FRENCH CYSTIC FIBROSIS REGISTRY

ANNUAL DATA REPORT 2019

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VAINCRE LA MUCOVISCIDOSE

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Editorial

A transitional year

2019 was a year of transition in the evolution of the treatment of cystic fibrosis. It was the era before Covid-19 but especially the era before Kaftrio® for which the nominative temporary authorization for use (ATU) was issued by the ANSM at the end of the year.

Also, the main indicators provided by the Registry data are interesting **in more ways.** Their evolution is fairly consistent with those of previous years and in particular of 2018, as evidenced by the increase in:

- the number of patients (+1.3% with 7,280 patients) thanks to the increase in the proportion of adults now at 58.6%
- the average age of 23.4 years (+ 6 months),
- the average age at death (34.7 years), i.e. more than one year of life gained compared to 2018

There are 41 deaths, which is still too high even if it represents a decrease of 28% compared to 2018.

The demography of the population affected by cystic fibrosis is continuing its favorable evolution, thanks to the impulses provided over the past 20 years. The best illustration is undoubtedly the tripling of the number of patients over 40 over the last ten years. They now represent 13.8% of the population.

Patient health indicators still remain a concern

While the median FEV1 is 10 points higher in 2019 than in 2009 for all or almost all age categories, it continues to decline inexorably with age. With age and from adolescence, kidney failure, diabetes and depression also gain ground.

The evolution of the infection with germs remains worrying since it progresses on almost all germs.

In 2019, the transplant is still the only way out

Transplantation is still sustained with 93 patients transplanted in 2019, the transplanted organ remains mainly pulmonary (80) but we also observe more kidney transplants. The 923 patients with a transplant represent 12.6% of the population (22% of adults) and are those for whom research must mobilize to provide them with treatment, since, for the moment, very few of them access the modulators.

The study conducted in 2020 by Pr. Pierre-Régis Burgel on patients benefiting from the nominative ATU of Kaftrio® (Burgel et al. AJRCCM 2021) highlighted the impact of this treatment, particularly for patients enrolled in a course of transplantation. Of the 53 patients concerned by the transplant (pre-transplant assessment or registered), 50 of them left this scheme. The data from the Biomedicine Agency for 2020 seem to confirm this perspective in view of the spectacular drop in the number of transplants concerning patients with pulmonary cystic fibrosis.Si le VEMS médian est supérieur de 10 points en 2019 à celui de 2009 sur toutes les catégories d'âge ou presque, il continue de diminuer inexorablement en vieillissant. Avec l'âge et dès l'adolescence, ce sont également l'insuffisance rénale, le diabète et la dépression qui gagnent du terrain.

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). Lung transplantation is the last resort in case of end stage respiratory disease. 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.

Data use

Statistical analysis is performed on anonymized data. Unless otherwise indicated, the results presented hereafter relate to the population seen during the year 2019.

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.

1. Demographics

Characteristics of the population

Figure 1.1. Evolution of the number of patients since 1992

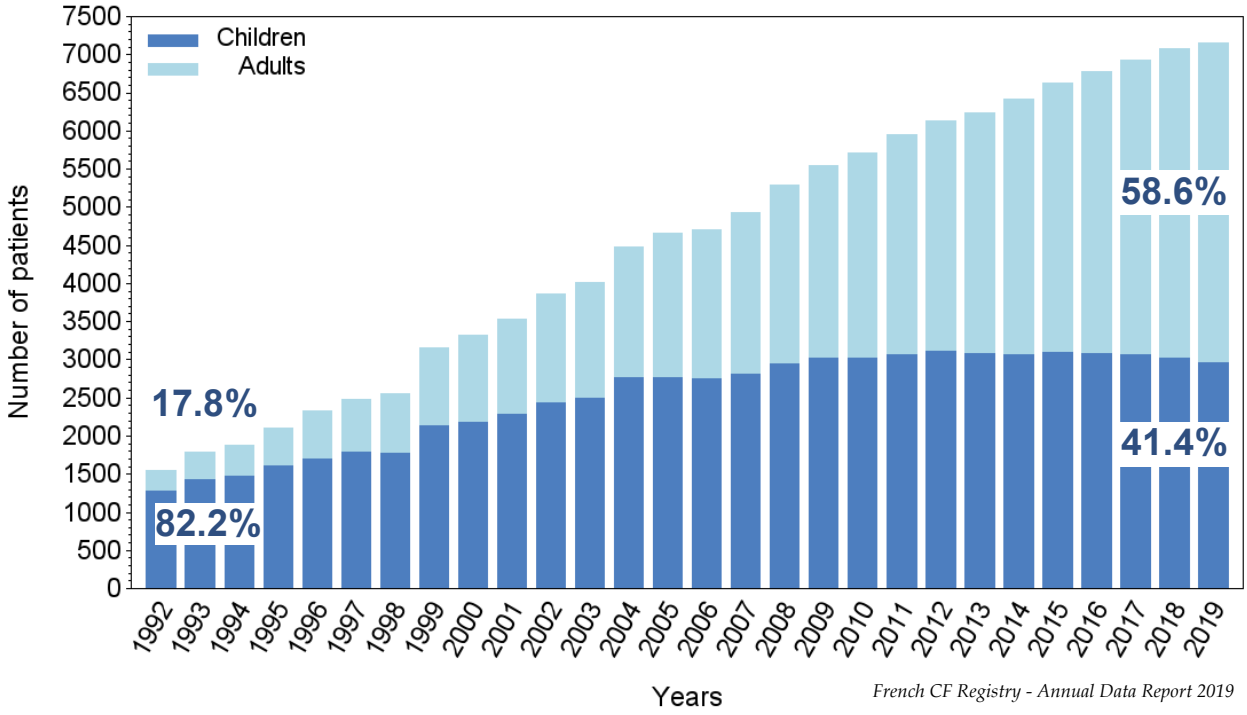

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Table 1.1. Annual evolution of the main indicators

	Years of follow-up										
Indicators	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
All patients*	5570	5715	5969	6139	6252	6428	6631	6787	7076	7181	7280
Patients seen during the year**	5551	5706	5957	6127	6241	6414	6621	6780	6933	7073	7160
Children	3017	3018	3068	3108	3085	3069	3096	3079	3061	3014	2967 (41.4 %)
Adults	2534	2688	2889	3019	3156	3345	3525	3701	3872	4059	4193 (58.6 %)
Over 40 years	309	339	399	452	509	586	668	758	825	910	987 (13.8 %)
Men	2889	2940	3085	3167	3223	3314	3442	3547	3616	3681	3735 (52.2 %)
Women	2662	2766	2872	2960	3018	3100	3179	3233	3317	3392	3425 (47.8 %)
Mean age (years)	18.1	18.5	19.1	19.5	20.1	20.7	21.2	21.8	22.3	22.9	23.4
Median age (years)	16.5	16.9	17.4	17.8	18.2	18.9	19.3	19.9	20.3	20.9	21.3
Minimum age (years)	0	0.1	0	0.1	0.1	0	0	0.1	0.1	0.1	0.1
Maximum age (years)	77.8	80	88	86.8	82.5	82.8	83.2	84.1	85.1	86.1	84.6

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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=24) were excluded from the analysis.

