Dutch Cystic Fibrosis Registry

Data on people with cystic fibrosis in the Netherlands

Annual report for 2019

Published in 2020

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NEDERLANDSE CYSTIC FIBROSIS STICHTING

Foreword

This online report of the Dutch CF Registry for 2019 has been realised with the cooperation of almost all people with Cystic Fibrosis (CF) and the efforts of many people working in the seven CF centres and at the Dutch Cystic Fibrosis Foundation (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.

The summary is shown as an infographic.

This report also presents the information for each centre separately and at a national level. It also includes information on indicators which are related to 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 pulmonary specialists, pulmonary specialists, paediatric gastroenterologists and paediatric nutritionists. At these meetings, the treatment, results and differences between the centres are discussed in an open and positive atmosphere, and points for improvement are determined.

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

The joint ambition of the CF centres and the NCFS remains unchanged: better care that results in a better and longer life for people with CF.

September 2020

Jacquelien Noordhoek, chair of the steering group of the Dutch CF Registry

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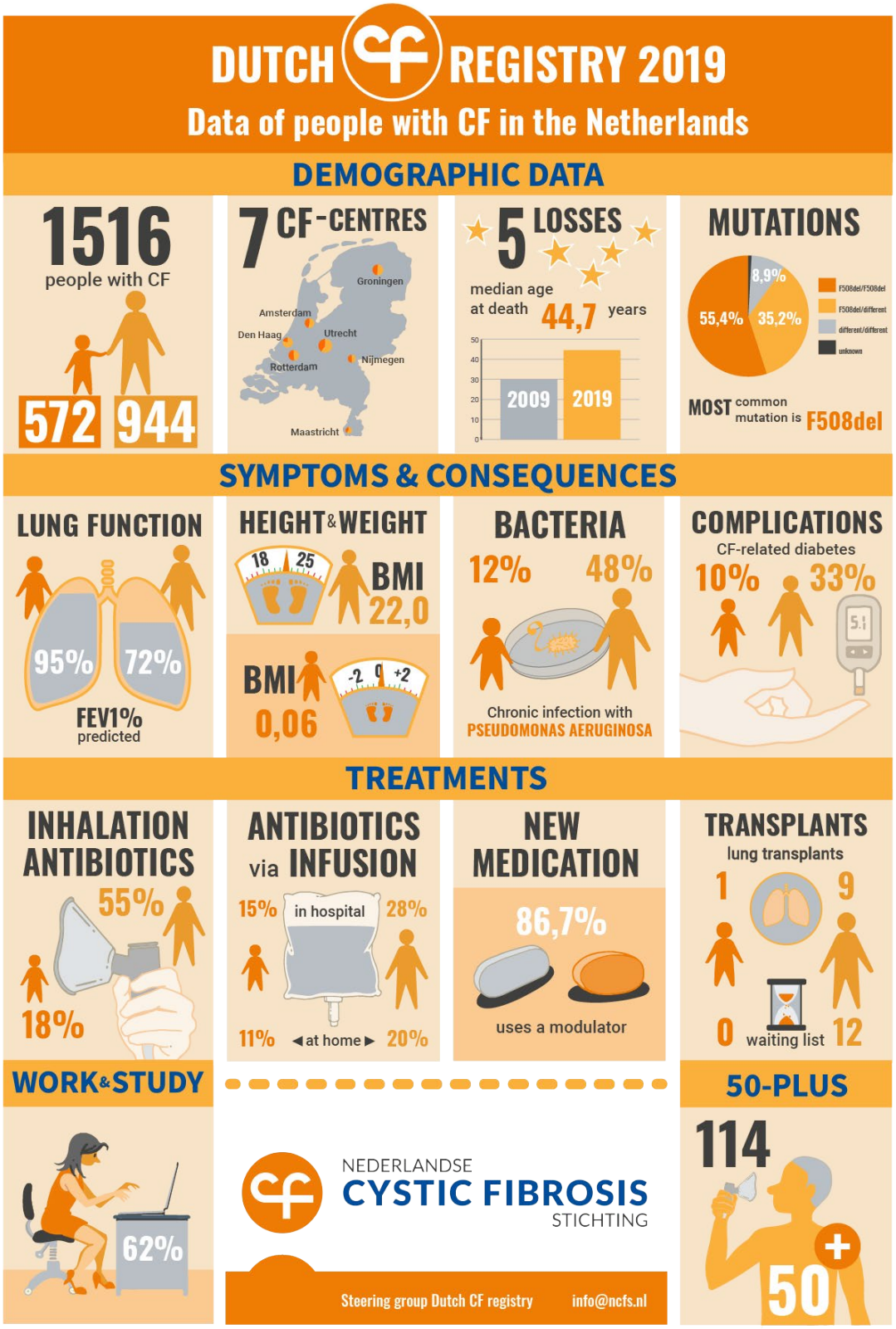
1. Summary


DUTCH REGISTRY 2019
Data of people with CF in the Netherlands
DEMOGRAPHIC DATA
1516
people with CF
572
944
7 CF-CENTRES
Groningen
Amsterdam
Den Haag
Utrecht
Nijmegen
Rotterdam
Maastricht
5 LOSSES
median age at death 44,7 years
50
40
30
20
10
0
2009
2019
MUTATIONS
8,9%
55,4%
35,2%
F508del/F508del
F508del/different
different/different
unknown
MOST common mutation is F508del
SYMPTOMS & CONSEQUENCES
LUNG FUNCTION
95%
72%
FEV1% predicted
HEIGHT & WEIGHT
18
25
BMI 22,0
BMI 0,06
-2
0
+2
BACTERIA
12%
48%
Chronic infection with PSEUDOMONAS AERUGINOSA
COMPLICATIONS
CF-related diabetes
10%
33%
5:1
TREATMENTS
INHALATION ANTIBIOTICS
55%
18%
ANTIBIOTICS via INFUSION
15%
in hospital
28%
11%
◄at home►
20%
NEW MEDICATION
86,7%
uses a modulator
TRANSPLANTS
lung transplants
1
9
0
waiting list
12
WORK & STUDY
62%
50-PLUS
114
50
NEDERLANDSE CYSTIC FIBROSIS STICHTING
Steering group Dutch CF registry
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2. Demographic data

How many people with CF and CF-related disease are there in the Netherlands? What is the age distribution? How many hospitals provide specialist CF care? These and other demographic characteristics are described in this chapter.

The demographic data include all people who were registered in the Dutch CF Registry in 2019. These are people with CF, but also people with CF-related disease (i.e. without a confirmed CF diagnosis) or people who have undergone a lung transplant.

Want to know more about CF? Go to the NCFS website.

The numbers

In 2019, data of 1,581 people was included in the Dutch CF Registry (Figure 1). We know that 81 people did not want their data to be included in the database. This means that the Registry covers 95% of the people who visit one of the seven CF centres for treatment. There may still be a very small number of people who do not visit a CF centre for care or treatment.

In 2018, we saw a temporary dip in the number of people who made their data available for the Registry, because a large number of people had not signed the consent form at the time the data were provided. In 2019, this problem was solved for the adults, but in the case of the children a few dozens consent forms were not signed yet.

Of the 1,581 people in the database in 2019, 1,516 have a confirmed CF diagnosis (the dot in Figure 1), namely 572 children and 944 adults. Every year, the number of adults goes up, but not the number of children.

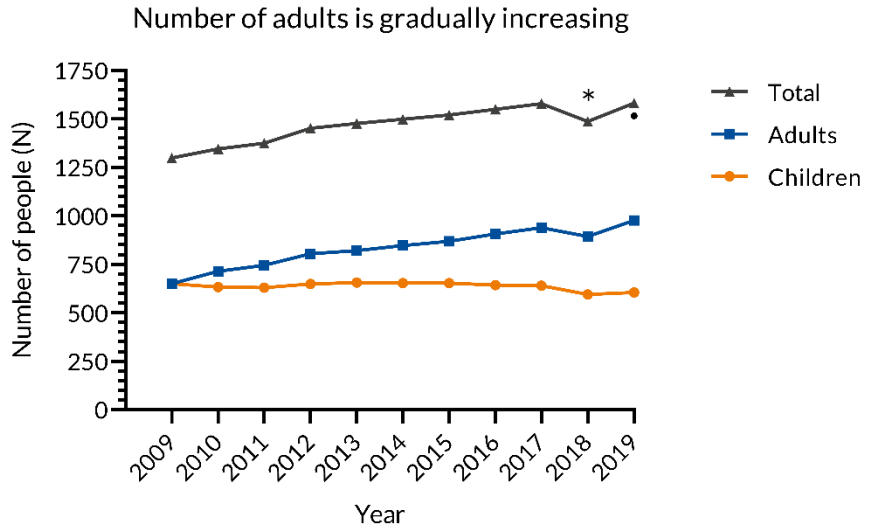

*Figure 1: Number of people in the Dutch CF Registry since 2009. In 2019, there were 1,581 people who gave permission for their data to be included in this database. Dot: the number of people in 2019 with a confirmed CF diagnosis (1,516). * In 2018, data on fewer people were included in the Registry because of problems with the (re)signing of consent forms.*

The distribution of the number of men and women in the Registry has been fairly stable for years: there are slightly more men (53.5%) than women (46.5%).

The Registry also includes a group of people without a confirmed CF diagnosis but who are receiving treatment at a CF centre. First of all, there is a group of children with CFSPID (a positive result on the heel prick screening, but no definitive CF diagnosis). Some of these children could develop CF in the

future. In addition, there is a group of adults with one or more symptoms that are consistent with CF, but whose CF diagnosis cannot be confirmed by two known CF mutations or a positive sweat test. These people do not have CF, but a so-called CF-related disease.

Age

The average age of people with CF or a CF-related disease continues to go up and was 24.5 years in 2019 (Figure 2). The median age is almost 23 years (22.8), which means that half of the people are younger than 22.8 years and the other half are older. The median age has gone up by almost five years in a period of ten years.

If we only look at the group of people with a confirmed CF diagnosis, the values are about the same: an average of 24.4 years and a median age of 22.9 years.

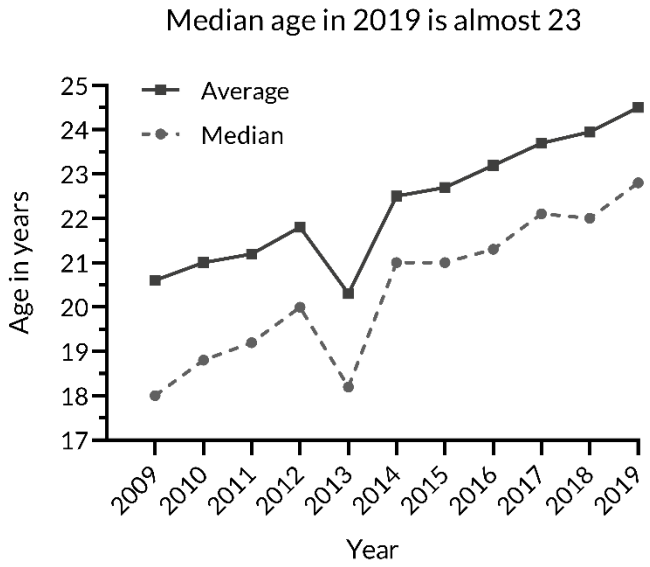

Figure 2: Average and median age of the people in the Dutch CF Registry since 2009. Median: half of the people are younger, half of the people are older. In 2019, the average age was 24.5 and the median age 22.8.

Figure 3 shows the number of people of a certain age. Only people with a confirmed CF diagnosis are included in this diagram. This diagram shows that a quarter of people with CF are 12 years or younger. Three-quarters of people are 33 years or younger.

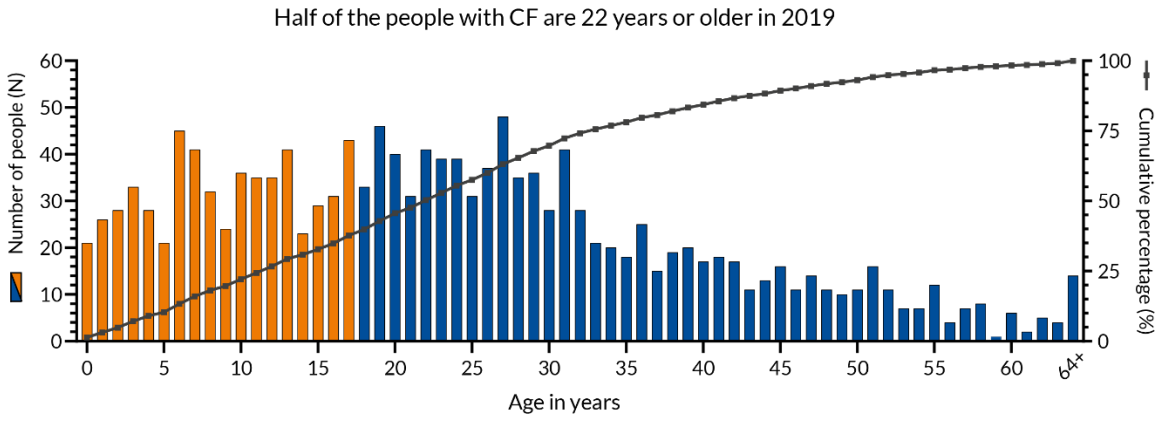

Figure 3: Ages of people with CF in 2019. Bars: the number of people by age (left axis), dotted line and right axis: percentage of people up to a certain age compared to the total group.

Deaths

Unfortunately, people with CF die every year. In 2019, five adults died but, for the first time since the start of the Dutch CF Registry, no children died (Figure 4). The median age of those who died was 44.7 years.

Since 2014, no more than 15 people have died each year, and in the last three years this dropped to less than 10 per year. We hope that this downward trend will continue.

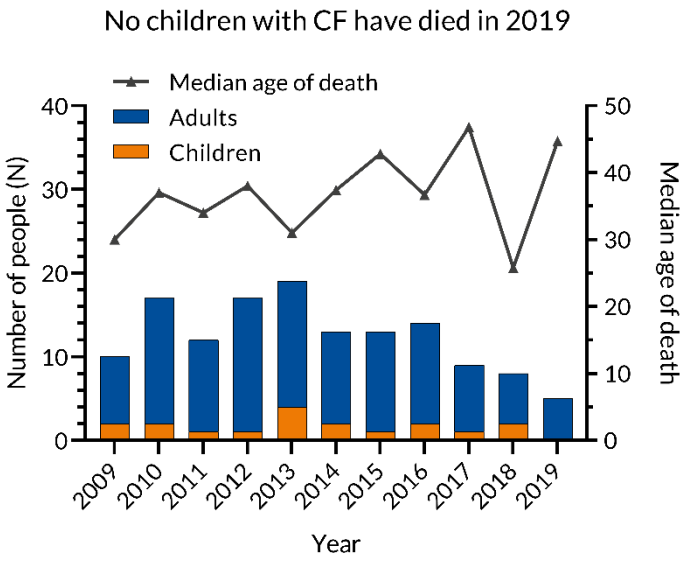

Figure 4: Number of people who have died since 2009. The bars indicate on the left axis how many people have died each year. The line above them shows the median age of death per year, indicated on the right axis. Median age of death: the age of death is lower for half of the people and higher for the other half of the people. Due to the ever decreasing numbers, the median age of death can vary greatly from year to year, as was the case in 2018.

CF centres

There are seven hospitals in the Netherlands that provide CF care to both children and adults. Figure 5 shows where the hospitals are located and how many children and adults were treated for CF or CF-related disease in 2019. Table 1 shows how many people have been treated at these hospitals in recent years.

Figure 5: Location of hospitals in the Netherlands that provide care and treatment of people with CF or CF-related disease. The number of children and adults under treatment in 2019 is specified by location.

Table 1. People treated at each CF centre. All people who signed consent forms for the Registry are included in this table, regardless of whether their CF diagnosis was confirmed or not.
**In 2018, the number of participants in the CF Registry was temporarily lower due to unsigned consent forms.*

	2014	2015	2016	2017	2018	2019
UMC Utrecht						
Children	206	196	190	191	158	146
Adults	231	245	260	281	251	308
Erasmus MC Rotterdam						
Children	149	143	140	149	135	141
Adults	121	120	139	138	122	134
HagaZiekenhuis (the Hague)						
Children	55	63	59	55	55	52
Adults	210	210	217	215	200	204
Amsterdam UMC						
Children	102	105	104	100	104	102
Adults	100	106	109	116	118	121
UMC Groningen						
Children	69	73	74	72	65	67
Adults	88	84	83	80	83	90
Radboud UMC Nijmegen						
Children	47	49	52	58	67	73
Adults	50	57	56	56	57	64
Maastricht UMC						
Children	34	28	26	27	29	28
Adults	37	42	40	40	43	51
TOTAL	**1499**	**1521**	**1549**	**1578**	**1487***	**1581**

3. Diagnosis

How many children are born with CF each year? What symptoms are seen and what is the role of the heel prick screening? What about CF and mutations? All these questions are addressed in this chapter on diagnosis. Therefore, this chapter will only use data from people with a confirmed CF diagnosis, whether or not they have had a lung transplant.

The diagnosis of CF can be made in different ways and at different moments during a person's life. It can be done before the birth, immediately after birth or in the first weeks or months. But it also happens that people do not find out that they have CF until they reach adulthood. Want to find out more? Read more on the website.

In the period 2014-2018, an average of 27 children with CF were born each year (Figure 6). In 2019, as far as is known in the Registry, 15 children were born with CF. This number is likely to increase if children are born in the last weeks of the year and diagnosed in the first few weeks of 2020, and because the signing of the Registry consent forms is sometimes delayed.

