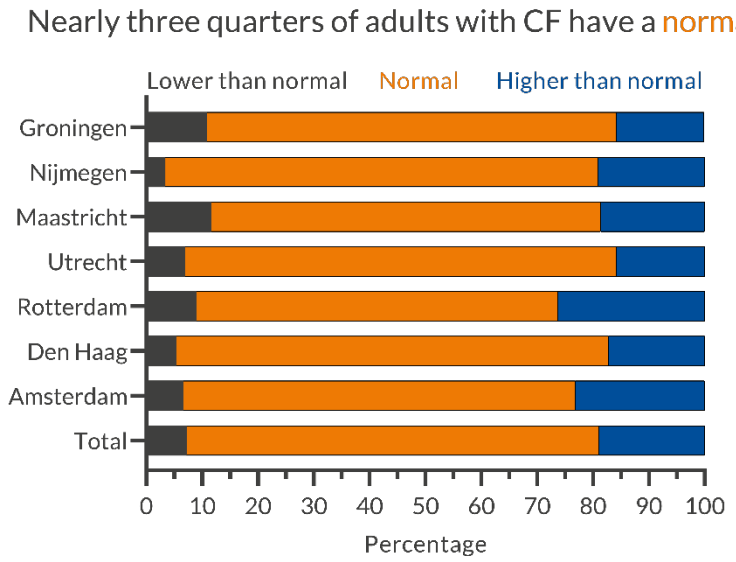

Figure 36. BMI groups by CF adult centre in 2020. A normal BMI is 18.5 or higher, but below 25. A lower than normal BMI is lower than 18.5. A BMI higher than normal is 25 or higher.

c. Differences between men and women

Figure 35 shows the BMI groups broken down by men and women. Women generally have a lower body weight than men. And with that, the differences become even more pronounced, because the BMI value aimed for is higher for women than for men with CF. 40.7% of men have a BMI below the (international) target value of 22. The percentage of women with a BMI lower than 22 is higher, namely 53.7%. Their target BMI is 23, and the percentage of women below that value is 67.2%.

In both men and women, there are also people who are overweight: 16.1% of women and 21.3% of men have a BMI higher than 25.

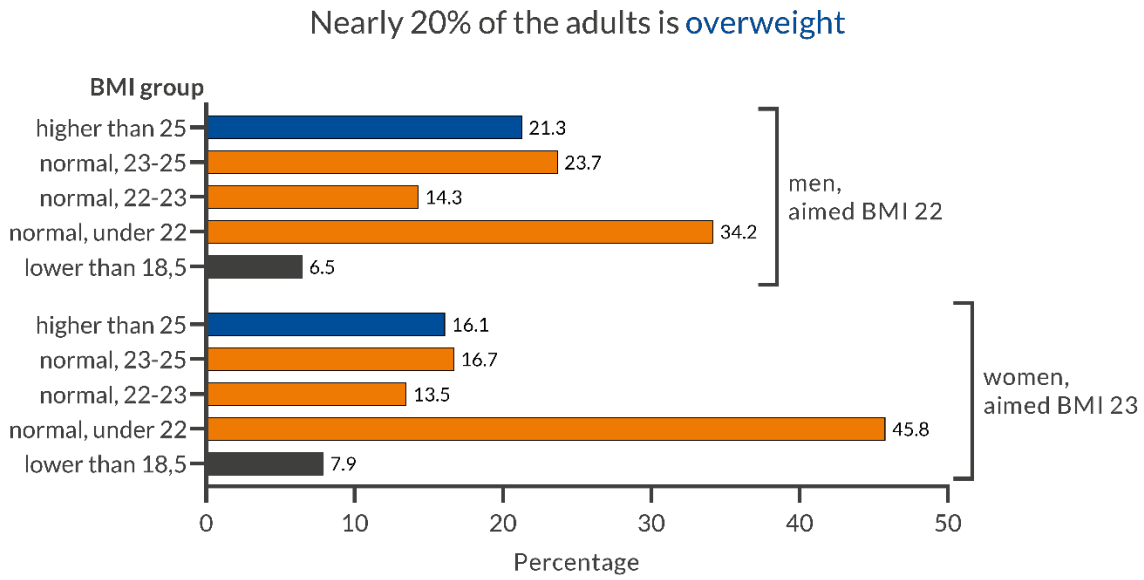

Figure 37. BMI groups of adult men and women with CF in 2020.

9. Bacterial and fungal infections

This chapter describes how common bacterial or fungal infections are. The data used are for all people with CF, who have not had a lung transplant, and who had at least one sputum culture done.

a. Age and infections

People with CF often have infections in the lungs. This is because bacteria or fungi get into the lungs and get stuck there in the tough mucus. Some bacteria are common (Figure 36), while others are rarer (Figure 37). Some bacteria primarily cause infections in young children (e.g. *Haemophilus influenzae*), while others are more common in adults (e.g. *Pseudomonas aeruginosa*).

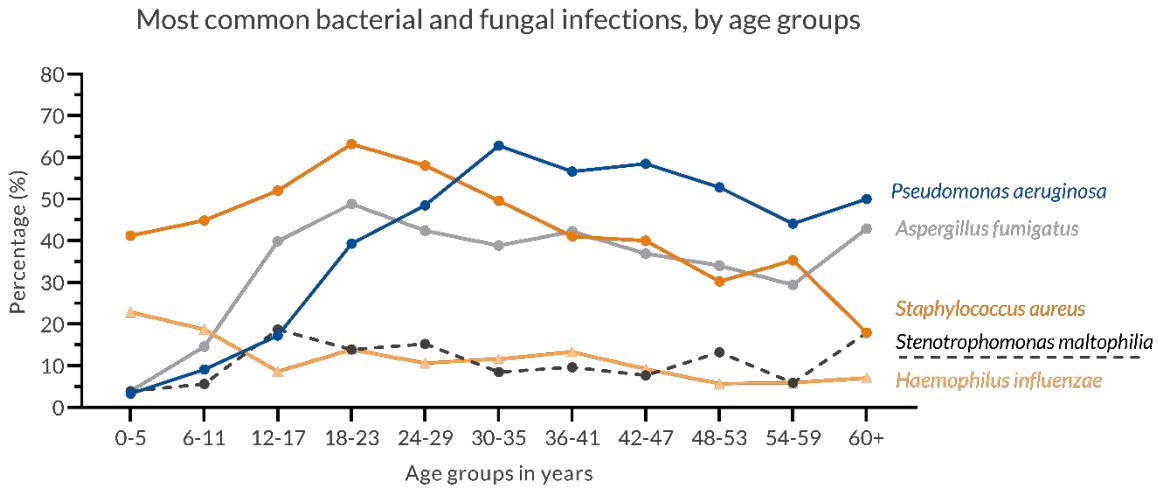

Figure 38. Most common bacterial and fungal infections in people with CF in 2020. Distribution by age group.

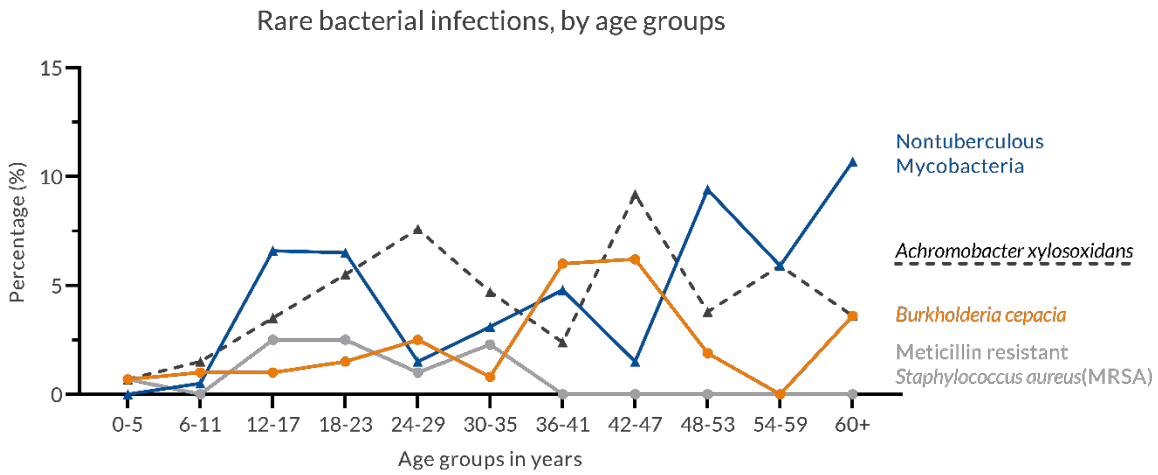

Figure 39. Infections with rarer bacteria in people with CF in 2020. Distribution by age group.

b. Common bacteria and fungi

There are four bacteria and one fungus that cause most of the pulmonary infections in people with CF (Figure 38). In 2020, significantly more people got infected with the *Staphylococcus aureus bacterium*. The largest decrease is seen in the number of infections caused by the *Haemophilus influenzae* bacterium.