1. Demographics

Characteristics of the population

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

Characteristics	2017		2018		**2019**	
	Men	Women	Men	Women	**Men**	**Women**
Patients seen during the year	3616	3317	3681	3392	**3735**	**3425**
Children	1584	1477	1542	1472	**1518**	**1449**
Adults	2032	1840	2139	1920	**2217**	**1976**
Mean age (years)	22.2	22.4	22.9	23	**23.4**	**23.4**
Median age (years)	20.5	20.1	21.3	20.5	**21.7**	**21**

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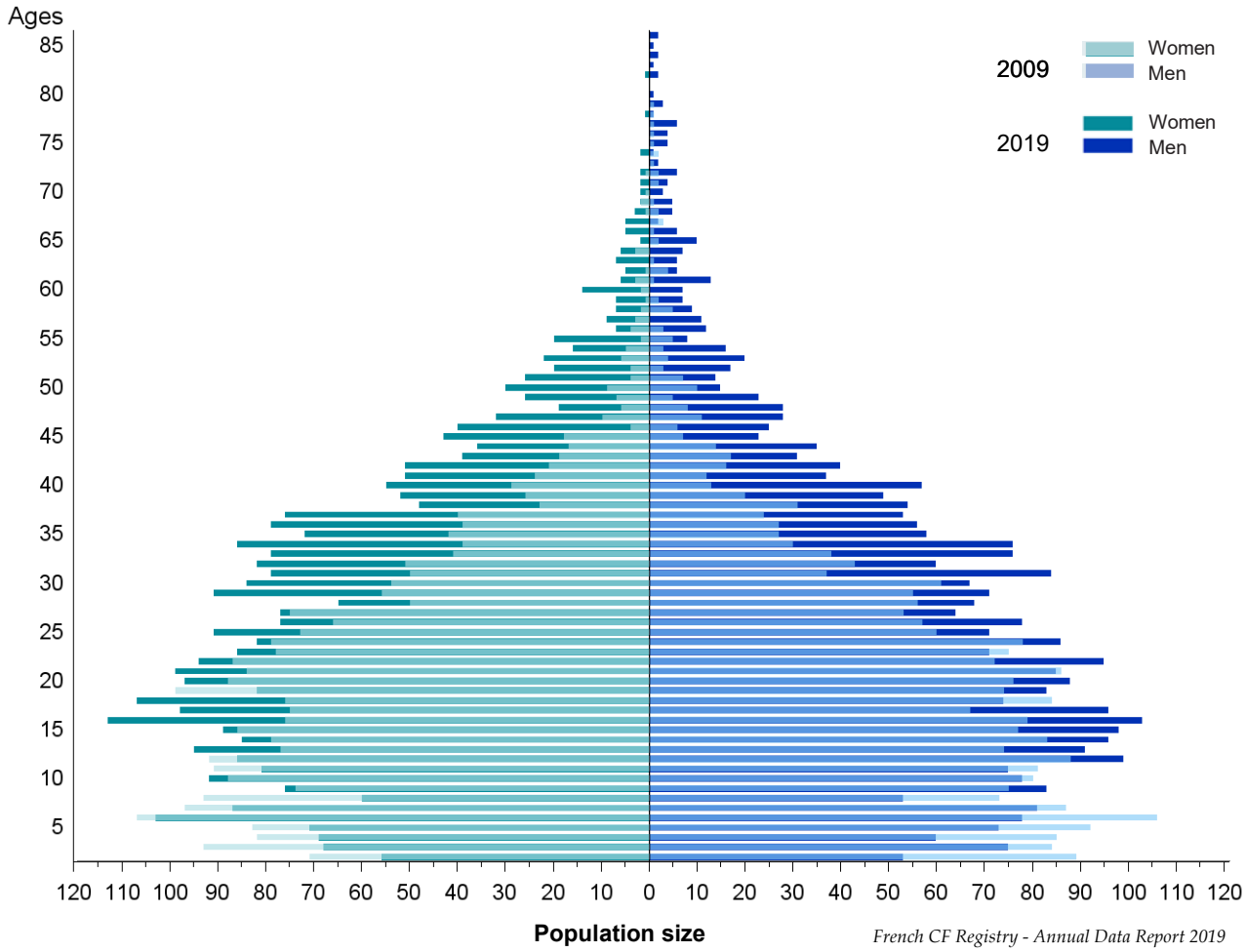
Figure 1.2. Population pyramid



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The number of babies born in 2019 (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 2020.

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	2154	30.1	127	0.1	63.9	10.5	10.9	9.4
Adult	14	2942	41.1	210	16.1	84.6	34.4	32.3	14.6
Paediatric/Adult	16	2025	28.3	127	0.1	82.7	21.4	18.6	19.5
Subtotal	47	7121	99.5	152	0.1	84.6	23.5	21.4	21.2
Other centres									
Paediatric	2	13 (b)	0.2	7	3.6	17.8	9.9	8.1	5.6
Paediatric/Adult	1	26 (c)	0.4	26	6.3	17.5	10.8	9.8	4.2
Subtotal	3	39	0.5	13	3.6	17.8	10.5	9.8	4.9
Total	50	7160	100	143	0.1	84.6	23.4	21.3	21.2

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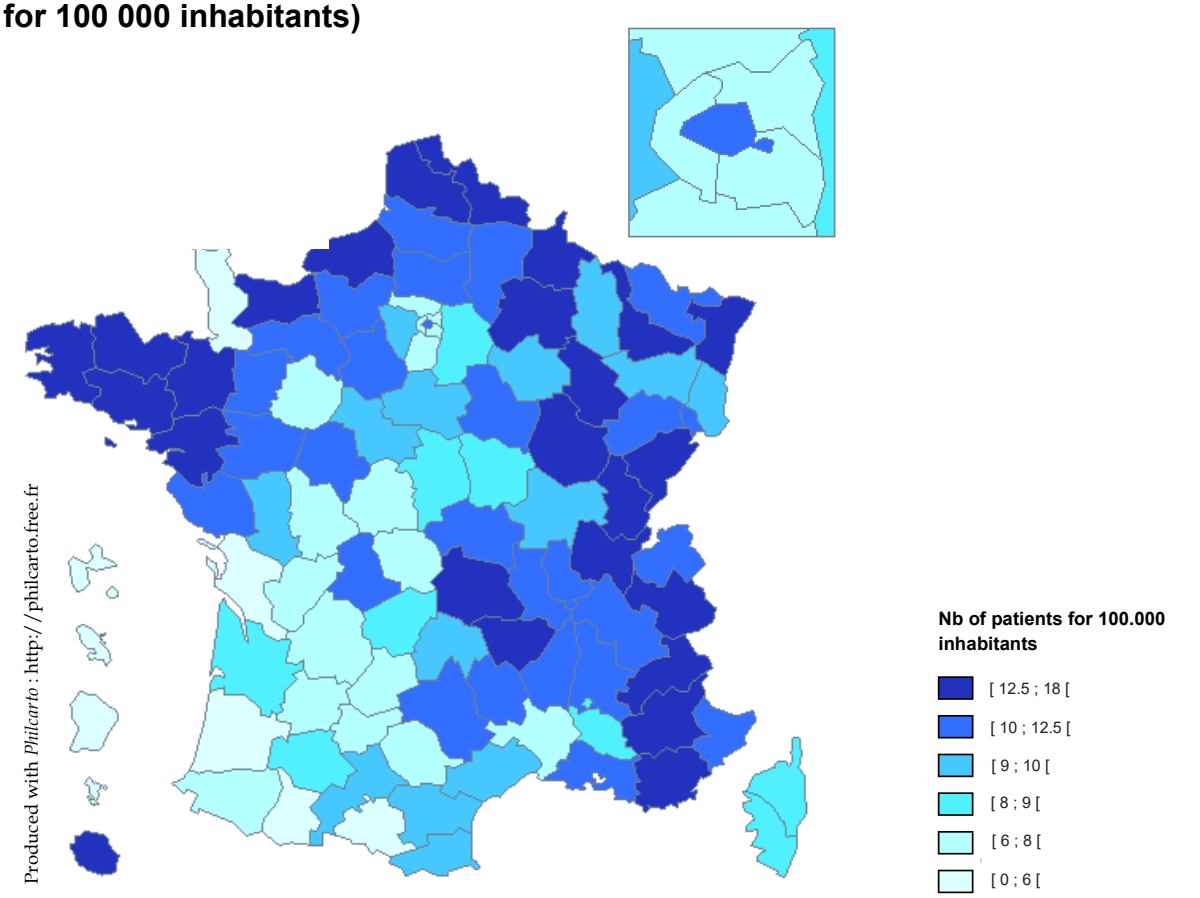
Notes : (a) Patients visiting at least 2 CF centres during the year were only counted in the one with the highest number of visits
(b) Including 1 patient also seen by a CF centre
(c) No patient also seen by a CF centre