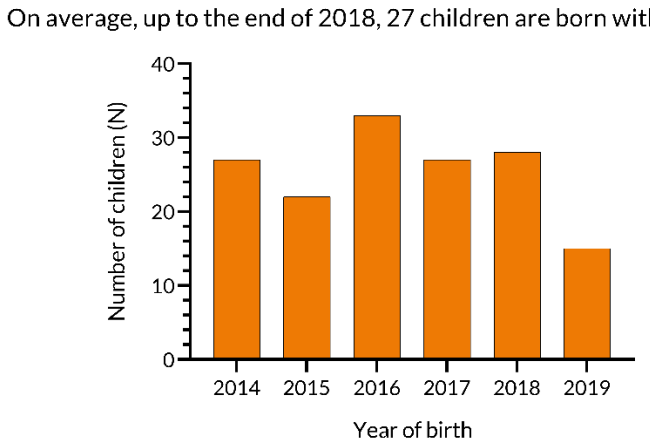

Figure 6: Number of children born with CF since 2014.

Symptoms at the time of diagnosis

Before the heel prick screening for CF was introduced, the diagnosis of CF was usually made on the basis of a number of symptoms. The Registry keeps a record of the symptoms that were seen at the time of diagnosis. Especially for children, we have very good records of this information.

In some cases there are already indications during pregnancy that the baby has CF because of abnormalities found during prenatal screening. Immediately after birth, it can also be clearly apparent, if a baby has *meconium ileus*. Meconium is the first (black) stool that a baby excretes in the first days after birth. In some babies, this meconium is so concentrated that it gets stuck (*meconium ileus*) and sometimes has to be surgically removed. In most cases, this is caused by CF.

Figure 7 summarises for all children with CF which of the most common symptoms were seen at the time of diagnosis. Not all children showed symptoms before the diagnosis, some did not yet show any symptoms, while the heel prick screening did indicate that they have CF.

Problems with growth and nutrition are most common at the time of diagnosis: these are seen in almost half of all children with CF. Respiratory complaints are also often reported.

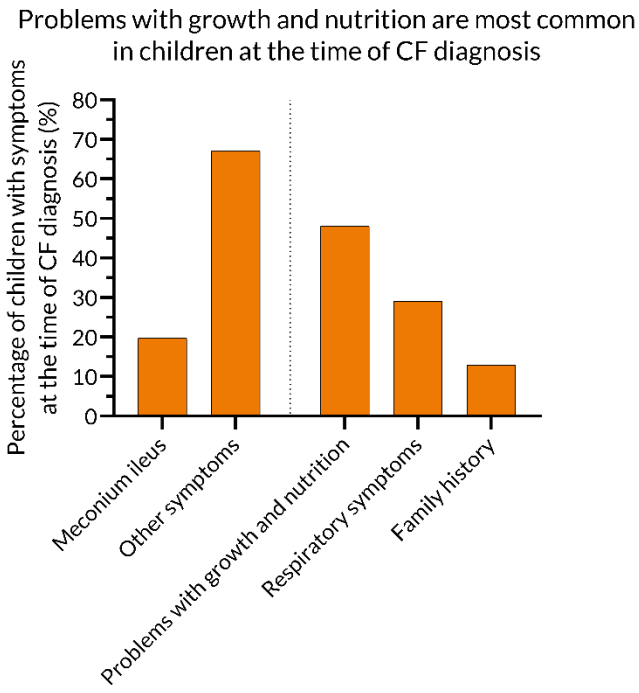

Figure 7: Symptoms children with CF have at the time of diagnosis. After the dotted line, the most common symptoms (other than meconium ileus) are specified.

There are some symptoms that are seen in only 2-5% of children that are diagnosed with CF:

- A deficiency or excess of electrolytes such as calcium, magnesium, chloride or bicarbonate is seen in 5.2% of children at the time of diagnosis;
- Liver problems in 4.5%;
- Abnormalities in prenatal screening in 4.5%;
- Nasal polyps or sinusitis in 3.1% of children with CF;
- Rectal prolapse (a piece of rectum protrudes from the anus) in 1.9%.

Heel prick screening

Since 2011, in principle, all new-borns in the Netherlands are screened for CF with the heel prick screening. Figure 8 shows, for the period 2012-2019, how many children were diagnosed with CF as a result of this screening. In 83% of children, the diagnosis of CF is made as a result of the heel prick screening. In Figure 8, 'Screening not done' means that the child did not have *meconium ileus* either. For positive, negative or unknown results of the heel prick screening, no distinction is made in whether or not *meconium ileus* occurred.

Sometimes the screening indicates that a child does not have CF, but the diagnosis is made at a later date (a so-called false-negative result). Such false results are becoming less and less common because the protocol has been amended as of April 2016. There are also a number of situations each year in which

screening is not carried out. This can be because the diagnosis of CF is known before birth, or because a baby is born with meconium ileus, clearly indicating that it has CF.

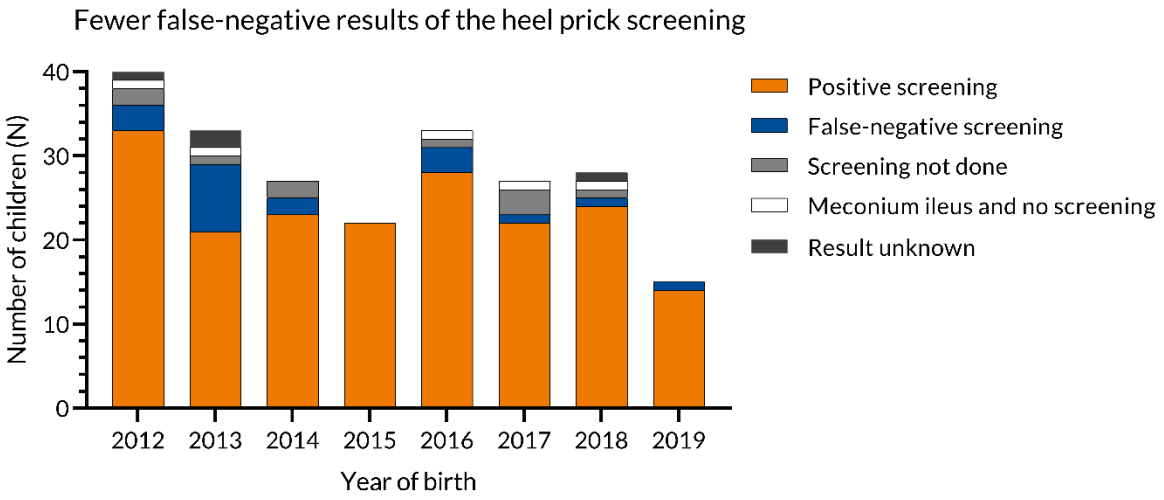

Figure 8: Number of children diagnosed with CF since 2012 by means of a heel prick screening or otherwise. Meconium ileus means that a new-born baby has an obstructed intestine. In most cases, the child will then turn out to have CF and sometimes the heel prick screening for CF will no longer be done.

In 2019, one child was missed at the heel prick screening. More children with CF may follow later whose diagnosis has been missed. This also applies to earlier years of birth, but with or without the heel prick screening, the diagnosis of CF is usually made in the first year of life; more information can be found in the section 'Age of diagnosis' in this chapter.

The symptoms at the time of diagnosis differ between children with CF diagnosed by means of a heel prick screening and children with CF identified via a different route (Figure 9). Since 2012, according to the registry, 225 children have been born with CF. Of those children, 187 had a positive heel prick screening for CF, and for 34 children the result was a false-negative, the result was unknown or no heel prick screening had been done.

Less than 5% of the children of both groups have:

- Liver problems: in 3.2% of children diagnosed with CF by means of a heel prick screening and in 2.6% of children with CF and an false-negative result or no heel prick screening;
- Rectal prolapse (in which a piece of bowel protrudes from the anus): in 1.6% of children with CF diagnosed by means of a heel prick screening and in none of the children with CF and a false-negative result or no heel prick screening.

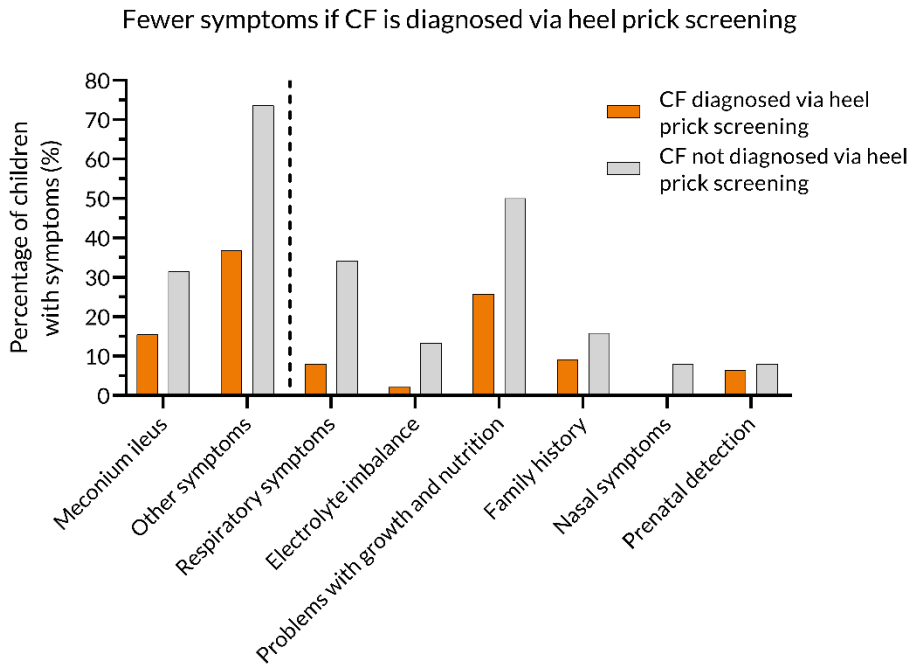

Figure 9: Symptoms in the lead-up to the CF diagnosis by means of a heel prick screening or otherwise, in children with CF born since 2012. After the dotted line, the various symptoms are specified.

Age of diagnosis

The age at which the diagnosis of CF is made varies greatly, also in the Netherlands (Figure 10). However, half of the people who were under the age of 40 in 2018 were diagnosed with CF well before their first birthday: at 0.1 years for the age group 0-19 and 0.7 years for the age group 20-39. For the group of over-40s, the age of diagnosis is much higher: half of them were younger than 12 years at the time of diagnosis.

11.8% of adults were diagnosed with CF after they reached the age of 18, with a median age of 32 years.

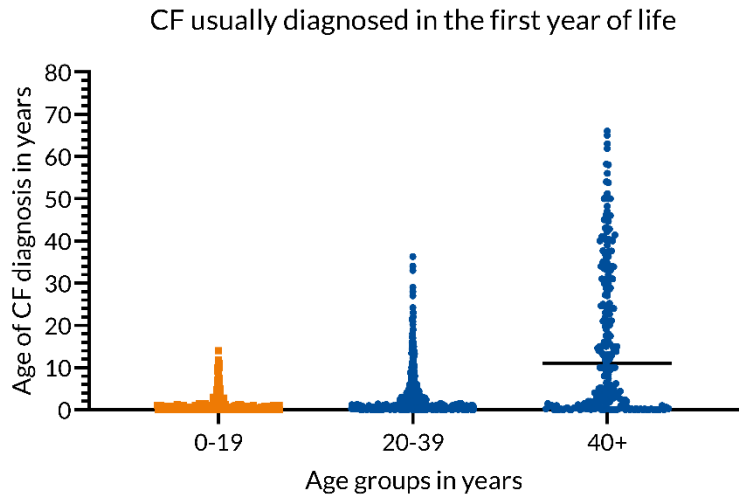

Figure 10: Age at which CF diagnosis is made, shown for three age groups. Median age of diagnosis is 0.1 years, 0.7 years and 11 years for the age groups 0-19, 20-39 and 40+, respectively.

Mutations

CF is caused by mutations in the DNA, on the CFTR gene. If both parents pass on a CFTR mutation to their child, then the child will get CF. It should be noted that not all CFTR mutations cause CF. There are more than 2,000 known mutations and at least 360 cause CF (source: cftr2.org).

The most common mutation worldwide is F508del. F508del is also the most common in the Netherlands, as can be seen in Figure 11, which shows the mutation distribution for all people with CF in 2019. 90% of all people with CF in the Netherlands have at least one F508del mutation.

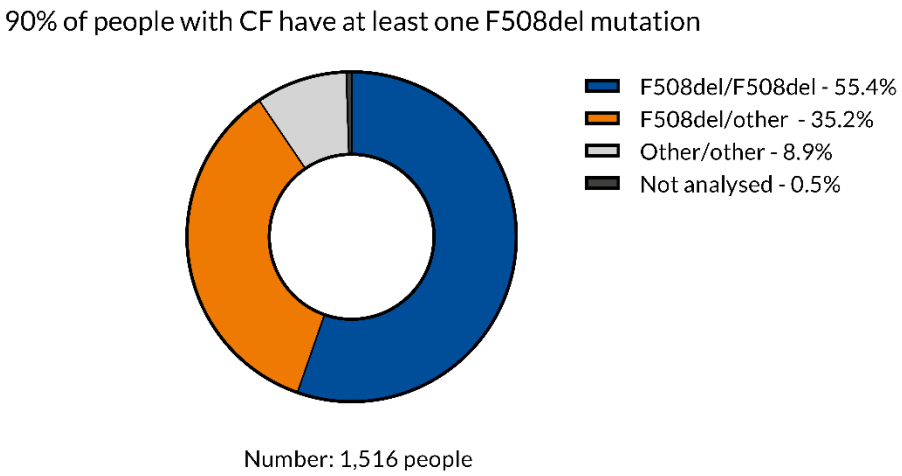

Figure 11: Mutation distribution for people with CF with F508del and/or another mutation.

Table 2 shows the most common mutations. The numbers and percentages are not calculated per person, but per allele. A gene consists of two alleles. Everyone inherits a set of alleles , one from each parent. In 2019, 1,516 people with a confirmed CF diagnosis were registered. The total of all alleles therefore results in a number that is twice as high: 3032.

The most common mutation after F508del is A455E. In other countries this is not the most common 'second mutation', which is why A455E is also called "the Dutch mutation".

Table 2. List of the fifteen most common mutations in people with CF in the Netherlands. These numbers are calculated based on the mutations of 1,516 people with CF. Because everyone with CF has a mutation on two sets of alleles (one from each parent), the total sum of the alleles is double that of the number of people: 3,032.

Mutation	Number	Percentage
F508del	2211	72.9%
A455E	122	4.0%
G542X	52	1.7%
1717-1G->A	45	1.5%
3272-26A->G	37	1.2%
S1251N	37	1.2%
R117H	36	1.2%
N1303K	33	1.1%
R1162X	32	1.1%
R553X	28	0.9%
2789+5G->A	24	0.8%
3849+10kbC->T	18	0.6%
E60X	18	0.6%
711+1G->T	14	0.5%
W1282X	14	0.5%
Unknown	25	0.8%
Not done	16	0.5%
Miscellaneous	270	8.9%
Total	3032	100.0%

For the 65 people in the Registry without a confirmed CF diagnosis (CF-related disease or CFSPID, for more information see 'The numbers'), the distribution of mutations is different again (Figure 12). Almost 60% has one F508del mutation, the rest has two other mutations or the analysis was not carried out.

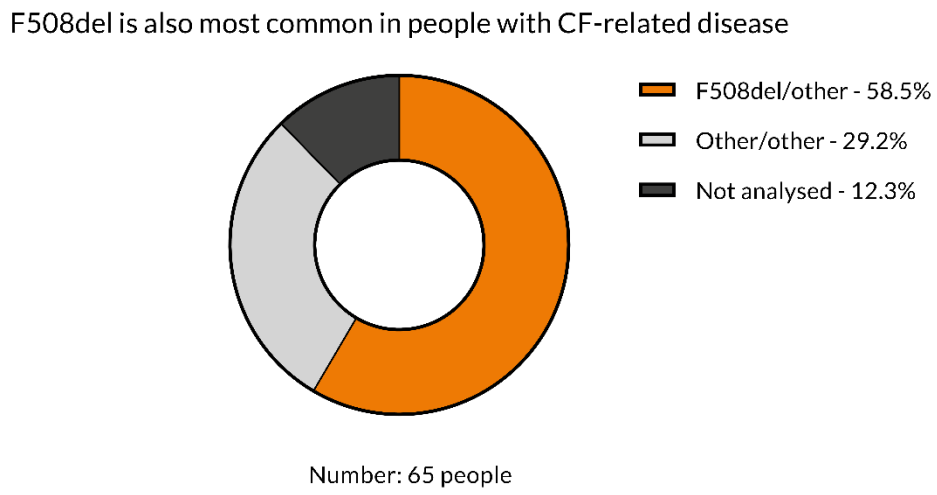

Figure 12: Mutation distribution for people with CF-related disease without a confirmed CF diagnosis.

4. Lung function

Lung function is one of the most important parameters in CF. Because of the tough mucus, the lungs, but also the nose and other parts of the respiratory tract, often suffer from (bacterial) infections and inflammation, which makes the lung function deteriorate further and further. This process has a major impact on the life expectancy of a person with CF. That is why their lung function is measured several times a year.

This chapter analyses the lung function measurements. For each person with CF, the best measurement of 2019 is included in the Registry. These measurements are compared between different age groups, between different CF centres and progression over time.

