German Cystic Fibrosis Registry

Annual Report | 2021

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Impressum

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Foreword

PD Dr. med. Lutz Nährlich

Medical Director
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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 in the 26th report which covers the year 2021 and also describes the development for selected cohorts for the first time.

The year 2021 will go down in the history of cystic fibrosis as the second year of the coronavirus pandemic and the year of the extension of approval of the highly effective CFTR modulator therapy (elexacaftor/tezacaftor/ivacaftor). A CFTR modulator therapy was available for approx. 73 % of all people with cystic fibrosis in Germany in 2021 and used in 81 % of these patients. The immediate effects on the state of health of this therapeutic development on all persons with cystic fibrosis can be seen for the first time. However, it should be borne in mind that the report does not make a distinction between people with cystic fibrosis with and without CFTR modulator therapy and therefore only partly reflects the individual effect.

Above all, the pulmonary function has significantly improved in all people with cystic fibrosis. This improvement has been demonstrated in all cohorts for several years now in the form of a stabilisation of the pulmonary function. This encouraging development has even been surpassed by the elimination of the characteristic and higher-than-average deterioration of the pulmonary function between the ages of 10 and 20 which was prevalent in the past. A reduction in the verifications of Pseudomonas aeruginosa at least once a year by a relative 30 % in patients between 12 and 30 years of age give grounds for optimism; however, they should be treated with caution as a result of the lower production of sputum associated with the modulator therapy. The rate of chronic Pseudomonas infection in children and adolescents is unchanged at 9.6 % and 53 % in adults. The decrease in the number of exacerbations treated with antibiotics and hospitalisations is another positive development: Only 26 % of all people with cystic fibrosis suffered such an exacerbation or received inpatient treatment compared with 35 % and 33 % respectively in 2020. The decrease in underweight, especially in adults, contrasts with an increase in overweight and adiposity in adults from 16 % to 20 %. The basic and indication therapy remained unchanged for the time being. All this underlines the continuing necessity for the close clinical care provided by the multidisciplinary cystic fibrosis team, in order to recognise and discuss the medium-term changes and challenges ahead on a collective basis. The German Cystic Fibrosis Registry can offer the (data) basis for this purpose.

With your support, we have continued to record COVID-19 positive patients in the Registry and once again provided information on this in the report. 929 COVID-19 infections were diagnosed (by means of PCR) from February 2020 to the middle of August 2022 and four people with cystic fibrosis unfortunately died as a result of their COVID-19 infections.

This detailed overview of the health status of people with cystic fibrosis would not have been possible without the trust you have placed 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 involved in data entry and analysis under the conditions of 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 team of the Interdisciplinary Center for Clinical Studies (IZKS) of the University of Mainz (Ms Wosniok, Ms Wollscheid, Ms Regenfuß, Mr Kronfeld, Mr Ruckes).

My special thanks go to Mr Burkhart of the Mukoviszidose Institut for his tireless efforts in project management.

Please keep supporting the Registry.

Collective description

The history data records of 6.776 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 2021. In addition, patients without history data were also included in the evaluations of new CF diagnoses and mortality (16 newly diagnosed patients and 13 deceased patients without history data in 2021).

All 369 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 6.407 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-yearold 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 statusfor 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 87 CF centers participating in the Registry in 2021.
A list of all CF facilities and the reported patient numbers can be found on page 62.
Write to us if your facility is not represented: mburkhart@muko.info

01

Brief overview

	2000	2005	2010	2015	2020	2021
Data status	27.06.2022	27.06.2022	27.06.2022	27.06.2022	12.07.2022	12.07.2022
Participating centers	78	83	81	89	88	87
Participating patients with annual data	3,642	4,720	5,106	5,751	6,647	6,776
of these, transplant patients	43	123	202	293	361	369
Age in years; median	14	16	18	20	21	22
Proportion of adults (≥ 18 years) in %	36.4	45.9	51.3	56.7	58.7	59.4
Male patients in %	52.4	52.1	51.9	52.0	52.0	51.8
New diagnoses in the reporting year[1]	223	205	214	223	218	150
Age for new diagnoses in years; Median[1]	1.34	0.83	0.92	0.92	0.17	0.08
of these, diagnosis via newborn screening	1.8	3.4	3.7	10.3	58.7	68.7
Maternities in the reporting year	4	8	13	19	33	37
Paternities in the reporting year	1	0	7	6	15	9
Deaths in the reporting year[1]	45	75	75	100	62	39
Deaths: % of all patients[1]	1.2	1.6	1.5	1.7	0.9	0.6
Age at death in years; median	21	26	28	31.5	34.5	42
(25^{th} – 75^{th} pctl)	(17 – 28)	(19 – 36)	(24 – 37)	(25 – 37)	(28 – 46)	(25 – 50)
Transplant patients in the reporting year[1]	9	36	33	33	31	10
Lung transplants[2]	7	32	29	30	27	9
Liver transplants[2]	2	3	4	6	5	1
Renal transplantation[2]	0	1	1	0	1	0
Pancreas transplantation[2]	0	0	0	1	0	0

Table 1: Brief overview of cystic fibrosis patients with follow-up data, valid informed consent and cystic fibrosis diagnosis in the reporting years 2000 – 2021 in Germany

[1] Data on new diagnoses, deaths, and transplant recipients include patients without follow-up data
[2] Multiple answers possible

Patient numbers development

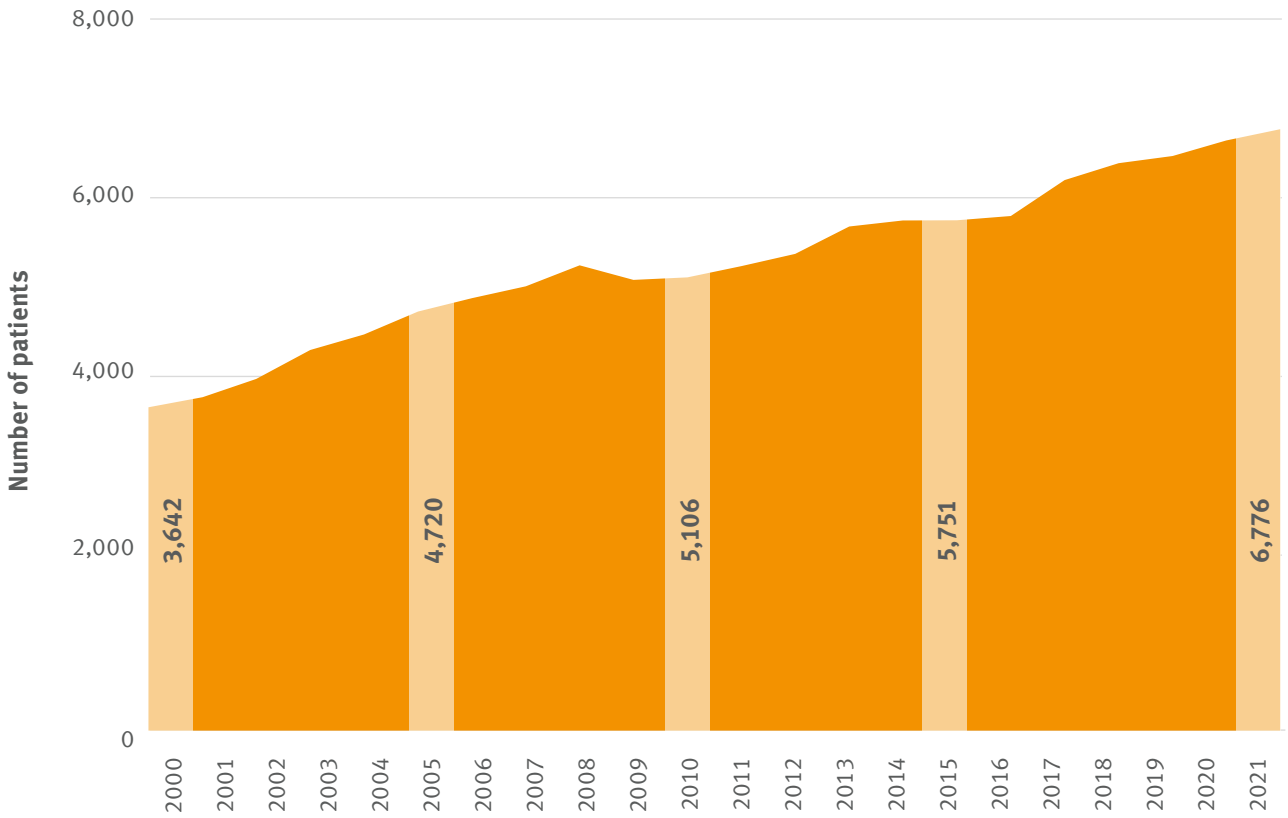

Figure 2: Number of patients documented in the registry 2000 – 2021

Reporting year	patients participating with annual data
2000	3,642
2001	3,756
2002	3,962
2003	4,287
2004	4,463
2005	4,720
2006	4,870
2007	5,005
2008	5,241
2009	5,077
2010	5,106

Reporting year	patients participating with annual data
2011	5,235
2012	5,372
2013	5,680
2014	5,746
2015	5,751
2016	5,798
2017	6,200
2018	6,391
2019	6,472
2020	6,647
2021	6,776

Table 2: Number of patients documented in the registry 2000 – 2021

03

Age structure

The age structure calculations include all 6,776 pwCF with annual data for 2021. 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.

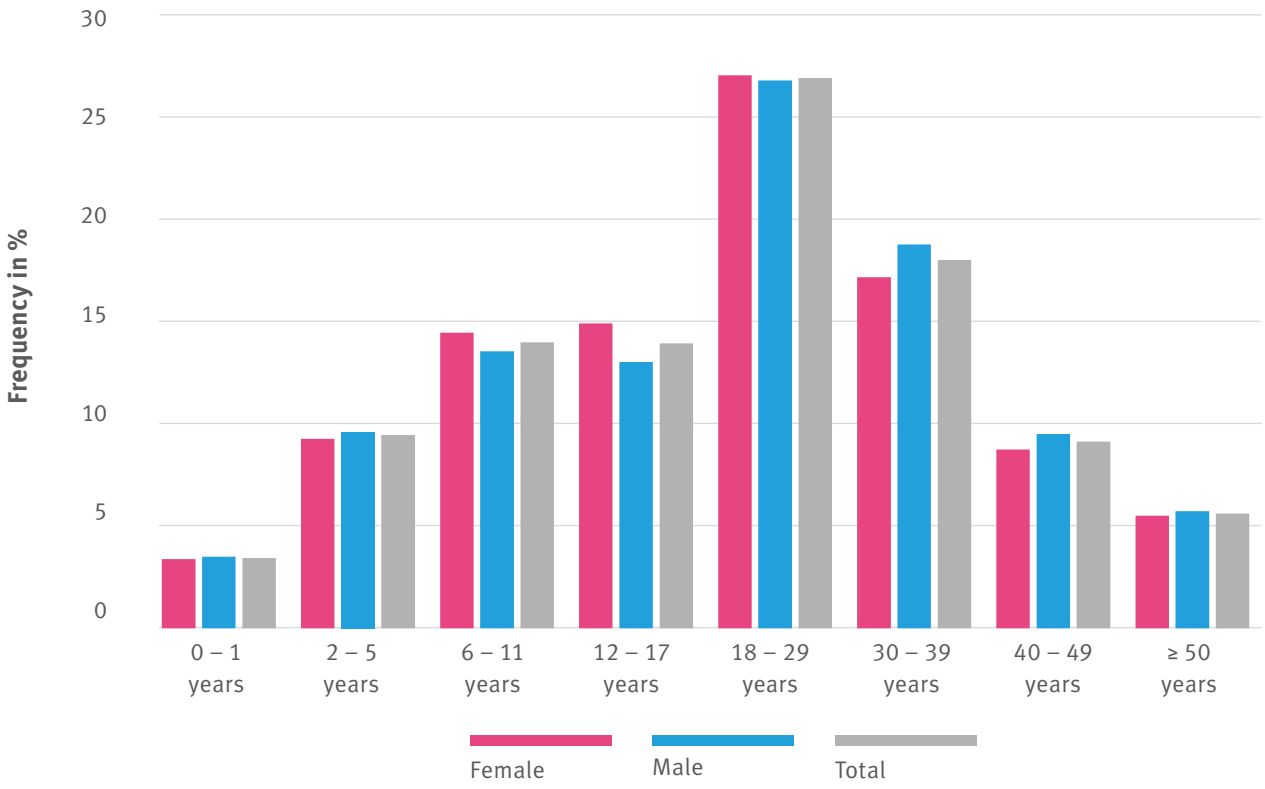

Figure 3: Age distribution of pwCF in 2021

	Male	Female	Total
Numbers	3,266	3,510	6,776
Mean value (years)	22.7	23.3	23.0
Median (years)	21.0	23.0	22.0
Minimum (years)	0	0	0
Maximum(years)	84	81	84
25th percentile (years)	11.0	11.0	11.0
75th percentile (years)	33.0	34.0	33.0
Number < 18 years	1,366	1,386	2,752
Number ≥ 18 years	1,900	2,124	4,024

Table 3: Age distribution of pwCF in 2021

Age structure

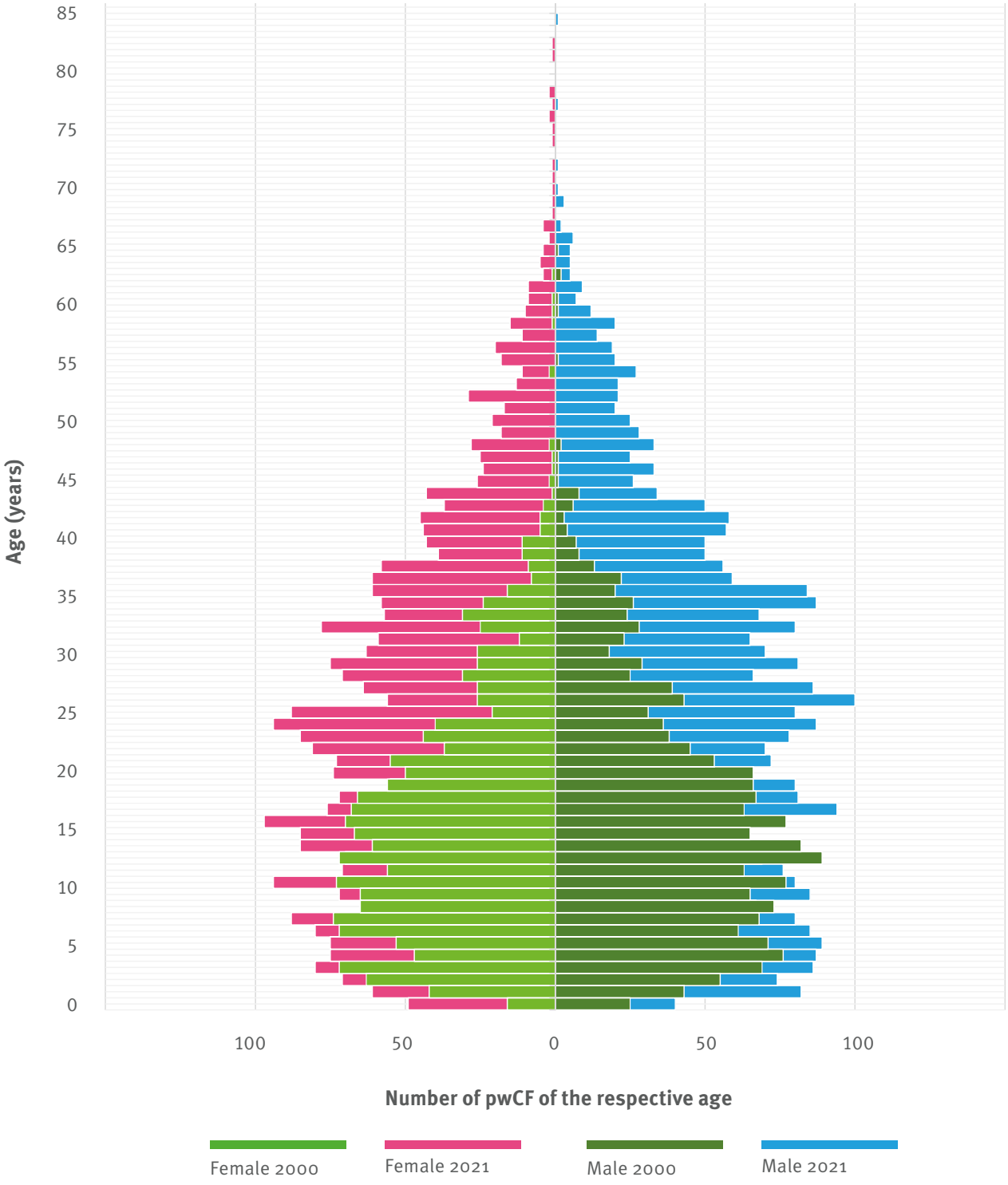

Figure 4: Age pyramid pwCF 2000 vs. 2021

03

Age structure

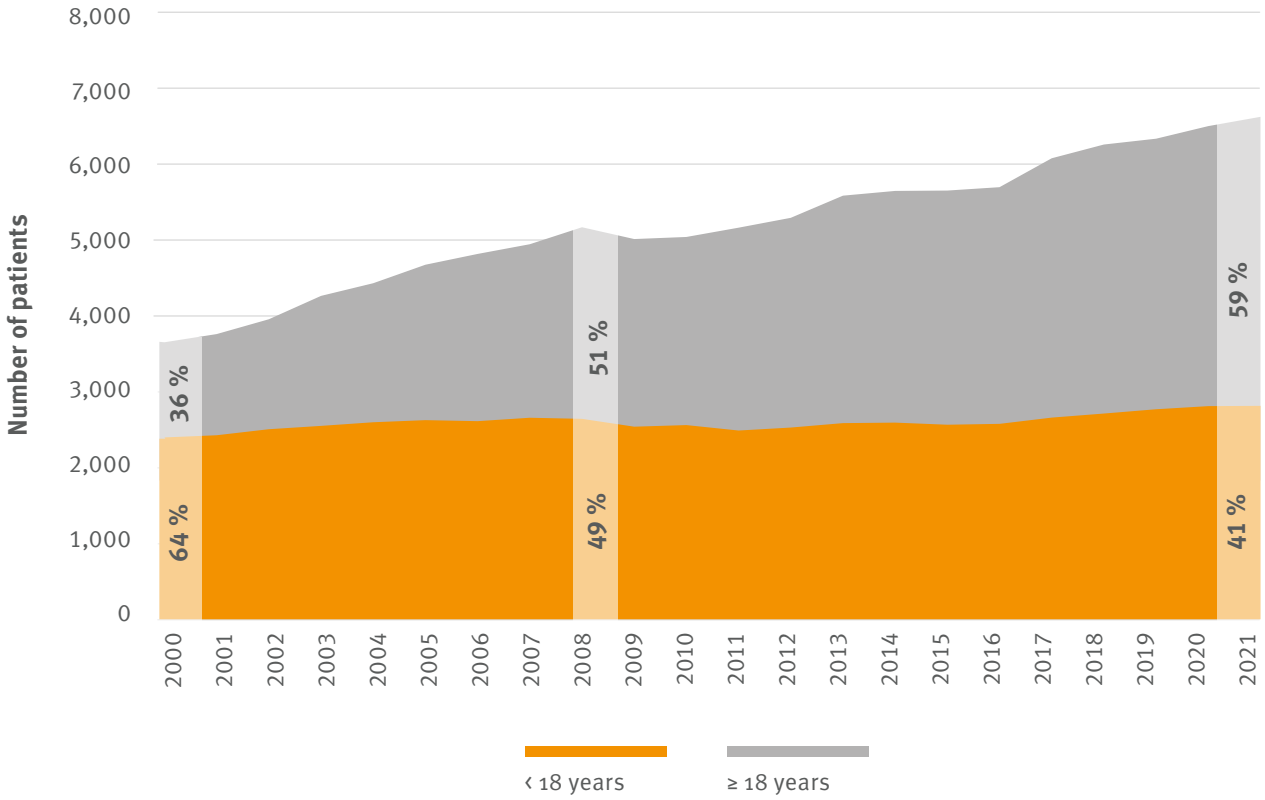

Figure 5: Development of age distribution (< 18 vs. ≥ 18 years) for the years 2000 – 2021

Age structure

Reporting year	Total	Prozentualer Anteil	
		< 18 years	≥ 18 Jahre
2000	3,642	63.6	36.4
2001	3,756	62.5	37.5
2002	3,962	61.3	38.7
2003	4,287	57.8	42.2
2004	4,463	56.6	43.4
2005	4,720	54.1	45.9
2006	4,870	52.2	47.8
2007	5,005	51.7	48.3
2008	5,241	49.1	50.9
2009	5,077	48.6	51.4
2010	5,106	48.7	51.3
2011	5,235	46.1	53.9
2012	5,372	45.7	54.3
2013	5,680	44.3	55.7
2014	5,746	43.9	56.1
2015	5,751	43.3	56.7
2016	5,798	43.2	56.8
2017	6,200	41.8	58.2
2018	6,391	41.4	58.6
2019	6,472	41.8	58.2
2020	6,647	41.3	58.7
2021	6,776	40.6	59.4

Table 4: Development of age distribution (<18 vs ≥ 18 years) for the years 2000 – 2021

04

Cystic fibrosis diagnosis

4a. Diagnoses in 2021

150 patients were diagnosed in 2021; annual data is available for 134 of these patients (89.3 %). The age distribution of all patients newly diagnosed in 2021 is shown in the following tables.