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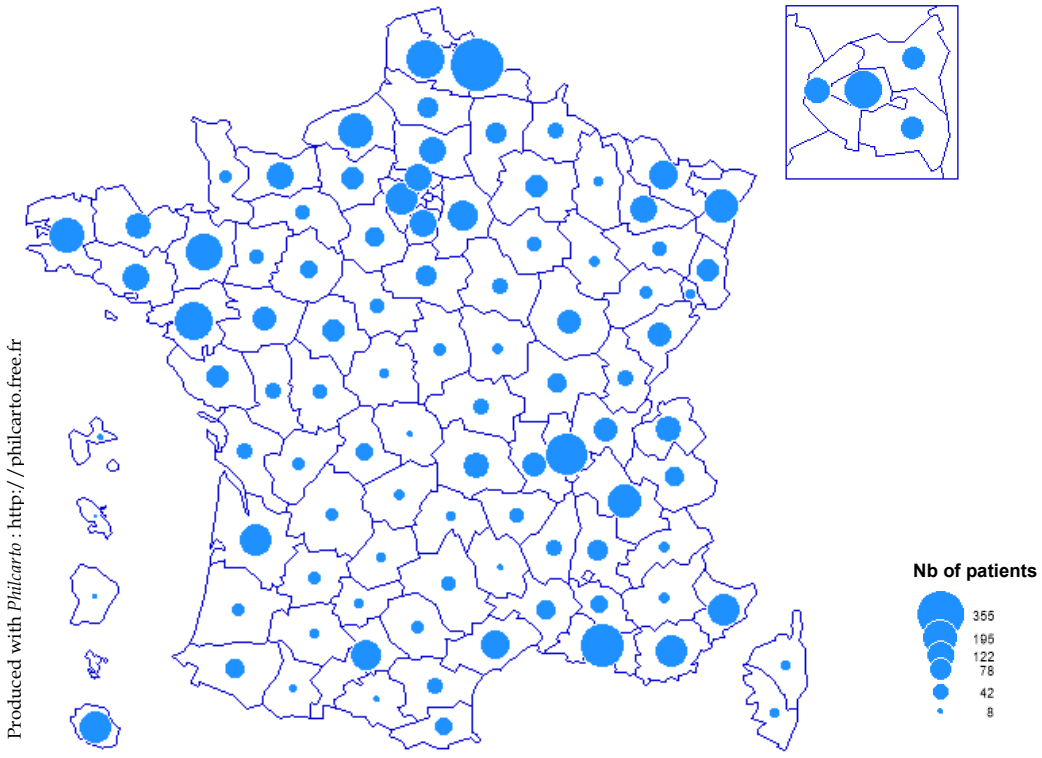
Map 1.2. Localisation of the patients by « département » of residence (absolute numbers)



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2. Mortality

Characteristics

Figure 2.1. Annual number of deaths since 1992

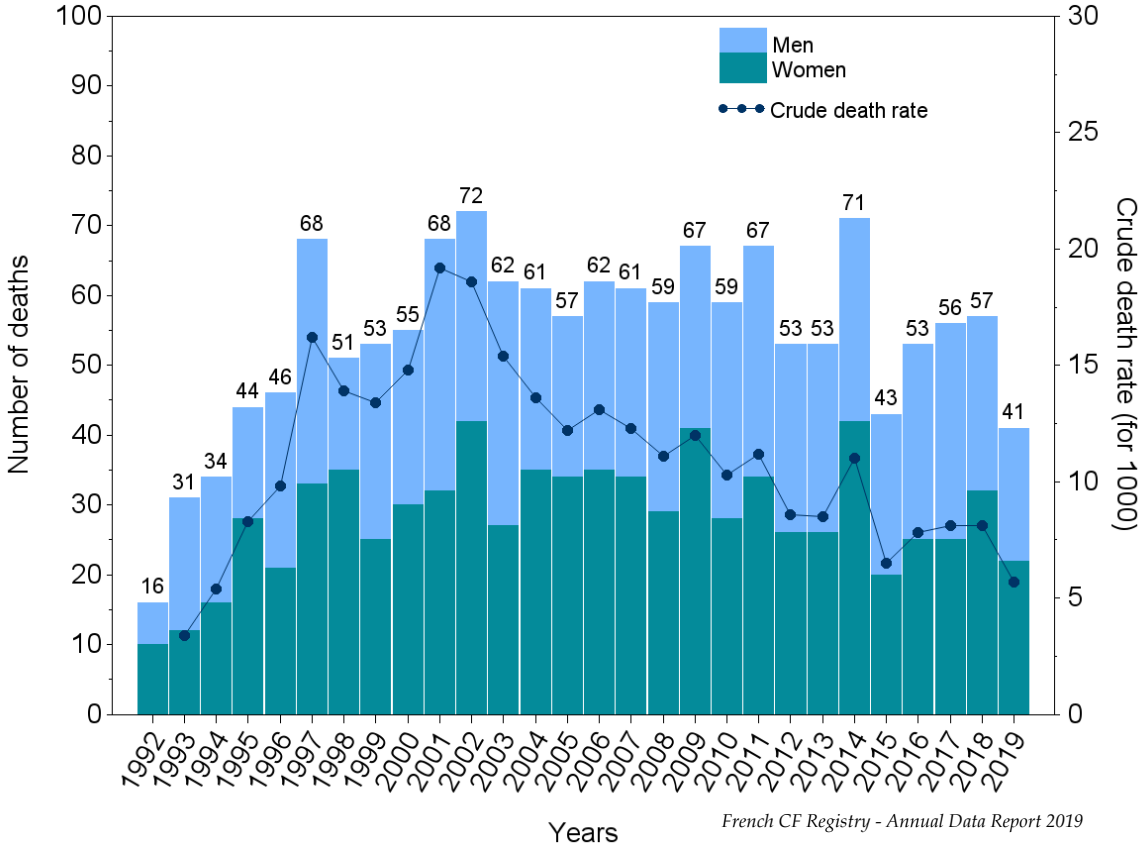

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Table 2.1. Mortality characteristics

Indicators	Years of follow-up										
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Number of deaths	67	59	67	53	53	71	43	53	56	57	41*
- including transplanted patients	34	32	33	27	29	41	22	37	33	36	21
Crude death rate (per 1000)	12.0	10.3	11.2	8.6	8.5	11.0	6.5	7.8	8.1	8.1	5.7
Mean age (years)	24.7	29.3	26.4	32.3	34.4	29.0	34.1	31.9	35.0	33.6	34.7
Median age (years)	23.3	27.6	24.9	27.8	30.7	27.1	31.8	28.0	33.8	31.0	34.0
Minimum age (years)	0.4	0.2	1.9	2.2	1.1	0.1	9.0	1.6	5.9	7.3	0.4
Maximum age (years)	73.4	68.9	55.5	88.4	82.5	71.2	83.2	76.0	74.3	80.9	65.9

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* 4 out of the 41 were not seen by a CF center in 2019.