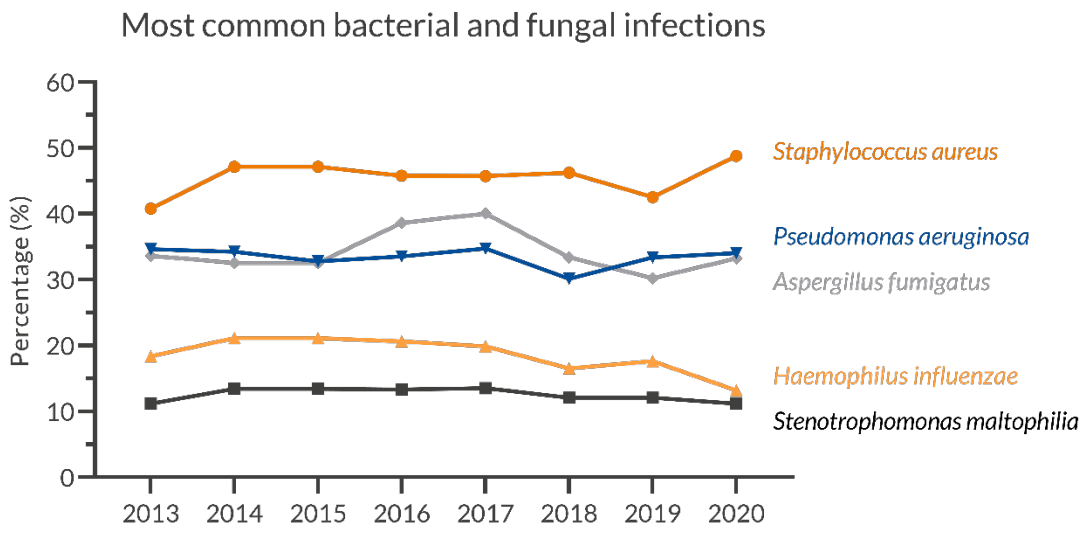

Figure 40. Percentage of people with CF with a common bacterial infection and fungal infection (Aspergillus fumigatus) between 2013 and 2020.

c. Rare bacteria

Other bacteria also cause infections in the lungs of people with CF, but are much less common (Figure 39). In 2020, there was a slight increase in the number of infections with a rare bacterium.

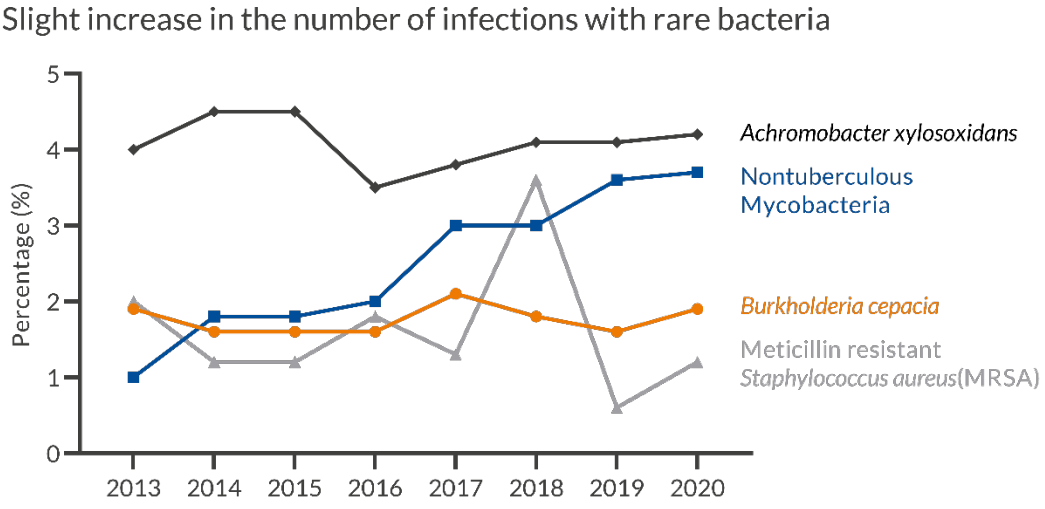

Figure 41. Percentage of people with CF with an infection with a rare bacterium between 2013 and 2020.

d. Nontuberculous mycobacteria (NTM)

In 2020, 3.7% of people with CF suffered an infection with an NTM. This may seem like a low percentage, but it goes up every year and these bacterial infections are difficult to treat.

From 2020 onwards, the Registry will include the type of NTM detected in the sputum culture of people with CF. The plan is to continue to specifically test for and monitor these bacteria in the coming years. In 2020, 49 people had an NTM in their sputum culture. 42.9% of infections were of the NTM abscessus type, 46.9% one of the three types of NTM avium complex, and the remaining group was a different or unknown variant.

e. Coronavirus in people with CF

Early 2020, the Coronavirus Sars-CoV-2 spread around the world and also arrived in the Netherlands. The Registry reported that 51 people with CF tested positive for Coronavirus in 2020. This is probably an underestimation.

10. Comorbidities with CF

People with CF often have additional conditions or illnesses, called comorbidities. Figure 4 shows how many people had which comorbidities in 2020. Data were used for people with CF who have not had a lung transplant and who were seen at a CF centre in 2020. The Registry contains data for a total of 1439 adults: 577 children and 862 adults.

The Dutch CF Registry keeps track of a large number of comorbidities. For the purposes of this report, they have been divided into four groups: most common, common, infrequent and rare comorbidities. Some groups are split into two, such as bone fractures in 2020 and bone fractures at any point in time. Virtually all comorbidities become more prevalent with advancing age. This means that adults are more likely to have one or more comorbidities than children.

a. Most common and common comorbidities

Figure 40 shows the most common comorbidities in 2020. A third of adults have diabetes and also a third suffer from bone weakness (the stage before osteoporosis). In contrast, liver disease is more common in children, with nearly 20% of children experiencing liver disease without scarring of the liver.

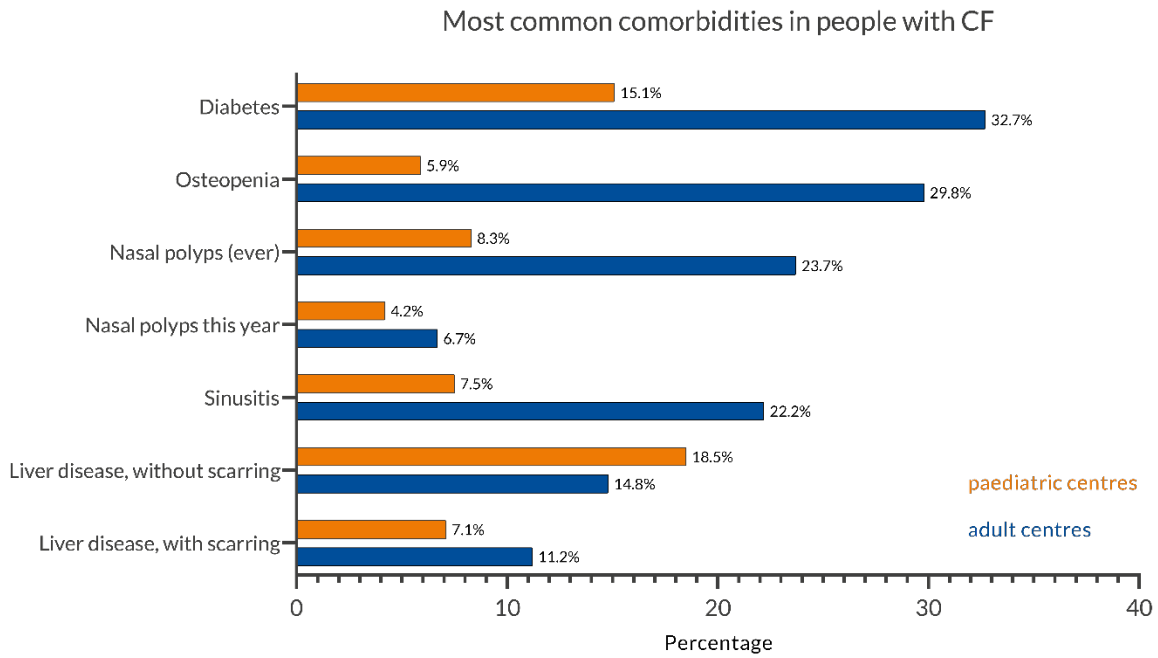

Figure 42. Most common comorbidities in people with CF in 2020.

Other comorbidities occur in 6-10% of adults, but almost not at all in children (Figure 41).

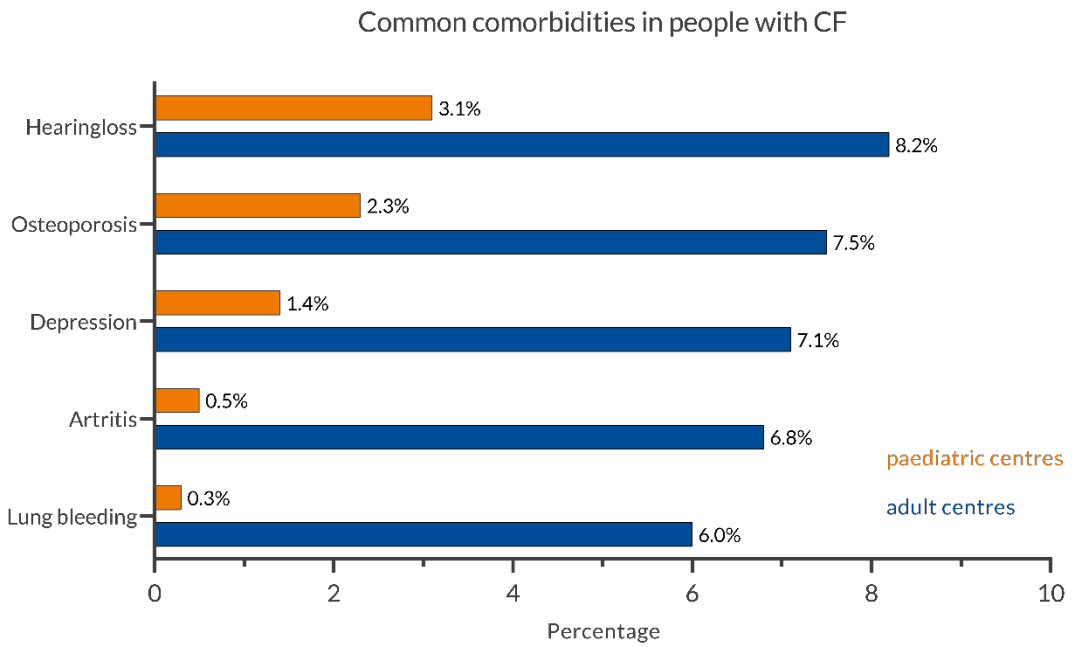

Figure 43. Common comorbidities in people with CF in 2020.

b. Infrequent and rare comorbidities

Some conditions occur in less than 5% of adults and children (Figure 42 and Figure 43). Figure 42 shows that an equal percentage of adults and children suffered an ABPA in 2020. An ABPA is an allergic respiratory reaction to the fungus *Aspergillus fumigatus*, and stands for allergic bronchopulmonary aspergillosis.