	N	Mean value	Median	Minimum	Maximum	25th percentile	75th percentile
Age in years	150	5.0	0.1	0.0	71.0	0.1	0.5

Table 5: Age at diagnosis of all cystic fibrosis patients diagnosed in 2021

Newborn screening was performed in 103 (68.7 %) of the pwCF diagnosed in 2021. 12 patients (8.1 %) had a meconium ileus. The age at diagnosis of the patients newly diagnosed via newborn screening in 2021 is as follows:

	N	Mean value	Median	Minimum	Maximum	25th percentile	75th percentile
Age in days	103	29.3	23.0	0.0	271	14	32

Table 6: Age at diagnosis of all pwCF diagnosed via newborn screening in 2021

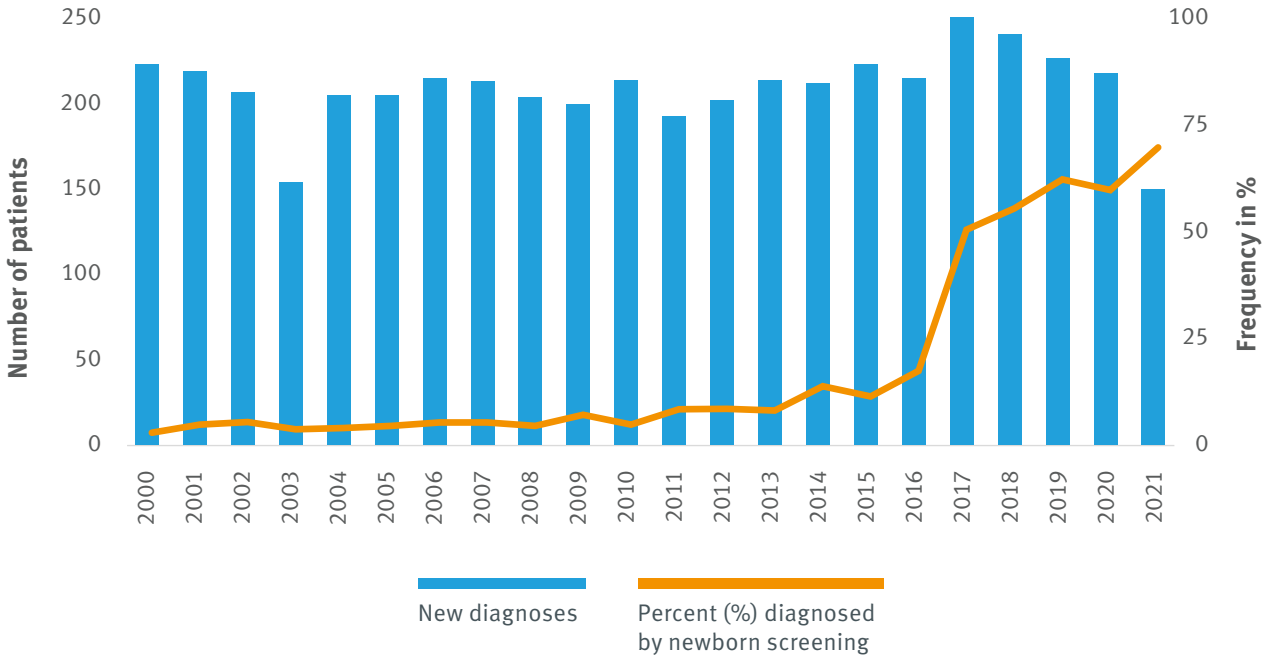

Figure 6: Number of new diagnoses and percentage of pwCF diagnosed by newborn screening 2000 – 2021

Cystic fibrosis diagnosis

4a. Diagnoses in 2021

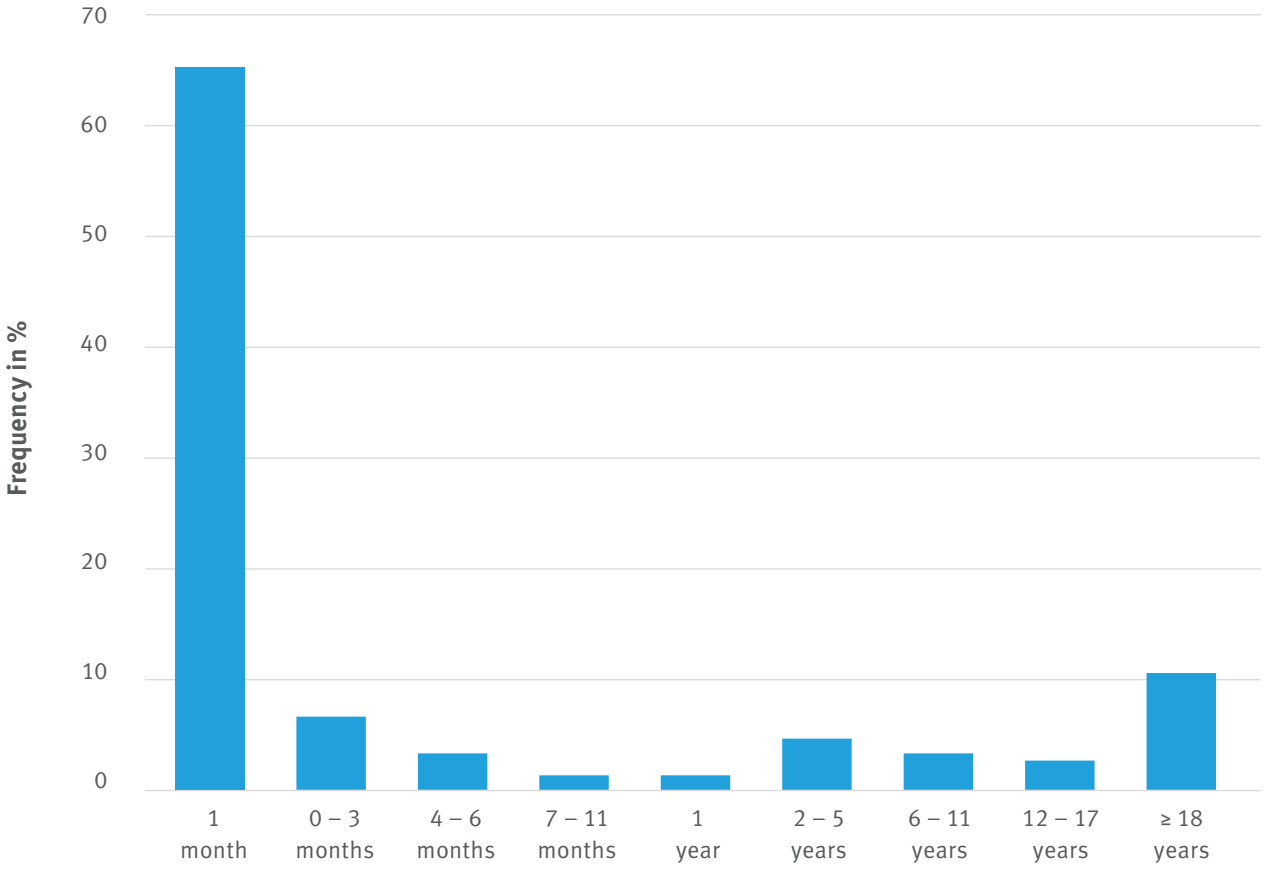

Figure 7: Age-related frequencies among pwCF diagnosed in 2021

Age at diagnoses	Frequency	Percent	Accumulated percentages
≤ 1 month	99	66.0	66.0
2 – 3 months	10	6.7	72.7
4 – 6 months	5	3.3	76.0
7 – 11 months	2	1.3	77.3
1 year	2	1.3	78.7
2 – 5 years	7	4.7	83.3
6 – 11 years	5	3.3	86.7
12 – 17 years	4	2.7	89.3
≥ 18 years	16	10.7	100.0

Table 7: Age at diagnosis in pwCF diagnosed in 2021

04

Cystic fibrosis diagnosis

4b. Age at diagnosis

The age distribution at diagnosis of the 6,776 patients with follow-up data in 2021 is shown in the following figures and tables. No information on the date of diagnosis was available for 242 patients (3.6 %).

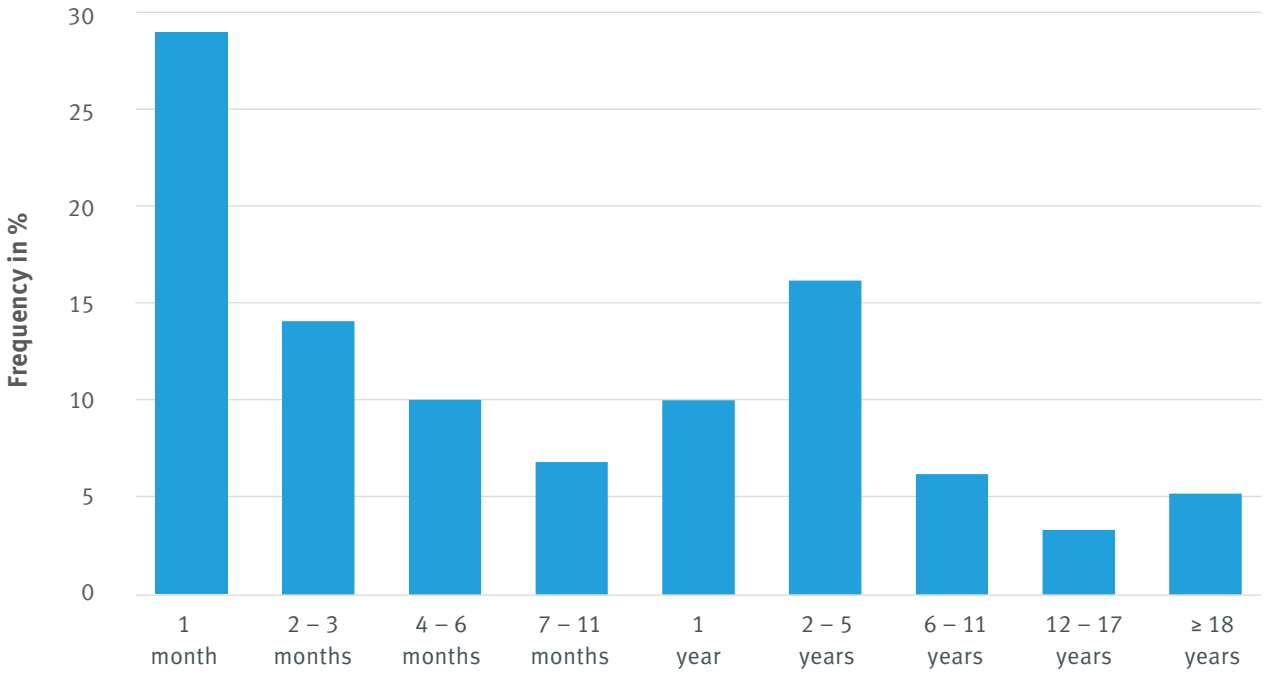

Figure 8: Age-related frequencies at diagnosis – all pwCF as of 2021

Age at diagnoses	Frequency	Percent	Accumulated percentages
≤ 1 month	1,878	28.7	28.7
2 – 3 months	913	14.0	42.7
4 – 6 months	651	10.0	52.7
7 – 11 months	442	6.8	59.4
1 year	648	9.9	69.4
2 – 5 years	1,048	16.0	85.4
6 – 11years	401	6.1	91.5
12 – 17 years	216	3.3	94.8
≥ 18 years	337	5.0	100.0
unknown	242	–	–

Table 8: Age at diagnosis – all pwCF as of 2021

Cystic fibrosis diagnosis

4c. Genotyping

Genotyping was available for 6710 patients (99.2 %). Missing data were treated as "mutation not identified" in the following presentation.

Mutationskombinationen	Frequency	Percent
F508del homozygot	3,159	46.6
F508del heterozygous: Second mutation identified	2,593	38.3
F508del heterozygous: Second mutation not identified	84	1.2
No verification of F508del: Both mutations identified	804	11.9
No verification of F508del: Only one mutation identified	35	0.5
No verification of F508del: No mutations identified	101	1.5
Total	6,776	100.0

Table 9: Mutation combinations pwCF 2021

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

Erste und zweite Mutation	Anzahl	Prozent
F508del (p.Phe508del/c.1521_1523delCTT)	8.995	67,1
G542X (p.Gly542X/c.1624G>T)	278	2,1
N1303K (p.Asn1303Lys/c.3909C>G)	268	2,0
R553X (p.Arg553X/c.1657C>T)	251	1,9
G551D (p.Gly551Asp/c.1652G>A)	211	1,6
CFTRdele2,3 (p.Ser18ArgfsX16/c.54-5940_273+10250del21kb)	198	1,5
R347P (p.Arg347Pro/c.1040G>C)	175	1,3
3849+10kbC->T (c.3718-2477C>T)	146	1,1
1717-1G->A (c.1585-1G>A)	111	0,8
2789+5G->A (c.2657+5G>A)	100	0,8
2183AA->G (p.Lys684SerfsX38/c.2051_2052delAAinsG)	92	0,7
W1282X (p.Trp1282X/c.3846G>A)	87	0,7
3272-26A->G (c.3140-26A>G)	68	0,5
M1101K (p.Met1101Lys/c.3302T>A)	64	0,5
R117H (p.Arg117His/c.350G>A)	60	0,5
2184insA (p.Gln685ThrfsX4 or p.Gln685Thrfs *4/c.2052dupA or c.2052dup)	58	0,4
621+1G->T (c.489+1G>T)	56	0,4
R1162X (p.Arg1162X/c.3484C>T)	56	0,4
I336K (p.Ile336Lys/c.1007T>A)	53	0,4
1677delTA (p.Tyr515X/c.1545_1546delTA)	51	0,4
Other Mutation	1.853	13,8
Unknown/Mutation not identified	184	1,4
Total	13.415	100,0

Table 10: CFTR genotyping pwCF 2021

05

Nutritional status

5a. Children and adolescents under 18 years

All patients from 2 – 17 years without a transplant with annual data in 2021 (n=2,539) were included. No information on the nutritional status was available for 9 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.

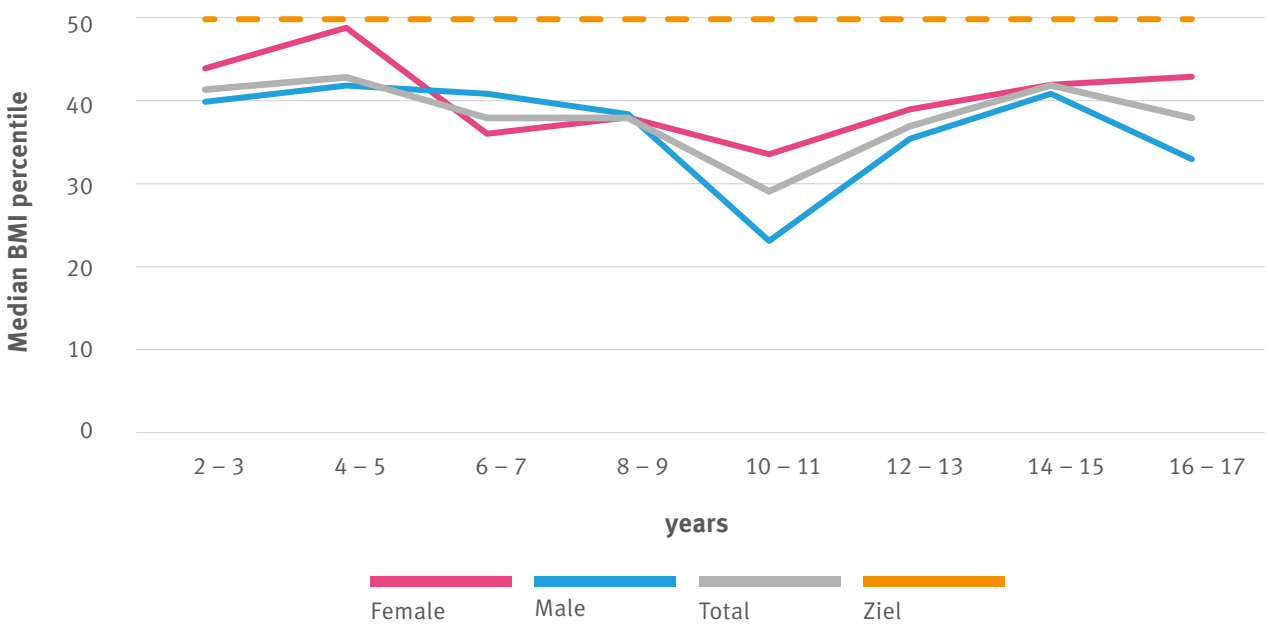

Figure 9: Median BMI percentiles of children and adolescents aged 2 – 17 years 2021

Age (years)	Male			Female			Total		
	N	Median	25th - 75th pctl.	N	Median	25th - 75th pctl.	N	Median	25th - 75th pctl.
2 – 3	164	40.0	18 – 62	152	44.0	15 – 72	316	41.5	18 – 66
4 – 5	201	42.0	15 – 71	167	49.0	19 – 70	368	43.0	17 – 70
6 – 7	157	41.0	21 – 60	164	36.0	20 – 58	321	38.0	20 – 59
8 – 9	164	38.5	22 – 60	164	38.0	18 – 60	328	38.0	19 – 60
10 – 11	137	23.0	11 – 51	122	33.5	17 – 56	259	29.0	14 – 54
12 – 13	140	35.5	15 – 56	167	39.0	18 – 60	307	37.0	17 – 56
14 – 15	142	41.0	21 – 66	175	42.0	21 – 66	317	42.0	21 – 66
16 – 17	174	33.0	14 – 55	140	43.0	21 – 68	314	38.0	16 – 62
Total	1,279	37.0	16 – 61	1.251	41.0	18 – 64	2.530	38.0	17 – 62

Table 11: BMI percentiles of children and adolescents aged 2 – 17 years 2021

Nutritional status

5a. Children and adolescents under 18 years

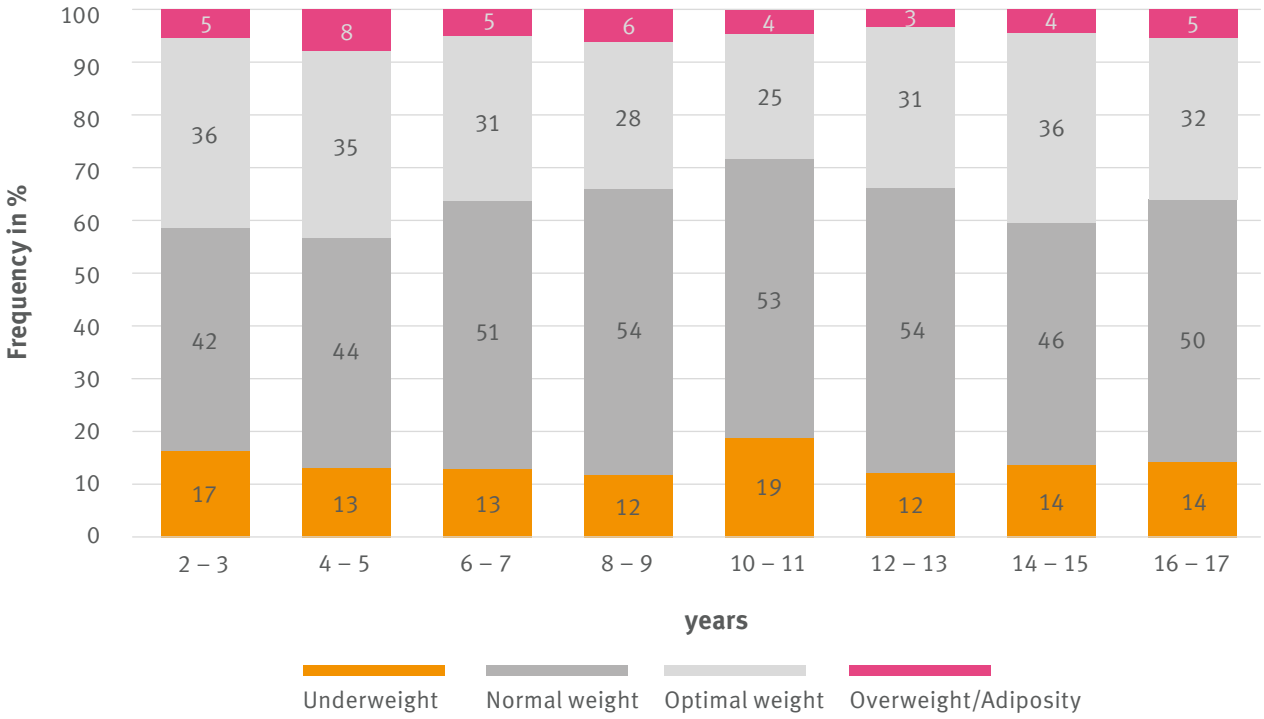

Figure 10: Weight categories of children and adolescents aged 2 – 17 (frequencies in %) 2021, Underweight: BMI percentiles < 10; Normal weight: BMI percentiles 10 – 49; Optimal weight: BMI percentiles 50 – 89; Overweight/Adiposity: BMI percentiles ≥ 90

BMI percentile KIGGS	Male	Female	Total
Underweight	15.1	13.2	14.2
Normal weight	49.8	48.0	48.9
Optimal weight	29.6	34.2	31.9
Overweight/Adiposity	5.6	4.6	5.1

Table 12: Weight categories of children and adolescents aged 2 – 17 (frequencies in %) 2021, 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	27.0	7.3	44.1	13.2	35.3	10.2
Normal weight	63.5	84.1	50.9	75.0	57.4	79.6
Overweight/Adiposity	9.5	8.7	5.1	11.8	7.4	10.2

Table 13: Weight categories of children under 2 years (frequencies in %) according to length/target weight (LSG) 2021, Underweight: LSG < 90 %; Normal weight: LSG 90 – 110 %; Overweight/obese: LSG > 110 %.

05

Nutritional status

5b. Adults 18 years and older

Adult patients without a transplant with annual data for 2021 (n=3,602) were included. No information on the nutritional status was available for 17 patients (0.5 %). The age was calculated at the time of the physical examination.

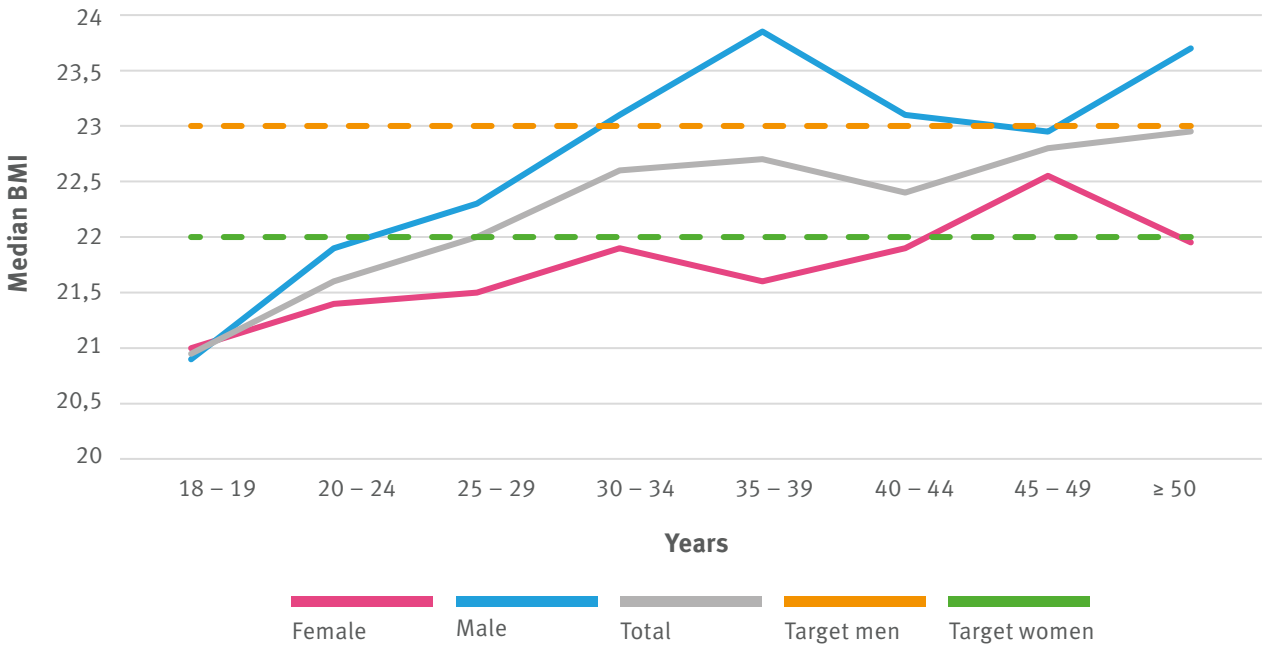

Figure 11: BMI of adults aged 18 and over 2021

Age (years)	Male			Female			Total		
	N	Median	25th - 75th pctl.	N	Median	25th - 75th pctl.	N	Median	25th - 75th pctl.
18 – 19	135	20.9	19 – 23	125	21.0	19 – 23	260	21.0	19 – 23
20 – 24	372	21.9	20 – 24	395	21.4	20 – 23	767	21.6	20 – 24
25 – 29	369	22.3	21 – 25	304	21.5	20 – 23	673	22.0	20 – 24
30 – 34	351	23.1	21 – 25	281	21.9	20 – 24	632	22.6	21 – 25
35 – 39	222	23.9	22 – 26	197	21.6	20 – 24	419	22.7	21 – 25
40 – 44	169	23.1	21 – 25	145	21.9	20 – 24	314	22.4	20 – 25
45 – 49	120	23.0	22 – 25	92	22.6	21 – 25	212	22.8	21 – 25
≥ 50	164	23.7	22 – 26	144	22.0	20 – 25	308	23.0	21 – 26
Total	1,902	22,7	21 – 25	1,683	21,6	20 – 24	3,585	22,1	20 – 24

