FRENCH CYSTIC FIBROSIS REGISTRY

ANNUAL DATA REPORT 2020

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VAINCRE LA MUCOVISCIDOSE

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Editorial

2020, Year One of the triple combination therapy era?

2020, year of the Covid-19 pandemic outbreak, but also and above all the beginning of the era of triple therapy for patients with cystic fibrosis. As part of compassionate use, 414 patients were prescribed Kaftrio® in 2020. Now, a third of patients benefit from CFTR modulators: Kalydeco® in 200 patients (+17% compared to 2019), Orkambi® in 1833 patients (+52%) and Kaftrio®/Trikafta®.

For the first year, indicators added recently in the annual survey have been integrated into the various chapters of this report, such as comorbidities, oral treatments, and social data.

The Kaftrio effect

The annual Registry report starts to show the spectacular effect of Kaftrio®: a 50% reduction in the number of lung transplants. Naturally, we will have to wait for the results of the real-life studies currently being carried out and financed by Vaincre la Mucoviscidose to be categorical and refine these results.

Annual reporting trends are confirmed

The number of patients identified continues to increase overall (+1%). However, the paediatric cohort continues its downward trend (-2%) observed since 2012. This can be compared to the constant decline in the birth rate in France between 2010 and 2020. The population comprises nearly 60% adults (+2. 7%).

The trend observed is also confirmed for the median age (nearly 22 years, + 6 months) and the median age at death (33 years, i.e. 1 year more than the average of the last 5 years).

CF centers were fully mobilized during the pandemic

Despite the health crisis and thanks to the strong mobilization of the CRCMs, follow-up was provided for all patients, whether by in-person or telehealth clinic visits.

Unsurprisingly, due to the health context, a smaller number of patients were able to benefit from the four visits recommended by the National Protocol for Diagnosis and Care. Fewer patients were hospitalized, and with shorter hospital stays. Conversely, the number of visits has increased, which is explained by the fact that many centers have included, in an exceptional way, telehealth clinic visits.

As regards treatments, the number of IV antibiotic courses has fallen by 21%, with a global shorter duration. No significant difference was observed in the prescription of oral or aerosol treatments.

A goldmine that remains to be explored

This report is the result once again of the hard work of caregivers, the French Cystic Fibrosis Registry team and Vaincre la Mucoviscidose, with the precious support of patients and the Muco/CFTR Network. Thank you to each of them for joining forces in the fight against the disease, the Registry being undoubtedly the mine that we need to explore more to identify paths of research and better understand the evolution of cystic fibrosis.

Thierry Nouvel
Chief Executive Officer

Lydie Lemonnier
Registry Lead

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Information
Percentages may not add up exactly to 100 due to rounding
Children are patients under 18 years of age, adults are patients aged 18 or more.

Cystic Fibrosis

Cystic fibrosis is a hereditary disease with autosomal recessive transmission: only subjects who have inherited two mutations – one from the father, the other from the mother – are affected.

The gene responsible for the disease, called *CFTR* (Cystic Fibrosis Transmembrane Conductance Regulator) was identified in 1989. It is located on the long arm of chromosome 7 (7q31) and codes for the CFTR protein, a protein involved in the regulation of chloride ion transport across the cell membrane. To date, more than 2,000 mutations have been identified, the most common (about 80% of patients) being F508del.

Before implementation of the systematic newborn screening program, the most common context for diagnosis was as follows: clinical symptoms (meconium ileus, steatorrhoea, bronchial obstruction, recurrent respiratory infections), confirmed by an elevated sweat chloride ions concentration. This would be followed by molecular analysis of the *CFTR* gene and identification of the disease causing mutations.

Newborn screening has been systematic in France and the French overseas territories since 2002. The screening technique uses measurement of immunoreactive trypsin (IRT) in the blood at age 3 days and detection of the most frequent *CFTR* mutations (30 then 29 up to 01/01/2015). The IRT protein is more abundant when there is pancreatic abnormality during foetal life and in the first few months of life. Measuring IRT concentrations enables 95% of newborn children with cystic fibrosis to be detected, though the test is not specific enough (it picks out some children who do not have cystic fibrosis) and is therefore linked with a molecular analysis.

After looking for the main *CFTR* mutations (F508del and about thirty others), three situations can arise:

– two mutations are identified. The newborn baby and its parents are asked to visit a cystic fibrosis care centre (*CRCM - Centre de Ressources et de Compétences de la Mucoviscidose*) to confirm the diagnosis based on a clinical assessment and a positive sweat test, and to initiate the necessary treatment and monitoring ;

– a single mutation is identified (the probability of not identifying a second mutation is around 10%). A sweat test must be carried out in a specialised centre. If the test is positive, the child is treated in the same way as the previous group. If negative, information concerning the heterozygous nature of the newborn will be given to the parents during genetic counselling ;

– the D3 IRT level is high and no mutation is found (or parents refused geneting testing). A second blotting paper sample test is carried out at age 21 days. If a raised IRT level persists at D21, the child is referred to a specialised centre for an additional assessment (sweat test).

A sweat test giving an intermediate value has to be repeated.

In case of IRT above the threshold and if the genetic study is not carried out due to the absence of parental consent, a control by blood sample on blotter around 21 days of life is carried out. Persistance of an elevated IRT will lead to a consultation in a CF center for further evaluation (sweat test).

In CF, functional abnormalities occur in the digestive tract, respiratory tract, sweat glands and genital tract. This wide range of abnormalities is associated with a broad spectrum of clinical expression, both regarding the age when the first symptoms appear and their subsequent evolution. The severity of respiratory symptoms affects life expectancy in the majority of cases.

Lifelong treatment is time consuming, demanding and aimed at symptomatic relief. It is essentially based on respiratory (physiotherapy, inhaled, antibiotic treatment, oxygen therapy), digestive and nutritional management (pancreatic enzyme supplements and a hypercaloric diet). During the last few years, new therapies targeting some CFTR mutations (CFTR modulators or correctors) impact the causative mechanism of the disease. Patient education is an integral part of care.

The French Cystic Fibrosis Registry

Objectives

In 1992, the medical Council of the association *Vaincre la Mucoviscidose*, set up a national cystic fibrosis observatory, the *Observatoire national de la mucovicidose* (ONM), with the following objectives:

- improving knowledge on medical and social characteristics
- gaining a better understanding of the socioeconomic cost of this disease with a view to obtaining sufficient resources to cover constantly growing needs
- improving information available to help both parents and patients in their personal choices, and institutional partners in strategic decisions
- helping research by facilitating pre-selection of patients eligible for clinical trials
- evaluating the impact of therapeutics and facilitate access to new treatments

Covering the entire population of patients in France, has since been added to the initial objectives. The patient organization has therefore transformed the ONM into a national cystic fibrosis registry. This initiative was approved in July 2006 by the Committee for Protection of Personal Data in Medical Research and in March 2007 by the Data Protection Agency. At the end of 2008 and then in 2011, 2015 and 2021, the registry was certified by the National Committee of Rare Disease Registries.

Population and data

The population is composed of people with cystic fibrosis followed in the French CF care centres (metropolitan France and Reunion Island). Data are collected once a year by means of an e-CRF or export from electronic medical records. They refer to the previous year and include semi-anonymous patient identification, diagnosis, medical follow-up, treatments, anthropometry, respiratory function, microbiology, evolution of the condition and social and family situation. Thematic questionnaires collect data on pregnancies, *Burkholderia Cepacia* complex and related, and inclusion in clinical trials, but also on CFTR modulators and atypical mycobacteria.

Due to the exceptional health situation in 2020, many centers have been included in the "Visits" the number of telehealth clinic visits.

Data use

Statistical analysis is performed on anonymized data. Unless otherwise indicated, the results presented hereafter relate to the population seen during the year 2020.

Data from different centers are now entered in one file per patient, thus allowing better data exhaustiveness and quality.

Missing data were considered an absence of event, some percentages can therefore be underestimated.

Data analysis

Ad hoc studies on various themes are conducted on the Registry data. Some are the subject of publications and communications at international congresses.

The French Registry sends anonymised data to the European Cystic Fibrosis Patient Registry in order to allow a wider use of the data along with other countries. Comparisons between indicators from national registries must be made with caution due to numerous biases linked in particular to the impact of neonatal screening, transplantation, socio-economic status but also to compliance with the measurement guidelines, population references and statistical limits, in particular in the event of an insufficient number of patients in an age group.

As part of a partnership with the Lyon Hospital and with the objective to carry out more in-depth analyzes, the Registry has been linked with the National Health Data System.

1. Demographics

Characteristics of the population

Figure 1.1. Evolution of the number of patients since 1992

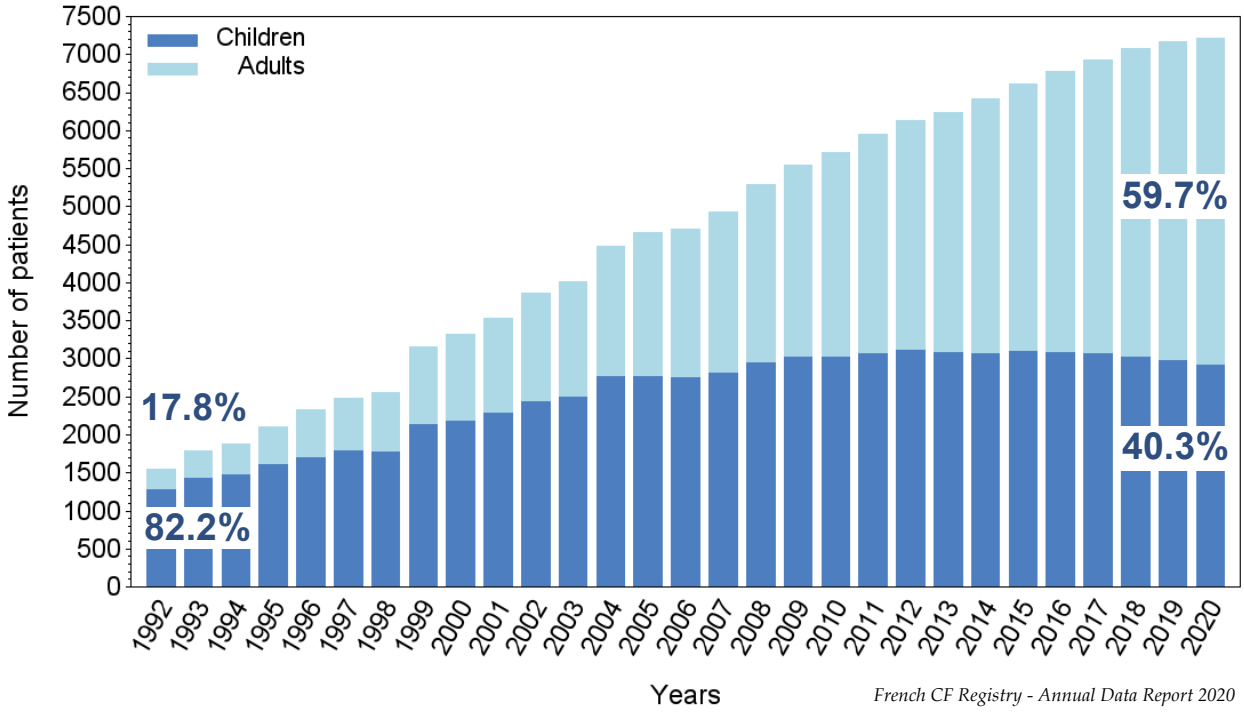

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Table 1.1. Annual evolution of the main indicators

	Years of follow-up										
Indicators	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
All patients*	5715	5969	6138	6252	6428	6630	6788	7078	7183	7290	7376
Patients seen during the year**	5706	5957	6126	6241	6414	6620	6781	6935	7075	7164	7216
Children	3018	3068	3108	3086	3070	3097	3081	3063	3016	2971	2909 (40.3 %)
Adults	2688	2889	3018	3155	3344	3523	3700	3872	4059	4193	4307 (59.7 %)
Over 40 years	339	399	452	509	586	668	758	825	910	986	1056 (14.6 %)
Men	2940	3085	3166	3223	3314	3442	3548	3618	3683	3739	3747 (51.9 %)
Women	2766	2872	2960	3018	3100	3178	3233	3317	3392	3425	3469 (48.1 %)
Mean age (years)	18.5	19.1	19.5	20.1	20.7	21.1	21.8	22.3	22.9	23.4	23.9
Median age (years)	16.9	17.4	17.8	18.2	18.9	19.3	19.9	20.3	20.9	21.3	21.9
Minimum age (years)	0.1	0	0.1	0.1	0	0	0.1	0.1	0.1	0.1	0
Maximum age (years)	80	88	86.8	82.5	82.8	83.2	84.1	85.1	86.1	84.6	85.6

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*Patients whose vital status is known, whether they visited or not a CF care centre.

**Reference patients for this report, excepted for survival.

This table is updated each year with the corrections made to previous year's data. Patients with unconfirmed or withdrawn diagnosis (N=26) were excluded from the analysis.

1. Demographics

Characteristics of the population

Table 1.2. Characteristics of the population, by sex and age

Characteristics	2018		2019		**2020**	
	Men	Women	Men	Women	**Men**	**Women**
Patients seen during the year	3683	3392	3739	3425	3747	3469
Children	1544	1472	1522	1449	1492	1417
Adults	2139	1920	2217	1976	2255	2052
Mean age (years)	22.9	23	23.4	23.4	23.9	23.9
Median age (years)	21.3	20.5	21.6	21	22.3	21.5

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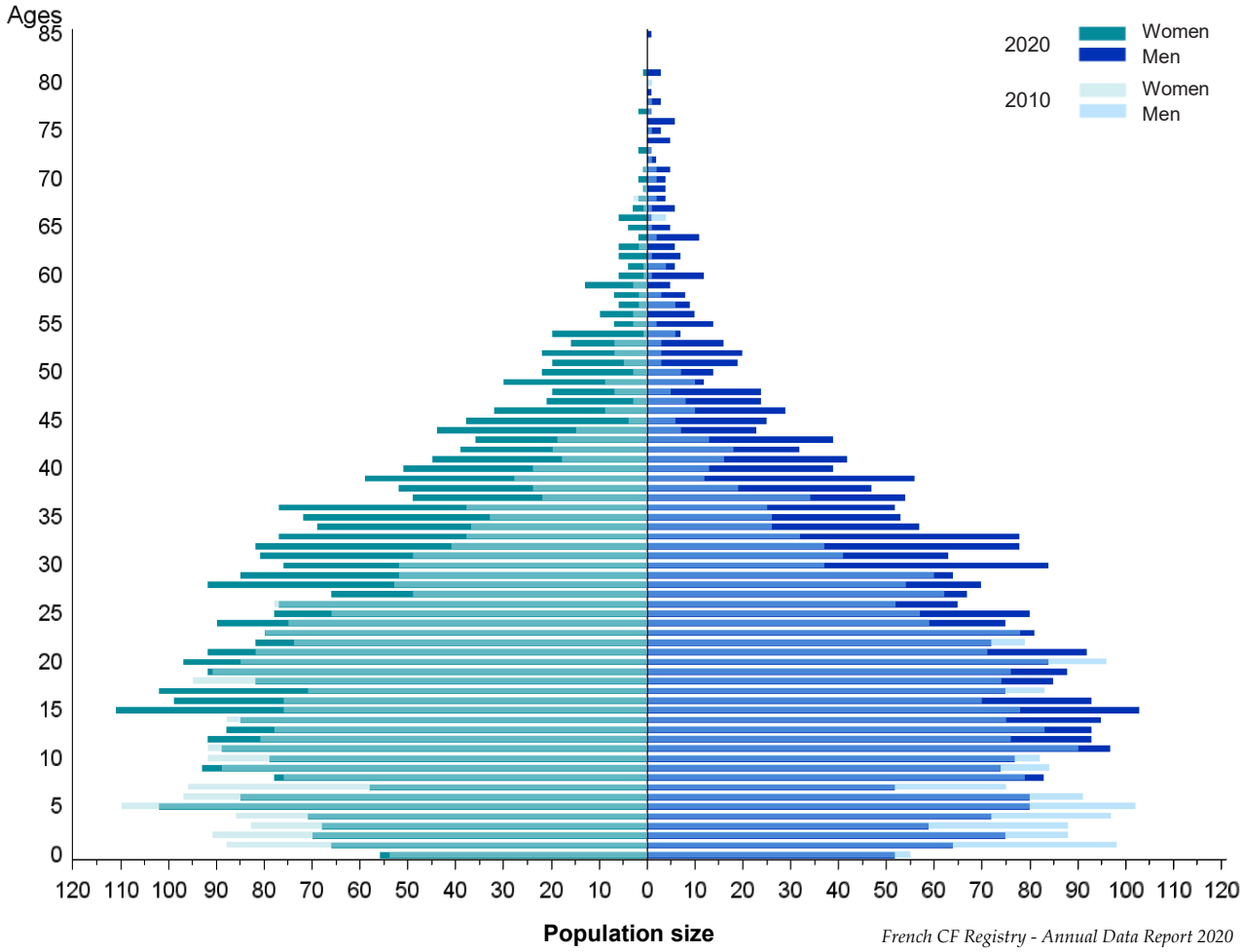
Figure 1.2. Population pyramid



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The number of babies born in 2020 (patients less than 1 year old) is slightly underestimated as it does not include those seen for the first time in a CF center in 2021.

The short bar corresponding to children born in 2013 has been validated with the newborn screening program data. To date there is no clear explanation.

1. Demographics

Location by type of centre

Table 1.3. Patients' characteristics by type of centre

		Patients' characteristics			Age of patients (years)				
Types of centres	Nb	Nb (a)	%	Mean nb by centre	Min*	Max*	Mean	Median	Inter-quartile
CRCMs									
Paediatric	17	2058	28.5	121.1	0	39.4	10.3	10.7	9.3
Adult	14	3091	42.8	220.8	16.5	85.6	34.5	32.5	14.9
Paediatric/Adult	16	2028	28.1	126.8	0.1	81.2	21.9	19.3	19.7
Subtotal	47	7177	99.5	152.7	0	85.6	24.0	22.0	21.4
Other centres									
Paediatric	2	12 (b)	0.2	6.0	4.6	17.7	10.3	9.0	5.6
Paediatric/Adult	1	27 (c)	0.4	27.0	1.9	18.5	11.4	10.8	4.3
Subtotal	3	39	0.5	13.0	1.9	18.5	11.1	10.3	5.0
Total	50	7216	100	144.3	0	85.6	23.9	21.9	21.5

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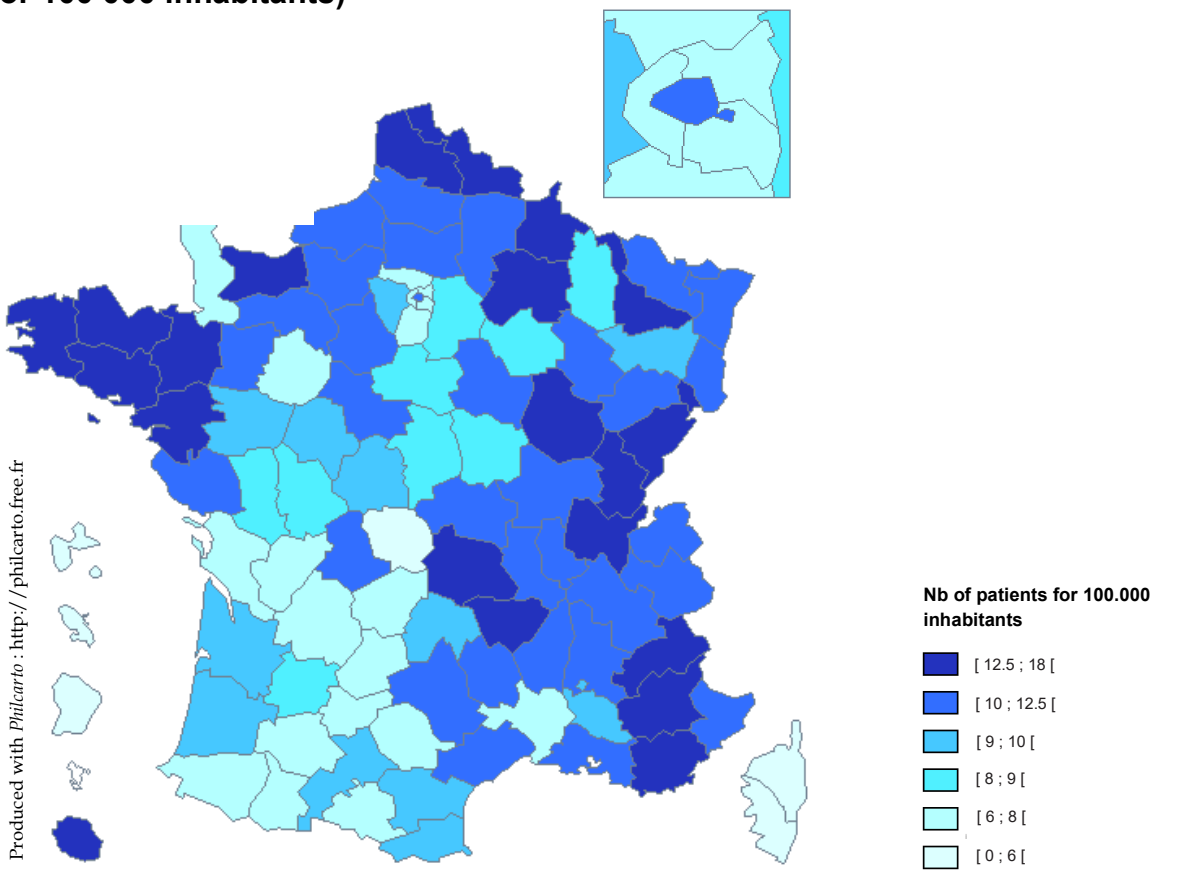
Notes : (a) Patients visiting at least 2 CF centres during the year were only counted in the one with the highest number of visits.
(b) Including 1 patient also seen by a CF centre.
(c) Including 2 patients also seen by a CF centre.