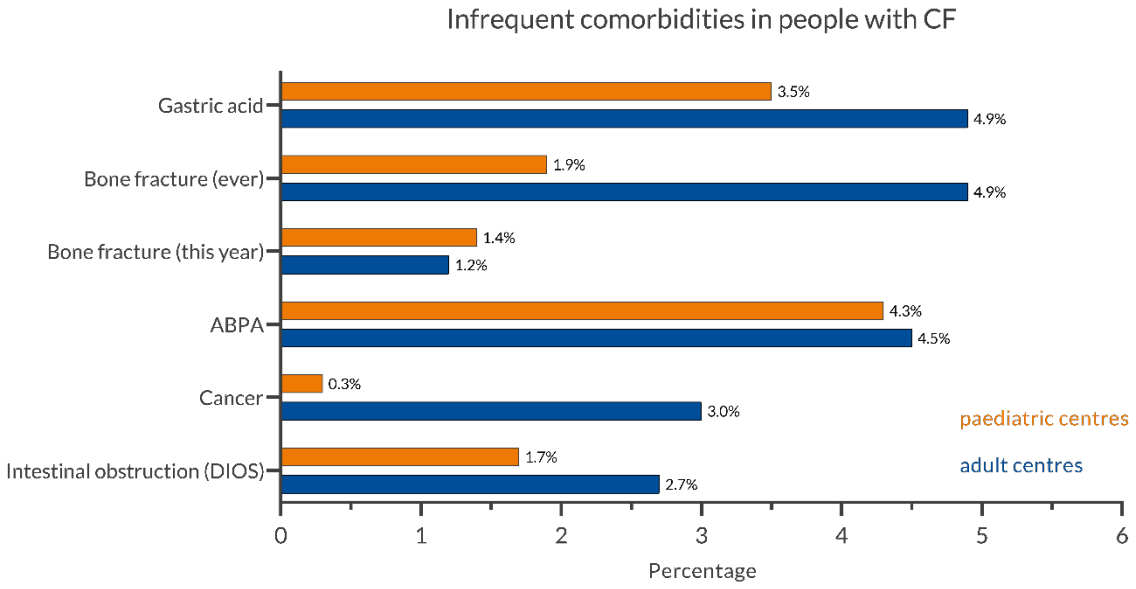

Figure 44. Infrequent comorbidities in people with CF in 2020. An ABPA is an allergic respiratory reaction to the fungus Aspergillus fumigatus (allergic bronchopulmonary aspergillosis).

Four people were diagnosed with cancer in 2020. Twenty-six people had previously been diagnosed with a form of cancer, e.g. colon cancer, testicular cancer, or breast cancer. There is no one form of cancer that was much more common than the others. Cancer is mainly seen in adults. The exact number of adults and children is not given here, as the numbers are too small (and therefore too personal).

Figure 43 lists the rarest comorbidities. They occur in fewer than 20 adults or children.

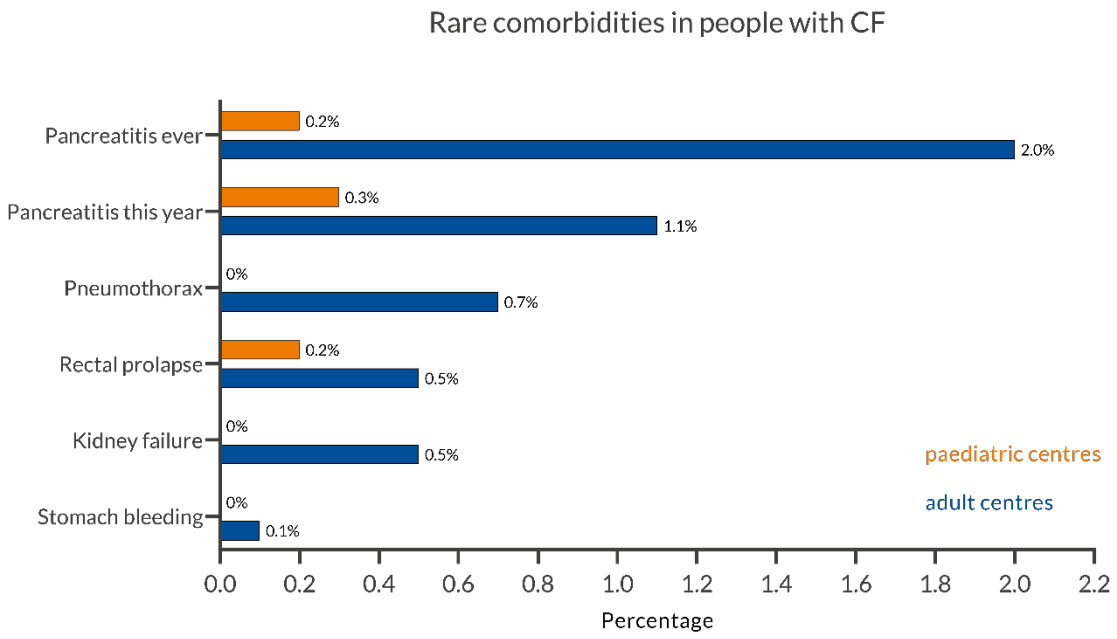

Figure 45. Rarest comorbidities in people with CF in 2020. Pancreatitis is an inflammation of the pancreas. Pneumothorax is a collapsed lung. Rectal prolapse means that a piece of bowel protrudes from the anus.

11. Work and family

For people with CF, studying and/or working is not automatically a given. This chapter shows how many people with CF are employed or are, on the other hand, unable to work. There is also information here about the number of pregnancies in women with CF. The Registry only used data for people with CF who receive treatment at an adult centre and who have not had a lung transplant. An additional requirement was that they had contact with a CF centre (in person or by telephone) in 2020.

a. Work and social life

A total of 862 adults with CF, who have not had a lung transplant, were seen at one of the hospitals in 2020. More than half of the people with CF have a job, and work from home or elsewhere. This percentage is up compared to 2019 (Figure 44). More than 15% of adults are in school or go to college or university. Fifteen percent of adults with CF are unable to work. What is notable, is that more men than women have jobs. It is important to note that volunteer work is not included in the Registry. This means that this is a limited representation of the percentage of people with CF who play an active role in society.

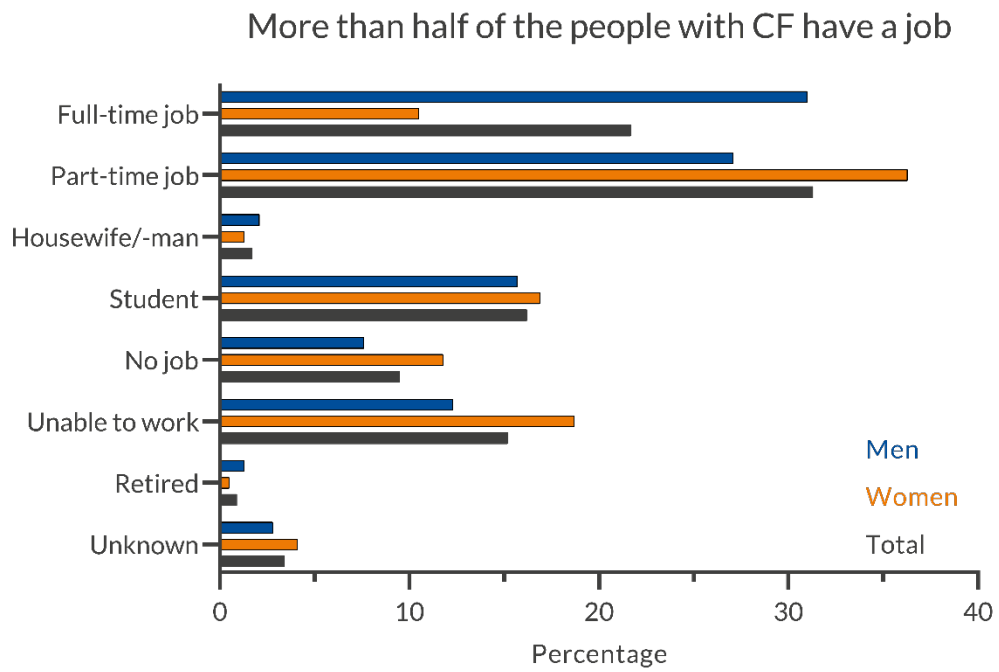

Figure 46. Social roles of people with CF in 2020.

b. Pregnancies

In 2020, 18 women were pregnant, out of 391 adult women with CF (who have not had a lung transplant). In total, since the Registry started, 99 pregnancies have been recorded. These resulted in the birth of 85 live and viable babies; the other cases ended in a miscarriage or abortion.

12. People who had a lung transplant

For the first time, there is a chapter with data on people who have CF *and* who had a lung transplant. In previous years, data was lacking for a large number of people in this group, which meant that their data could not be analysed as a group.

This chapter includes data from people who have CF *and* who had a lung transplant. They were also seen at a centre at least once this year. The Registry contains data for 107 adults, And there are at least 20 more people for whom no data is available.

a. Through the years

Figure 45 shows how many people with CF received new lungs each year. Since 2009, four or more people with CF had a lung transplant every year. Of those who have had multiple lung transplants (a handful receive donor lungs more than once), only the most recent transplant year was used.