Table 14: BMI of adults aged 18 and over 2021

Nutritional status

5b. Adults 18 years and older

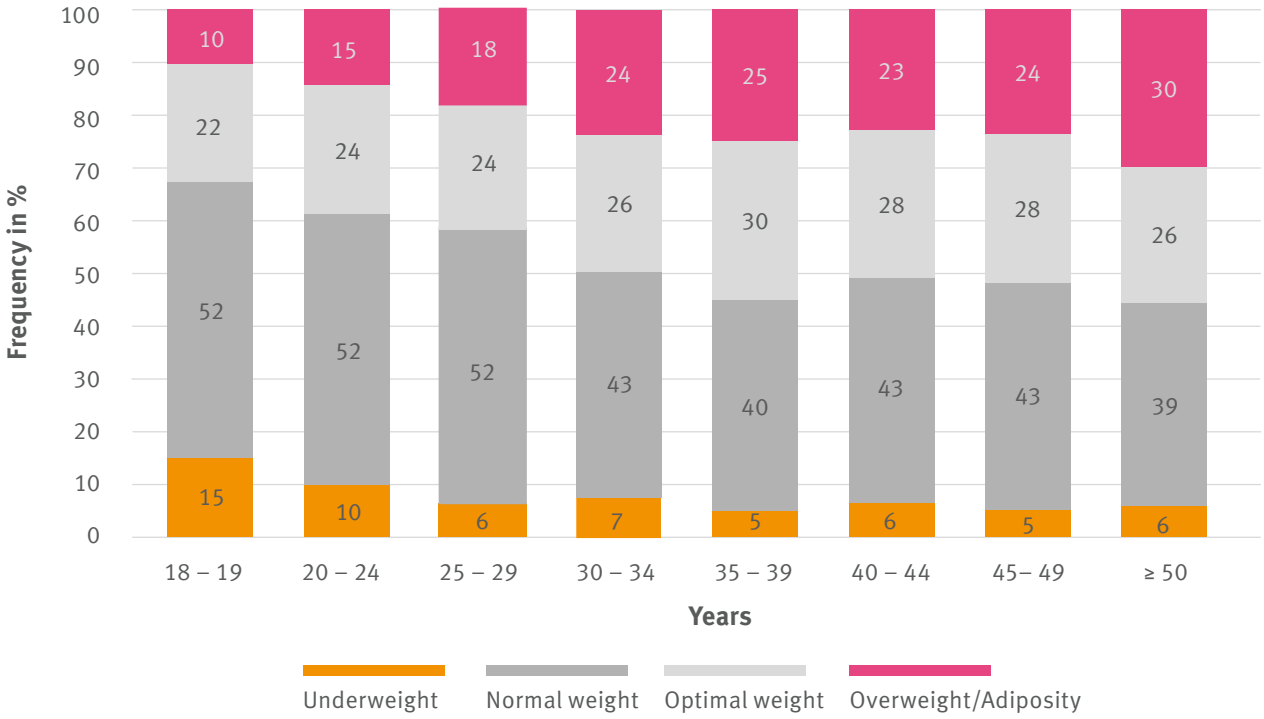

Figure 12: Weight categories adults 18 years and older (frequencies in %) 2021,
Underweight: BMI ‹ 18.5 kg/sqm; Normal weight: BMI men 18.5 – 22.9 kg/sqm; BMI women 18.5 – 21.9 kg/sqm;
Optimal weight: BMI men 23.0 – 24.9 kg/sqm, BMI women 22.0 – 24.9 kg/sqm; Overweight/Adiposity: BMI ≥ 25 kg/sqm

	Male	Female	Total
Underweight	6.7	8.7	7.6
Normal weight	46.5	46.2	46.4
Optimal weight	22.1	29.8	25.7
Overweight/Adiposity	24.7	15.3	20.3

Table 15: Weight categories adults 18 years and older (frequencies in %) 2021
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

05

Nutritional status

5c. Development of nutritional status 2000 – 2021 Children and adolescents under 18 years of age

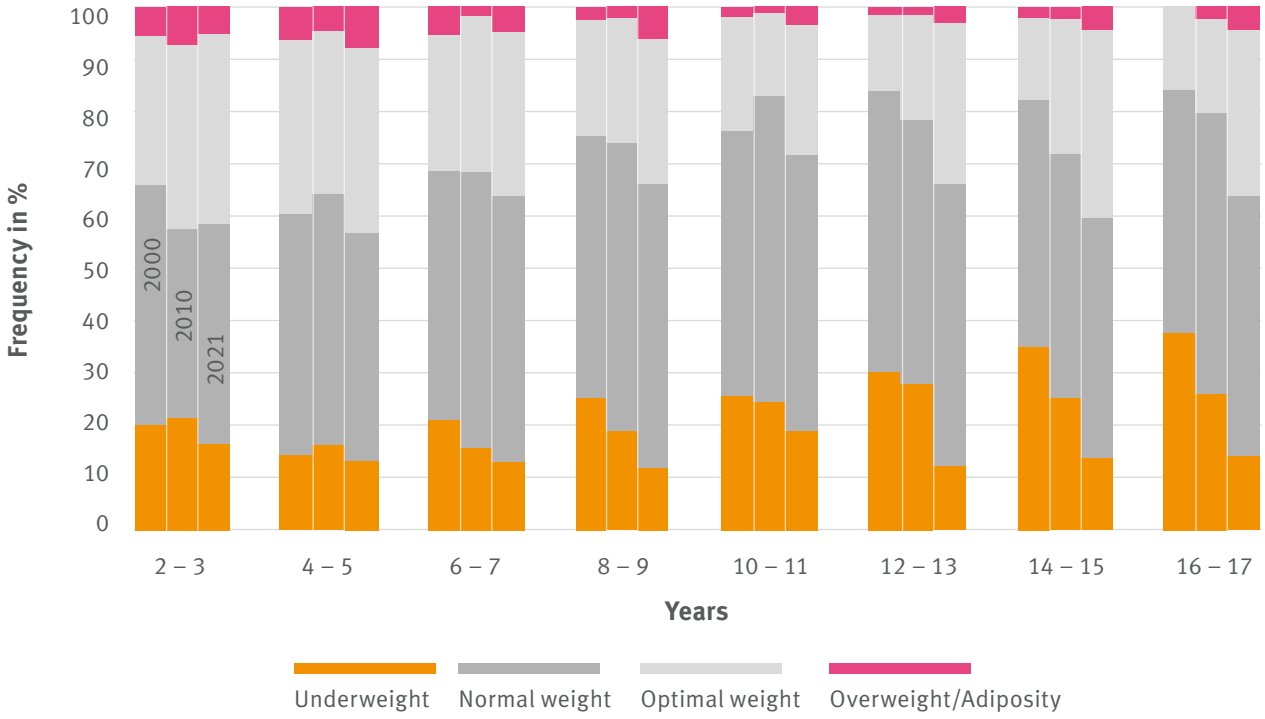

Figure 13: Development of weight categories of children and adolescents up to 17 years (frequencies in %) 2000 – 2021, Underweight: BMI percentiles < 10; normal weight: BMI percentiles 10 - 49; optimal weight: BMI percentiles 50 – 89; Overweight/Adiposity: BMI percentiles ≥ 90

Weight categories	Reporting year	Age (years)							
		2 – 3	4 – 5	6 – 7	8 – 9	10 – 11	12 – 13	14 – 15	16 – 17
Underweight	2000	20.2	14.5	21.2	25.3	25.8	30.4	35.2	37.5
	2010	21.5	16.4	15.7	19.1	24.6	28.1	25.4	26.0
	2021	16.5	13.3	13.1	11.9	18.9	12.4	13.9	14.3
Normal weight	2000	45.9	46.1	47.7	50.2	50.6	53.6	47.2	46.2
	2010	36.1	47.9	52.8	55.0	58.3	50.5	46.7	53.6
	2021	42.1	43.5	50.8	54.3	52.9	53.8	45.7	49.7
Optimal weight	2000	28.5	33.2	25.8	22.1	21.7	14.5	15.6	15.9
	2010	35.1	31.1	29.7	23.7	15.8	19.9	25.7	18.1
	2021	36.1	35.3	31.2	27.7	24.7	30.6	36.0	31.5
Overweight/ Adiposity	2000	5.5	6.2	5.4	2.4	1.9	1.5	2.0	0.4
	2010	7.3	4.6	1.8	2.3	1.4	1.5	2.2	2.3
	2021	5.4	7.9	5.0	6.1	3.5	3.3	4.4	4.5

Table 16: Development of weight categories of children and adolescents up to 17 years (frequencies in %) 2000 – 2021 Underweight: BMI-Perzentile < 10; Normal weight: BMI-Perzentile 10 – 49; Optimal weight: BMI-Perzentile 50 – 89; Overweight/Adiposity: BMI-Perzentile ≥ 90

Nutritional status

5c.i Median BMI percentiles by birth cohort

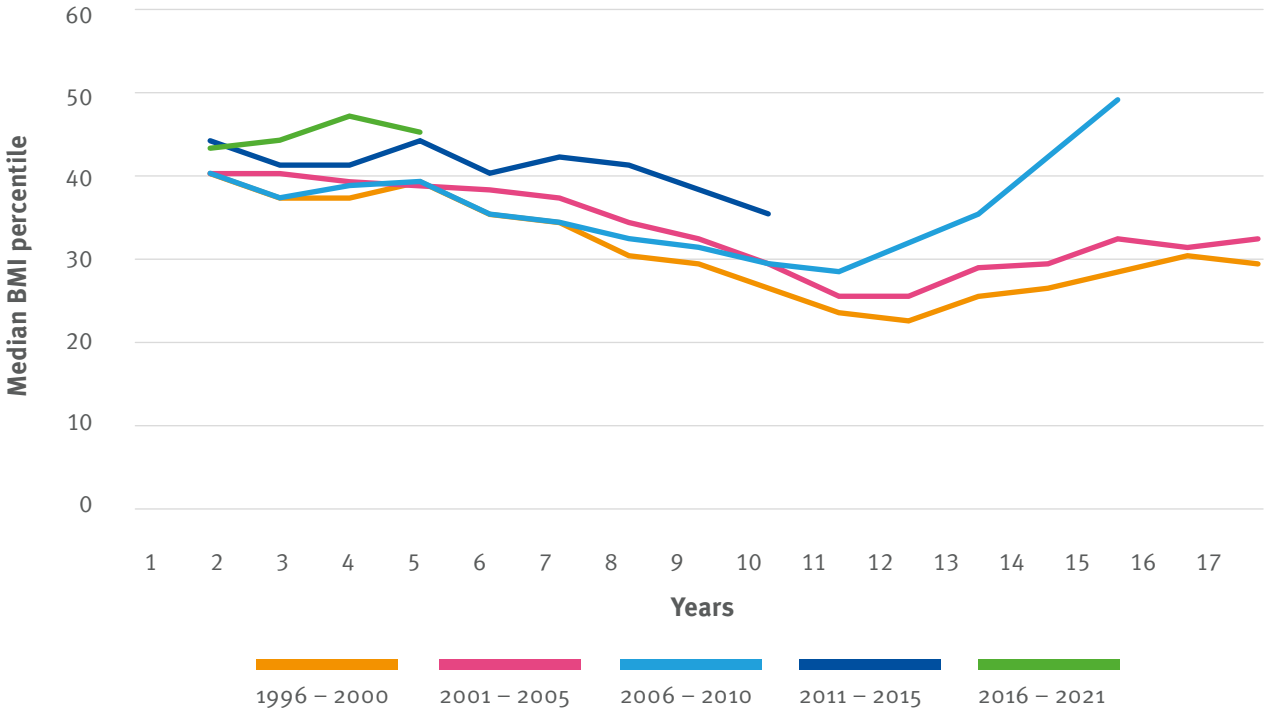

Figure 14: Development of median BMI percentiles of children and adolescents under 18 years by birth cohorts 1996 – 2021 for the data of the years 1996 – 2021. Until 2014, the BMI recorded was the BMI close to the date of birth; from 2014, the BMI recorded was the BMI at the time of the best lung function of the calendar year.

Birth Cohort	Age (years)															
	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1996 – 2000	40	37	37	39	35	34	30	29	26	23	22	25	26	28	30	29
2001 – 2005	40	40	39	39	38	37	34	32	29	25	25	29	29	32	31	32
2006 – 2010	40	37	39	39	35	34	32	31	29	28	32	35	42	49	–	–
2011 – 2015	44	41	41	44	40	42	41	38	35	–	–	–	–	–	–	–
2016 – 2020	43	44	47	45	–	–	–	–	–	–	–	–	–	–	–	–

Table 17: Development of median BMI percentiles of children and adolescents under 18 years by birth cohorts 1996 – 2021 for the data of the years 1996 – 2021. Until 2014, the BMI recorded was the BMI close to the date of birth; from 2014, the BMI recorded was the BMI at the time of the best lung function of the calendar year.

05

Nutritional status

5d. Development of nutritional status 2000 – 2021 Adults aged 18 and over

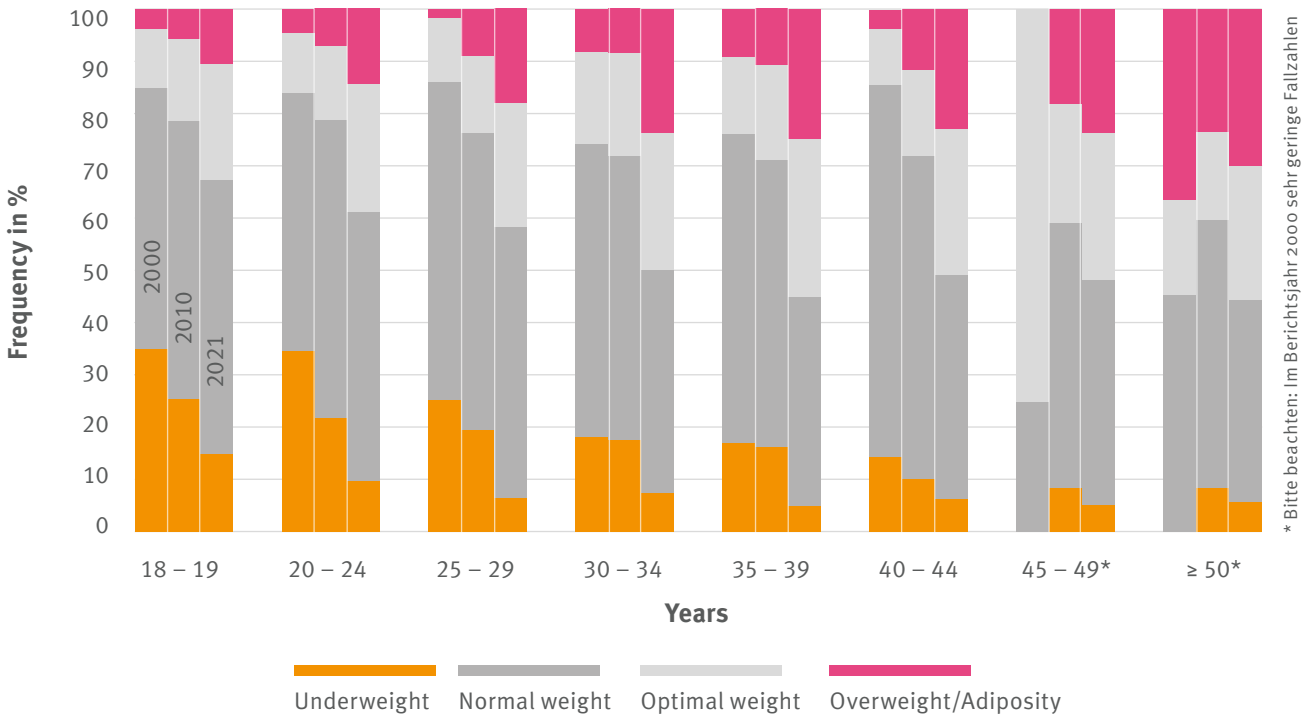

Figure 15: Development of weight categories of adults aged 18 and over (frequencies in %) 2000 – 2021,
Underweight : BMI ‹ 18.5 kg/sqm; Normal weight: BMI men 18.5 – 22.9 kg/sqm; BMI women 18.5 – 21.9 kg/sqm;
Optimal weight: BMI men 23.0 – 24.9 kg/sqm, BMI women 22.0 – 24.9 kg/sqm; Overweight/Adiposity: 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	35.1	34.6	25.3	18.2	17.1	14.3	0.0	0.0
	2010	25.4	21.9	19.5	17.6	16.4	10.1	8.4	8.5
	2021	15.0	9.8	6.4	7.4	5.0	6.4	5.2	5.8
Normal weight	2000	50.0	49.4	61.1	56.0	59.1	71.4	25.0	45.5
	2010	53.3	56.9	56.7	54.4	54.7	61.9	50.6	51.1
	2021	52.3	51.5	52.0	42.7	39.9	42.7	42.9	38.6
Optimal weight	2000	11.2	11.5	12.1	17.7	14.8	10.7	75.0	18.2
	2010	15.6	14.1	14.9	19.6	18.2	16.4	22.9	17.0
	2021	22.3	24.3	23.6	26.1	30.3	28.0	28.3	25.7
Overweight/ Adiposity	2000	3.7	4.5	1.6	8.1	9.1	3.6	0.0	36.4
	2010	5.7	7.2	8.8	8.5	10.8	11.6	18.1	23.4
	2021	10.4	14.5	18.0	23.7	24.8	22.9	23.6	29.9

Table 18: Development of weight categories of adults aged 18 and over (frequencies in %) 2000 – 2021
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

Nutritional status

5d.i Median BMI percentiles by birth cohort

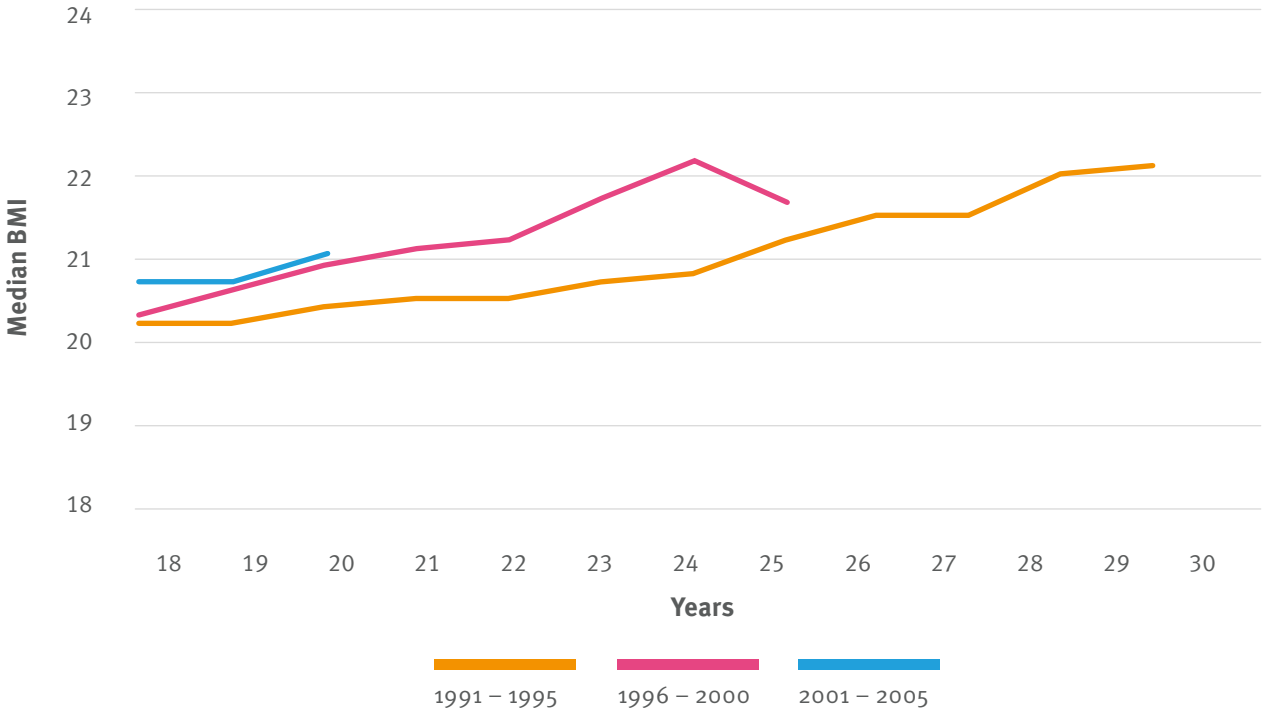

Figure 16: Development of median BMI of adults aged 18 years and older by birth cohorts 1991 – 2005 for 2009 – 2020 data.
Until 2014, BMI close to birth date was recorded, from 2014 onwards BMI at the time of recording the best FEV1% of the calendar year.

Birth Cohort	Age (years)												
	18	19	20	21	22	23	24	25	26	27	28	29	30
1991 – 1995	20.2	20.2	20.4	20.5	20.5	20.7	20.8	21.2	21.5	21.5	22	22.1	–
1996 – 2000	20.3	20.6	20.9	21.1	21.2	21.7	22.2	21.7	–	–	–	–	–
2001 – 2005	20.7	20.7	21.1	–	–	–	–	–	–	–	–	–	–

Table 19: Development of median BMI of adults aged 18 years and older by birth cohorts 1991 – 2005 for 2009 – 2020 data.
Until 2014, BMI close to birth date was recorded, from 2014 onwards BMI at the time of recording the best FEV1% of the calendar year.

06

Lung function

6a. Overview of lung function

All patients of 6 years and older without a transplant with a pulmonary function measurement in 2021 were included in the evaluations of the lung function. A total of 5,347 data sets were available.