* Cases when a child's follow up is made by an adult centre or vice versa are very rare.

1. Demographics

Geographical location

Map 1.1. Prevalence of cystic fibrosis by « département » of residence (number of patients for 100 000 inhabitants)



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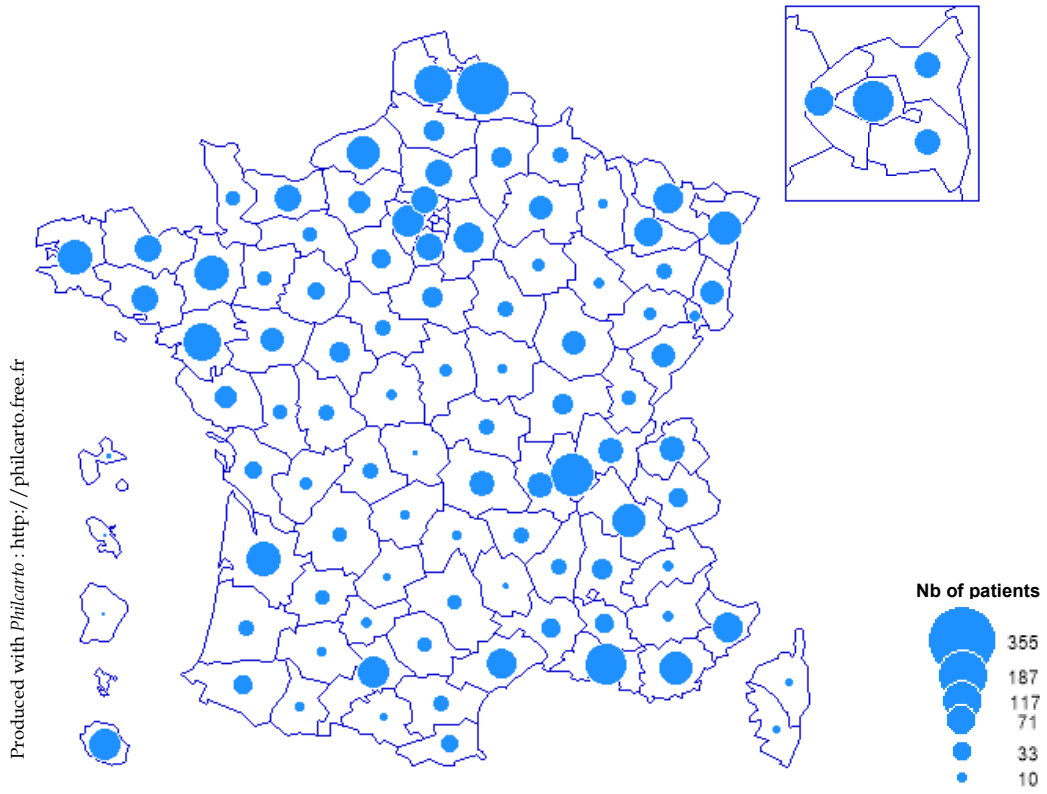
Map 1.2. Localisation of the patients by « département » of residence (absolute numbers)



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2. Mortality

Characteristics

Figure 2.1. Annual number of deaths since 1992

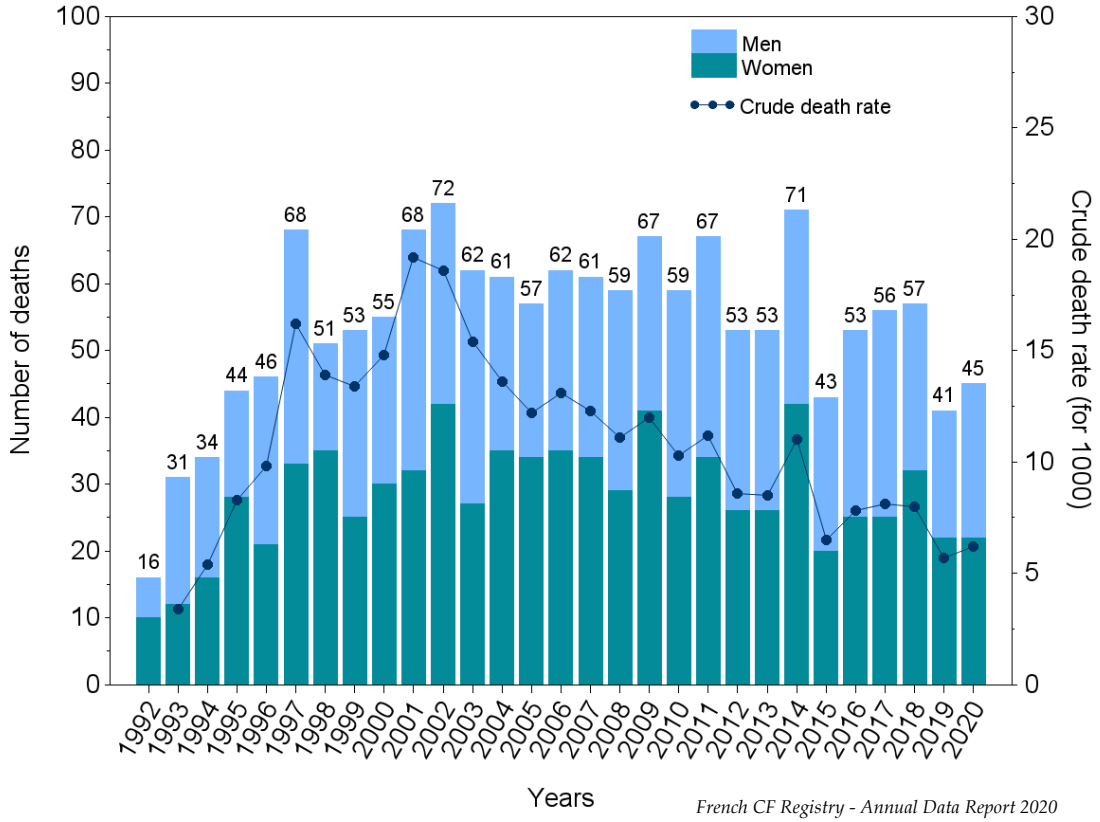

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Table 2.1. Mortality characteristics

Indicators	Years of follow-up										
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number of deaths	59	67	53	53	71	43	53	56	57	41	45*
- including transplanted patients	32	33	27	29	41	22	37	33	36	21	25
Crude death rate (per 1000)	10.3	11.2	8.6	8.5	11.0	6.5	7.8	8.1	8.0	5.7	6.2
Mean age (years)	29.3	26.4	32.3	34.4	29.0	34.1	31.9	35.0	33.6	34.7	36.5
Median age (years)	27.6	24.9	27.8	30.7	27.1	31.8	28.0	33.8	31.0	34.0	32.8
Minimum age (years)	0.2	1.9	2.2	1.1	0.1	9.0	1.6	5.9	7.3	0.4	0.3
Maximum age (years)	68.9	55.5	88.4	82.5	71.2	83.2	76.0	74.3	80.9	65.9	85.8

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* 10 out of the 45 were not seen by a CF center in 2020.

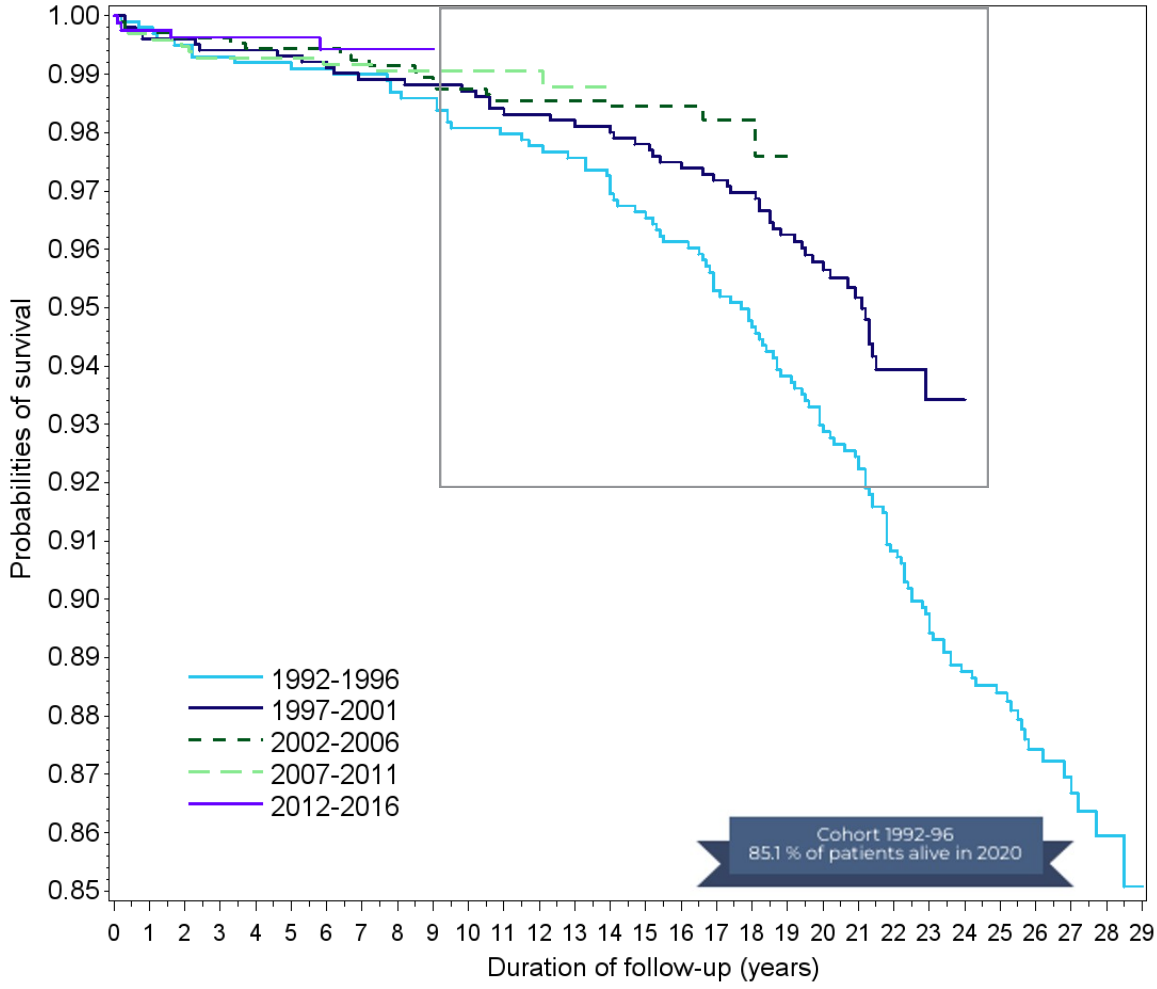
2. Mortality

Survival analysis

Figure 2.2. Survival curves by birth cohort (Kaplan-Meier method)

In order to show the evolution of health status of the patients, a survival analysis was performed on 5 birth cohorts; the numbers of patients and of deaths are:

- Births from 1992 to 1996 (in 2020 this cohort was followed during 29 years maximum): 997 patients, 122 deaths
- Births from 1997 to 2001 (maximum 24 years of follow up): 1019 patients, 52 deaths
- Births from 2002 to 2006 (maximum 19 years of follow up): 1070 patients, 18 deaths
- Births from 2007 to 2011 (maximum 14 years of follow up): 968 patients, 10 deaths
- Births from 2012 to 2016 (maximum 9 years of follow up): 813 patients, 4 deaths



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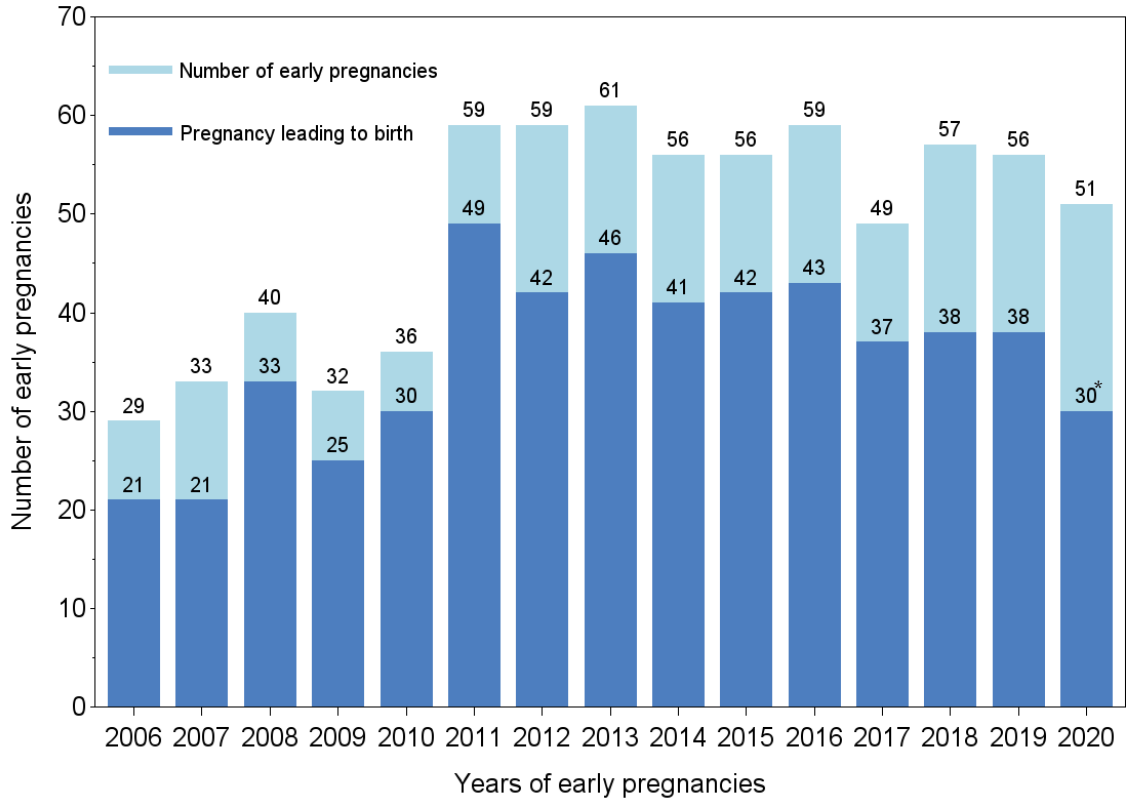
Until the age of 9, there is no difference in survival between the different birth cohorts.

After this age, a difference in survival between the two oldest cohorts (1992-1996 and 1997-2001) appears, and this difference is statistically significant (Log-Rank test = 8.5, p = 0.0035).

Survival analysis by sex is available on annex 1.

3. Pregnancy – Paternity

Figure 3.1. Annual number of early pregnancies, evolution since 2006



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Of the 51 early pregnancies in 2020, 30 resulted in a birth (in 2020 or 2021).

* Some pregnancy outcomes were not known at the time of data collection. Figures given for 2020 are therefore presented for information purposes and should not be considered as definitive.

Table 3.1. Early pregnancy characteristics

Characteristics	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number of early pregnancies	29	33	40	32	36	59	59	61	56	56	59	49	57	56	51
Pregnancy rates in women aged 15 to 49 years (for 1000)	26.1	28.5	32.4	24.2	25.9	40.1	38.2	37.8	33.1	31.6	32.2	25.9	29.4	28.2	24.9
Mean age at 31st December of the year of early pregancy	27.2	27	26.7	27.5	28.8	28.4	28.3	28.5	28.6	30.9	28.2	29.9	29.9	29.8	29.6
Number of lung transplanted women starting a pregnancy	1	2	1	3	3	3	7	4	1	3	4	4	10	11	4

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3. Pregnancy – Paternity

Table 3.2. Paternities

Characteristics	N	Proportion (%)
Number of paternities, including:	33	
- Natural father	3	9.1
- Medically assisted reproduction, including:	30	90.9
+ Intracytoplasmic Sperm Injection / in vitro fertilization	28	93.3
+ Artificial insemination with sperm donor	1	3.3

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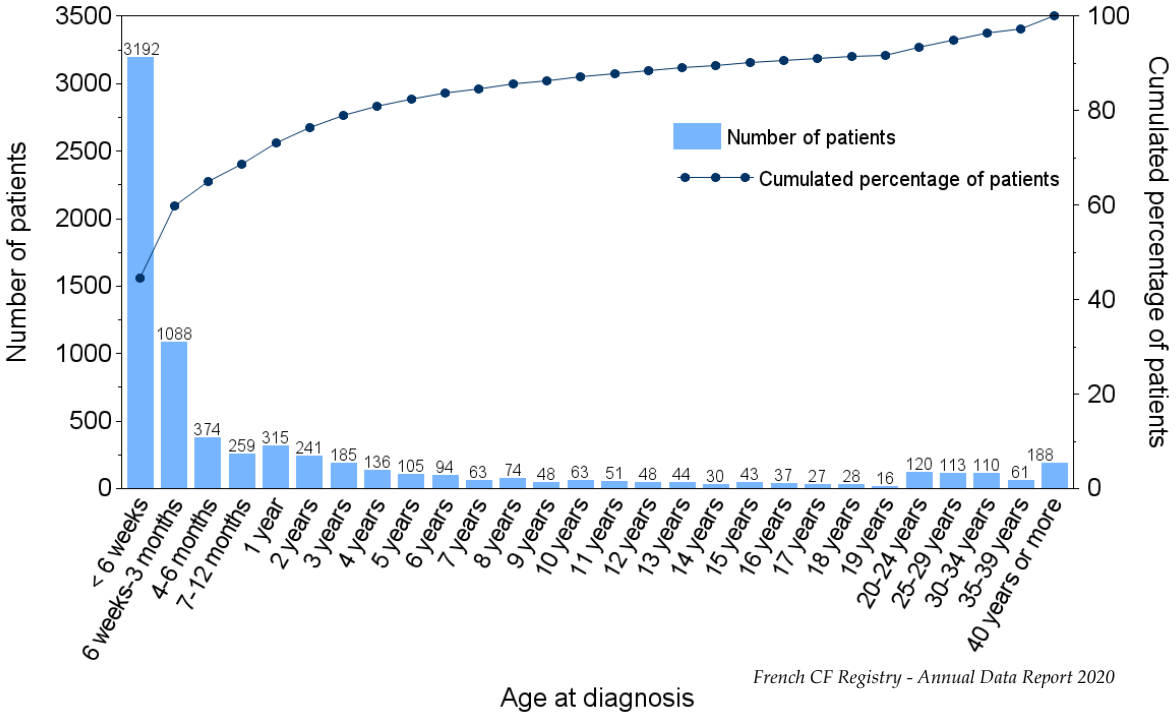
Note: precision on medically assisted reproduction was missing for 1 patient.

4. Diagnosis

Main characteristics

Figure 4.1. Number of patients and cumulative percentage of patients by age at diagnosis

N = 7153 (number of patients whose age at diagnosis is known).



