

German Cystic Fibrosis Registry

Annual Data Report | 2020

L. Nährlich (ed.), M. Burkhart, J. Wosniok

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Registry Work Group:

PD Dr. Lutz Nährlich (Medical director), Gießen
Manuel Burkhart (Project leader), Bonn
Enno Buss, Cologne
Clemens Basler, Karlsruhe
PD Dr. Anna-Maria Dittrich, Hannover
Prof. Dr. Helmut Ellemunter, Innsbruck
Prof. Dr. Helge Hebestreit, Würzburg
Dr. Oliver Nitsche, Mainz
Dr. Inka Held, Hamburg
Dr. Christina Smaczny, Frankfurt
PD Dr. Doris Staab, Berlin
Dr. Sivagurunathan Sutharsan, Essen

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Mukoviszidose e.V. & Mukoviszidose Institut gGmbH
In den Dauen 6, 53117 Bonn
E-Mail: info@muko.info
www.muko.info

The publishers are represented by:

PD Dr. Lutz Nährlich, Gießen
Justus-Liebig-Universität Gießen
E-Mail: lutz.naehrlich@paediat.med.uni-giessen.de
Manuel Burkhart, Bonn
Mukoviszidose Institut gGmbH
Qualitätsmanagement
E-Mail: mburkhart@muko.info

Data Management &

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Johannes Gutenberg Universität
Interdisziplinäres Zentrum Klinische Studien (IZKS)
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Foreword



**PD Dr. med.
Lutz Nährlich**

Medical Director
German
Cystic Fibrosis
Registry

In addition to the current state of health of people with cystic fibrosis in Germany, the German Cystic Fibrosis Registry presents the development of the last two decades for the first time in the 26th report and also describes the challenges for the future. The 2020 report presents the data of 6,648 people from 88 outpatient clinics. The proportion of adults is 59 % and the median age is 21 years. A CFTR genotyping, which is important in the age of mutation-specific therapies, shows an F508del mutation on at least one allele in 86 % of all people with cystic fibrosis. Of the people diagnosed with cystic fibrosis in 2020, 63 % were diagnosed via newborn screening. 80 % of the children (from 2 years of age) and adolescents and 73 % of the adults have a normal nutritional status. 69 % of the adolescents have an age-appropriate FEV₁%pred of more than 80 % at the age of 16 – 17 years. A chronic *Pseudomonas aeruginosa* infection can be found in 10 % of the children and adolescents and 53 % of the adults. At least one mucolytic therapy is used by 93 % of the children and adolescents and 87 % of the adults. Three inhalative therapies (inhalative antibiotics, mucolytics, DNase) are used in 12 % of the children and adolescents and 30 % of the adults. An increase in CFTR modulator therapies was recorded in all age groups – 31 % instead of 21 % of all children and adolescents and 58 % instead of 36 % of all adults were treated with CFTR modulators in 2020. The median survival age for the period 2015 – 2019 was 52.41 years and has therefore improved by 2 years compared with the period 2014 – 2018.

The year 2020 will go down in the history of cystic fibrosis as the year of the coronavirus pandemic and the introduction of the highly effective CFTR modulator therapy (elixacaftor/tezacaftor/ivacaftor).

With your support, we have started recording COVID-19 positive patients in the Registry and will report on the impacts on cystic fibrosis patients in Germany in Muko.web on the homepage of the Mukoviszidose e.V. in the near future and also in the report for the first time. 114 COVID-19

infections were diagnosed (by means of PCR) from February 2020 to the middle of August 2021 (corresponds to 1.7 % of all people reported with cystic fibrosis in 2020). Unfortunately, two people with cystic fibrosis died of their COVID-19 infections.

A CFTR modulator therapy was approved for approx. 68 % of the people with cystic fibrosis in Germany at the end of the year 2020 and used in 43 % of the people with cystic fibrosis in Germany in 2020. The impacts of the approval as extended in 2021 on the use and the health status will not be reflected until the next report.

We are presenting the developments that have taken place in age distribution, diagnoses, nutritional status, the severity level of the pulmonary function and the verification of *Pseudomonas* since 2000 for the first time. This impressively demonstrates the long-term positive development of the treatment results, as well as the challenges ahead, such as the treatment of underweight and the premature restricted pulmonary function which occurs in children, adolescents and young adults to some extent.

This detailed overview of the health status of people with cystic fibrosis would not have been possible without the trust you have placed in us. I would like to express my thanks to all the outpatient clinic teams and the people with cystic fibrosis who allow us to document and evaluate their data. Many thanks to all those who input and evaluate the data under the difficult conditions caused by the corona pandemic. My thanks also go to the Registry Work Group, the axaris company (Ms Jaumann, Mr Müller, Mr Volk) and the data management and statistics team of the Interdisciplinary Center for Clinical Studies (IZKS) of the University of Mainz (Ms Wosniok, Ms Wollscheid, Ms Regenfuß, Mr Kronfeld, Mr Ruckes, Mr Engelmann). My special thanks go to Mr Burkhart of the Mukoviszidose Institut for his tireless efforts in project management.

Please keep supporting the Registry.

Kollektivbeschreibung

The history data records of 6.648 people with cystic fibrosis (pwCF) are included in the analyses of the demography, Cystic Fibrosis diagnosis, mortality and structure of care for the reporting year 2020. In addition, patients without history data were also included in the evaluations of new CF diagnoses and mortality (23 newly diagnosed patients and 12 deceased patients without history data in 2020).

All 353 transplant patients were excluded from the evaluations of nutritional status, pulmonary function, lung infections, complications and therapies, regardless of the type of transplant. This results in a number of 6295 patients for the analysis of the history data.

Further definitions apply to the various evaluation groups in some cases. These are described in more detail in the respective chapters.

A current declaration of consent is available for all evaluated patients, or they died before consent could be renewed. Patients who withdrew their consent before death were excluded from the mortality analyses. The age of the patients was calculated in completed years at the end of the respective reporting year for patients not documented as deceased. The age at the time of death was calculated in completed years for patients who died during the reporting year. The age was calculated in completed years at the end of the reporting year for deceased patients for whom no date of death was documented. The age of newly diagnosed patients was calculated at the time of diagnosis.

The pulmonary function was calculated and reported using the reference values of the Global Lung Function Initiative (Quanjer et al; Eur Respir J 2012; 40: 1324).

The reference values according to the KiGGS study were used for calculation of the BMI percentiles for 2 – 18-year-old patients (Robert Koch Institute: Reference percentiles for anthropometric measures and blood pressure based on the German Health Interview and Examination Survey for Children and Adolescents (KiGGS); Berlin: RKI-Hausdruckerei; 2013).

Missing values were not taken into account for the calculation of the percentages.

The history data records are documented once a year in the so-called Level 1 documentation as the status for the entire calendar year or are aggregated from the visit-related data records of the so-called Level 2 documentation. The examination date with the best FEV₁%pred and the relevant body measurements are selected as the examination time point in the reporting year for patients older than 6 years with a pulmonary function measurement. The last body measurements available in the reporting year are used in the absence of an FEV₁ value and for children younger than 6 years. A complication occurring at least once a year or a longterm therapy, microbiological indication or a chronic infection determine the intensity for the entire reporting year. If history data sets from several outpatient clinics are available for a patient, they are aggregated in a single data set for the annual data report in accordance with the above rules.

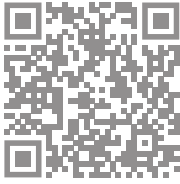
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Map of participating CF centers



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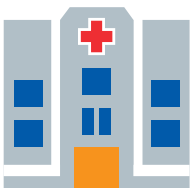


Figure 1: CF centers participating in 2020

The map shows all 88 CF centers participating in the Registry in 2020. A list of all CF facilities and the reported patient numbers can be found on page 58. Write to us if your facility is not represented: mburkhart@muko.info

Brief overview

	2000	2005	2010	2015	2019	2020
Data status	09.12.2020	09.12.2020	09.12.2020	09.12.2020	09.12.2020	10.06.2021
Participating centers	78	83	81	89	87	88
Participating patients with annual data	3,595	4,700	5,102	5,682	6,473	6,648
of these, transplant patients	50	128	200	280	365	353
Age in years; median	14	16	18	20	21	21
Proportion of adults (≥ 18 years) in %	36.3	45.7	51.3	56.4	58.2	58.7
Male patients in %	52.3	52.0	51.9	51.9	51.8	52.1
New diagnoses in the reporting year¹	223	202	212	216	217	195
Age for new diagnoses in years; Median¹	1.34	0.83	0.92	0.84	0.16	0.08
of these, diagnosis via newborn screening	2.7	4	5.2	10.6	61.3	63.1
Deaths in the reporting year¹	35	57	73	94	59	57
Deaths: % of all patients ¹	1	1.2	1.4	1.6	0.9	0.9
Age at death in years; median	22	27	28	30.5	35	35
(25 th – 75 th pctl)	(15 – 28)	(20 – 33)	(24 – 37)	(24 – 37)	(27 – 45)	(28 – 43)
Transplant patients in the reporting year¹	8	35	33	32	46	27
of these, lung transplants ²	6	31	29	29	41	23
of these, liver transplants ²	2	3	4	6	6	5
of these, renal transplantation ²	0	1	1	0	0	1
of these, pancreas transplantation ²	0	0	0	1	0	0
of these, Transplants other organs ²	0	1	0	0	0	0

Table 1: Brief overview of pwCF with annual data, valid declaration of consent and Cystic Fibrosis diagnosis in Germany in the reporting year 2019

¹ The values for new diagnoses, deaths and transplant patients also include patients without history data

² Multiple responses allowed

Patient numbers development

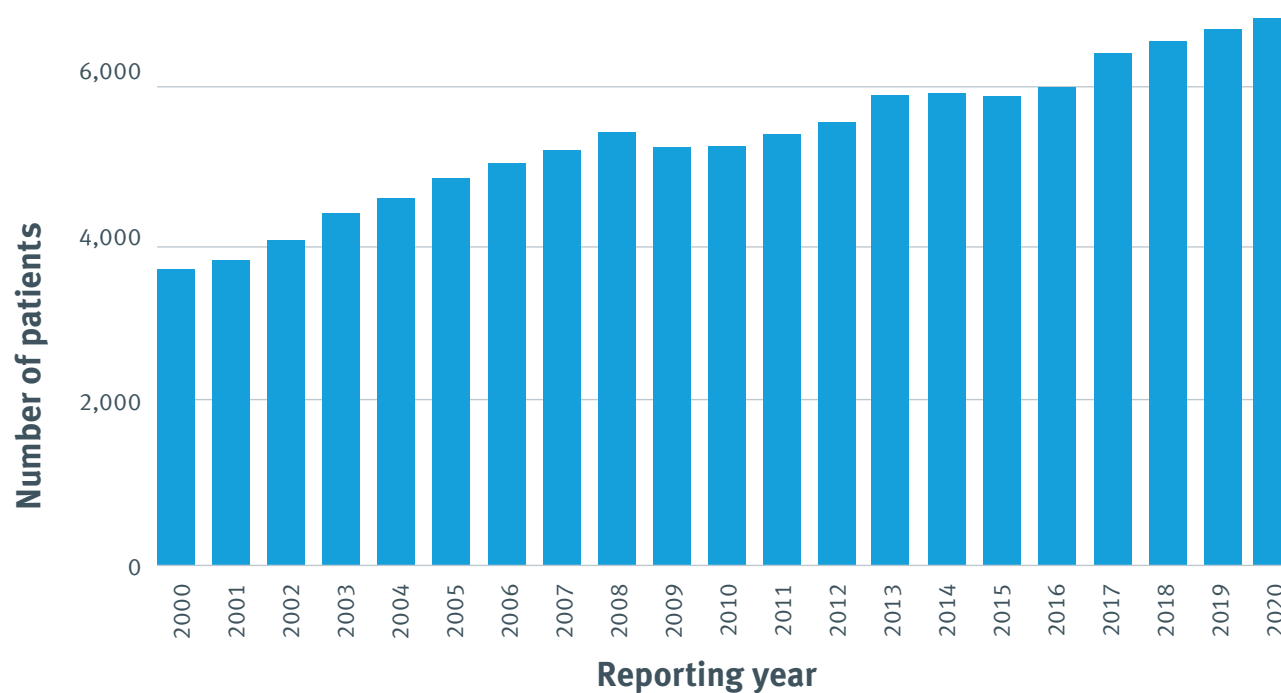


Figure 2: Number of patients documented in the registry 2000 – 2020

Reporting year	pwCF with annual data	Reporting year	pwCF with annual data
2000	3,595	2011	5,234
2001	3,713	2012	5,370
2002	3,926	2013	5,677
2003	4,260	2014	5,744
2004	4,440	2015	5,682
2005	4,700	2016	5,797
2006	4,854	2017	6,195
2007	4,995	2018	6,385
2008	5,237	2019	6,473
2009	5,075	2020	6,648
2010	5,102		

Table 2: Number of patients documented in the registry 2000 – 2020

Age structure

The age structure calculations include all 6,648 pwCF with annual data for 2020. The age of the patients was calculated in completed years at the end of the respective reporting year for patients not documented as deceased as well as for those without a date of death. The age at the time of death was calculated in completed years if the date of death was available.

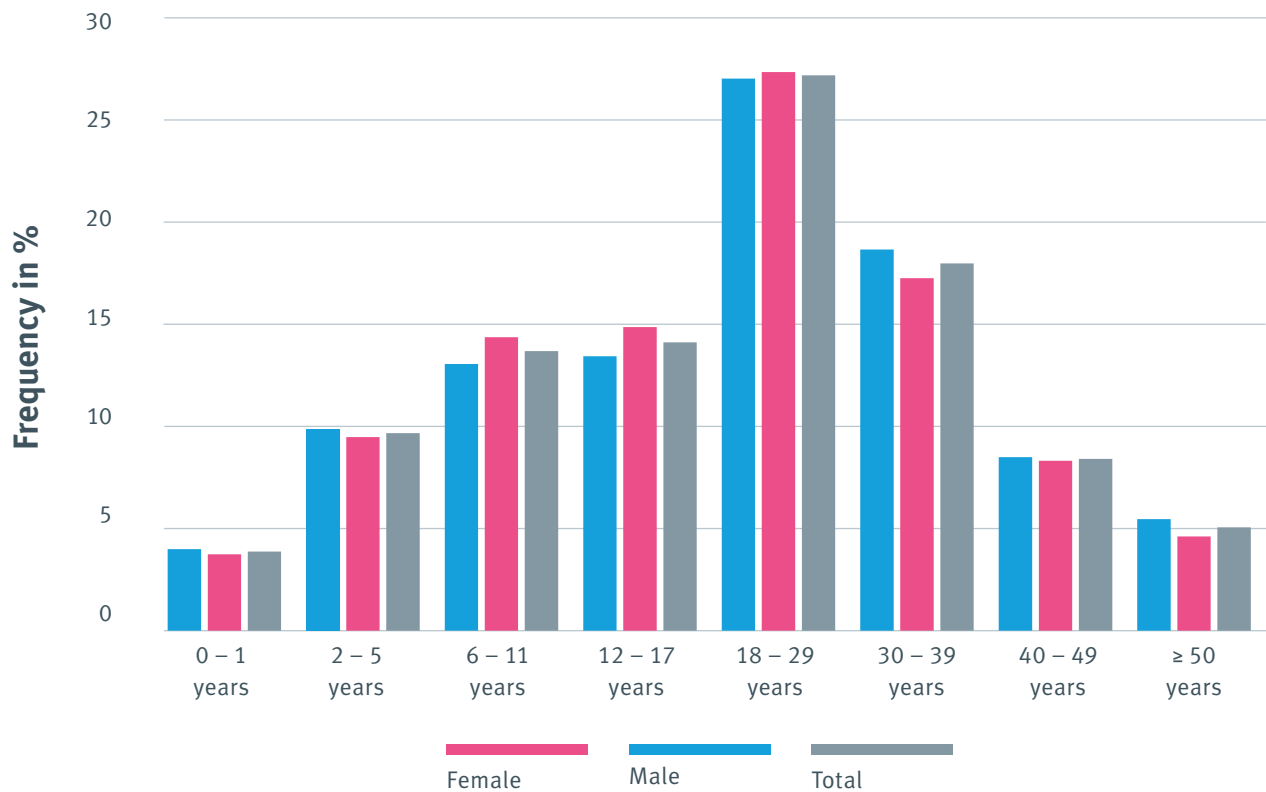


Figure 3: Age distribution of pwCF in 2020

	Male	Female	Total
Numbers	3,187	3,461	6,648
Mean value (years)	22.2	22.9	22.5
Median (years)	21	22	21
Minimum (years)	0	0	0
Maximum (years)	78	82	82
25th percentile (years)	10	11	10
75th percentile (years)	32	33	32
Number < 18 years	1,353	1,396	2,749
Number ≥ 18 years	1,834	2,065	3,899

Table 3: Age distribution of pwCF in 2020

Age structure

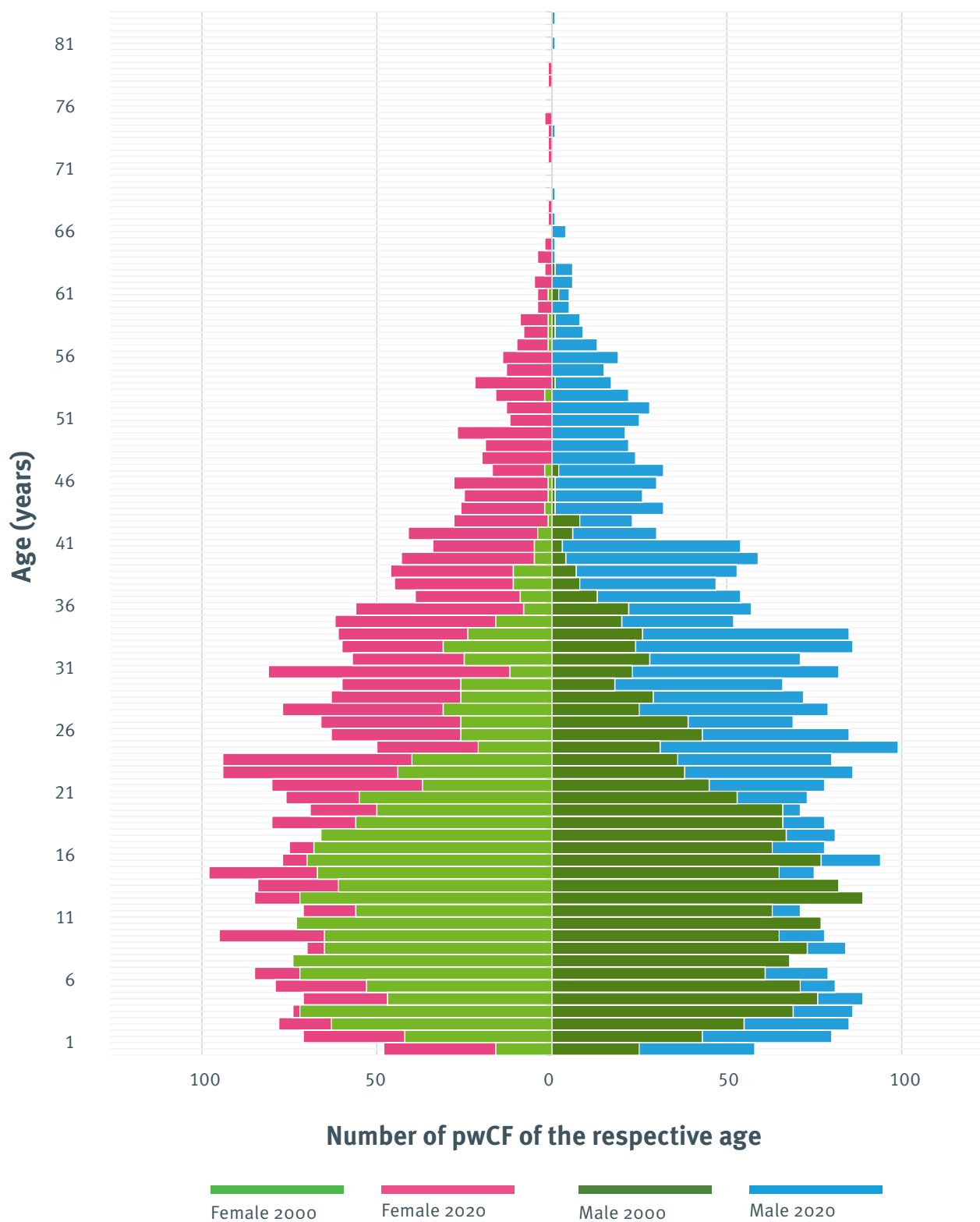


Figure 4: Age pyramid pwCF 2000 vs. 2020

Age structure

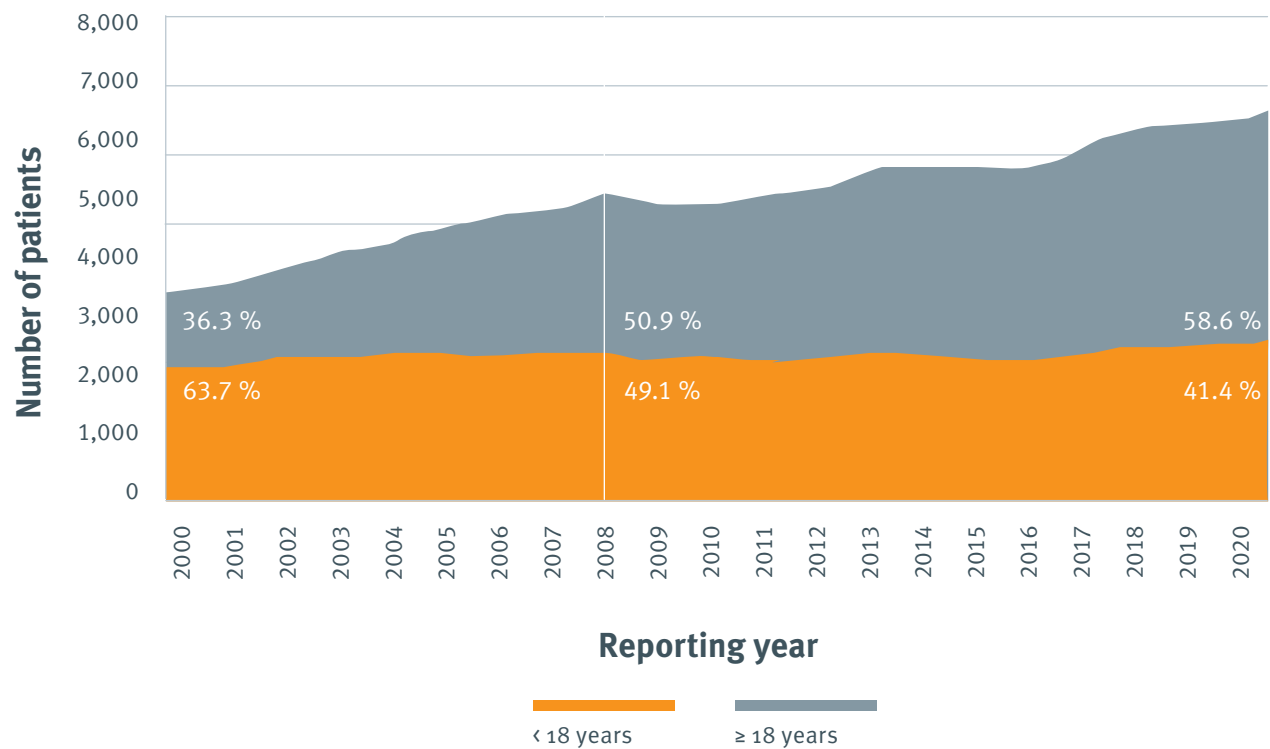


Figure 5: Development of age distribution (< 18 vs ≥ 18 years) for the years 2000 – 2020

Age structure

Reporting year	Total	< 18 years	≥ 18 years
2000	3,595	63.7	36.3
2001	3,713	62.5	37.5
2002	3,926	61.4	38.6
2003	4,260	57.8	42.2
2004	4,440	56.7	43.3
2005	4,700	54.3	45.7
2006	4,854	52.2	47.8
2007	4,995	51.7	48.3
2008	5,237	49.1	50.9
2009	5,075	48.5	51.5
2010	5,102	48.7	51.3
2011	5,234	46.0	54.0
2012	5,370	45.7	54.3
2013	5,677	44.2	55.8
2014	5,744	43.9	56.1
2015	5,682	43.6	56.4
2016	5,797	43.2	56.8
2017	6,195	41.8	58.2
2018	6,385	41.4	58.6
2019	6,473	41.8	58.2
2020	6,648	41.4	58.6

Table 4: Development of age distribution (<18 vs ≥ 18 years) for the years 2000 – 2020

Cystic fibrosis diagnosis

4a. Diagnoses in 2020

195 patients were diagnosed in 2020; annual data is available for 172 of these patients (88.2 %). The age distribution of all patients newly diagnosed in 2020 is shown in the following tables.