Lung function and age

From the age of six, the lung function of a person with CF is tested several times a year. The lung function is usually measured as the volume that a person can force out of their lungs in one second, the FEV1. The measurement is given as a percentage of the healthy population: peers of the same age, height and sex, without CF or other pulmonary disease. We call this the FEV1% of predicted.

Figure 13 shows the course of lung function by age group. The height of the bars indicates the median value: half of the people in that age group has a higher lung function and the other half has a lower lung function. Above the bars is the number of people used for the calculation for that age group.

Lung function deteriorates slightly with age. In childhood, the median lung function decreases from 100% to 82%. The strongest deterioration can be seen up to an age of approx. 40 years. From age 40 onwards, the deterioration in lung function is no longer as evident. This can be explained by the fact that most people between 30 and 40 years of age die or get a lung transplant around that age. The over-40s group includes people with a relatively better lung function.

Most people with CF over 65 years of age have one or two relatively mild CFTR mutations with associated high lung function.

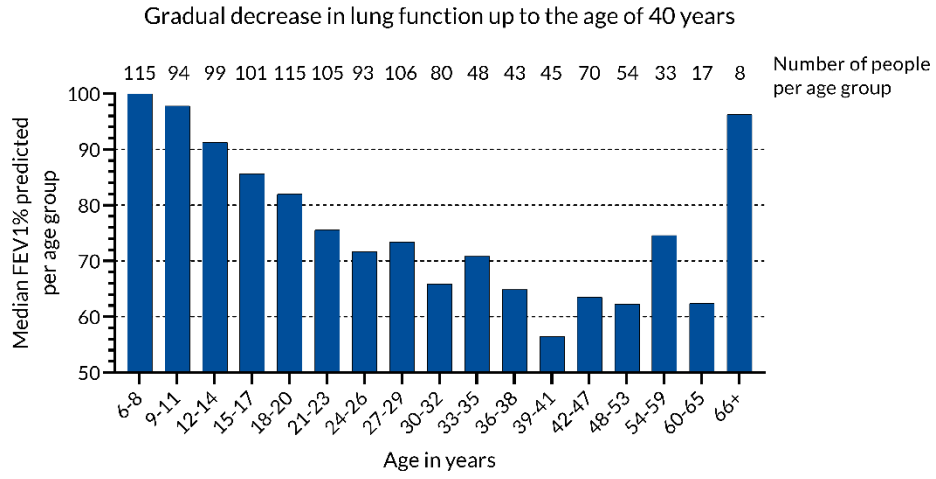

Figure 13: Lung function for people with CF in 2019, divided into three-year age brackets (up to the age of 42) or six-year age brackets (from age 42 upward). The FEV1% of predicted is a measure of lung function: the volume that a person can force out in one second, compared to their peers without CF. The median value indicates that half of the people in this age group had a higher lung function and the other half a lower lung function. Above the bars, the number of people used to calculate the value is given.

In order to have a better overview of all lung function values, the lung function values are often divided into categories, which is also done internationally. The lung function values for the period 2017-2019 are divided into four groups (see Figure 14): lower than 40%, between 40 and 70%, between 70 and 90% and higher than 90%. A lung function value of 90% or higher is considered normal.

The differences between children and adults are significant. More than half of the children had a normal lung function of at least 90% in the past years, while less than a quarter of adults had a normal lung function. The percentage of children and adults with a normal lung function is slightly higher in 2019 than in previous years.

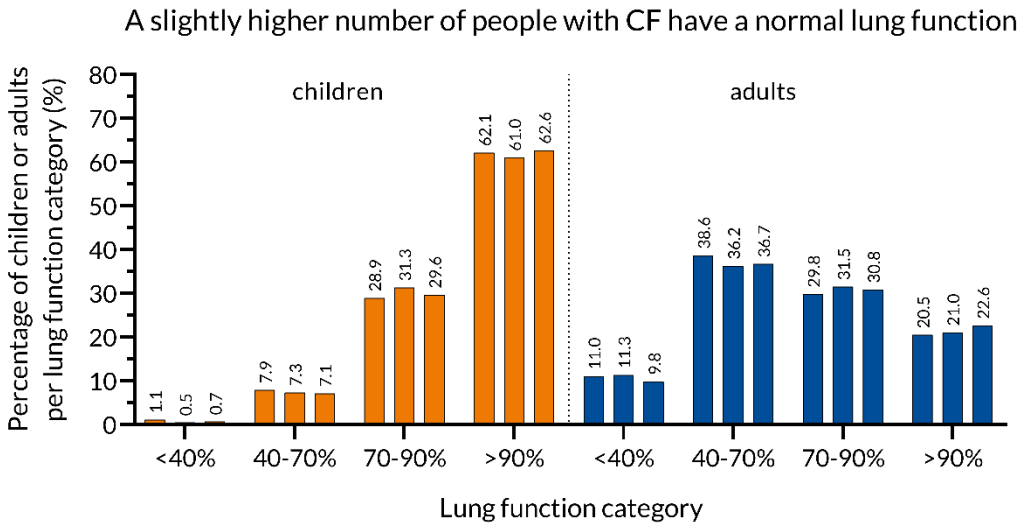

Figure 14: Pulmonary function values for children and adults in the period 2017-2019, divided into (international) categories. A pulmonary function of 90% or higher is considered normal.

Lung function per centre

Figure 15 shows the lung function values for children in the period 2017-2019. The differences in lung function values between and within CF centres are small, but the progression over time is sometimes different. One of the reasons for this difference is that a number of children move to a centre for adults every year, and a number of adults move to a different centre, for example because they move house.

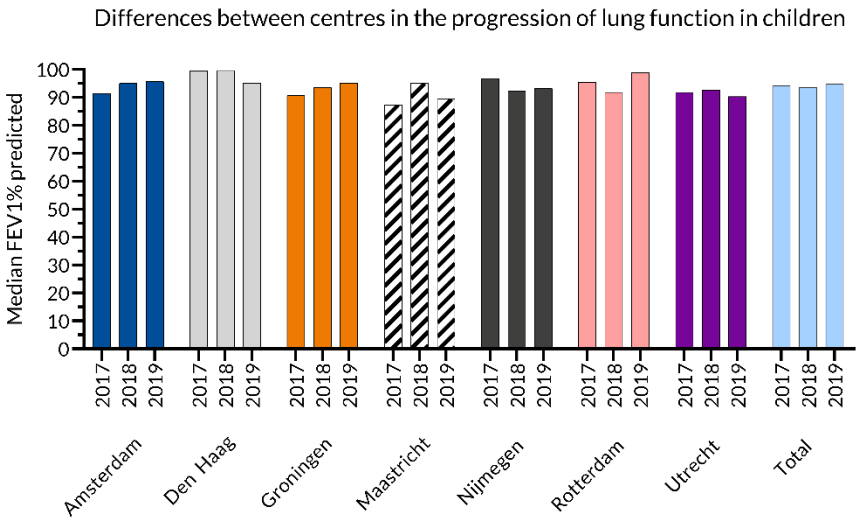

Figure 15: Lung function for children with CF in the period 2017-2019 by CF centre. The bars indicate the median value: half of the children have a higher lung function and the other half a lower lung function.

Converted to lung function categories (Figure 16), it appears that at all the centres most children have a normal lung function of 90% or higher. Some centres treat a number of children with a lung function lower than 40%.

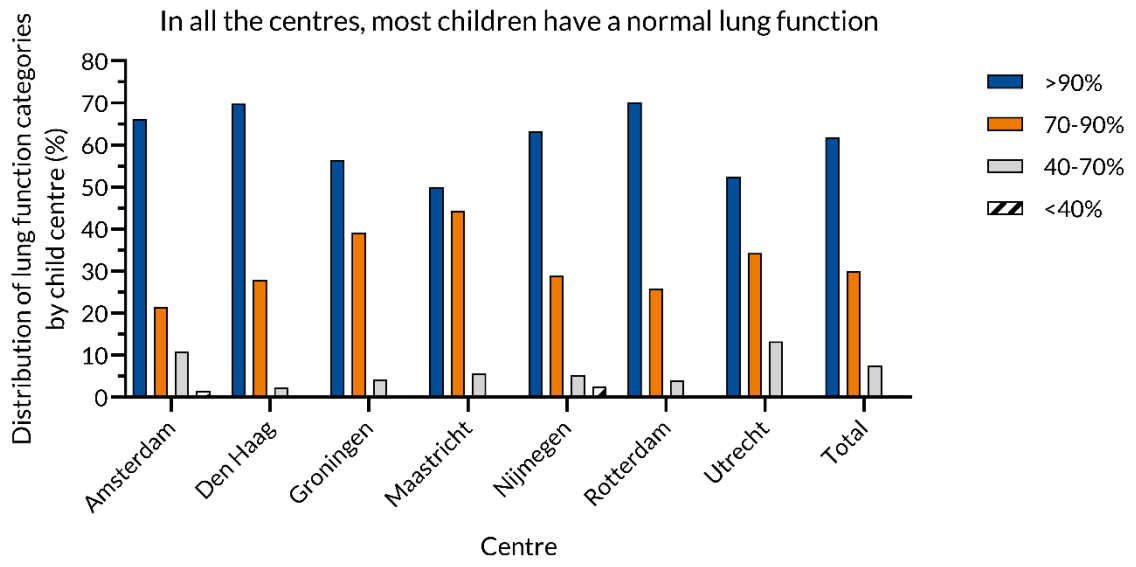

Figure 16: Lung function for children by centre in 2019, divided into (international) lung function categories. A lung function of 90% or higher is considered normal.

For the adult centres, the lung functions are much lower, as can be seen in Figure 17. Here too, the changes in the past three years have been minimal, and the median lung function is going up at most centres.

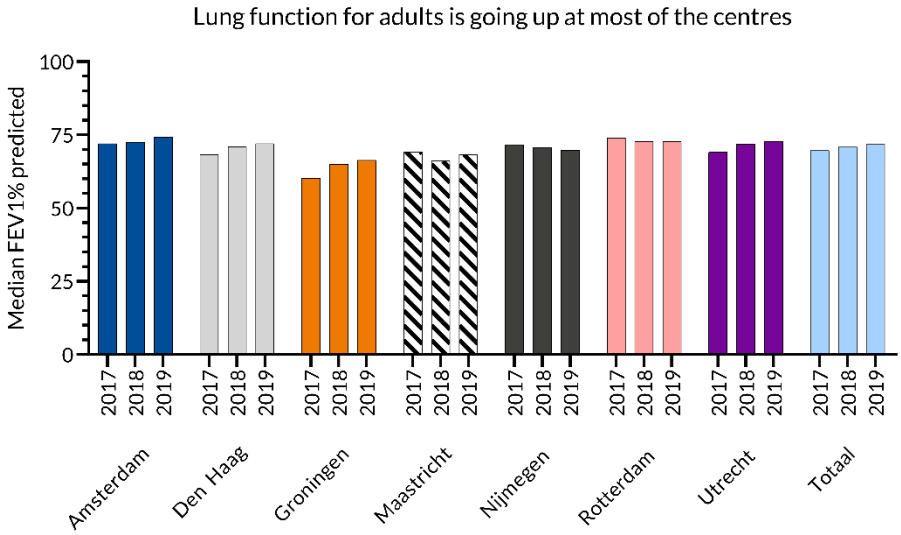

Figure 17: Lung function for adults with CF in the period 2017-2019 by CF centre. The bars indicate the median value: half of the adults have a higher lung function and the other half a lower lung function in that year (and at that centre).

Figure 18 shows the lung function values for adults divided into categories. The figure clearly shows that a lung function lower than 40% is much more common in adults than in children with CF. Here, too, the differences between the CF centres are small. At most centres, most adults have a lung function between 40 and 70%.

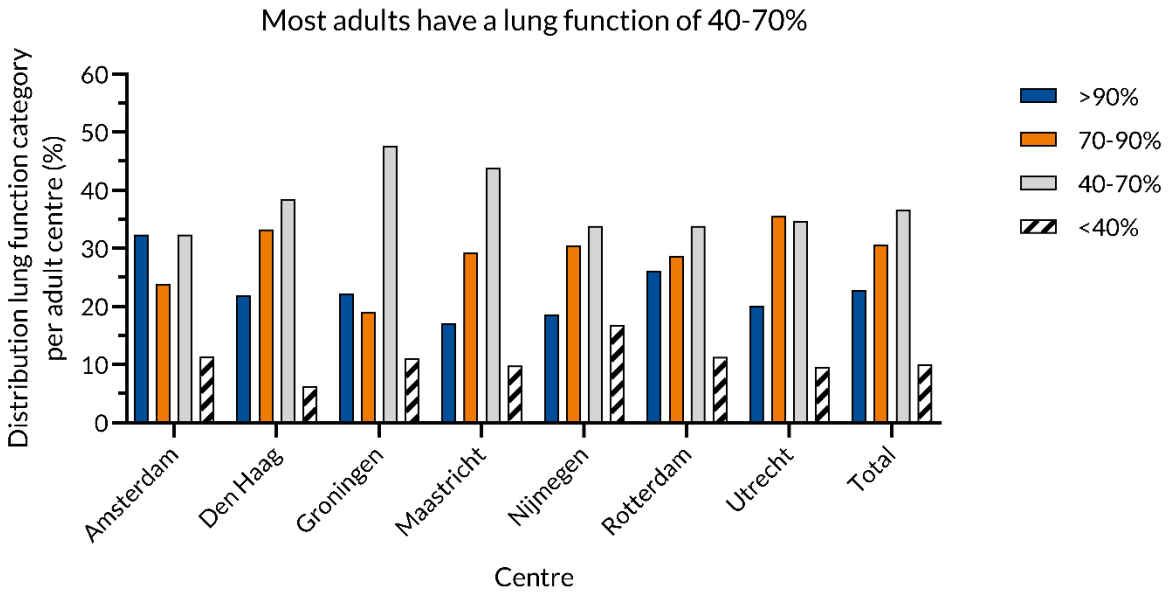

Figure 18: Lung function for adults by centre in 2019, divided into (international) lung function categories. A lung function of 90% or higher is considered normal.

5. Bacteria and fungi

Bacteria and fungi are micro-organisms, living creatures (*organisms*) that are only visible under the microscope (*micro*). Micro-organisms can be useful; bacteria in the intestine, for instance, break down food and strengthen our immune system. However, there are also micro-organisms that cause disease.

People with CF can suffer more from infections with 'bad' micro-organisms, because the tough mucus in the lungs is less able to remove these pathogens. That is why we pay close attention to whether, and if so which, bacteria and fungi are detected in the respiratory tract.

Infections are fought with antibiotics; more information can be found in the chapter 'Treatment'.

Presence of bacteria and fungi

At each stage of their life, different micro-organisms can be found in the respiratory tract of a person with CF. Figure 19 shows the percentage of people with CF who had a certain bacterium or fungus, by age group.

Figure 19 shows, for example, that infections with the fungus *Aspergillus fumigatus* and the bacterium *Pseudomonas aeruginosa* become more frequent with age.

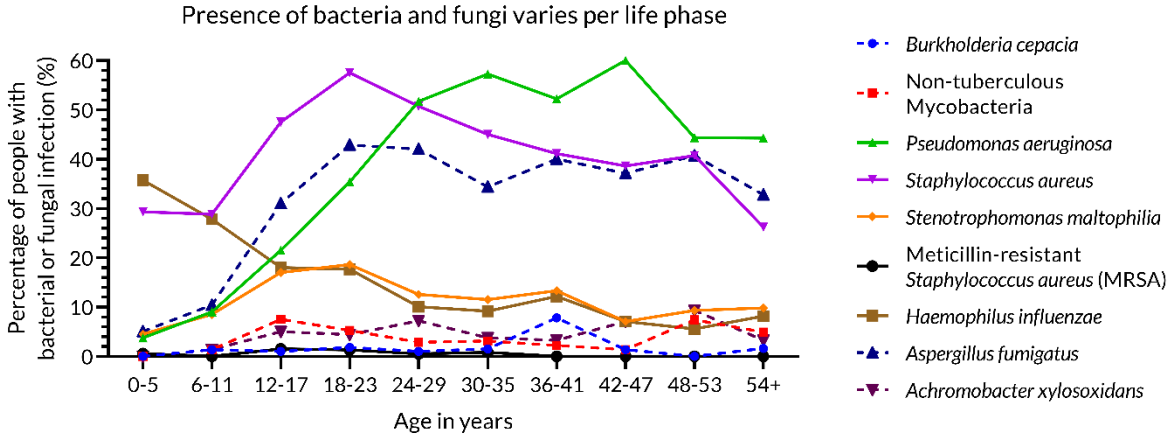

Figure 19: Percentage of people within an age group with a bacterial or fungal infection in 2019. The calculations are done by age group (per 6-year age bracket plus the group of 54 years and over).

Bacteria and fungi by age

The data in Figure 19 are only from 2019. The presence of micro-organisms has been fairly stable over the years, as shown in Figure 20 with data for the period 2013-2019.

Figure 20 shows the percentages of the most common micro-organisms (seen in 10-50% of people with CF). The numbers do not vary very much over the years. However, for the second year in a row we are seeing a decrease in the number of infections with the fungus *Aspergillus fumigatus*.