Half of them were older than 32 years of age; the other half were younger. The youngest recipient was 8 years old, the oldest 60 years old.

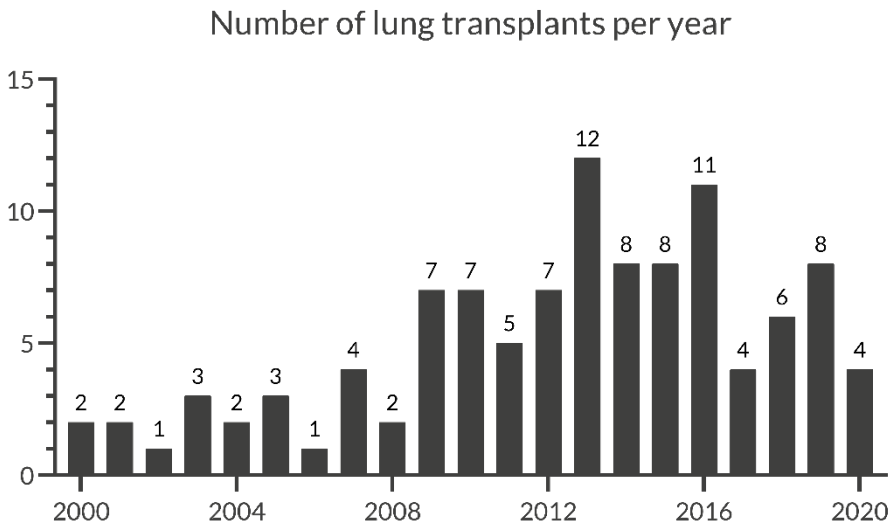

Figure 47. Lung transplants in people with CF, shown by year. Some people received new lungs more than once, the most recent year is given.

b. Demographics

Of the 107 people with CF who had a lung transplant, 58.9% were male. Four people received new lungs in 2020. Six people died in 2020.

Figure 46 shows that most people have at least one F508del mutation: 88.7%.

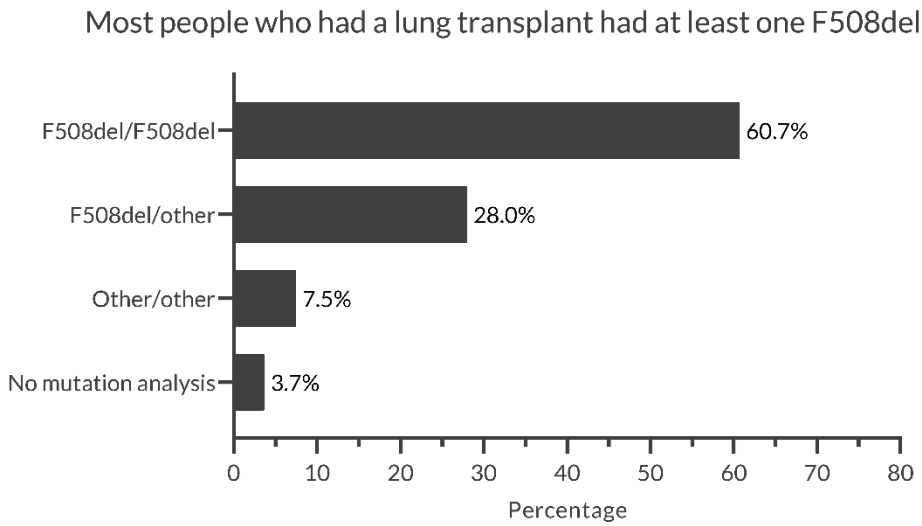

Figure 48. Mutation distribution in people with CF who had a lung transplant.

Of all the people with CF who received a new lung, half were between 30 and 41 years old (Figure 47). Almost a quarter of them was 48 years or older. There is a difference in age between men and women: half of them men were over 39.7 years old in 2020. For women, the median value is a bit lower, namely 34.2 years.

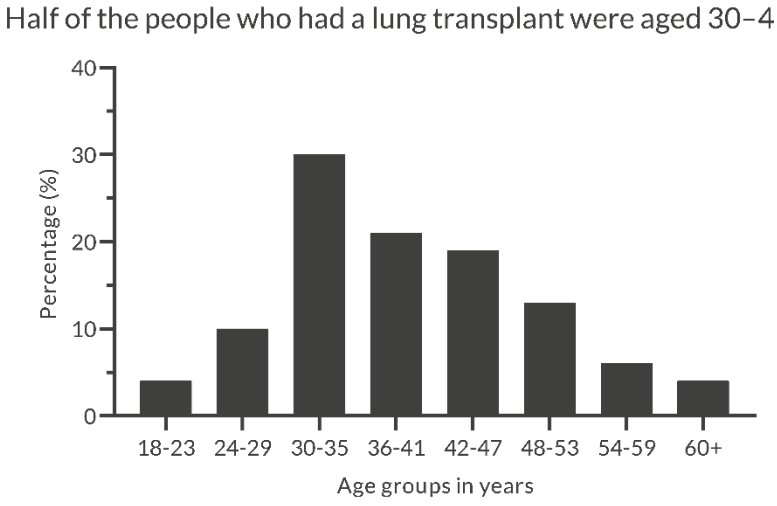

Figure 49. Age distribution for people with CF who had a lung transplant in 2020. The age is given in 6-year brackets.

c. Medication

Nearly all lung transplant recipients used pancreatic enzymes, according to the data for 2020 (Figure 48). More than 30% required nutritional supplements; in the group of people with CF who did not have a lung transplant, this was about 40%. In the lung transplant group, most of these supplements were nutritional drinks.

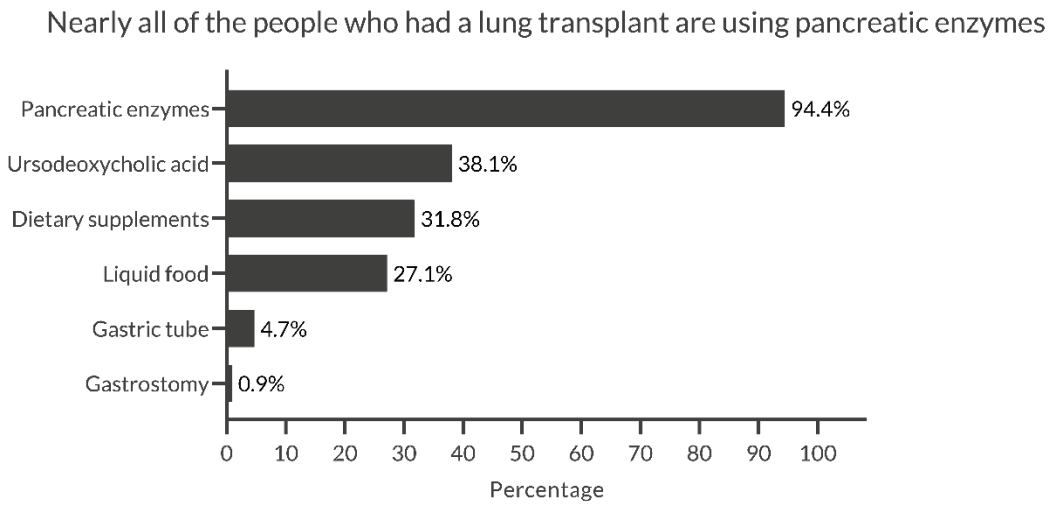

Figure 50. Treatment of gastrointestinal problems in people with CF who had a lung transplant in 2020.

d. Comorbidities

People with CF who had a lung transplant often have comorbidities (as do people with CF who have not had a lung transplant). Nearly 80% of all lung transplant recipients have diabetes (Figure 49). Osteoporosis is also common, as are bone weakness and liver disease.

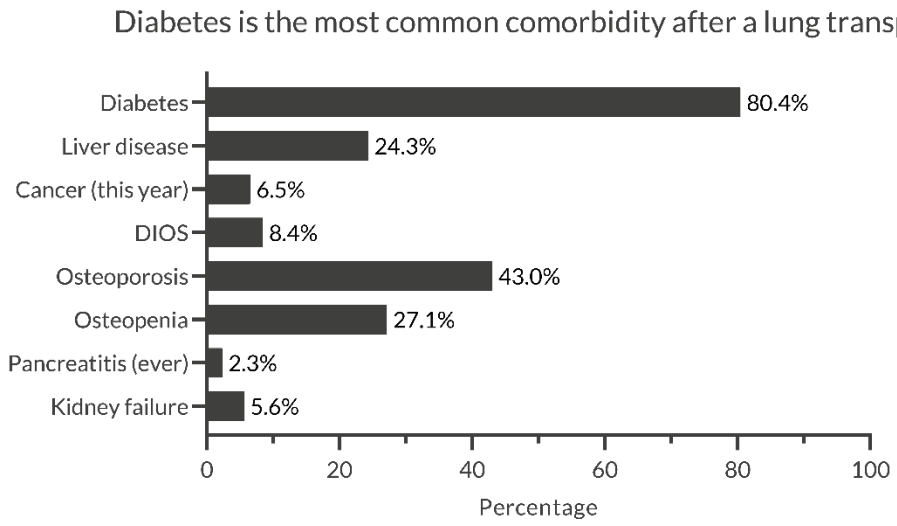

Figure 51. Comorbidities in people with CF who had a lung transplant, according to the data for 2020. DIOS is a severe intestinal obstruction.

e. Height and weight

Most of the women who had a lung transplant have a normal BMI (Figure 50). Less than 10% of the women have a lower or higher BMI than normal. For the men, more than a quarter have a BMI that is not within the normal range. Half of the women have a BMI higher than 20.9. For the men, that median value is 22.2.