	N	Mean value	Median	Minimum	Maximum	25 th percentile	75 th percentile
Age in years	195	4.4	0.1	0.0	67.7	0.1	2.7

Table 5: Age at diagnosis of all pwCF diagnosed in 2020

Newborn screening was performed in 123 (63.1 %) of the pwCF diagnosed in 2020. 21 patients (10.8 %) had a meconium ileus. The age at diagnosis of the patients newly diagnosed via newborn screening in 2020 is as follows:

	N	Mean value	Median	Minimum	Maximum	25 th percentile	75 th percentile
Age in years	123	32.7	25.0	0.0	213.0	17.0	39.0

Table 6: Age at diagnosis of allpwCF diagnosed via newborn screening in 2020

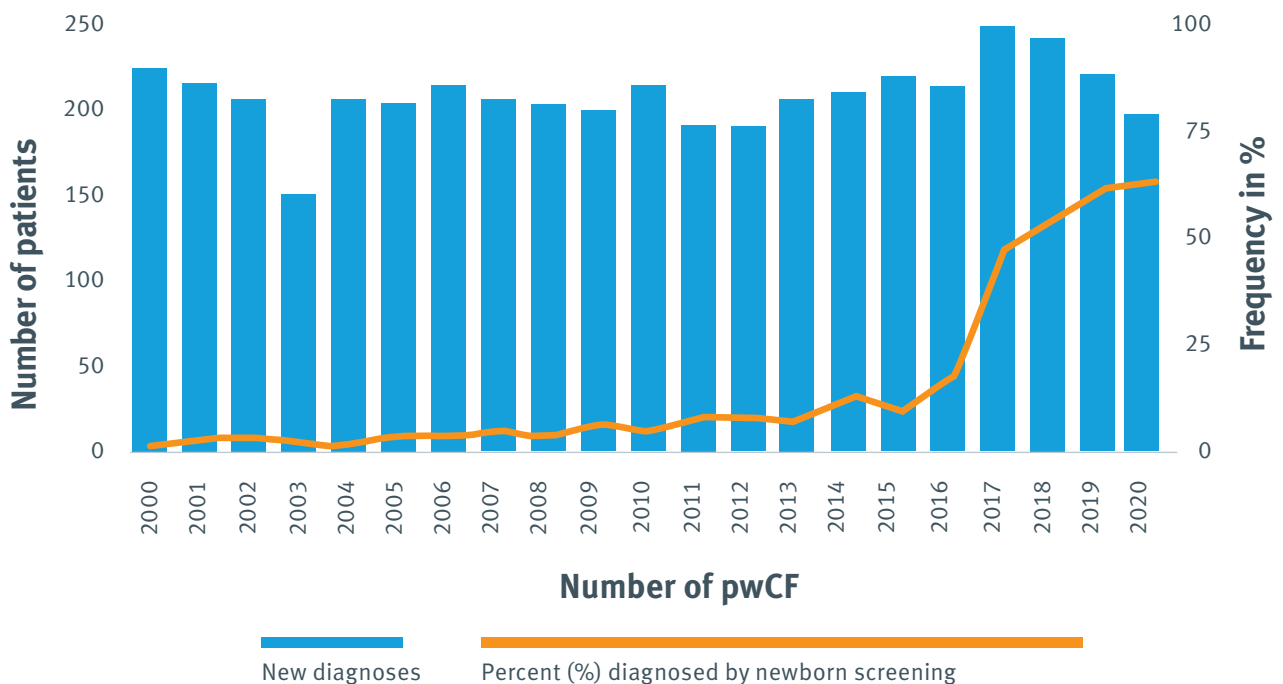


Figure 6: Number of new diagnoses and percentage frequency of pwCF diagnosed by newborn screening 2000 – 2020

Cystic fibrosis diagnosis

4a. Diagnoses in 2020

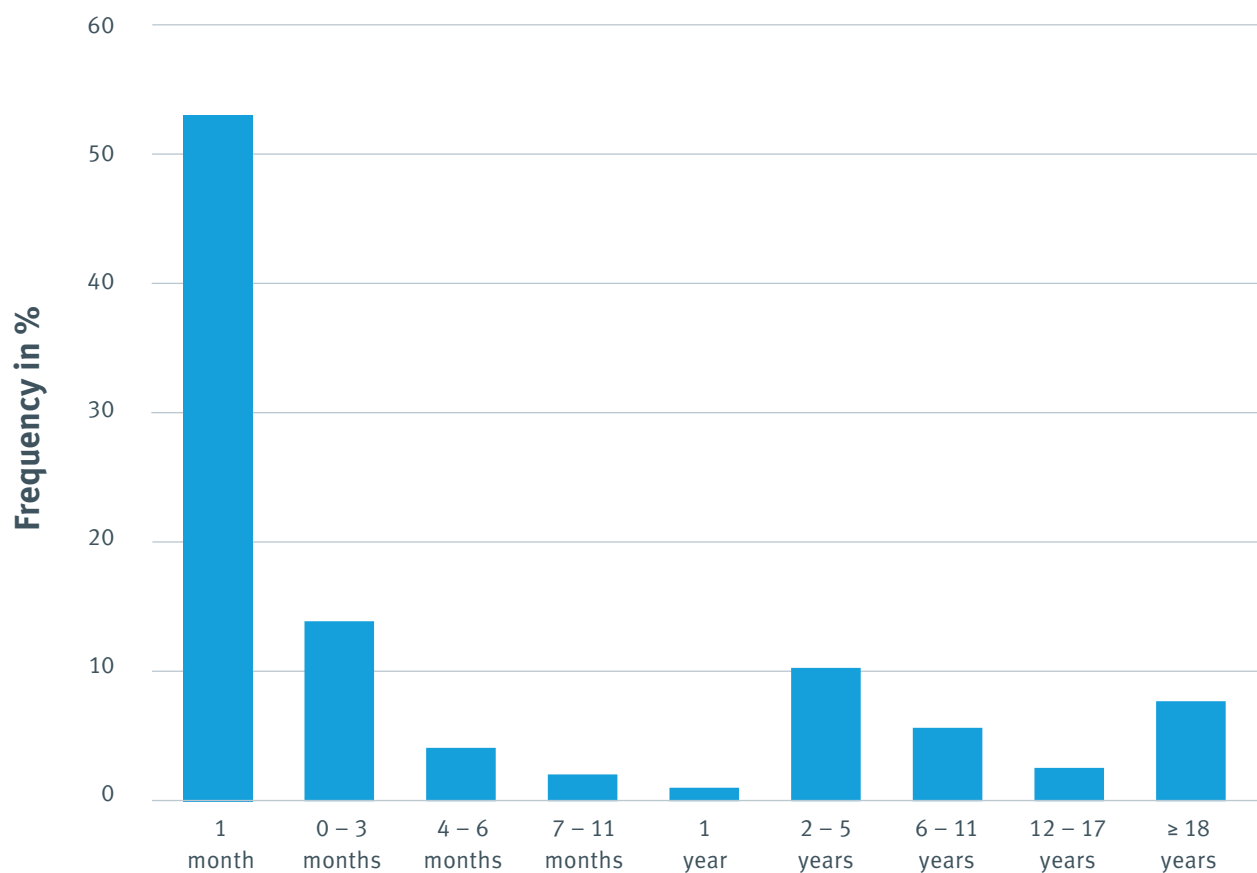


Figure 7: Age-related frequencies among pwCF diagnosed in 2020

Age at diagnoses	Frequency	Percent	Accumulated percentages
≤ 1 month	103	52.8	52.8
2 – 3 months	27	13.9	66.7
4 – 6 months	8	4.1	70.8
7 – 11 months	4	2.1	72.8
1 year	2	1.0	73.9
2 – 5 years	20	10.3	84.1
6 – 11 years	11	5.6	89.8
12 – 17 years	5	2.6	92.3
≥ 18 years	15	7.7	100.0

Table 7: Age at diagnosis among pwCF diagnosed in 2020

Cystic fibrosis diagnosis

4b. Age at diagnosis

The age distribution at diagnosis of the 6,648 patients with follow-up data in 2020 is shown in the following figures and tables. No information on the date of diagnosis was available for 238 patients (3.6 %).

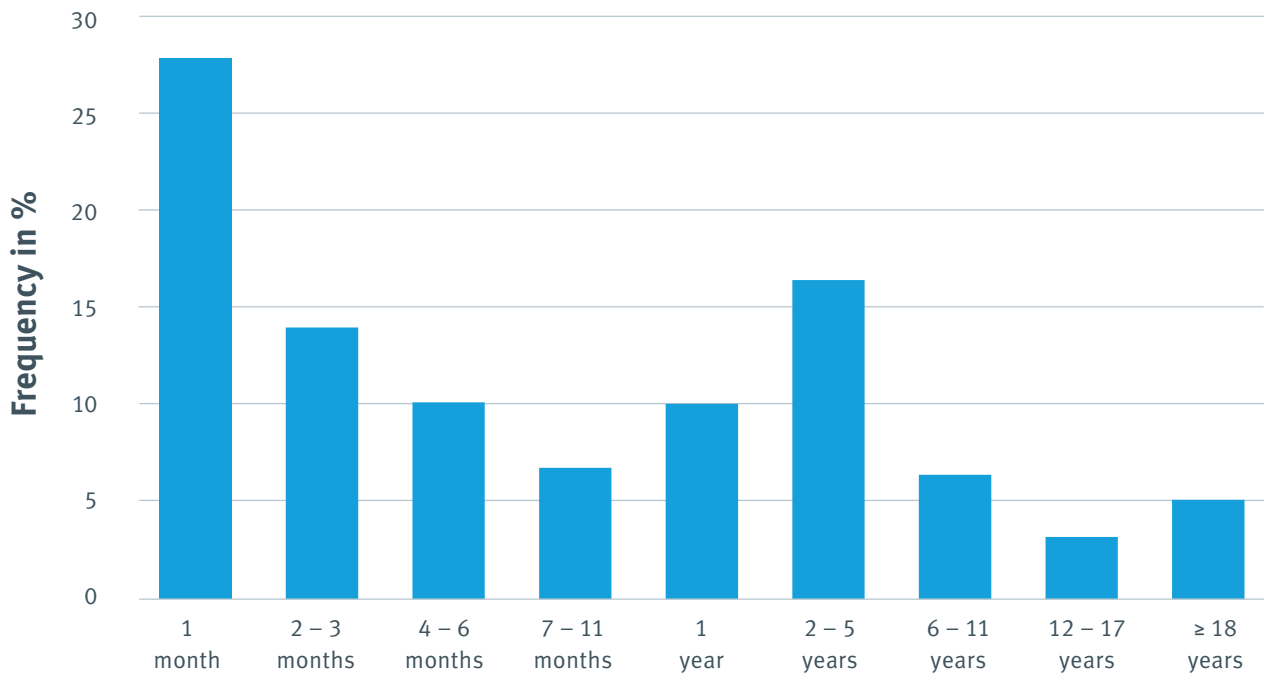


Figure 8: Age-related frequencies at diagnosis – all pwCF as of 2020

Age at diagnoses	Frequency	Percent	Accumulated percentages
≤ 1 month	1,785	27.9	27.9
2 – 3 months	897	14.0	41.8
4 – 6 months	650	10.1	52.0
7 – 11 months	434	6.8	58.8
1 year	645	10.1	68.8
2 – 5 years	1,054	16.4	85.3
6 – 11 years	411	6.4	91.7
12 – 17 years	206	3.2	94.9
≥ 18 years	328	5.1	100.0
unknown	238		

Table 8: Age at diagnosis – all pwCF as of 2020

Cystic fibrosis diagnosis

4c. Genotyping

Genotyping was available for 6,589 patients (99.4 %). Missing data were treated as "mutation not identified" in the following presentation.

Mutation combinations	Frequency	Percent
F508del homozygot	3,040	45.7
F508del heterozygous: Second mutation identified	2,472	37.2
F508del heterozygous: Second mutation not identified	187	2.8
No verification of F508del: Both mutations identified	779	11.7
No verification of F508del: Only one mutation identified	66	1.0
No verification of F508del: No mutations identified	104	1.6
Total	6,648	100.0

Table 9: Mutation combinations pwCF 2020

The frequencies for the individual alleles are shown below, whereby only those with an absolute frequency of at least 50 are shown individually:

First and second mutation	Frequency	Percent
F508del (p.Phe508del/c.1521_1523delCTT)	8,739	66.4
G542X (p.Gly542X/c.1624G>T)	264	2.0
N1303K (p.Asn1303Lys/c.3909C>G)	262	2.0
R553X (p.Arg553X/c.1657C>T)	252	1.9
G551D (p.Gly551Asp/c.1652G>A)	220	1.7
CFTRdele2,3 (p.Ser18ArgfsX16/c.54-5940_273+10250del21kb)	189	1.4
R347P (p.Arg347Pro/c.1040G>C)	179	1.4
3849+10kbC>T (c.3718-2477C>T)	147	1.1
1717-1G>A (c.1585-1G>A)	109	0.8
2789+5G>A (c.2657+5G>A)	101	0.8
2183AA>G (p.Lys684SerfsX38/c.2051_2052delAAinsG)	92	0.7
W1282X (p.Trp1282X/c.3846G>A)	90	0.7
3272-26A>G (c.3140-26A>G)	62	0.5
M1101K (p.Met1101Lys/c.3302T>A)	59	0.5
R117H (p.Arg117His/c.350G>A)	57	0.4
2184insA (p.Gln685ThrfsX4 or p.Gln685Thrfs *4/c.2052dupA or c.2052dup)	54	0.4
621+1G>T (c.489+1G>T)	52	0.4
Other Mutation	1,907	14.5
Unknown/Mutation not identified	323	2.5
Total	13,158	100.0

Table 10: CFTR genotyping pwCF 2020

Nutritional status

5a. Children and adolescents under 18 years

All patients from 2 – 17 years without a transplant with annual data in 2020 (n=2,503) were included. No information on the nutritional status was available for 6 patients (0.2 %). The BMI percentiles according to KiGGS were used to assess the nutritional status of children and adolescents. The age was calculated at the time of the physical examination.

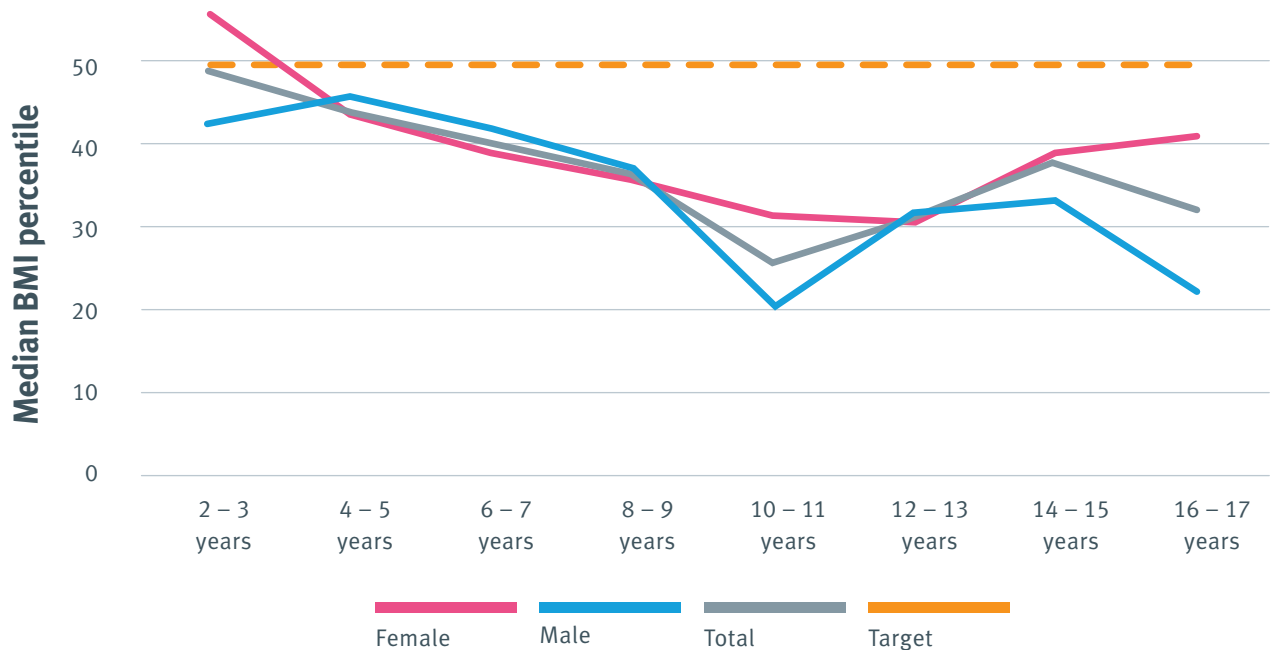


Figure 9: BMI percentiles of children and adolescents aged 2 – 17 years 2020

Age (years)	Male			Female			Total		
	N	Median	25 th – 75 th pctl.	N	Median	25 th – 75 th pctl.	N	Median	25 th – 75 th pctl.
2 – 3	167	43.0	18 – 70	156	55.5	30 – 77	323	49.0	22 – 72
4 – 5	189	46.0	20 – 70	163	44.0	22 – 71	352	44.0	22 – 70
6 – 7	150	42.0	22 – 60	147	39.0	14 – 62	297	41.0	20 – 60
8 – 9	153	37.0	21 – 61	171	36.0	19 – 62	324	36.5	20 – 61
10 – 11	142	21.0	10 – 47	134	31.5	15 – 51	276	26.0	13 – 50
12 – 13	137	32.0	15 – 54	181	31.0	13 – 49	318	31.0	13 – 52
14 – 15	166	33.5	14 – 63	163	39.0	21 – 61	329	38.0	17 – 61
16 – 17	158	22.5	9 – 51	120	41.0	20 – 65	278	32.5	13 – 59
Total	1,262	35.0	15 – 60	1,235	38.0	19 – 63	2,497	37.0	17 – 62

Table 11: BMI percentiles of children and adolescents aged 2 – 17 years 2020

Nutritional status

5a. Children and adolescents under 18 years

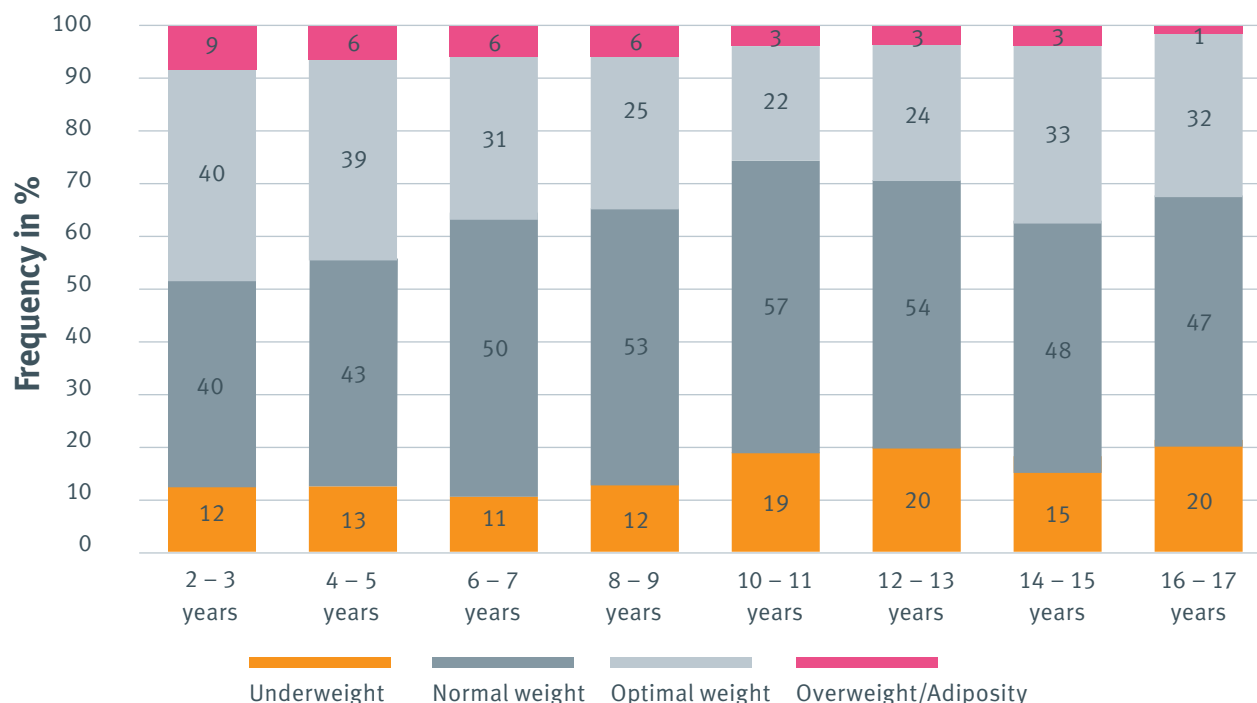


Figure 10: Weight categories of children and adolescents aged 2 – 17 (frequencies in %) 2020, Underweight: BMI percentiles < 10; Normal weight: BMI percentiles 10 – 49; Optimal weight: BMI percentiles 50 – 89; Overweight/Adiposity: BMI percentiles ≥ 90

BMI percentile KIGGS	Male	Female	Total
Underweight	16.6	13.7	15.2
Normal weight	48.5	48.7	48.6
Optimal weight	29.6	33.3	31.4
Overweight/Adiposity	5.2	4.4	4.8

Table 12: Weight categories of children and adolescents aged 2 – 17 years 2020, Underweight: BMI percentiles < 10; Normal weight: BMI percentiles 10 – 49; Optimal weight: BMI percentiles 50 – 89; Overweight/Adiposity: BMI percentiles ≥ 90

Nominal length weight	Male		Female		Total	
	0 – 12 months	13 – 24 months	0 – 12 months	13 – 24 months	0 – 12 months	13 – 24 months
Underweight	22.5	8.3	37.1	13.6	29.8	10.5
Normal weight	67.6	85.7	54.3	74.6	61	81.1
Overweight/Adiposity	9.9	6.0	8.6	11.9	9.2	8.4

Table 13: Weight categories of children under 2 years (frequencies in %) according to length/target weight (LSG) 2020/Underweight: LSG < 90 %; Normal weight: LSG 90 – 110 %; Overweight/obese: LSG > 110 %.

Nutritional status

5b. Adults 18 years and older

Adult patients without a transplant with annual data for 2020 (n=3,496) were included. No information on the nutritional status was available for 15 patients (0.4 %). The age was calculated at the time of the physical examination.