4. Diagnosis

Main characteristics

Table 4.1. Diagnosis characteristics

Characteristics	**2020**
ALL PATIENTS	
Patients whose age at diagnosis is known - N (%) *	7153 (99.1 %)
Age at diagnosis	
- Median age (months)	1.9
- Mean age (years)	4.6
- Minimum age (years)	0
- Maximum age (years)	81
NEW PATIENTS DIAGNOSED DURING THE YEAR	
Number of patients	
New patients - N (%)	158 (2.2 %)
- Including 2020 newborn patients - N	108
Age at diagnosis	
- Median age (months)	1.1
- Mean age (years)	7.2
- Minimum age (years)	0
- Maximum age (years)	81
Context of diagnosis	
1. Screened positive newborns (NBS)	**118**
- including Prenatal diagnosis - N (%)	7 (5.9 %)
- including Meconium ileus - N (%)	11 (9.3 %)
2. Diagnosis on symptoms (NBS excluded)	**40**
- including Meconium ileus - N (%)	1 (2.5 %)
- including Symptoms (other than MI):- N (%)	39 (97.5 %)
- Mean age at diagnosis (years)	28.4

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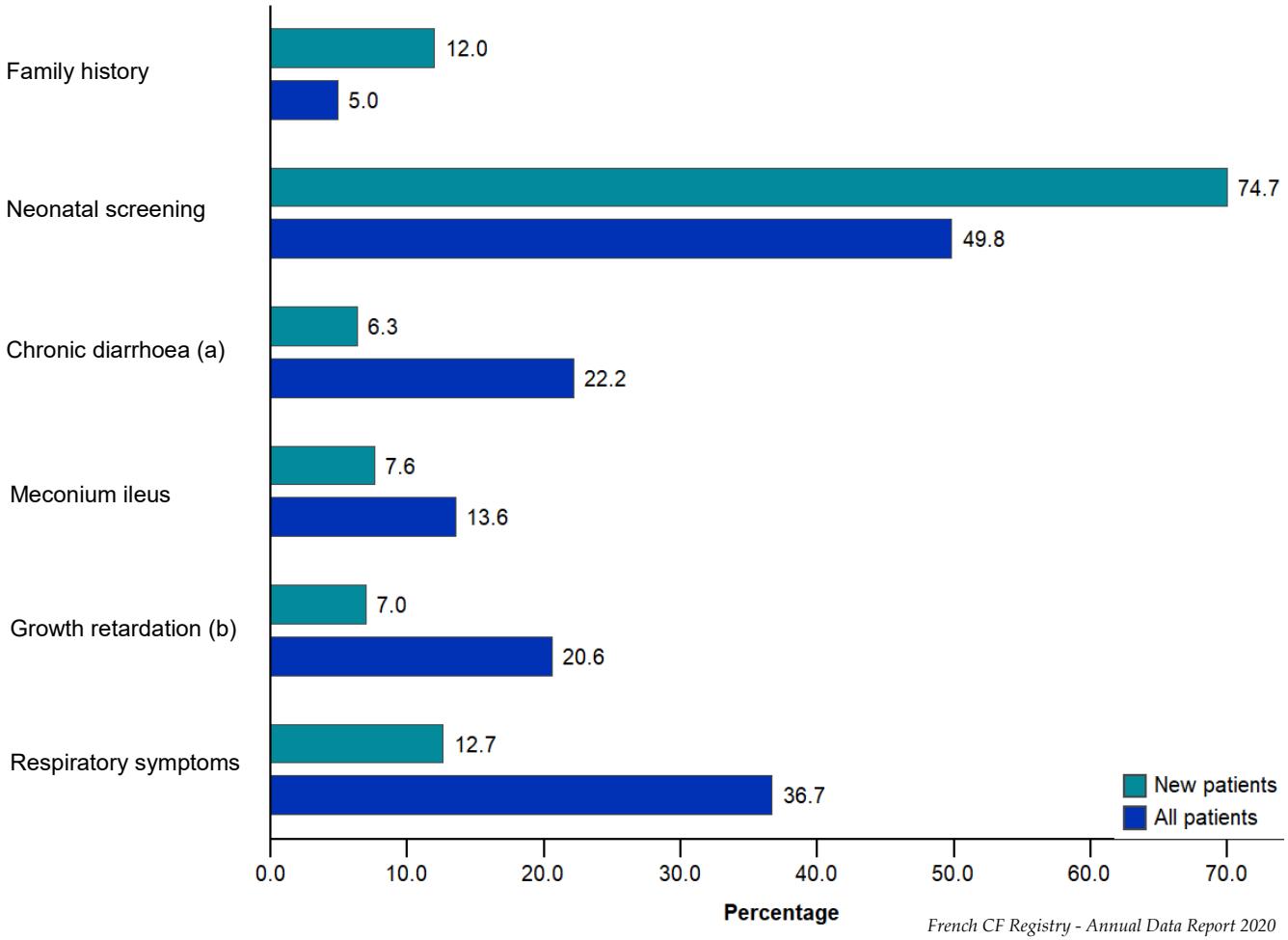
Among the 158 new patients, 108 were born in 2020. The method used to compile this report (patients seen in a care centre in 2020) means that infants born in 2020 and seen for the first time in 2021 are not included yet. For information purposes only, 17 newborns in 2019 were diagnosed in 2020 through neonatal screening. In the 2019 age pyramide, the number of patients aged 0 was 109 and should have been 109+17=126.

The number of patients diagnosed by neonatal screening (118) given in this report is not the actual number for France during the year, but represents the patients for whom screening resulted in diagnosis. It excludes patients for whom the diagnosis was made before the result of screening.

4. Diagnosis

Diagnosis signs

Figure 4.2. Diagnosis signs (most frequent ones)

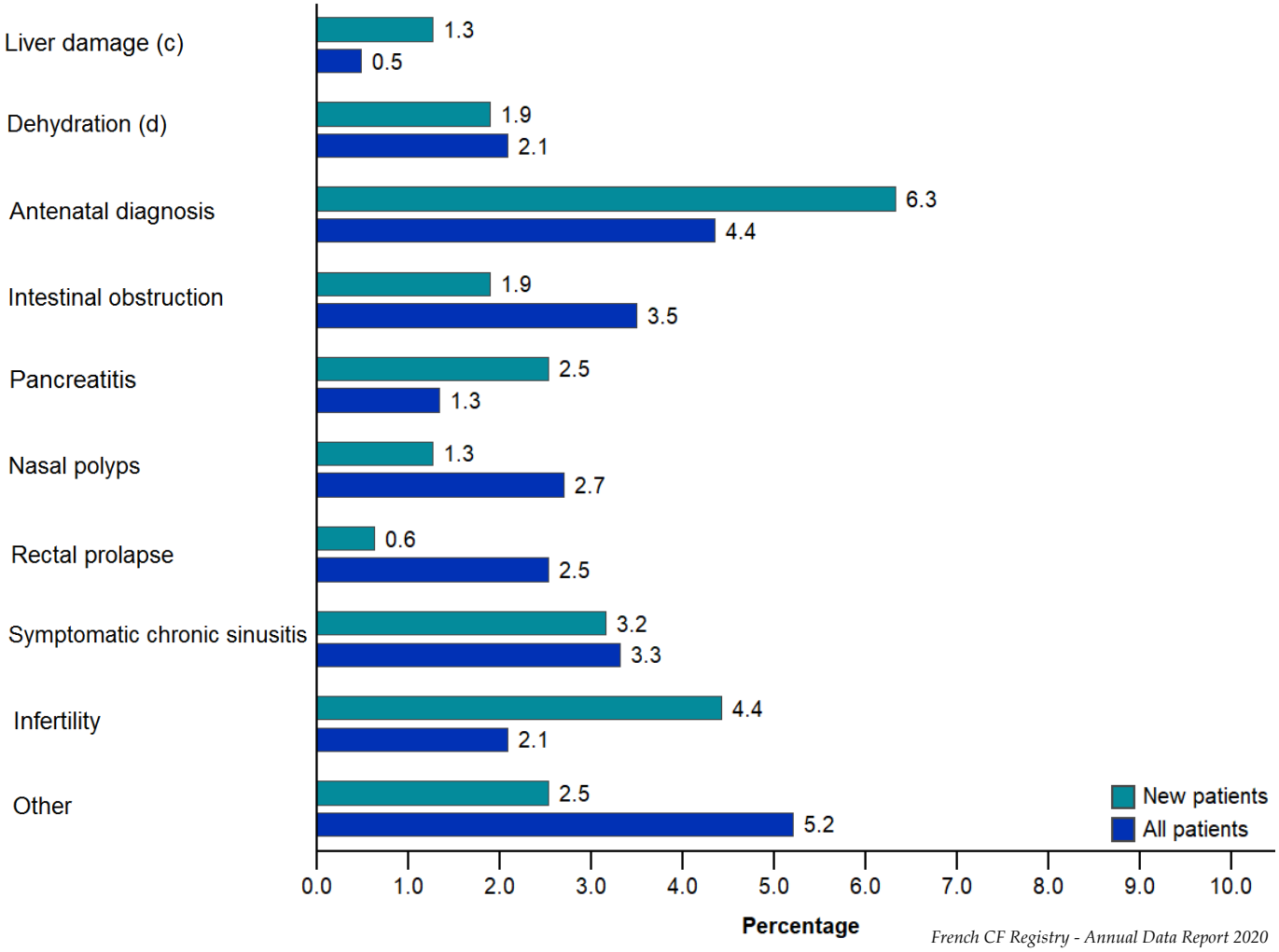


(a) Chronic diarrhoea / Steatorrhoea / Malabsorption
(b) Growth retardation / Malnutrition

4. Diagnosis

Diagnosis signs

Figure 4.3. Diagnosis signs (less frequent ones)



(c) Liver damage / Jaundice / Portal hypertension
(d) Dehydration / Electrolyte inbalance

4. Diagnosis

Genotypes

Table 4.2. Prevalence of the 40 most common mutations

Mutations	Number of patients *	Proportion (%)
F508del	5999	83.1
G542X	395	5.5
N1303K	303	4.2
2789+5G>A	190	2.6
1717-1G>A	153	2.1
R117H	132	1.8
G551D	127	1.8
R553X	127	1.8
W1282X	110	1.5
3849+10kbC>T	106	1.5
L206W	96	1.3
I507del	88	1.2
711+1G>T	86	1.2
3272-26A>G	82	1.1
Y122X	80	1.1
2183AA>G	75	1.0
D1152H	75	1.0
R347P	72	1.0
3120+1G>A	60	0.8
R1162X	59	0.8
G85E	53	0.7
R334W	53	0.7
Y1092X	53	0.7
R347H	47	0.7
3659delC	46	0.6
A455E	46	0.6
S945L	43	0.6
1078delT	40	0.6
1811+1.6kbA>G	36	0.5
394delTT	35	0.5
E60X	34	0.5
621+1G>T	33	0.5
R1066C	33	0.5
W846X	32	0.4
S1251N	26	0.4
L997F	23	0.3
E585X	22	0.3
1677delTA	21	0.3
Q220X	21	0.3
2711delT	19	0.3

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* With at least one copy of the considered mutation.

4. Diagnosis

Genotypes

Table 4.3. Age of patients by genotype

Genotypes	Patients		Age (years)		
	Number	%	Mean	Median	Max
F508del / F508del	2978	41.3	22.6	21.6	66.1
F508del / Other	2984	41.4	24.3	21.8	78.6
Other/ Other	1109	15.4	24.1	21.1	81.9
Subtotal (non missing genotypes)	7071	98.0	23.5	21.6	81.9
F508del / Missing	37	0.5	41.5	40.4	85.6
Other/ Missing	57	0.8	42.3	39.4	79.5
Missing/ Missing	51	0.7	40.1	36.2	76.7
Subtotal (partial genotypes / missing)	145	2.0	41.3	38.7	85.6
Total	7216	100			

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Table 4.4. Age of patients with a gating, nonsense or R117H mutation

	Patients		Age (years)		
	Number	%	Mean	Median	Max
At least one gating mutation	209	2.9	25.8	22.9	70.0
At least one nonsense mutation	1128	15.6	22.3	20.4	78.8
At least one R117H mutation	132	1.8	20.5	15.8	77.2

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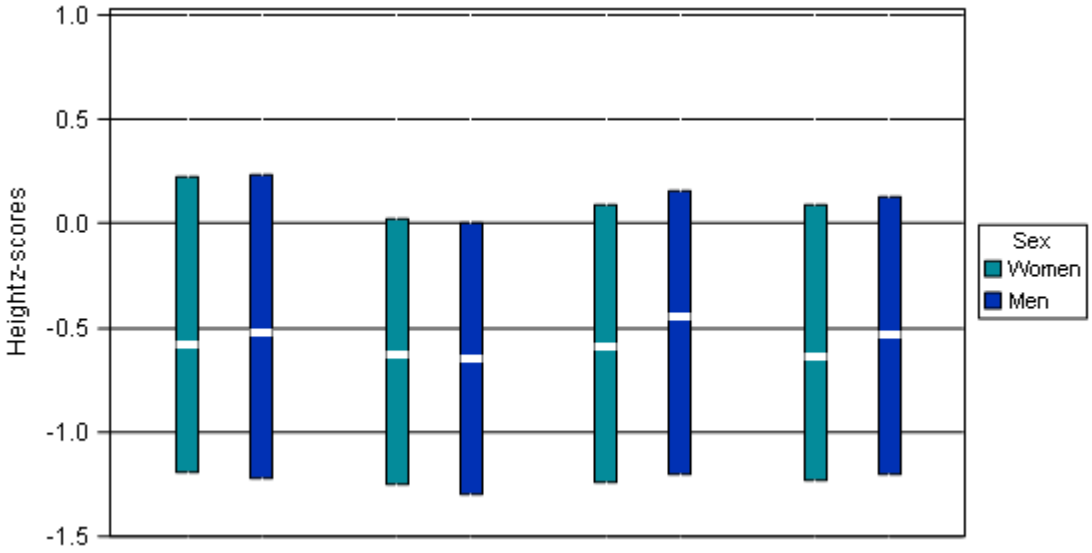
Gating mutations doesn't prevent the CFTR protein from reaching the cell membrane but alter choride transport.

Nonsense mutations cause a premature stop codon thus an absence of CFTR protein production.

5. Anthropometry

Height and weight

Figure 5.1. Height z-scores* in children, by age group and sex



Age groups (years)		00-04	05-09	10-14	15-18	Total
Mean height z-score	Women	-0.47	-0.64	-0.57	-0.64	-0.58
	Men	-0.46	-0.62	-0.51	-0.56	-0.54
Median height z-score	Women	-0.59	-0.63	-0.59	-0.64	-0.62
	Men	-0.53	-0.65	-0.45	-0.54	-0.55

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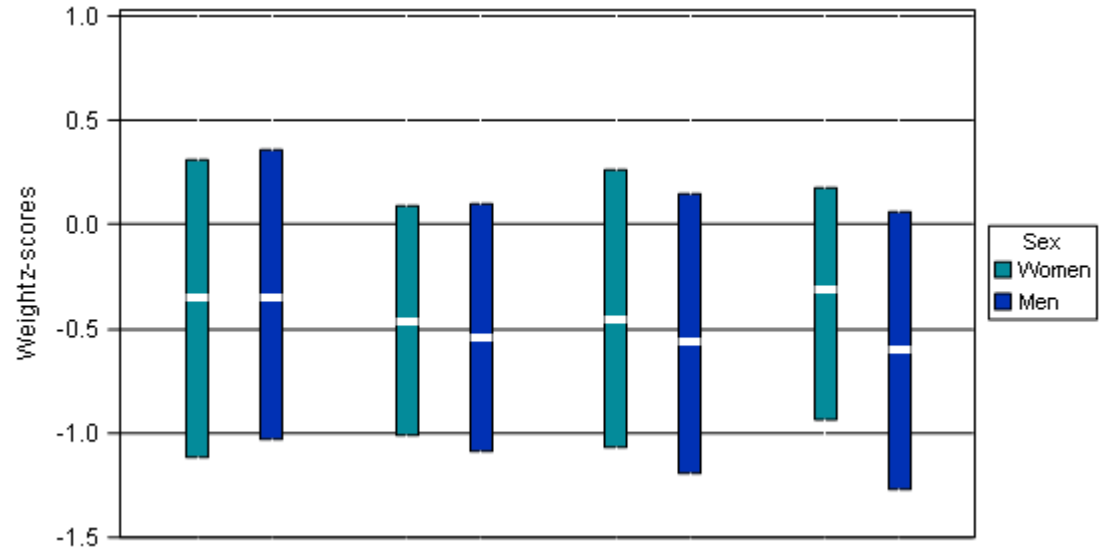
Figure 5.2. Weight z-scores* in children, by age group and sex



Age groups (years)		00-04	05-09	10-14	15-18	Total
Mean weight z-score	Women	-0.38	-0.45	-0.39	-0.38	-0.40
	Men	-0.33	-0.47	-0.49	-0.60	-0.48
Median weight z-score	Women	-0.36	-0.47	-0.46	-0.31	-0.42
	Men	-0.36	-0.54	-0.56	-0.60	-0.53

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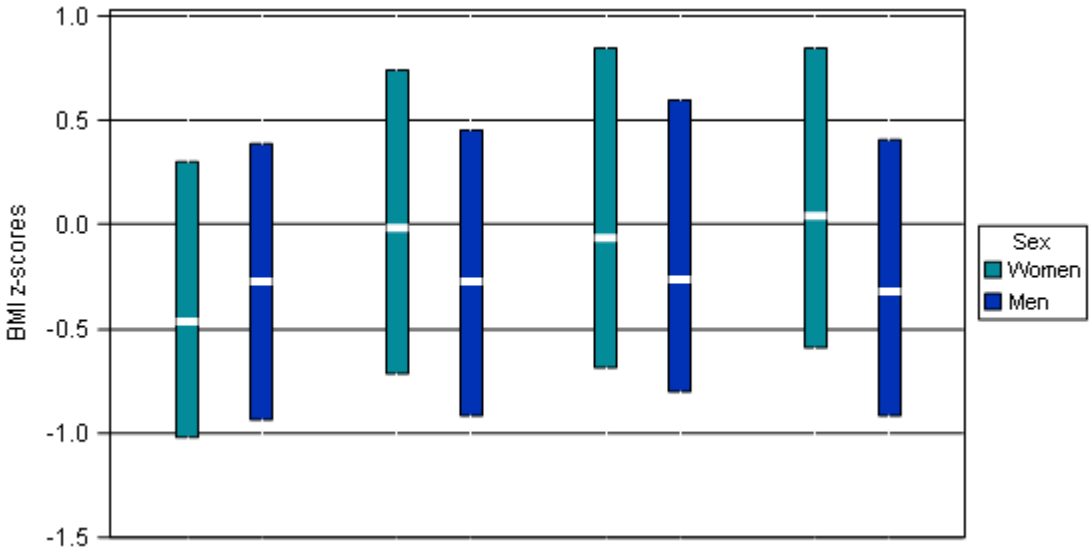
*See explicative note p 22

5. Anthropometry

Body Mass Index (BMI)

Figure 5.3. BMI z-scores in children, by age group and sex



Age groups (years)		00-04	05-09	10-14	15-18	Total
Mean BMI z-score	Women	-0.32	0.13	0.16	0.20	0.06
	Men	-0.25	-0.16	-0.01	-0.19	-0.15
Median BMI z-score	Women	-0.47	-0.02	-0.07	0.04	-0.09
	Men	-0.28	-0.27	-0.26	-0.32	-0.28
BMI z-score >=0 (% of patients)	Women	34.6	49.9	49.0	51.7	46.8
	Men	39.4	40.9	41.0	40.4	40.5

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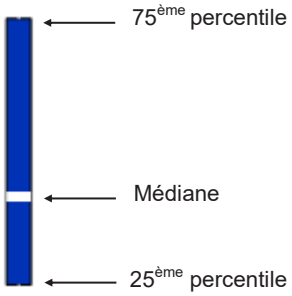
The z-score is a anthropometric reduced centered variable (Z = [measure-mean]/standard deviation), ajusted for gender and age; the mean and standard deviation are taken from the French reference population with the same gender and age as the patient. This index measures the difference with population norms and a negative score means growth retardation.

- Since this 2020 report, reference population used for the calculation of Z-scores for height and weight is the French reference population AFPA-CRESS/Inserm -CompuGroup Medical 2018.

- BMI z-score was calculated with respect to the French reference population (Rolland-Cachera MF et al. A. Body Mass Index variations: centiles from birth to 87 years. Eur J Clin Nutr 1991;45:13-21).

Explanation for figures pages 21 to 24

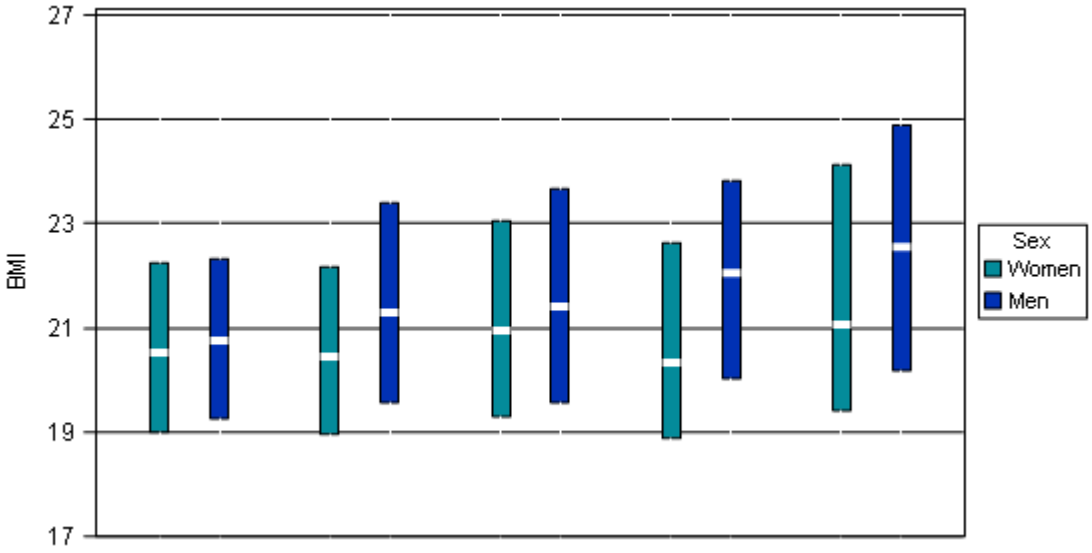
Those figures represent z-scores of anthropométrie and spirometry values.
For each age and sex group, median values are the white lines, extremes are the 25th and 75th percentiles.