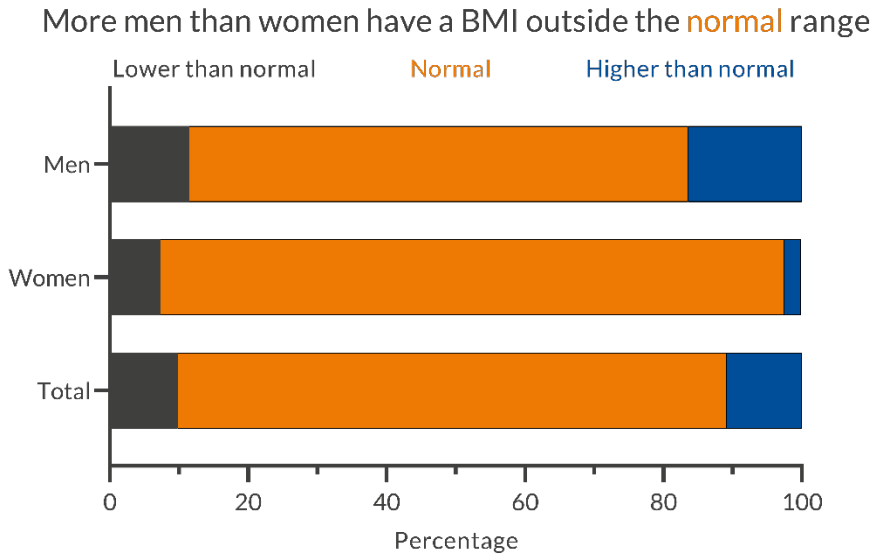

Figure 52. BMI for men and women with CF who had a lung transplant, divided into three groups. A normal BMI in the range 18.5 to 25.

f. Pulmonary function

The best pulmonary function (FEV1% predicted) in 2020 was recorded for 94 people. The women, as a group, had a better pulmonary function than the men. Half of the women had a pulmonary function higher than 80.9%. For the men, the median value was 78.2%.

A few people had a pulmonary function below 40% (FEV1% predicted, Figure 51). More women than men had a normal pulmonary function of 90% or higher.

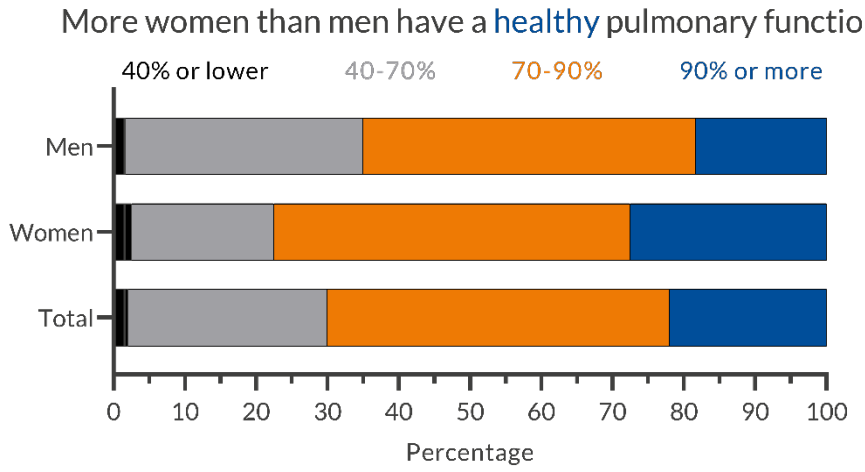

Figure 53. Pulmonary function for men and women with CF who had a lung transplant in 2020, divided into three groups.

g. Other types of transplants

Some people with a lung transplant have also received other organs. In the whole group, three people had a liver transplant, three had a kidney transplant, and one person received an unknown organ.

13. Over-50s and CF

More and more people with CF live beyond the age of 50. There are 133 over-50s with CF who were seen at the treating hospital according to the data for 2020. Of those 133 people, 19 have had a lung transplant. They are not included in this chapter.

a. Age and mutations by centre

The Registry contains data for 114 people with CF, who have not had a lung transplant, aged 50 years or older. Most people are 50-59 years old, a third are 60 years old or older (Figure 52).

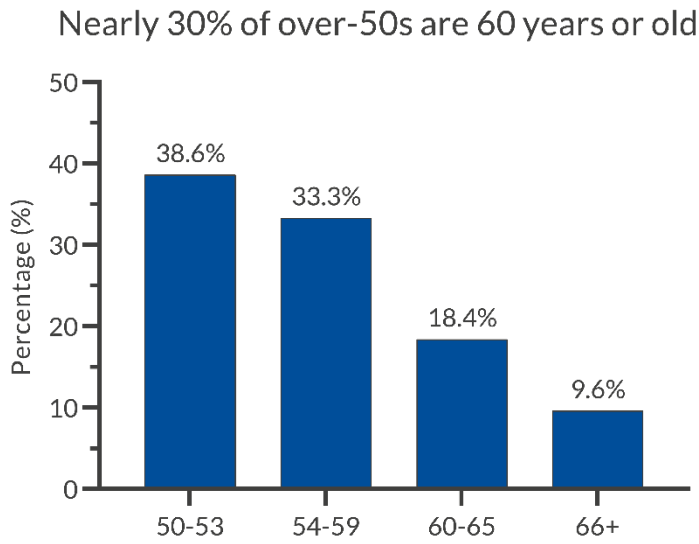

Figure 54. Age distribution of people with CF, who have not had a lung transplant, and who are aged 50 years or older (in 2020).

The mutation combination F508del/F508del is less common in people over 50 (about 20%, Figure 53) than in the whole group of people with CF in the Netherlands (more than 50%, Chapter 3 CF and mutations, page 14). Still, 84.3% of the over-50s have at least one F508del mutation.

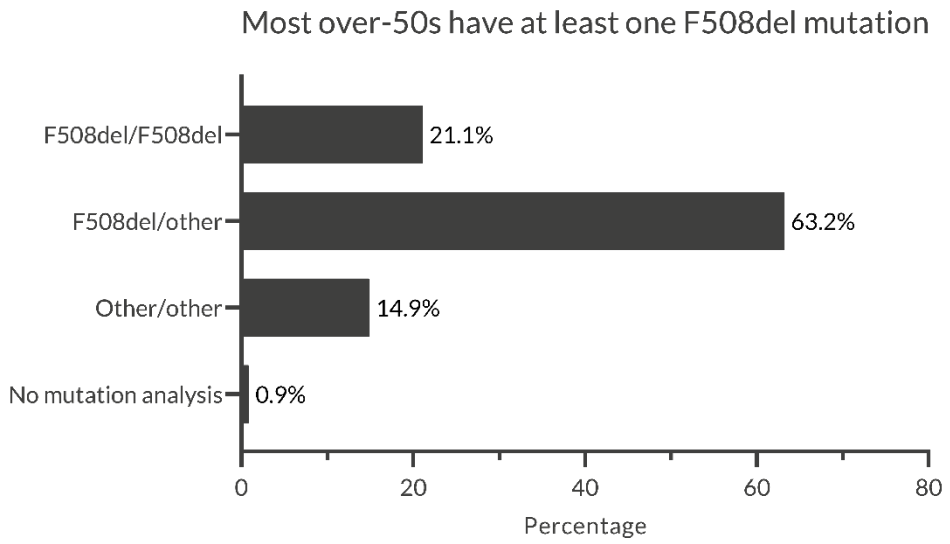

Figure 55. Mutation distribution in the over-50s with CF in 2020.

The CF centres at The Hague and Nijmegen treat the most people over 50 with CF, who have not had a lung transplant (Figure 54).

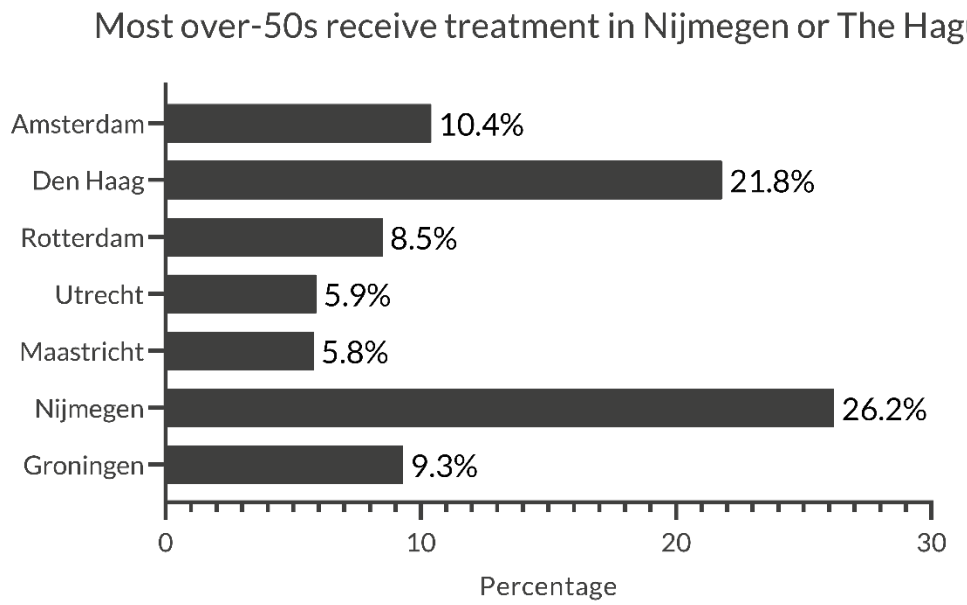

Figure 56. Percentage of over-50s by CF centre in 2020.

b. Pulmonary function

Half of those over 50 have a pulmonary function higher than 65.4%. The differences between men and women are minimal.

The largest group of people over 50 have a pulmonary function that falls into the 40–70% category (Figure 55). 18.1% have a healthy pulmonary function of 90% or higher.