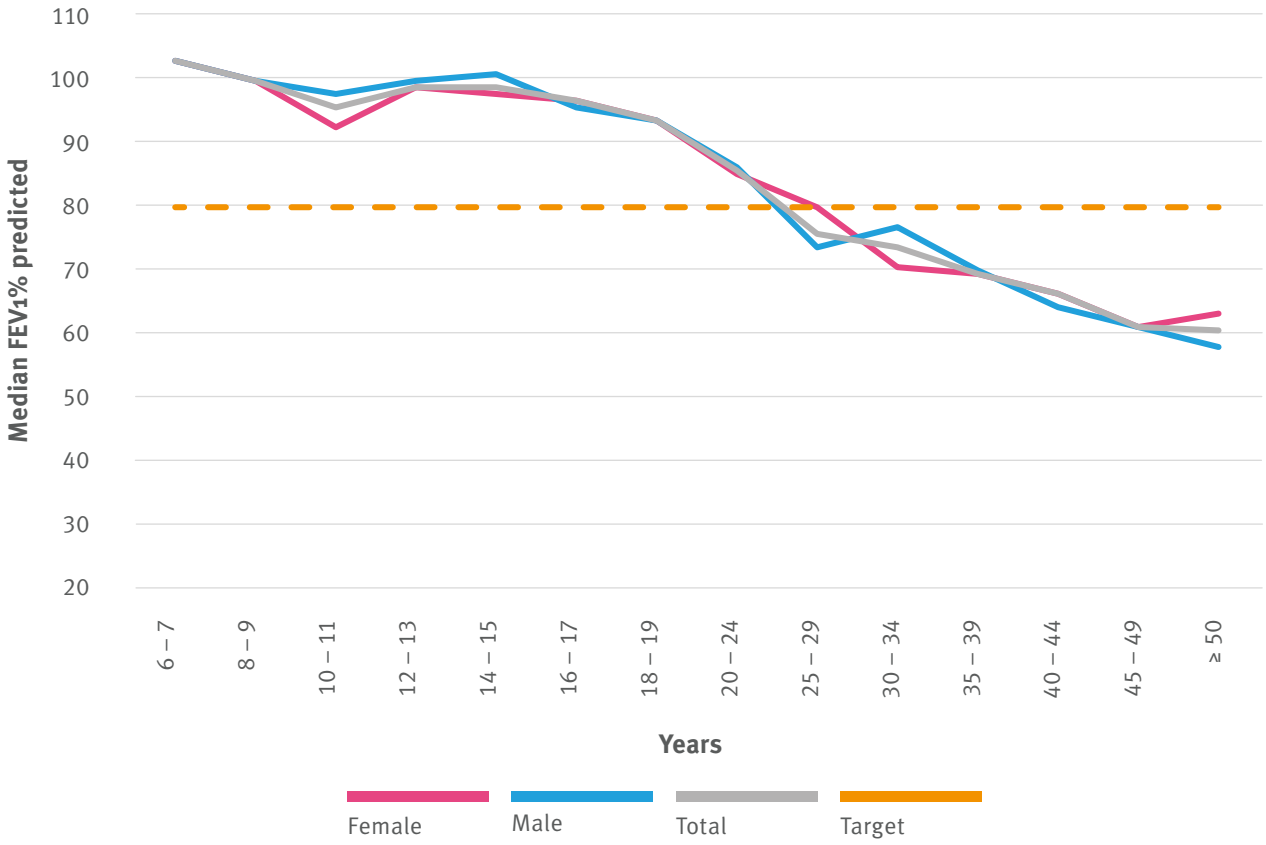

Figure 17: FEV1% value 2021 according to Global Lung Function Initiative (GLI)

Lung function

Age (years)	Male			Female			Total		
	N	Median	25th – 75th pctl.	N	Median	25th – 75th pctl.	N	Median	25th – 75th pctl.
6 – 7	152	102	92 – 110	153	102	93 – 109	305	102	92 – 109
8 – 9	161	99	91 – 107	161	99	89 – 106	322	99	90 – 106
10 – 11	133	97	85 – 104	121	92	83 – 105	254	95	85 – 105
12 – 13	139	99	90 – 106	166	98	87 – 108	305	98	88 – 107
14 – 15	141	100	86 – 109	175	97	86 – 106	316	98	86 – 107
16 – 17	169	95	88 – 104	138	96	86 – 107	307	96	87 – 106
18 – 19	136	93	81 – 103	125	93	76 – 101	261	93	79 – 102
20 – 24	370	86	68 – 98	392	85	65 – 99	762	86	66 – 98
25 – 29	365	74	57 – 94	301	80	60 – 96	666	76	58 – 95
30 – 34	347	77	56 – 93	278	71	55 – 90	625	74	55 – 92
35 – 39	216	71	50 – 90	190	70	54 – 87	406	70	51 – 88
40 – 44	166	65	45 – 85	141	67	54 – 85	307	67	49 – 85
45 – 49	115	62	45 – 79	90	62	46 – 75	205	62	46 – 78
≥ 50	163	59	41 – 81	143	64	49 – 78	306	62	45 – 80
Total	2,773	86	64 – 100	2,574	86	66 – 100	5,347	86	65 – 100

Table 20: FEV1% value 2021 according to Global Lung Function Initiative (GLI)

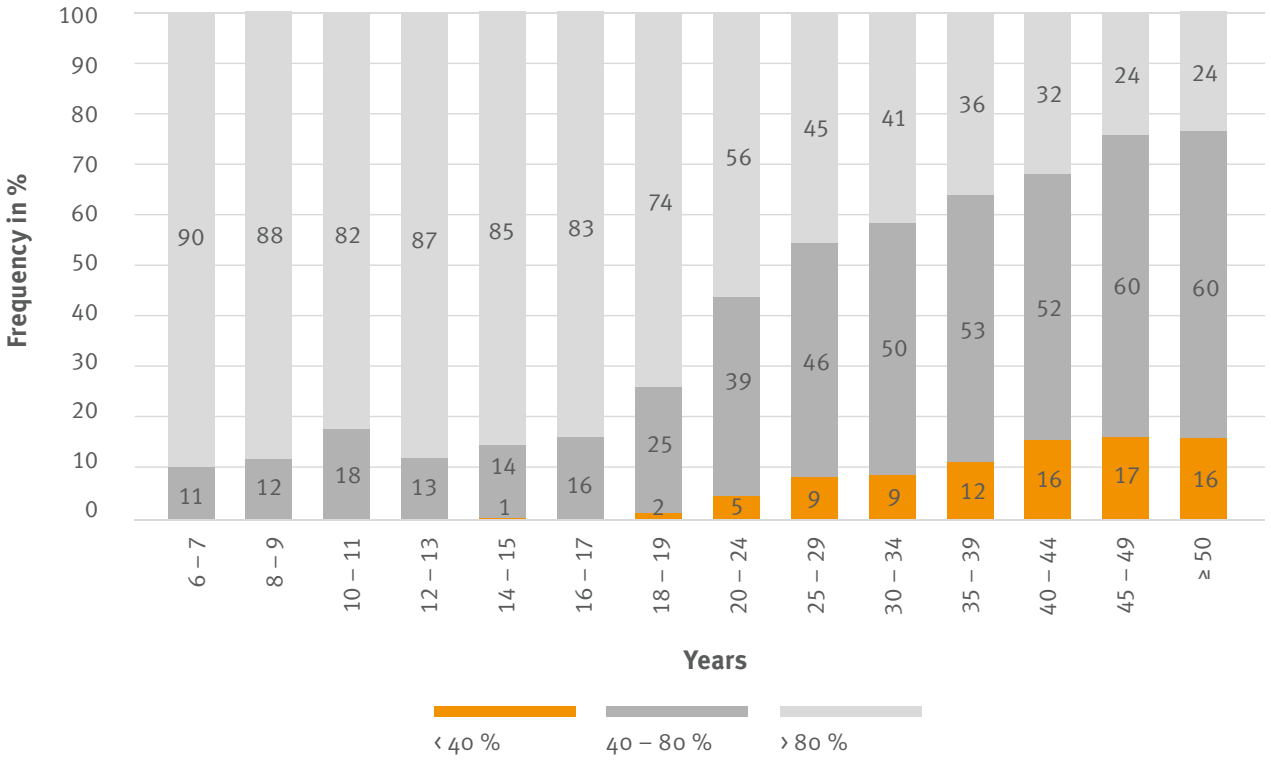

Figure 18: Severity of FEV1% (categories ‹ 40 %, 40 – 80 %, › 80 %) 2021 according to Global Lung Function Initiative (GLI)

06

Lung function

6b. Development of lung function 2000 – 2021

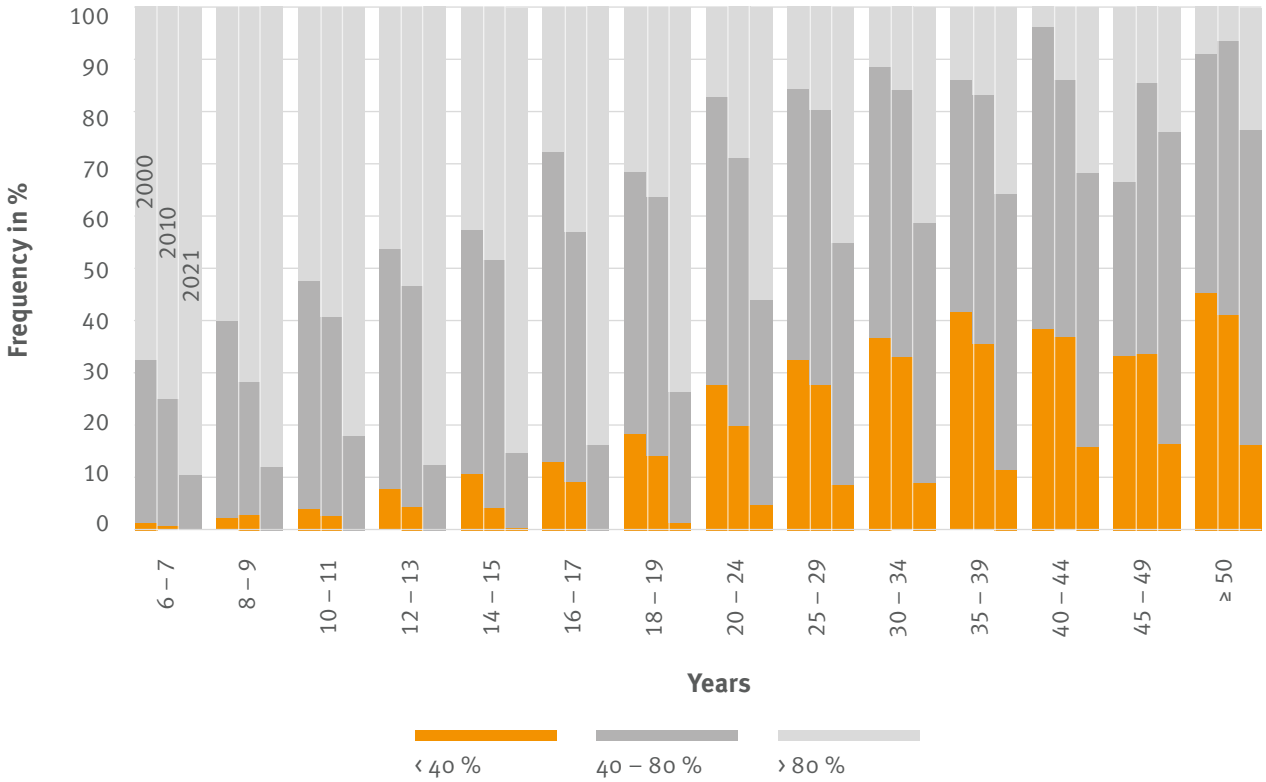

Figure 19: Development of age-related frequencies (in %) of FEV1% severity according to the Global Lung Initiative (GLI) 2000 – 2021

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	1.4	2.3	4.1	8.0	10.8	13.1	18.5	27.7	32.6	36.8	41.8	38.5	33.3	45.5
	2010	0.9	3.1	2.7	4.6	4.4	9.3	14.2	19.9	27.8	33.2	35.7	37.0	33.7	41.3
	2021	0.0	0.3	0.0	0.3	0.6	0.3	1.5	4.9	8.6	9.1	11.6	16.0	16.6	16.3
40 – 80 %	2000	31.1	37.8	43.6	45.8	46.6	59.3	50.0	55.2	51.7	51.8	44.3	57.7	33.3	45.5
	2010	24.2	25.3	38.1	42.1	47.4	47.8	49.6	51.3	52.5	50.9	47.6	49.2	51.8	52.2
	2021	10.5	12.1	18.1	12.5	14.2	16.3	24.9	39.1	46.3	49.6	52.7	52.4	59.5	60.1
› 80 %	2000	67.6	59.9	52.3	46.2	42.6	27.6	31.5	17.1	15.7	11.4	13.9	3.9	33.3	9.1
	2010	74.9	71.6	59.2	53.3	48.2	42.9	36.2	28.9	19.7	15.9	16.7	13.8	14.5	6.5
	2021	89.5	87.6	81.9	87.2	85.1	83.4	73.6	56.0	45.2	41.3	35.7	31.6	23.9	23.5

Table 21: Development of age-related frequencies (in %) of FEV1% severity according to Global Lung Initiative (GLI) 2000 – 2021

Lung function

6c. Median FEV1% by birth cohort

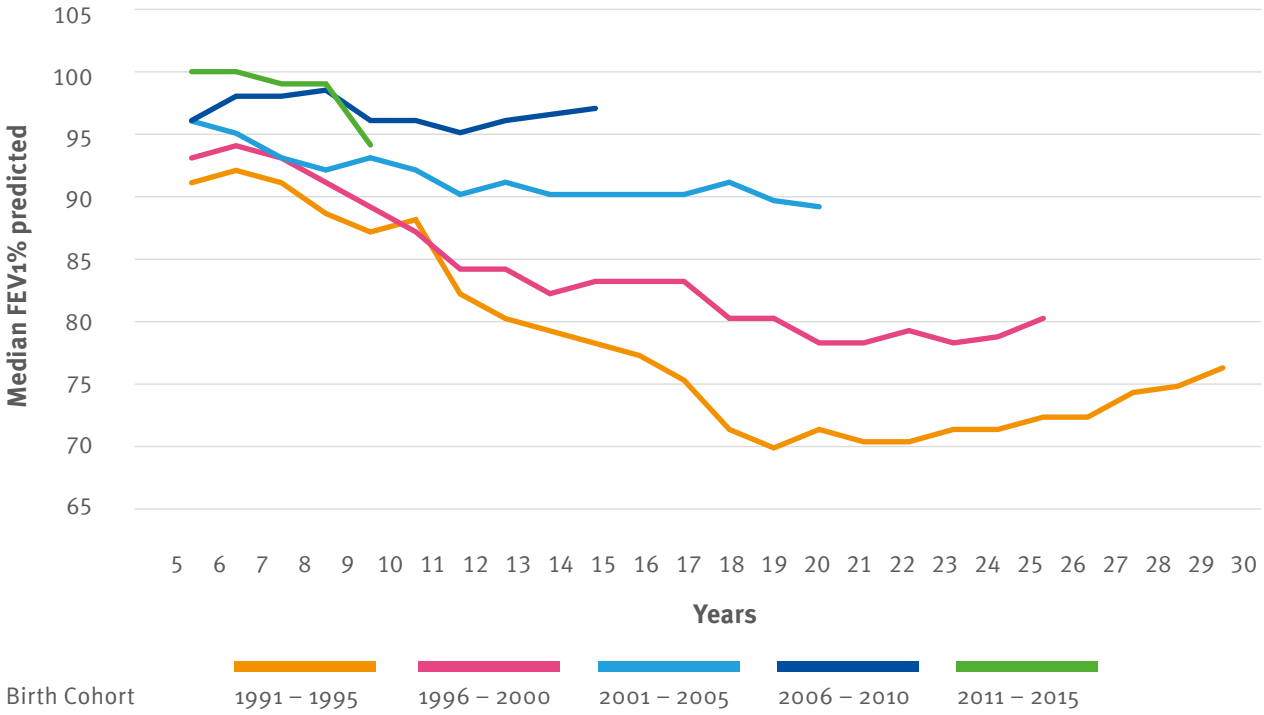

Figure 20: Development median FEV1% of children and adults by birth cohorts 1991 – 2015 for the years 1997 – 2020 data.
Until 2014, the near-birthday FEV1% was recorded; from 2014, the best FEV1% of the calendar year was recorded.

Birth Cohort	Age (years)																								
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
1991 – 1995	91	92	91	89	87	88	82	80	79	78	77	75	71	70	71	70	70	71	71	72	72	74	75	76	–
1996 – 2000	93	94	93	91	89	87	84	84	82	83	83	83	80	80	78	78	79	78	79	80	–	–	–	–	–
2001 – 2005	96	95	93	92	93	92	90	91	90	90	90	90	91	90	89	–	–	–	–	–	–	–	–	–	–
2006 – 2010	96	98	98	99	96	96	95	96	97	97	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2011 – 2015	100	100	99	99	94*	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

Table 22: Development median FEV1% of children and adults by birth cohorts 1991 – 2015 for the years 1997 – 2020 data.
Until 2014, the near-birthday FEV1% was recorded; from 2014, the best FEV1% of the calendar year was recorded.
* Limited explanatory power because of small cohort size

07

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=6,259). No information on a microbiological test in the calendar year was available for 148 patients (2.3 %).

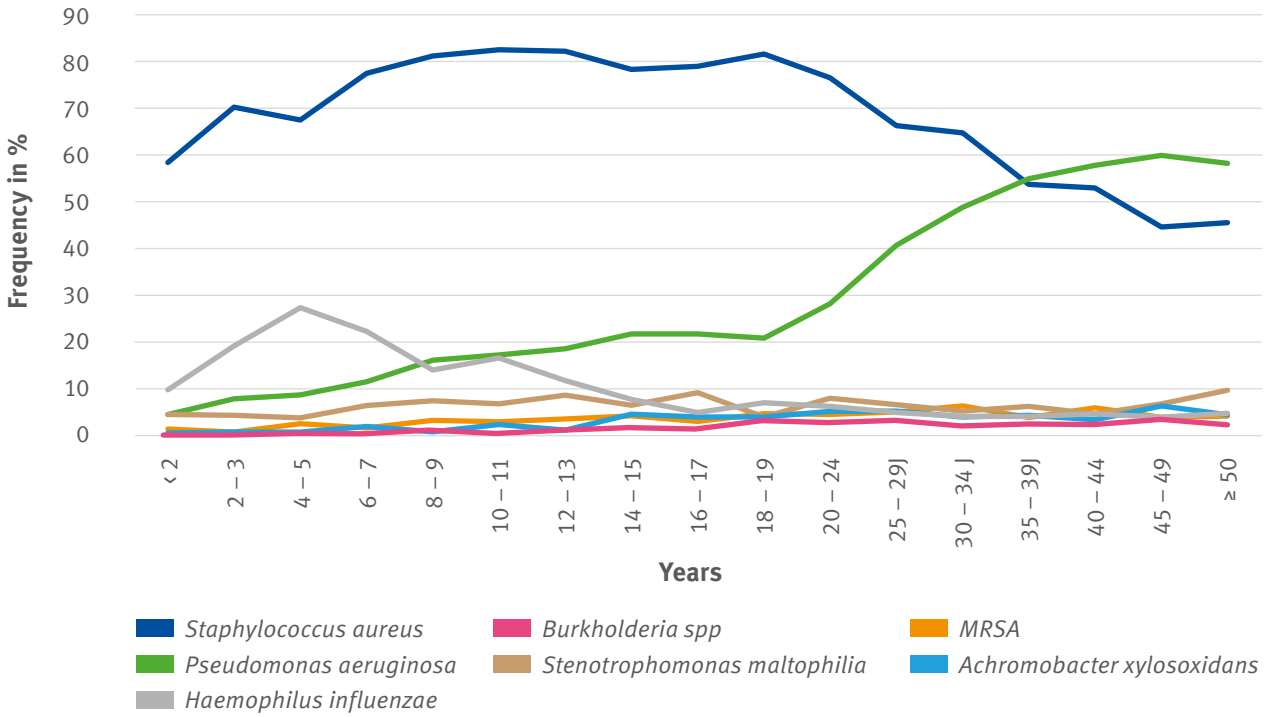

Figure 21: Bacteria detection in pwCF with microbiological examination 2021

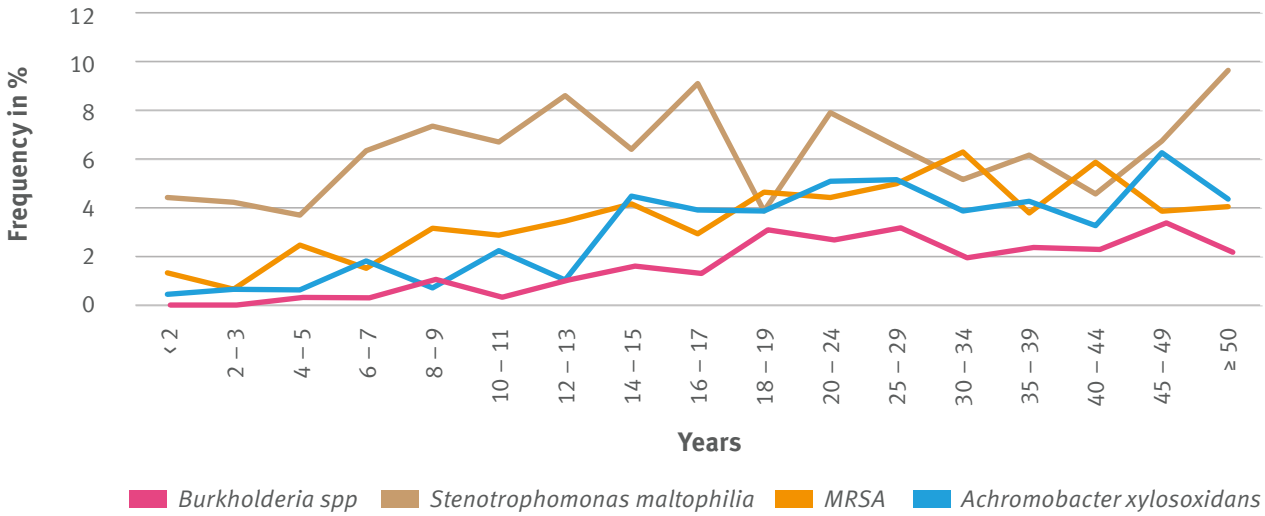

Figure 22: Bacteria detection in pwCF with microbiological examination (without the representation of Pseudomonas aeruginosa and Staphylococcus aureus) 2021

Lung infections

7a. Annual verification at least once

Age (years)	*Staphylococcus aureus inklusive MRSA*	*MRSA*	*Pseudomonas aeruginosa (PSA)*	*Burkholderia spp*	*Stenotro-phomonas maltophilia*	*Achromobacter xylosoxidans*	*Haemophilus influenzae*
< 2	58.6	1.3	4.4	0.0	4.4	0.4	9.7
2 – 3	70.5	0.7	7.8	0.0	4.2	0.7	19.2
4 – 5	67.7	2.5	8.6	0.3	3.7	0.6	27.4
6 – 7	77.7	1.5	11.5	0.3	6.3	1.8	22.3
8 – 9	81.5	3.2	16.1	1.1	7.3	0.7	14.0
10 – 11	82.8	2.9	17.2	0.3	6.7	2.2	16.6
12 – 13	82.5	3.4	18.6	1.0	8.6	1.0	11.7
14 – 15	78.6	4.2	21.7	1.6	6.4	4.5	7.7
16 – 17	79.2	2.9	21.8	1.3	9.1	3.9	4.9
18 – 19	81.9	4.6	20.9	3.1	3.9	3.9	7.0
20 – 24	76.8	4.4	28.2	2.7	7.9	5.1	6.2
25 – 29	66.5	5.0	40.8	3.2	6.5	5.1	4.8
30 – 34	65.0	6.3	49.0	1.9	5.2	3.9	4.0
35 – 39	53.9	3.8	55.1	2.4	6.2	4.3	4.0
40 – 44	53.1	5.9	58.0	2.3	4.6	3.3	4.6
45 – 49	44.7	3.9	60.1	3.4	6.7	6.3	3.9
≥ 50	45.7	4.0	58.4	2.2	9.6	4.4	4.7
Total	69.0	3.8	31.2	1.8	6.4	3.4	9.3
< 18	75.9	2.5	14.4	0.7	6.3	1.8	15.1
≥ 18	63.7	4.9	44.0	2.6	6.5	4.5	4.9

Table 23: Detection of bacteria in pwCF with microbiological examination (frequencies in %) 2021

07

Lung infections

7b. Development of infections with Pseudomonas aeruginosa 2000 – 2021

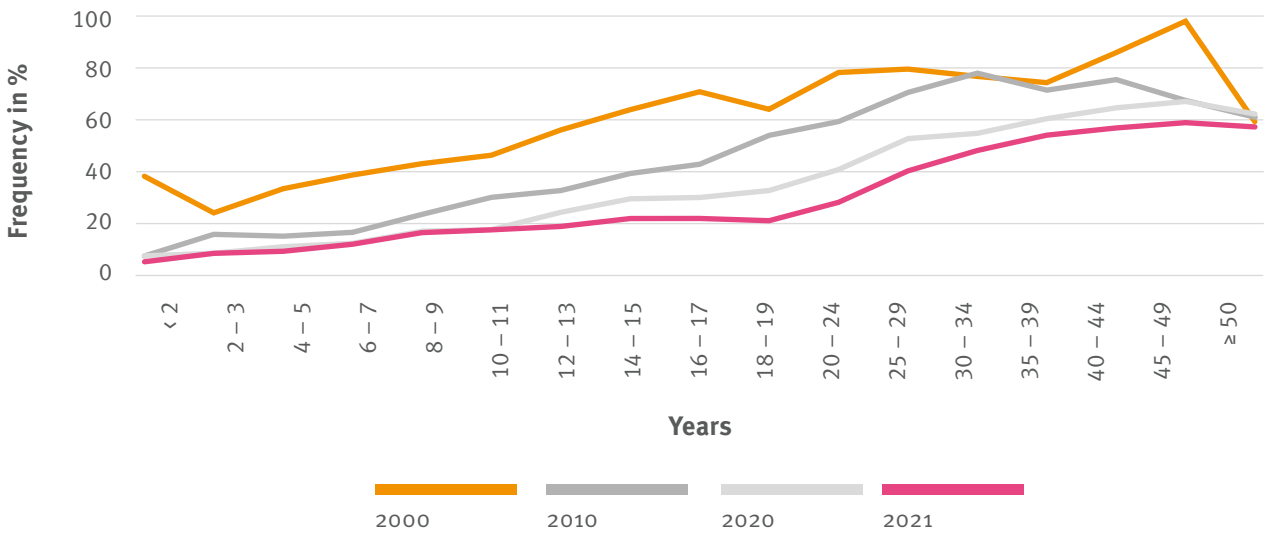

Figure 23: Development of Pseudomonas aeruginosa detections in pwCF with microbiological examination (frequencies in %) 2000 – 2021

Age (years)	2000	2010	2020	2021
< 2	38.3	6.7	6.8	4.4
2 – 3	23.7	15.3	7.8	7.8
4 – 5	33.3	14.6	10.4	8.6
6 – 7	38.8	16.1	11.8	11.5
8 – 9	43.3	23.3	16.6	16.1
10 – 11	46.7	30.1	17.3	17.2
12 – 13	56.7	32.8	24.2	18.6
14 – 15	64.8	39.6	29.6	21.7
16 – 17	71.9	43.3	30.1	21.8
18 – 19	65.0	54.8	32.9	20.9
20 – 24	79.6	60.3	41.3	28.2
25 – 29	81.0	71.9	53.6	40.8
30 – 34	78.1	79.6	55.7	49.0
35 – 39	75.6	72.8	61.6	55.1
40 – 44	87.5	77.0	65.9	58.0
45 – 49	100.0	68.7	68.5	60.1
≥ 50	60.0	62.0	63.4	58.4

Table 24: Development of Pseudomonas aeruginosa detections in pwCF with microbiological examination (frequencies in %) 2000 – 2021

German Cystic Fibrosis Registry:
Annual Reports

Since 1995, the annual report volume with evaluations from the German Cystic Fibrosis Registry has been published. Since 2015, the report is also available in English translation. In addition, we offer a report volume for patients and families that is easy to understand for laypersons.