5. Anthropometry

Body Mass Index (BMI)

Figure 5.4. BMI in adults, by age group and sex



Age groups (years)		19-24	25-29	30-34	35-39	40 ou +	Total
Mean BMI	Women	21.0	20.9	21.5	21.1	22.3	21.4
	Men	21.1	21.7	21.9	22.1	22.8	21.9
Median BMI	Women	20.5	20.5	21.0	20.3	21.1	20.7
	Men	20.8	21.3	21.4	22.1	22.6	21.5
BMI ≥ 22 (%)	Women	28	28	36	30	39	33
BMI ≥ 23 (%)	Men	17	28	31	35	44	31
BMI < 18.5 (%)	Women	18	17	13	20	14	16
	Men	1	13	14	10	11	13

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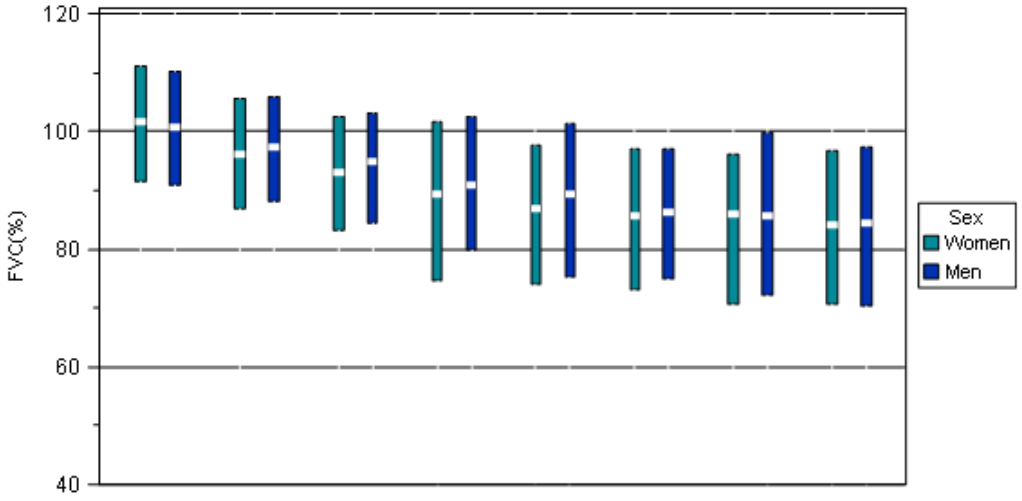
In adults, mean height was 172 cm for men and 160 cm for women.

In adults, mean weight was 65 kg for men and 55 kg for women.

6. Spirometry

95.2% Patients aged 6 and over carried out spirometry

Figure 6.1. FVC (% predicted)*, by age group and sex



Age groups (years)		05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +	Total
Mean FVC	Women	101.3	95.5	92.1	88.2	85.2	84.6	84.2	83.0	89.1
	Men	99.7	96.8	93.7	90.4	87.1	85.0	85.0	83.2	89.8
	All patients	100.5	96.1	92.9	89.3	86.2	84.8	84.6	83.1	**89.5**
Median FVC	Women	101.7	95.9	93.0	89.5	86.8	85.7	85.8	84.2	90.6
	Men	100.8	97.3	95.0	90.9	89.4	86.3	85.6	84.3	91.6
	All patients	101.4	96.8	94.4	90.3	87.6	86.1	85.7	84.2	**91.0**

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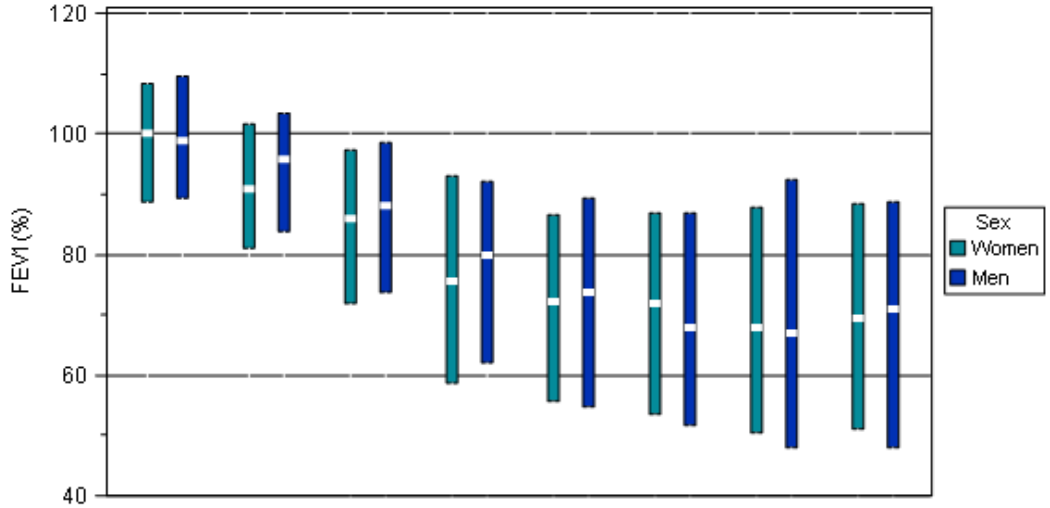
Figure 6.2. FEV_1 (% predicted)*, by age group and sex



Age groups (years)		05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +	Total
Mean FEV_1	Women	98.0	90.1	83.5	75.7	72.0	70.4	69.9	69.7	78.5
	Men	97.9	92.7	85.6	77.5	72.6	68.6	69.3	69.0	78.9
	All patients	97.9	91.3	84.6	76.7	72.3	69.5	69.6	69.3	**78.7**
Median FEV_1	Women	100.0	91.0	86.1	75.6	72.2	71.9	67.8	69.5	80.6
	Men	98.8	95.7	88.1	79.9	73.6	67.9	67.0	71.1	82.0
	All patients	99.1	93.3	87.2	78.2	73.2	69.6	67.3	70.0	**81.4**

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The pulmonary function tests need an active participation of the patient, difficult to obtain before 6 years of age.
The forced vital capacity (FCV) and the forced expiratory volume in the first second (FEV1) are given in % predicted (Quanjer PH *et al*. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012;40(6):1324–1343).

*See explicative note p 22.

6. Spirometry

Figure 6.3. FEV_1 (% predicted) classes

Values of FEV1(% predicted) are classified in four « functional » groups according to various degrees of bronchial obstruction.

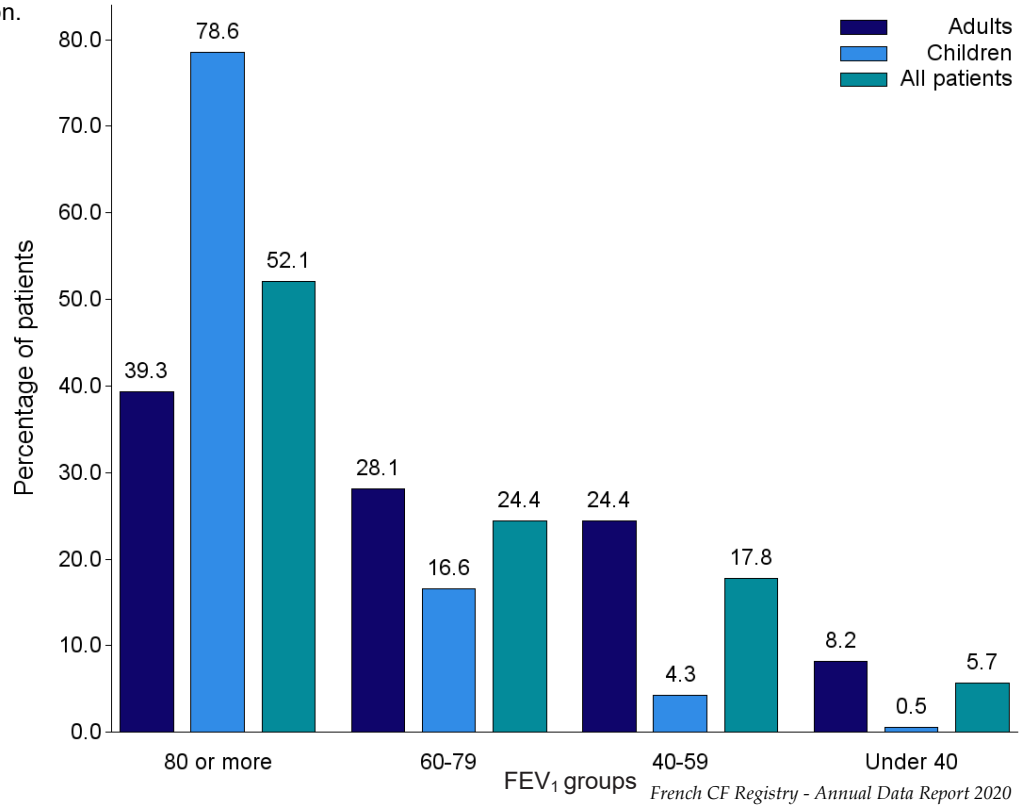
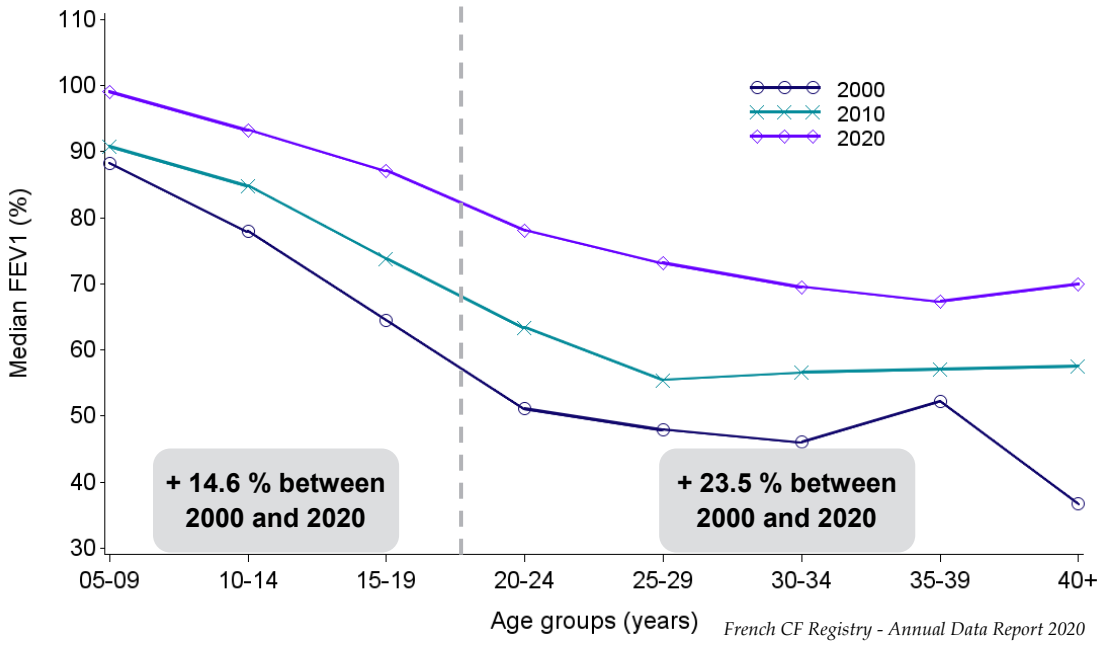


Figure 6.4. Median FEV_1 (% predicted) in 2020 compared with 2000 and 2010



Last FEV1 (%) value of the year was collected from 1992 to 2010, and best value since 2011.

The median FEV1 was 78.2 % for patients aged 6 to 19 years in 2000, and 92.8 % in 2020. It was 48.9 % in 2000 and 72.4 % in 2020 for patients aged 20 years or more.

See appendix 2 for additional information on spirometry and transplantation

7. Microbiology

Table 7.1. Sputum cultures

Patients with at least one sputum	N	*Proportion (%)*
All patients	6015	*83.4 %*
Children	2801	*96.3 %*
Adults	3214	*74.6 %*

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In 2020, 83.4 % of the patients had at least one sputum culture. Among the patients without sputum culture (N=1201), 59.1 % of them were transplanted.

Table 7.2. Distribution of the respiratory germs

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%*
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	
Patients with at least one sputum	**621**	**763**	**858**	**886**	**725**	**564**	**545**	**375**	**678**	**6015**	**83.4 %**
Normal flora	289	294	281	192	66	42	37	34	58	1293	17.9 %
Pseudomonas aeruginosa, including:	*106*	*151*	*263*	*343*	*383*	*334*	*348*	*238*	*400*	*2566*	*35.6 %*
- Chronic P. aeruginosa	*11*	*32*	*95*	*170*	*234*	*224*	*254*	*180*	*289*	*1489*	*20.6 %*
Staphylococcus, including:	427	595	717	743	580	430	363	232	347	4434	61.4 %
- MSSA	*414*	*582*	*698*	*710*	*541*	*401*	*314*	*209*	*311*	*4180*	*57.9 %*
- Chronic *MSSA*	*171*	*298*	*419*	*464*	*355*	*233*	*183*	*130*	*181*	*2434*	*33.7 %*
- MRSA	*18*	*18*	*29*	*62*	*63*	*49*	*63*	*30*	*45*	*377*	*5.2 %*
- Chronic *MRSA*	*4*	*8*	*14*	*37*	*29*	*24*	*49*	*18*	*29*	*212*	*2.9 %*
Achromobacter spp.	*15*	*30*	*51*	*92*	*81*	*51*	*64*	*34*	*41*	*459*	*6.4 %*
Burkholderia cepacia	*1*	*7*	*12*	*20*	*32*	*27*	*17*	*14*	*20*	*150*	*2.1 %*
- Chronic B. cepacia	*.*	*5*	*9*	*14*	*18*	*23*	*13*	*9*	*12*	*103*	*1.4 %*
Stenotrophomonas maltophilia	*56*	*70*	*114*	*113*	*95*	*63*	*61*	*37*	*58*	*667*	*9.2 %*
Haemophilus influenzae	*106*	*166*	*115*	*102*	*93*	*71*	*59*	*45*	*54*	*811*	*11.2 %*
Pneumococcus	32	22	12	3	4	6	10	7	13	109	1.5 %
Enterobacteria	72	29	35	45	67	44	57	21	70	440	6.1 %

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* Percentage with respect to the entire population.

Chronic colonization: more than 50 % of positive test results in the last 12 months (with at least 4 tests during this period) and/or significant increase in anti-PA antibodies (according to the laboratory).

7. Microbiology

Figure 7.1. Clinically important bacteria

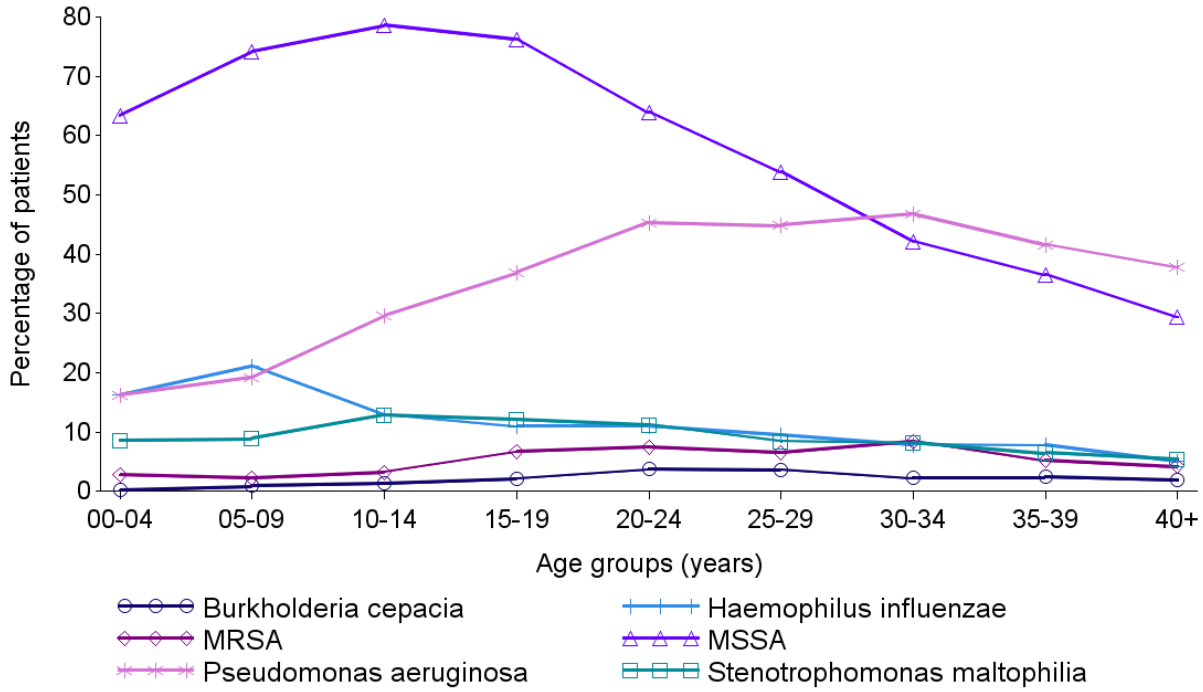

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Table 7.3. Bcc species

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%*
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	
Patients with *Bcc*	*1*	*7*	*12*	*20*	*32*	*27*	*17*	*14*	*20*	*150*	
B. multivorans	.	4	5	8	14	12	6	4	9	62	41.3 %
B. cenocepacia	.	.	1	1	1	5	5	2	4	19	12.7 %
B. cepacia	1	.	4	5	7	4	3	5	4	33	22.0 %
B. stabilis	.	.	.	.	.	1	.	.	.	1	0.7 %
B. vietnamiensis	.	.	.	.	1	1	.	.	.	2	1.3 %
B. gladioli	.	3	2	6	6	2	3	1	2	25	16.7 %
Any other Burkholderia	.	.	.	.	2	.	.	.	1	3	2.0 %

* Percentage of the number of patients colonized by Bcc.