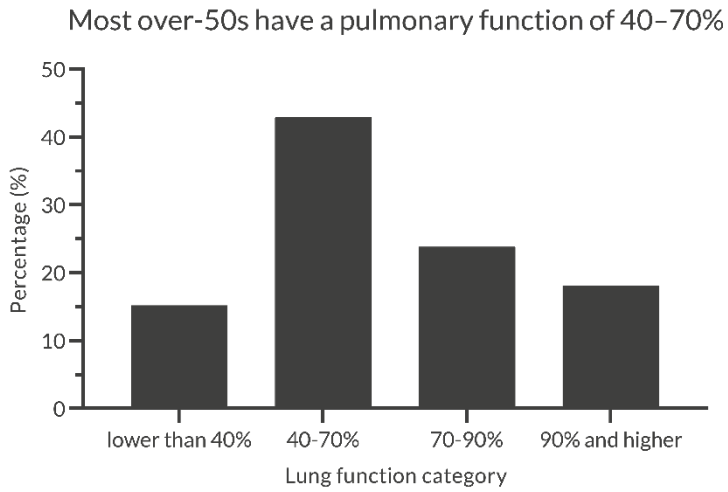

Figure 57. Pulmonary function in the over-50s with CF in 2020 who have not had a lung transplant, by pulmonary function group.

c. BMI

The BMI for the over-50s is relatively high. The median value is 23.3, which means that half of the people have a BMI higher than 23.3. The other half have a lower BMI.

Figure 56 shows that more than a third of over-50s are overweight: they have a BMI higher than the maximum normal value of 25.

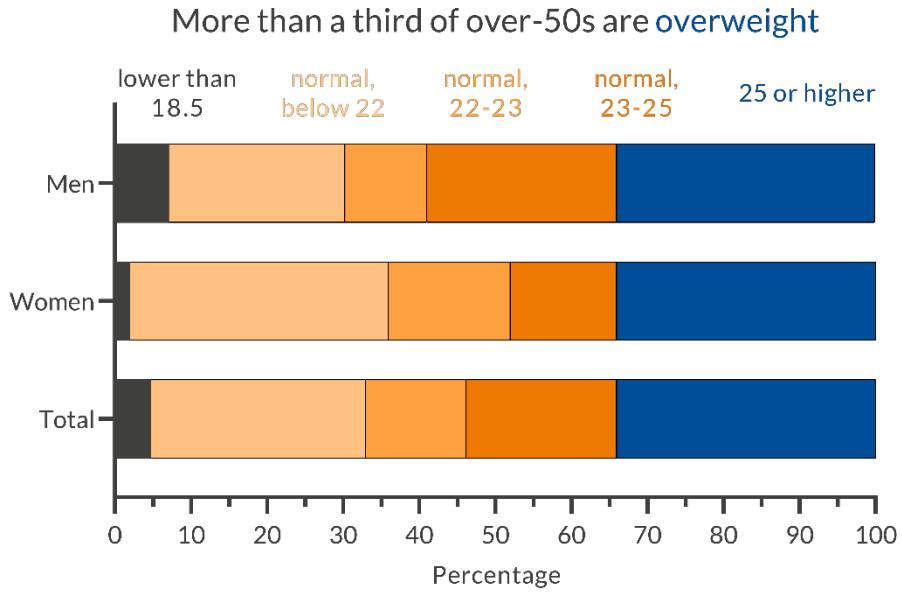

Figure 58. BMI groups for the over-50s with CF in 2020.

d. Treatment, comorbidities

Half of over-50s use pancreatic enzymes (Figure 57). This is a lower percentage than for the whole group of people with CF in the Netherlands (about 80%, Figure 21). Other characteristics of this group are also listed in Figure 57.

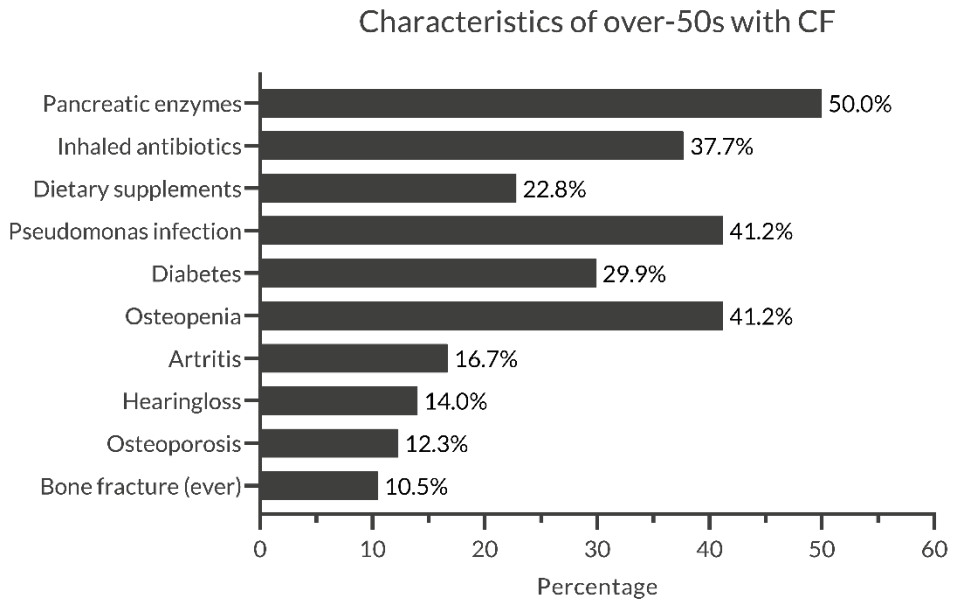

Figure 59. Various characteristics of the group of 50+ with CF in 2020 who have not had a lung transplant. Treatment, infections, and comorbidities are shown in percentages.

e. Employment

Many over-50s engage in social activities (Figure 58). A quarter of them work full-time, and another quarter work part-time. However, a quarter are unable to work and 7% are retired. A few people are stay-at-home parents.

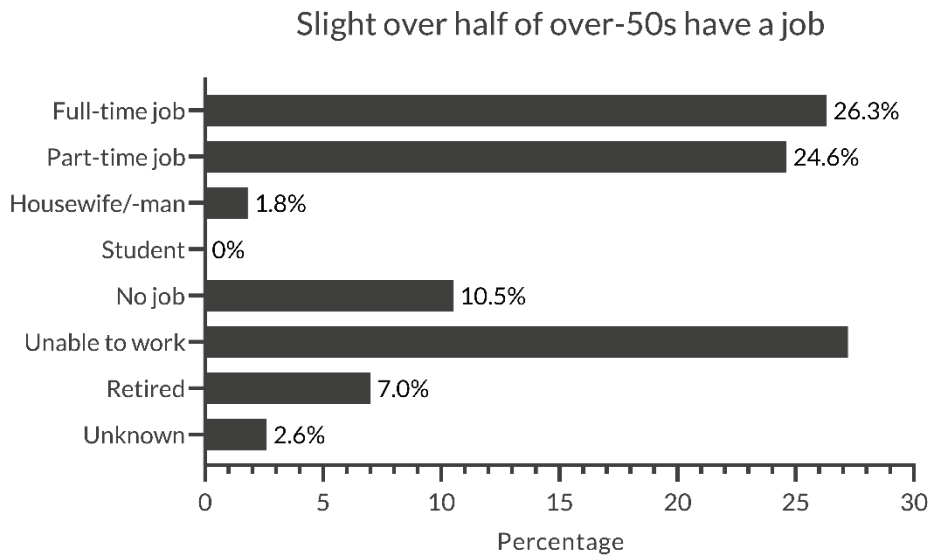

Figure 60. Social roles of over-50s with CF in 2020.

14. Quality of care

Quality of care is an important issue. For many years, data has been collected for the Dutch CF Registry to be able to reflect the quality of care provided by the CF centres.

This chapter presents a dataset that has been analysed for many years. This year the Registry Steering Group has arrived at an expansion of the set of characteristics to provide information on the quality of care. The reason behind this change is that the health of people with CF has improved, especially for the younger generation. It does not seem necessary for everyone to visit a CF centre four times a year (this is one of the characteristics from the old dataset). In addition, it became clear in 2020 that care can often also be provided remotely as well.

In this chapter, various characteristics are broken down by CF centre. The information here is based on data for people with a confirmed CF diagnosis, who have not had a lung transplant. They must also have been seen throughout the year (meaning they did not transfer to another CF centre or come in later after being diagnosed). In total, the Registry has data for 1,383 people. Additional conditions apply to pulmonary function measurements and the glucose tolerance test.

One of the characteristics in the dataset is how often people with CF visit the outpatient clinic. Most people (88.4%) visited the clinic at least three times in 2020 (Figure 59). Of the children, 90.7% visited the clinic three or more times, for the adults this was 87%.