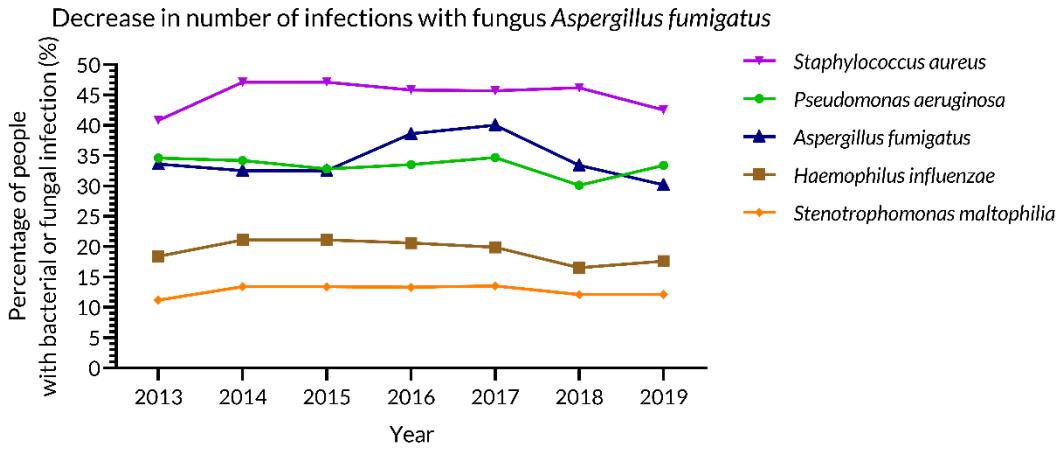

Figure 20: Presence of common bacteria and one fungus (Aspergillus) in people with CF, from 2013 onwards.

Other bacteria are less common, and are seen in less than 5% of people with CF. By zooming in on these small numbers, it becomes clear that there is an increase in people who get an infection with the non-tuberculous mycobacterium (NTM). At the time of writing this report, the steering group of the Dutch CF Registry, together with NTM experts, is investigating which risk factors contribute to the development of an NTM infection, whether there is an exchange between people with CF and whether there are differences between CF centres and if so, what those difference are. With the results of this analyses, the hope is that the increase in NTM infections can be halted.

2018 appears to show a peak in the number of MRSA infections. A large number of people with MRSA were registered in 2018, but in view of the numbers for the years before and after, this is unlikely to be a correct registration. It is important to note that MRSA is not easy to shake off.

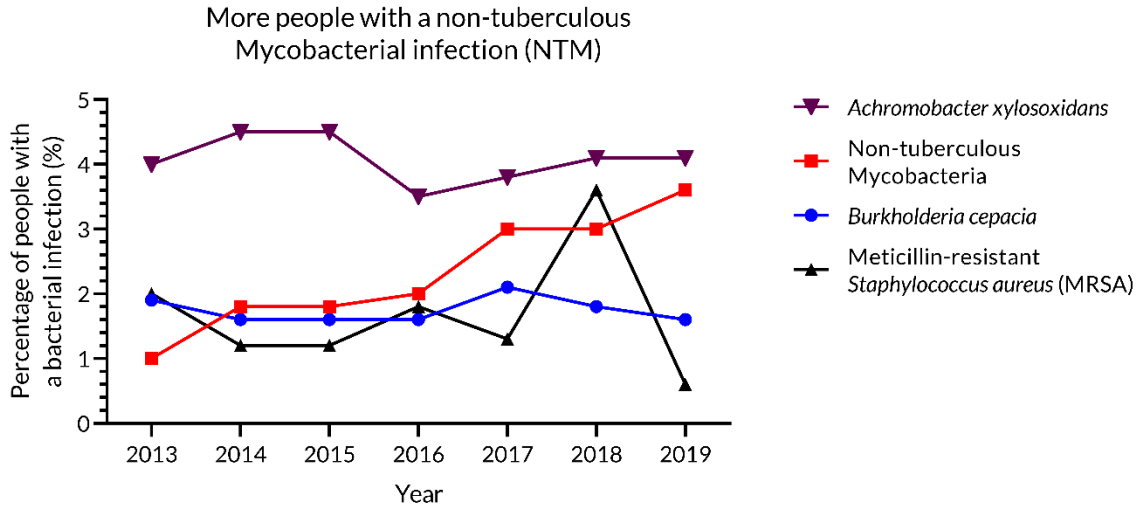

Figure 21: Presence of rarer bacteria in people with CF, from 2013 onwards.

6. Height and weight

The relationship between height and body weight says something about a person's nutritional status. Nutritional status' is the medical term for the balance between the intake of energy and nutrients and how they are used. It is important to have a good nutritional status, among other things to ensure a healthy immune system and good growth in children. This is all the more true for people with CF who have problems with the digestion of fats. For that reason, height and weight are measured several times a year.

Height and weight in children

The Body Mass Index (BMI) is an important measure to gain insight into a person's nutritional status. Other ways to look at this are height-for-age, weight-for-age and weight-for-height. For children, these values are converted to Standard Deviation Scores (SDS), also called Z-scores, to correct for age and gender. A Z-score of 0 is average, 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.

Figure 22 shows all measurements for height and weight in children with CF. This shows that the height-for-age is relatively low at all centres. This does not apply to the other measuring methods. In fact, for the BMI, at almost all centres half the children have a Z-score of 0 or higher.

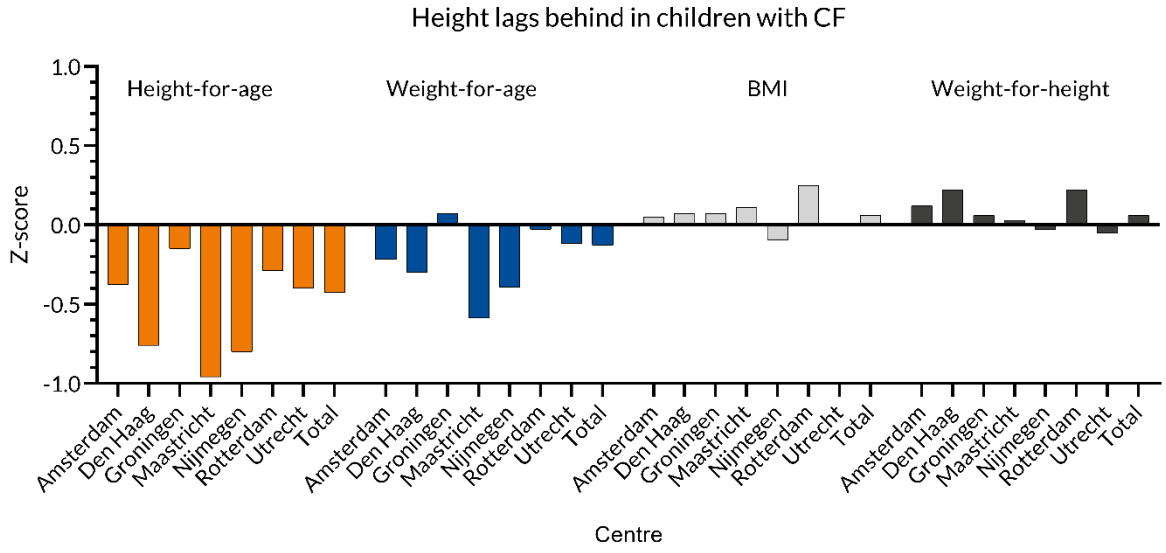

Figure 22: Four ways to look at the height and weight of children with CF. The diagram shows the data for 2019 by centre. The values have been converted to Z-scores to compare with peers with and without CF. A Z-score with a value of 0 is average. A Z-score higher than 2 or lower than -2 is considered to be strongly deviating with regard to weight, height or BMI. The median value is the middle one of all the values measured: half of the people have a higher Z-score and the other half a lower score.

The BMI of all children together went up slightly for a number of years, so that the median Z-score was above 0 from 2011 onwards (Figure 23). In 2016 and 2017, the BMI fell slightly. In 2018 and 2019, the BMI for children with CF has increased again to above 0.

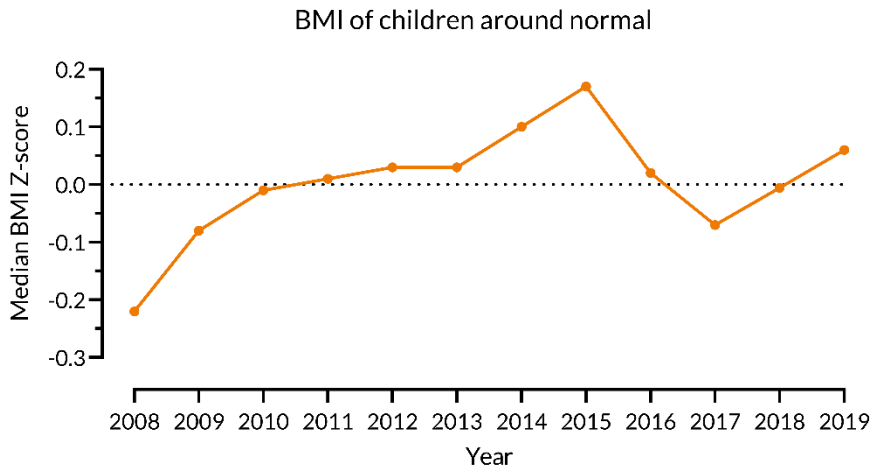

Figure 23: BMI for children with CF in the period 2008-2019. The BMI values are converted to Z-scores to correct for age and gender. A Z-score of approx. 0 is normal. A Z-score higher than 2 or lower than -2 is considered to be strongly deviating with regard to the BMI. The median value indicates that half of the children had a lower BMI and the other half a higher one.

The increase in BMI Z-score in 2019 for children with CF can be partly explained by the increase in the weight-for-age, but the median height-for-age decreased compared to previous years (Figure 24).

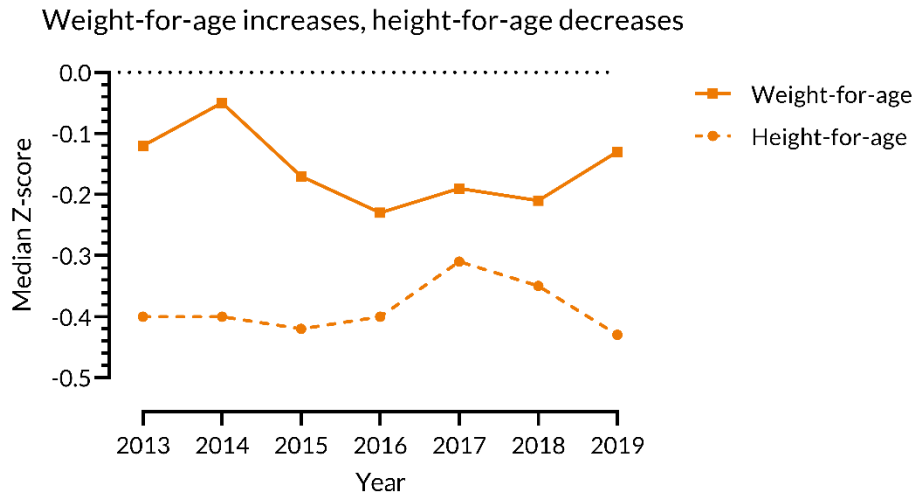

Figure 24: Weight-for-age and height-for-age for children with CF from 2013 onwards. The pulmonary functions are converted to Z-scores to correct for age and gender. A Z-score of approx. 0 is normal. A Z-score higher than 2 or lower than -2 is considered to be strongly deviating with regard to weight or height. The median value indicates that half of the children had a lower weight or height and the other half a higher one.

Categories of height and weight of children

Another way to look at the differences in nutritional status is to divide the Z-score into groups. This visualises how often the nutritional status is good and when it deviates significantly for the norm. A Z-

score lower than -2 or higher than 2 is considered to be strongly deviating. In this section, the BMI, height-for-age, and weight-for-age are divided into these Z-score groups.

Figure 25 shows that over 96% of children have a normal BMI. Only a few children have a BMI that deviates strongly.

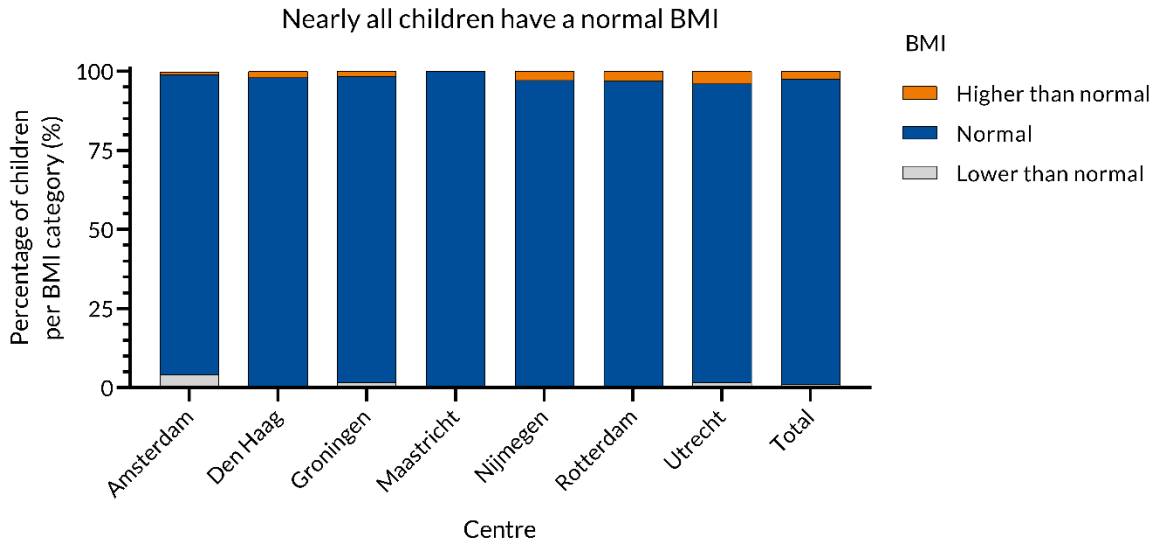

Figure 25: BMI values for CF children in 2019, divided into three BMI Z-score groups. Z-scores higher than 2 or lower than -2 indicate that the BMI deviates significantly from the normal value (too high or too low, respectively).

Comparing the weight of children with CF by age, and with peers without a pulmonary disease, shows that most children (more than 94%) have a healthy weight (Figure 26).

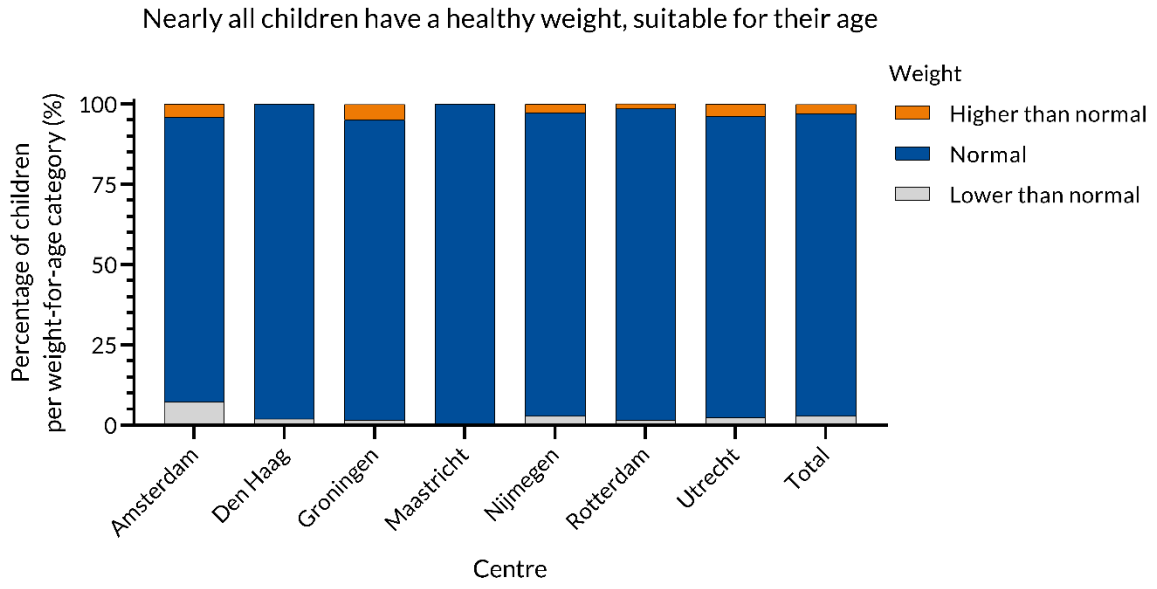

Figure 26: Weight-for-age for children with CF in 2019. Higher than normal means a Z-score of 2 or higher, lower than normal means a Z-score of -2 or lower.

By calculating the height-for-age in relation to the healthy population of children, it appears that the height is lagging behind in 7.2% of the children (Figure 27).