7. Microbiology

Figure 7.2. Comparison of germs in 2020 and in 2010

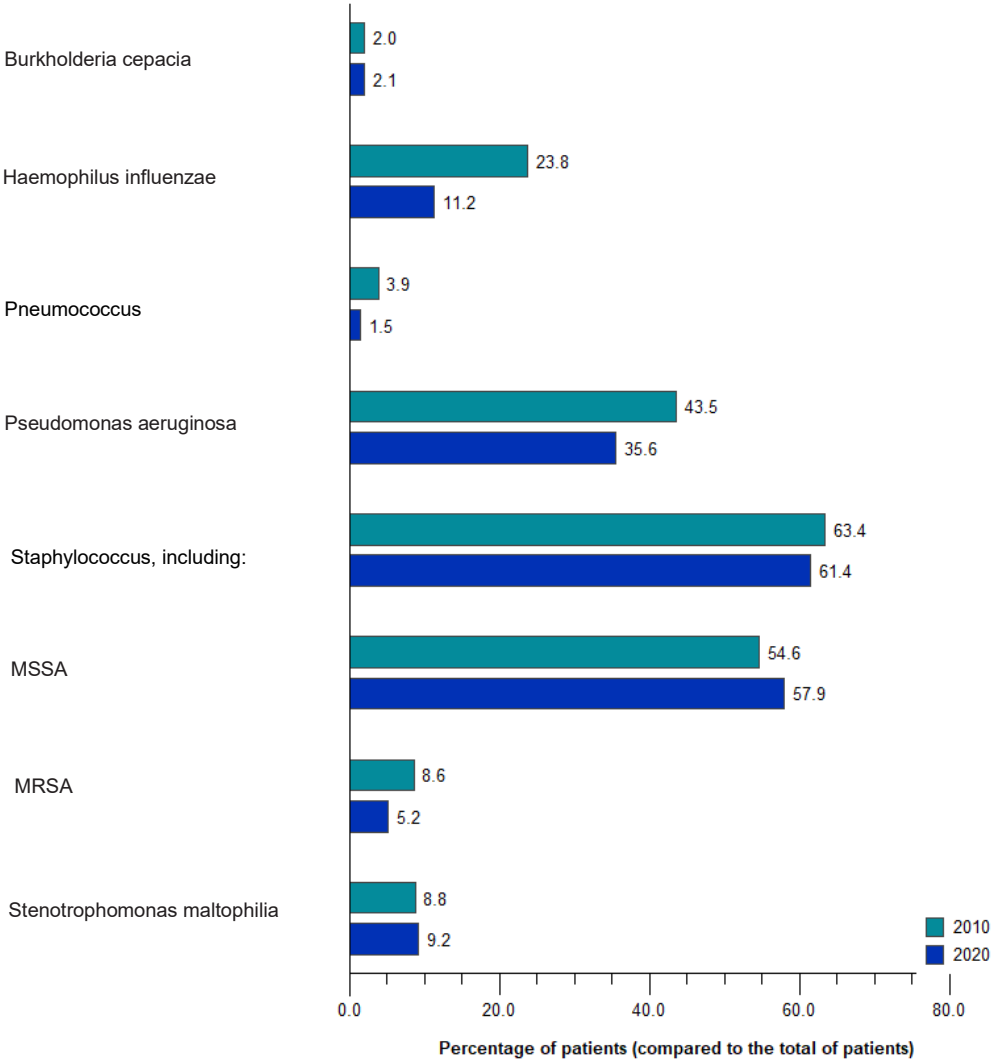

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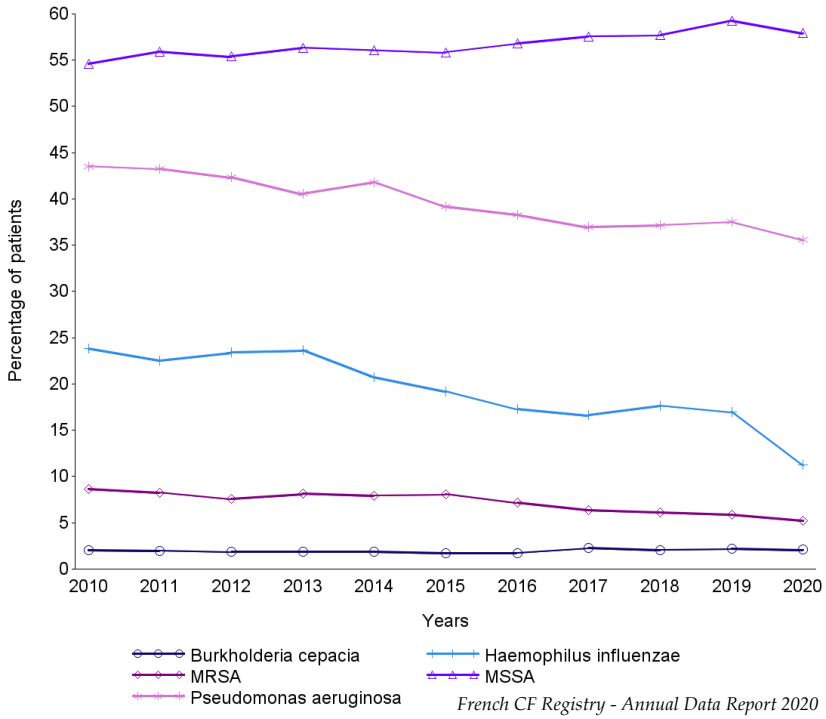
Figure 7.3. Evolution of respiratory germs since 2010



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7. Microbiology

Table 7.4. Fungal elements, mycobacteria and viruses

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%*
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*745*	*571*	*1055*	*7216*	
Aspergillus fumigatus	23	80	214	284	304	219	197	134	213	1668	23.1
Other aspergillus	4	14	29	35	33	30	32	17	44	238	3.3
Candida albicans	81	144	213	276	283	212	227	159	252	1847	25.6
Candida non albicans	50	40	68	66	75	61	69	57	91	577	8.0
Search for mycobacteria	311	487	583	646	542	397	383	274	457	4080	56.5
- Abscessus complex	.	2	6	10	7	6	4	1	4	40	0.6
- Avium complex	.	.	1	2	1	1	2	.	2	9	0.1
- Other mycobacteria	10	5	23	28	46	33	32	10	24	211	2.9
Search for viruses	128	105	115	135	83	72	80	64	104	886	12.3
- Coronavirus	11	8	14	9	4	15	9	8	20	98	1.4
- Influenza A	3	.	5	9	3	5	4	5	5	39	0.5
- Influenza B	1	5	6	2	.	3	4	1	.	22	0.3

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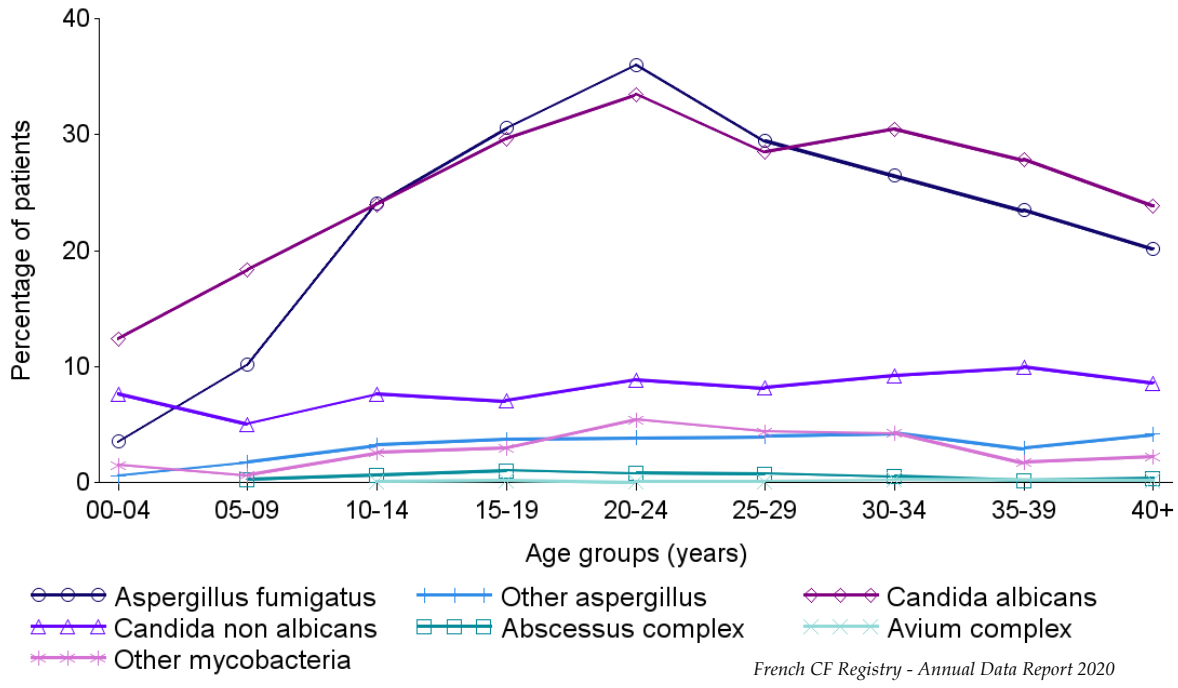
Figure 7.4. Fungal elements, mycobacteria and viruses



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8. Complications

Respiratory

Table 8.1. Respiratory complications and ENT

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	
Pneumothorax	.	.	.	6	9	11	6	1	2	35	0.5
Haemoptysis	.	1	17	60	61	50	71	33	48	341	4.7
ABPA	5	20	57	89	91	68	61	40	51	482	6.7
Non APBA aspergillosis	3	4	10	9	18	17	19	9	18	107	1.5
Pulmonary arterial hypertension	1	.	1	3	5	6	3	7	12	38	0.5
Asthma	115	176	215	223	177	148	137	106	172	1469	20.4
Nasal polyps	18	105	177	196	179	169	159	122	196	1321	18.3
Symptomatic chronic rhinosinusitis	17	67	70	95	139	114	124	120	205	951	13.2
Deafness / Hypoacusia	2	4	8	10	31	97	110	93	195	550	7.6

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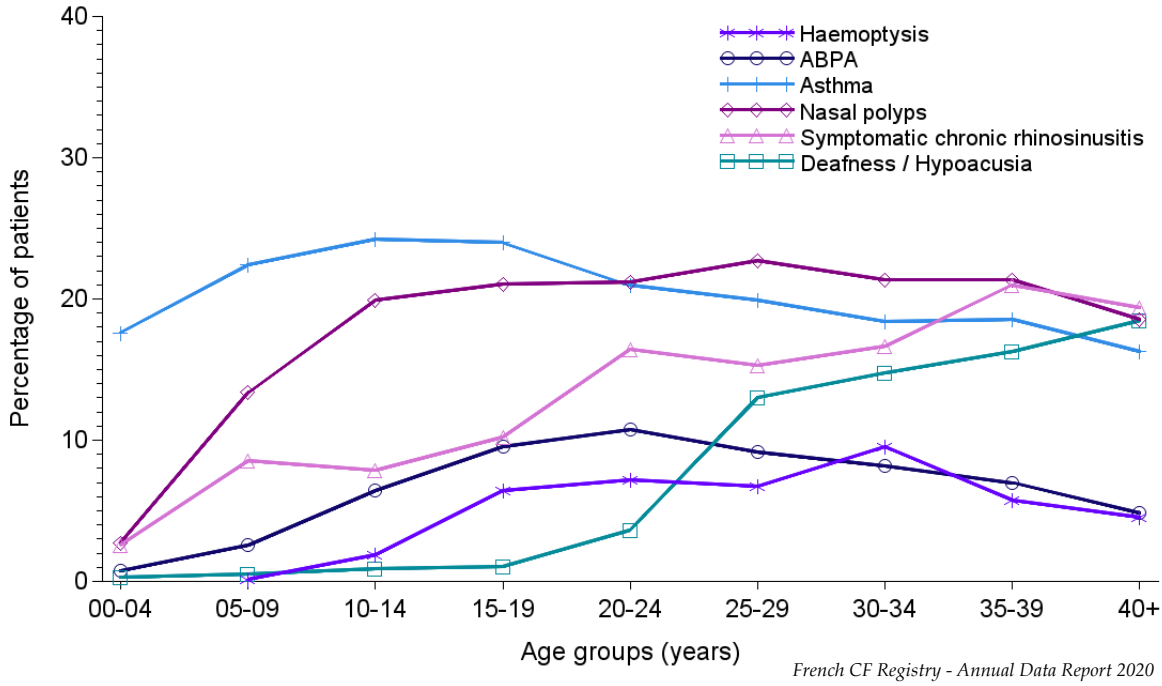
Figure 8.1. Respiratory complications and ENT

Percentage of age groups reporting complications.



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8. Complications

Gastro-intestinal

Table 8.2. Gastro-intestinal complications

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	
Abnormal exocrine pancreatic function	517	621	719	754	727	631	631	480	736	5816	80.6 %
Treated gastro-oesophageal reflux disease	117	99	127	163	253	265	273	247	413	1957	27.1 %
Hepatic disease	30	83	168	229	188	138	136	105	122	1199	16.6 %
- Hepatic disease without cirrhosis	25	67	123	155	130	105	101	78	77	861	11.9 %
- Cirrhosis without portal hypertension	1	3	14	32	27	19	9	7	11	123	1.7 %
- Cirrhosis with portal hypertension	3	13	29	35	28	14	20	19	25	186	2.6 %
Digestive Hemorrhage	.	.	.	1	1	1	2	1	3	9	0.1 %
Gallstones	4	10	14	16	23	31	31	36	42	207	2.9 %
Intestinal obstruction	11	7	18	19	35	21	30	21	40	202	2.8 %
Acute pancreatitis	.	1	5	13	11	6	6	12	14	68	0.9 %

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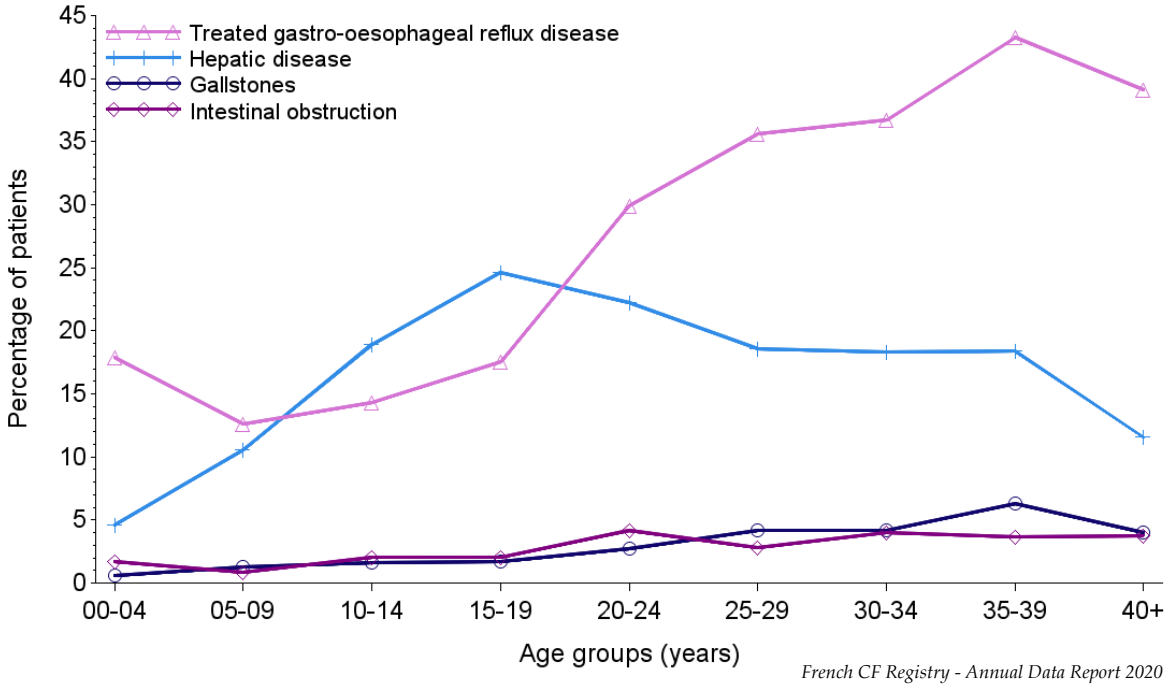
Figure 8.2. Gastro-intestinal complications

Percentage of age groups reporting complications.



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8. Complications

Metabolic complications

32.5% of adult patients are with diabetes mellitus

Table 8.3. Metabolic complications

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	
OGTT done	3	28	326	319	260	145	153	79	129	1442	20.0 %
Glucose intolerancy	1	16	144	194	182	100	107	82	106	932	12.9 %
Total diabetes	.	11	79	170	194	229	260	239	399	1581	21.9 %
Non insulin-dependent diabetes	.	5	22	43	33	34	24	25	35	221	3.1 %
Diabetes traited with oral antidiabetic agent	.	.	2	7	9	11	9	11	44	93	1.3 %
Insulin-dependent diabetes	.	6	58	125	157	189	229	207	329	1300	18.0 %
Degenerative complications of diabetes	.	.	.	1	4	11	20	20	29	85	1.2 %
- Retinopathy	.	.	.	.	1	10	14	10	18	53	0.7 %
- Nephropathy	.	.	.	1	2	4	13	11	15	46	0.6 %
- Neuropathy	.	.	.	.	1	.	.	2	5	8	0.1 %
- Diabetic macroangiopathy	.	.	.	.	.	2	.	.	1	3	0.0 %
Adrenal insufficiency	5	3	4	10	9	10	12	15	23	91	1.3 %

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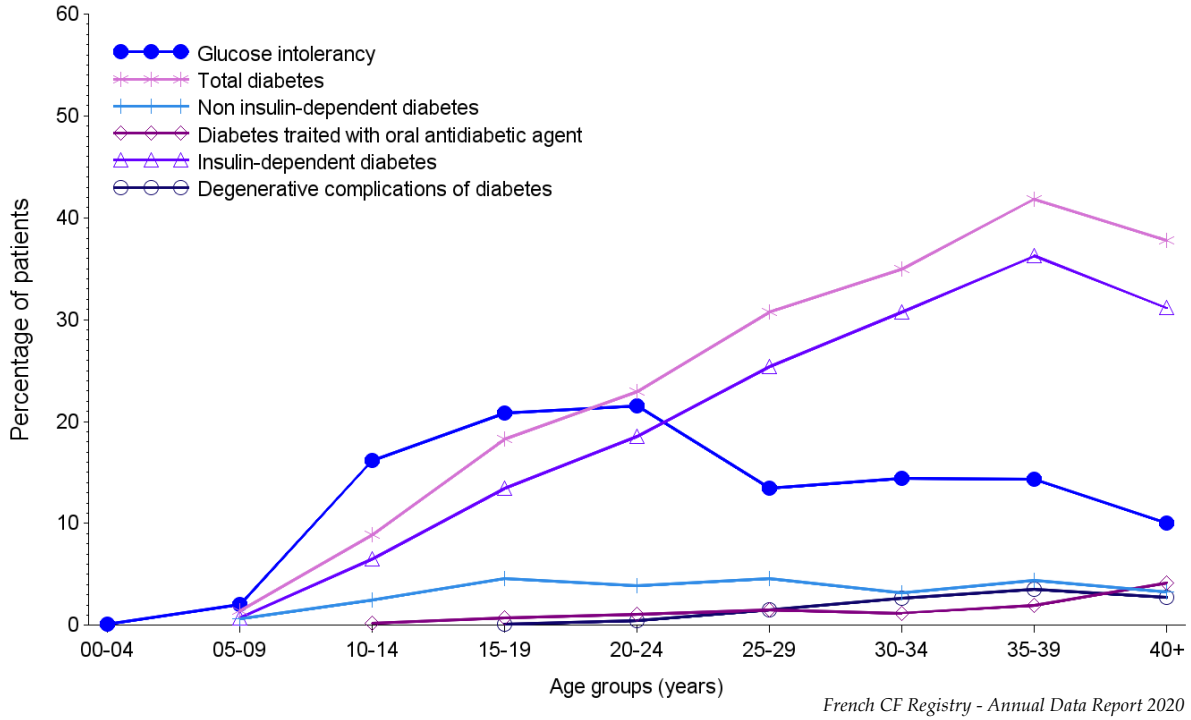
The line « Total diabetes » sums the number of patients having at least one type of diabetes. Among the 1581 patients, 10 patients presented with both types of diabetes during the year.

Figure 8.3. Metabolic complications

Percentage of age groups reporting complications.



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8. Complications

Other complications

Table 8.4. Other complications

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	
Cancer	1	.	2	2	6	4	10	17	41	83	1.2 %
Osteopenia / osteoporosis	.	4	20	75	133	160	163	180	345	1080	15.0 %
Bone fracture	3	.	4	1	7	6	8	7	11	47	0.7 %
Arthropathy	1	2	7	17	18	21	21	39	72	198	2.7 %
Urinary incontinence	.	2	4	2	7	11	8	8	26	68	0.9 %
Renal lithiasis	1	1	1	3	3	11	13	13	16	62	0.9 %
Treated arterial hypertension	.	1	2	4	17	39	83	112	237	495	6.9 %
Terminal renal failure	.	.	1	.	1	2	3	12	20	39	0.5 %
Depression	.	4	31	36	67	76	88	93	193	588	8.1 %

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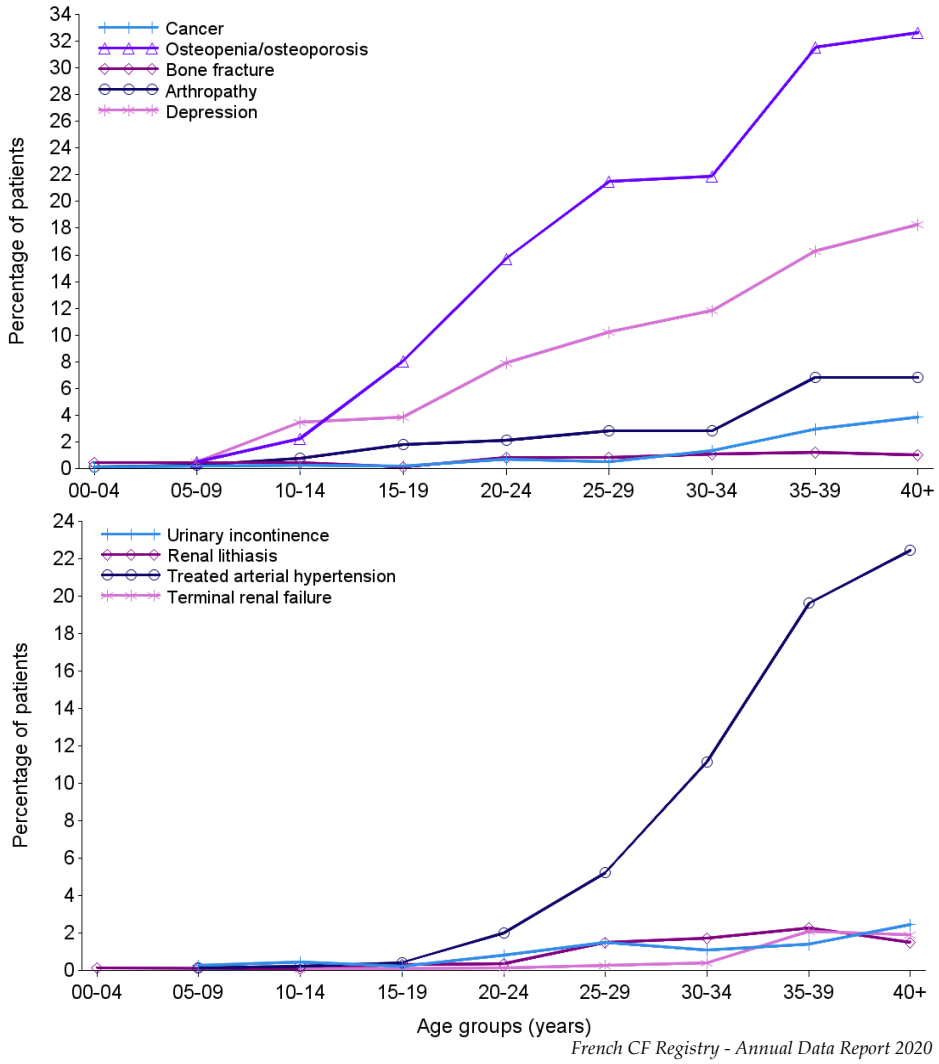
Figure 8.4. Other complications

Percentage of age groups reporting complications.