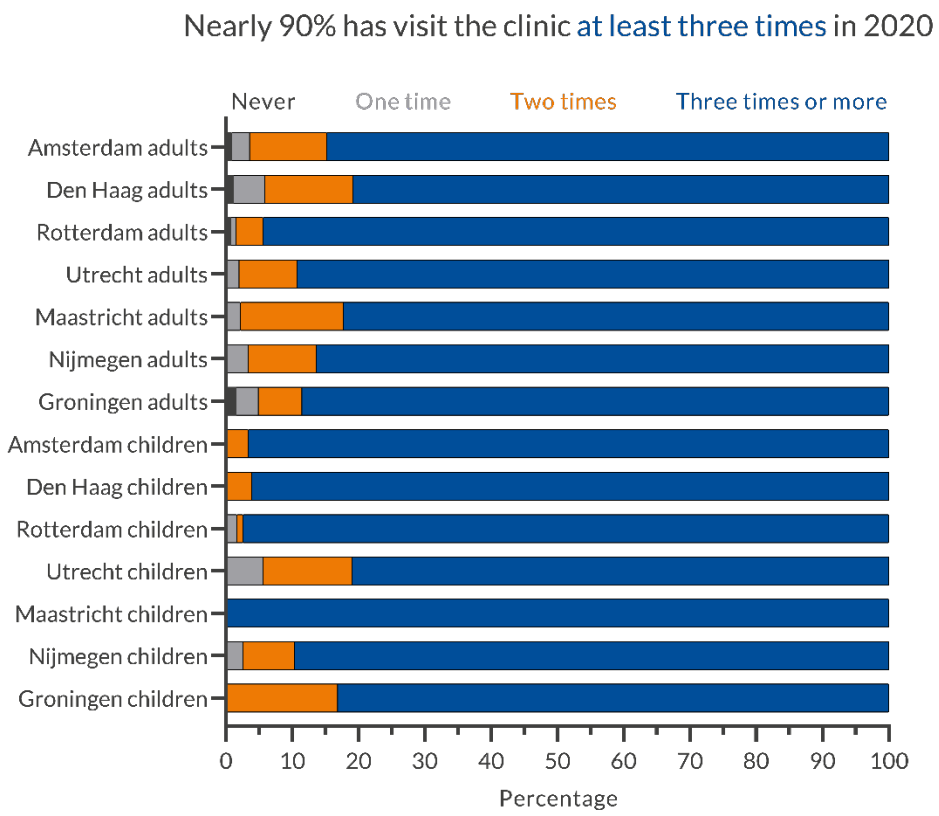

Figure 61. Number of visits to the outpatient clinic in 2020 by people with CF, who have not had a lung transplant, by paediatric/adult centre.

An outpatient visit often includes a sputum test. This culture is used to see what bacteria and fungi grow in the lungs of a person with CF. Figure 60 shows how often this was done per CF centre. Overall, 66.7% of people had at least three sputum cultures taken in 2020. The differences between children and adults are significant: 87.2% of children had three or more sputum cultures taken, while or the adults, this was 53.6%.

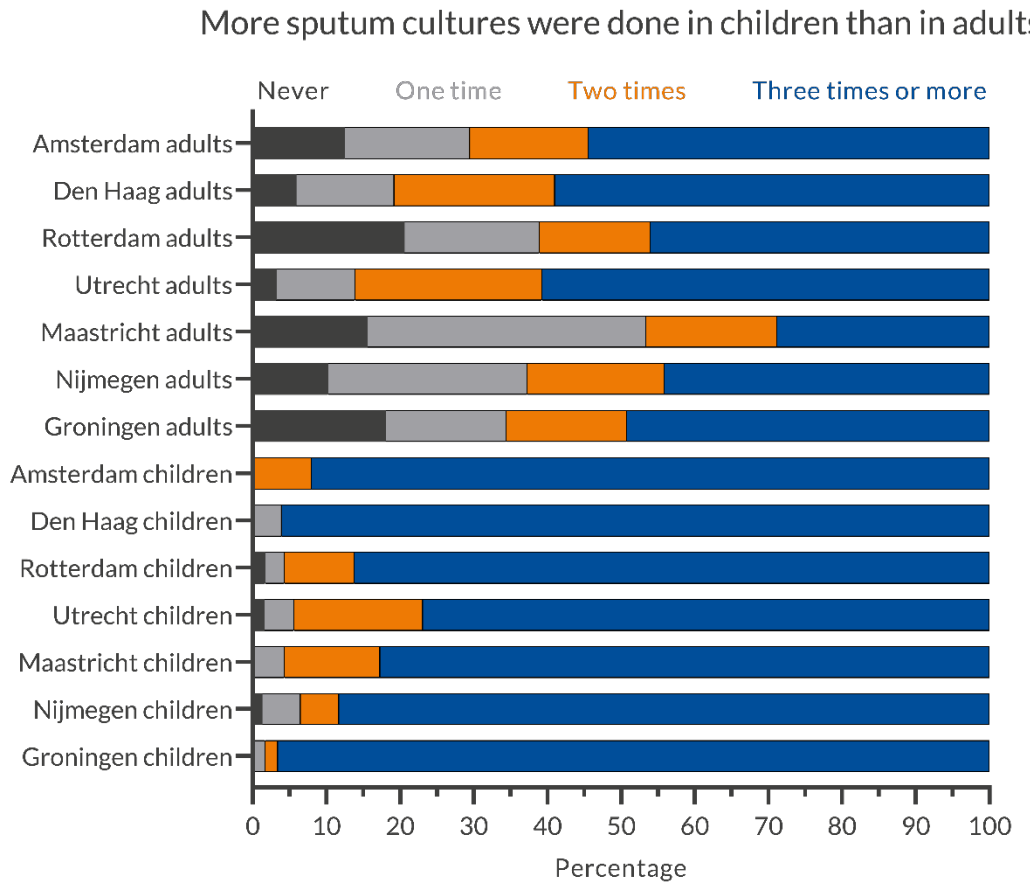

Figure 62. Number of sputum cultures at CF centres in 2020 for people with CF, who have not had a lung transplant, by paediatric/adult centre.

Another measure of the quality of care is how often a pulmonary function measurement was taken (FEV1 measurement). In 2020, nearly all people with CF, aged six years and older, were given a device to measure their pulmonary function at home. That data was not recorded. Figure 61 shows the pulmonary function measurements taken at CF centres. The Registry contains data for 1,282 people.

Almost everyone had at least one pulmonary function measurement done at a CF centre in 2020 (96.2%). The remaining people have not had any measurements done at the hospital. 61.0% of people had three or more pulmonary function measurements done. The differences between children and adults are significant. 83.8% of children had three or more pulmonary function measurements done at the hospital. For adults, this was less than half: 49.9%.

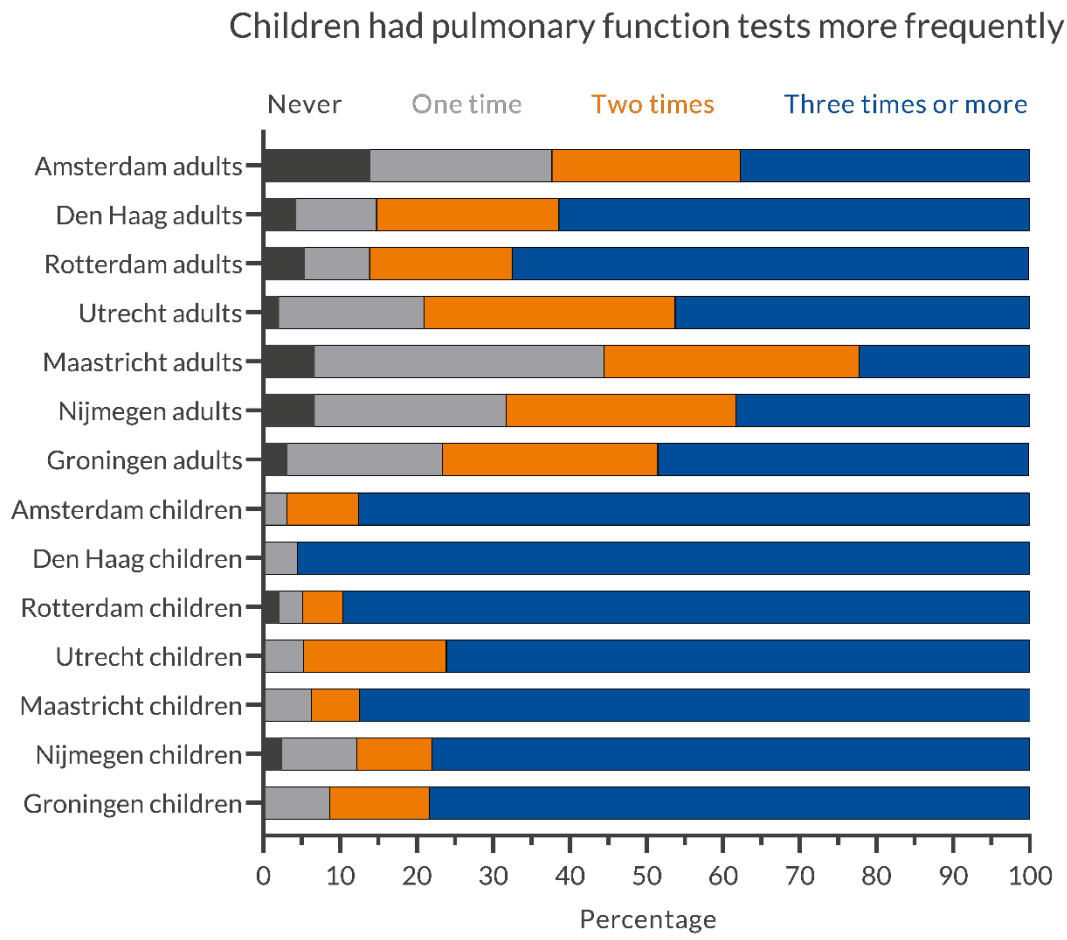

Figure 63. Number of pulmonary function measurements at CF centres in 2020 for people with CF, who have not had a lung transplant, by paediatric/adult centre.

The glucose tolerance test is performed every year, by appointment. This test checks to see if someone is developing diabetes. The test is not done on all people with CF, but on a subset of the group: anyone who uses pancreatic enzymes, who is at least ten years old and who does not have CF-related diabetes.

In 2020, 558 people with CF were eligible for the glucose tolerance test. Figure 62 shows the percentage of people per CF centre who have taken such a test. Almost half of people (49.1%) took the test in 2020. More children than adults took the test: 69.9% compared to 40.3%.