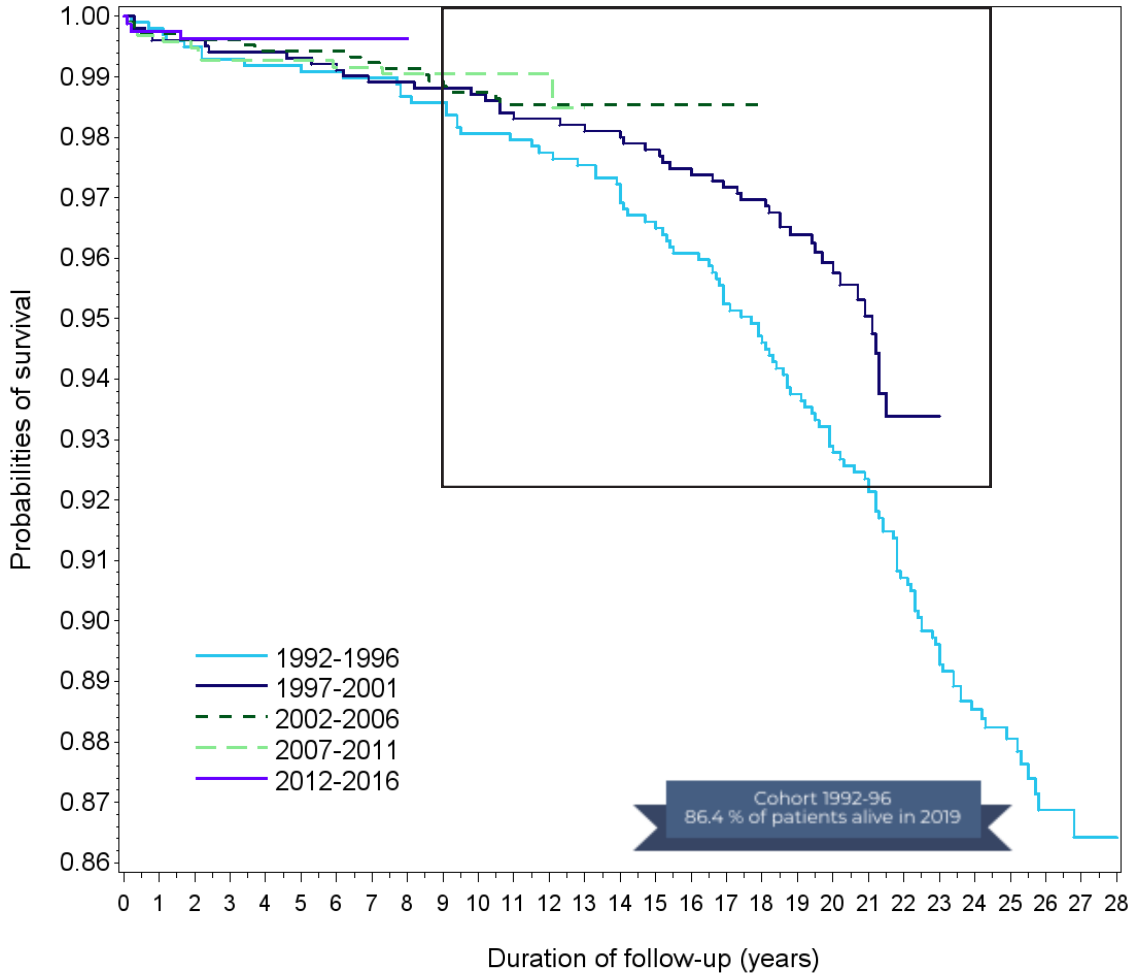
2. Mortality

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 2019 this cohort was followed during 28 years maximum): 986 patients, 112 deaths
- Births from 1997 to 2001 (maximum 23 years of follow up): 1016 patients, 47 deaths
- Births from 2002 to 2006 (maximum 18 years of follow up): 1065 patients, 15 deaths
- Births from 2007 to 2011 (maximum 13 years of follow up): 962 patients, 10 deaths
- Births from 2012 to 2016 (maximum 8 years of follow up): 811 patients, 3 deaths



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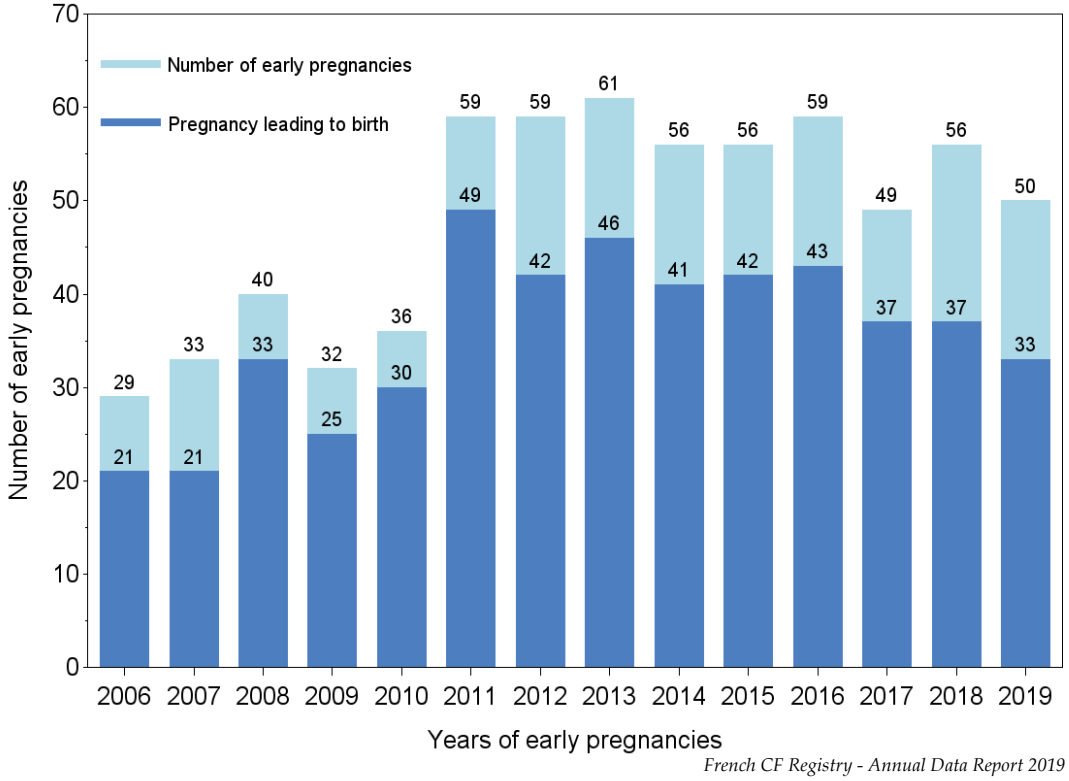
Until the age of 9, there is no difference in survival between the different birth cohorts.

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 = 6.6, p = 0.0103.

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 50 early pregnancies in 2019, 33 resulted in a birth (in 2019 or 2020).