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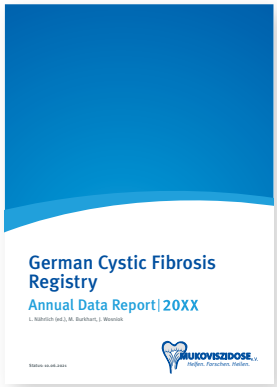
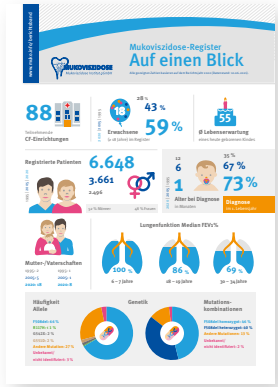
German Cystic Fibrosis Registry Annual Report



German Cystic Fibrosis Registry Annual Report, English

Numbers, Data & Facts for patients and families



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07

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=6,259). No information on a microbiological test in the calendar year was available for 148 patients (2.3 %).

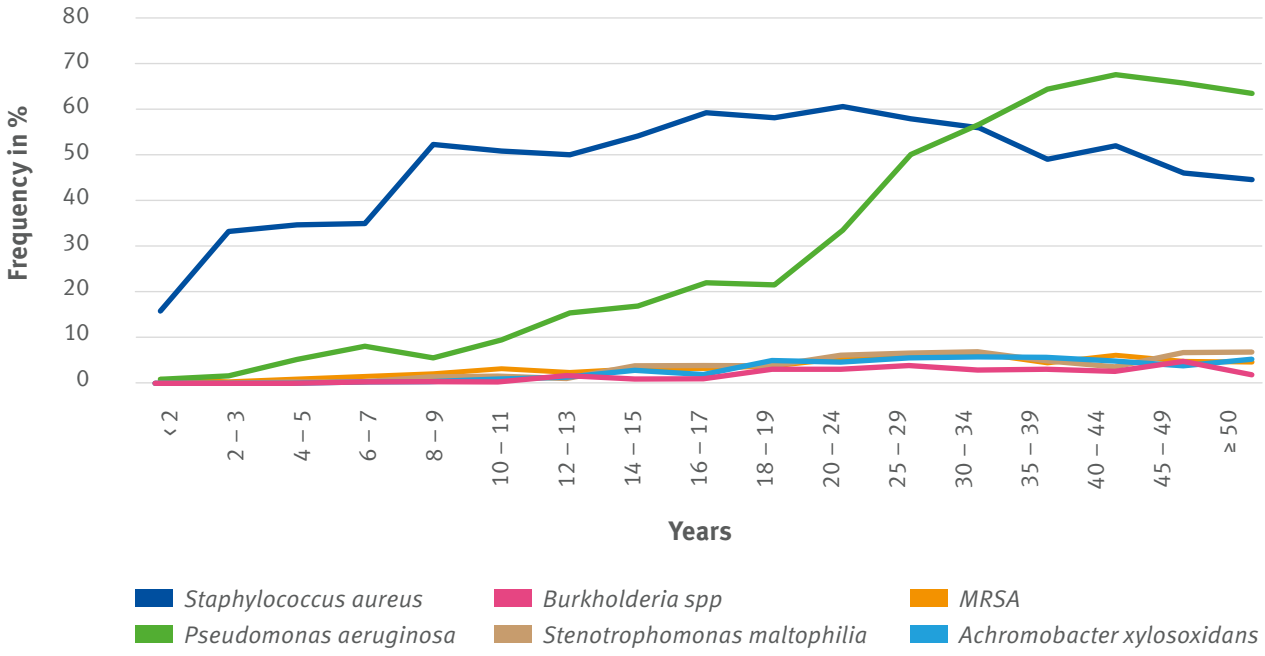

Figure 24: Chronic lung infections in pwCF with microbiological examination 2021

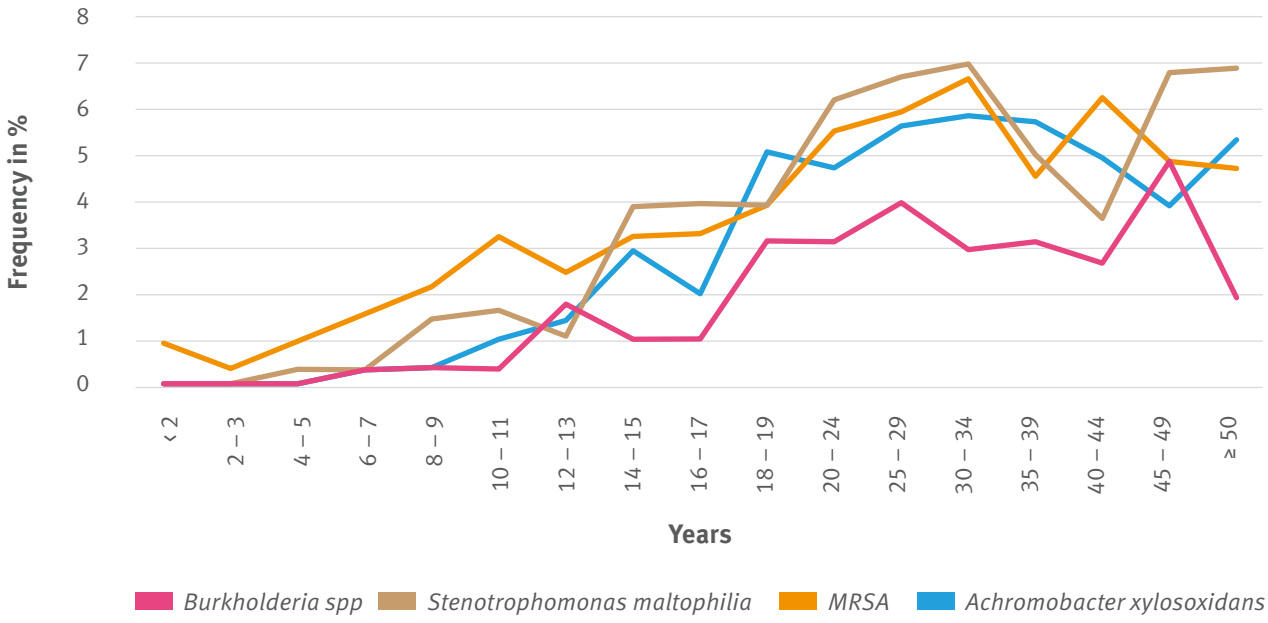

Figure 25: Chronic lung infections in pwCF with microbiological examination (without the representation of Pseudomonas aeruginosa and Staphylococcus aureus) 2021

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	0.9	0.9	0.0	0.0	0.0
2 – 3	33.3	0.3	1.6	0.0	0.0	0.0
4 – 5	34.8	0.9	5.2	0.0	0.3	0.0
6 – 7	35.1	1.5	8.2	0.3	0.3	0.3
8 – 9	52.5	2.1	5.6	0.4	1.4	0.4
10 – 11	51.0	3.2	9.6	0.3	1.6	1.0
12 – 13	50.2	2.4	15.5	1.7	1.0	1.4
14 – 15	54.3	3.2	16.9	1.0	3.8	2.9
16 – 17	59.4	3.3	22.1	1.0	3.9	2.0
18 – 19	58.3	3.9	21.6	3.1	3.9	5.0
20 – 24	60.8	5.5	33.6	3.1	6.1	4.7
25 – 29	58.1	5.9	50.2	3.9	6.6	5.6
30 – 34	56.1	6.6	56.8	2.9	6.9	5.8
35 – 39	49.2	4.5	64.5	3.1	5.0	5.7
40 – 44	52.1	6.2	67.8	2.6	3.6	4.9
45 – 49	46.2	4.8	65.9	4.8	6.7	3.9
≥ 50	44.7	4.7	63.7	1.9	6.8	5.3
Total	50.0	4.0	33.3	2.0	4.0	3.3
< 18	43.5	2.0	9.7	0.5	1.4	0.9
≥ 18	54.8	5.5	51.2	3.2	5.9	5.2

Table 25: Chronic lung infections in pwCF with microbiological examination (frequencies in %) 2021

07

Lung infections

7d. Atypical mycobacteria

All patients without a transplant who had at least one microbiological test for mycobacteria in 2021 were included in the analyses (n=1,634).

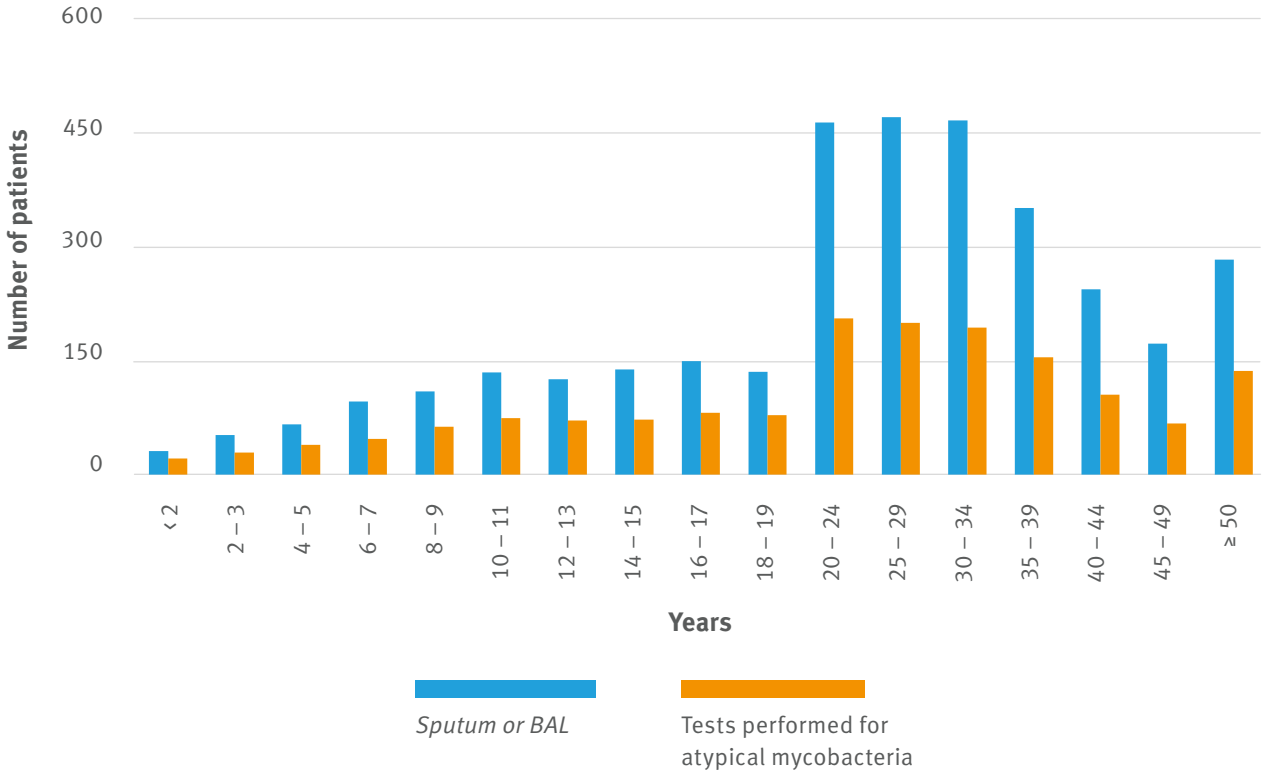

Figure 26: Number of patients with sputum or BAL and the number of tests performed for atypical mycobacteria 2021

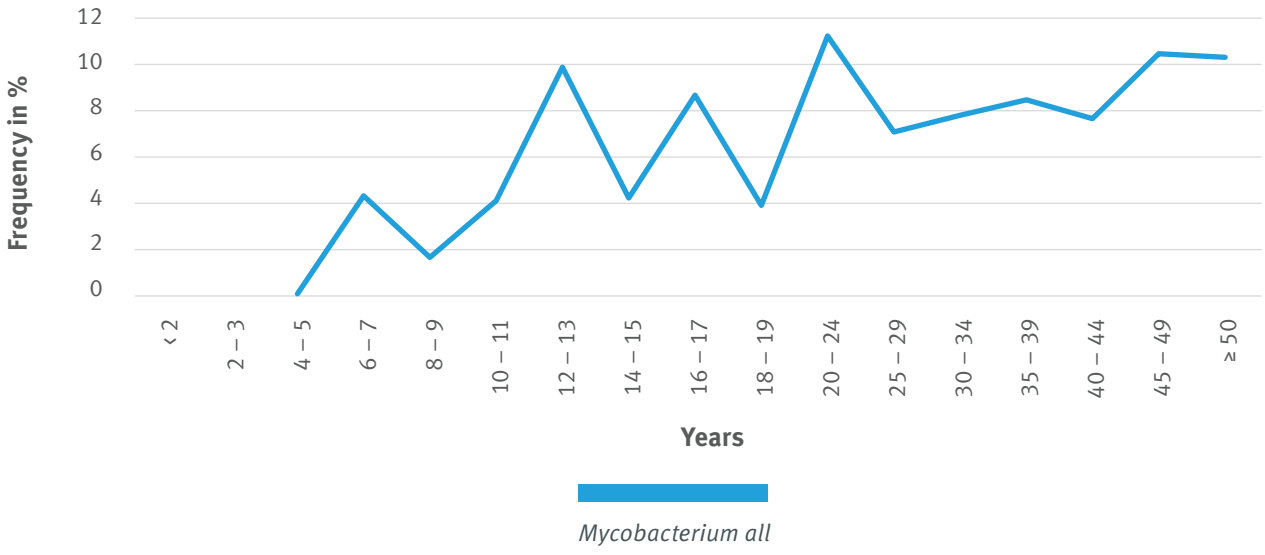

Figure 27: Age-dependent frequency in % of patients with examinations for atypical mycobacteria 2021

Lung infections

7d. Atypical mycobacteria

Age (years)	Sputum or BAL performed	Testing for atypical mycobacteria performed	Mykobakterium all
< 2	13.7	67.7	0.0
2 – 3	16.9	55.8	0.0
4 – 5	20.3	59.1	0.0
6 – 7	28.9	49.0	4.3
8 – 9	38.1	57.8	1.6
10 – 11	42.7	55.2	4.1
12 – 13	43.0	56.8	9.9
14 – 15	44.1	52.2	4.2
16 – 17	48.4	54.4	8.6
18 – 19	52.1	57.8	3.9
20 – 24	61.6	44.4	11.2
25 – 29	70.7	42.4	7.0
30 – 34	74.8	41.5	7.8
35 – 39	82.6	44.0	8.4
40 – 44	79.1	43.2	7.6
45 – 49	82.7	39.0	10.5
≥ 50	87.6	48.2	10.3
Total	55.6	47.0	7.3
< 18	33.3	55.2	4.6
≥ 18	73.0	44.0	9.0

Table 26: pwCF tested for atypical mycobacteria (frequency in %), based on patient population, in whom microbiology was performed with sputum or BAL 2021

08

Complications extended

All patients without transplant for whom the question about complications was documented were included in the analysis of complications. A total of 6,388 data sets were available. A total of 19 patients (0.3 %) did not answer the question about complications.

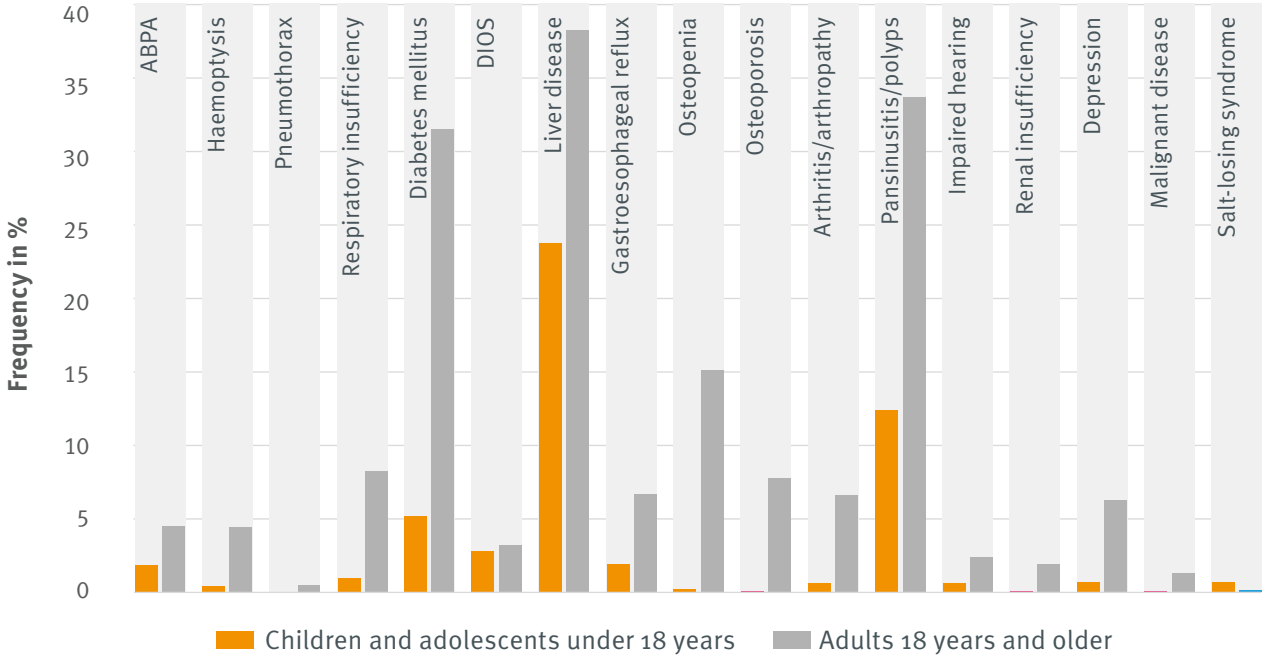

Figure 28: pwCF with complications (not showing pancreatic insufficiency) 2021

Complications extended

8a. Children and adolescents under 18 years

Complications	0 – 5 years	6 – 11 years	12 – 17 years	< 18 Jahre
Pulmonary complications				
Allergic bronchopulmonary aspergillosis	0.2	1.9	3.3	1.8
Haemoptysis	0.1	0.1	1.0	0.4
of these, at least one serious episode (› 240 ml in 24h)	0.0	0.0	0.0	0.0
Pneumothorax	0.0	0.0	0.0	0.0
of these, requiring drainage	-	-	-	-
Respiratory insufficiency	0.7	1.1	1.1	1.0
of these, partial insufficiency	66.7	70.0	80.0	73.1
of these, global insufficiency	33.3	0.0	20.0	15.4
Gastrointestinal complications				
Exocrine pancreatic insufficiency	91.4	92.2	89.8	91.1
Distal intestinal obstruction syndrome (DIOS)	1.7	3.5	3.0	2.8
Liver disease	10.7	21.7	38.1	23.7
of these, liver cirrhosis	1.1	8.3	20.2	13.7
of these, with portal hypertension	1.1	3.4	6.8	5.0
of these, without portal hypertension	0.0	4.4	8.8	6.2
Gastroesophageal reflux	0.6	1.6	3.4	1.9
Other complications/comorbidities				
Diabetes mellitus	0.4	2.0	12.9	5.2
of these, Type 3	0.0	89.5	91.6	89.4
of these, not Type 3	100.0	10.5	8.4	10.6
Bone disease				
Osteopenia	0.0	0.1	0.3	0.2
Osteoporosis	0.0	0.0	0.1	0.0
Arthritis/Arthropathy	0.0	0.4	1.3	0.6
Pansinusitis/Polyps	2.3	13.7	20.5	12.4
Impaired hearing	0.4	0.3	1.2	0.6
Renal insufficiency	0.0	0.0	0.1	0.0
Depression	0.0	0.0	2.1	0.7
Malignant disease	0.0	0.0	0.1	0.0
Salt-losing syndrome	1.4	0.5	0.1	0.7