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9. Transplantation

21.6% of adult patients are living with a transplant

Table 9.1. Characteristics of the patients on waiting list and of transplant recipients

Were included in this table all the patients seen and/or dead in 2020.

	All years	2020
WAITING LIST	All waiting patients	Listed in 2020
Nb of patients	**88**	**30**
Mean age (years) and standard deviation (SD)	32.4 ± 10.9	31.9 ± 11.2
Extremes of age (years)	9.5-59.3	13.0-59.3
Deaths on waiting list	0	0
TRANSPLANTATION	All transplanted *	Transplanted in 2020
Nb of patients	**955**	**50**
Single organ transplant:		
- bilateral lung - N (%)	909 (95.2 %)	36 (72.0 %)
- liver - N (%)	32 (3.4 %)	4 (8.0 %)
- kidney - N (%)	71 (7.4 %)	6 (12.0 %)
- bilobar lung transplantation, N(%)	1 (0.1 %)	
- single lung - N (%)	9 (0.9 %)	
- pancreatic islets, N(%)	1 (0.1 %)	
- bone marrow - N (%)	1 (0.1 %)	
Multiple organ transplant:		
- heart-lung - N (%)	23 (2.4 %)	
- heart-lung / liver - N (%)	2 (0.2 %)	
- bilateral lung / liver - N (%)	27 (2.8 %)	2 (4.0 %)
- bilateral lung / kidney - N (%)	7 (0.7 %)	2 (4.0 %)
- bilateral lung / islet of Langerhans - N (%)	10 (1.0 %)	
- liver / single lung - N (%)	1 (0.1 %)	
- liver / pancreas - N (%)	1 (0.1 %)	
- liver / pancreatic islets - N (%)	1 (0.1 %)	
- kidney / pancreas - N (%)	4 (0.4 %)	
Mean age (years)	36.9	30
SD	10.2	11.3
Extremes of age (years)	6.51-71.3	9.48-59.3
Post-transplantation deaths	25	1

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*** 134 patients underwent two or more organ transplants.**

9. Transplantation

Figure 9.1. Annual number of transplanted patients, since 1992

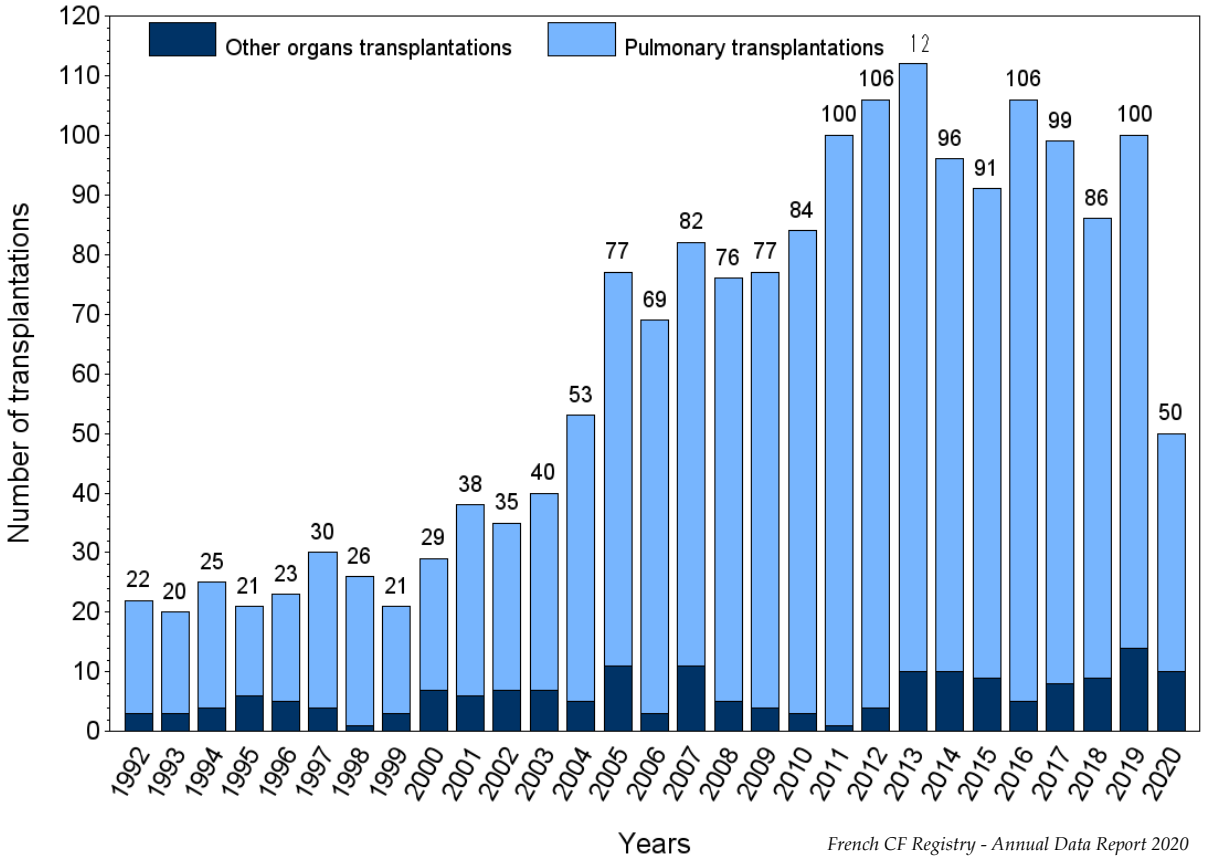

Table 9.2. Annual number of transplanted patients, since 1992

	Years													
Transplant type	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Pulmonary*	71	71	73	81	99	102	102	86	82	101	91	77	86	40
Other organs	11	5	4	3	1	4	10	10	9	5	8	9	14	10

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* single lung, bilobar lung transplantation, bilateral lung or heart-lung (alone or combined with another organ).

Table 9.3. Annual number of surgeries, since 1992

	Types of surgeries			
	Abdominal	Thoracic	ENT	Other
Number of surgeries in 2020	148	81	94	176

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10. Outpatient and inpatient visits

Table 10.1. Characteristics of the visits

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*
< 4 visits per year	127	201	199	224	347	316	273	220	516	2423
≥ 4 visits per years	526	584	689	706	498	428	471	351	540	4793
Outpatient visits*										
Number of patients with at least one outpatient visit	*430*	*497*	*556*	*614*	*612*	*515*	*530*	*393*	*731*	*4878*
Median number of visits	3.0	2.0	3.0	3.0	3.0	3.0	3.0	3.0	2.0	3.0
Mean number of visits	3.2	2.8	3.0	3.2	3.5	3.4	3.6	3.4	3.2	3.2
One-day hospitalizations										
Number of patients with at least one one-day visit	*610*	*749*	*832*	*843*	*664*	*562*	*580*	*448*	*768*	*6056*
Median number of visits	4.0	3.0	3.0	3.0	2.0	2.0	2.0	2.0	2.0	3.0
Mean number of visits	3.7	3.1	3.3	3.2	2.5	2.7	2.7	2.8	2.5	3.0
Inpatient visits										
Number of patients with at least one inpatient visit	*113*	*104*	*186*	*243*	*220*	*202*	*231*	*170*	*281*	*1750*
Median number of visits	1.0	1.0	1.0	1.0	2.0	1.0	1.0	1.0	1.0	1.0
Mean number of visits	1.6	1.6	1.8	2.0	2.2	2.4	1.9	2.0	2.0	2.0
Median duration (days)	5.5	5.0	8.0	9.0	9.0	8.0	7.0	8.0	8.0	8.0
Mean duration (days)	13.9	14.5	15.7	15.2	18.8	17.9	13.8	15.9	16.8	16.0

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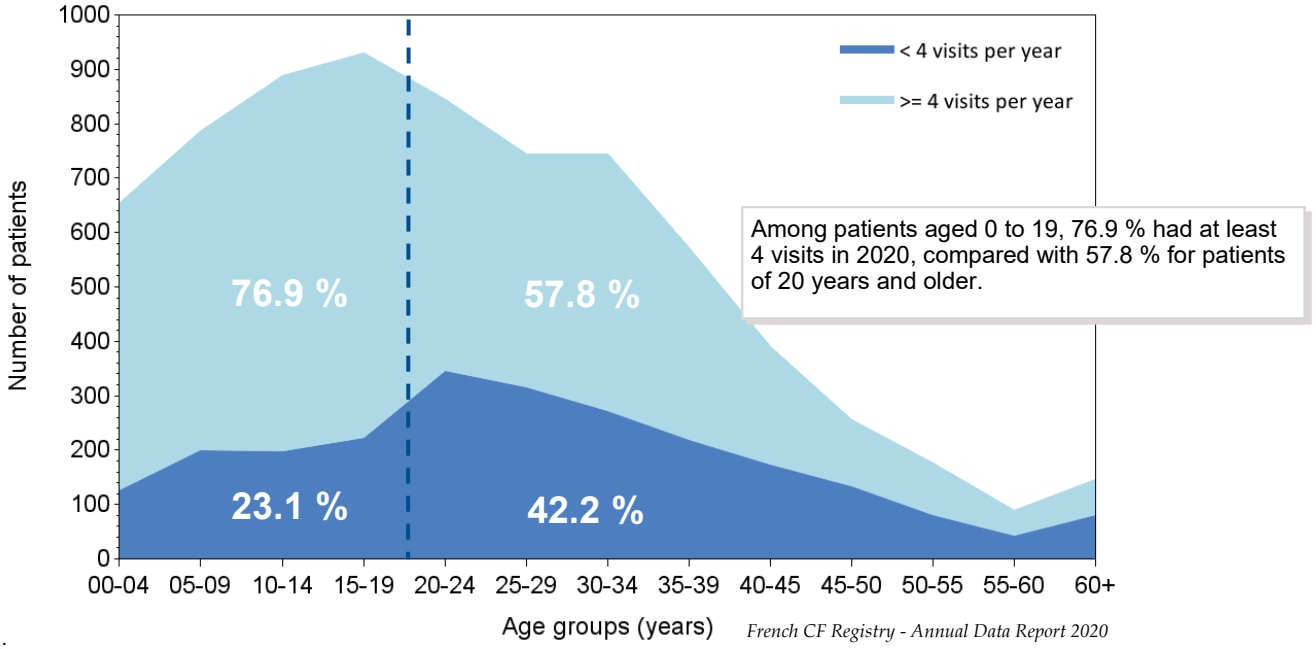
Figure 10.1. Number of visits



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Notes:
- Visits include outpatient, one-day hospitalizations and inpatient visits.
- Mean and median are calculated on patients with at least one visit (any type).

* Due to the exceptional health situation in 2020, many centers have been included in the "Visits" the number of telehealth clinic visits.

11. Therapeutic management

Antibiotic courses – TIVAD

Table 11.1. IV antibiotic courses

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	
All patients	653	785	888	930	845	744	744	571	1056	7216
Nb of patients with at least one course	52 (8.0%)	78 (9.9%)	172 (19.4%)	262 (28.2%)	312 (36.9%)	258 (34.7%)	270 (36.3%)	182 (31.9%)	258 (24.4%)	1844 (25.6%)
- and with TIVAD*	4	22	66	92	112	128	133	79	120	756
- PICC Line	19	21	34	62	76	44	51	43	46	396
- Peripheral venous catheter (PVC)	20	35	51	79	55	44	41	30	47	402
- Midline	7	4	15	37	41	24	28	13	16	185
Nb of courses	65	128	317	513	609	549	584	323	513	3601
Nb of days of courses including:	912	1785	5052	8014	9520	9092	9219	4639	7096	55329
- at hospital	662	860	2118	2521	2110	1752	1533	1176	1628	14360
- at home	250	925	2958	5400	7082	6807	7115	3166	5031	38734
TIVAD* (with or without course)	5	24	72	97	122	140	150	98	148	856

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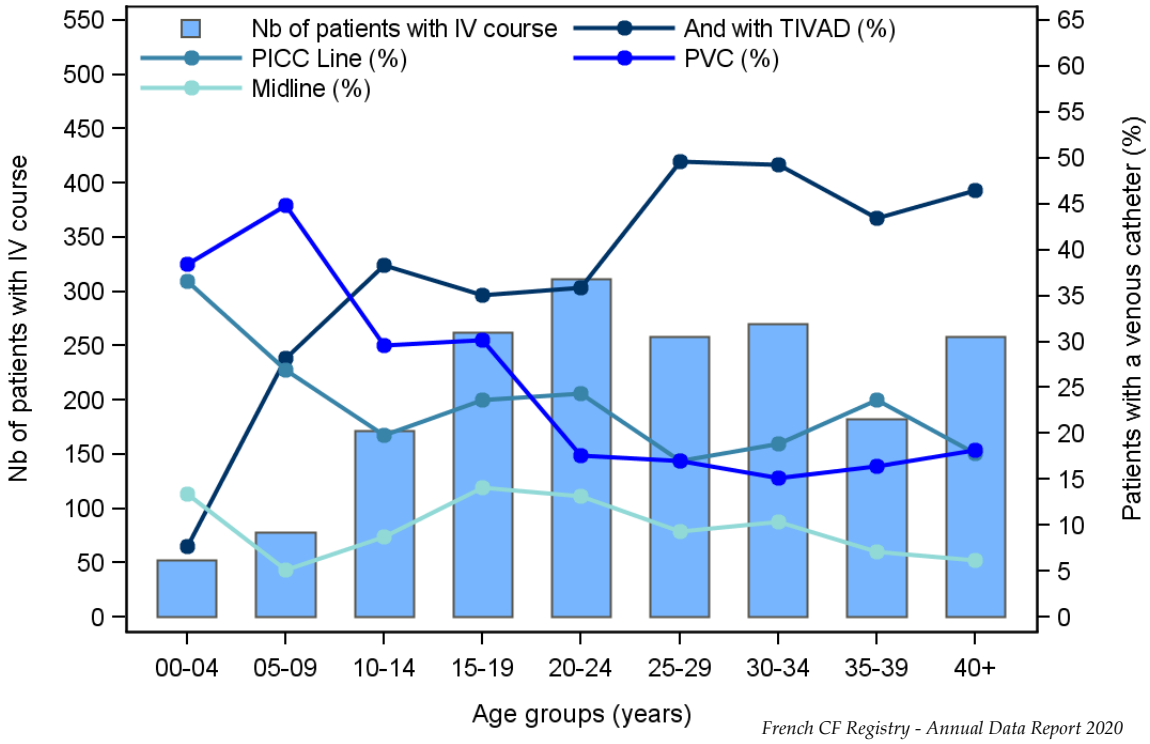
Figure 11.1. Patients with at least one IV antibiotic course and a TIVAD *



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* TIVAD: Totally Implantable Vascular Access Device

11. Therapeutic management

IV antibiotic courses

Table 11.2. Mean number of IV antibiotic courses and of days of courses *

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	
Courses										
Mean number of courses	1.3	1.6	1.9	2.0	2.0	2.1	2.2	1.8	2.0	2.0
SD	0.5	1.2	1.4	1.3	1.5	1.5	2.0	1.3	1.8	1.6
Day of courses		.	.	.	.	.	.	.	.	.
Mean duration of courses (days)	17.5	23.2	29.9	31.1	31.0	36.2	35.9	26.8	29.2	31.0
SD	8.3	19.9	27.0	27.1	32.2	43.0	43.4	21.1	25.9	32.4
Median duration of courses (days)	14.0	14.0	15.0	21.0	20.0	27.0	22.0	15.0	16.0	18.0
1st quartile (Q1)	14.0	14.0	14.0	14.0	14.0	14.0	14.0	14.0	14.0	14.0
3rd quartile (Q3)	16.0	28.0	33.0	42.0	34.0	42.0	37.0	31.0	35.0	35.0

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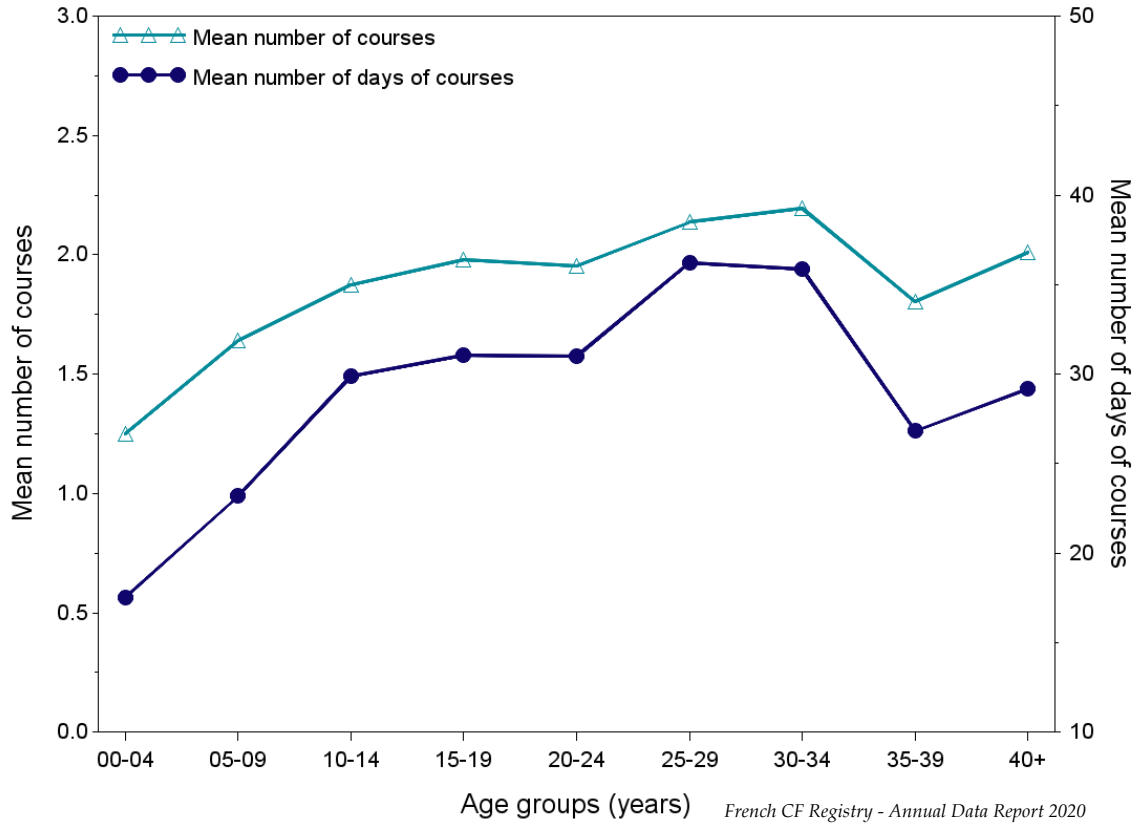
Figure 11.2. Mean number of IV antibiotic courses and of days of courses *



* Among patients having received at least one IV course.