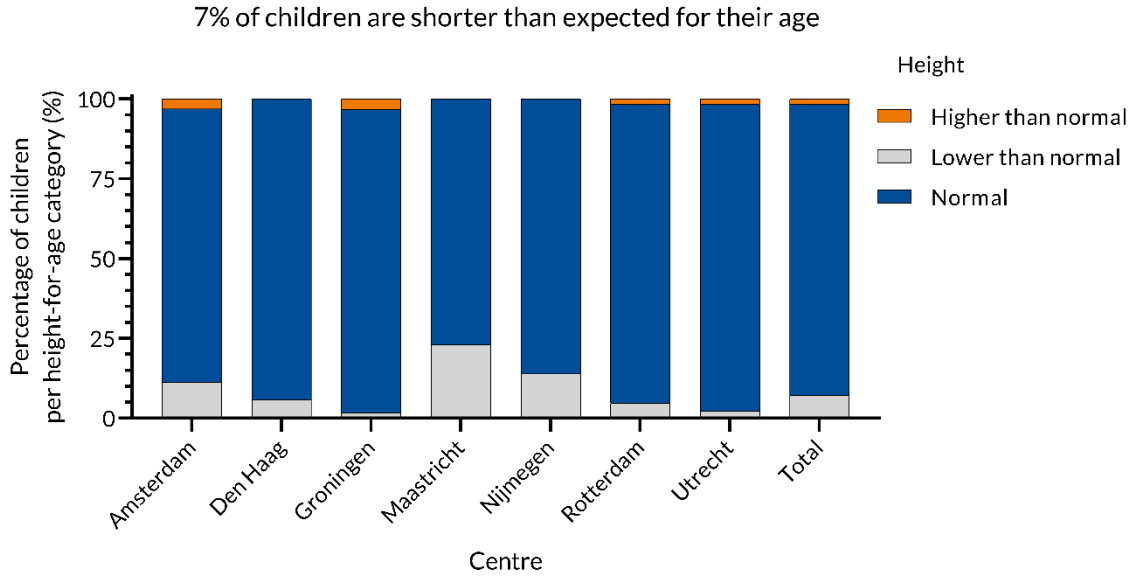

Figure 27: Height-for-age of children with CF in 2019. A child is in the 'normal height' category if the Z-score (value corrected for age and gender) is higher than -2 or lower than 2. Taller than normal means a Z-score of 2 or higher, shorter than normal means a Z-score of -2 or lower.

Adults

The nutritional status of adults with CF is calculated using the BMI. Figure 28 shows the median BMI for each age group (half of the people have a higher BMI, the other half a lower one). As people age, their BMI gradually goes up. The median BMI remains in the healthy area between 18.5 and 25.

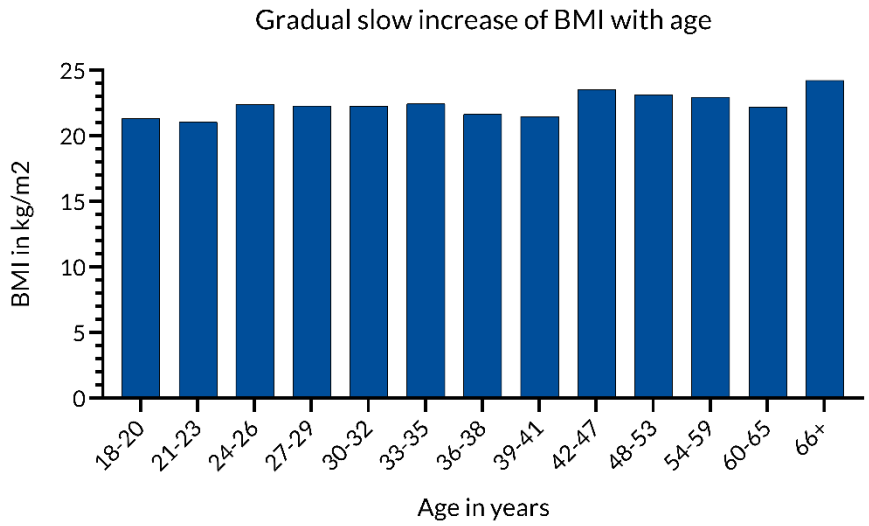

Figure 28: BMI for adults with CF in 2019, given in 3-year or 6-year age brackets. The bars indicate the median BMI value by age group: half of the people in that age group has a higher BMI, and the other half a lower BMI.

Over the years, the BMI in adults goes up a bit, but not for all centres (Figure 29).

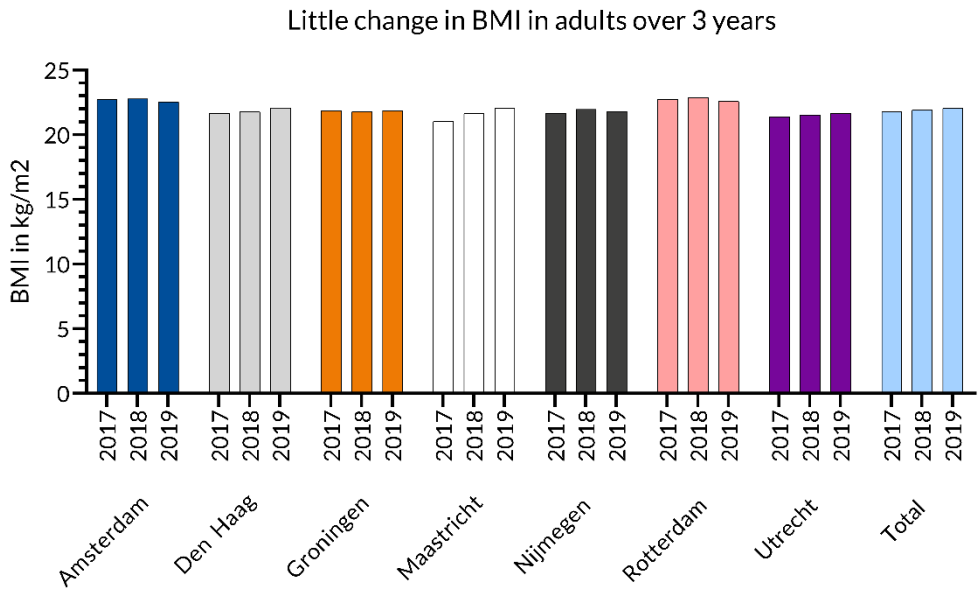

Figure 29: BMI for adults with CF by centre from 2017 onwards. Each bar indicates the median BMI: half of the people in that year (and at that centre) have a higher BMI and the other half a lower BMI.

However, almost 25% of adults with CF have a strongly deviating BMI (lower than 18.5 or higher than 25). Almost 75% of that group has a high BMI, just over a quarter has a low BMI.

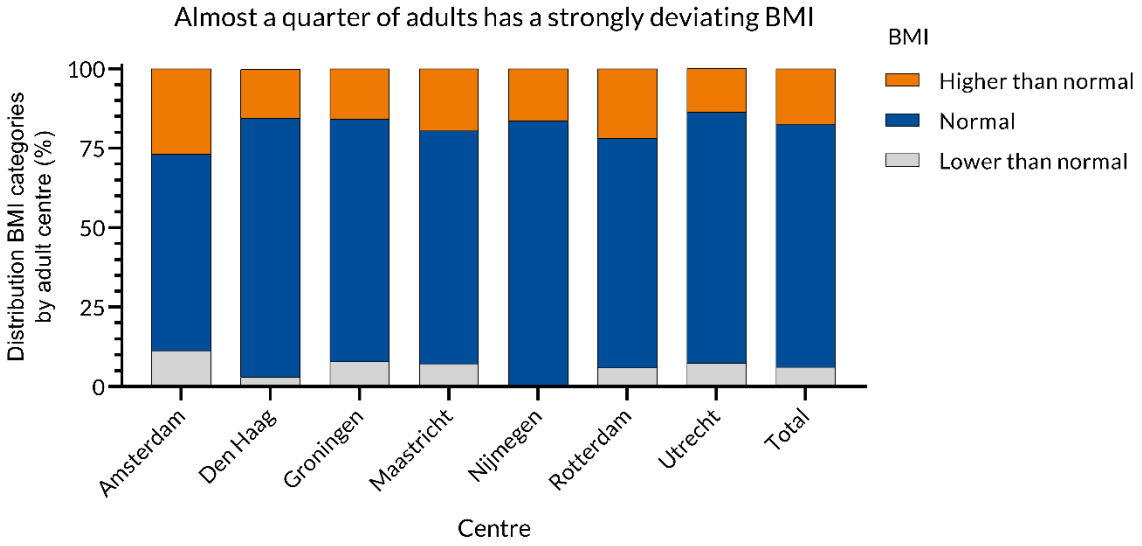

Figure 30: Percentage of adults with CF with a normal BMI or an deviating BMI in 2019, by centre. A BMI between 18.5 and 25 is considered normal.

For adult men with CF, a BMI of 22 is an international target number. For women, this is 23.

In 2019, about 40% of adult men were below the target number, but almost everyone was in the healthy range from 18.5 upwards (Figure 31). More than half of the men have a BMI that is higher than the target number. About 20% of adult men with CF are overweight (BMI of 25 or higher).

Within the group of adult men with a BMI above the target number, almost 30% are overweight (BMI between 25 and 30) and 6% are obese (BMI of 30 or higher).

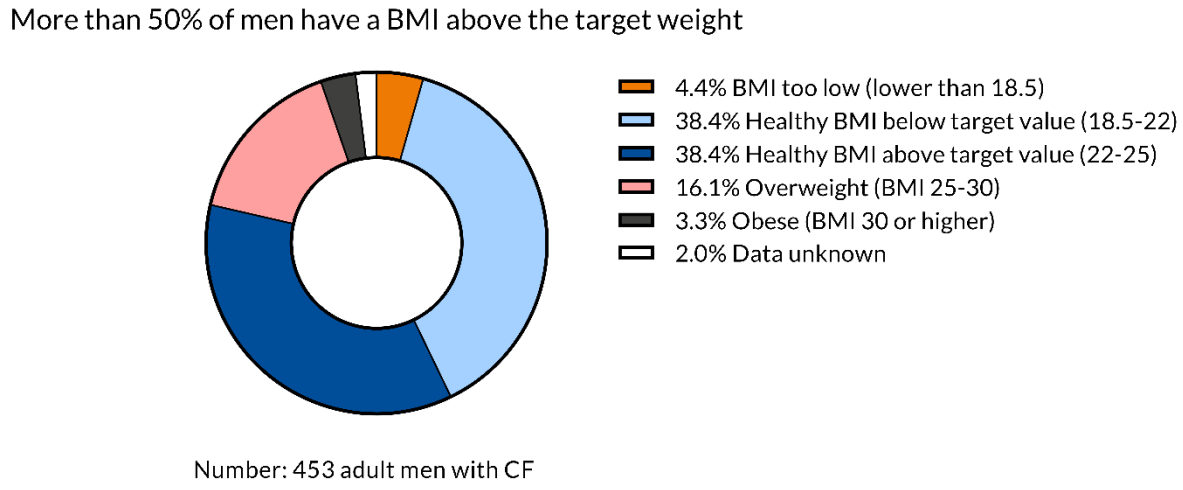

Figure 31: BMI categories of adult men with CF

Among adult women with CF, almost 70% had a BMI below the target number. Still, 60% of all women were in the healthy range from 18.5 upwards. Nearly 30% of adult women with CF have a BMI above the target number of 23. Fifteen percent of women are overweight (BMI of 25 or higher).

Of the group of adult women with CF with a BMI above the target number, 35% are overweight (BMI between 25 and 30) and 15% are obese (BMI of 30 or higher). In other words, half of the women with a BMI above the target weight have a BMI that is too high.

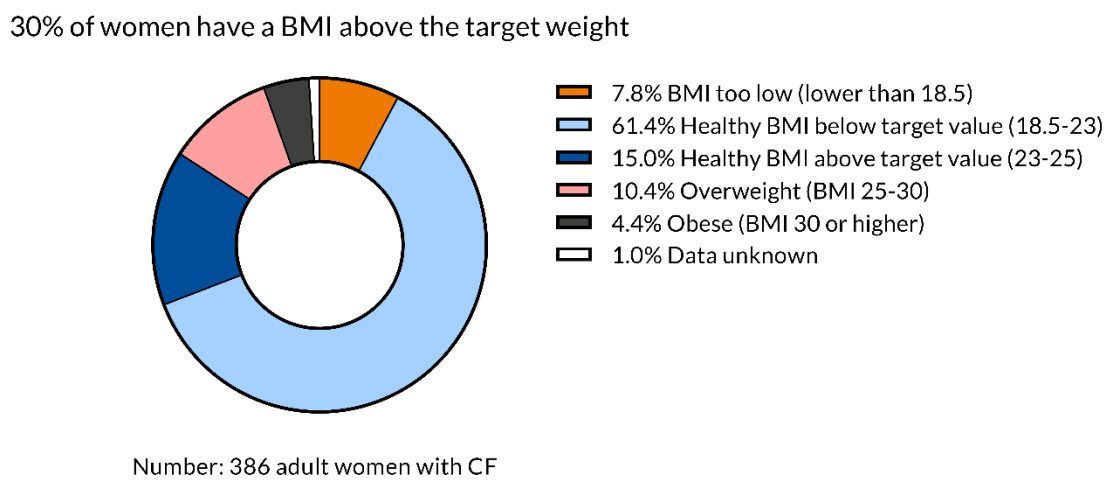

Figure 32: BMI categories of adult women with CF

3.8% of all adults with CF are obese (BMI of 30 or higher). Being overweight is more common in men with CF than in women, but obesity is more common in women. This distribution of being overweight and being obese also applies to the Dutch population, but with much higher percentages.

7. Comorbidity

Comorbidity is the generic term for diseases or conditions that can occur when patients have a particular disease, such as CF. This chapter shows how often people with CF suffer from comorbidity and zooms in on CF-related diabetes.

Presence of other diseases or conditions

There are many different conditions that a person with CF can get, varying from liver disease to nasal polyps. Figure 33 shows how often each disorder occurs in children and in adults. Almost all comorbidities are more prevalent in adults than in children.

Compared to last year, more adults had an ABPA (allergic reaction to the fungus *Aspergillus*). More adults also had sinusitis.

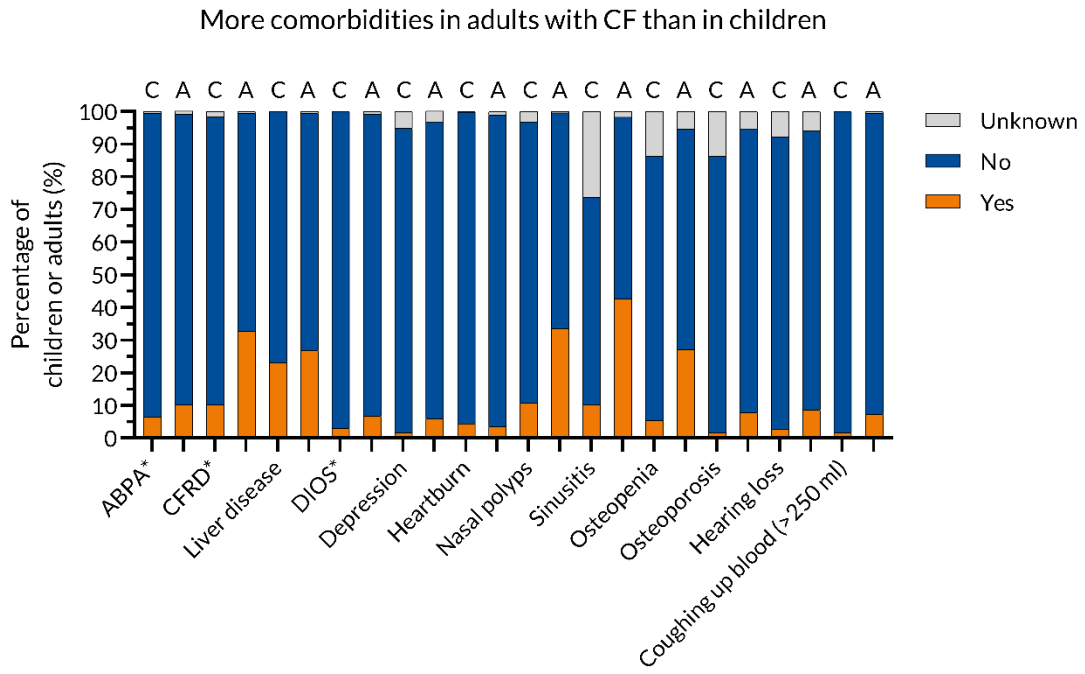

*Figure 33: Comorbidities for children and adults with CF in 2019. Comorbidity is an 'additional' disorder or disease, and per comorbidity you can see the percentage of children (C) and adults (A). These data are not known for everyone. * Abbreviations: ABPA stands for an allergic reaction to the fungus Aspergillus fumigatus, CFRD for CF-related diabetes and DIOS for distal intestinal obstruction syndrome.*

CF-related diabetes

One comorbidity which has been specifically monitored in recent years in people with CF is CF-related diabetes (CFRD). CFRD can be caused by pancreatic scarring, due to years of obstruction of that organ by tough mucus. The production of insulin takes place in the pancreas and can deteriorate due to scarring. CFRD therefore resembles diabetes (type 1 and type 2) but is not exactly the same. Want to know more about CFRD? The NCFS website gives more information.

In principle, people with CF who are at risk of getting CFRD are tested every year; see Chapter 11 on quality of care. Of all people with CF, the percentage that has CFRD has increased slightly compared to last year (Figure 34). This is true for both children and adults (not in diagram).

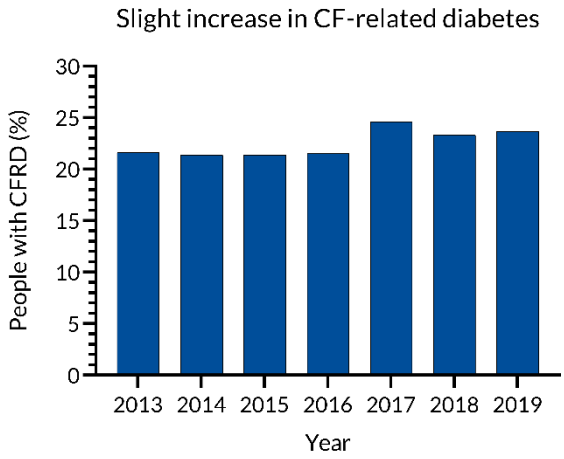

Figure 34: Percentage of people with CF who also have CF-related diabetes (CFRD). Given per year from 2013 onwards.