Table 27: pwCF under 18 years with complications (frequencies in %) 2021

08

Complications extended

8b. Adults 18 years and older

Complications	18 – 29 years	30 – 39 years	≥ 40 years	≥ 18 years
Pulmonary complications				
Allergic bronchopulmonary aspergillosis	4.7	5.2	3.1	4.5
Haemoptysis	3.5	5.7	4.8	4.4
of these, at least one serious episode (› 240 ml in 24h)	3.8	1.9	2.9	2.8
Pneumothorax	0.4	0.4	0.6	0.4
of these, requiring drainage	85.7	100.0	100.0	93.8
Respiratory insufficiency	5.6	7.6	14.3	8.2
of these, partial insufficiency	61.1	75.6	74.0	70.3
of these, global insufficiency	27.4	14.6	14.6	18.7
Gastrointestinal complications				
Exocrine pancreatic insufficiency	92.3	90.9	85.7	90.3
Distal intestinal obstruction syndrome (DIOS)	3.4	3.3	2.7	3.2
Liver disease	39.9	37.6	36.1	38.3
of these, liver cirrhosis	19.9	14.0	14.4	17.0
of these, with portal hypertension	8.2	6.9	7.1	7.6
of these, without portal hypertension	6.3	3.2	4.2	4.9
Gastroesophageal reflux	5.6	6.2	9.4	6.7
Other complications/comorbidities				
Diabetes mellitus	24.5	33.1	43.5	31.5
of these, Type 3	96.4	94.7	95.5	95.6
of these, not Type 3	3.6	5.3	4.5	4.4
Bone disease				
Osteopenia	8.8	17.3	25.0	15.1
Osteoporosis	4.1	7.5	15.3	7.8
Arthritis/Arthropathy	4.2	8.6	9.0	6.6
Pansinusitis/Polyps	32.0	34.4	36.5	33.8
Impaired hearing	1.1	2.1	5.0	2.3
Renal insufficiency	1.2	1.8	3.6	1.9
Depression	6.7	6.4	5.2	6.3
Malignant disease	0.1	0.5	4.6	1.3
Salt-losing syndrome	0.1	0.0	0.1	0.1

Table 28: pwCF aged 18 and over with complications (frequencies in %) 2021

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	65.8	17.4	9.2	4.5	1.4	1.3	0.5
6 – 11	72.0	16.8	5.8	2.7	1.9	0.8	0.0
12 – 17	80.2	12.8	4.5	1.4	0.3	0.2	0.6
18 – 29	75.1	15.4	5.2	2.0	0.6	1.1	0.6
30 – 39	75.9	15.0	4.9	1.1	1.0	0.5	1.7
≥ 40	75.5	15.5	5.0	1.6	0.6	0.3	1.5
Total	74.4	15.4	5.6	2.1	0.9	0.7	0.8
< 18	72.9	15.6	6.4	2.8	1.2	0.8	0.4
≥ 18	75.4	15.3	5.1	1.6	0.7	0.7	1.1

Table 29: Number of exacerbations treated with antibiotics per pwCF (frequencies in %) 2021

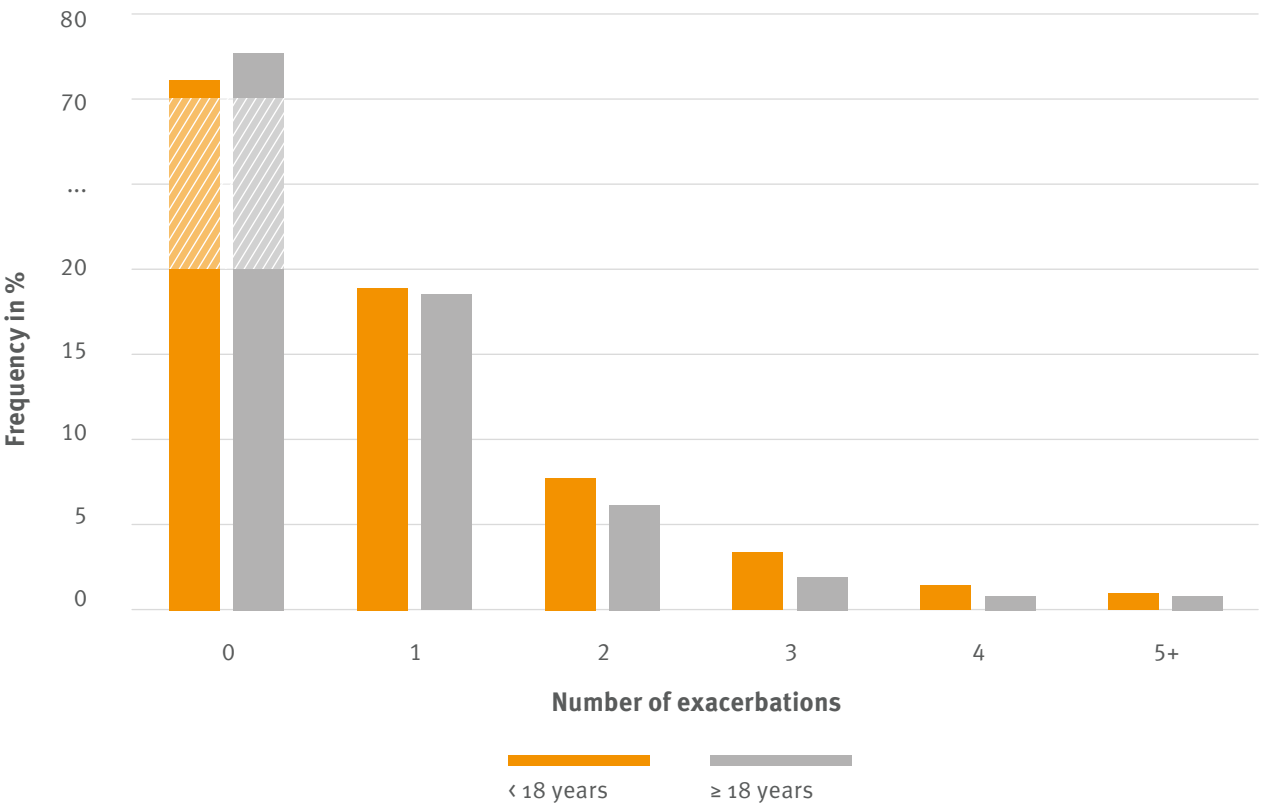

Figure 29: Number of exacerbations treated with antibiotics per pwCF (frequencies in %) 2021

09

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 2,732 patients under 18 years and 3,662 patients 18 years and older are included in the analyses. A total of 8 patients (0.1 %) 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	14.3	51.1	64.6	44.0
Mannitol	0.0	0.0	0.3	0.1
Hypotonic saline solution (≥3 %)	89.3	95.4	92.6	92.5
of these 3 – 5,7 %	30.2	27.6	22.9	26.8
of these ≥ 5,8 %	69.8	72.4	77.1	73.2
At least one mucolytic therapy (Mannitol, DNAse, Hypertonic saline solution ≥3 %)	89.5	97.0	95.2	94.0
ß2-sympathomimetics				
Short-acting (SABA)	60.0	74.1	73.0	69.2
Long-acting (LABA)	4.8	15.3	25.3	15.3
Anticholinergics	7.2	13.5	15.2	12.1
Antistaphylococcal therapy	6.5	8.5	10.4	8.5
Steroids				
Nasal	7.9	23.5	27.9	20.0
Inhalative	8.2	19.8	26.6	18.4
Orale	0.6	2.7	4.2	2.5
Vitamins				
Vitamin A	81.1	85.0	83.8	83.3
Vitamin D	95.6	96.7	96.2	96.2
Vitamin E	72.8	78.6	82.5	78.1
Vitamin K	76.1	77.8	76.2	76.7
Hormonal contraception for women[1]	–	–	9.2	23.4

Table 30: pwCF under 18 years with basic therapy (frequencies in %) 2021
[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 (2,732 patients). 131 patients (4.8 %) of these did not receive any inhalation therapy.

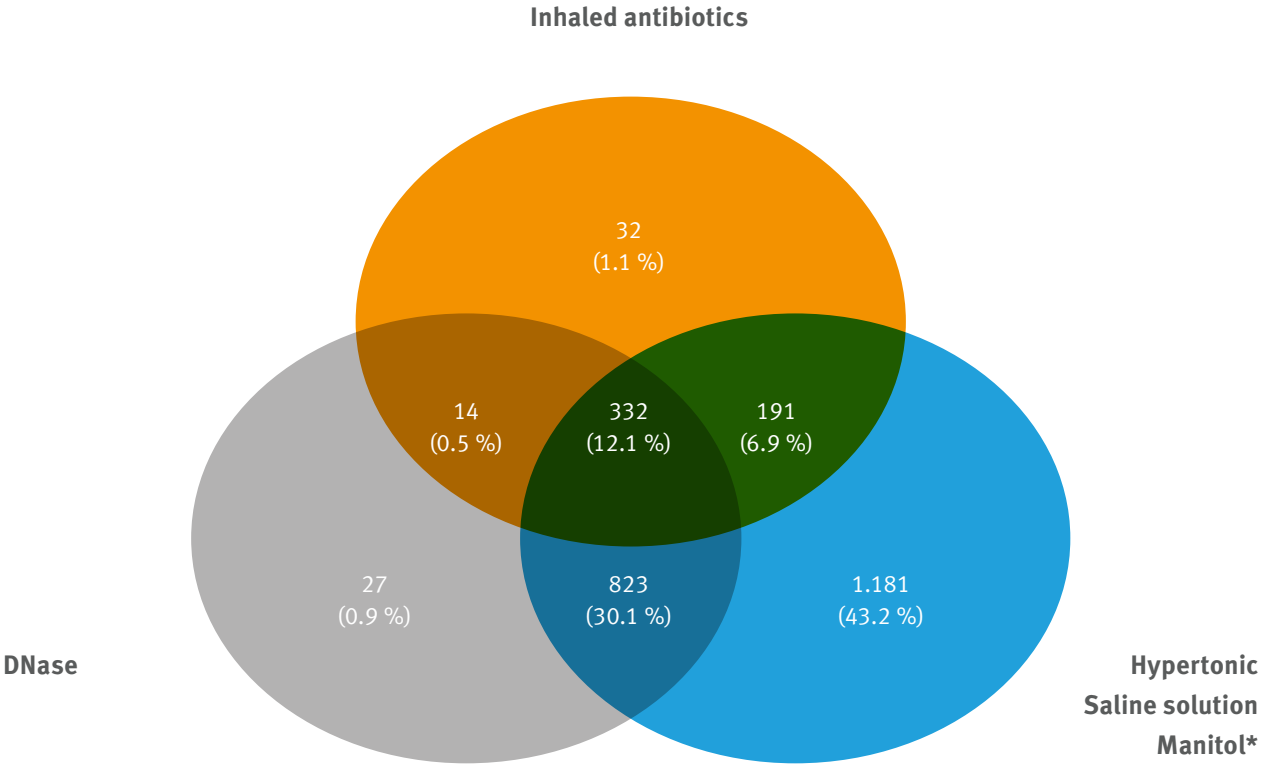

Figure 30: Inhalation and combination therapies in pwCF under 18 years 2020
*Hypertonic saline solution ≥ 3 %

09

Therapies

9a. Basic therapy

9a.iii. Adults 18 years and older

Basic therapy	18 – 29 years	30 – 39 years	≥ 40 years	Total
DNase	62.5	52.6	44.6	55.4
Mannitol	4.6	7.6	5.2	5.6
Hypotonic saline solution (≥3 %)	81.4	74.1	66.9	75.8
of these 3 – 5,7 %	23.4	23.3	26.3	24.0
of these ≥ 5,8 %	76.6	76.7	73.8	76.0
At least one mucolytic therapy (Mannitol, DNAse, Hypertonic saline solution ≥3 %)	90.5	86.8	80.7	87.1
ß2-sympathomimetics				
Short-acting (SABA)	67.9	63.3	65.5	66.0
Long-acting (LABA)	49.1	65.0	74.0	59.7
Anticholinergics	38.9	53.4	65.2	49.4
Antistaphylococcal therapy	8.4	5.6	4.8	6.7
Steroids				
Nasal	25.7	24.3	20.4	24.0
Inhalative	38.7	53.7	58.4	47.8
Orale	5.5	8.0	10.2	7.4
Vitamins				
Vitamin A	80.3	71.9	63.5	73.9
Vitamin D	95.0	93.9	92.6	94.1
Vitamin E	79.9	69.4	61.5	72.5
Vitamin K	75.3	67.1	59.6	69.2
Hormonal contraception for women[1]	30.9	20.2	11.8	21.2

Table 31: pwCF aged 18 and over with basic therapy (frequencies in %) 2021

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 (3,662 patients). 249 patients (6.8 %) of these did not receive any inhalation therapy.

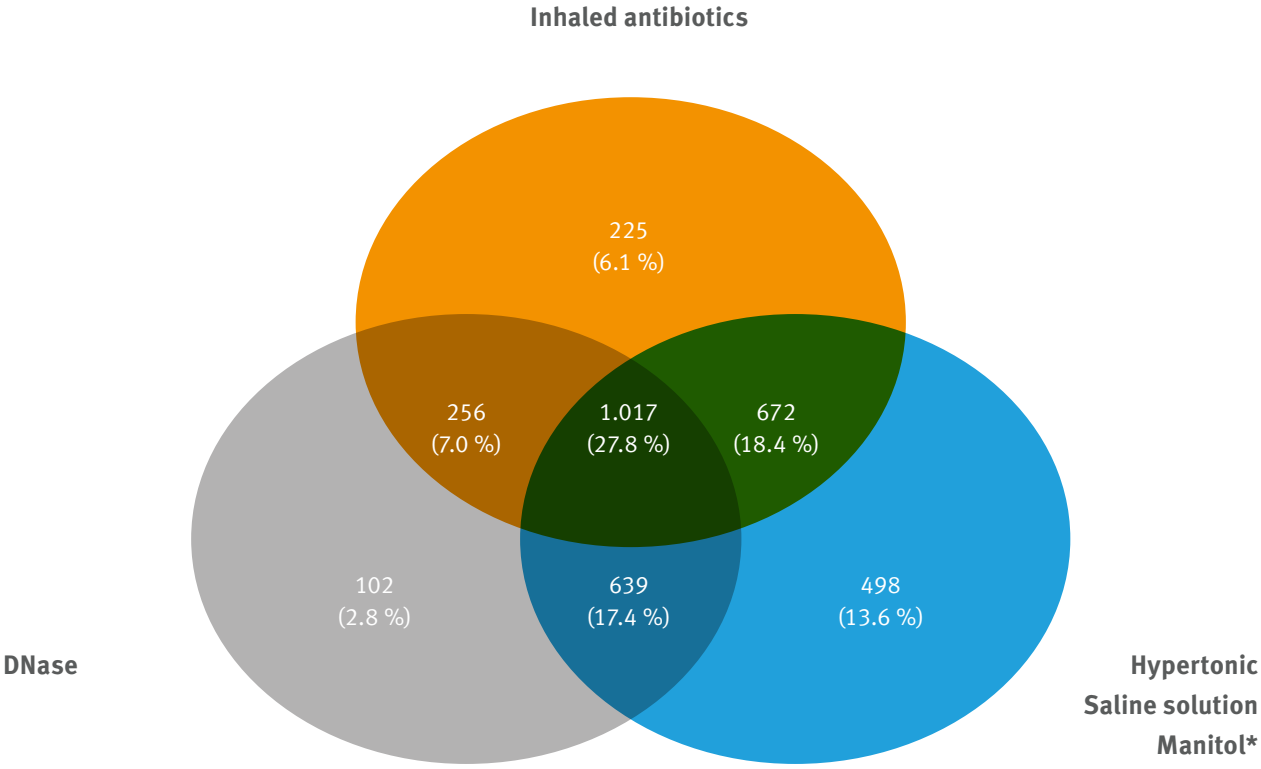

Figure 31: Inhalation and combination therapies in pwCF over 18 years 2021
*Hypertonic saline solution ≥ 3 %

09

Therapies

9b. Indication therapy

9b.i. Children and adolescents under 18 years

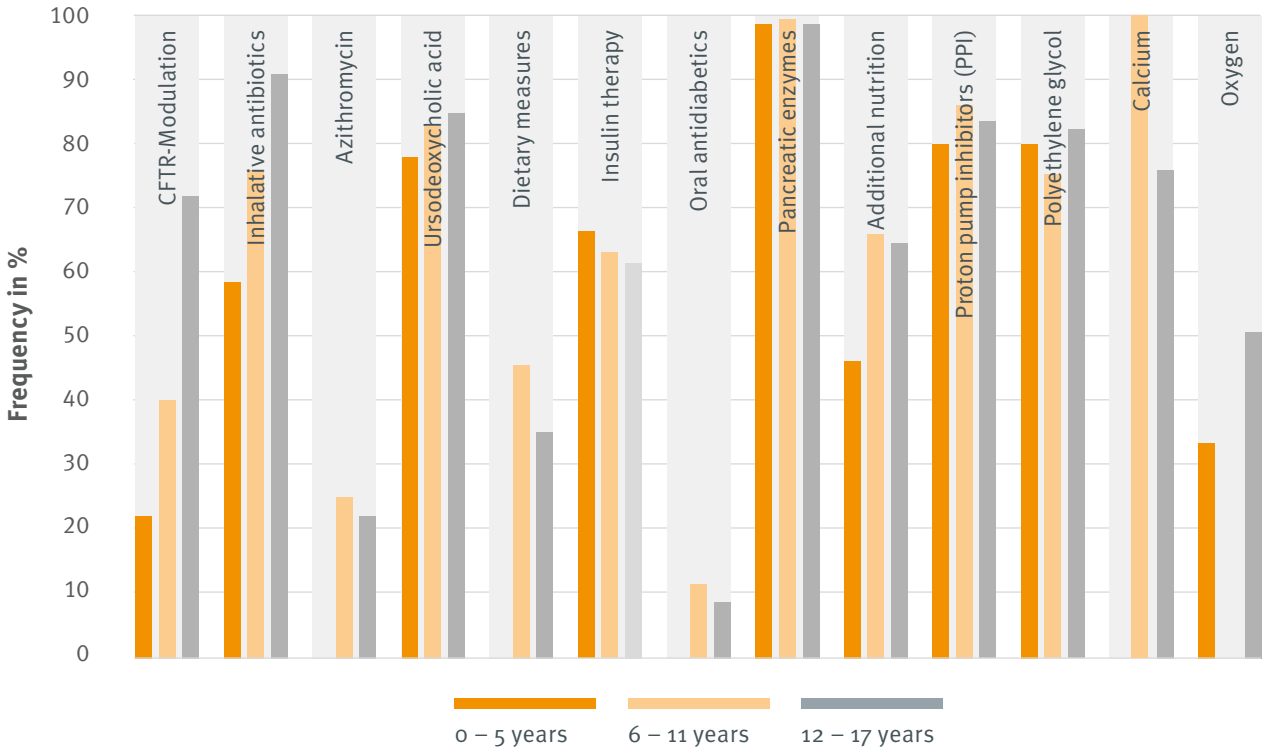

Figure 32: pwCF under 18 years with indication therapy 2021

Status of approval of CFTR modulators 31.12.2021
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 and since 2021 for all patients aged 12 and older with at least one F508del 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	22.4	39.7	72.0	45.1
of these, Ivacaftor[1]	1.9	3.6	3.7	3.1
of these, Lumacaftor/Ivacaftor[2]	20.3	30.7	10.8	20.7
of these, Tezacaftor/Ivacaftor[3]	0.0	3.6	6.5	3.4
of these, Elexacaftor/Tezacaftor/Ivacaftor[4]	0.0	3.8	63.3	22.8
Inhalative antibiotics *with chronic Pseudomonas infection*	58.3	74.0	90.3	82.8
of these, inhalative tobramycin	29.2	46.6	53.1	49.0
of these, inhalative aztreonam	45.8	53.4	59.9	56.8
of these, inhalative aztreonam	4.2	9.6	19.1	15.1
of these, DPI tobramycin	0.0	0.0	7.3	4.6
of these, DPI colistin	0.0	1.4	11.1	7.3
of these, levofloxacin	0.0	0.0	1.9	1.2
of these, inhalative gentamicin	0.0	1.4	0.6	0.8
of these, others	0.0	2.7	1.9	1.9
Azithromycin with *chronic Pseudomonas infection*	0.0	24.7	21.6	20.5
Ursodeoxycholic acid *with liver disease*	78.5	82.8	84.9	83.3
Dietary measures *with Diabetes mellitus*	0.0	47.4	34.5	35.5
Insulin therapy *with Diabetes mellitus*	66.7	63.2	61.0	61.4
Oral antidiabetics *with Diabetes mellitus*	0.0	10.5	8.5	8.6
Pancreatic enzymes *with exocrine pancreatic insufficiency*	98.9	99.2	99.4	99.2
Additional nutrition *with underweight*	44.6	63.4	61.8	56.1
Additional oral nutrition	39.9	59.7	52.0	50.1
PEG	2.0	3.0	10.6	4.9
Proton pump inhibitors (PPI) *with gastroesophageal reflux*	80.0	86.7	83.9	84.3
Polyethylene glycol *with DIOS*	80.0	75.8	82.1	79.0
Calcium *with osteoporosis/osteopenia*	0.0	100.0	75.0	80.0
Oxygen *with respiratory insufficiency*	33,3	0,0	50,0	26,9

Table 32: pwCF under 18 years with indication therapy (frequencies in %)

09

Therapies

9b. Indication therapy

9b.ii. Adults 18 years and older

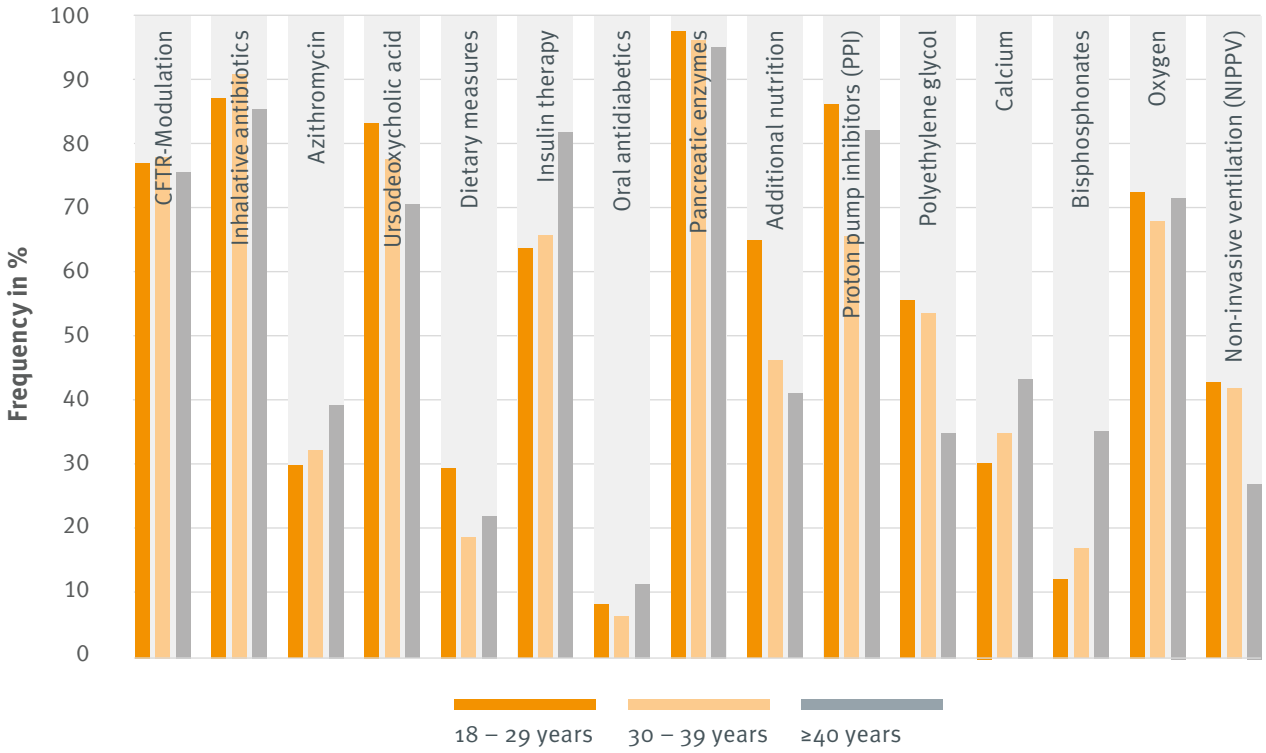

Figure 33: pwCF aged 18 and over with indication therapy 2021

Status of approval of CFTR modulators 31.12.2021
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 and since 2021 for all patients aged 12 and older with at least one F508del mutation.