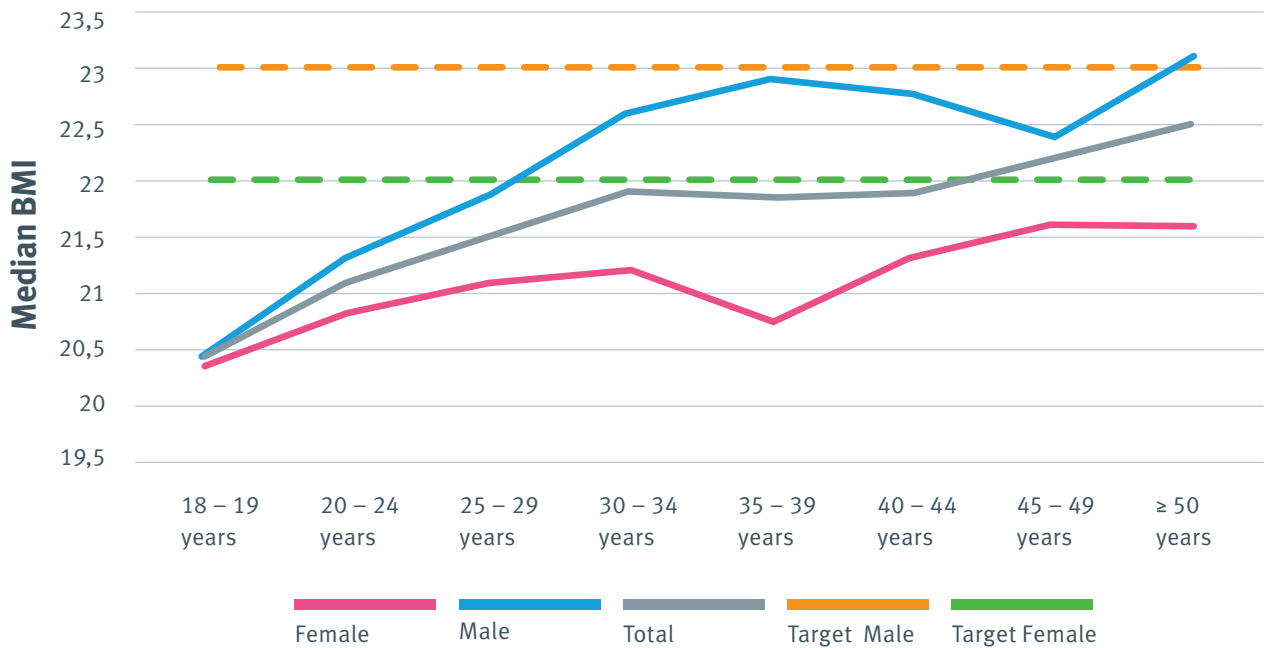


Figure 11: BMI of adults aged 18 and over 2020

Age (years)	Male			Female			Total		
	N	Median	25 th – 75 th pctl.	N	Median	25 th – 75 th pctl.	N	Median	25 th – 75 th pctl.
18 – 19	134	20.5	19 – 23	140	20.4	19 – 22	274	20.4	19 – 22
20 – 24	397	21.3	20 – 23	366	20.9	19 – 23	763	21.1	20 – 23
25 – 29	356	21.9	20 – 24	313	21.1	20 – 23	669	21.5	20 – 24
30 – 34	338	22.6	21 – 25	270	21.2	19 – 23	608	21.9	20 – 24
35 – 39	235	22.9	21 – 26	191	20.8	20 – 23	426	21.9	20 – 25
40 – 44	128	22.8	21 – 24	123	21.3	20 – 23	251	21.9	20 – 24
45 – 49	121	22.4	21 – 25	88	21.6	20 – 25	209	22.2	21 – 25
≥ 50	150	23.1	21 – 26	131	21.6	20 – 24	281	22.5	21 – 25
Total	1,859	22.1	20 – 24	1,622	21.1	20 – 23	3,481	21.5	20 – 24

Table 14: BMI of adults aged 18 and over 2020

Nutritional status

5b. Adults 18 years and older

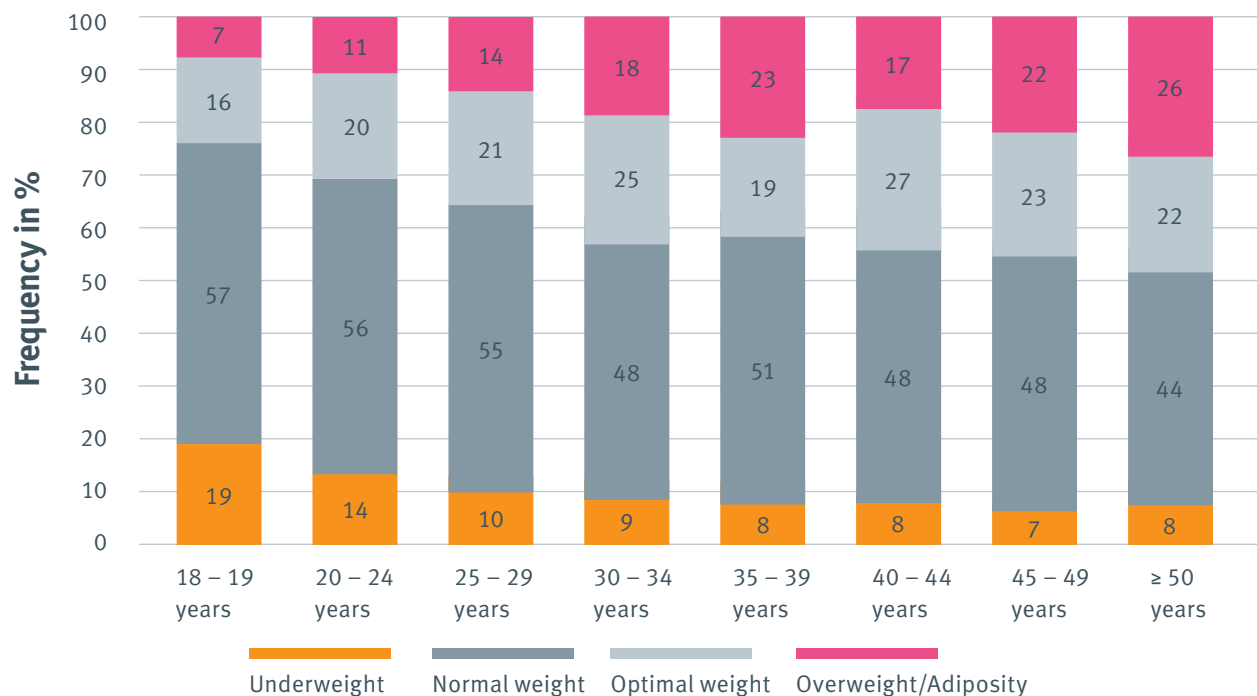


Figure 12: Weight categories adults 18 years and older (frequencies in %) 2020

Underweight: BMI < 18.5 kg/sqm; Normal weight: BMI men 18.5 – 22.9 kg/sqm; BMI women 18.5 – 21.9 kg/sqm;

Optimal weight: BMI men 23.0 – 24.9 kg/sqm, BMI women 22.0 – 24.9 kg/sqm; Overweight/Adiposity: BMI ≥ 25 kg/sqm

	Male	Female	Total
Underweight	8.9	12.8	10.7
Normal weight	51.6	52.1	51.9
Optimal weight	19.5	23.4	21.3
Overweight/Adiposity	20.0	11.7	16.1

Table 15: Weight categories of adults aged 18 and over (frequencies in %) 2020

Underweight : BMI < 18.5 kg/sq m; Normal weight: BMI men 18.5 – 22.9 kg/sq m; BMI women 18.5 – 21.9 kg/sq m;

Optimal weight: BMI men 23.0 – 24.9 kg/sqm, BMI women 22.0 – 24.9 kg/sqm; Overweight/Adiposity: BMI ≥ 25 kg/sqm

Nutritional status

5d. Development of nutritional status 2000 – 2020 Children and adolescents under 18 years of age

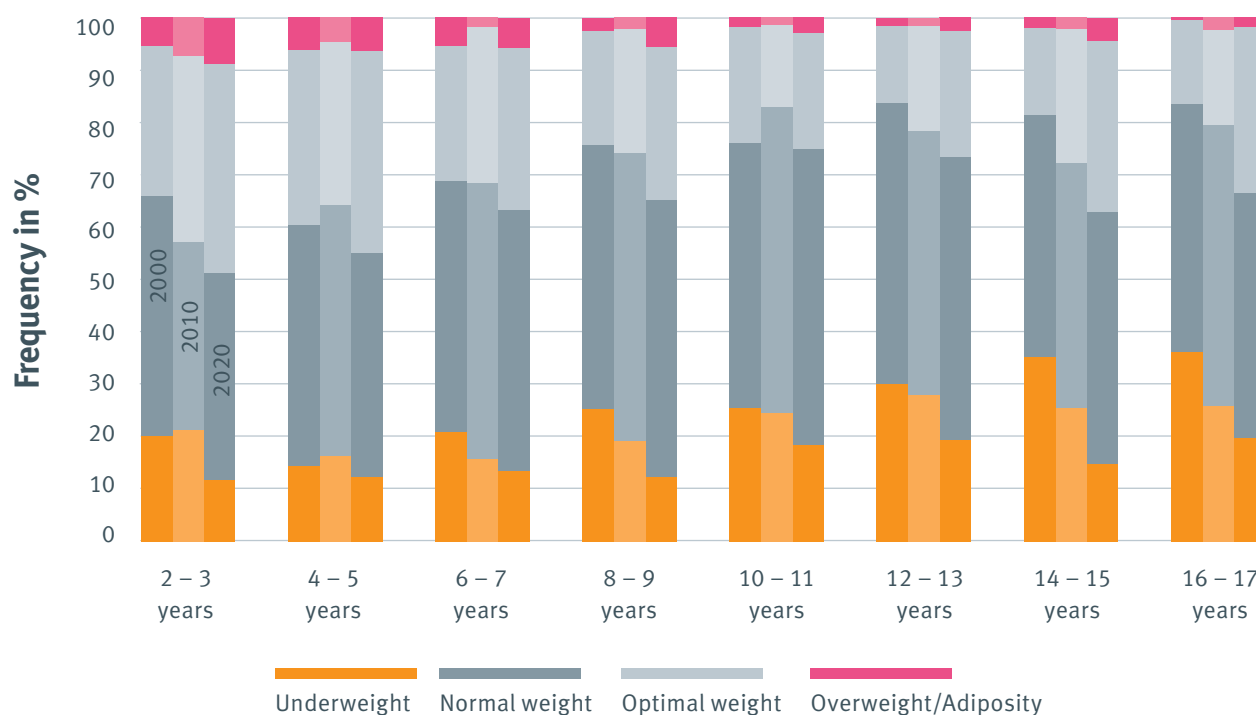


Figure 13: Development of weight categories of children and adolescents up to 17 years (frequencies in %) 2000 – 2020
Underweight: BMI percentiles < 10; normal weight: BMI percentiles 10 - 49; optimal weight: BMI percentiles 50 – 89;
Overweight/Adiposity: BMI percentiles ≥ 90

Weight categories	Reporting year	Age (years)							
		2 – 3	4 – 5	6 – 7	8 – 9	10 – 11	12 – 13	14 – 15	16 – 17
Underweight	2000	20	15	21	26	26	30	35	36
	2010	21	16	16	19	25	28	26	26
	2020	12	13	14	12	19	20	15	20
Normal weight	2000	46	46	48	50	51	54	46	47
	2010	36	48	53	55	58	51	47	54
	2020	40	43	50	53	57	54	48	47
Optimal weight	2000	29	33	26	22	22	15	16	16
	2010	35	31	30	24	16	20	26	18
	2020	40	39	31	29	22	24	33	32
Overweight/Adiposity	2000	6	6	5	2	2	2	2	–
	2010	7	5	2	2	1	2	2	2
	2020	9	6	6	6	3	3	4	2

Table 16: Development of weight categories of children and adolescents up to 17 years (frequencies in %) 2000 – 2020
Underweight: BMI-Perzentile < 10; Normal weight: BMI-Perzentile 10 – 49; Optimal weight: BMI-Perzentile 50 – 89;
Overweight/Adiposity: BMI-Perzentile ≥ 90

Nutritional status

5e. Development of nutritional status 2000 – 2020 Adults aged 18 and over

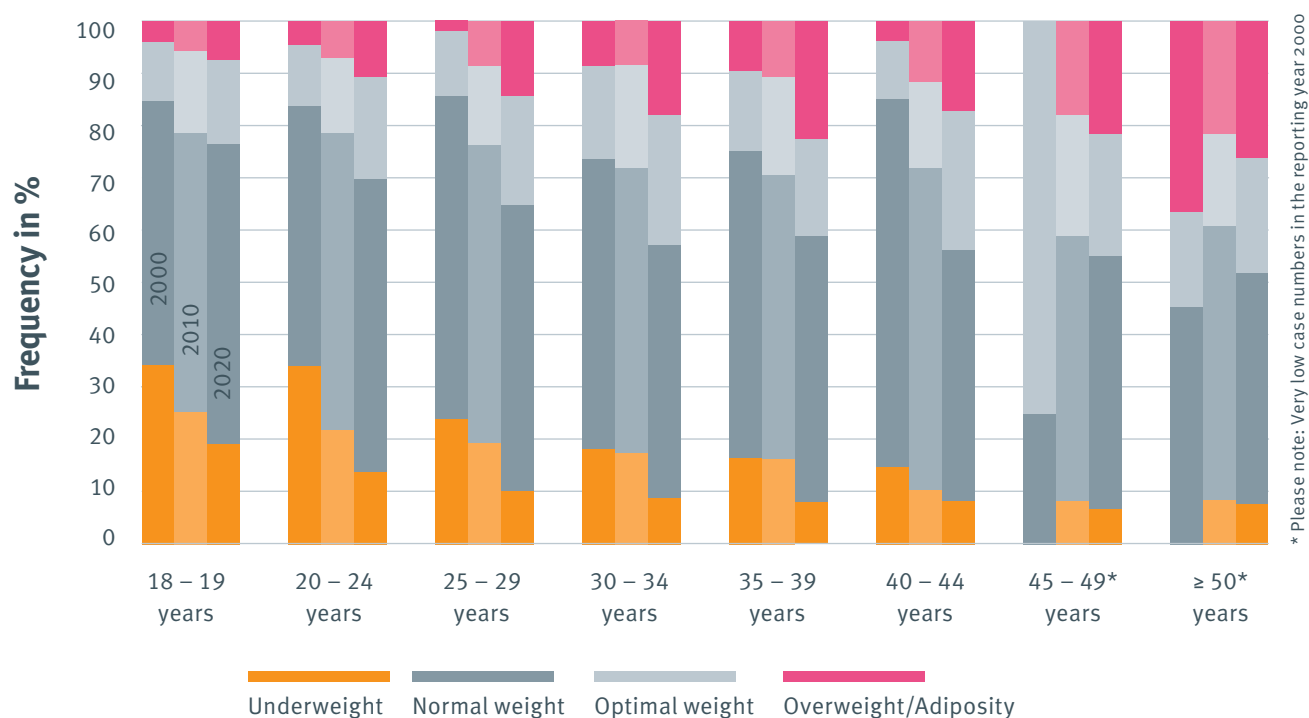


Figure 14: Development of weight categories of adults aged 18 and over (frequencies in %) 2000 – 2020
 Underweight : BMI < 18.5 kg/sqm; Normal weight: BMI men 18.5 – 22.9 kg/sqm; BMI women 18.5 – 21.9 kg/sqm;
 Optimal weight: BMI men 23.0 – 24.9 kg/sqm, BMI women 22.0 – 24.9 kg/sqm; Overweight/Adiposity: BMI ≥ 25 kg/sqm

Weight categories	Reporting year	Age (years)							
		18 – 19	20 – 24	25 – 29	30 – 34	35 – 39	40 – 44	45 – 49	≥ 50
Underweight	2000	34	34	24	18	17	15	---	---
	2010	25	22	20	18	16	11	8	9
	2020	19	14	10	9	8	8	7	8
Normal weight	2000	51	50	62	55	59	70	25	46
	2010	53	57	57	54	54	62	51	52
	2020	57	56	55	48	51	48	48	44
Optimal weight	2000	11	12	12	18	15	11	75	18
	2010	16	14	15	20	19	16	23	17
	2020	16	20	21	25	19	27	23	22
Overweight/Adiposity	2000	4	5	2	9	9	4	–	36
	2010	6	7	9	9	11	12	18	22
	2020	7	11	14	18	23	17	22	26

Table 17: Development of weight categories of adults aged 18 and over (frequencies in %) 2000 – 2020
 Underweight : BMI < 18.5 kg/sqm; Normal weight: BMI men 18.5 – 22.9 kg/sqm; BMI women 18.5 – 21.9 kg/sqm;
 Optimal weight: BMI men 23.0 – 24.9 kg/sqm, BMI women 22.0 – 24.9 kg/sqm; Overweight/Adiposity: BMI ≥ 25 kg/sqm

Lung function

6a. Overview of lung function

All patients of 6 years and older without a transplant with a pulmonary function measurement in 2020 were included in the evaluations of the lung function. A total of 5,187 data sets were available.

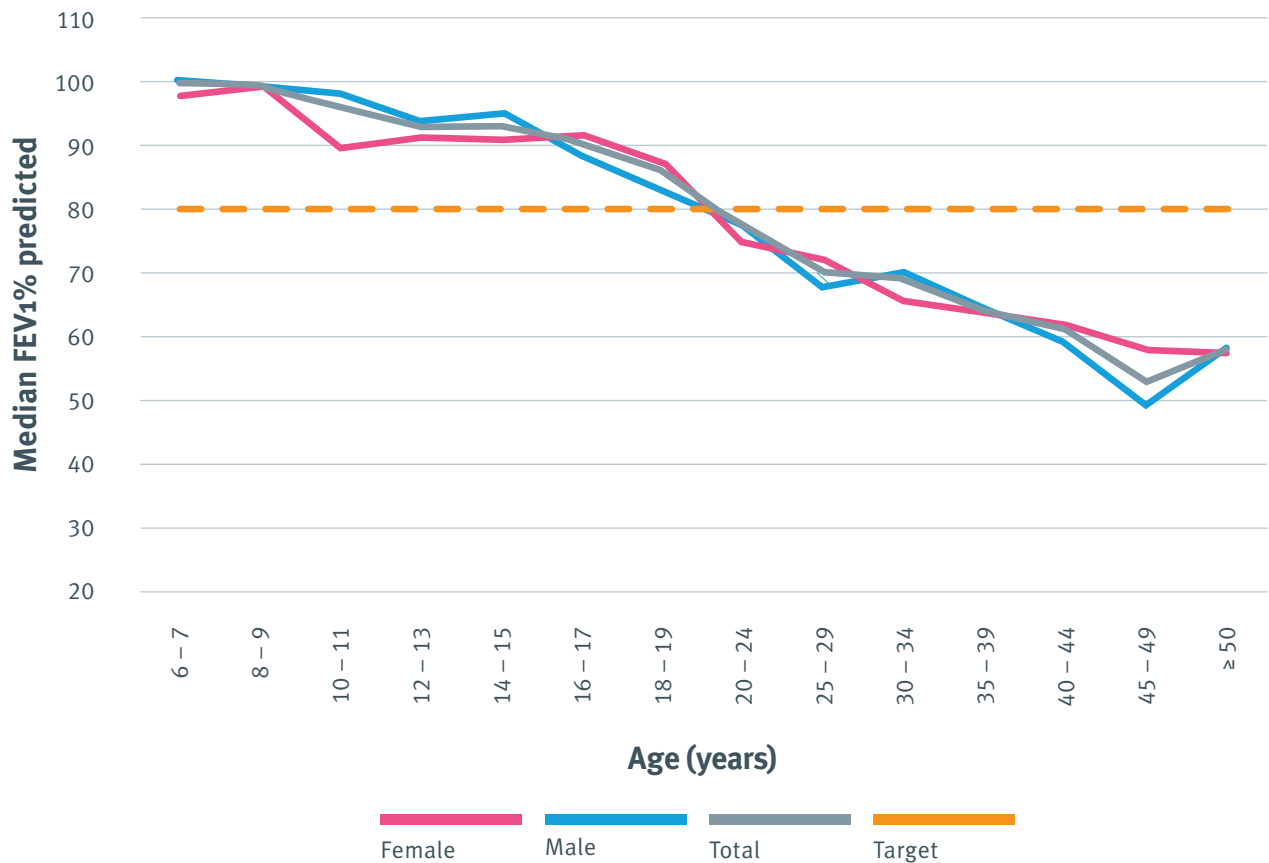


Figure 15: FEV1% value 2020 according to Global Lung Function Initiative (GLI)

Lung function

Age (years)	Male			Female			Total		
	N	Median	25 th –75 th pctl.	N	Median	25 th –75 th pctl.	N	Median	25 th –75 th pctl.
6 – 7	146	100	90 – 112	141	98	89 – 107	287	100	90 – 109
8 – 9	150	99	88 – 106	164	99	90 – 106	314	99	89 – 106
10 – 11	136	98	90 – 105	133	90	83 – 104	269	96	85 – 105
12 – 13	136	94	84 – 104	179	91	80 – 101	315	93	82 – 103
14 – 15	164	95	85 – 103	159	91	81 – 103	323	93	83 – 103
16 – 17	157	89	75 – 99	119	91	77 – 100	276	90	76 – 100
18 – 19	132	84	69 – 96	138	87	62 – 99	270	86	66 – 98
20 – 24	390	77	58 – 92	361	75	56 – 91	751	77	57 – 91
25 – 29	347	69	51 – 89	305	72	54 – 91	652	70	53 – 90
30 – 34	335	70	51 – 87	265	66	50 – 84	600	69	50 – 86
35 – 39	226	65	42 – 85	187	64	47 – 80	413	64	46 – 82
40 – 44	119	59	40 – 79	122	62	49 – 80	241	61	44 – 79
45 – 49	118	50	40 – 71	85	58	42 – 69	203	53	41 – 71
≥ 50	147	58	38 – 80	126	58	44 – 72	273	58	41 – 77
Total	2,703	81	58 – 97	2,484	81	59 – 96	5,187	81	58 – 97

Table 18: FEV₁% value 2020 according to Global Lung Function Initiative (GLI)