Table 3.1. Early pregnancy characteristics

Characteristics	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Number of early pregnancies	29	33	40	32	36	59	59	61	56	56	59	49	56	50
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	28.9	25.2
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	29.5
Number of lung transplanted women starting a pregnancy	1	2	1	3	3	3	7	4	1	3	4	4	10	10

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3. Pregnancy – Paternity

Table 3.2. Paternities

Characteristics	N	Proportion (%)
Number of paternities, including:	28	
- Natural father	3	10.7
- Medically assisted reproduction, including:	23	82.1
+ Intracytoplasmic Sperm Injection / in vitro fertilization	22	95.7

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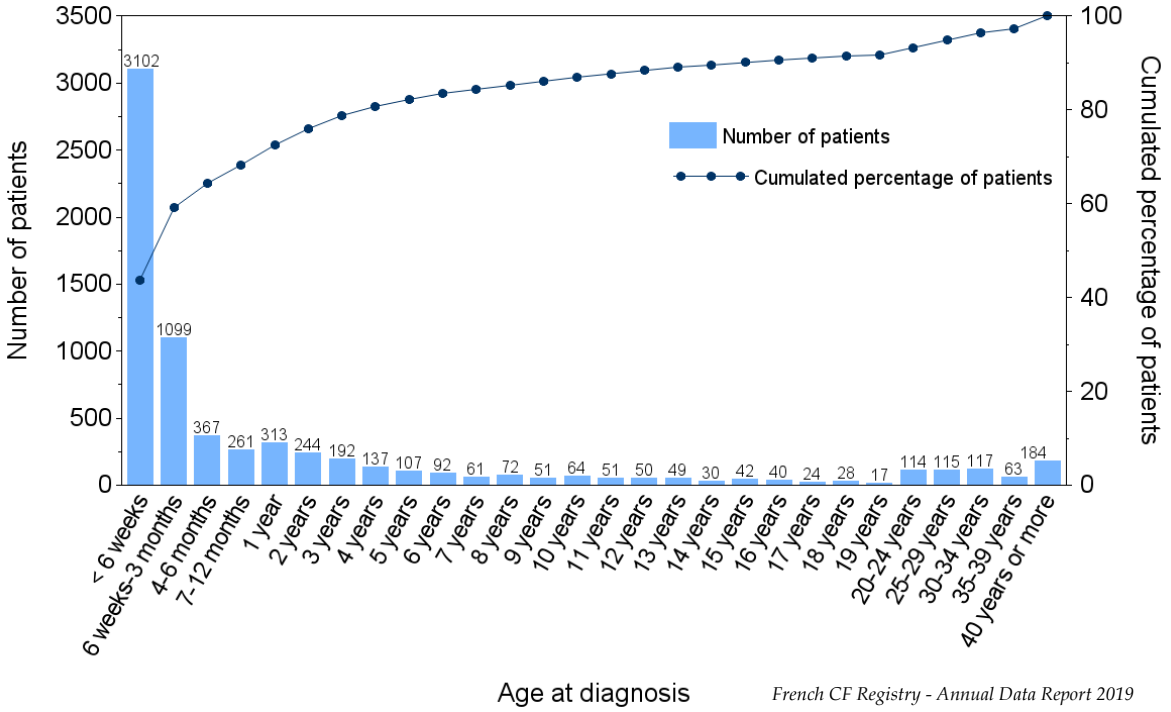
Note: precision on paternity was missing for 2 patients.

4. Diagnosis

Main characteristics

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

N = 7086 (number of patients whose age at diagnosis is known).



4. Diagnosis

Main characteristics

Table 4.1. Diagnosis characteristics

Characteristics	**2019**
ALL PATIENTS	
Patients whose age at diagnosis is known - N (%) *	7086 (99 %)
Age at diagnosis	
- Median age (months)	2.0
- Mean age (years)	4.7
- Minimum age (years)	0
- Maximum age (years)	79
NEW PATIENTS DIAGNOSED DURING THE YEAR	
Number of patients	
New patients - N (%)	163 (2.3 %)
- Including 2019 newborn patients - N	109
Age at diagnosis	
- Median age (months)	1.1
- Mean age (years)	7.5
- Minimum age (years)	0
- Maximum age (years)	76
Context of diagnosis	
1. Screened positive newborns (NBS)	**123**
- including Prenatal diagnosis - N (%)	8 (6.5 %)
- including Meconium ileus - N (%)	17 (13.8 %)
2. Diagnosis on symptoms (NBS excluded)	**40**
- including Meconium ileus - N (%)	4 (10.0 %)
- including Symptoms (other than MI):- N (%)	36 (90.0 %)
- Mean age at diagnosis (years)	29.8

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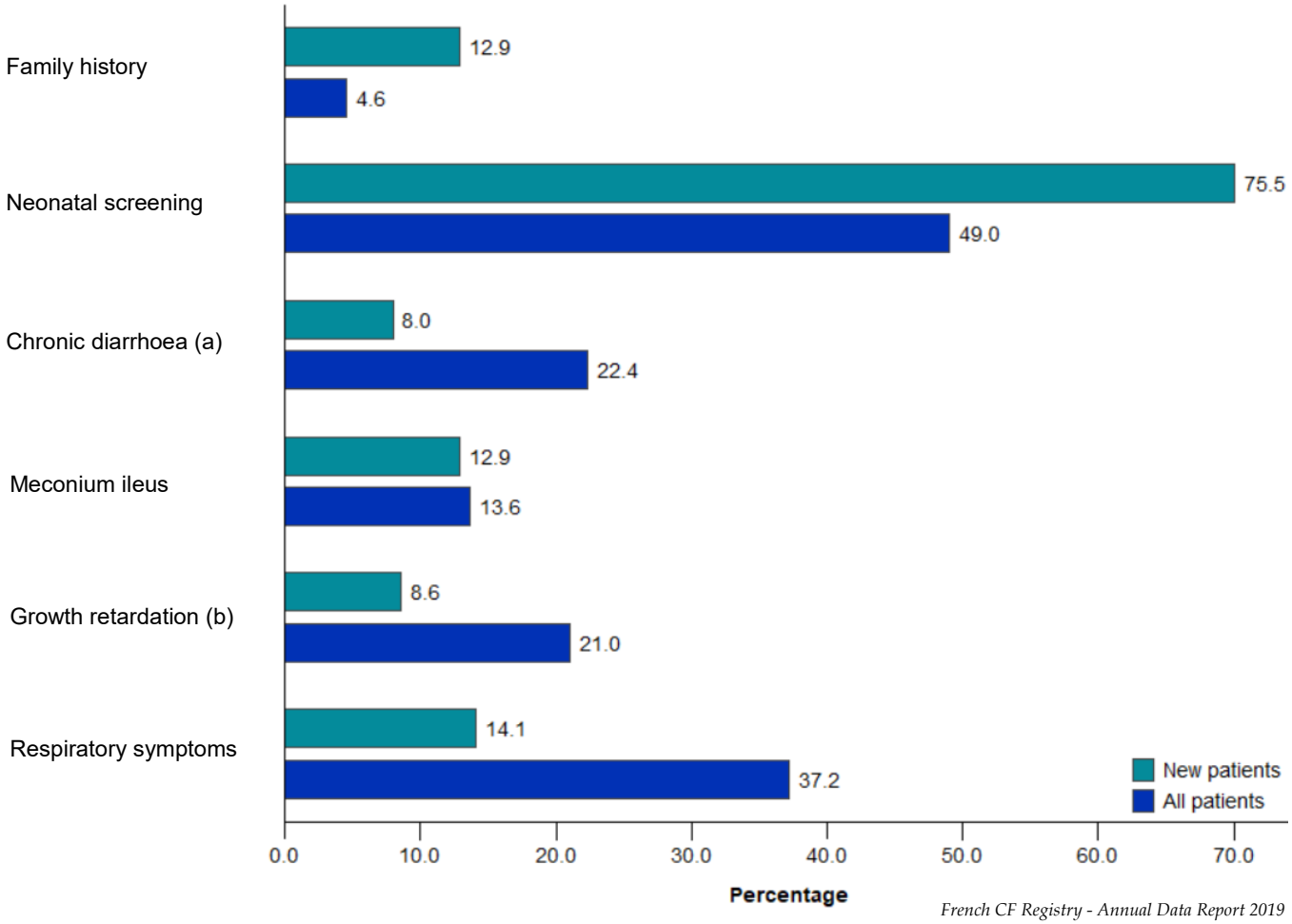
Among the 163 new patients, 109 were born in 2019. The method used to compile this report (patients seen in a care centre in 2019) means that infants born in 2019 and seen for the first time in 2020 are not included yet. For information purposes only, 17 newborns in 2018 were diagnosed in 2019 through neonatal screening. In the 2018 age pyramide, the number of patients aged 0 was 119 and should have been 119+17=136.