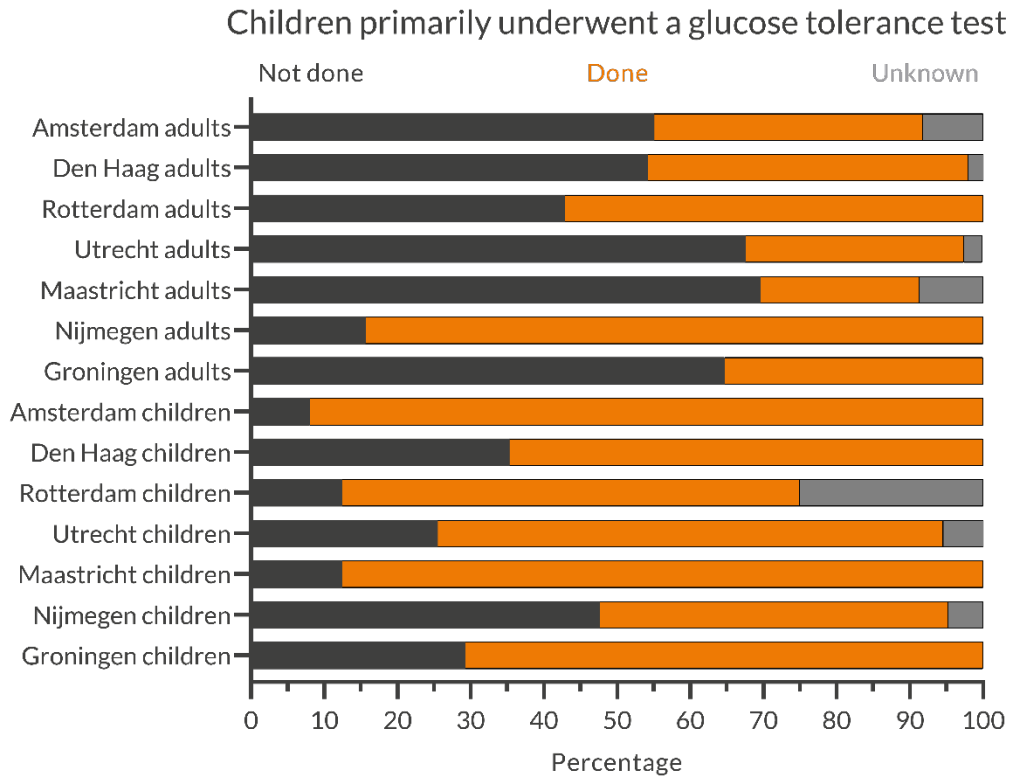

Figure 64. Glucose tolerance test in 2020 for people with CF, who have not had a lung transplant, by paediatric/adult centre.

The course of the median FEV1% predicted over the past three years is shown in Table 3 per centre. The course differs per centre in terms of decrease or improvement and in the degree of change. In most cases the differences are small.

Table 3. Median FEV1% predicted by centre from 2018-2020.

Centre	2018	2019	2020
Amsterdam adults	72.4	74.4	74.0
Den Haag adults	71.0	72.0	72.2
Rotterdam adults	72.9	72.7	71.3
Utrecht adults	71.9	72.7	71.2
Maastricht adults	66.1	68.4	64.5
Nijmegen adults	70.8	69.7	68.4
Groningen adults	65.0	66.4	64.1
Amsterdam children	95.1	95.7	95.7
Den Haag children	99.6	95.0	94.1
Rotterdam children	91.8	98.9	97.6
Utrecht children	92.7	90.3	90.8
Maastricht children	95.1	89.4	88.1
Nijmegen children	92.4	93.1	90.8
Groningen children	93.6	95.2	94.6

Another way to gather information on the quality of care is based on the height-to-weight ratio of people with CF at a centre. For this purpose, the BMI is calculated. For children, the BMI is then converted relative to peers without CF of the same gender and with a similar ethnic background. Table 4 shows that an increased number of centres have a median value around 0 (for children) and around 22 (for adults).

Table 4. Distribution of Z-score for the BMI by paediatric centre and BMI per adult centre from 2018-2020. The Z-score is a child's BMI relative to peers of the same gender and ethnic background without CF. Normal values are between -2 and 2. The median value is the midpoint of a distribution, with half of the children/adults above this value and the other half below. Yellow are the values above 0 (for children) or above 22 (for adults), with higher values being darker yellow. Values around 0 or 22 are white. All values below 0 or 22 are red, with lower values being darker red.

	Paediatric centres (sdsBMI)			Adult centres (BMI)		
	2018	2019	2020	2018	2019	2020
Amsterdam	0.10	0.05	0.15	22.8	22.6	22.2
Den Haag	0.11	0.07	0.09	21.8	22.1	22.2
Groningen	0.01	0.25	0.13	22.9	22.6	23.0
Maastricht	-0.10	0.02	-0.08	21.6	21.7	22.1
Nijmegen	0.14	0.11	0.04	21.6	22.1	22.4
Rotterdam	-0.11	-0.10	-0.04	22.0	21.8	21.9
Utrecht	-0.01	0.07	0.07	21.8	21.9	21.9

Annex 1. Methods

For this report, seven CF centres collected the medical data for almost all people with CF in the Netherlands. This data was then sent to the NCFS, that manages the Registry, does the calculations and prepares the report. The data is encrypted and cannot be identified or traced back to individuals by the NCFS. In total, about 160 different data or variables are collected per person. The data has been collected in this way for 10 years.

International harmonisation

Each year, a part of data from the Dutch Registry is forwarded to the European CF Society Patient Registry (ECFSPR). The European database now contains data on more than 50,000 people from 39 countries.

For years, data for people with CF has also been collected in America and Canada and on other continents. In order to compare the data properly, all countries collect the data in the same way as far as possible. For example, the highest pulmonary function value for each year (and not of the most recent visit) and the height and weight of that same day are collected. Or an infection with the *Pseudomonas* bacterium is classed as chronic/persistent if three of the four sputum cultures have come back positive.

Calculations

Two calculations were carried out for the data in this report, which are explained below:

1. Pulmonary function: the centres entered the highest value per person of all the measurements done in 2020. The relationship between the data and the reference group with international reference values was then examined (Global Lung Initiative 2012).
2. The height and weight of children were converted to Z-scores in order to be able to combine the different age groups (and boys and girls). These Z-scores were calculated using the Growth Analyser programme of the Foundation for Child and Growth [Stichting Kind en Groei] in Rotterdam. The reference values used are those of the Dutch, Turkish and Moroccan populations from the last national study carried out in 2010.

The analyses were done using IBM SPSS Statistics version 25 and GraphPad Prism version 9.

Terms used

This report makes use of and explains various terms:

- The median value is the middle value (midpoint) of all values in a distribution. Half of the people have a higher value and the other half has a lower value than the median value. The average value is calculated differently: the sum of all values is divided by the total number of values in a distribution.
- Z-score: In some cases, the pulmonary function and heigh-weight values are converted to Z-scores to correct for age and gender. A Z-score of 0 means an average value and 95% of healthy children in the Netherlands have a Z-score between -2 and 2. A Z-score lower than -2 or higher than 2 is considered to be strongly deviating.

Abbreviations

The abbreviations used in this report are explained again here.

- ABPA is an allergic respiratory reaction to the fungus *Aspergillus fumigatus*, and stands for allergic bronchopulmonary aspergillosis.
- BMI stands for body mass index, and says something about the ratio of weight to height: the weight (in kilograms) is divided by the height squared (in metres).
- CF is short for cystic fibrosis.
- DIOS stands for distal intestinal obstruction syndrome, a severe obstruction of the last part of the small intestine.
- FEV1% predicted is a measure of the pulmonary function. The FEV1 is the amount of air a person can expel in one second (Forced Expiratory Volume in the first (1) second). This value is displayed in litres. In order to be able to compare the values of people with CF with peers of the same height and gender without a lung disease, the volumes are converted into percentages. These percentages are called FEV1% predicted, often abbreviated to FEV1%.

Annex 2. Registry Steering Group

Representatives of all seven CF centres and the NCFS together form the Dutch CF Registry Steering Group. The Steering Group determines the policy of the Registry and determines which data will be included in the Registry, in consultation with the European CF Registry. The results are discussed each year to improve CF care in the Netherlands.

Steering Group

NCFS

Drs. J.J. Noordhoek-van der Staay, director NCFS, chair of the Steering Group

Dr. V.A.M. Gulmans, Head of Research and Quality of Care NCFS, secretary of the Steering Group

Dr. D.D. Zomer-van Ommen, Co-ordinator Dutch CF Registry

CF centres

Prof. Dr. H.G.M. Heijerman, pulmonologist, UMC Utrecht

Dr. K.M. de Winter-de Groot, paediatric pulmonologist, UMC Utrecht

Dr. H.M. Janssens, paediatric pulmonologist, Erasmus MC Rotterdam

Drs. R. Hoek, pulmonologist/transplant doctor, Erasmus MC Rotterdam

Drs. R. van der Meer, pulmonologist, HagaZiekenhuis, The Hague

Dr. M. Nuijsink, paediatric pulmonologist, HagaZiekenhuis, The Hague

Dr. J. Altenbrug, pulmonologist, Amsterdam UMC

Dr. S.W.J. Terheggen-Lagro, paediatric pulmonologist, Amsterdam UMC

Dr. H. van der Vaart, pulmonologist, UMC Groningen

Prof. Dr. G.H. Koppelman, paediatric pulmonologist, UMC Groningen

Dr. P.J.F.M. Merkus, paediatric pulmonologist, Radboud UMC Nijmegen

Dr. J.J.E. Hendriks, paediatric pulmonologist, Maastricht UMC (until February 2021)

Drs. L.H. Conemans, pulmonologist, Maastricht UMC (from February 2021)

Drs. M.A.G.E. Bannier, pulmonologist, Maastricht UMC (from February 2021)

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