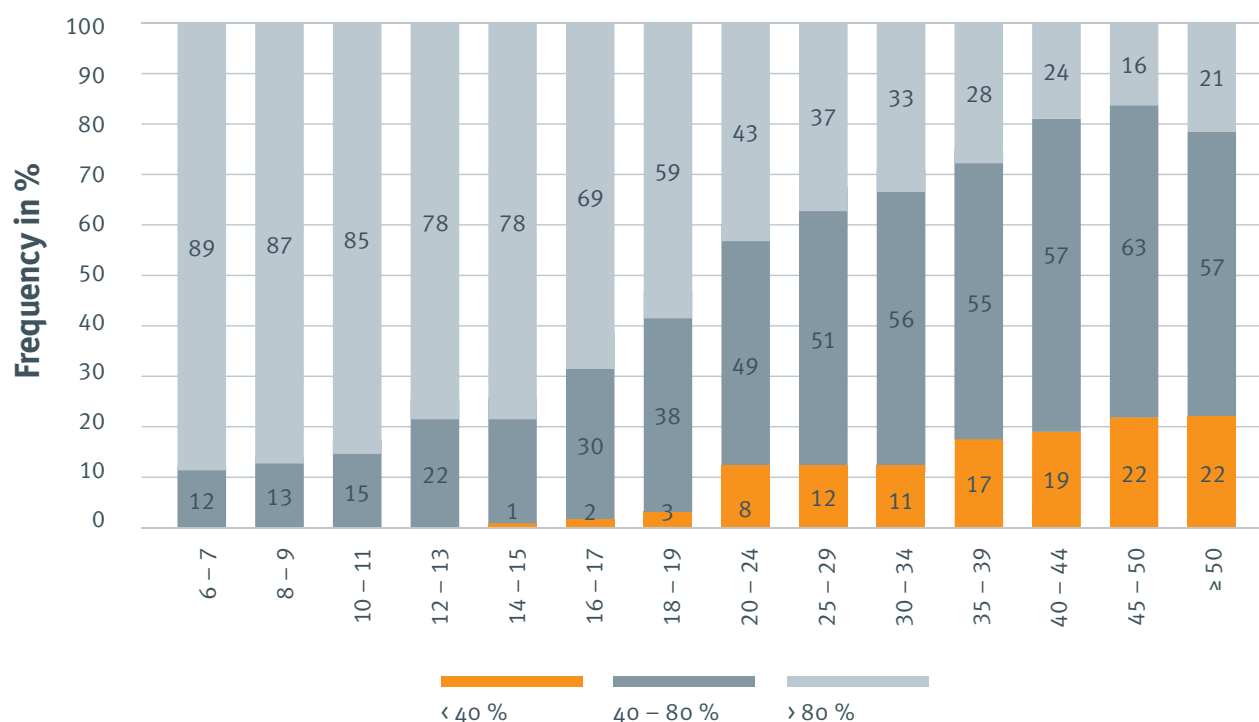


Figure 16: Severity of FEV₁% (categories < 40 %, 40 - 80 %, > 80 %) 2020 according to Global Lung Function Initiative (GLI)

Lung function

6b. Development of lung function 2000 – 2020

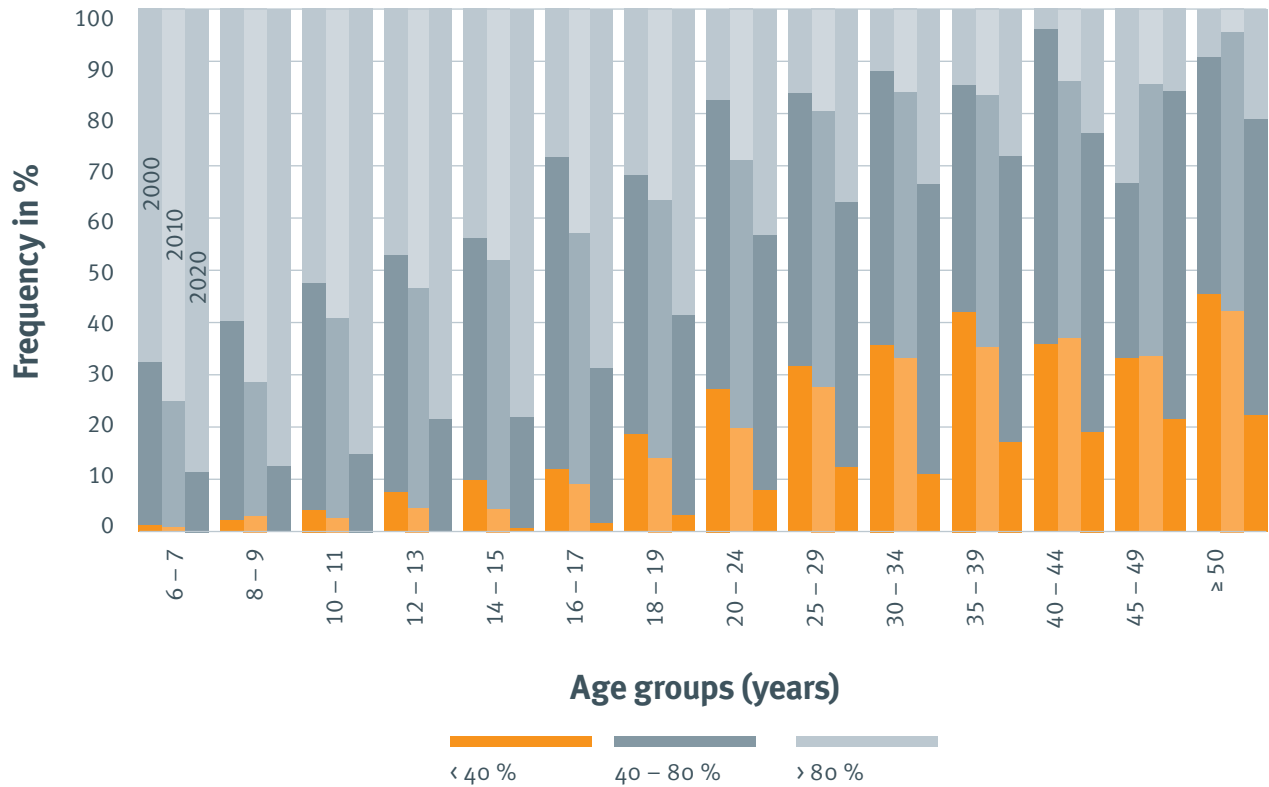


Figure 17: Development of age-related frequencies (in %) of FEV1% severity according to the Global Lung Initiative (GLI) 2000 – 2020

Severity levels of FEV1%	Reporting year	Age groups (years)													
		6 – 7	8 – 9	10 – 11	12 – 13	14 – 15	16 – 17	18 – 19	20 – 24	25 – 29	30 – 34	35 – 39	40 – 44	45 – 49	≥ 50
< 40 %	2000	1	2	4	8	10	12	19	27	32	36	42	36	33	46
	2010	1	3	3	5	4	9	14	20	28	33	35	37	34	42
	2020	---	---	---	---	1	2	3	8	12	11	17	19	22	22
40 – 80 %	2000	31	38	43	45	46	60	50	55	52	52	43	60	33	46
	2010	24	26	38	42	48	48	50	51	53	51	48	49	52	53
	2020	12	13	15	22	21	30	38	49	51	56	55	57	63	57
> 80 %	2000	67	60	53	47	44	28	32	17	16	12	15	4	33	9
	2010	75	71	59	54	48	43	36	29	20	16	17	14	15	4
	2020	89	87	85	78	78	69	59	43	37	33	28	24	16	21

Table 19: Development of age-related frequencies (in %) of FEV1% severity according to Global Lung Initiative (GLI) 2000 – 2020

Lung infections

7a. Annual verification at least once

All patients without a transplant who had at least one microbiological test in the calendar year were included in the evaluations of lung infections (n=6,150). No information on a microbiological test in the calendar year was available for 145 patients (2.3 %).

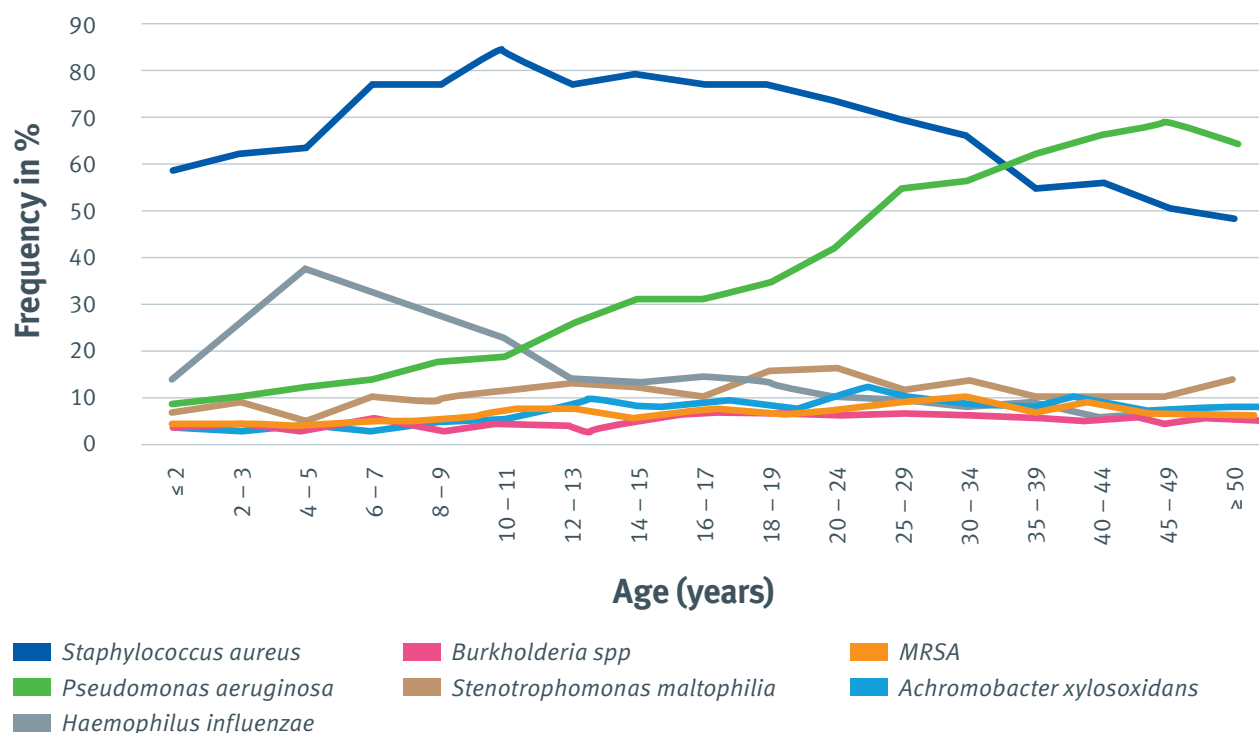


Figure 18: Bacteria detection in pwCF with microbiological examination 2020

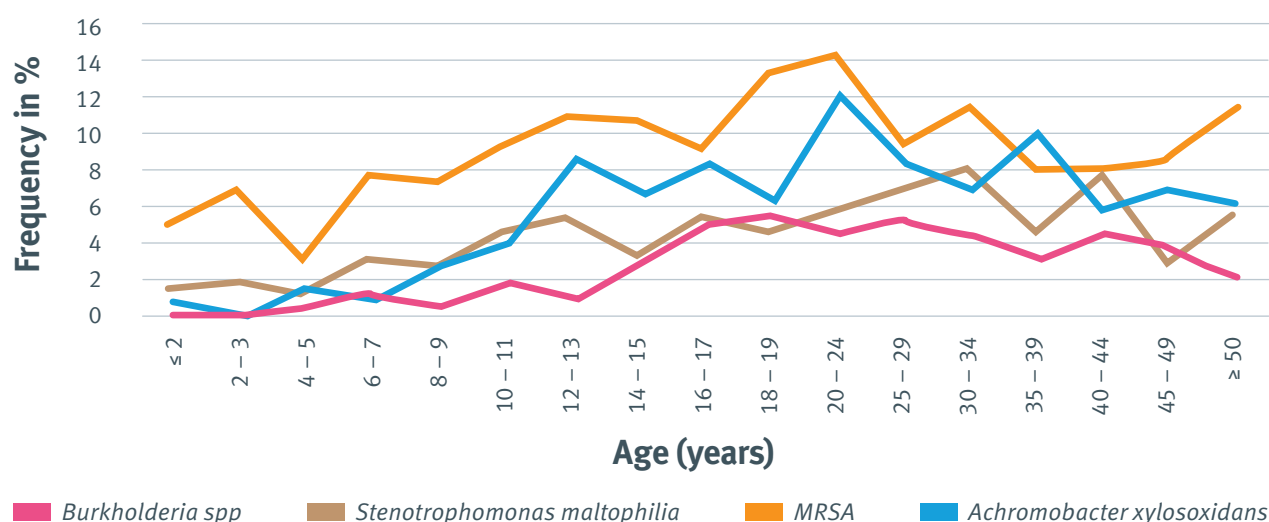


Figure 19: Bacteria detection in pwCF with microbiological examination (without the representation of *Pseudomonas aeruginosa* and *Staphylococcus aureus*) 2020

Lung infections

7a. Annual verification at least once

Age (years)	Staphylococcus aureus inklusive MRSA	MRSA	Pseudomonas aeruginosa (PSA)	Burkholderia spp	Stenotrophomonas maltophilia	Achromobacter xylosoxidans	Haemophilus influenzae
< 2	57.9	1.6	6.8	0.0	5.2	0.4	12.7
2 – 3	61.8	1.9	7.5	0.0	6.9	0.0	24.8
4 – 5	63.6	1.6	10.4	0.3	3.1	1.3	36.1
6 – 7	76.6	3.1	12.1	0.7	7.6	0.7	30.7
8 – 9	77.8	2.8	16.4	0.3	7.4	2.2	25.9
10 – 11	83.9	4.6	17.2	1.4	9.1	3.2	21.4
12 – 13	77.5	5.3	24.2	0.7	10.9	6.6	11.9
14 – 15	78.8	3.3	29.6	2.4	10.8	5.1	11.0
16 – 17	77.9	5.4	29.7	4.0	9.1	6.5	12.3
18 – 19	76.4	4.6	33.5	4.2	13.4	4.9	10.9
20 – 24	73.9	5.5	41.2	3.6	14.3	9.5	8.0
25 – 29	68.7	6.7	53.6	3.9	9.4	6.4	7.5
30 – 34	65.5	8.2	55.6	3.4	11.4	5.6	6.1
35 – 39	54.9	4.5	61.5	2.5	8.1	7.8	7.1
40 – 44	55.7	7.6	65.7	3.4	8.0	4.6	3.8
45 – 49	50.0	2.9	68.3	2.9	8.7	5.3	4.8
≥ 50	47.6	5.5	63.8	1.7	11.4	4.8	4.1
Total	68.2	4.8	37.4	2.3	9.6	5.0	13.1
< 18	73.0	3.3	17.2	1.1	7.8	2.9	21.0
≥ 18	64.4	6.0	53.2	3.3	11.0	6.6	6.9

Table 20: Detection of bacteria in pwCF with microbiological examination (frequencies in %) 2020

Lung infections

7b. Development of infections with *Pseudomonas aeruginosa* 2000 – 2020

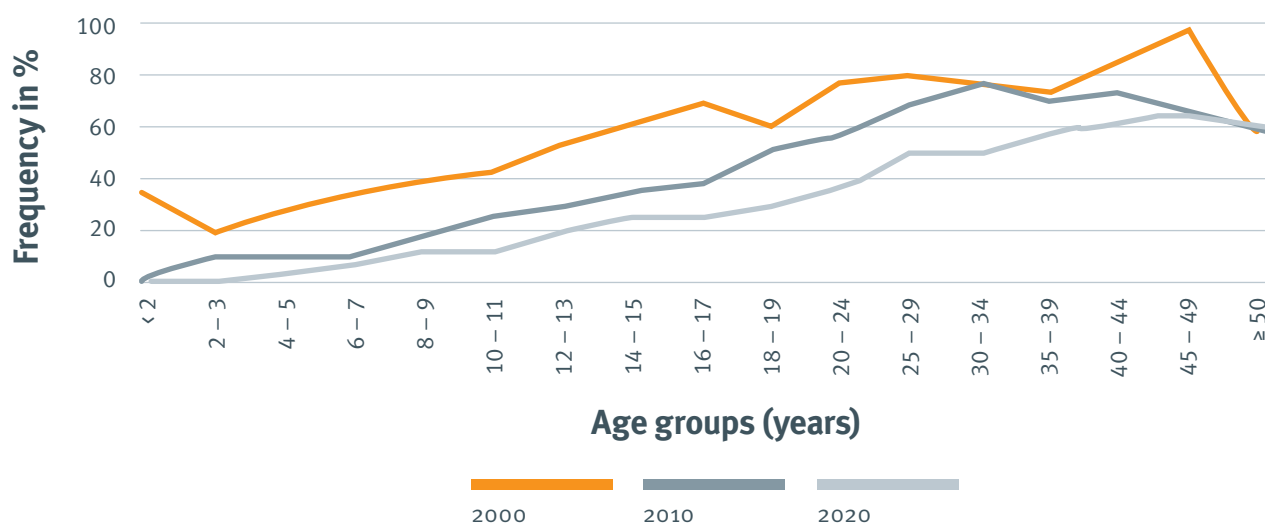


Figure 20: Development of *Pseudomonas aeruginosa* detections in pwCF with microbiological examination (frequencies in %) 2000 – 2020

Age (years)	2000	2010	2020
< 2	38.3	6.7	6.75
2 – 3	23.7	15.3	7.52
4 – 5	33.3	14.6	10.38
6 – 7	39.1	16.1	12.07
8 – 9	43.3	23.2	16.36
10 – 11	46.7	30.1	17.19
12 – 13	57.1	32.9	24.17
14 – 15	64.5	39.6	29.55
16 – 17	72.2	43.1	29.71
18 – 19	64.2	54.8	33.45
20 – 24	79.7	60.4	41.2
25 – 29	81.0	71.8	53.61
30 – 34	78.1	79.6	55.56
35 – 39	75.6	72.9	61.46
40 – 44	87.5	76.6	65.65
45 – 49	100.0	68.7	68.27
≥ 50	60.0	62.0	63.79

Table 21: Development of *Pseudomonas aeruginosa* detections in pwCF with microbiological examination (frequencies in %) 2000 – 2020

Lung infections

7c. Chronic lung infections

All patients without a transplant who had at least one microbiological test in the calendar year were included in the evaluations of chronic lung infections (n=6,150). No information on a microbiological test in the calendar year was available for 145 patients (2.3 %).

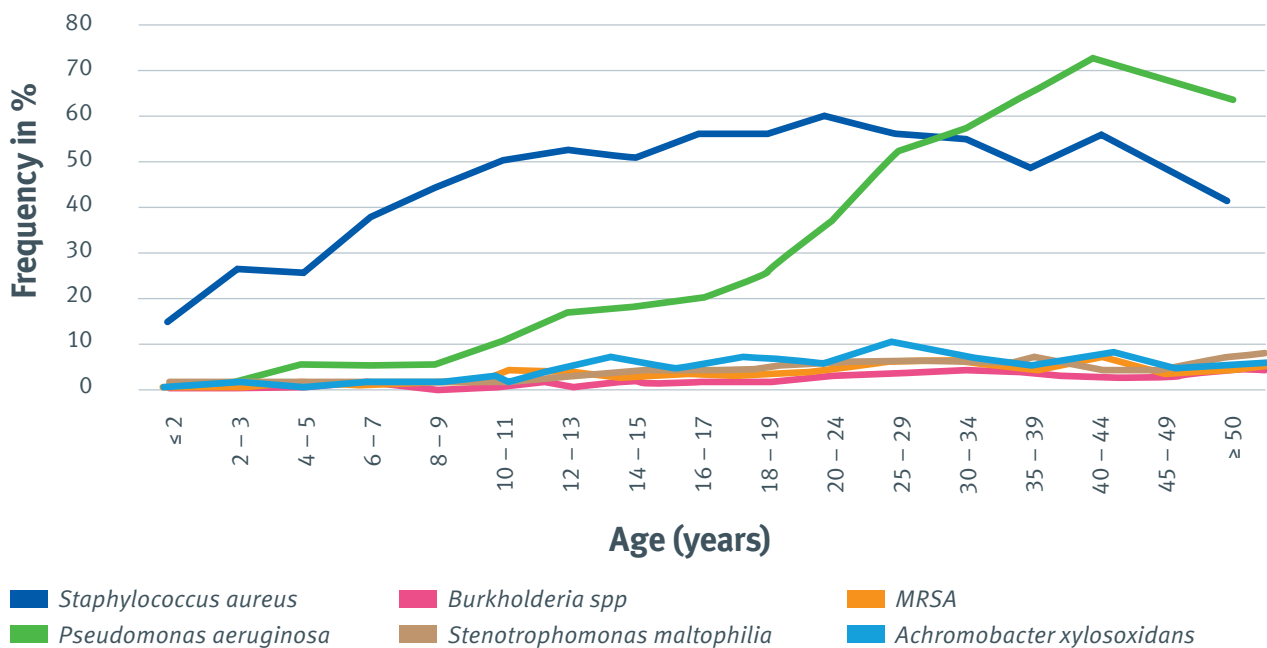


Figure 21: Chronic lung infections in pwCF with microbiological examination 2020

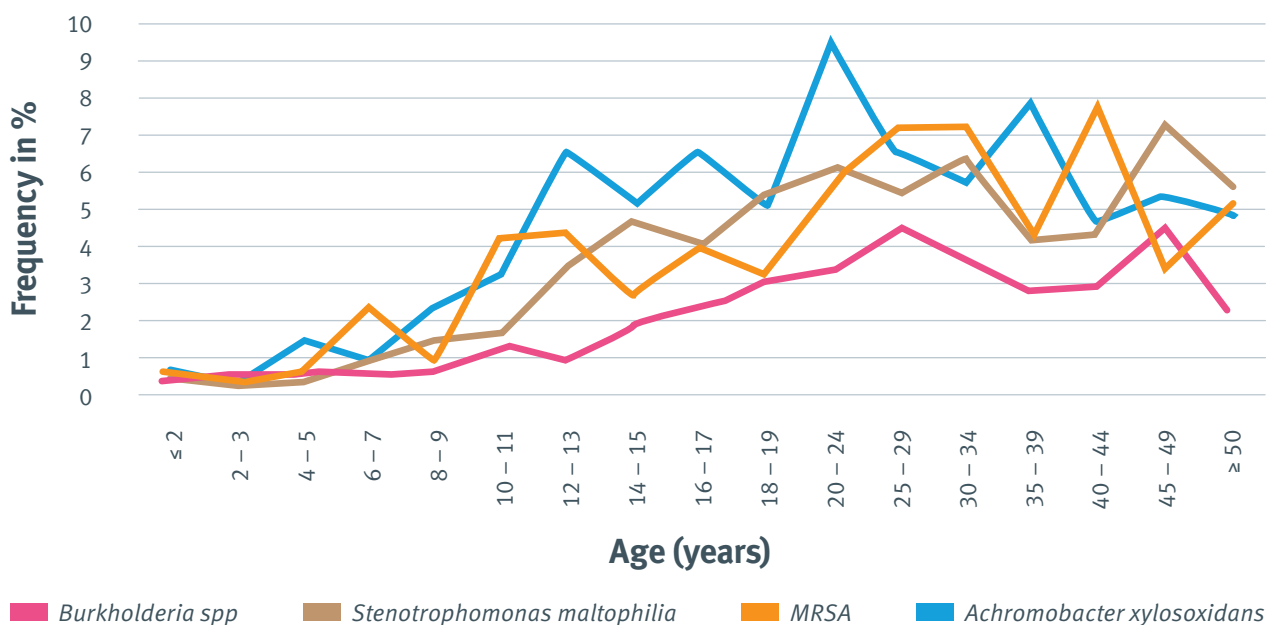


Figure 22: Chronic lung infections in pwCF with microbiological examination (without the representation of *Pseudomonas aeruginosa* and *Staphylococcus aureus*) 2020

Lung infections

7c. Chronic lung infections

Age (years)	Staphylococcus aureus inklusive MRSA chronic	MRSA chronic	Pseudomonas aeruginosa (PSA) chronic	Burkholderia spp chronic	Stenotrophomonas maltophilia chronic	Achromobacter xylosoxidans chronic
< 2	15.9	0.4	0.8	0.0	0.4	0.0
2 – 3	26.3	0.6	1.6	0.0	0.0	0.0
4 – 5	25.7	0.6	5.7	0.3	0.0	0.0
6 – 7	37.9	2.4	5.2	0.3	0.7	0.0
8 – 9	44.1	0.9	5.3	0.3	1.2	1.2
10 – 11	50.2	4.2	11.2	1.1	1.4	1.1
12 – 13	52.3	4.3	17.2	0.7	3.3	3.3
14 – 15	51.6	2.7	18.8	1.8	4.5	1.8
16 – 17	55.8	4.0	20.3	2.2	4.0	3.3
18 – 19	56.3	3.2	26.4	2.8	5.3	4.6
20 – 24	59.0	5.8	37.3	3.2	6.0	6.6
25 – 29	55.3	7.2	52.5	4.4	5.3	5.3
30 – 34	55.3	7.2	56.5	3.5	6.4	5.5
35 – 39	48.1	4.3	64.8	2.5	4.1	8.4
40 – 44	55.6	7.8	72.8	2.7	4.3	2.7
45 – 49	47.6	3.4	68.9	4.4	7.3	5.3
≥ 50	41.0	5.2	63.1	2.1	5.5	4.5
Total	47.8	4.3	33.6	2.2	3.9	3.7
< 18	40.2	2.2	9.6	0.7	1.7	1.2
≥ 18	53.7	5.9	52.6	3.3	5.6	5.7

Table 22: Chronic lung infections in pwCF with microbiological examination (frequencies in %) 2020

Lung infections

7d. Atypical mycobacteria

All patients without a transplant who had at least one microbiological test for mycobacteria in 2020 were included in the analyses (n=2,112).