The number of patients diagnosed by neonatal screening (123) 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)



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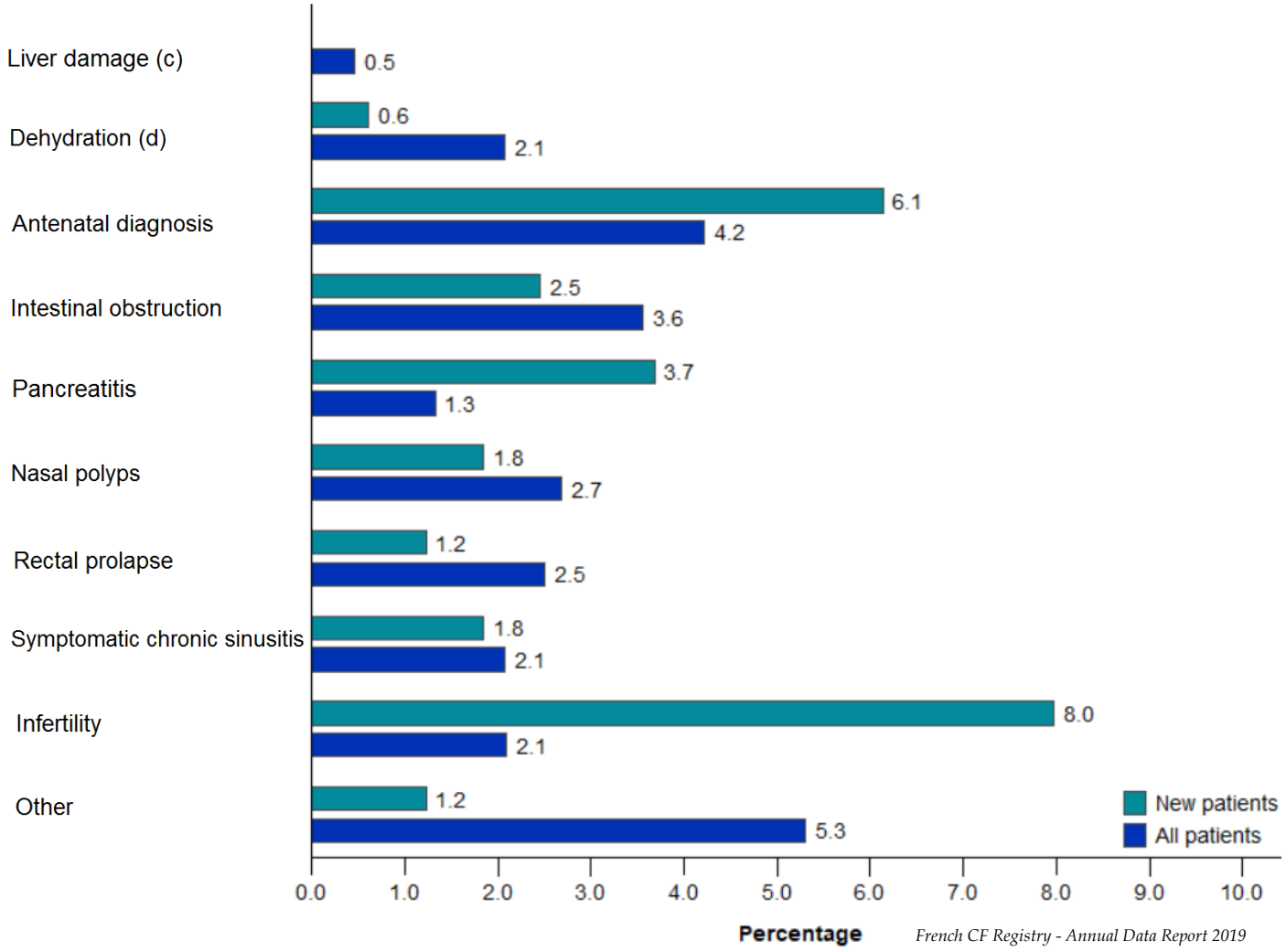
(a) Chronic diarrhoea / Steatorrhoea / Malabsorption
(b) Growth retardation / Malnutrition

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	5957	83.2
G542X	398	5.6
N1303K	296	4.1
2789+5G>A	187	2.6
1717-1G>A	151	2.1
R117H	146	2.0
R553X	132	1.8
G551D	127	1.8
W1282X	108	1.5
3849+10kbC>T	103	1.4
L206W	98	1.4
3272-26A>G	87	1.2
D1152H	84	1.2
711+1G>T	82	1.1
Y122X	81	1.1
I507del	80	1.1
2183AA>G	73	1.0
R347P	71	1.0
3120+1G>A	58	0.8
R1162X	57	0.8
G85E	53	0.7
R334W	53	0.7
Y1092X	50	0.7
A455E	47	0.7
R347H	46	0.6
S945L	45	0.6
3659delC	42	0.6
1078delT	39	0.5
1811+1.6kbA>G	36	0.5
394delTT	35	0.5
R1066C	34	0.5
E60X	33	0.5
621+1G>T	32	0.4
W846X	32	0.4
S1251N	26	0.4
1677delTA	24	0.3
E585X	22	0.3
L997F	22	0.3
Q220X	21	0.3
4005+1G>A	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	2933	41.0	22.1	21.0	65.1
F508del / Other	2981	41.6	23.8	21.2	82.7
Other/ Other	1090	15.2	23.7	20.6	84.0
Subtotal (non missing genotypes)	7004	97.8	23.1	21.2	84.0
F508del / Missing	43	0.6	37.5	36.9	84.6
Other/ Missing	53	0.7	38.4	36.8	78.5
Missing/ Missing	60	0.8	39.1	35.7	84.2
Subtotal (partial genotypes / missing)	156	2.2	38.4	35.9	84.6
Total	7160	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	207	2.9	25.0	21.9	69.0
At least one nonsense mutation	1126	15.7	21.8	19.7	77.8
At least one R117H mutation	146	2.0	20.1	14.6	84.0