8. Treatment

CF can be treated in different ways. This chapter shows how many people with CF are prescribed a CFTR modulator. CFTR modulators are drugs that address the cause of CF. Unfortunately, not everyone is eligible for such a drug yet, because it depends on the mutations that someone has.

People with CF have to deal with various problems of their airways , intestines or pancreas. How many people take medication for these problems is described in this chapter. It also contains information on organ transplants in 2019.

Modulators

The first CFTR modulator available in the Netherlands is ivacaftor (Kalydeco). This drug is now available for people with CF with one of nine specific mutations (G551D, S549N, G551S, S1255P, G1244E, G178R, S549R, S1251N or G1349D) and who are aged one and older. People who have an R117H mutation and who are 18 years of age or older were also eligible for ivacaftor (Kalydeco) in 2019. Since 2020, ivacaftor (Kalydeco) has been available to everyone with one of the nine mutations aged six months and older. People with an R117H mutation can be prescribed this drug from the age of 18.

Figure 35 shows that approximately 50 people have now been prescribed ivacaftor (Kalydeco).

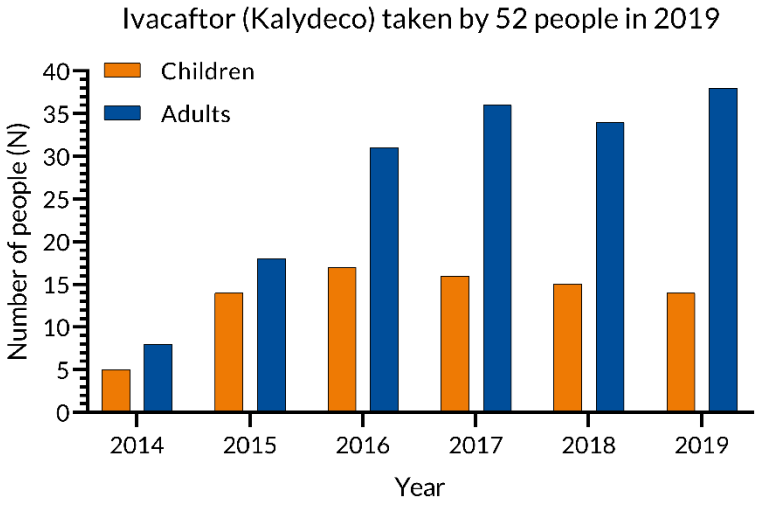

Figure 35: The number of people prescribed ivacaftor (Kalydeco) in the period 2014-2019.

Ivacaftor/lumacaftor (Orkambi) is the second modulator that can be prescribed in the Netherlands to people with CF. This drug can be prescribed to people aged two years and older with two F508del mutations and in 2019 it was prescribed to 380 people (Figure 36). This is much lesser than the number in 2018. The reason is that more than 200 people switched to a third modulator in 2019. Tezacaftor/ivacaftor (Symkevi) has been available to people with two F508del mutations since mid-2019, but only for those aged of twelve and older (Figure 37). Over 300 people were prescribed this modulator. Three people switched back to lumacaftor/ivacaftor (Orkambi).

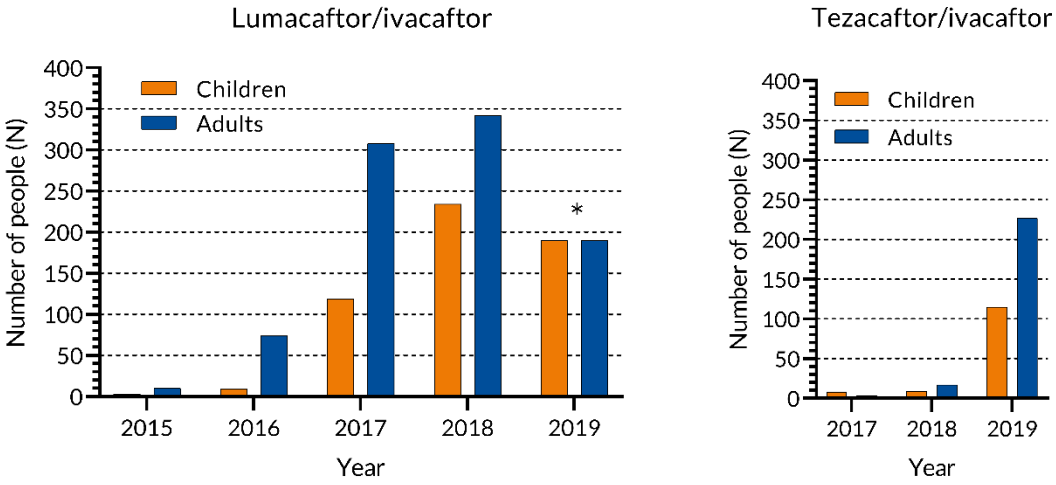

*Figure 36: The number of people prescribed lumacaftor/ivacaftor (Orkambi) or tezacaftor/ivacaftor (Symkevi) in the period 2015-2019. * The number of users of lumacaftor/ivacaftor (Orkambi) for 2019 does not include those people who switched to tezacaftor/ivacaftor (Symkevi), and vice versa.*

Not everyone eligible for a CFTR modulator was prescribed one in 2019. Figure 37 shows, by drug and age group, the percentage of eligible people who actually got this prescription in 2019.

For ivacaftor (Kalydeco) this was 88.2% of the people with one of the nine mutations aged 1 year and older. That is down from the year before. Within the group of people with an R117H mutation, this drug was prescribed to 33.3%, more than in 2018.

Children with two F508del mutations up to the age of 11 years are eligible to be given lumacaftor/ivacaftor (Orkambi). In the age group 2 to 6 years, 86.2% were prescribed this drug, in the age group 6 to 12 years, this was 95.2%.

Children and adults with two F508del mutations aged twelve years and older are eligible for both lumacaftor/ivacaftor (Orkambi) and tezacaftor/ivacaftor (Symkevi) since mid-2019. 34% were prescribed lumacaftor/ivacaftor (Orkambi) and did not switch to tezacaftor/ivacaftor (Symkevi). The latter drug was prescribed to 52.3% of people.

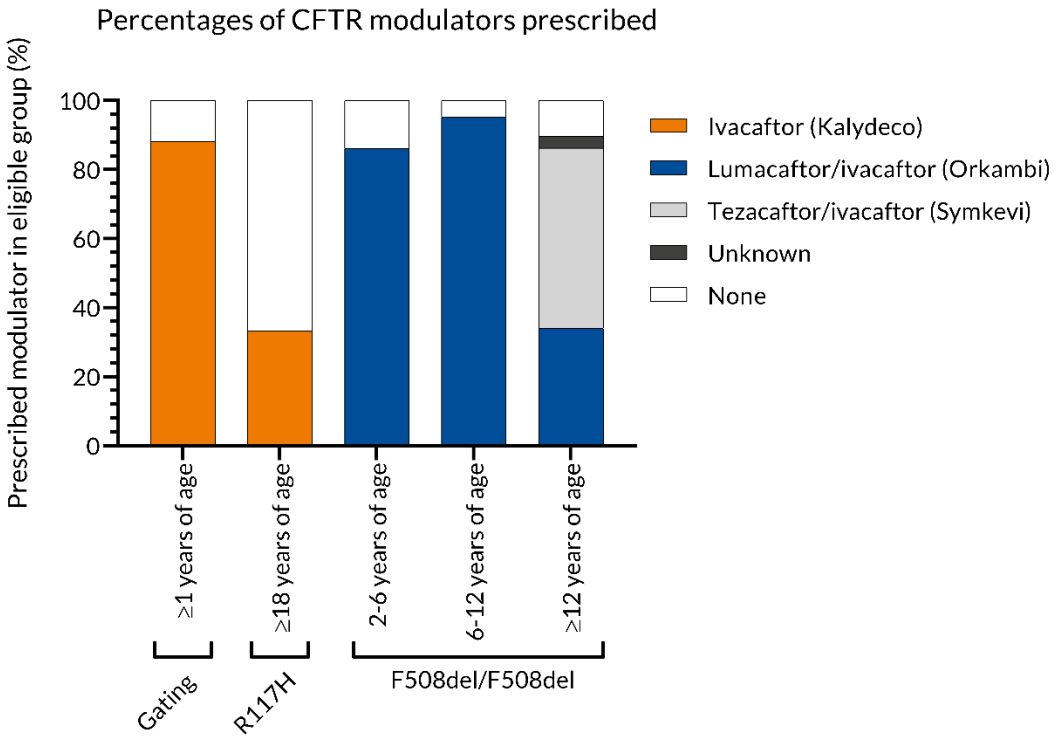

Figure 37: People who were eligible for one of the CFTR modulators reimbursed in the Netherlands in 2019, broken down by drug and subgroup according to the percentage of people who were prescribed a modulator or not (or unknown).

Respiratory tract

With CF, it is important to keep the respiratory tract as clean as possible and thus prevent infections. There are several drugs available that can help, such as expectorants (dornase alpha (Pulmozyme) and hypertonic saline) or medicines that dilate the airways. Other respiratory treatment methods may help in case of severe shortness of breath , such as extra oxygen through a nasal tube or mask, or extra support when breathing with a mask (non-invasive ventilation).

Figure 38 shows the percentage of children and adults who received respiratory drugs or treatment in 2019. These percentages are comparable to 2018.

It appears that expectorants and airway dilators are the most commonly used. It also becomes clear that adults were more often prescribed medication to relieve respiratory complaints than children, which is to be expected since adults usually have a lower lung function than children (see Chapter 4 on lung function for more information). When anti-inflammatory drugs (corticosteroids) are needed, the variants that need to be inhaled are more often prescribed than the corticosteroids that are taken in pill form.

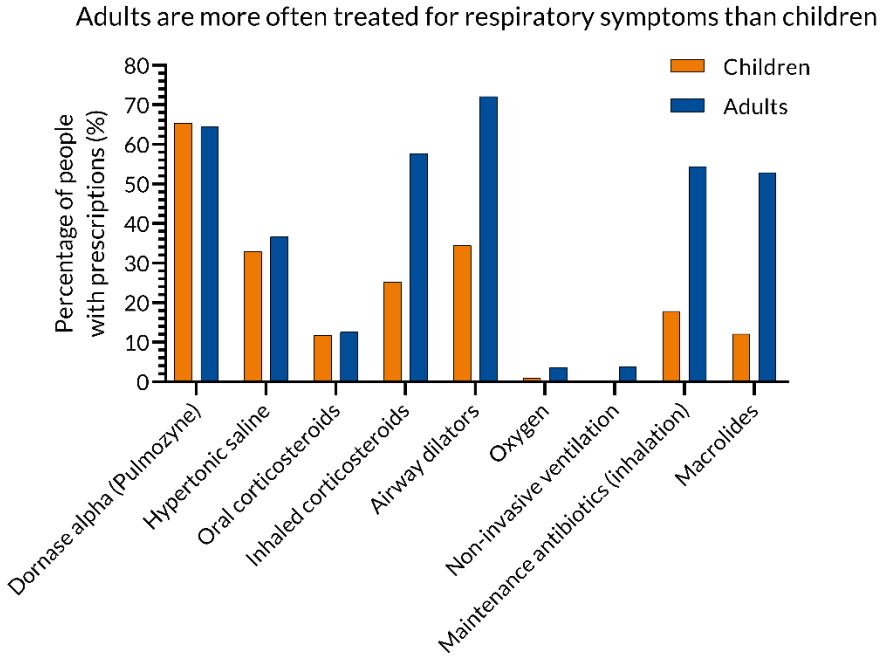

Figure 38: Treatment of respiratory problems in people with CF. The percentage of children and adults is shown for each medication or treatment prescribed in 2019.

Figure 39 further zooms in on the different types of inhaled antibiotics in order to treat or prevent (maintenance) infections. 18% of children used inhaled antibiotics in 2019, primarily tobramycin and colistin. As far as the group of adults is concerned, more than half of them (54.4%) took maintenance antibiotics and all five drugs were regularly prescribed. Compared to 2018, there has hardly been any change.

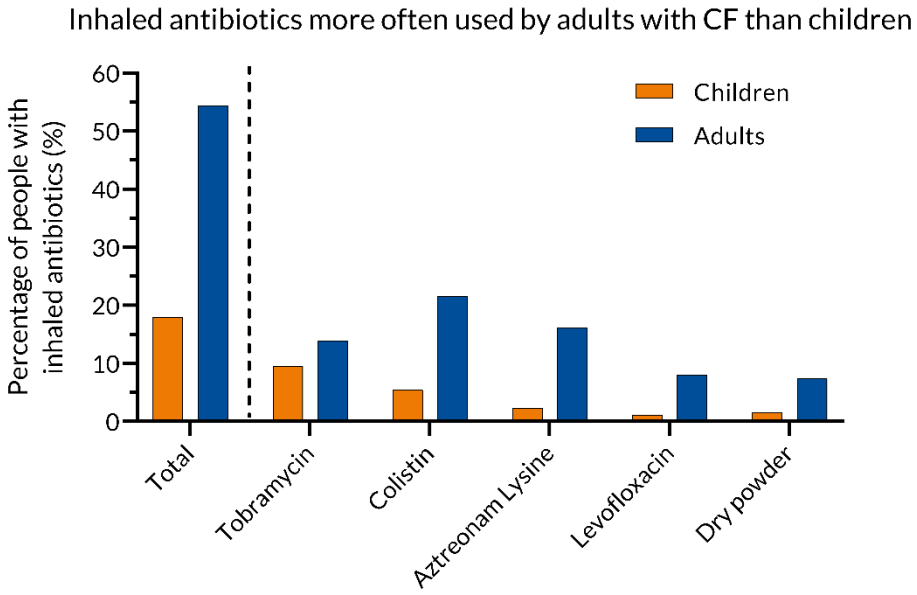

Figure 39: Inhaled antibiotics used by people with CF in 2019. The percentage of children and adults prescribed inhaled antibiotics is shown, as a total and behind the dotted line also broken down by drug. These are liquids that are inhaled using a nebulizer or as a dry powder (which can be tobramycin or colistin).

Treatment of *Pseudomonas* infection

The chapter on Bacteria and fungi (Chapter 5) includes information on how many people with CF have had a chronic infection with the *Pseudomonas Aeruginosa* bacterium in recent years. In Figure 40 below, these data are linked to the treatment of this infection with antibiotics that were inhaled into the lungs (inhaled antibiotics). The data are shown per CF centre and for each centre for children and adults separately.

Pseudomonas infections are much less common in children than in adults. Most people are then treated with inhaled antibiotics. However, there are also differences between the centres. One of the reasons is that a person sometimes immediately receives intravenous (IV) antibiotics.

12% of the children and 48% of the adults with CF had an *Pseudomonas* infection in 2019, the same percentage as in 2018. 85% of people with a *Pseudomonas* infection were treated with inhaled antibiotics: 77% of the children and 87% of the adults. In 2018, this was 78% for both groups, which means an increase in the number of adults treated with inhaled antibiotics.

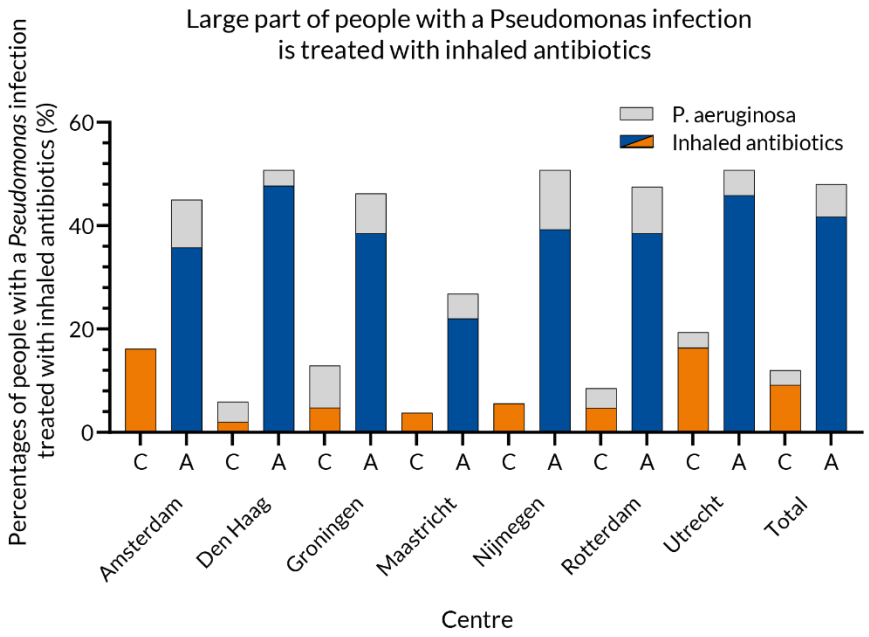

Figure 40: Percentage of people with a chronic Pseudomonas aeruginosa infection and how many of them were treated with inhaled antibiotics in 2019. Broken down by centre and for children (C) and adults (A).

IV antibiotics

If inhaled antibiotics or antibiotics in pill form do not work sufficiently, and someone with CF still has a bacterial or fungal infection, antibiotics are administered directly into a blood vessel . This is called an intravenous (IV) treatment.

Figure 41 shows the percentage of people receiving IV treatment in 2019, broken down by age group and for home or hospital treatment. IV antibiotics are usually administered in the hospital (22.4%), but it can also often be done at home (16.3%, after starting treatment in the hospital). Data are available for 1,404 people in 2019 (567 children and 837 adults). Of the children, 14.6% received IV treatment in hospital and 11.1% at home. For adults, this was 27.6% in hospital and 19.8% at home.