Therapies

9b. Indication therapy

9b.ii. Adults 18 years and older

Indication therapy	18 – 29 years	30 – 39 years	≥40 years	Total
CFTR-Modulation	77.0	78.9	75.0	77.1
of these, Ivacaftor[1]	3.8	4.5	6.1	4.6
of these, Lumacaftor/ Ivacaftor[2]	5.5	2.5	2.1	3.8
of these, Tezacaftor/ Ivacaftor[3]	8.6	10.2	11.6	9.8
of these, Elexacaftor/ Tezacaftor/ Ivacaftor[4]	69.8	73.0	67.2	70.1
Inhalative antibiotics *with chronic Pseudomonas infection*	87.2	90.6	86.5	88.2
of these, inhalative tobramycin	31.3	26.4	19.6	26.0
of these, inhalative aztreonam	54.3	56.2	53.5	54.7
of these, inhalative aztreonam	25.6	37.8	37.5	33.4
of these, DPI tobramycin	16.7	14.5	6.4	12.8
of these, DPI colistin	15.2	16.1	14.3	15.2
of these, levofloxacin	9.9	15.4	19.7	14.8
of these, inhalative gentamicin	0.3	0.5	0.0	0.3
of these, others	3.4	3.6	3.7	3.5
Azithromycin with *chronic Pseudomonas infection*	29.4	31.4	39.9	33.3
Ursodeoxycholic acid *with liver disease*	83.7	77.6	70.1	78.9
Dietary measures *with Diabetes mellitus*	29.7	18.6	21.4	23.6
Insulin therapy *with Diabetes mellitus*	63.0	65.6	81.6	69.9
Oral antidiabetics *with Diabetes mellitus*	8.4	7.0	10.2	8.5
Pancreatic enzymes *with exocrine pancreatic insufficiency*	98.0	96.1	95.3	96.8
Additional nutrition *with underweight*	63.4	47.2	40.8	55.3
Additional oral nutrition	54.0	43.1	38.0	48.4
PEG	8.7	8.3	2.0	7.4
Proton pump inhibitors (PPI) *with gastroesophageal reflux*	86.3	65.7	82.7	79.4
Polyethylene glycol *with DIOS*	55.2	52.8	34.8	50.4
Calcium *with osteoporosis/osteopenia*	29.8	35.4	43.6	37.3
Bisphosphonates *with osteoporosis*	12.9	17.5	34.9	24.5
Oxygen *with respiratory insufficiency*	72.3	68.3	71.5	70.9
Non-invasive ventilation (NIPPV) *with respiratory global insufficiency*	42.3	41.7	27.8	37.5

Table 33: pwCF aged 18 and over with indication therapy (frequencies in %) 2021

09

Therapies

9c. Development of CFTR modulation therapy 2018 – 2021

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.

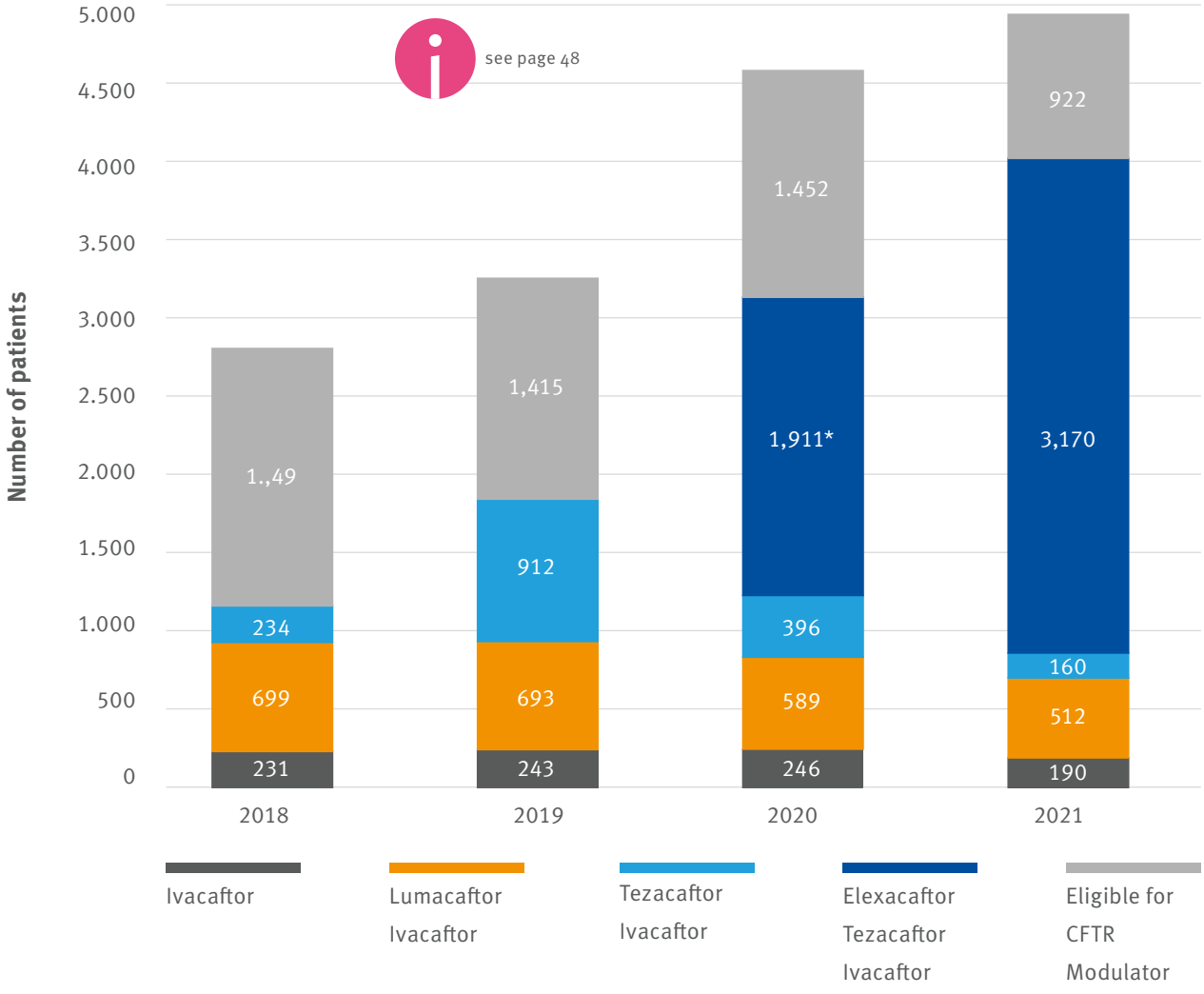

Figure 34: Number of pwCF with modulation therapy and number of patients for whom a suitable modulator is approved 2018

* There is a difference in the representation of patients who received Kaftrio therapy in 2020 between the 2020 and 2021 report volumes. The discrepancy in the data is due to the retrospective recording of the start of Kaftrio therapy at the end of 2020 in the 2021 reporting year.

Mortality

39 patients (17 girls/women and 22 boys/men) died in the reporting year 2021. The main causes of death were cardio-pulmonary diseases (33.3 %), transplants (5.1 %), liver diseases/failure (2.6 %) and malignant diseases (10.3 %). Other or unknown causes were present in 48.7 % of cases. The age at death is broken down as follows:

	Mean value	Median	Minimum	Maximum	25th percentile	75th percentile
Age at death in full years	37.6	42.0	1	64	25.0	50.0

Table 34: Age at death 2021

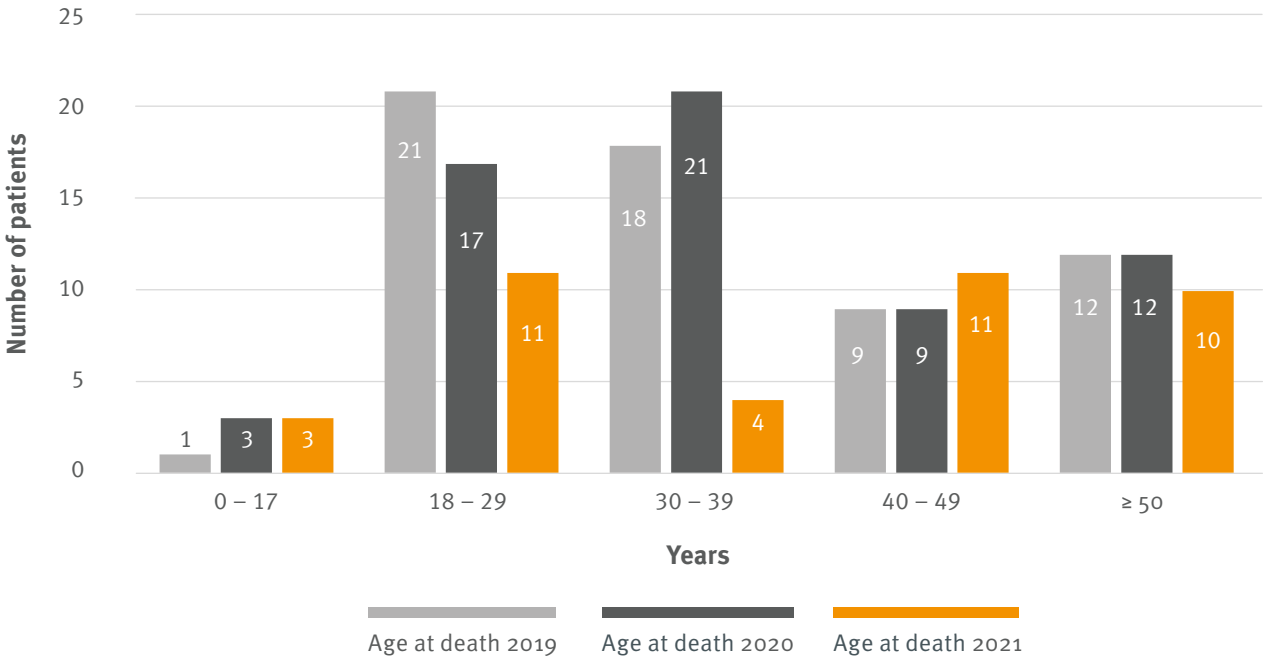

Figure 35: Deceased pwCF in the years 2019 – 2021

Age (years)	2019		2020		2021	
	Number	Percent	Number	Percent	Number	Percent
0 – 17	1	1.6	3	4.8	3	7.7
18 – 29	21	34.4	17	27.4	11	28.2
30 – 39	18	29.5	21	33.9	4	10.3
40 – 49	9	14.8	9	14.5	11	28.2
≥ 50	12	19.7	12	19.4	10	25.6
Total	61	100.0	62	100.0	39	100.0

Table 35: Deceased pwCF in 2021

10

Mortality

(Data status: 27.06.2022)

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 2021, we decided to report the current median age at death for the year 2021 as well as the average survival age and the life expectancy with respect to the period 2016 – 2020.

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 42 (35) years in the reporting year 2021 (2020).

Median survival age 2020

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. 7,991 people with Cystic Fibrosis (including patients with transplants) and 392 deaths were recorded In the 5-year window between 2016 and 2020. 2017 patients (2.7 %) were lost from the follow-up. The median survival age was 54.3 years (confidence interval: 52.3 to 57.2).

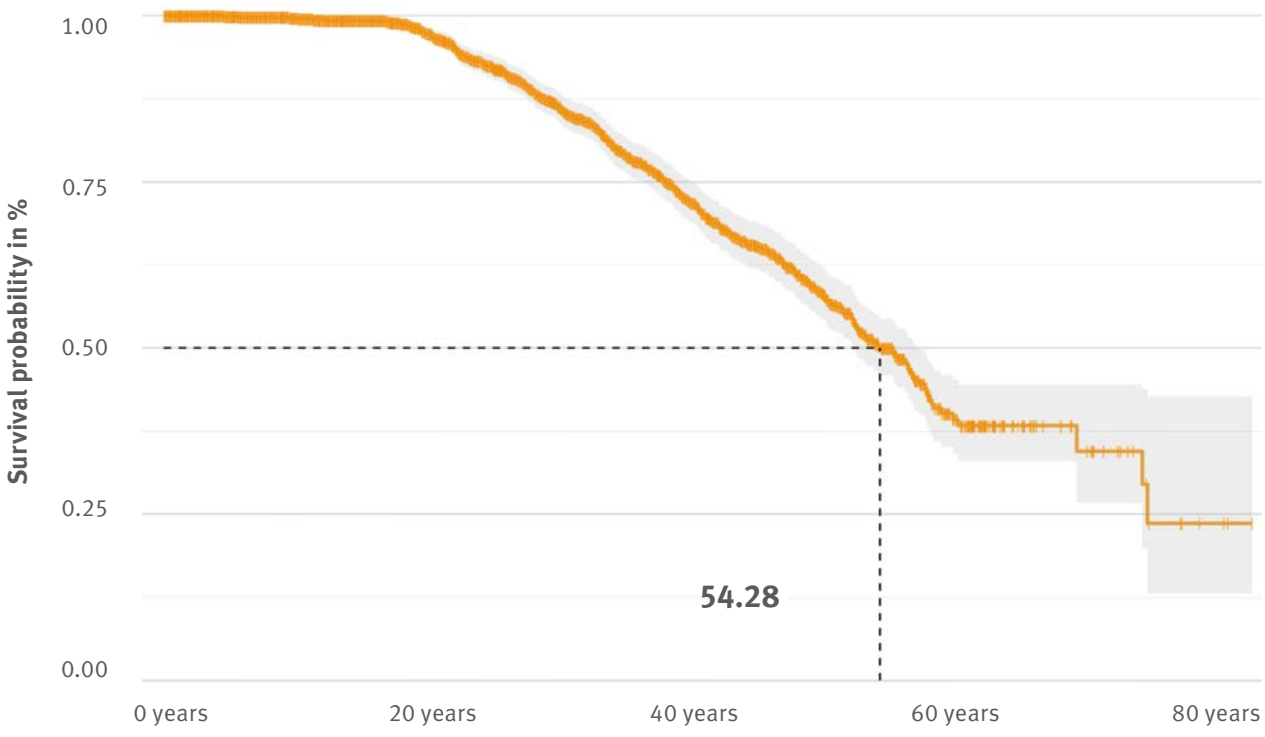

Figure 36: Median survival age for pwCF for the period 2016 – 2020

Mortality

Life expectancy 2021

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.

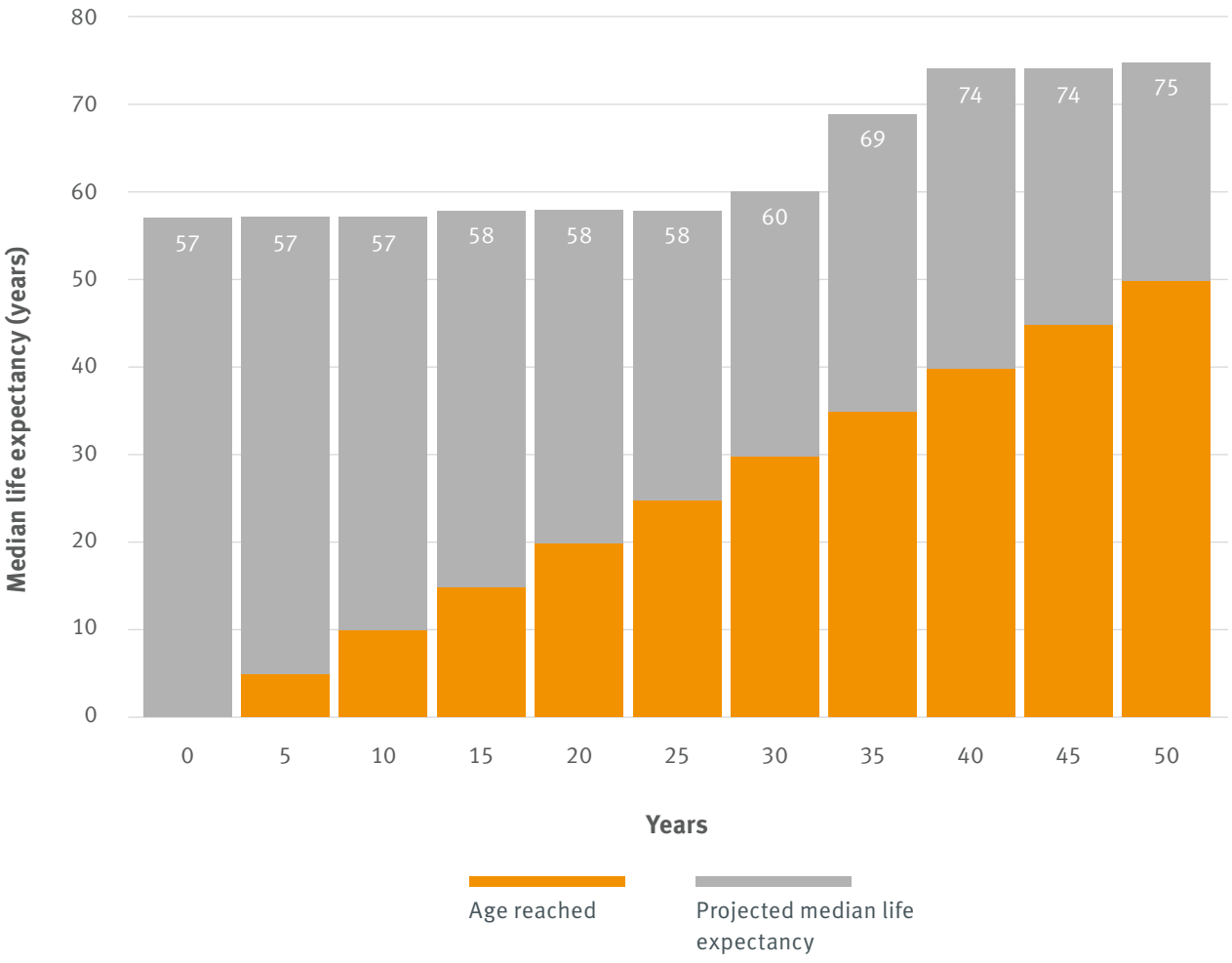

Figure 37: Projected median life expectancy for pwCF 2020

11

COVID 19

(Status: 20.10.2022)

The data basis is data for the period from 02.02.2020 - 20.10.2022. 80 CF outpatient clinics took part in the COVID-19 documentation in the German Cystic Fibrosis Registry. Cystic Fibrosis Registry, 80 CF outpatient clinics participated. 6,062 tests were documented. For 929 patients a positive result was documented by PCR diagnostics. 6.9 % of all patients tested positive had to be hospitalized, of which 0.9 % required intensive care. 4 (0.43%) of the patients who tested positive by PCR diagnostics died as a result of their COVID-19 infection. The following graphs are based solely on the proportion of positive PCR tests (n=929).

			Severity levels			Hospitalisation	
	Total	Sympto-matic	light case	heavy case	critical case	non-intensiv care	Intensive care unit
Total	**929**	82.3	97.5	1.8	0.6	5.9	0.9
Sex							
Female	48.3	84.4	97.6	2.0	0.4	6.7	0.7
Male	51.7	80.4	97.5	1.7	0.8	5.2	1.0
Age							
0 – 11 years	22.3	78.7	100.0	0.0	0.0	3.4	0.0
12 – 17 years	14.5	82.2	98.5	0.7	0.7	0.7	0.7
18 – 29 years	27.6	81.3	96.9	3.1	0.0	7.0	0.0
30 – 49 years	29.7	85.9	96.7	2.2	1.1	8.0	1.4
≥ 50 years	5.9	83.6	92.7	3.6	3.6	12.7	5.5
Transplanted							
No	92.4	81.8	98.1	1.6	0.2	4.1	0.5
Yes	7.3	89.7	89.7	4.4	5.9	29.4	5.9
Unknown	0.1	0.0	100.0	0.0	0.0	0.0	0.0
Mutation							
F508del homozygot	44.5	80.4	99.0	0.7	0.2	6.1	0.2
F508del heterozygot	38.4	85.2	98.0	1.4	0.6	4.2	0.8
Other	15.6	81.4	93.8	4.1	2.1	8.3	2.1
Unknown	1.5	78.6	78.6	21.4	0.0	21.4	7.1

Table 36: Overview COVID-19 in pwCF (frequencies in %) 2020 – 2022

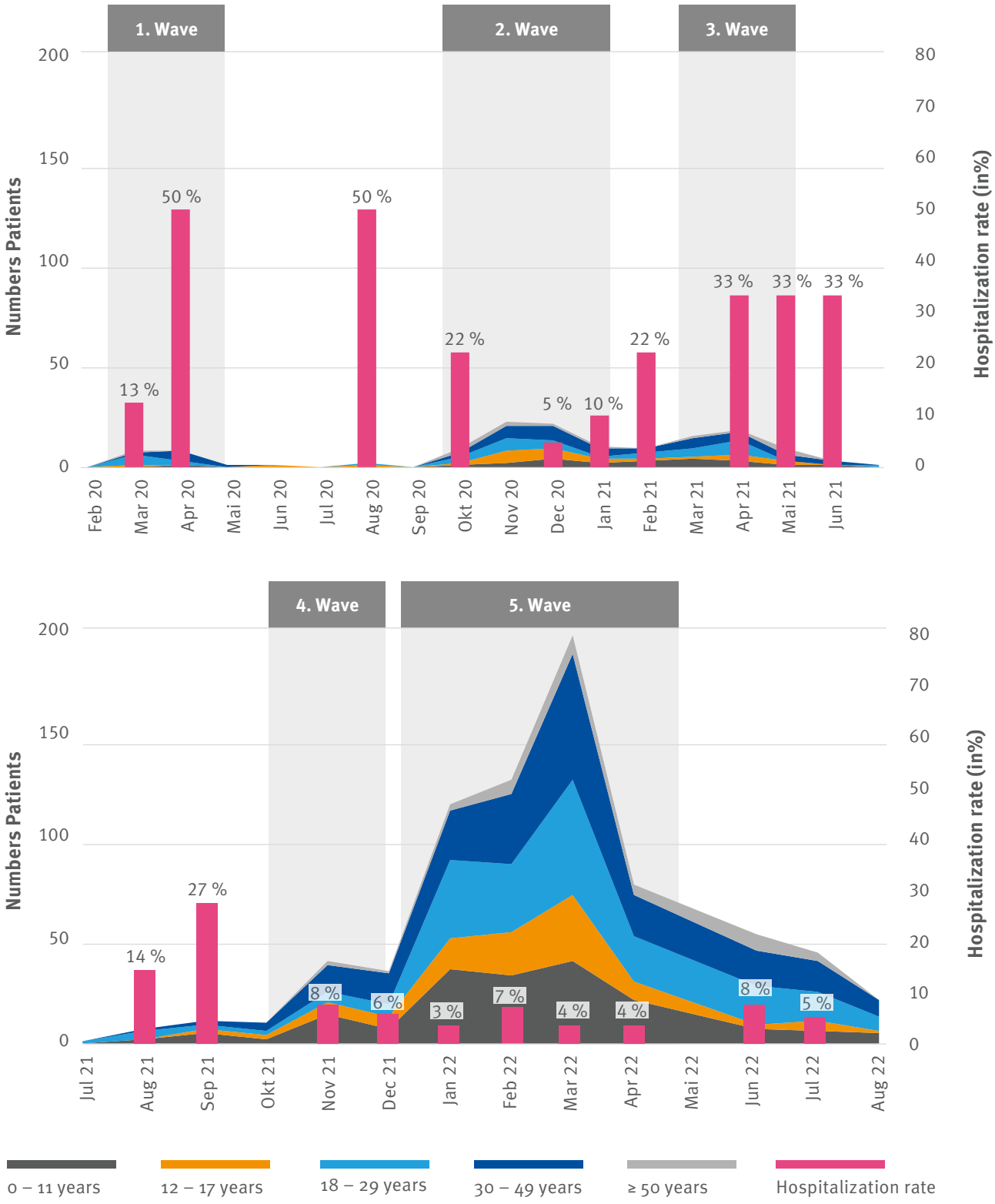

Figure 38: Age-group-specific frequencies of positive PCR tests and hospitalization rates in pwCF 2020 – 2022

12

Structure of care

12a. Size of the participating CF-centers

87 CF-centers participated in the Cystic Fibrosis Registry in the reporting year 2021. 43 centers cared for less than 50 patients and 50 centers cared for more than 50 patients. Over 86 % of the patients documented in the Registry are cared for in these centers.