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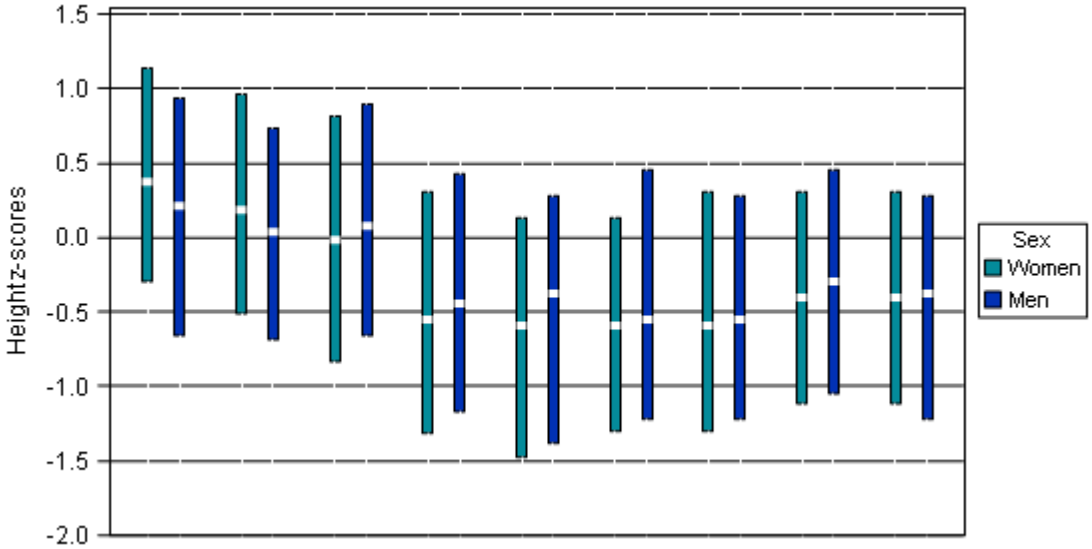
Gating mutations doesn't prevent the CFTR protein from reaching the cell membrane but alter choride transport.

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*, by age group and sex



Age groups (years)		00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +	Total
Mean height z-score	Women	0.39	0.17	0.02	-0.57	-0.68	-0.61	-0.47	-0.42	-0.40	-0.29
	Men	0.19	0.07	0.09	-0.39	-0.48	-0.48	-0.53	-0.33	-0.43	-0.26
Median height z-score	Women	0.38	0.18	-0.02	-0.55	-0.59	-0.59	-0.59	-0.41	-0.41	-0.31
	Men	0.21	0.04	0.08	-0.45	-0.38	-0.55	-0.55	-0.30	-0.38	-0.26

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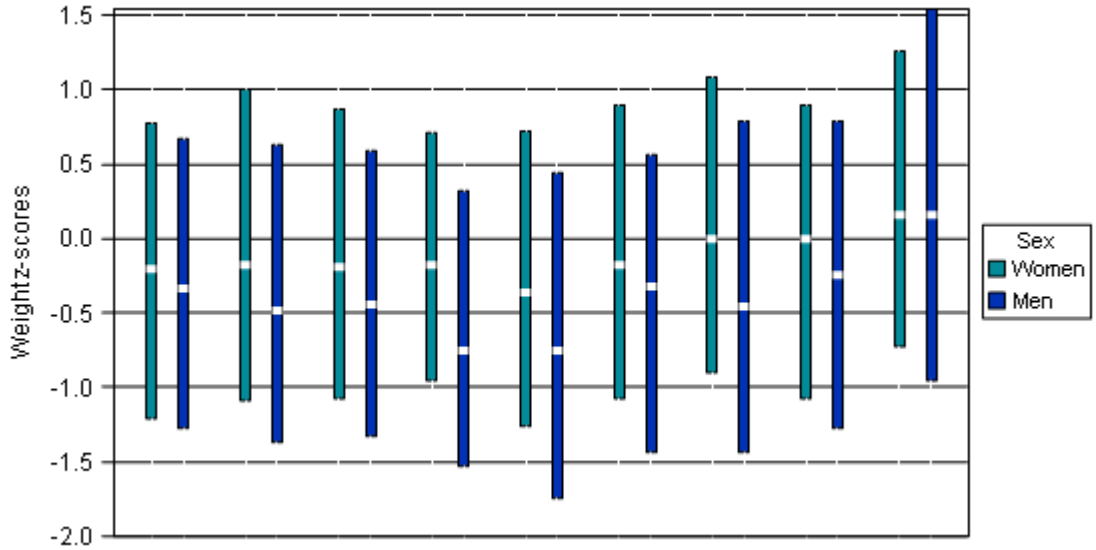
Figure 5.2. Weight z-scores*, by age group and sex



Age groups (years)		00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +	Total
Mean weight z-score	Women	-0.16	-0.02	-0.03	-0.13	-0.25	-0.02	0.21	-0.01	0.31	-0.01
	Men	-0.28	-0.31	-0.28	-0.57	-0.58	-0.34	-0.23	-0.14	0.24	-0.28
Median weight z-score	Women	-0.20	-0.17	-0.20	-0.17	-0.36	-0.18	0.00	0.00	0.16	-0.17
	Men	-0.34	-0.49	-0.45	-0.76	-0.76	-0.32	-0.46	-0.24	0.16	-0.44

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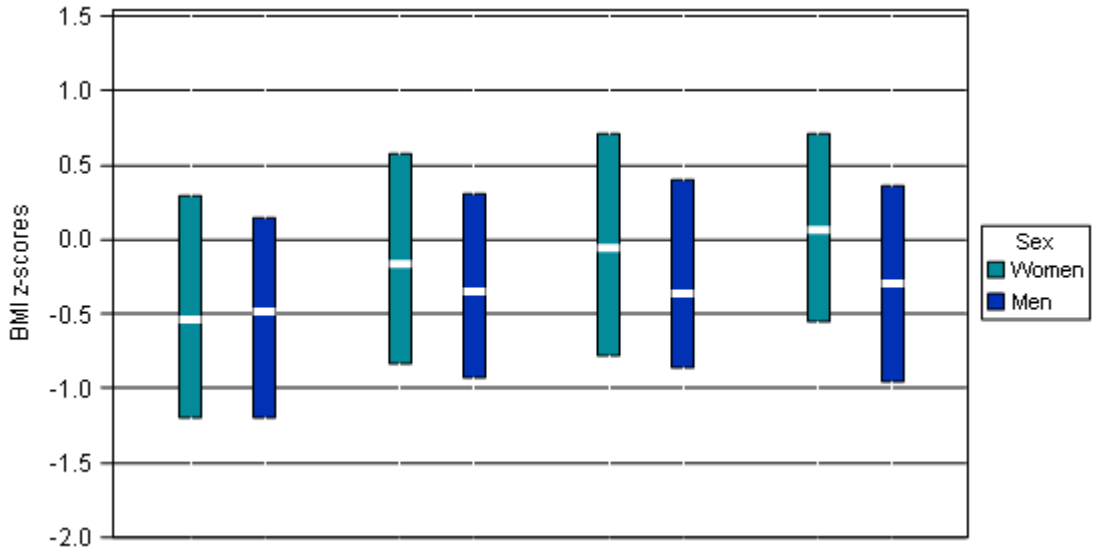
*See explicative note p 22

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	15-19	Total
Mean BMI z-score	Women	-0.41	-0.03	0.07	0.14	-0.03
	Men	-0.47	-0.27	-0.13	-0.22	-0.26
Median BMI z-score	Women	-0.54	-0.17	-0.05	0.07	-0.13
	Men	-0.48	-0.35	-0.36	-0.30	-0.37
BMI z-score >=0 (% of patients)	Women	35.6	42.1	49.7	54.3	46.4
	Men	30.6	34.6	38.6	37.1	35.6

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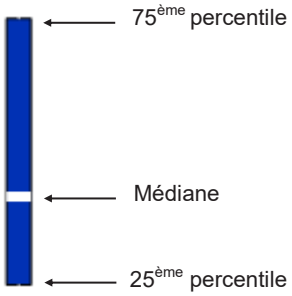
The z-score is a anthropometric reduced centered variable (Z = [measure-mean]/standard deviation), ajusted for gender and age; the mean and standard deviation are taken from the French reference population with the same gender and age as the patient. This index measures the difference with population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

- Height and weight z-scores have been calculated with respect to the French reference population (Sempé M., 1997, Auxologie – Méthode et séquences, Méditions, Lyon, 205 p.).