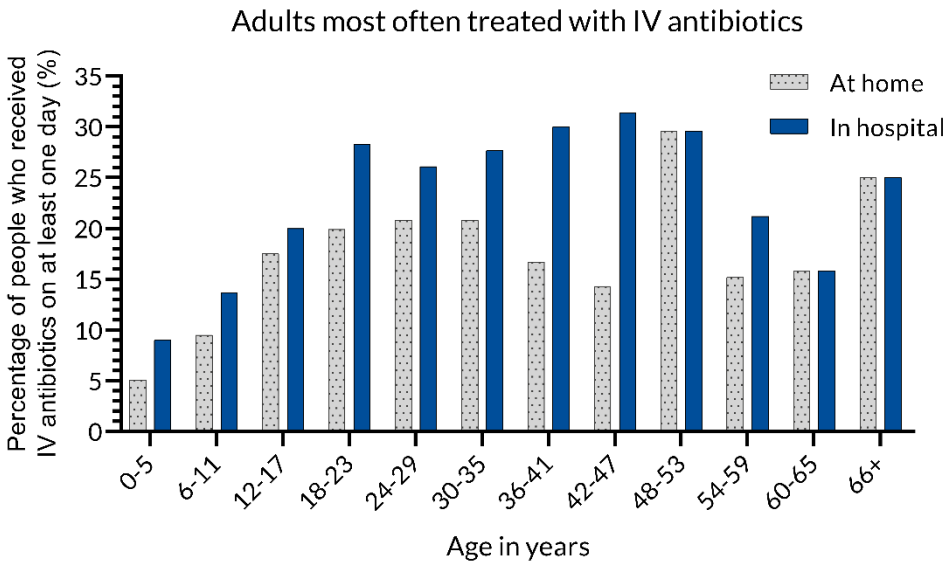

Figure 41: Percentage of people with CF who got IV antibiotics administered on at least one day in 2019. The data are broken down by home and hospital treatment and by age group.

Figure 42 gives the calculation of the average number of days of IV antibiotics administered by age group, at home or in hospital. For this purpose, data from all people with CF who were administered IV antibiotics on at least one day in 2019 were used.

On average, people with CF spent 16.8 days in hospital for IV treatment and received 24.7 days of home treatment. On average, the children received IV antibiotics on more days than adults: 19.8 days in the hospital and 26.1 days at home. Adults spent an average of 15.7 days in the hospital for treatment and had 24.1 days of home treatment.

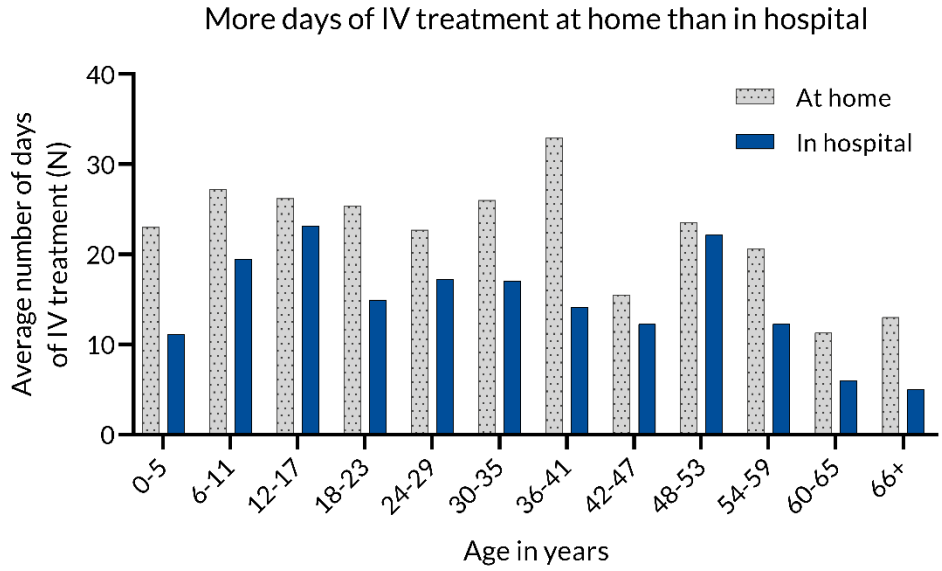

Figure 42: Average number of days of treatment with IV antibiotics at home or in the hospital. Calculated within the group of people who received treatment on at least one day, by age group.

Whether or not IV antibiotics are prescribed has been recorded in the Dutch CF Registry for many years. Figure 43 shows that the percentage of children and adults remains fairly stable over the years, although the percentage of children given IV antibiotics is decreasing for the second year in a row, both with regard to treatment at home and in hospital.

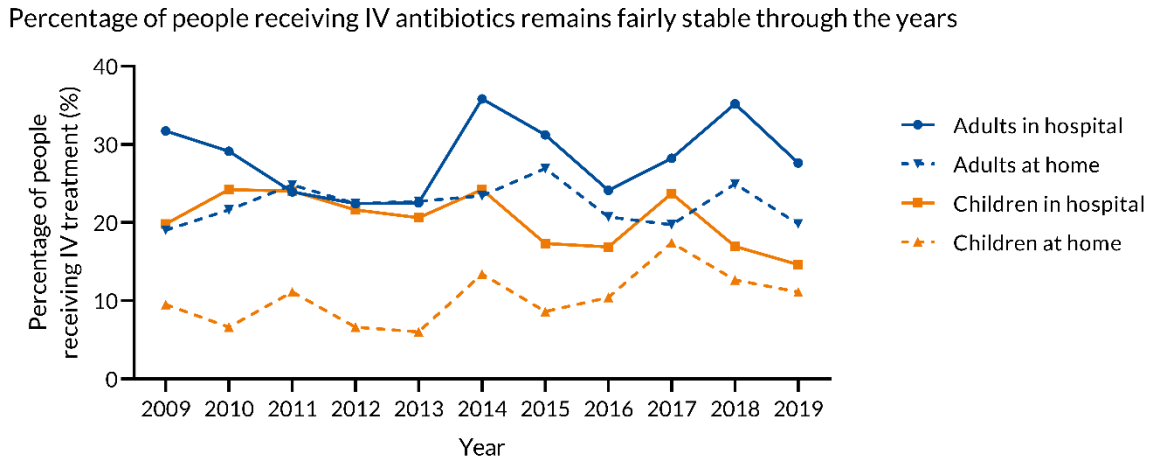

Figure 43: Percentage of people with CF who received IV antibiotics on at least one day, in the period 2009-2019. Broken down by year for children and adults and by treatment location, at home or in hospital.

Digestive system

In addition to respiratory problems, people with CF often also suffer from a poorly functioning digestive system (such as the intestines, the liver and the pancreas). Figure 44 shows which drugs were prescribed to people with CF in 2019 in order to combat digestive problems. There are usually small differences between children and adults, but proton pump inhibitors were less prescribed in children (also compared to 2018). It also appears that pancreatic enzymes (which digest food and thus also improve the absorption of food) are by far the most commonly used.

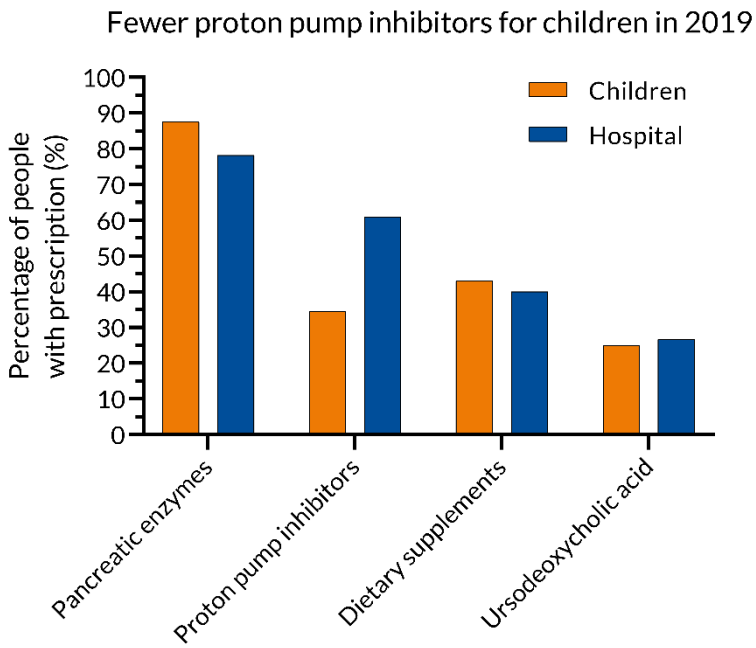

Figure 44: Treatment of problems of the digestive system in people with CF in 2019. The percentage of children and adults is shown for each medication or treatment prescribed. Pancreatic enzymes digest the food, so that it is better absorbed by the

body, proton pump inhibitors help against heartburn. Dietary supplements help you gain weight or maintain your weight. Ursodeoxycholic acid can improve gallbladder function.

Figure 45 shows the different forms of dietary supplements prescribed to children and adults in 2019. Nearly everyone received liquid dietary supplements as part of the treatment. A gastric tube or gastrostomy are much less common. Both methods are used more often in children than in adults.

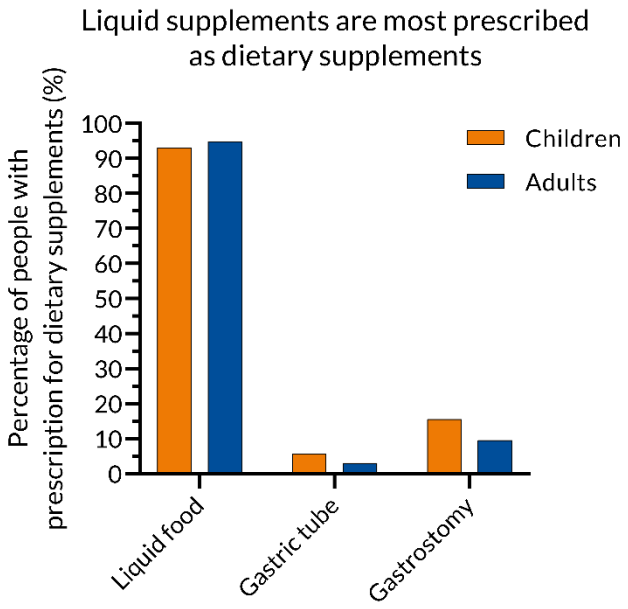

Figure 45: Type of dietary supplements prescribed in 2019. Percentages by type of dietary supplement relative to the group that was prescribed dietary supplements (see Figure 41). The percentage of children and adults is shown for each type of dietary supplement prescribed.

Transplants

In a person with CF, the function of some organs often deteriorates with time. They may be eligible for a transplant if the lungs, liver or kidneys have almost stopped working.

In people with CF, lung transplants are the most common, liver transplants are much less common and kidney transplants are very rare (kidney transplants are not recorded in the Registry).

In the Netherlands, transplants are carried out at three hospitals: Groningen, Utrecht and Rotterdam. According to the data in the Registry, ten people underwent a lung transplant in 2019. Twelve people were still waiting for new lungs on 31-12-2019.

The Dutch Transplant Foundation collects transplant data from all transplanted people every year. They have the same data for 2019: 10 people have undergone a lung transplant and 12 people are still on the waiting list.

Liver transplants are less common than lung transplants. In 2019, one person underwent a liver transplant and three people with CF were still on the waiting list.

9. Work and family

For those who have CF, work and study are not self-evident. How many adults with CF are capable of hold down a job or go to school or university? This chapter also gives information about pregnancies in women with CF.

Work and education

Social participation is not only reserved for people who work or study. Volunteering or helping friends/family is also considered to be social participation. The Dutch CF Registry keeps general data about the social participation of adults with CF in 2019.

Based on the data in the Registry, approximately half of the people have a job in 2019, at home or elsewhere (Figure 46). 17% was in education in 2019.

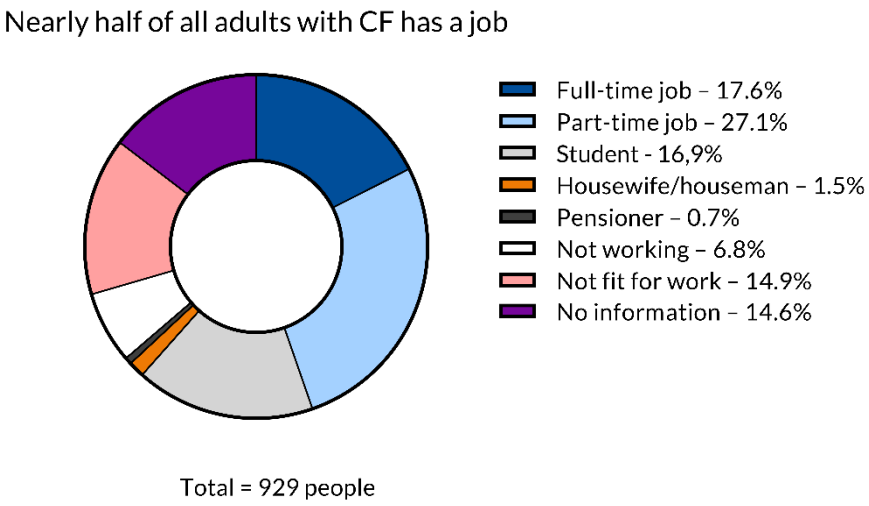

Figure 46: Various roles of adults with CF in society in 2019.

Pregnancies

The Dutch CF Registry records which women with CF are pregnant and/or have had a child. It does not track whether men with CF have become a father.

In 2019, twelve women with CF were pregnant. Of the group of women with CF aged 18 and over in 2019, 93 women had been pregnant in previous years.

Want to know more about CF and having children? The website gives more information and also contains references to other websites.

10. Over-50s and CF

According to the 2019 Registry, there are 128 people in the Netherlands who have CF or a CF-related disease and who are aged 50 and over, namely 70 men and 58 women. Of this group, 114 people had a confirmed CF diagnosis. More information about these people can be found in this chapter on the age distribution and mutations.

Age

Of the 114 people with CF who are over 50, half are between 50 and 55. Three-quarters of the people are between 50 and 60 (Figure 47). The oldest person with CF turned 78 in 2019.

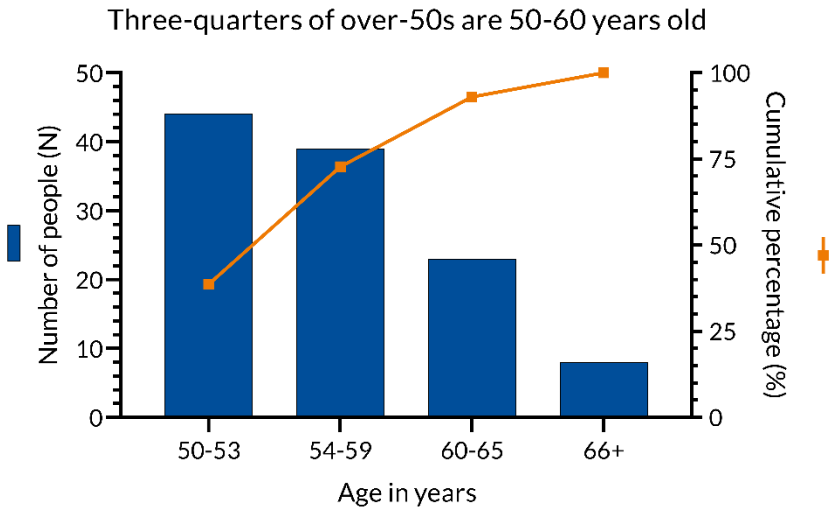

Figure 47: Age distribution of people with CF aged 50 and over in 2019. The bars indicate the number of people per age category (see left axis for scale). The orange dotted line marks the percentage up to the age group (see right axis for correct scale).

Mutations

The mutation distribution within the group of people aged 50 and over is different from that for the entire group of people with CF (Figure 48). The most common mutation is still F508del. But when we look at the mutation combination, the double F508del mutation is no longer the most common, but F508del with another (often milder) mutation.

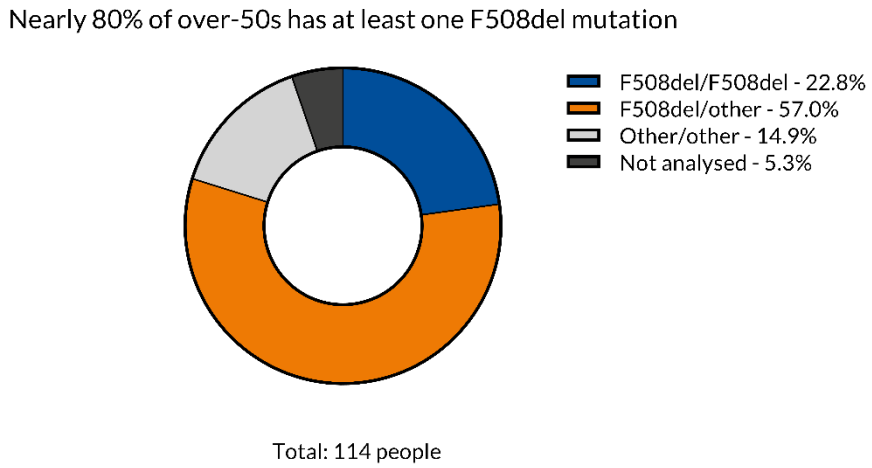

Figure 48: Mutation distribution for people with CF with a F508del and/or another mutation who are over 50.