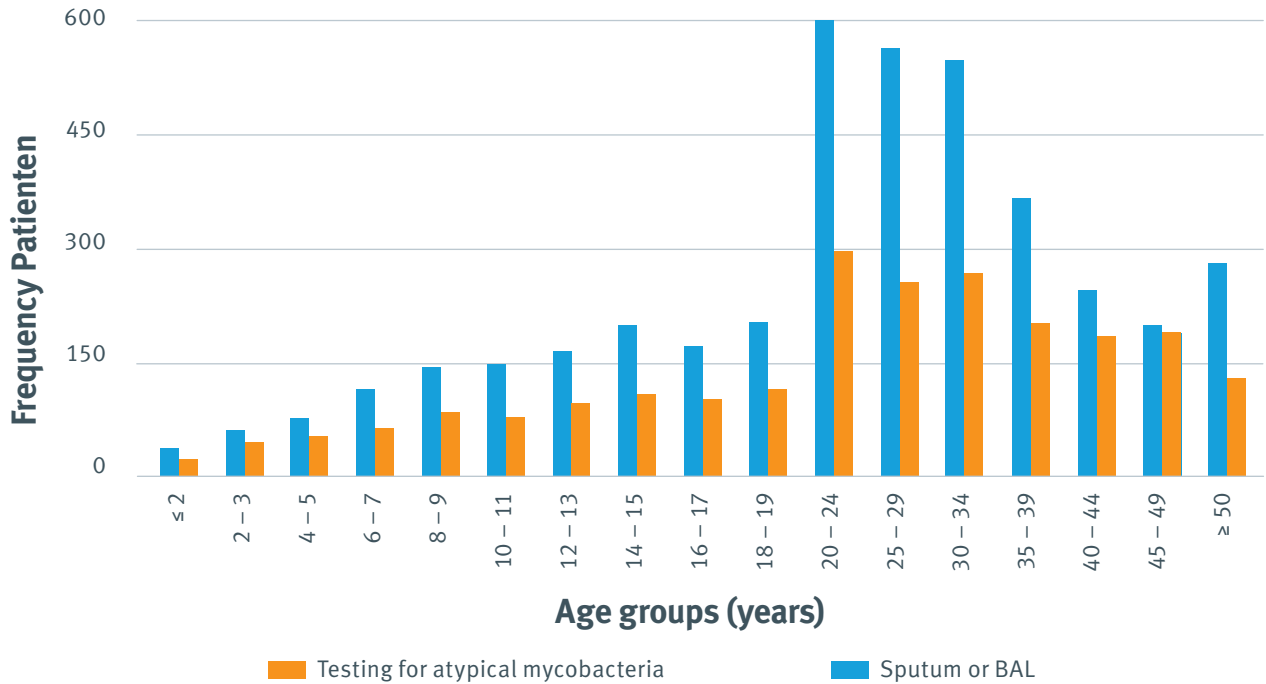


Figure 23: Number of patients with sputum or BAL and the number of tests performed for atypical mycobacteria 2020

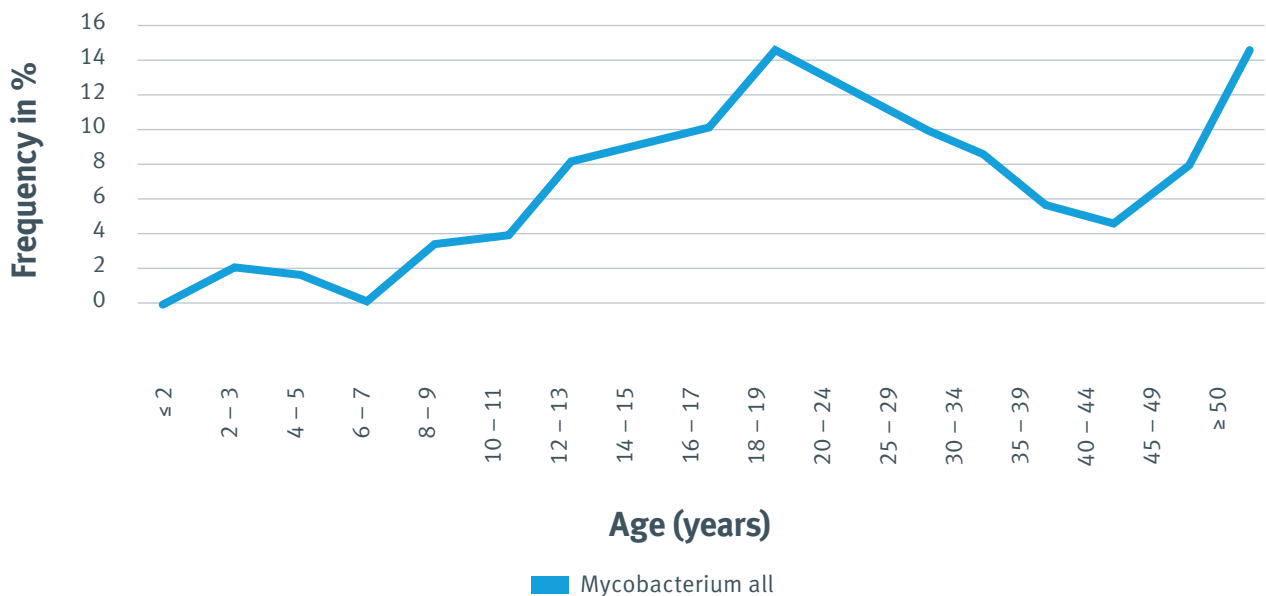


Figure 24: Age-dependent frequency in % of patients with examinations for atypical mycobacteria 2020

Lung infections

7d. Atypische Mykobakterien

Age (years)	Sputum or BAL performed	Testing for atypical mycobacteria performed	Mykobakterium all
< 2	15.9	65.0	0.0
2 – 3	19.8	76.2	2.1
4 – 5	25.4	70.4	1.8
6 – 7	40.0	57.8	0.0
8 – 9	44.4	59.7	3.5
10 – 11	52.3	54.4	3.7
12 – 13	54.6	60.0	8.1
14 – 15	60.0	54.2	9.2
16 – 17	62.3	59.3	9.8
18 – 19	71.1	57.9	14.5
20 – 24	79.8	49.3	12.5
25 – 29	87.8	45.3	10.3
30 – 34	88.8	49.3	8.6
35 – 39	92.0	48.0	5.7
40 – 44	92.8	43.2	4.8
45 – 49	96.2	46.0	7.6
≥ 50	95.9	47.5	14.4
Total	67.1	51.3	8.5
< 18	41.9	59.7	5.3
≥ 18	86.9	48.1	10.0

Table 23: pwCF tested for atypical mycobacteria (frequency in %), based on patient population, in whom microbiology was performed with sputum or BAL 2020

Complications extended

All patients without transplant for whom the question about complications was documented were included in the analysis of complications. A total of 6,234 data sets were available. A total of 55 patients (0.9 %) did not answer the question about complications.

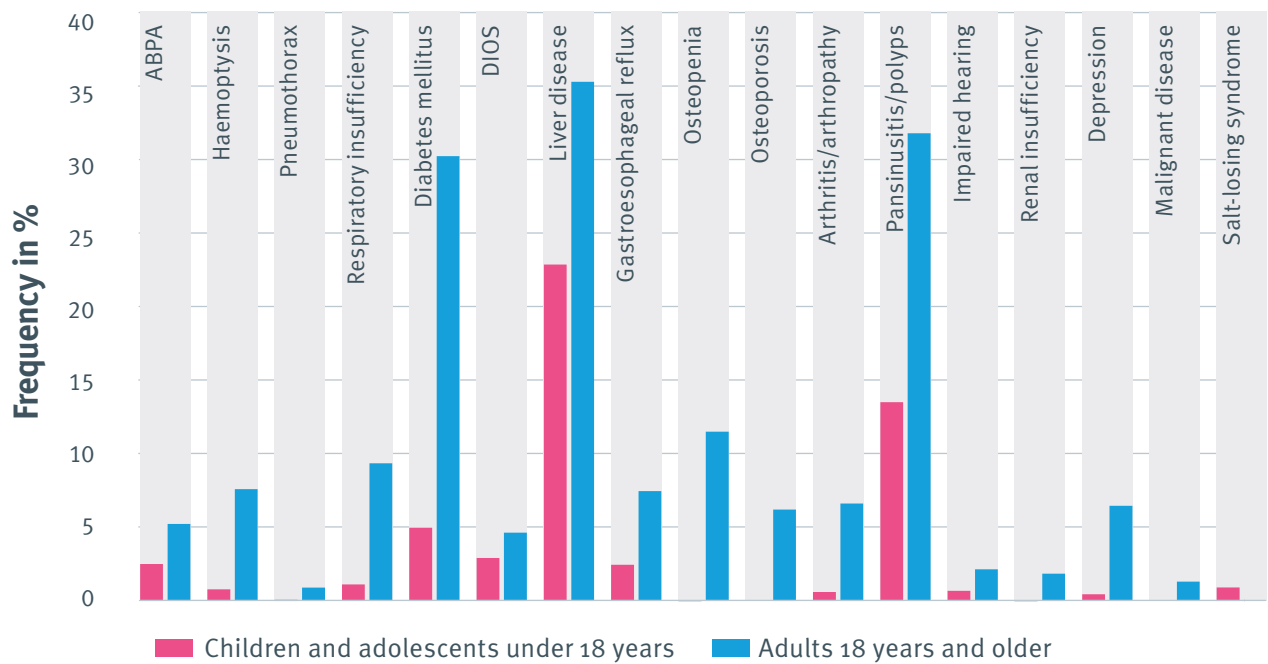


Figure 25: pwCF with complications (not showing pancreatic insufficiency) 2020

Complications extended

8a. Children and adolescents under 18 years

Complications	0 – 5 years	6 – 11 years	12 – 17 years	< 18 years
Pulmonary complications				
Allergic bronchopulmonary aspergillosis	0.0	2.0	5.2	2.4
Haemoptysis	0.0	0.3	2.0	0.8
of these, at least one serious episode (> 240 ml in 24h)	0.0	0.0	5.6	4.8
Pneumothorax	0.0	0.1	0.1	0.1
of these, requiring drainage	0.0	100.0	0.0	50.0
Respiratory insufficiency	0.9	1.0	1.3	1.1
of these, partial insufficiency	87.5	77.8	83.3	82.8
of these, global insufficiency	0.0	0.0	16.7	6.9
Gastrointestinal complications				
Exocrine pancreatic insufficiency	91.4	91.3	90.4	91.0
Distal intestinal obstruction syndrome (DIOS)	2.3	3.2	3.3	2.9
Liver disease	10.0	22.8	35.7	22.9
of these, liver cirrhosis	1.1	8.7	19.2	13.1
of these, with portal hypertension	0.0	4.4	7.6	5.5
of these, without portal hypertension	1.1	3.4	6.7	4.8
Gastroesophageal reflux	1.2	1.9	4.1	2.4
Other complications/comorbidities				
Diabetes mellitus	0.1	1.9	12.7	4.9
of these, Type 3	0.0	94.1	94.0	93.3
of these, not Type 3	100.0	5.9	6.0	6.7
Bone disease				
Osteopenia	0.0	0.0	0.2	0.1
Osteoporosis	0.0	0.0	0.1	0.0
Arthritis/Arthropathy	0.0	0.2	1.4	0.6
Pansinusitis/Polyps	3.1	15.3	22.2	13.6
Impaired hearing	0.3	0.7	0.9	0.6
Renal insufficiency	0.0	0.0	0.3	0.1
Depression	0.0	0.2	1.2	0.5
Malignant disease	0.0	0.0	0.2	0.1
Salt-losing syndrome	1.8	0.9	0.0	0.9

Table 24: pwCF under 18 years with complications (frequencies in %) 2020

Complications extended

8b. Adults 18 years and older

Complications	18 – 29 years	30 – 39 years	≥ 40 years	≥ 18 years
Pulmonary complications				
Allergic bronchopulmonary aspergillosis	5.9	5.0	4.0	5.2
Haemoptysis	6.5	9.2	7.9	7.6
of these, at least one serious episode (> 240 ml in 24h)	2.7	4.3	3.3	3.4
Pneumothorax	1.1	0.7	0.8	0.9
of these, requiring drainage	64.7	71.4	100.0	73.3
Respiratory insufficiency	7.2	9.1	14.4	9.3
of these, partial insufficiency	61.8	68.8	68.5	66.1
of these, global insufficiency	21.1	18.3	19.8	19.9
Gastrointestinal complications				
Exocrine pancreatic insufficiency	91.8	90.8	85.3	90.0
Distal intestinal obstruction syndrome (DIOS)	4.9	4.9	4.2	4.7
Liver disease	38.2	34.1	31.3	35.5
of these, liver cirrhosis	18.1	16.3	18.7	17.7
of these, with portal hypertension	8.3	8.0	8.3	8.2
of these, without portal hypertension	4.9	4.3	5.8	4.9
Gastroesophageal reflux	5.7	8.0	10.4	7.4
Other complications/comorbidities				
Diabetes mellitus	23.6	32.1	43.5	30.4
of these, Type 3	97.0	94.8	96.1	96.1
of these, not Type 3	3.0	5.2	3.9	3.9
Bone disease				
Osteopenia	7.3	13.0	19.0	11.5
Osteoporosis	3.3	5.9	13.0	6.2
Arthritis/Arthropathy	4.0	8.2	10.4	6.6
Pansinusitis/Polyps	30.4	33.3	32.2	31.6
Impaired hearing	1.1	2.0	4.9	2.2
Renal insufficiency	1.2	2.1	2.9	1.8
Depression	7.1	6.0	5.6	6.4
Malignant disease	0.2	0.6	4.4	1.2
Salt-losing syndrome	0.1	0.0	0.1	0.1

Table 25: pwCF aged 18 and over with complications (frequencies in %) 2020

Complications extended

8c. Exacerbations treated with antibiotics

Age (years)	Number of antibiotic-treated exacerbations per patient						
	0	1	2	3	4	5+	unknown
0 – 5	70.9	16.0	8.4	2.2	1.3	1.0	0.1
6 – 11	69.8	16.5	8.2	2.9	1.3	1.0	0.3
12 – 17	67.6	16.6	8.2	3.7	1.8	1.7	0.3
18 – 29	61.0	18.5	9.1	5.0	2.8	3.0	0.7
30 – 39	62.9	17.2	9.9	3.0	2.3	1.3	3.4
≥ 40	65.9	17.5	7.2	3.9	1.8	1.2	2.5
Total	65.5	17.3	8.6	3.7	2.0	1.7	1.2
< 18	69.4	16.4	8.3	2.9	1.5	1.2	0.3
≥ 18	62.7	17.9	8.9	4.2	2.4	2.1	1.9

Table 26: Number of exacerbations treated with antibiotics per pwCF (frequencies in %) 2020

Therapies

9a. Basic therapy

All patients without transplant for whom the question about gastrointestinal and pulmonary long-term therapy was documented were included in the evaluation of the basic therapies. The data sets of 2,724 patients under 18 years and 3,522 patients 18 years and older are included in the analyses. A total of 49 patients (0.8 %) did not answer the question about gastrointestinal and pulmonary long-term therapy.

9a.i. Children and adolescents under 18 years

Basic therapy	0 – 5 years	6 – 11 years	12 – 17 years	Total
DNase	14.6	52.2	67.0	44.7
Mannitol	0.0	0.0	0.6	0.2
Hypotonic saline solution (≥ 3 %)	88.4	94.7	90.3	91.1
of these 3 – 5,7 %	33.0	29.9	24.0	28.9
of these $\geq 5,8$ %	67.0	70.1	76.0	71.1
At least one mucolytic therapy (Mannitol, DNase, Hypertonic saline solution)	89.1	96.2	93.7	93.0
β2-sympathomimetics				
Short-acting (SABA)	60.7	74.2	73.0	69.3
Long-acting (LABA)	4.8	18.7	26.9	16.9
Anticholinergics	8.6	15.2	16.8	13.6
Antistaphylococcal therapy	7.2	8.1	10.2	8.5
Steroids				
Nasal	7.1	26.1	26.6	20.0
Inhalative	8.9	22.4	28.6	20.0
Orale	0.6	2.9	5.6	3.0
Vitamins				
Vitamin A	79.8	82.8	81.0	81.2
Vitamin D	95.3	95.5	94.7	95.2
Vitamin E	73.9	77.4	79.7	77.0
Vitamin K	73.2	74.4	72.2	73.3
Hormonal contraception for women¹	–	–	9.2	9.2

Table 27: pwCF under 18 years with basic therapy (frequencies in %) 2020

¹ Survey 14 years and older

Therapies

9a.ii. Inhalation and combination therapies Children and adolescents under 18 years of age

In the graph on inhalation and combination therapies, all minors were considered who answered the question about continuous pulmonary therapy (2,724 patients). 157 patients (5.8 %) of these did not receive any inhalation therapy.

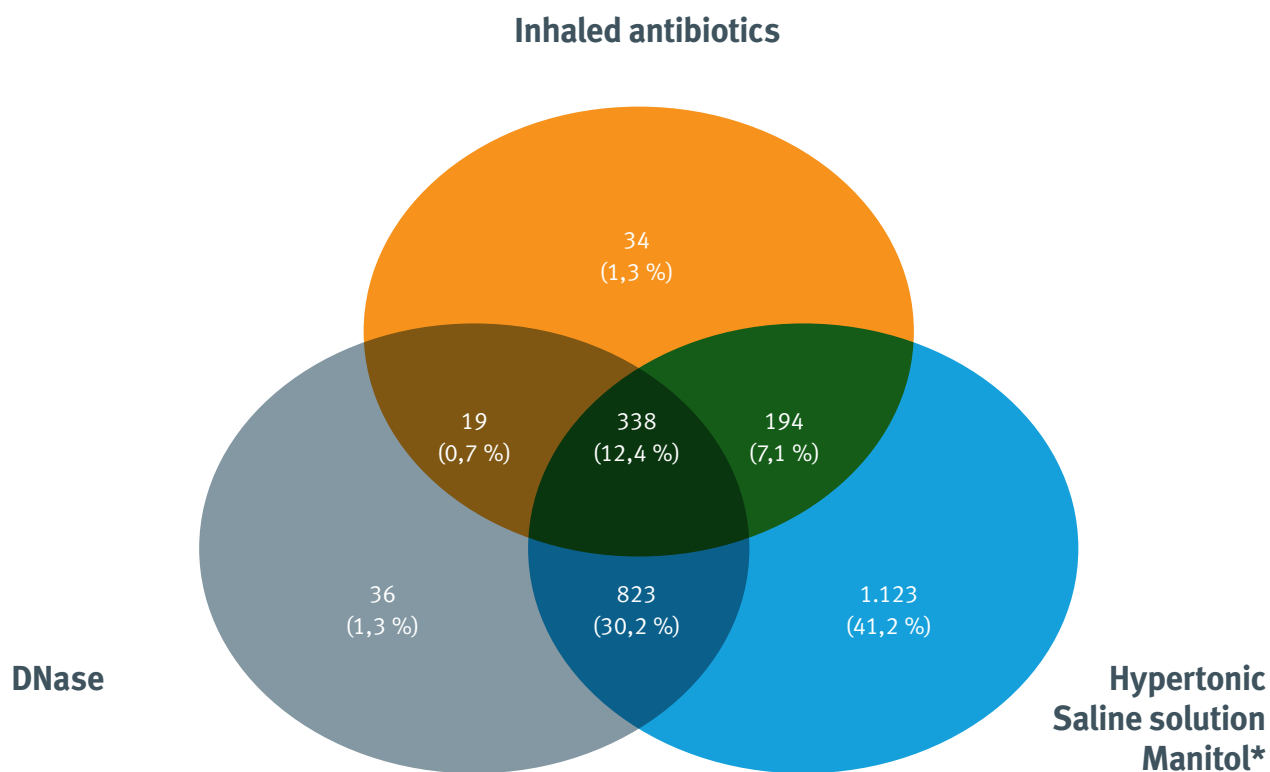


Figure 26: Inhalation and combination therapies in pwCF under 18 years 2020

*Hypertonic saline solution ≥ 3 %

Therapies

9a. Basic therapy

9a.iii. Adults 18 years and older

Basistherapie	18 – 29 years	30 – 39 years	≥ 40 years	Total
DNase	62.8	54.9	45.5	56.7
Mannitol	4.7	8.5	5.4	6.0
Hypotonic saline solution (≥3 %)	79.1	74.0	66.1	74.8
of these 3 – 5,7 %	23.0	23.2	26.4	23.7
of these ≥ 5,8 %	77.0	76.9	73.6	76.3
At least one mucolytic therapy (Mannitol, DNase, Hypertonic saline solution)	90.2	86.8	79.6	86.9
β2-sympathomimetics				
Short-acting (SABA)	66.5	63.7	66.4	65.7
Long-acting (LABA)	52.2	66.5	74.1	61.2
Anticholinergics	39.6	53.3	65.1	49.2
Antistaphylococcal therapy	8.9	5.9	4.4	7.0
Steroids				
Nasal	23.8	23.0	20.1	22.7
Inhalative	40.8	52.8	57.2	48.0
Orale	6.8	9.2	11.2	8.5
Vitamins				
Vitamin A	79.1	69.6	62.6	72.7
Vitamin D	94.5	93.0	90.7	93.2
Vitamin E	78.0	67.6	62.3	71.5
Vitamin K	73.0	62.5	57.9	66.6
Hormonal contraception for women	29.5	20.0	10.1	22.6

Table 28: pwCF aged 18 and over with basic therapy (frequencies in %) 2020

Therapies

9a.iii. Inhalation and combination therapies Adults 18 years and older

In the graph on inhalation and combination therapies, all minors were considered who answered the question about continuous pulmonary therapy (3,522 patients). 250 patients (7.1 %) of these did not receive any inhalation therapy.