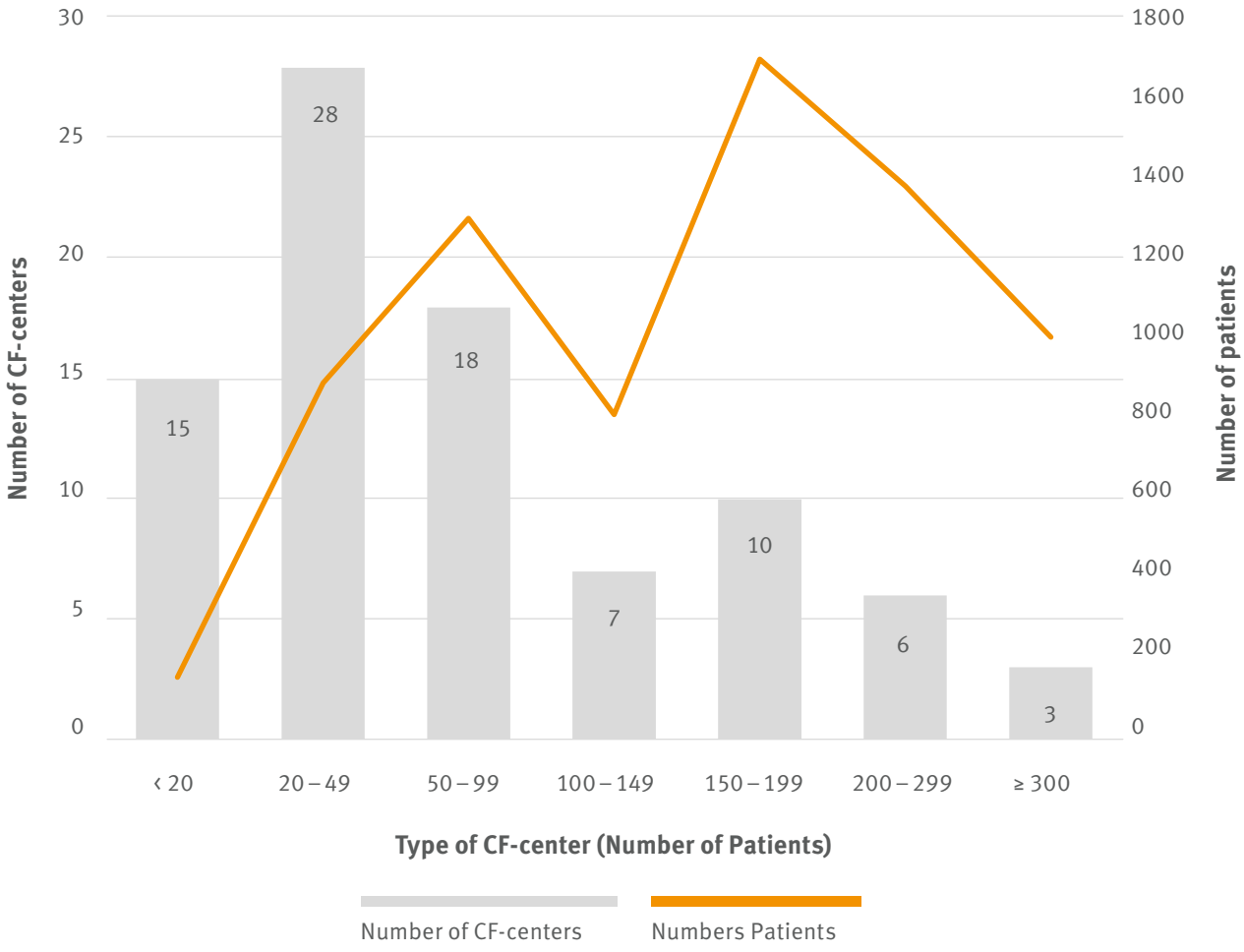

Figure 39: Number of documented pwCF and number of CF centers 2021

Structure of care

12b. Outpatient care

All patients with annual data in 2021 (n=6,776) 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 *in the outpatient clinic*	64.9	62.5	62.3	50.0	38.8	43.3	52.4
Nutritional therapy *in the outpatient clinic*	58.7	47.1	44.4	23.1	15.9	16.9	31.8
Psychosocial support *in the outpatient clinic*	53.0	46.8	48.2	35.8	22.6	25.0	37.3
Anxiety and depression screening[1]	–	–	28.9	32.6	31.4	33.4	31.8
Imaging							
Thorax	53.9	53.7	54.3	49.6	45.3	48.1	50.4
Abdomen	66.0	66.3	62.1	50.9	48.9	46.9	55.6
Bone density measurement	0.3	0.4	4.2	8.8	11.3	15.4	7.3
Laboratory	89.3	90.9	95.0	96.8	97.4	96.8	94.9
Rehabilitation stay	5.9	6.5	4.3	3.1	3.3	4.1	4.3
oGT test[2] *in patients without diabetes mellitus in the previous year*	–	12.4	40.9	30.8	25.2	20.6	22.4

Table 37: pwCF with outpatient care (frequencies in %) 2021
[1] referred to pwCF aged 12 years and older;
[2] referred to pwCF aged 6 years and over

12

Structure of care

12c. CF-related hospitalisations

Age (years)	Number of CF-relevant hospitalisations per patient						
	0	1	2	3	4	5+	unknown
0 – 5	70.1	18.8	3.8	0.9	0.3	0.2	5.9
6 – 11	71.4	15.7	3.2	2.4	0.7	0.1	6.5
12 – 17	67.2	16.7	4.3	2.0	1.6	0.5	7.7
18 – 29	72.2	14.3	4.8	1.5	0.7	0.4	6.1
30 – 39	81.5	11.8	3.0	1.1	0.4	0.3	1.8
≥ 40	79.8	13.1	3.9	0.7	0.6	0.5	1.4
Total	73.9	14.8	3.9	1.4	0.7	0.4	4.9
< 18	69.5	17.0	3.7	1.8	0.9	0.3	6.7
≥ 18	76.9	13.2	4.1	1.2	0.6	0.4	3.7

Table 38: Number of cystic fibrosis-related hospitalisations per patient (frequencies in %) 2021

Overview of Registry requests

Receipt	Applicant	Institution	Subject / Title	Status
2017	Dittrich	Universität Heidelberg	Referenzperzentilen für FEV1 und BMI bei Mukoviszidose	Under evaluation
2017	Schwarz	Charité Universitätsmedizin Berlin	Art4Fun/Schimmelpilz-assoziierte Erkrankungen	Completed – Published (MIQ)
2017	Prinz	Universität Ulm	Mukoviszidose und Glukosetoleranz	Completed – Published (MIQ)
2017	Grehn	Charité Universitätsmedizin Berlin	Arthropathie bei Patienten mit Mukoviszidose	Completed – Published (MIQ)
2017	Chiesi Farmaceutici S.p.A	---	Quinsair PASS	Studie läuft
2018	Ballmann	Kinder-und Jugendklinik Universitätsmedizin Rostock	Diabetes Sonderauswertung	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	Waiting list
2018	Hogardt	Universitätsklinikum Frankfurt	Prävalenz des B. cepacia-Komplex bei CF-Patienten	Completed – Published (MIQ)
2019	Steindor/ Ringshausen	Universitätsklinik Essen/Medizinische Hochschule Hannover	NTM bei CF-Patienten in Deutschland	Under evaluation
2019	Moos-Thiele/Muko.fit	Mukoviszidose e.V.	Kontrollgruppe aus Register zur Überprüfung der Repräsentanz der Muko.fit Gruppe	Study in progress
2019	Hebestreit	Universitätsklinikum Würzburg	Kontrollgruppe aus Register zur Überprüfung der Repräsentanz der VEMSE-Population	Completed
2019	Nährig/Schulte-Hubbert	Klinikum der Universität München/Uniklinikum Dresden	Datenanalyse zur antibiotischenInhalationstherapie bei CF-Patienten mit chron. Pseudomonas-Infektion	Completed
2019	Stanke	Medizinische Hochschule Hannover	Genetische Prädiktoren für schwere CF bei europäischen Zwillingen und Geschwistern	Under evaluation
2019	Hogardt	Universitätsklinikum Frankfurt	Molekulare Epidemiologie von Mycobacterium abscessus bei CF-Patienten aus Deutschland	Completed
2020	Vertex Pharmaceuticals (Germany) GmbH	---	Dossier Nutzenbewertung Triple-Therapie	Completed
2020	Eickmeier/Gardecki	Universitätsklinikum Frankfurt	Patient Science zur Erforschung Seltener Erkrankungen – eine bürgerwissenschaftliche Studie am Beispiel der Mukoviszidose	Completed
2020	Müller	Universität Siegen	Einfluß hormoneller Kontrazeptiva auf Pneumonien bei CF Patientinnen	Under evaluation
2020	Van Dullemen	Universitätsklinikum Frankfurt	Mutationsspezifische Therapie - Übergewicht bei CF (DMT 2020 Vortrag)	Completed
2020	Vertex Pharmaceuticals (Germany) GmbH	---	Dossier Nutzenbewertung Triple-Therapie - Indikationserweiterung	Completed
2020	Vertex Pharmaceuticals	---	Kaftrio PASS	Study in progress
2021	Vertex Pharmaceuticals (Germany) GmbH	Vertex	Dossier Nutzenbewertung Triple-Therapie	Completed
2022	Dittrich, Tümmler	Medizinische Hochschule Hannover	MicroChange: Changes in Culture-dependent Microbiology after initiation of highly-effective CFTR modulator therapy	Under evaluation
2022	Splisense, Israel		Number of CF patients carrying the 3849 +10kb C->T mutation in Germany	Completed
2022	Nährig, Smaczny	Klinikum der Universität München/ Universitätsklinikum Frankfurt	Verlauf von Schwangerschaften	Under preparation
2022	Mukoviszidose Institut gGmbH	ETI Publikationsinitiative	ETI Auswirkungen auf FEV1%, BMI & HbA1c, Schweißtest, Exazerbationen, Basistherapie	Under evaluation

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Participating CF centers 2021

City	CF center	Department	Documentation level[1]	Number of patients[2]
Aachen	Kinderarztpraxis Laurensberg	Aachener Mukoviszidose Ambulanz für Kinder und Jugendliche	Level 1	47
Aachen	Luisenhospital Aachen	Mukoviszidose-Zentrum für Erwachsene, Innere Medizin	Level 1	89
Aachen	Universitätsklinik der RWTH Aachen	Klinik für Kinder- und Jugendmedizin	Level 1	47
Aue	HELIOS Klinikum Aue - CF-Ambulanz	Klinik für Kinder- und Jugendmedizin	Level 1	10
Augsburg	Josefinum KJF	Krankenhaus für Kinder und Jugendliche, CF Ambulanz	Level 2	17
Augsburg	Klinikum Augsburg	II. Klinik für Kinder und Jugendliche, Kinderpneumologie - Allergologie, Mukoviszidose Ambulanz	Level 1	30
Baden Baden	Klinikum Mittelbaden GmbH	Baden-Baden Balg, Lungenzentrum, Mukoviszidose Ambulanz	Level 1	7
Berlin	Sana Klinkum 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	326
Berlin	HELIOS Klinikum Berlin- Buch	Klinik für Kinder- und Jugendmedizin - Pulmologie, Mukoviszidose, Allergologie	Level 1	35
Bielefeld	Evangelisches Klinikum Bethel gGmbH	Lehrkrankenhaus der Universität Münster, Klinik für Kinder- und Jugendmedizin, Tagesklinik für Allergologie und Pneumologie	Level 2	31
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	69
Brandenburg	Medizinische Hochschule Brandenburg (MHB) Klinikum West-Brandenburg	Kinder- und Jugendklinik, CF-Ambulanz	Level 2	30
Bremen	Gesundheit Nord	Eltern-Kind-Zentrum Prof. Hess	Level 2	74
Chemnitz	Poliklinik Chemnitz gGmbH	Praxis für Kinder- und Jugendmedizin	Level 1	2
Cottbus	Carl-Thiem-Klinikum Cottbus	Akademisches Lehrkrankenhaus der Charité, Klinik für Kinder- und Jugendmedizin	Level 2	28
Donaustauf	Klinik Donaustauf	Pneumologische Ambulanz	Level 2	42
Dresden	Universitätsklinikum Carl Gustav Carus	Klinik und Poliklink für Kinder- und Jugendmedizin, Mukoviszidose-Centrum "Christiane Herzog"	Level 2	170
Düsseldorf	UKD Universitätsklinikum Düsseldorf	Klink für Allgemeine Pädiatrie, Neonatologie & Kinder-kardiologie, Ambulanz f. Kinderpneumologie & Allergologie	Level 1	30
Erfurt	HELIOS Klinikum Erfurt	Kinderklinik und Jugendmedizin, CF-Ambulanz	Level 1	18
Erlangen	Universitätsklinikum Erlangen	Kinder- und Jugendklinik, Sozialpädiatrisches Zentrum	Level 2	172
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	310
Frankfurt	Universitätsklinikum Frankfurt	Goethe Universität, Christiane Herzog CF-Zentrum für Kinder, Jugendliche und Erwachsene	Level 2	233
Frankfurt	Frankfurter Rotkreuz-Kliniken e. V.	Klinik für Pneumologie	Level 2	29
Frankfurt/O.	Klinikum Frankfurt (Oder) GmbH	Kinderzentrum	Level 2	8
Freiburg	Universitätsklinikum Freiburg	Klinik für Allgemeine Kinder- und Jugendmedizin, Ambulanz und Arbeitsgruppe Pneumologie, Allergologie und Mukoviszidose	Level 2	69
Freiburg	Universitätsklinikum Freiburg	Abteilung Pneumologie, Erwachsenenambulanz	Level 2	47
Gießen	Universitätsklinik Gießen und Marburg GmbH	Zentrum für Kinder- und Jugendmedizin, Mukoviszidose-Zentrum	Level 2	104
Gießen	Universitätsklinik Gießen	CF Ambulanz für Erwachsene, Justus-Liebig-Universität, Med. Klinik II	Level 2	97

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

City	CF center	Department	Documentation level[1]	Number of patients[2]
Greifswald	Ernst-Moritz-Arndt Universität	Universitätsmedizin Greifswald, Klinik und Poliklinik für Kinder- und Jugendmedizin	Level 2	22
Halle	Universitätsklinikum Halle (Saale) (UKH)	Medizinische Fakultät der Martin-Luther-Universität, Mukoviszidose-Zentrum	Level 2	70
Hamburg	Kinder- und Jugendärztliche Gemeinschaftspraxis	Kinderärzte im Friesenweg, CF Centrum Altona	Level 2	149
Hamburg	Universitätsklinikum Eppendorf	II. Medizinische Klinik	Level 2	39
Hamm	Evangelisches Krankenhaus Hamm (EVK) gGmbH	Klinik für Kinder- und Jugendmedizin, Pulmologie/Allergologie	Level 1	11
Hannover	Medizinische Hochschule Hannover	Klinik für Pädiatrische Pneumologie, Allergologie und Neonatologie	Level 2	186
Hannover	Medizinische Hochschule Hannover	Klinik für Innere Medizin, Pneumologische Ambulanz (Erwachsene)	Level 2	238
Heidelberg	Universitätsklinikum Heidelberg	Sektion Pädiatrische Pneumologie, Allergologie und Mukoviszidose-Zentrum	Level 2	128
Heidelberg	Thoraxklinik am Universitätsklinikum Heidelberg	Abteilung für Pneumologie und Beatmungstherapie, CF Ambluanz für Erwachsene	Level 2	215
Heilbronn	SLK-Kliniken Heilbronn GmbH	Klinik für Kinder- und Jugendmedizin, Klinikum am Gesundbrunnen, Perinatalzentrum	Level 2	20
Homburg	Universitätsklinikum des Saarlandes	Klinik für Allgemeine Pädiatrie und Neonatologie	Level 2	53
Homburg	Universitätsklinikum des Saarlandes	Innere Medizin 5, CF-Ambulanz für Erwachsene	Level 1	58
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	25
Kassel	Klinikum Kassel	Klinik für Kinder- und Jugendmedizin, Pneumologie, CF-Ambulanz	Level 2	45
Kiel	Städtisches Krankenhaus Kiel GmbH	Klinik für Kinder- und Jugendmedizin, Christiane Herzog Zentrum Nord – Kinder	Level 2	47
Kiel	Mukoviszidose Zentrum für Erwachsene	Städtisches Klinikum Kiel, 4. Medizinische Klinik, Christiane Herzog Zentrum Nord – Erwachsene	Level 2	110
Koblenz	Gemeinschaftsklinikum Mittelrhein gGmbH	Klinik für Kinder- und Jugendmedizin, Pädiatrische Pneumologie und Allergologie, Mukoviszidose Ambulanz	Level 2	45
Köln	Universitätsklinikum Köln	Klinik und Poliklinik für Kinder- und Jugendmedizin, Mukoviszidose-Zentrum	Level 2	237
Köln	Kliniken der Stadt Köln	Lungenklinik Merheim	Level 2	79
Krefeld	Helios Klinikum Krefeld	Zentrum für Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	41
Leipzig	Universitätsklinikum Leipzig	Klinik und Poliklinik für Kinder- und Jugendmedizin, CF-Ambulanz	Level 2	62
Löwenstein	SLK Lungenklinik Löwenstein 296	Medizinische Klinik I, Pneumologie	Level 2	20
Lübeck	Universitätsklinkum Schleswig Holstein (UKSH)	Campus Lübeck, Klinik für Kinder- und Jugendmedizin, Pädiatrische Pneumologie	Level 1	30
Magdeburg	Otto-von-Guericke Universitätsklinikum Magdeburg	Klinik für Allgemeinpädiatrie und Neonatologie, CF-Ambulanz	Level 2	22
Magdeburg	Otto-von-Guericke Universitätsklinikum Magdeburg	Universitätsklinik für Pneumologie	Level 2	11
Mainz	Universitätskinderklinik Mainz	Pädiatrische Pneumologie, Allergologie, Mukoviszidose	Level 2	109
Mannheim	Universitätsklinikum Mannheim	Klinik für Kinder- und Jugendmedizin, Pulmologie, Infektiologie und Allergologie	Level 2	18

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

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Participating CF centers 2021

City	CF center	Department	Documentation level[1]	Number of patients[2]
Marburg	Zentrum für Kinderheilkunde	Mukoviszidose-Ambulanz	Level 2	13
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 2	31
München	LMU Klinikum der Universität München	Campus Innenstadt, Medizinische Klinik – Pneumologie	Level 2	217
München	LMU Klinikum der Universität München	Kinderklinik und Kinderpoliklinik im Dr. von Hauner-schen Kinderspital, Christiane Herzog-Ambulanz	Level 2	311
München	Lungenheilkunde München Pasing	Mukoviszidose-Zentrum München West	Level 2	167
Münster	Clemenshospital	Mukoviszidose-Ambulanz	Level 2	119
Münster	Universitätsklinikum Münster UKM	Klinik für Kinder- und Jugendmedizin, Allgemeine Pädiatrie Mukoviszidose-Ambulanz	Level 1	61
Neubranden-burg	Dietrich Bonhoeffer Klinikum	Klinik für Kinder- u. Jugendmedizin	Level 2	23
Oldenburg	Klinikum Oldenburg AöR	Klinik für Pädiatrische Pneumologie und Allergologie, Neonatologie und Intensivmedizin	Level 1	94
Osnabrück	Christliches Kinderhospital Osnabrück	Zentrum für Kinder- und Jugendmedizin, Mukoviszidose Ambulanz	Level 2	59
Passau	Kinderklinik Dritter Orden	Zentrum für Kinder- und Jugendgesundheit, Sozialpädiatrisches Zentrum	Level 2	22
Potsdam	Klinikum Westbrandenburg gGmbH	Kinder- und Jugendklinik, Mukoviszidose ASV-Ambulanz	Level 2	193
Ravensburg	Oberschwabenklinik (OSK) gGmbH Ravensburg	Krankenhaus St. Elisabeth, Klinik für Kinder und Jugendliche	Level 1	3
Regensburg	KUNO Klinik St. Hedwig	Kinder- und Jugendmedizin	Level 2	91
Rostock	Universitätsmedizin Rostock	Kinder- und Jugendmedizin	Level 2	36
Schwerin	HELIOS Kliniken Schwerin	Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	26
Stuttgart	Klinikum Stuttgart	Olgahospital, Pädiatrie 3, Mukoviszidose Ambulanz	Level 2	176
Stuttgart-Gerlingen	Robert Bosch Krankenhaus RBK	Klinik Schillerhöhe, Mukoviszidose Ambulanz	Level 2	154
Trier	Klinikum Mutterhaus der Borromäerinnen gGmbH	Kinder-u. Jugendmedizin	Level 2	21
Trier	Klinikum Mutterhaus der Borromäerinnen gGmbH	Klinikum Mutterhaus Mitte, Innere Medizin 1	Level 1	29
Tübingen	Universitätsklinik Tübingen	Klinik für Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	151
Ulm	Universitätsklinikum Ulm	Klinik für Kinder- und Jugendmedizin, Mukoviszidose-Ambulanz	Level 2	114
Vechta	St. Marienhospital Vechta gGmbH	Klinik für Kinder- und Jugendmedizin, Allergologie und Pulmologie	Level 1	2
Wangen	Fachkliniken Wangen	Waldburg Zeil Kliniken, Klinik für Pneumologie	Level 2	22
Wangen	Fachkliniken Wangen gGmbH	Waldburg-Zeil Kliniken, Klinik für Pädiatrische Pneumologie und Allergologie, CF-Ambulanz, Rehabilitationsklinik für Kinder und Jugendliche	Level 2	8
Wesel	Marien-Hospital Wesel	Akademisches Lehrkrankenhaus der Westfälischen Wilhelms-Universität Münster, Klinik für Kinder- und Jugendmedizin	Level 2	32
Worms	Klinikum Worms gGmbH	Klinik für Kinder- und Jugendmedizin	Level 2	50
Würzburg	Universitäts-Kinderklinik Würzburg	Christiane-Herzog-Ambulanz für Mukoviszidose	Level 2	148
Zwickau	Heinrich Braun Klinikum gGmbH	Standort Zwickau, Kinderzentrum	Level 1	9

[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 *Aspergillus fumigatus*.
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.
ß2-sympathomimetics	Betasympathomimetics 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 FEV1 value is part of the pulmonary function and can be measured in a pulmonary function test.
FEV1% predicted	The FEV1% is the percentage value of the average FEV1 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.

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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 = Q3 - Q1.
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.
Median survival prognosis	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.
MRSA	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 sacciform 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.
Pseudomonas aeruginosa	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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