11. Therapeutic management

Respiratory /CFTR gene modulators

Table 11.3. Respiratory therapeutics (≥ 3 months)

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	·
Aerosol therapy*	340	616	789	816	725	613	599	432	787	5717	79.2 %
Oral corticosteroids	4	6	16	37	92	156	162	175	305	953	13.2 %
Azithromycin (or other	58	167	245	309	368	361	383	311	534	2736	37.9 %
Oxygen therapy	1	.	8	27	39	41	32	38	95	281	3.9 %
Nasal ventilation	2	5	19	39	24	26	27	31	77	250	3.5 %
Pulmonary rehabilitation	6	5	20	48	61	58	39	38	68	343	4.8 %

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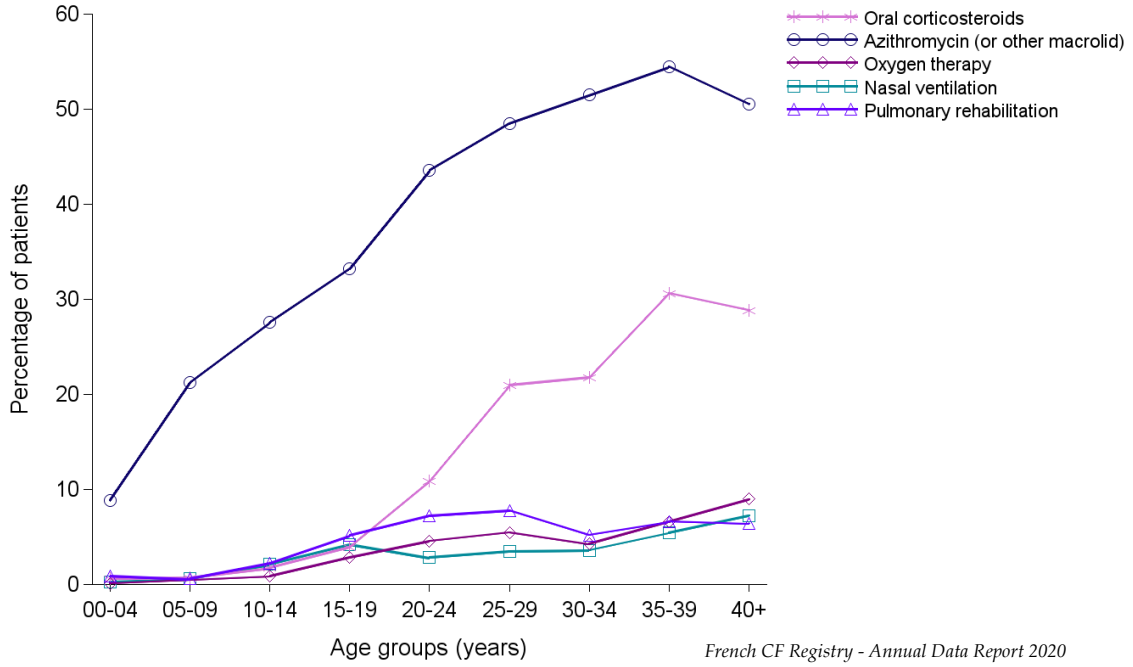
Figure 11.3. Respiratory therapeutics (≥ 3 months)



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* By nebulization, spray or powder

Table 11.4. CFTR gene modulators

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	·
Ivacaftor	11	17	31	26	23	17	15	16	40	196	2.7 %
Lumacaftor + ivacaftor	156	263	320	302	252	157	135	81	71	1737	24.1 %
Tezacaftor-elexacaftor-ivacaftor / ivacaftor	.	1	13	40	65	63	76	62	91	411	5.7 %

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This table counts the lattest treatment declared in the year. Thus, the 4 patients on ivacaftor and 101 patients on lumacaftor-ivacaftor who changed to triple therapy are only counted in the line of triple therapy.

11. Therapeutic management

Aerosoltherapy

Table 11.5. Aerosoltherapy treatments (≥ 3 months)

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	·
Patients under aerosol therapy*	**340**	**616**	**789**	**816**	**725**	**613**	**599**	**432**	**787**	**5717**	**79.2 %**
Inhaled antibiotics, including:	99	160	278	367	411	358	364	268	406	2711	37.6 %
- Tobramycin	*35*	*73*	*136*	*195*	*225*	*170*	*161*	*88*	*130*	*1213*	*16.8 %*
- Colistin	*35*	*64*	*152*	*221*	*236*	*205*	*220*	*187*	*266*	*1586*	*22.0 %*
- Aztreonam	*1*	*2*	*10*	*15*	*26*	*38*	*31*	*33*	*48*	*204*	*2.8 %*
Bronchodilators	203	383	550	583	572	475	477	352	610	4205	58.3 %
- inhaled alone	168	264	360	395	430	375	377	289	446	3104	43.0 %
- nebulized	29	21	22	37	27	27	31	32	60	286	4.0 %
Corticosteroids	101	334	484	497	470	386	390	272	514	3448	47.8 %
- inhaled alone	94	73	58	51	33	22	39	23	48	441	6.1 %
- nebulized	25	21	10	14	15	14	15	10	18	142	2.0 %
- association of inhaled bronchodilators and cortico-steroids	29	156	233	210	233	179	189	125	231	1585	22.0 %
- intranasal corticosteroids	62	233	365	395	365	296	289	215	400	2620	36.3 %
Inhaled hypertonic saline	80	124	180	189	100	74	60	52	81	940	13.0 %
RhDNase	89	422	611	596	450	316	277	172	294	3227	44.7 %

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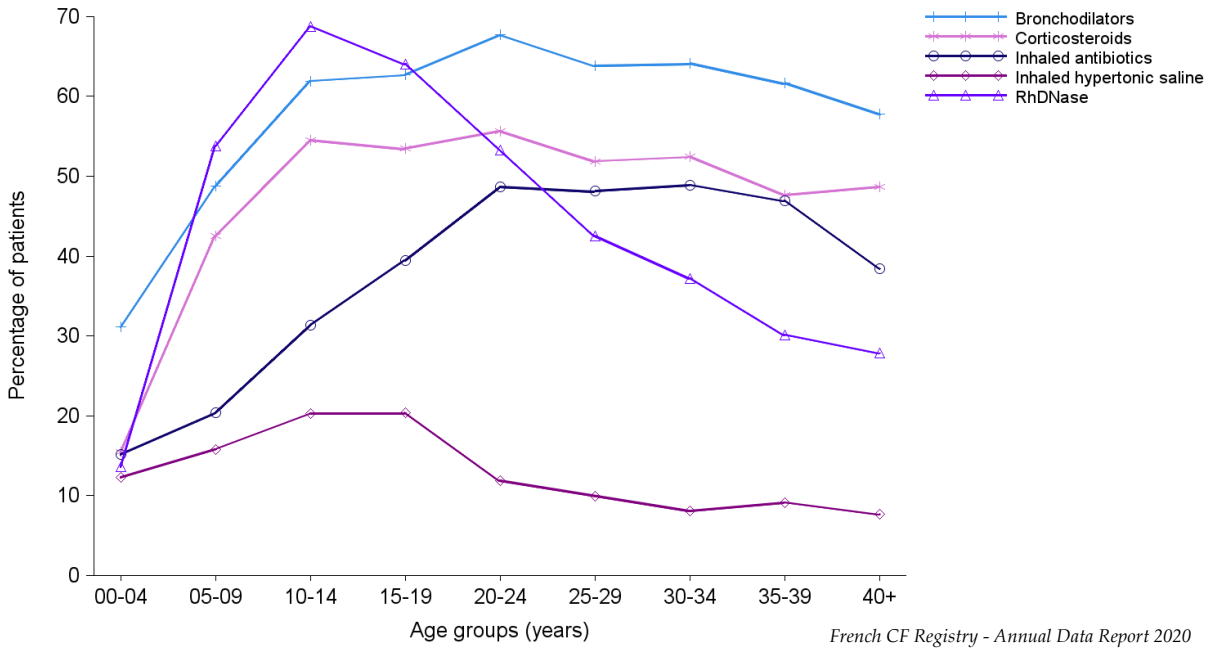
* By nebulization, spray or powder

Figure 11.4. Aerosoltherapy treatments (≥ 3 months)



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11. Therapeutic management

Hepatic, digestive and nutritional

Table 11.6. Hepatic, digestive and nutritional treatments (≥ 3 months)

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	·
Ursodeoxycholic acid	37	94	211	292	267	217	215	163	199	1695	23.5 %
Acid blockers	160	204	289	355	403	405	410	338	602	3166	43.9 %
Pancreatic enzymes	517	618	717	747	727	638	636	487	735	5822	80.7 %
Supplemental tube feeding	34	50	61	62	51	30	20	10	26	344	4.8 %
Oral supplemental feeding	134	237	317	299	336	299	262	195	286	2365	32.8 %
Fat-soluble vitamins	572	722	835	859	774	667	636	499	841	6405	88.8 %

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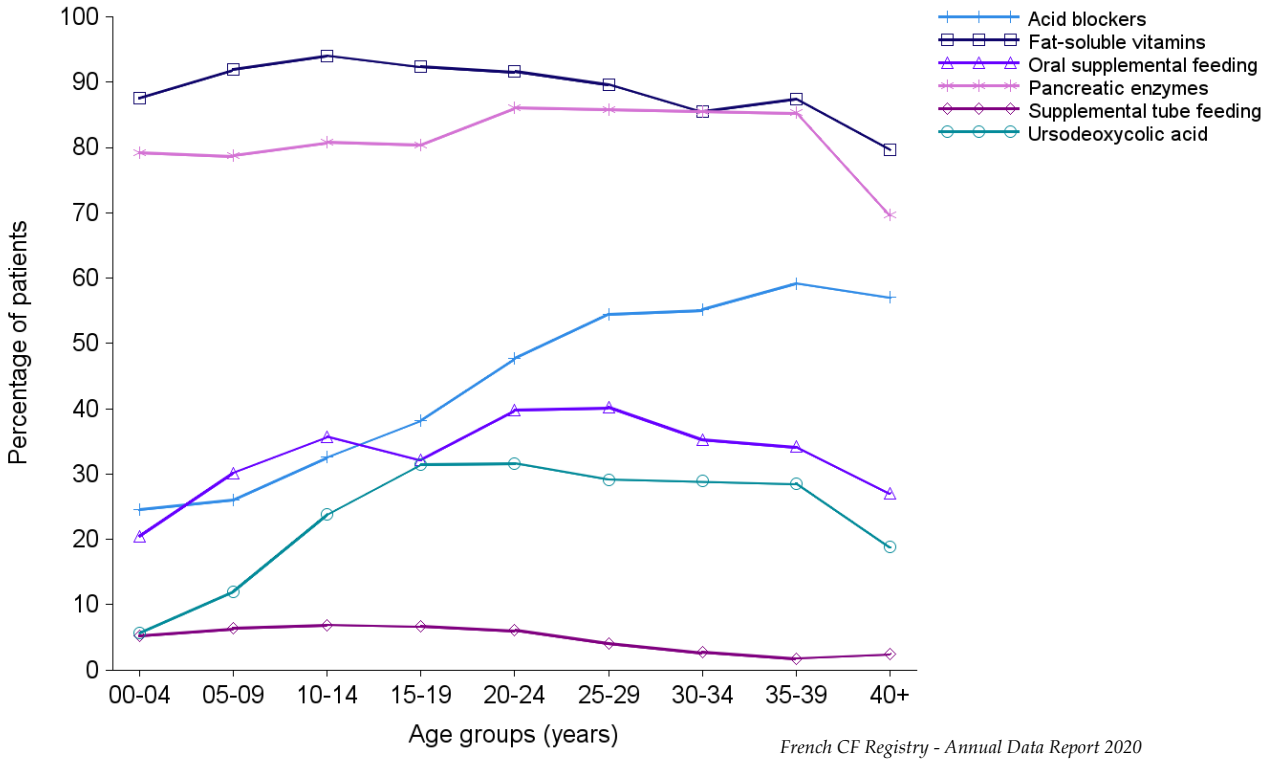
Figure 11.5. Hepatic, digestive and nutritional treatments (≥ 3 months)



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11. Therapeutic management

Other treatments

Table 11.7. Other treatments

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*653*	*785*	*888*	*930*	*845*	*744*	*744*	*571*	*1056*	*7216*	
Antifungals	5	18	63	89	90	59	58	44	83	509	7.1 %
Anti-mycobacterial treatment	1	2	4	10	9	13	9	5	13	66	0.9 %
Anti-leukotrienes	14	27	25	22	34	36	39	27	48	272	3.8 %
Contraception	.	.	1	60	128	118	120	74	58	559	7.7 %*

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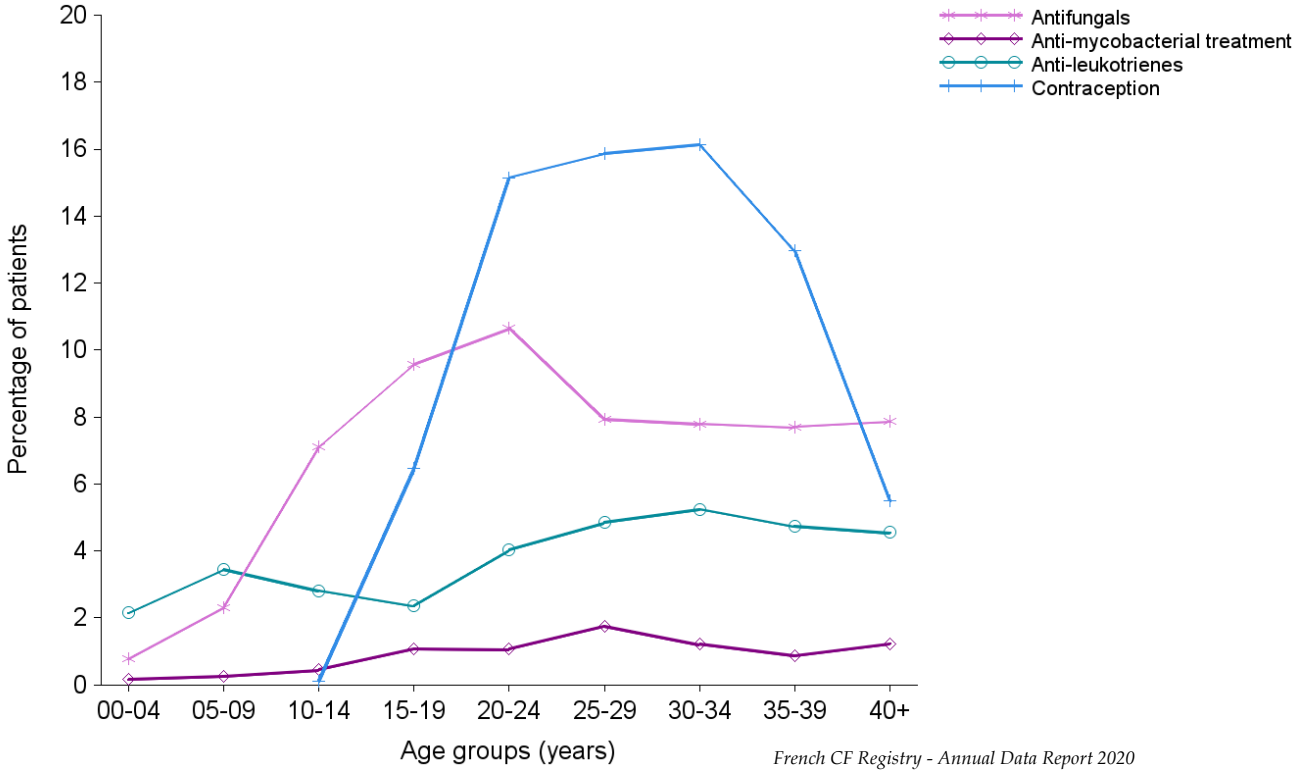
* Percent of women aged 15-49 currently using the pill is around 26%.

Figure 11.6. Other treatments



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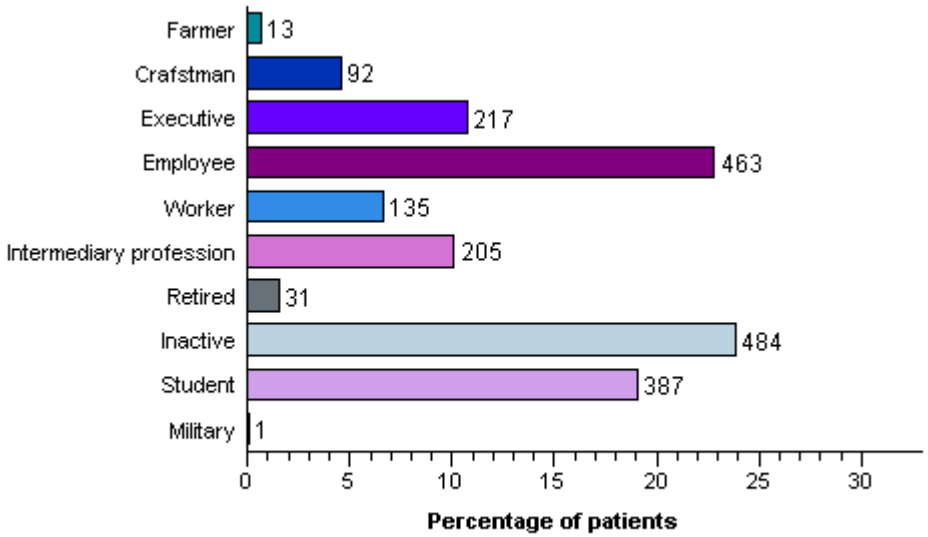
12. Social data

Employment

Figure 12.1. Employment of men ≥ 18 years

N = 2028 (number of men with a known employment situation, corresponding to 89.9 % of adults men).



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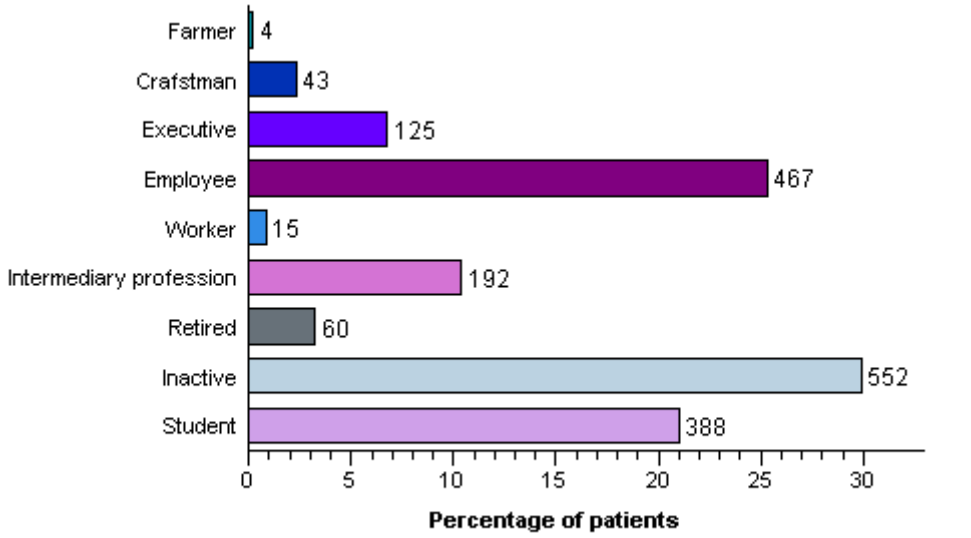
Among men aged 18 to 65, 50.3 % are workers.

Among men aged 18 to 25, 54.2 % are studiants.

Figure 12.2. Employment of women ≥ 18 years

N = 1846 (number of women with a known employment situation, corresponding to 90.0 % of adults women).



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Among women aged 18 to 65, 42.3 % are workers.

Among women aged 18 to 25, 56.5 % are studiants.

12. Socioeconomic characteristics of adults

15% of patients have at least one child

Figure 12.3. Family and marital status

Status is known for 2108 men (93.5 % of adult men), and 1935 women (94.3 % of adult women).