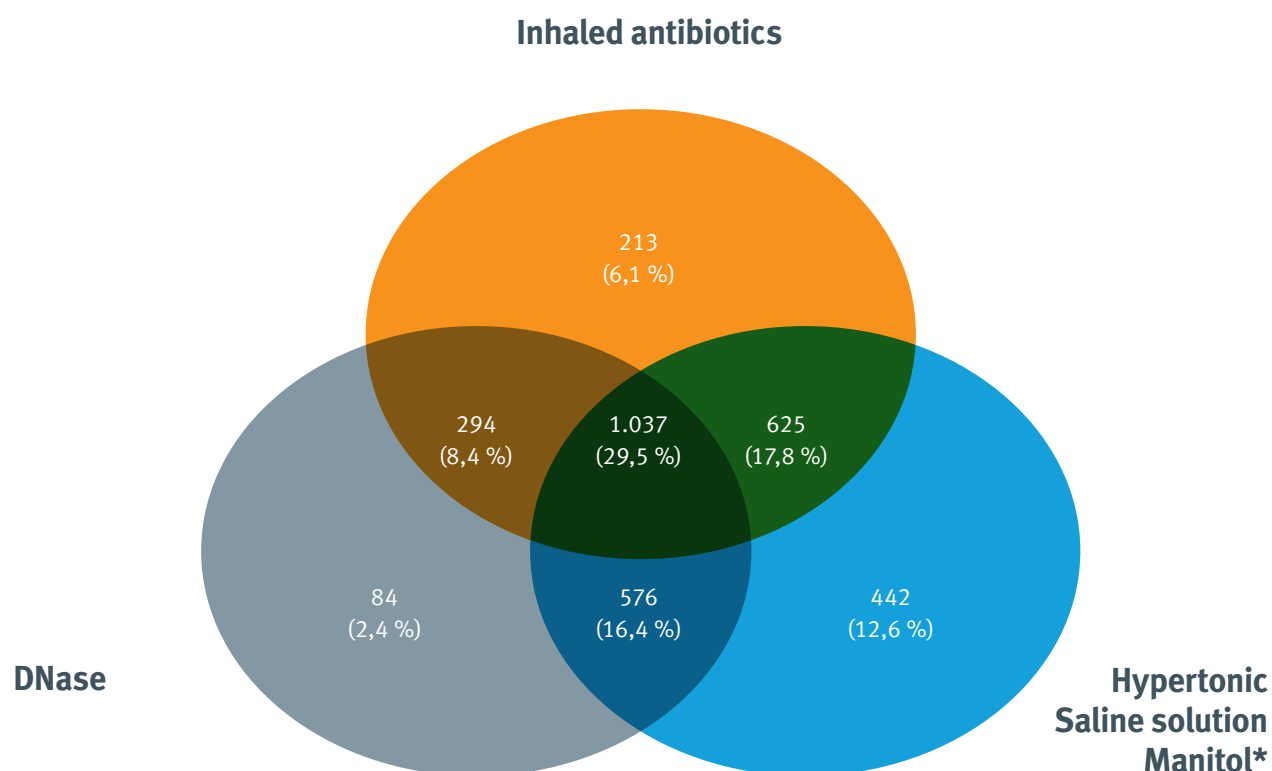


Figure 27: Inhalation and combination therapies in pwCF over 18 years 2020

*Hypertonic saline solution ≥ 3 %

Therapies

9b. Indication therapy

9b.i. Children and adolescents under 18 years

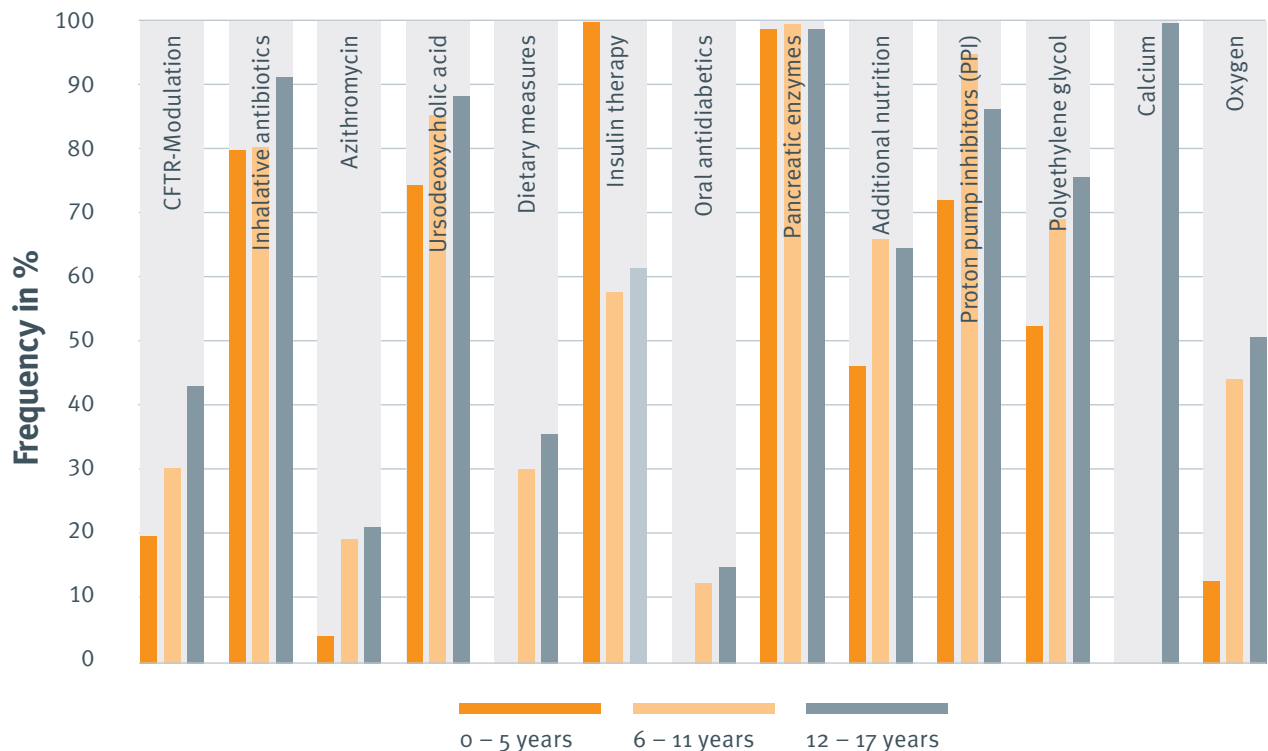


Figure 28: pwCF under 18 years with indication therapy 2020

Status of approval of CFTR modulators 31.12.2020

Only the most recently used modulator in the reporting year is shown here.

- ¹ Ivacaftor has been approved since 2018 from the 1st year of life and since 2020 from the 4th month of life for patients with the G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R mutations. For patients with the R117H mutation, ivacaftor has been approved in over 18s since 2018, since 2020, also from 4 months of age
- ² Lumacaftor/ivacaftor has been approved for F508del homozygous patients since 2018 from 6 years of age. and since 2019 from 2 years of age.
- ³ Tezacaftor/ivacaftor has been approved for F508del homozygous patients from 12 years of age since 2019. or for F508del heterozygous patients with any of the following mutations: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T.
- ⁴ Elexacaftor/tezacaftor/ivacaftor has been available since 2020 from age 12 for F508del homozygous patients or F508del heterozygous patients with a minimal function (MF) mutation.



Therapies

9b. Indication therapy

9b.i. Children and adolescents under 18 years

Indication therapy	0 – 5 years	6 – 11 years	12 – 17 years	Total
CFTR-Modulation	19,3	30,4	43,8	31,2
of these, Ivacaftor ¹	1,9	3,4	4,3	3,2
of these, Lumacaftor/Ivacaftor ²	17,4	26,3	15,1	19,6
of these, Tezacaftor/Ivacaftor ³	0,1	0,4	11,5	4,0
of these, Elexacaftor/Tezacaftor/Ivacaftor ⁴	0,0	0,1	14,7	5,0
Inhalative antibiotics <i>with chronic Pseudomonas infection</i>	80,0	81,3	91,2	87,7
of these, inhalative tobramycin	44,0	58,7	48,5	50,6
of these, inhalative aztreonam	52,0	62,5	58,5	58,9
of these, inhalative aztreonam	8,0	11,1	19,3	16,2
of these, DPI tobramycin	0,0	1,6	13,5	9,3
of these, DPI colistin	0,0	0,0	12,9	8,5
of these, levofloxacin	0,0	3,2	2,3	2,3
of these, inhalative gentamicin	0,0	0,0	0,0	0,0
of these, others	4,0	1,6	1,2	1,5
Azithromycin with chronic Pseudomonas infection	4,0	19,1	20,5	18,5
Ursodeoxycholic acid with liver disease	74,4	84,0	88,1	84,8
Dietary measures with Diabetes mellitus	0,0	29,4	36,2	35,1
Insulin therapy with Diabetes mellitus	100,0	58,8	61,2	61,2
Oral antidiabetics with Diabetes mellitus	0,0	11,8	14,7	14,2
Pancreatic enzymes <i>with exocrine pancreatic insufficiency</i>	99,2	99,6	99,3	99,4
Additional nutrition with underweight	46,6	66,1	64,6	59,4
Additional oral nutrition	42,9	62,1	56,7	53,9
PEG	2,3	3,2	8,5	5,0
Proton pump inhibitors (PPI) <i>with gastroesophageal reflux</i>	72,7	94,1	86,8	86,4
Polyethylene glycol with DIOS	52,4	69,0	76,7	67,5
Calcium with osteoporosis/osteopenia	0,0	0,0	100,0	100,0
Oxygen with respiratory insufficiency	12,5	44,4	50,0	37,9

Table 29: pwCF under 18 years with indication therapy (frequencies in %) 2020

Therapies

9b. Indikationstherapie

9b.ii. Adults 18 years and older

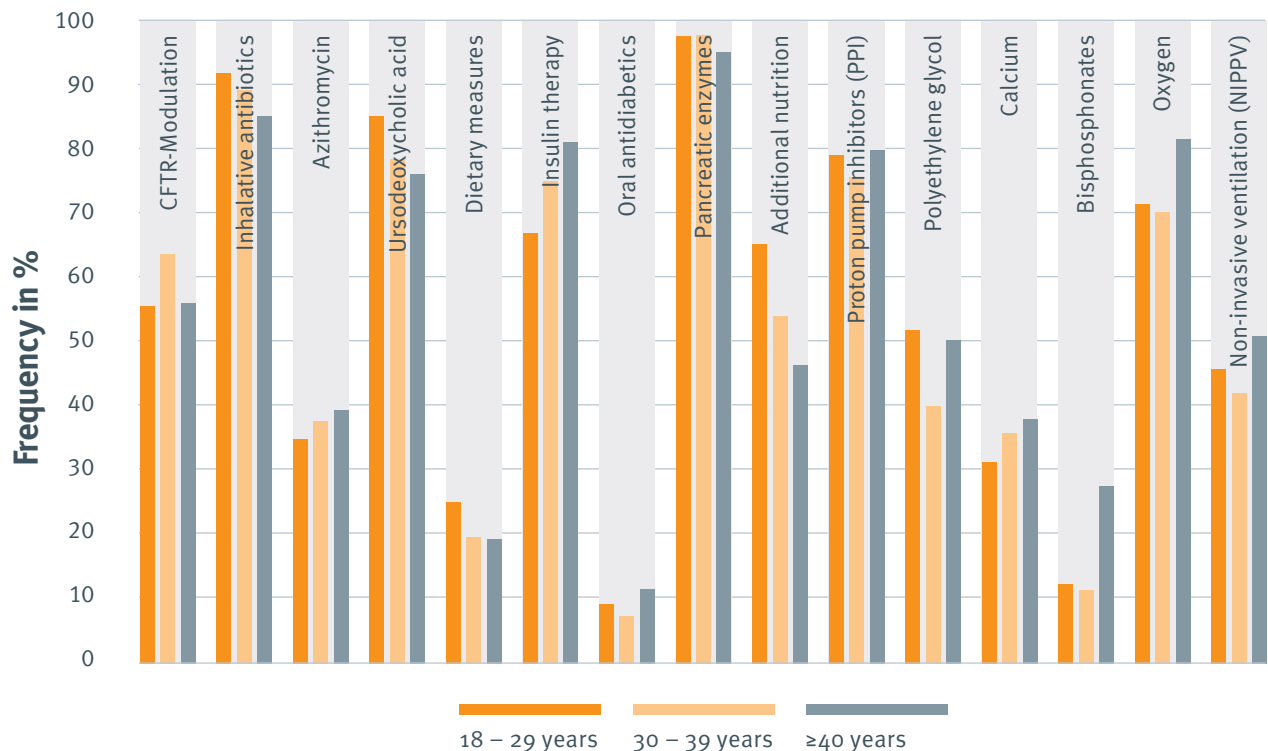


Figure 29: pwCF aged 18 and over with indication therapy 2020

Status of approval of CFTR modulators 31.12.2020

Only the most recently used modulator in the reporting year is shown here.

- ¹ Ivacaftor has been approved since 2018 from the 1st year of life and since 2020 from the 4th month of life for patients with the G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R mutations. For patients with the R117H mutation, ivacaftor has been approved in over 18s since 2018, since 2020, also from 4 months of age
- ² Lumacaftor/ivacaftor has been approved for F508del homozygous patients since 2018 from 6 years of age. and since 2019 from 2 years of age.
- ³ Tezacaftor/ivacaftor has been approved for F508del homozygous patients from 12 years of age since 2019. or for F508del heterozygous patients with any of the following mutations: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G and 3849+10kbC→T.
- ⁴ Elexacaftor/tezacaftor/ivacaftor has been available since 2020 from age 12 for F508del homozygous patients or F508del heterozygous patients with a minimal function (MF) mutation.



Therapies

9b. Indikationstherapie

9b.ii. Erwachsene ab 18 Jahren

Indication therapy	18 – 29 years	30 – 39 years	≥40 years	Total
CFTR-Modulation	55,8	62,2	56,9	57,9
of these, Ivacaftor ¹	3.9	4.6	6.8	4.8
of these, Lumacaftor/ Ivacaftor ²	10.8	9.3	6.0	9.3
of these, Tezacaftor/ Ivacaftor ³	23.2	26.5	28.6	25.4
of these, Elexacaftor/ Tezacaftor/ Ivacaftor ⁴	20.8	24.9	21.6	22.1
Inhalative antibiotics	91.1	89.1	86.6	89.2
with chronic <i>Pseudomonas</i> infection				
of these, inhalative tobramycin	33.7	27.2	18.5	27.2
of these, inhalative aztreonam	58.0	53.6	52.3	54.9
of these, inhalative aztreonam	28.8	38.8	37.3	34.5
of these, DPI tobramycin	17.4	14.5	7.3	13.6
of these, DPI colistin	15.5	15.7	12.5	14.7
of these, levofloxacin	13.1	19.1	20.3	17.1
of these, inhalative gentamicin	0.2	0.5	0.2	0.3
of these, others	2.5	2.7	4.1	3.0
Azithromycin with chronic <i>Pseudomonas</i> infection	34.1	37.3	39.1	36.6
Ursodeoxycholic acid with liver disease	85.0	78.8	75.5	81.4
Dietary measures with Diabetes mellitus	24.4	19.8	19.6	21.5
Insulin therapy with Diabetes mellitus	67.4	73.6	81.9	73.9
Oral antidiabetics with Diabetes mellitus	8.2	7.3	10.1	8.5
Pancreatic enzymes	98.9	98.0	96.8	98.2
with exocrine pancreatic insufficiency				
Additional nutrition with underweight	64.9	52.4	46.7	59.3
Additional oral nutrition	56.9	44.2	42.6	51.8
PEG	9.2	9.3	3.3	8.3
Proton pump inhibitors (PPI)	79.6	75.6	80.0	78.5
with gastroesophageal reflux				
Polyethylene glycol with DIOS	51.2	40.0	50.0	47.6
Calcium with osteoporosis/osteopenia	30.4	36.7	38.1	35.4
Bisphosphonates with osteoporosis	10.5	10.0	27.0	18.0
Oxygen with respiratory insufficiency	70.7	69.9	81.1	74.0
Non-invasive ventilation (NIPPV)	46.2	41.2	50.0	46.2
with respiratory global insufficiency				

Table 30: pwCF aged 18 and over with indication therapy (frequencies in %) 2020

Therapies

9c Development of CFTR modulation therapy 2018 – 2020

For the presentation of CFTR modulation therapy, all patients without transplantation and with modulator use were taken into account or all patients for whom a suitable modulator is approved in the respective reporting year.

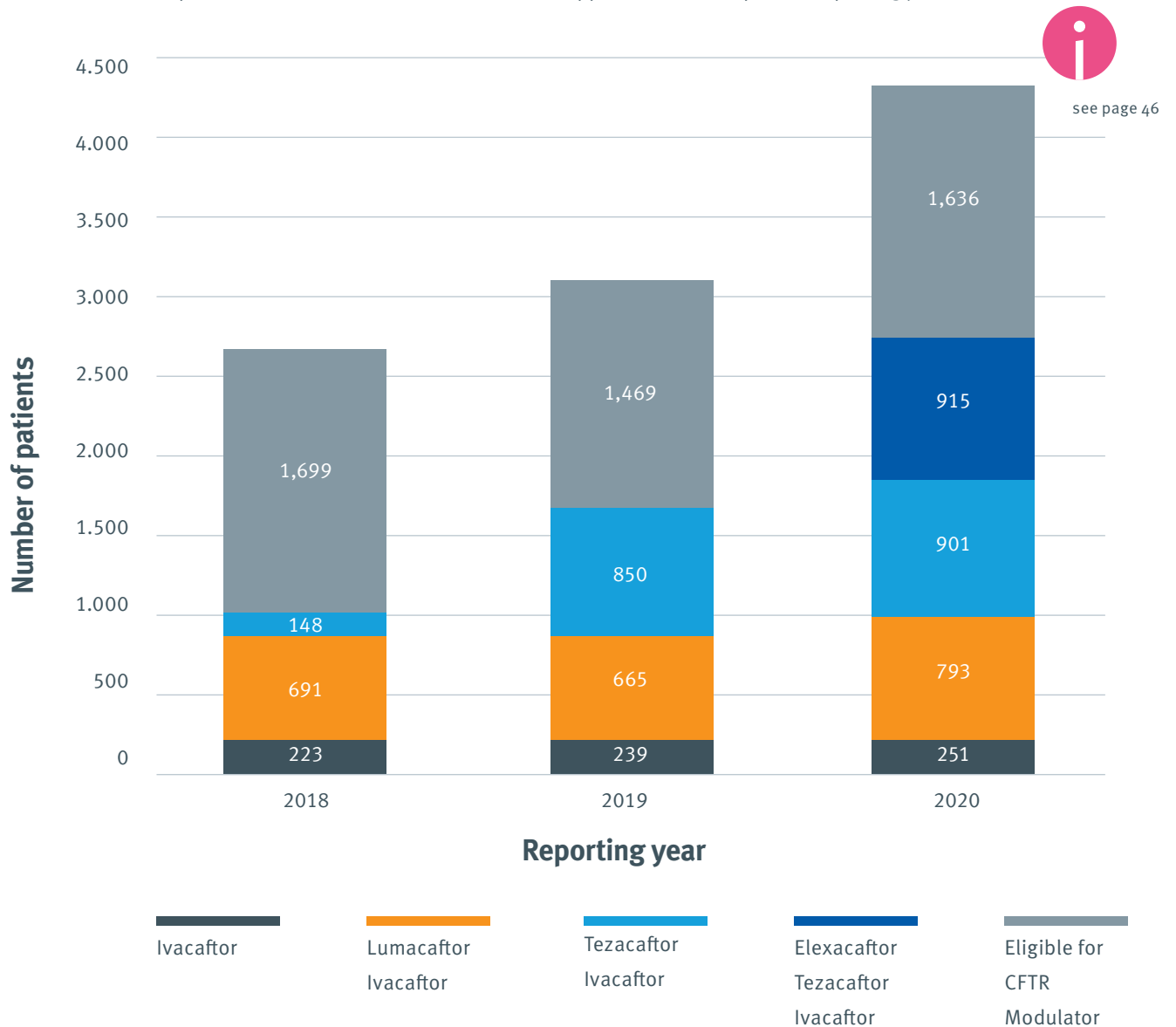


Figure 30: Number of pwCF with modulation therapy and number of patients for whom a suitable modulator is approved 2018 – 2020

Mortality

57 patients (25 girls/women and 32 boys/men) died in the reporting year 2020. The main causes of death were cardio-pulmonary diseases (43.9 %), transplants (3.5 %), liver diseases/failure (12.3 %) and malignant diseases (7.0 %). Other or unknown causes were present in 33.3 % of cases. The age at death is broken down as follows:

	Mean value	Median	Minimum	Maximum	25 th percentile	75 th percentile
Age at death in full years	36	35	5	58	28	43

Table 31: Age at death 2020

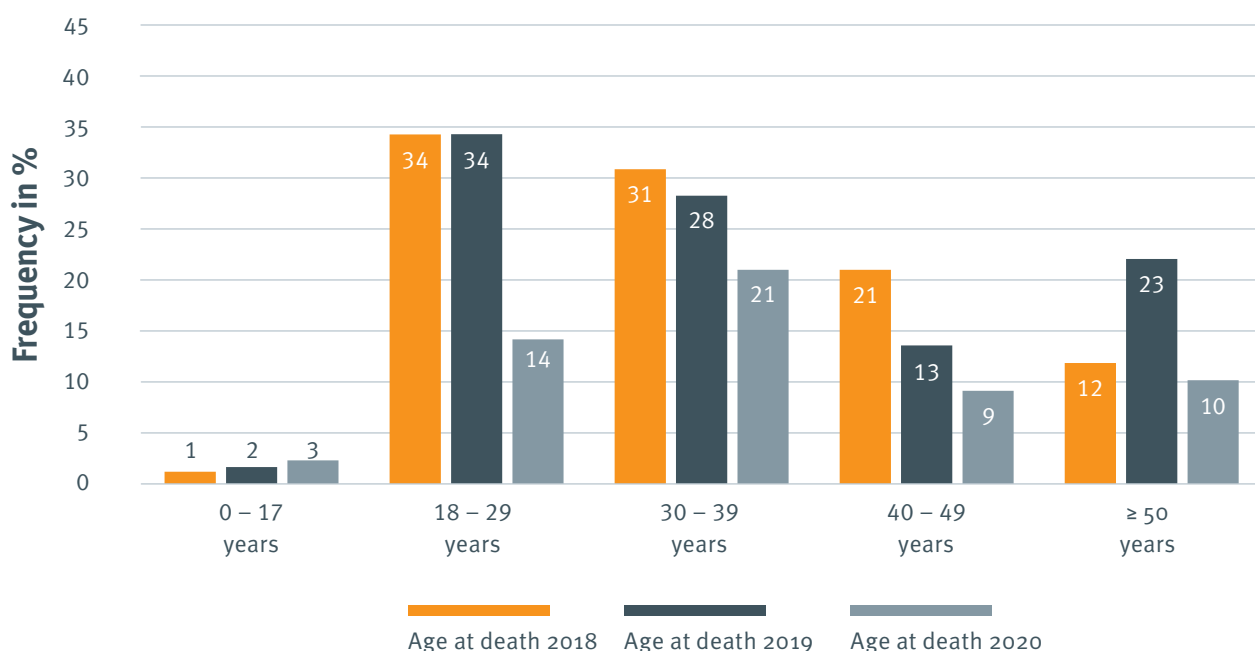


Figure 31: Deceased pwCF in the years 2018 – 2020

Age (years)	Number	Percent
0 – 17	3	5.3
18 – 29	14	24.6
30 – 39	21	36.8
40 – 49	9	15.8
≥ 50	10	17.5
Total	57	100.0

Table 32: Deceased pwCF in 2020

Mortality

(Data status: 13.09.2021)

The lifespan is described by the average age at death, the median survival age and the average age-specific life expectancy. We will present these statistical values in this annual data report on the basis of internationally accepted and comparable analytical methods. Owing to the higher number of patients lost from the follow-up for the reporting year 2020, we decided to report the current median age at death for the year 2020 as well as the average survival age and the life expectancy with respect to the period 2015 – 2019.

Average age at death

The average age at death for a given year describes the age at which half of the patients died. The average age at death was 35 (34) years in the reporting year 2020 (2019).