Other properties

Of the 114 people with CF aged 50 or over, 12 have had a lung transplant in the past, and 2 had a transplant this year. These 14 people were not included in the description of properties below (Figure 49), such as hearing loss, bone weakness or chronic bacterial infection. The reason is that after a lung transplant, both the treatment and the symptoms often change dramatically.

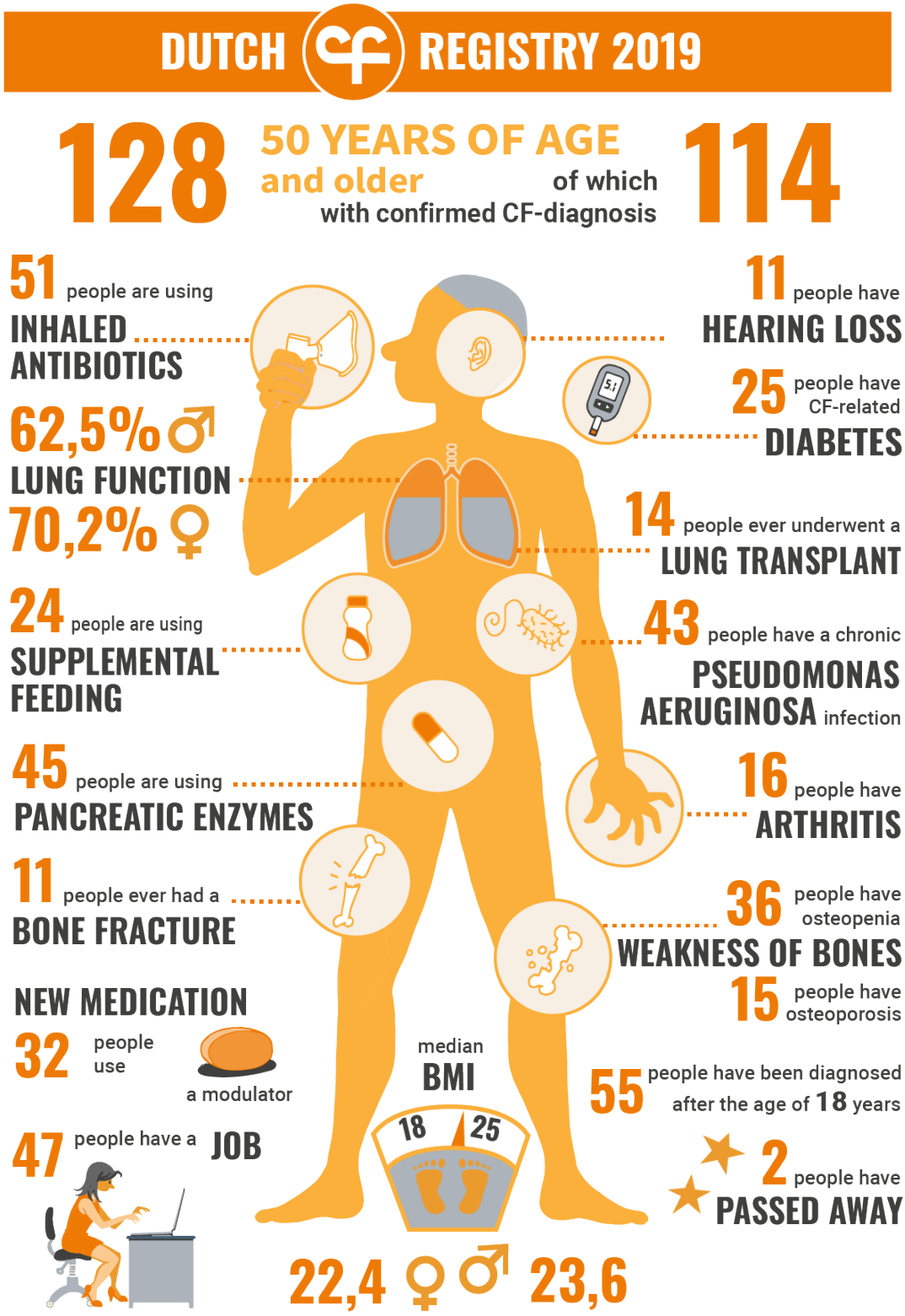

Figure 49: Infographic for people aged 50 and over and with CF.

11. Quality of care

How good is the quality of CF care in hospitals? The National Health Care Institute [Zorginstituut Nederland] tries to establish this every year by collecting data, the so-called indicators. One indicator, for example, is how many people with CF visited the CF centre four times or more in a year.

In this annual report of the Dutch CF Registry, the indicators for CF are presented as a separate chapter. For the calculations, we used the data of people with a confirmed CF diagnosis who did not undergo a lung transplant, who were seen in the same hospital all year 2019 (e.g. those who did not move to another centre during the year).

Visits to the outpatient clinic

In principle, people with CF visit the outpatient clinic of the CF centre four times a year for a check-up. During this check-up, a number of things are measured, such as lung function and height and weight. A sputum sample is also taken.

Some people with CF have fewer symptoms and have agreed fewer check-ups with the CF centre. Figure 50 shows that nearly 80% of people visited the outpatient clinic four times or more in 2019. This is down from 2018, when more than 80% visited the outpatient clinic at least four times.

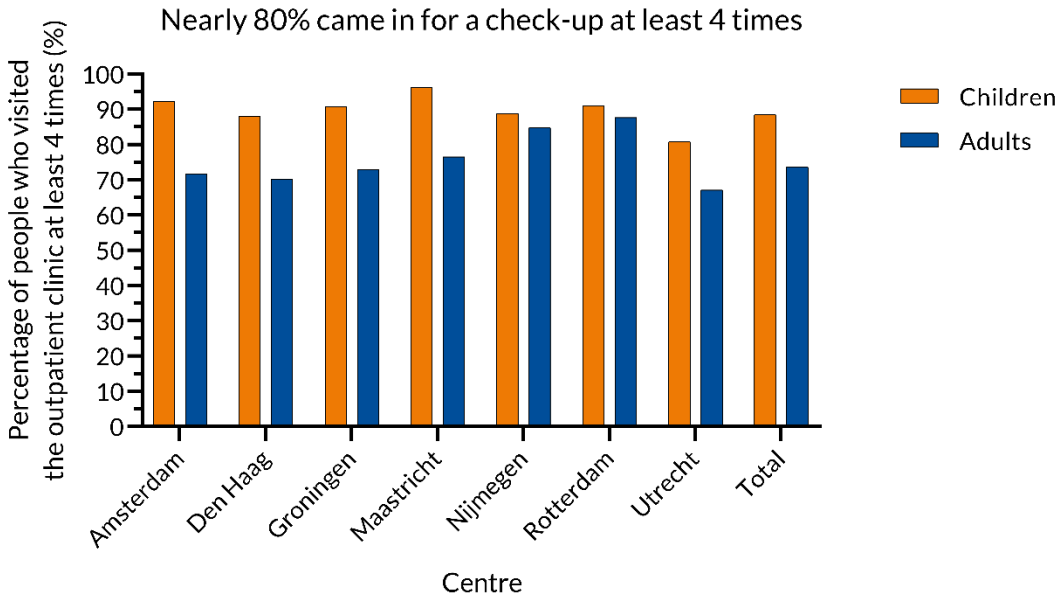

Figure 50: Percentage of people with CF who have had at least four check-ups at the outpatient clinic in 2019.

Lung function test

In principle, lung function is also tested during the regular (four) visits to the outpatient clinic. Figure 51 shows that more than three-quarters of people (aged 6 years and over) underwent at least four lung function tests in 2019. This is up from 2018, when 70% of people had at least four tests.

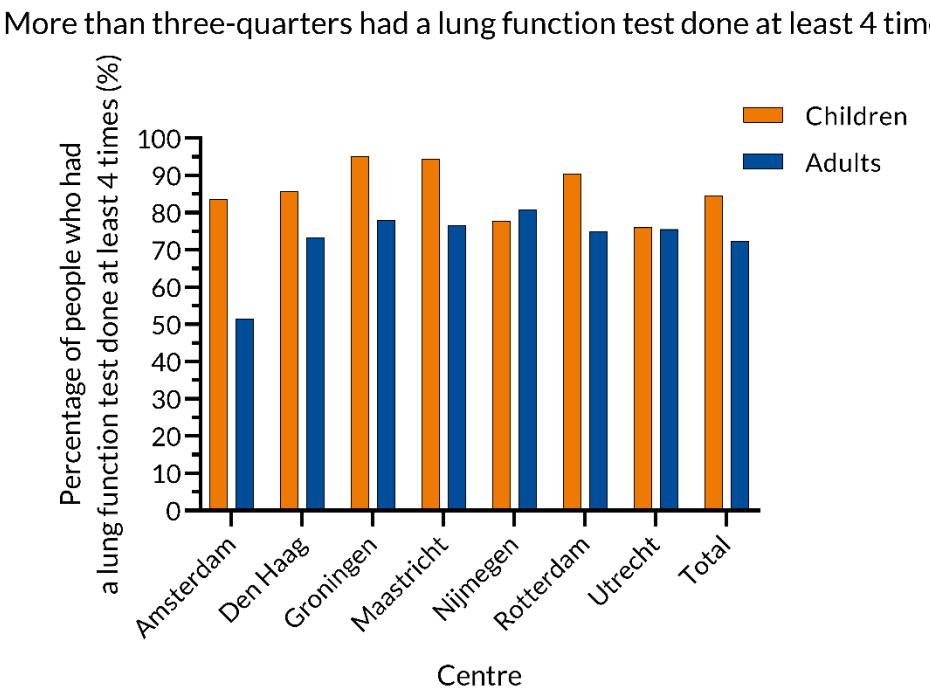

Figure 51: Percentage of people with CF who had at least four lung function tests in 2019.

Sputum sample

Taking a sample of the sputum (the mucus produced in the lungs) is also a standard part of a regular outpatient clinic check-up. The sputum is then tested for bacteria and fungi (more information in Chapter 5).

Figure 52 shows that nearly 90% of the children had at least four sputum samples taken in 2019, to test for the presence of bacteria and fungi. For adults, the average percentage was nearly 70% (more than the year before). A total of three-quarters of people with CF had at least four sputum samples taken.

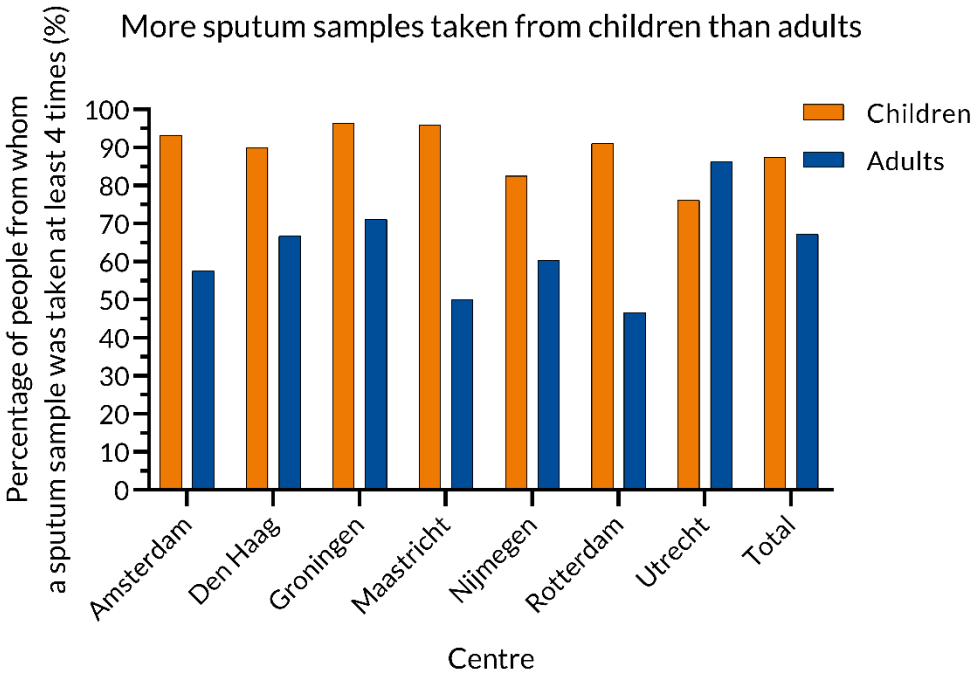

Figure 52: Percentage of people with CF who had at least four sputum samples taken and tested in 2019. Sputum is mucus produced in the lungs, which is sampled to test for the presence of bacteria and fungi.

Glucose tolerance test

Some people with CF have an increased risk of CF-related diabetes (CFRD). The production of insulin can be affected by scarring of the pancreas. Insulin is a hormone that ensures good glucose levels in the blood.

For this reason, the Dutch guideline stipulates that all people with CF who take pancreatic enzymes and are not known with CFRD, undergo a glucose tolerance test every year from the age of ten. This glucose tolerance test shows whether someone is developing or already has CFRD.

The risk group consists of 532 people of whom almost three-quarters did a glucose tolerance test in 2019 (Figure 53). More children and adults were tested compared to the year before (almost 85% of children and almost 70% of adults).

Want to know more about CFRD? Check out the website for more information.

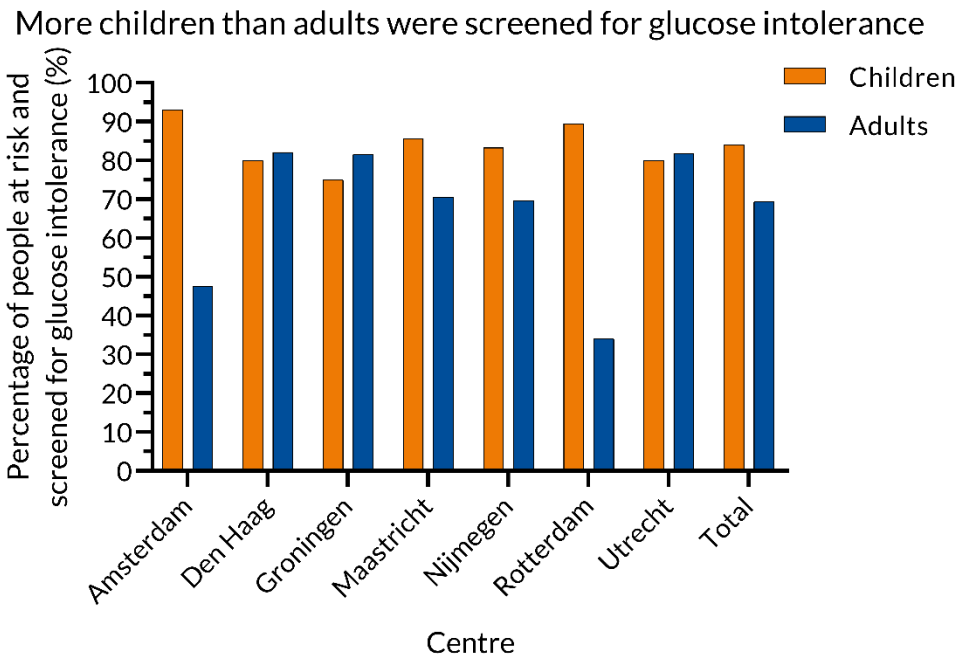

Figure 53: Percentage of people with CF who were screened for glucose intolerance in 2019. The percentages are calculated within the risk group: people with CF who are at risk of developing CF related diabetes, use pancreatic enzymes, and are 10 years or over.

Annex 1. Methods

For this report, seven CF centres collected the medical data on 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.

How is this coordinated with other countries? How are the calculations made and what assumptions are used? This chapter explains the methods and process. It also explains a number of the terms and abbreviations used.

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 38 countries. Want to know more about the ECFSPR? Read more here.

For years, data from people with CF have also been collected in North-America, Australia and Canada and on other continents. In order to compare the data properly, all countries have to collect the data in the same way as far as possible. An example is that the highest lung function value of each year and the height and weight of the same day are collected. Or that an infection with the *Pseudomonas* bacterium is classed as chronic if three of the four sputum cultures come back positive.

The way data is recorded is becoming more and more standardised internationally, which also makes the data more reliable to compare.

Calculations

In addition to Chapter 2, 'Demographic data', and a few other exceptions (as described) the analyses in this report have only used data on people with CF who did not undergo a lung transplant.

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

1. Lung function: the centres entered the highest value per person of all measurements done in 2019. 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 8.

Concepts

This report makes use of and explains various terms:

- The median value is the middle value of all values together. 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.
- Z-score: In some cases, the lung 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 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 square of the height (in metres).
- **CF** is short for cystic fibrosis.
- **CF-related disease** is a disease where a person has CFTR mutations but not a confirmed CF diagnosis, for example because they had a normal sweat test (not influenced by a CFTR modulator) or because one of the CFTR mutations does not cause CF.
- **CFRD** is CF-related diabetes.
- **DIOS** stands for distal intestinal obstruction syndrome, a severe obstruction of the last part of the small intestine.
- **FEV1% of predicted** is a measure of lung function. The FEV1 is the amount of air a person can force out 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 age, height and sex without a lung disease, the volumes are converted into percentages. These percentages are called FEV1% of predicted.

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 close agreement 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, CEO 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, Coordinator Dutch CF Registry

CF centres

Prof. Dr. H.G.M. Heijerman, chest physician, 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, chest physician/transplant specialist, Erasmus MC Rotterdam

Drs. R. van der Meer, chest physician, HagaZiekenhuis, The Hague

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

Dr. C.M. Majoor, chest physician, Amsterdam UMC (up to February 2020)

Dr. J. Altenbrug, chest physician, Amsterdam UMC (from February 2020)

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

Dr. H. van der Vaart, chest physician, 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