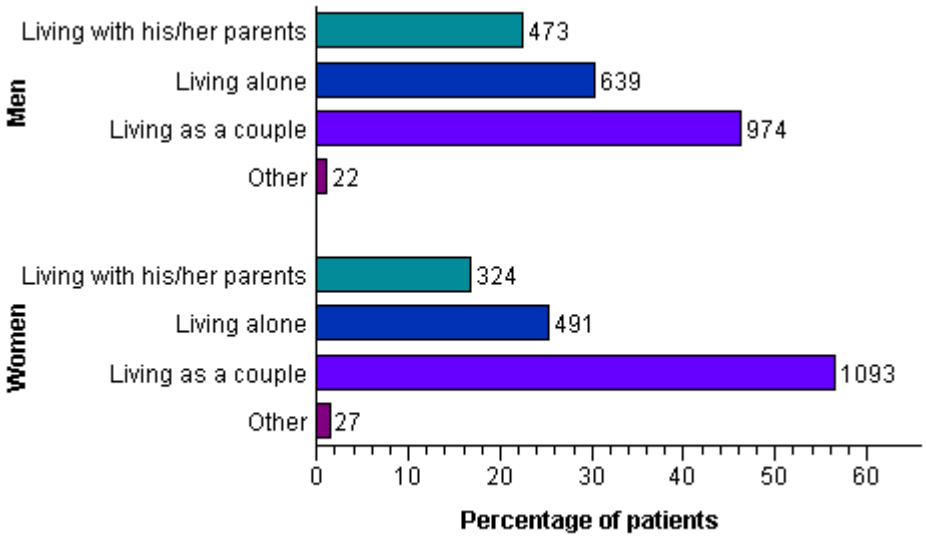

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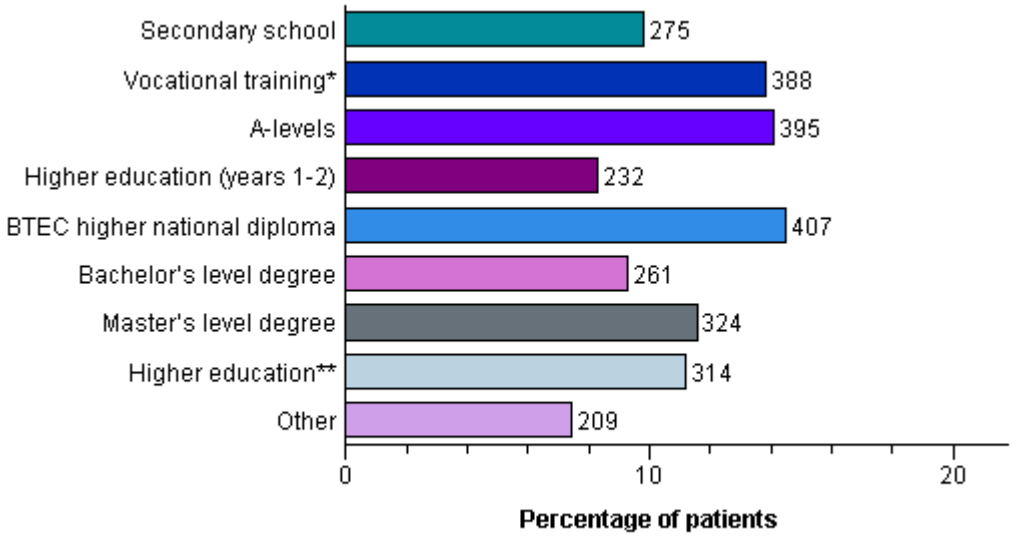
Figure 12.4. Education

Education is known for 2805 patients (65.1 % of adults).



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* and Technical school certificate

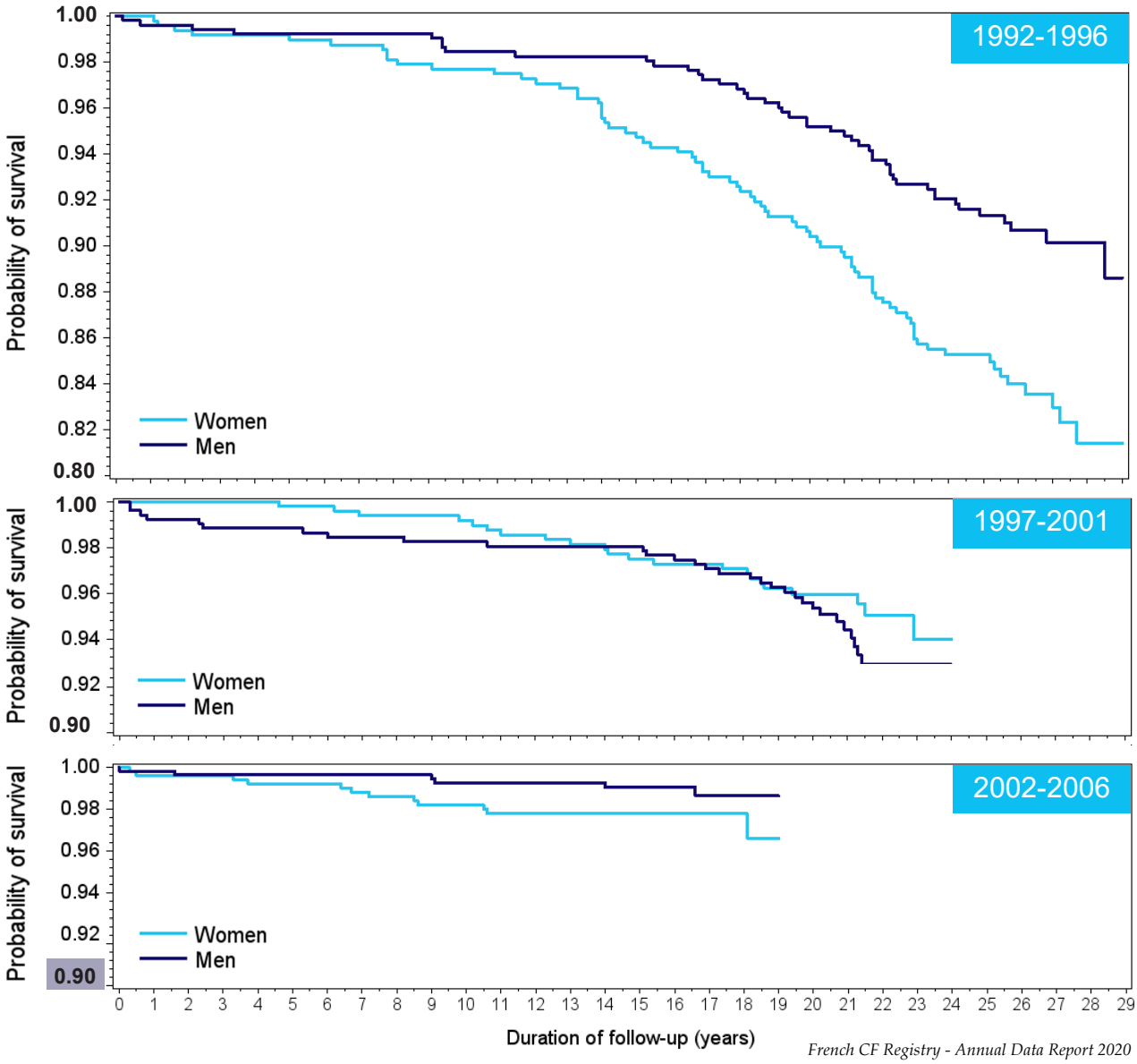
** Level not specified

Annex 1

- Complement on survival analysis – stratification by sex

Figure A1.1. Survival curves by birth cohort and sex (Kaplan-Meier method)

Birth cohorts	Men		Women	
	Patients (N)	Deaths (N)	Patients (N)	Deaths (N)
1992-1996	517	46	480	76
1997-2001	520	30	499	22
2002-2006	556	6	514	12



In the 1992-1996 cohort, women had a lower survival, from the age of 6 years compared with men gender group. This no longer appears in the 1997-2001 birth cohort, suggesting an improvement in the health status of women over time.

In the most recent cohort (2002-2006), a slight gender gap appears, but this cohort is followed for only 18 years.

Annex 2

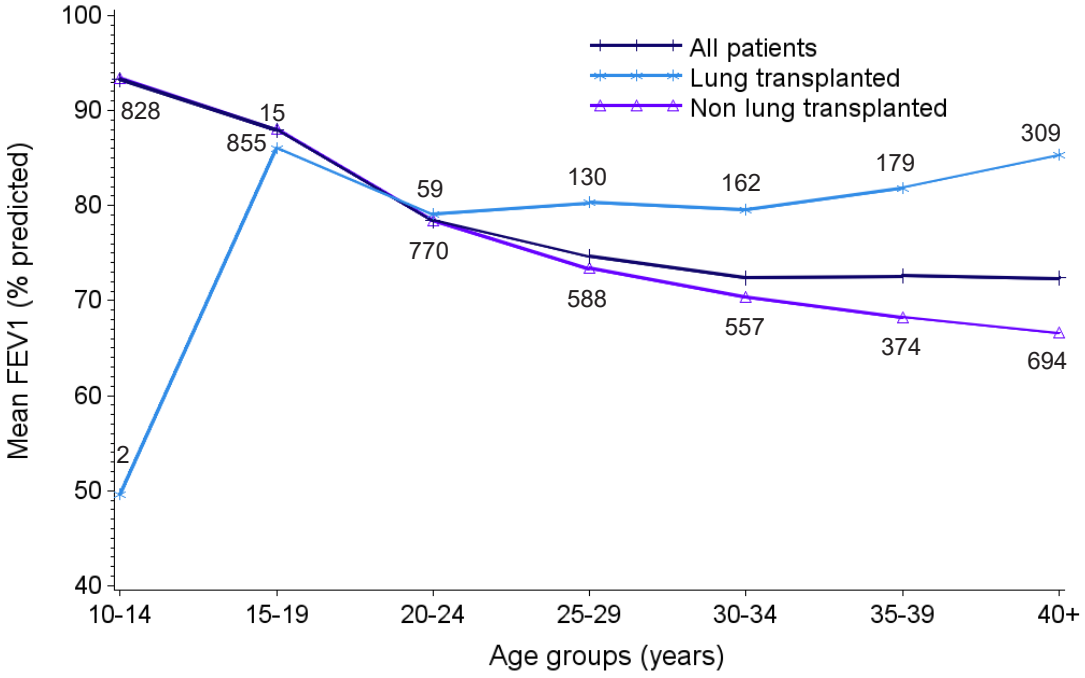
Spirometry and transplantation

This complementary analysis compares by age group the whole CF population to: 1) double lung or heart-lung transplant recipients and, 2) non transplanted patients in terms of FEV_1(%).

The curves of the whole population and of non-transplanted patients are identical up to age 20-24, as the number of patients transplanted before 20 is low. Above 25 years, FEV_1 (%) of non-transplanted patients drops more sharply, with a difference of almost 5% at ages 35-39.

Among patients aged 35 or above, an upward trend is observed in all groups, suggesting a selection bias of patients with the mildest forms of CF at these ages.

Figure A2.1. Mean FEV_1 (% predicted) and transplantation



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Curve « Lung transplant recipients »:
- The values **above** the curve represent the number of lung transplant recipients with a FEV1 value (eg: 130 patients in the 25-29 age group).
- No pulmonary transplantation has been reported in patients under 10.

Curve « Non lung transplant recipients »:
- The values **below** the curve represent the number of non lung transplant recipients with a FEV1 value (eg: 588 patients in the 25-29 age group).

Annex 3 (1/2)

Participating centres

Table A3.1. List of the participating CF care centres

CF care centres	Number of patients*
Paediatric CF care centres	
Besançon	69
Bordeaux	170
Grenoble	115
Lille	176
Lyon	261
Marseille	137
Nancy	132
Nantes	107
Paris Necker	187
Paris Robert Debré	145
Paris Trousseau	54
Rennes St Brieuc	121
Saint Denis de la Réunion	58
Strasbourg	118
Toulouse	114
Tours	125
Versailles	67
Adults CF care centres	
Besançon	68
Bordeaux	184
Grenoble	101
Lille	210
Lyon	409
Marseille	255
Nancy	94
Nantes	255
Paris Cochin	579
Rennes	124
Strasbourg	164
Suresnes Foch	515
Toulouse	215
Tours	89
Paediatric and Adults CF care centres	
Amiens	109
Angers-Le Mans	134
Caen	116
Clermont-Ferrand	148
Créteil	120
Dijon	123
Dunkerque	90
Giens	191
Limoges	67
Montpellier	233
Nice	110
Reims	142
Roscoff	171
Rouen	210
Saint Pierre de la Réunion	83
Vannes-Lorient	92

Annex 3 (2/2)

Participating centres

Table A3.2. List of the non-CF specific participating centres

Centres	Number of patients*
Paediatric local centres	
Brest	1
Le Havre	17
Paediatric and Adults local centres	
Lens	26

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* Number of patients who visited the centre during the year. Patients followed by a centre and who did not visit it in 2020 were excluded from those statistics.

Annex 4 (1/2)

Table A4.1. Summary of data

	2018	2019	2020
Patients seen during the year and centres participating to the registry			
- Patients registered* (N):	7183	7290	7376
- Patients seen during the year in a centre** (N):	7075	7164	7216
- Centres (N) :			
Paediatric CRCMs:	17	17	17
Adult CRCMs:	14	14	14
Paediatric and Adult CRCMs:	16	16	16
Other centres:	3	3	3
Demographics			
- Male patients (%):	52.1	52.2	51.9
- Age of patients, in years (mean):	22.9	23.4	23.9
- Age of patients, in years (median):	20.9	21.3	21.9
- Age of patients. in years (min-max):	0.1-86.1	0.1-84.6	0-85.6
- Patients aged 18 years and over (%):	57.4	58.5	59.7
- Early pregnancies in the year (N):	57	56	51
- Pregnancy rates in women aged 15 to 49 years (for 1000):	29.4	28.2	24.9
- Age at 31st December of the year of early pregancy (mean):	29.9	29.8	29.6
- Deaths (N):	57	41	45
- Crude death rate (for 1 000):	8.0	5.7	6.2
- Age at death, in years (mean):	33.6	34.7	36.5
- Age at death, in years (median):	31.0	34.0	32.8
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	2	2	1.9
- New patients diagnosed during the year (N):	177	162	158
- Age at diagnosis of the new patients, in years (median):	1.2	1.1	1.1
- Age at diagnosis of the new patients, in years (min-max):	0-81	0-76	0-81
- Full genotypes identified (%):	98	98	98
F508del / F508del:	40.9	40.9	41.3
F508del / Other:	41.6	41.8	41.4
Other / Other:	15.5	15.3	15.4
F508del / Missing:	0.4	0.5	0.5
Other / Missing:	0.6	0.7	0.8
Missing / Missing:	0.9	0.8	0.7
Anthropometry			
- Patients aged 17 years and less, Height z-score (mean):	-0.61	-0.6	-0.55
Weight z-score (mean):	-0.53	-0.54	-0.43
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - GLI (mean):	92	91.7	92.4
- Patients aged 18 years and over, FEV_1 (% predicted) - GLI (mean):	71.7	71.4	72.2

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* Patients whose vital status is known, whether they visited or not a centre during the year.

** Reference patients for the statistics of this report, with the exclusion of survival data.

Annex 4 (2/2)

Table A4.1. Summary of data

	2018	2019	2020
Microbiology			
- Patients with at least one sputum during the year (%):	86	85.9	83.4
H. influenzae:	17.7	17	11.2
MSSA:	57.7	59.3	57.9
MRSA:	6.1	5.9	5.2
P. aeruginosa:	37.2	37.5	35.6
S. maltophilia:	10.3	10.4	9.2
B. cepacia:	2.1	2.2	2.1
Achromobacter spp. :	6.7	6.9	6.4
Aspergillus fumigatus :	26	27.8	23.1
Complications and transplantations			
- ABPA (%) :	7.1	7.7	6.7
- Non APBA aspergillosis (%) :	1.7	1.2	1.5
- Abnormal exocrine pancreatic function (%) :	80.3	80	80.6
- Treated gastro-oesophageal reflux (%) :	27.3	26	27.1
- Osteopenia/osteoporosis (%) :	15.1	14.5	15
- Haemoptysis (%):	5.3	5.9	4.7
- Hepatic disease (%):	13.5	15.7	16.6
- Total diabetes (%):	20.8	21.4	21.9
- Transplanted patients (N):	892	922	955
Including patients transplanted during the year:	84	94	50
- Patients on waiting list (N):	136	154	88
Including patients listed during the year:	88	100	30
Deaths on waiting list:	2	4	0
Therapeutic management			
- IV courses (%):	29	29.1	25.6
- Oxygenotherapy (%):	4.9	4.6	3.9
- Nasal ventilation (%):	4.6	4.6	3.5
- Azithromycin (or other macrolid) (%):	33.7	36.1	37.9
- Inhaled antibiotics (%):	37.7	38.9	37.6
- Bronchodilators (%):	59	59.4	58.3
- RhDNase (%):	43.4	39.5	44.7
- Corticosteroids (%):	48.7	47.7	47.8
- Pancreatic enzymes (%):	80	80.3	80.7

Annex 5

Table A5.1. Summary of data - Transplanted vs non transplanted patients

	Transplanted patients	Non transplanted patients	2020 data
- Patients seen during the year in a centre* (N):	950	6266	7216
Demographics			
- Age of patients, in years (mean):	36.9	21.9	23.9
- Age of patients, in years (median):	36.3	19.4	21.9
- Patients aged 18 years and over (%):	97.8	53.9	59.7
- Early pregnancies during the year (N):	5	46	51
- Deaths (N):	25	20	45
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	5	1.7	1.9
- Full genotypes identified (%):	97.5	98.1	98
F508del / F508del:	49.1	40.1	41.3
F508del / Other:	37.5	41.9	41.4
Other / Other:	10.9	16	15.4
F508del / Missing:	0.7	0.5	0.5
Other / Missing:	0.6	0.8	0.8
Missing / Missing:	1.2	0.6	0.7
Anthropometry			
- Patients aged 17 years and less, Height z-score (mean):	-1.64	-0.54	-0.55
Weight z-score (mean):	-1.59	-0.43	-0.43
BMI z-score (mean):	-0.8	-0.04	-0.04
- Patients aged 18 years and over, BMI (mean):	20.4	21.9	21.6
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - GLI (mean):	78.1	92.5	92.4
- Patients aged 18 years and over, FEV_1 (% predicted) - GLI (mean):	78.5	70.4	72.2
Complications			
- Treated aspergillosis (%)	4.3	7	6.7
- Non APBA aspergillosis (%) :	2.1	1.4	1.5
- Abnormal exocrine pancreatic function (%) :	93.2	78.7	80.6
- Treated gastro-oesophageal reflux disease (%) :	55.5	22.8	27.1
- Osteopenia/osteoporosis (%) :	39.2	11.3	15
- Haemoptysis (%):	2.4	5.1	4.7
- Hepatic disease (%):	17.1	16.5	16.6
- Total diabetes (%):	65.8	15.3	21.9
Therapeutic management			
- Pancreatic enzymes (%) :	94.6	78.6	80.7
- Oral steroids (%) :	78.2	3.4	13.2

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** The difference between the number of transplanted patients page 34 (955) and the number of patients shown in this table (950) are the patients who died and were not seen in 2020.*

Annex 6

Table A6.1. Summary of data - classical vs atypical CF

Atypical CF includes CFSPID/CRMS and mono-symptomatic CFTR-RD.

	CF	Atypical CF	2020 data
- Patients seen during the year in a centre* (N):	6602	443	7216
Demographics			
- Age of patients, in years (mean):	23.5	25.1	23.9
- Age of patients, in years (median):	21.6	17.4	21.9
- Patients aged 18 years and over (%):	59.6	47.9	59.7
- Early pregnancies during the year (N):	47	2	51
- Deaths (N):	39	2	45
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	1.7	25.5	1.9
- Full genotypes identified (%):	98.9	85.8	98
F508del / F508del:	44.3	0.2	41.3
F508del / Other:	40.2	58.9	41.4
Other / Other:	14.4	26.6	15.4
F508del / Missing:	0.3	2.5	0.5
Other / Missing:	0.3	7	0.8
Missing / Missing:	0.4	4.7	0.7
Anthropometry			
- Patients aged 17 years and less, Height z-score (mean):	-0.58	-0.21	-0.55
Weight z-score (mean):	-0.47	-0.04	-0.43
BMI z-score (mean):	-0.07	0.27	-0.04
- Patients aged 18 years and over, BMI (mean):	21.4	23.9	21.6
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - GLI (mean):	91.8	100.7	92.4
- Patients aged 18 years and over, FEV_1 (% predicted) - GLI (mean):	71.6	86.2	72.2
Complications			
- Treated aspergillosis (%)	7	2	6.7
- Non APBA aspergillosis (%) :	1.5	0.9	1.5
- Abnormal exocrine pancreatic function (%) :	85.7	11.7	80.6
- Treated gastro-oesophageal reflux disease (%) :	28.3	10.6	27.1
- Osteopenia/osteoporosis (%) :	15.4	4.1	15
- Haemoptysis (%):	4.8	1.6	4.7
- Hepatic disease (%):	17.6	2.7	16.6
- Total diabetes (%):	23	2.9	21.9
Therapeutic management			
- Pancreatic enzymes (%) :	85.6	14	80.7
- Oral steroids (%) :	13.8	1.6	13.2

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** Diagnosis type is missing for 171 patients.*

FRENCH CYSTIC FIBROSIS REGISTRY

Coordinated by the patient organization Vaincre la Mucoviscidose, the French Cystic Fibrosis Registry collects annual clinical data from the CF care centers. This epidemiological database allows evaluation of the CF patients' characteristics, health status and care monitoring.
It is also used for research and feasibility studies.

In partnership with the French Cystic Fibrosis-CFTR Network.

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