Median survival age 2019

The median survival age describes the expected age at which only 50 % of the patients are still alive. A COX PH regression analysis according to Sykes (Journal of Clinical Epidemiology 2016; 70: is conducted over a 5-year period to compensate for variations in the annual number of deaths. 7,807 people with Cystic Fibrosis (including patients with transplants) and 392 deaths were recorded in the 5-year window between 2015 and 2019. 213 patients (2.73 %) were lost from the follow-up. The median survival age was 52.41 years (confidence interval: 50.05 to 55.27).

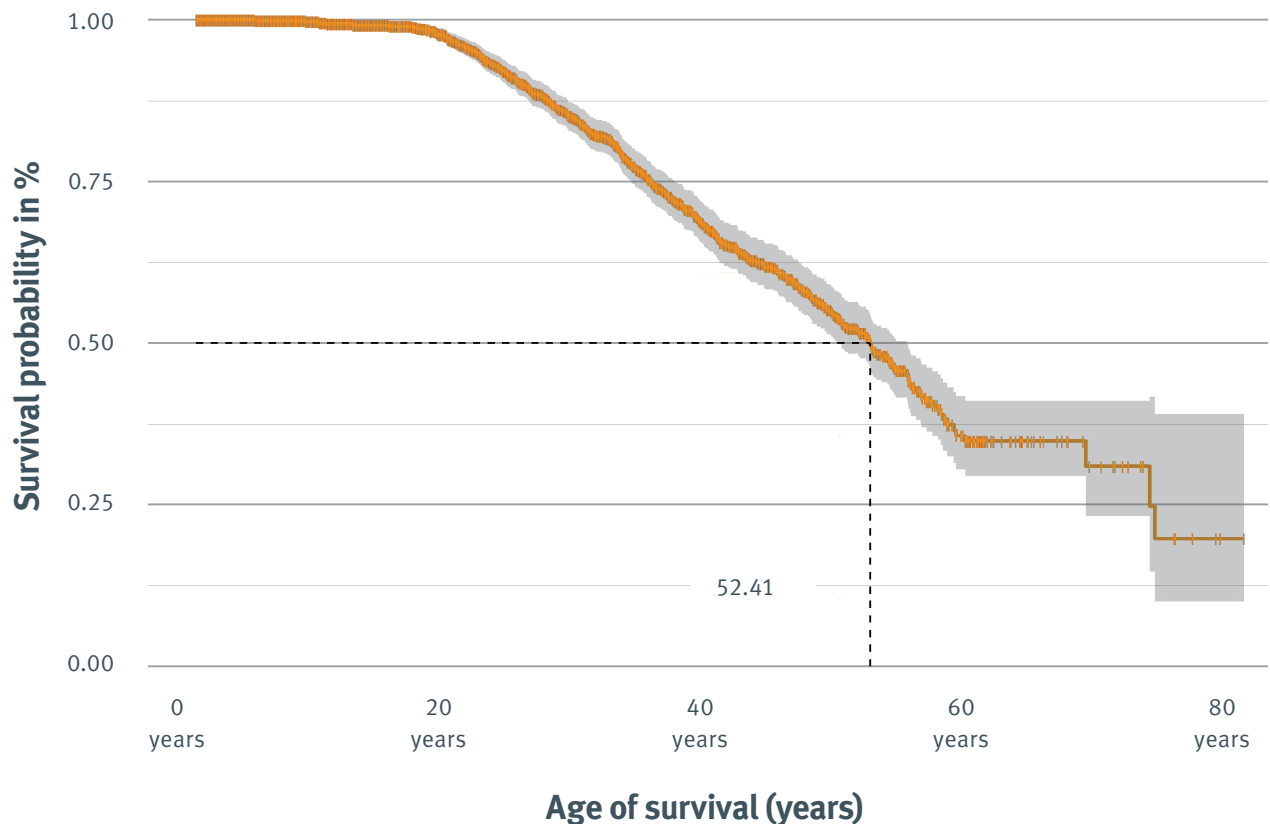


Figure 32: Median survival age for pwCF for the period 2015 – 2019

Mortality

Life expectancy 2020

Life expectancy is the average time a person can be expected to live from a specified age until death. It is calculated for a fixed period of time and is based on current and age-specific death rates. Currently the life expectancy of a healthy male newborn in Germany is 78 years and that of a female newborn 83 years (www.statista.de). The life expectancy is different for each age and does not correspond to the median survival age.

All statistical values refer to the population of Cystic Fibrosis patients in Germany, who vary greatly from individual to individual. As a result, only allow limited conclusions can be drawn about the individual. According to the literature, important influencing factors include gender, the existing gene mutation and the exocrine pancreatic function. All calculations are based on the current death rate, which has fortunately been steadily decreasing over the past years.

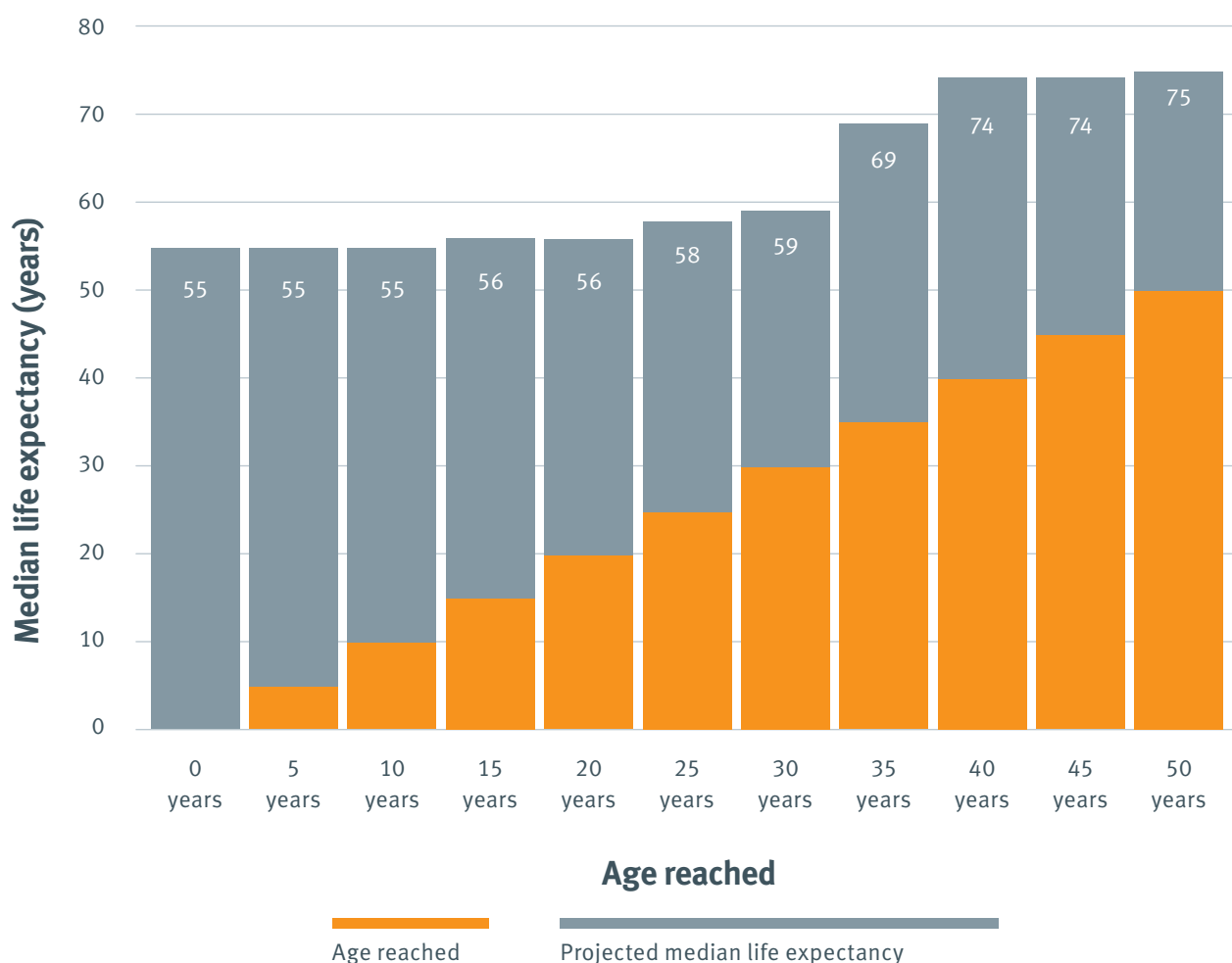


Figure 33: Projected median life expectancy for pwCF 2020

COVID 19

The data basis are data for the period from 02.02.2020 – 15.08.2021. 74 CF outpatient clinics took part in the COVID-19 documentation in the German Cystic Fibrosis Registry. 74 CF centers participated. 3,259 tests in 1,872 patients were documented. 145 tests yielded a positive result, of which 114 (79 %) with PCR diagnostics, 24 (17 %) by serology and 4 (3 %) by antigen testing. For 3 (2 %) of the patients, the procedure was unknown. 2 (1.8 %) of the patients who were positive by PCR diagnosis died as a result of their COVID-19 infection. The following graphs are based exclusively on the proportion of positive PCR tests (n=114).

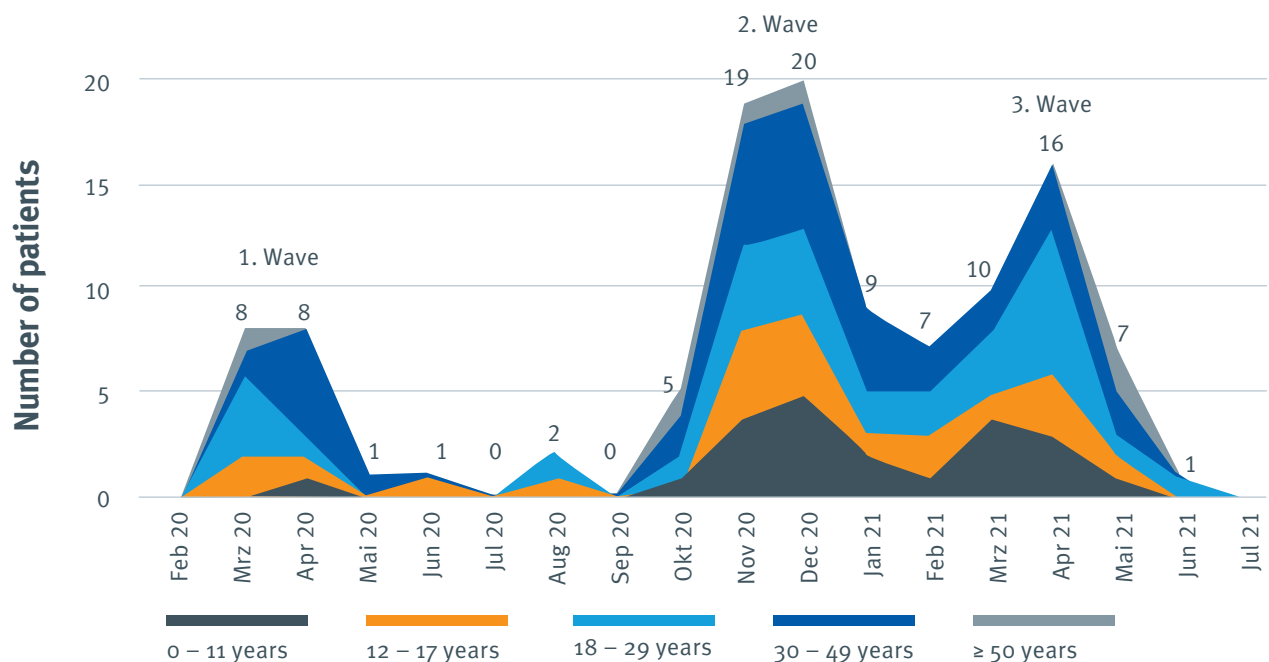


Figure 34: Monthly age group-specific frequencies of positive PCR tests in cystic fibrosis patients 2020/21

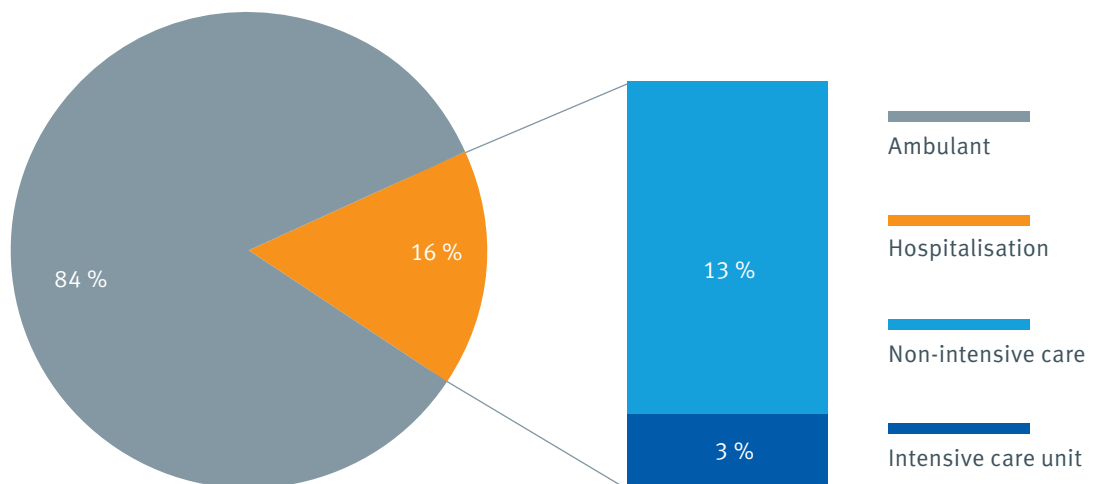


Figure 35: Treatment site (in %) of COVID-19 infection in cystic fibrosis patients 2020/21

COVID 19

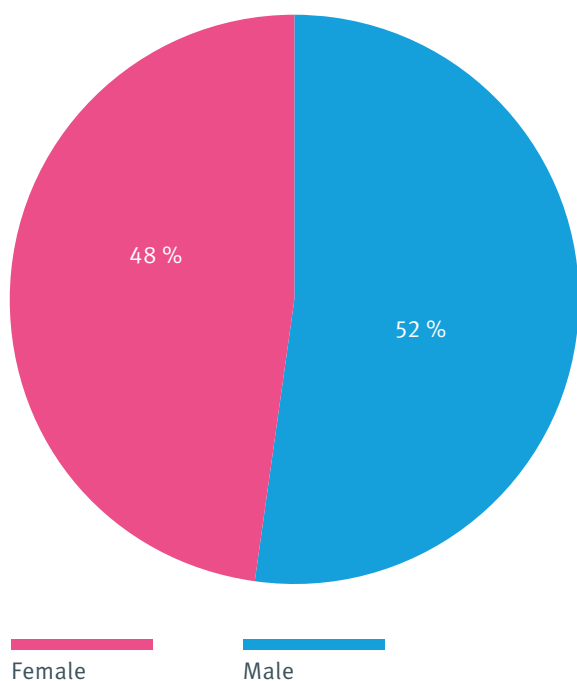


Figure 36: Percentage gender-specific frequency of a COVID-19 infection in pwCF 2020/21

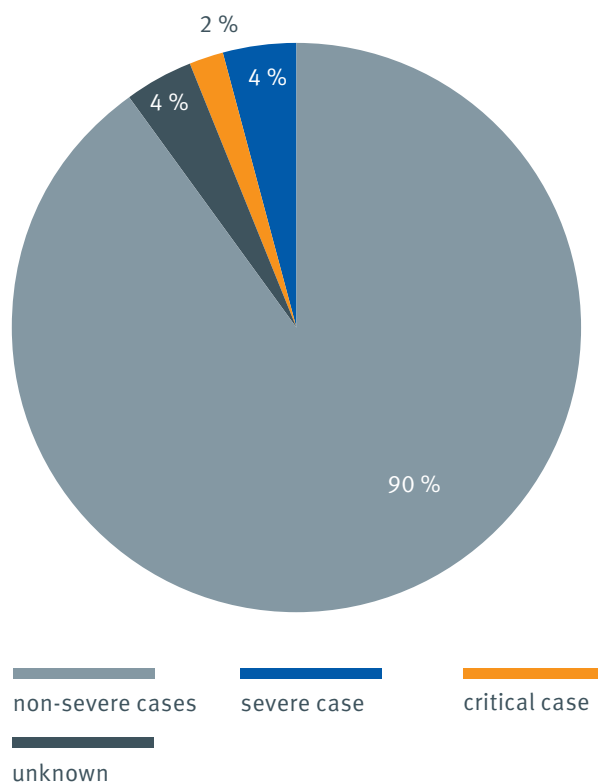


Figure 37: Percentage frequency of severity of COVID-19 infection in pwCF 2020/21

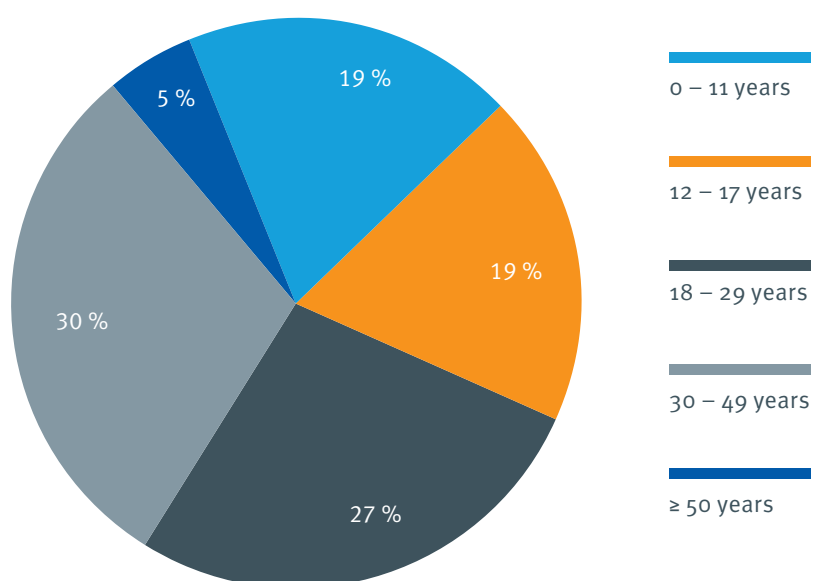


Figure 38: Age group-specific frequencies (in %) of positive PCR tests in pwCF 2020/21

Structure of care

12a. Size of the participating CF-centers

88 CF-centers participated in the Cystic Fibrosis Registry in the reporting year 2020. 46 centers cared for less than 50 patients and 42 centers cared for more than 50 patients. Over 84 % of the patients documented in the Registry are cared for in these centers.

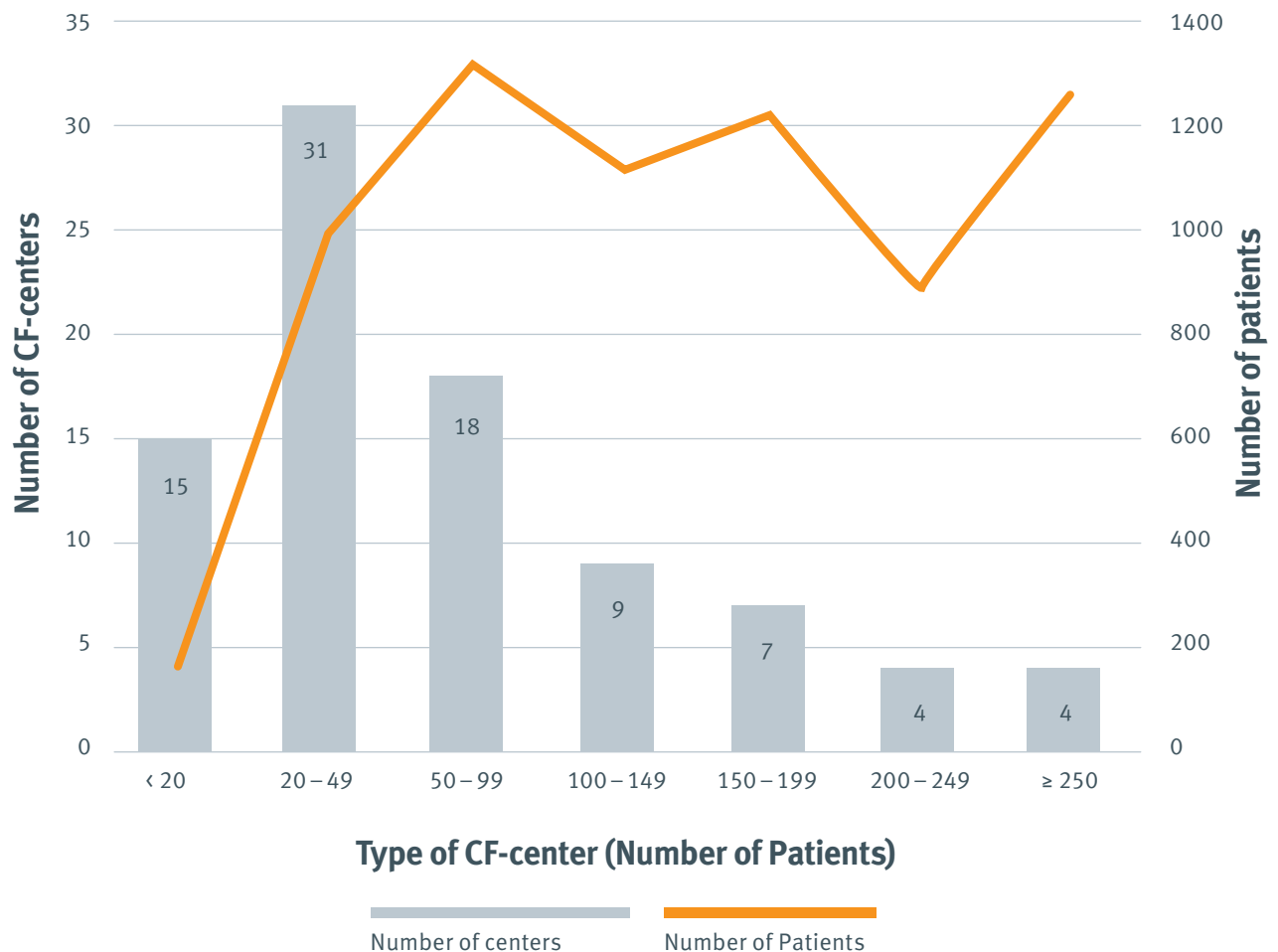


Figure 39: Number of documented pwCF and number of CF centers 2020

Structure of care

12b. Outpatient care

All patients with annual data in 2020 (n=6,483) were included in the following evaluations.

	0 – 5 years	6 – 11 years	12 – 17 years	18 – 29 years	30 – 39 years	≥ 40 years	Total
Physiotherapy <i>in the outpatient clinic</i>	62.8	63.4	65.3	49.8	43.7	42.7	53.6
Nutritional therapy <i>in the outpatient clinic</i>	55.2	45.1	41.8	23.3	16.7	15.4	31.0
Psychosocial support <i>in the outpatient clinic</i>	46.7	41.0	47.1	36.9	26.4	21.3	36.2
Anxiety and depression screening¹	–	–	22.8	31.8	27.2	24.3	27.5
Imaging							
Thorax	50.8	56.7	57.9	51.4	47.0	43.8	51.1
Abdomen	63.9	66.3	63.5	48.9	45.8	42.8	54.0
Bone density measurement	0.0	0.7	3.7	7.9	13.7	11.3	6.7
Laboratory	89.2	93.0	94.7	95.8	96.1	95.5	94.4
Rehabilitation stay	4.0	6.5	6.3	3.3	2.6	3.7	4.2
oGT test² in patients without diabetes mellitus in the previous year	0.3	10.0	43.9	32.2	25.7	17.7	22.7

Table 33: pwCF with outpatient care (frequencies in %) 2020

¹ referred to pwCF aged 12 years and older;

² referred to pwCF aged 6 years and over

Structure of care

12c. CF-relevant hospitalisations

Age (years)	Number of CF-relevant hospitalisations per patient						
	0	1	2	3	4	5+	unknown
0 – 5	69.2	19.0	4.9	0.7	0.4	0.1	5.7
6 – 11	69.5	17.9	3.4	1.4	0.8	0.8	6.3
12 – 17	59.9	16.3	8.1	3.9	2.0	1.5	8.3
18 – 29	61.9	16.8	7.6	4.3	1.9	1.7	5.8
30 – 39	70.4	18.6	5.2	3.1	1.5	0.5	0.7
≥ 40	73.4	17.0	5.1	2.1	1.2	0.9	0.2
Total	66.7	17.5	6.0	2.9	1.4	1.0	4.5
< 18	66.1	17.7	5.5	2.0	1.1	0.8	6.8
≥ 18	67.1	17.4	6.3	3.4	1.6	1.1	2.9

Table 34: Number of cystic fibrosis-related hospitalisations per patient (frequencies in %) 2020

Overview of Registry requests

Receipt	Applicant	Institution	Subject / Title	Status
2017	Dittrich	University of Heidelberg	Reference percentiles for FEV ₁ and BMI for cystic fibrosis	Under evaluation
2017	Schwarz	Charité Medical University Berlin	Art4Fun/diseases associated with mould	Completed – Published
2017	Prinz	University of Ulm	Cystic Fibrosis and glucose tolerance	Completed – Published
2017	Grehn	Charité Medical University Berlin	Arthropathy in patients with Cystic Fibrosis	Completed
2017	Chiesi Farmaceutici S.p.A	–	Quinsair PASS	Study in progress
2018	Ballmann	Clinic for Children and Adolescents Rostock University	Diabetes special evaluation	Completed
2018	Vertex Pharmaceuticals	–	TEZ/IVA PASS	Study in progress
2018	Waldmann	Universität Erlangen/ Nürnberg	Advanced Statistical Inference in Joint Models for Longitudinal and Time to Event Data	Warteliste
2018	Hogardt	Medical Center Frankfurt University Hospital	Prevalence of the B. cepacia complex in CF patients	Completed – Published (MIQ)
2019	Steindor/Ringshausen	Essen University Hospital / Hanover Medical School	NTM in CF patients in Germany	Under evaluation
2019	Moos-Thiele/ Muko.fit	Mukoviszidose e.V.	Control group from the Registry for verification of the representation of the Muko.fit group	Under preparation
2019	Hebestreit	Würzburg University Clinic	Control group from the Registry for verification of the representation of the VEMSE population	Completed
2019	Nährig/Schulte-Hubbert	University of Munich Medical Centre/Dresden University Hospital	Data analysis for antibiotic inhalation therapy in CF patients with chron. Pseudomonas infection	Completed
2019	Stanke	Hanover Medical School	Genetic predictors for severe CF in European twins and siblings	Under evaluation
2019	Hogardt	Frankfurt University Hospital	Molecular epidemiology of Mycobacterium abscessus in CF patients from Germany	Completed
2020	Vertex Pharmaceuticals (Germany) GmbH	–	Clinical benefit dossier assessment of triple therapy	Completed
2020	Eickmeier/Gardecki	Frankfurt University Hospital	Patient science for the research of rare diseases – a civic science study taking Cystic Fibrosis as an example	Completed
2020	Müller	University of Siegen	Influence of hormonal contraceptives on pneumonias in CF patients	Under evaluation
2020	Van Dullemen	Frankfurt University Hospital	Mutation-specific therapy - Overweight in CF	Completed
2020	Vertex Pharmaceuticals (Germany) GmbH	–	Clinical benefit dossier assessment of triple therapy – indication extension	Completed
2020	Vertex Pharmaceuticals	–	Kaftrio PASS	Study in progress
2021	Vertex Pharmaceuticals (Germany) GmbH	Vertex	Clinical benefit dossier assessment of triple therapy – indication extension	Completed

Participating CF centers 2020

City	CF center	Department	Documentation level ¹	Number of patients ²
Aachen	Kinderarztpraxis Laurensberg	Aachener Mukoviszidose Ambulanz für Kinder und Jugendliche	Level 1	46
Aachen	Luisenhospital Aachen	Mukoviszidose-Zentrum für Erwachsene, Innere Medizin	Level 1	87
Aachen	Universitätsklinik der RWTH Aachen	Klinik für Kinder- und Jugendmedizin	Level 1	46
Aue	HELIOS Klinikum Aue - CF-Ambulanz	Klinik für Kinder- und Jugendmedizin	Level 1	11
Augsburg	Klinikum Augsburg	II. Klinik für Kinder und Jugendliche, Kinderpneumologie - Allergologie, Mukoviszidose Ambulanz	Level 1	28
Augsburg	Josefinum KJF	Krankenhaus für Kinder und Jugendliche, CF Ambulanz	Level 2	33
Baden Baden	Klinikum Mittelbaden GmbH	Baden-Baden Balg, Lungenzentrum, Mukoviszidose Ambulanz	Level 1	7
Berlin	HELIOS Klinikum Berlin-Buch	Klinik für Kinder- und Jugendmedizin - Pulmologie, Mukoviszidose, Allergologie	Level 1	41
Berlin	Sana Klinikum Lichtenberg	Oskar-Ziethen-Krankenhaus, Klinik für Kinder- und Jugendmedizin, Pneumologie, Mukoviszidose-Zentrum, Allergologie	Level 2	63
Berlin	Charité	Christiane Herzog-Zentrum Berlin, Klinik für Pädiatrie m. S. Pädiatrische Pneumologie und Immunologie	Level 2	382
Bielefeld	Evangelisches Klinikum Bethel gGmbH	Lehrkrankenhaus der Universität Münster, Klinik für Kinder- und Jugendmedizin, Tagesklinik für Allergologie und Pneumologie	Level 1	21
Bochum	Universitätsklinikum der Ruhr-Universität Bochum	St. Josef-Hospital am Katholischen Klinikum Bochum, Klinik für Kinder- und Jugendmedizin, Christiane Herzog Zentrum Ruhr (CHCR)	Level 2	63
Brandenburg	Medizinische Hochschule Brandenburg (MHB) Klinikum West-Brandenburg	Kinder- und Jugendklinik, CF-Ambulanz	Level 2	28
Bremen	Gesundheit Nord	Eltern-Kind-Zentrum Prof. Hess	Level 2	91
Chemnitz	Poliklinik Chemnitz gGmbH	Praxis für Kinder- und Jugendmedizin	Level 1	44
Cottbus	Carl-Thiem-Klinikum Cottbus	Akademisches Lehrkrankenhaus der Charité, Klinik für Kinder- und Jugendmedizin	Level 2	28
Donaustauf	Klinik Donaustauf	Pneumologische Ambulanz	Level 2	41
Dresden	Universitätsklinikum Carl Gustav Carus	Klinik und Poliklinik für Kinder- und Jugendmedizin, Mukoviszidose-Zentrum "Christiane Herzog"	Level 2	167
Düsseldorf	UKD Universitätsklinikum Düsseldorf	Klinik für Allgemeine Pädiatrie, Neonatologie und Kinderkardiologie, Ambulanz für Kinderpneumologie und Allergologie	Level 1	33
Erfurt	HELIOS Klinikum Erfurt	Kinderklinik und Jugendmedizin, CF-Ambulanz	Level 1	16
Erlangen	Universitätsklinikum Erlangen	Medizinische Klinik 1, Schwerpunkt Pneumologie, CF-Ambulanz für Erwachsene	Level 1	30
Erlangen	Universitätsklinikum Erlangen	Kinder- und Jugendklinik, Sozialpädiatrisches Zentrum	Level 2	154
Essen	Universitätsklinikum Essen	Zentrum für Kinder- und Jugendmedizin, Pädiatrische Pneumologie und Schlafmedizin, Christiane Herzog Centrum Ruhr	Level 2	98
Essen	Universitätsmedizin Essen	Ruhrlandklinik - Pneumologie	Level 2	303
Esslingen	Städtische Kliniken Esslingen/Neckar	Klinik für Kinder und Jugendliche	Level 1	8
Frankfurt	Frankfurter Rotkreuz-Kliniken e. V.	Klinik für Pneumologie	Level 2	29
Frankfurt	Universitätsklinikum Frankfurt	Goethe Universität, Christiane Herzog CF-Zentrum für Kinder, Jugendliche und Erwachsene	Level 2	251
Frankfurt/Oder	Klinikum Frankfurt (Oder) GmbH	Kinderzentrum	Level 2	8
Freiburg	Universitätsklinikum Freiburg	Abteilung Pneumologie, Erwachsenenambulanz	Level 2	47

¹ Vgl. die Kollektivbeschreibung für die Definition der Dokumentationsstufe, ² Patienten können in mehreren Ambulanzen dokumentiert worden sein

Participating CF centers 2020

City	CF center	Department	Documentation level ¹	Number of patients ²
Freiburg	Universitätsklinikum Freiburg	Klinik für Allgemeine Kinder- und Jugendmedizin, Ambulanz und Arbeitsgruppe Pneumologie, Allergologie und Mukoviszidose	Level 2	66
Gießen	Universitätsklinik Gießen	CF Ambulanz für Erwachsene, Justus-Liebig-Universität, Med. Klinik II	Level 2	94
Gießen	Universitätsklinik Gießen und Marburg GmbH	Zentrum für Kinder- und Jugendmedizin, Mukoviszidose-Zentrum	Level 2	111
Greifswald	Ernst-Moritz-Arndt Universität	Universitätsmedizin Greifswald, Klinik und Poliklinik für Kinder- und Jugendmedizin	Level 2	23
Halle	Universitätsklinikum Halle (Saale) (UKH)	Medizinische Fakultät der Martin-Luther-Universität, Mukoviszidose-Zentrum	Level 2	84
Hamburg	Universitätsklinikum Eppendorf	II. Medizinische Klinik	Level 2	13
Hamburg	Kinder- und Jugendärztliche Gemeinschaftspraxis	Kinderärzte im Friesenweg, CF Centrum Altona	Level 2	193
Hamm	Evangelisches Krankenhaus Hamm (EVK) gGmbH	Klinik für Kinder- und Jugendmedizin, Pulmologie/Allergologie	Level 1	12
Hannover	Medizinische Hochschule Hannover	Klinik für Pädiatrische Pneumologie, Allergologie und Neonatologie	Level 2	198
Hannover	Medizinische Hochschule Hannover	Klinik für Pneumologie, Mukoviszidose-Ambulanz im Christiane-Herzog-Zentrum	Level 2	234
Heidelberg	Universitätsklinikum Heidelberg	Sektion Pädiatrische Pneumologie, Allergologie und Mukoviszidose-Zentrum	Level 2	127
Heidelberg	Thoraxklinik am Universitätsklinikum Heidelberg	Abteilung für Pneumologie und Beatmungstherapie, CF Ambulanz für Erwachsene	Level 2	219
Heilbronn	SLK-Kliniken Heilbronn GmbH	Klinik für Kinder- und Jugendmedizin, Klinikum am Gesundbrunnen, Perinatalzentrum	Level 2	22
Homburg	Universitätsklinikum d. Saarlandes	Innere Medizin 5, CF-Ambulanz für Erwachsene	Level 1	58
Homburg	Universitätsklinikum d. Saarlandes	Klinik für Allgemeine Pädiatrie und Neonatologie	Level 2	64
Jena	Universitätsklinikum Jena	Klinik für Kinder- und Jugendmedizin, Ambulanz für Pädiatrische Pneumologie, Allergologie, Mukoviszidosezentrum	Level 2	166
Karlsruhe	Städtisches Klinikum Karlsruhe gGmbH	Klinik für Kinder- und Jugendmedizin	Level 2	22
Kassel	Klinikum Kassel	Klinik für Kinder- und Jugendmedizin, Pneumologie, CF-Ambulanz	Level 2	48
Kiel	Städtisches Krankenhaus Kiel GmbH	Klinik für Kinder- und Jugendmedizin, Christiane Herzog Zentrum Nord – Kinder	Level 2	48
Kiel	Mukoviszidose Zentrum für Erwachsene	Städtisches Klinikum Kiel, 4. Medizinische Klinik Christiane Herzog Zentrum Nord – Erwachsene	Level 2	107
Koblenz	Gemeinschaftsklinikum Mittelrhein gGmbH	Klinik f. Kinder- u. Jugendmedizin, Pädiatrische Pneumologie und Allergologie, Mukoviszidose Ambulanz	Level 2	54
Cologne	Kliniken der Stadt Köln	Lungenklinik Merheim	Level 2	79
Cologne	Universitätsklinikum Köln	Klinik und Poliklinik für Kinder- und Jugendmedizin, Mukoviszidose-Zentrum	Level 2	240
Krefeld	Helios Klinikum Krefeld	Zentrum für Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	44
Leipzig	Universitätsklinikum Leipzig	Klinik und Poliklinik für Kinder- und Jugendmedizin, CF-Ambulanz	Level 2	61
Lübeck	Universitätsklinikum Schleswig Holstein (UKSH)	Campus Lübeck, Klinik für Kinder- und Jugendmedizin, Pädiatrische Pneumologie	Level 1	32
Magdeburg	Otto-von-Guericke Universitätsklinikum Magdeburg	Universitätsklinik für Pneumologie	Level 2	14
Magdeburg	Otto-von-Guericke Universitätsklinikum Magdeburg	Klinik f. Allgemeinpädiatrie u. Neonatologie, CF-Ambulanz	Level 2	22
Mainz	Universitätskinderklinik Mainz	Pädiatrische Pneumologie, Allergologie, Mukoviszidose	Level 2	103

Participating CF centers 2020

City	CF center	Department	Documentation level ¹	Number of patients ²
Mannheim	Universitätsklinikum Mannheim	Klinik für Kinder- und Jugendmedizin, Pulmologie, Infektiologie und Allergologie	Level 2	18
Marburg	Zentrum für Kinderheilkunde	Mukoviszidose-Ambulanz	Level 2	12
Memmingen	Klinikum Memmingen	Klinik für Kinder- und Jugendmedizin, Sozialpädiatrisches Zentrum	Level 1	9
München	Klinik für Kinder- und Jugendmedizin München Klinik Schwabing und Harlaching	CF-Ambulanz	Level 1	36
München	Klinikum Rechts der Isar der TU München	Mukoviszidose-Zentrum München West	Level 2	173
München	Lungenheilkunde München Pasing	Campus Innenstadt, Medizinische Klinik - Pneumologie	Level 2	218
München	LMU Klinikum der Universität München	Kinderklinik und Kinderpoliklinik im Dr. von Hauner-schen Kinderspital, Christiane Herzog-Ambulanz	Level 2	332
Münster	Universitätsklinikum Münster UKM	Klinik für Kinder- und Jugendmedizin, Allgemeine Pädiatrie Mukoviszidose-Ambulanz	Level 1	67
Münster	Clemenshospital	Mukoviszidose-Ambulanz	Level 2	120
Neubrandenburg	Dietrich Bonhoeffer Klinikum	Klinik für Kinder- u. Jugendmedizin,	Level 2	21
Oldenburg	Klinikum Oldenburg AöR	Klinik für Pädiatrische Pneumologie und Allergologie, Neonatologie und Intensivmedizin	Level 1	98
Osnabrück	Christliches Kinderhospital Osnabrück	Zentrum für Kinder- und Jugendmedizin, Mukoviszidose Ambulanz	Level 2	60
Passau	Kinderklinik Dritter Orden	Zentrum für Kinder- und Jugendgesundheit, Sozialpädiatrisches Zentrum	Level 2	25
Potsdam	Klinikum Westbrandenburg gGmbH	Kinder- und Jugendklinik, Mukoviszidose ASV-Ambulanz	Level 2	35
Ravensburg	Oberschwabenklinik (OSK) gGmbH Ravensburg	Krankenhaus St. Elisabeth, Klinik für Kinder u. Jugendliche	Level 1	5
Regensburg	KUNO Klinik St. Hedwig	Kinder- und Jugendmedizin	Level 2	84
Rostock	Universitätsmedizin Rostock	Kinder- und Jugendmedizin	Level 2	38
Schwerin	HELIOS Kliniken Schwerin	Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	25
Stuttgart	Klinikum Stuttgart	Olgahospital, Pädiatrie 3, Mukoviszidose Ambulanz	Level 1	172
Stuttgart-Gerlingen	Robert Bosch Krankenhaus RBK	Klinik Schillerhöhe, Mukoviszidose Ambulanz	Level 2	149
Trier	Klinikum Mutterhaus der Borromäerinnen gGmbH	Kinder- und Jugendmedizin	Level 2	23
Trier	Klinikum Mutterhaus der Borromäerinnen gGmbH	Klinikum Mutterhaus Mitte, Innere Medizin 1	Level 1	27
Tübingen	Universitätsklinik Tübingen	Klinik für Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	145
Ulm	Universitätsklinikum Ulm	Klinik für Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	120
Vechta	St. Marienhospital Vechta gGmbH	Klinik für Kinder- und Jugendmedizin, Allergologie und Pulmologie	Level 1	2
Wangen	Fachkliniken Wangen gGmbH	Waldburg-Zeil Kliniken, Klinik für Pädiatrische Pneumologie und Allergologie, CF-Ambulanz, Rehabilitationsklinik für Kinder und Jugendliche	Level 2	8
Wangen	Fachkliniken Wangen	Waldburg Zeil Kliniken, Klinik für Pneumologie	Level 2	21
Wesel	Marien-Hospital Wesel	Akad. Lehrkrankenhaus der Westfälischen Wilhelms-Universität Münster, Klinik f. Kinder- u. Jugendmedizin	Level 2	30
Worms	Klinikum Worms gGmbH	Klinik für Kinder- und Jugendmedizin	Level 2	50
Würzburg	Universitäts-Kinderklinik Würzburg	Christiane-Herzog-Ambulanz für Mukoviszidose	Level 2	145
Zwickau	Heinrich Braun Klinikum gGmbH	Standort Zwickau, Kinderzentrum	Level 1	11

¹ See the collective description for the definition of the documentation level; ² patients may have been documented in several outpatient clinics.

Glossary

Term	Definition
ABPA Allergic bronchopulmonary aspergillosis	Development of an allergic reaction to <i>Aspergillus fumigatus</i> .
Anticholinergics	An anticholinergic has a relaxing effect on the smooth musculature and inhibits secretion.
Arthritis	A condition which causes pain and inflammation in the joints.
Arthropathy	A condition which causes pain in the joints.
Pancreas	An organ in the digestive system which produces insulin and digestive enzymes.
β₂-sympathomimetics	Betasymphomimetics are pharmaceutical substances which stimulate the beta receptors of the sympathetic nervous system.
BMI (Body Mass Index)	A measure for evaluating a person's body weight in relation to their height.
Burkholderia cepacia	Burkholderia cepacia is a species of bacterium in the Burkholderia genus. Several of these bacteria are a potential threat to the health of people with Cystic Fibrosis.
CF (Cystic fibrosis)	Mucoviscidosis; Cystic Fibrosis
CFTR Regulator of the transmembrane conductance in Cystic Fibrosis	A protein on the cell surface which controls the sodium and water balance of a cell. The gene which causes Cystic Fibrosis is the blueprint for the CFTR protein. Every person has two copies of the gene for CFTR. Both CFTR genes must be affected by a mutation which causes CF, in order for someone to be born with Cystic Fibrosis.
Enzymes	Biological molecules present in the body (i.e. molecules occurring as metabolic products in the living cell) which support complex reactions such as the digestion of food.
FEV₁ one-second capacity	The one-second capacity is the largest-possible quantity of air which can be forced out of the lungs within 1 second. The FEV ₁ value is part of the pulmonary function and can be measured in a pulmonary function test.
FEV₁% predicted	The FEV ₁ % is the percentage value of the average FEV ₁ which healthy people of the same age, gender and height can achieve. It is normally between 80 – 120%.
Gastroesophageal reflux disease	A chronic symptom of damage caused by gastric acid rising from the gastric mucosa.
Genotype	A characteristic part of the genetic structure of a cell, an organism or an individual.
Haemophilus influenza	Haemophilus influenza is a bacterium which can cause severe illness.
Haemoptysis	Coughing up blood.
Hepatobiliary disease	A liver or biliary disease.

Glossary

Term	Definition
Heterozygous	Everyone living with Cystic Fibrosis has two mutations of the gene for CFTR. One mutation is inherited from the mother and one from the father. If both mutations (or genotypes) are different, the person is heterozygous.
Homozygous	Everyone living with Cystic Fibrosis has two mutations of the gene for CFTR. One mutation is inherited from the mother and one from the father. If both mutations (or genotypes) are the same, the person is homozygous.
Interquartile range	The interquartile range is a measure of dispersion in descriptive statistics. If the sample is sorted by size, it indicates the width of the interval in which the mean 50% of the sample elements lie. It shows the difference between the upper and lower quartile: $IQR = Q_3 - Q_1$.
Confidence interval	An expectancy range to express how confident we are about our statistical estimates of a clinical measure. It shows a series of results which are likely to include the correct values for the population under study. A narrow confidence interval indicates a more accurate estimate. A wide confidence interval indicates greater uncertainty about the exact value of the measurement, often because only a small group of patients was studied.
Digestive tract / Gastrointestinal tract (GI)	The gastrointestinal tract (GI) is the main part of the digestive system which extends from the oesophagus to the anus. The GI is an organ system responsible for digesting food, absorbing nutrients and excreting faeces.
Median	The middle number when all numbers are arranged from the smallest to the largest number.
<i>Median survival prognosis</i>	A mathematical formula which can be used to predict the age which half the people born with CF today will reach. For example: 50 % of the people born today will reach the age of at least 47. The other 50% of these people will probably die before they reach this age.
Mean value	An average value calculated by adding up all the values and dividing by the number of values.
Average age at death	The average age at death is based on the people with CF who died in one year.
<i>MRSA</i>	Methicillin-resistant Staphylococcus aureus is a bacterial species which is resistant to a series of widely-used antibiotics.
Mutation	A mutation is an alteration to a gene. If both parents of a child are carriers of a mutation which causes Cystic Fibrosis, there is a 25% chance that the child will have CF. There are over 1,400 different mutations of the CFTR gene.
Hepatobiliary disease	Small saciform growths caused by chronic inflammation of the nasal mucosa.

Glossary

Term	Definition
Newborn screening	Newborn screening is an examination of newborns which aims to detect congenital diseases at an early stage, e.g. Cystic Fibrosis.
Non-tuberculous mycobacteria (NTM)	A mycobacterium which does not cause tuberculosis but can still be the cause of respiratory tract infections. Several types are known.
Osteopenia	A disease which is less severe than osteoporosis and in which the mineral content of bones is reduced.
Osteoporosis	A condition in which the bones become brittle due to the loss of tissue.
Percentile	A percentile indicates where a value is relative to the rest of the data. If a value is higher than 90% of the rest of the data, it is referred to as the 90th percentile.
Pneumothorax	An accumulation of air in the cavity between the lung and the chest wall which can cause a pulmonary collapse on the affected side.
Prevalence	The total number of people with this disease in the last 12 months.
<i>Pseudomonas aeruginosa</i>	A strain of bacteria which rarely affects healthy people but can lead to a variety of infections in a weakened immune system. These infections often become chronic.
Liver cirrhosis	A chronic liver disease.

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Mukoviszidose e.V.

In den Dauen 6 | 53117 Bonn

Tel.: 0228 9 87 80-0 | Fax: 0228 9 87 80-77

info@muko.info | www.muko.info