- The 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

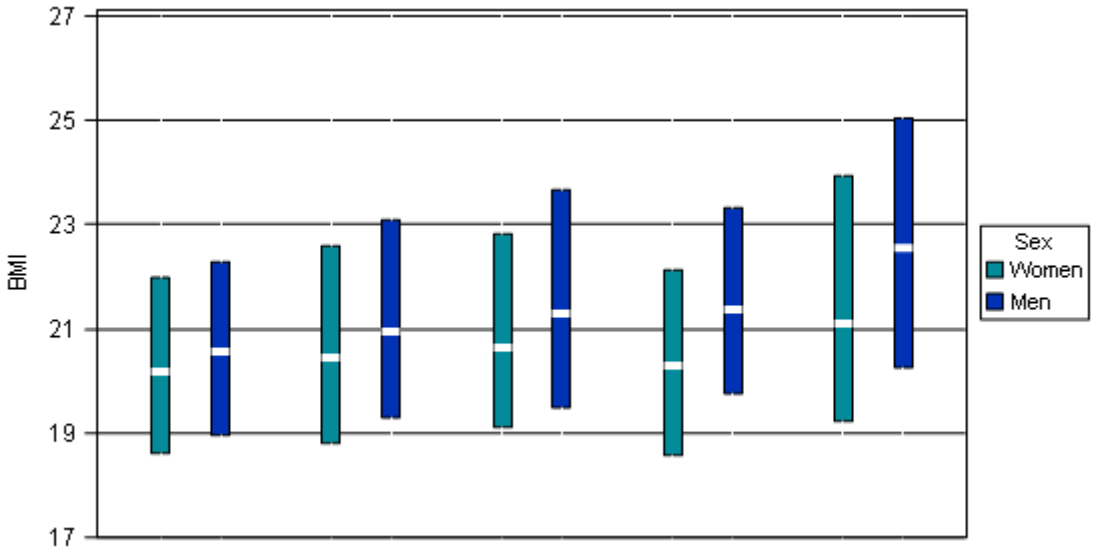
Those figures represent z-scores of anthropométrie and spirometry values.
For each age and sex group, median values are the white lines, extremes are the 25th and 75th percentiles.



5. Anthropometry

Body Mass Index (BMI)

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



Age groups (years)		20-24	25-29	30-34	35-39	40 +	Total
Mean BMI	Women	20.5	20.9	21.3	20.7	22.2	21.2
	Men	20.8	21.4	21.7	21.7	22.9	21.7
Median BMI	Women	20.2	20.5	20.6	20.3	21.1	20.5
	Men	20.6	21.0	21.3	21.4	22.6	21.3
BMI ≥ 22 (%)	Women	24	30	34	26	37	31
BMI ≥ 23 (%)	Men	18	26	31	29	44	30
BMI < 18.5 (%)	Women	23	20	17	24	16	20
	Men	20	15	17	14	12	15

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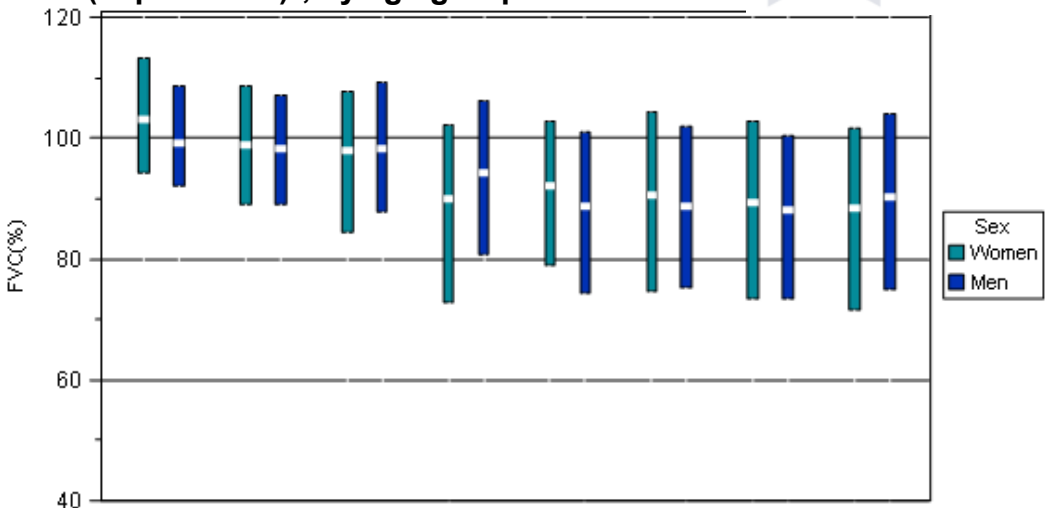
6. Spirometry

96.4% 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	102.4	97.7	95.0	87.6	90.3	88.9	88.5	87.4	92.0
	Men	99.4	97.5	97.1	91.9	86.5	87.3	86.1	88.5	91.8
	All patients	100.8	97.6	96.1	89.8	88.3	88.0	87.3	87.9	**91.9**
Median FVC	Women	103.0	99.0	97.9	89.9	92.2	90.5	89.4	88.6	94.8
	Men	99.1	98.2	98.2	94.4	88.6	88.9	88.1	90.2	94.3
	All patients	101.4	98.5	98.2	92.4	90.2	89.3	88.7	89.7	**94.5**

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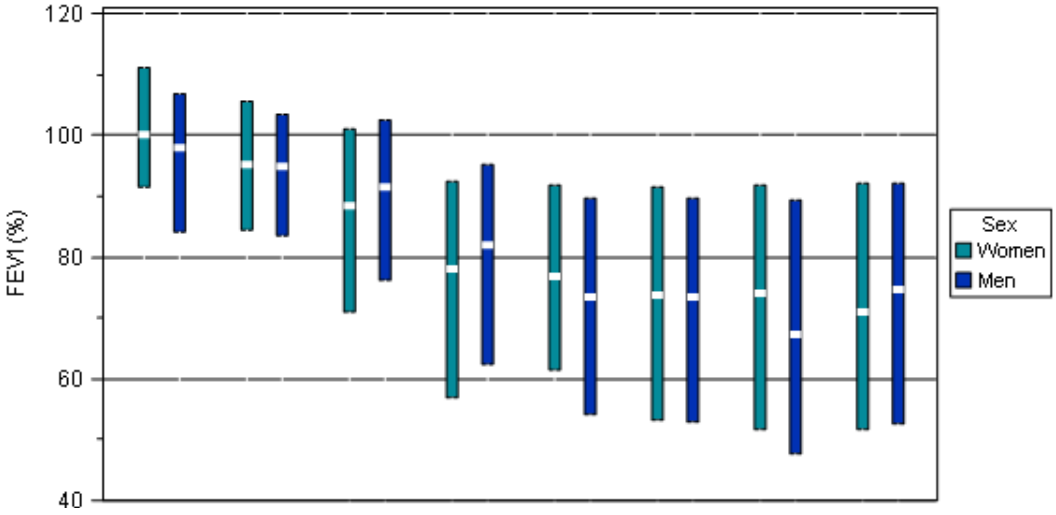
Figure 6.2. FEV_1 (% predicted)*, by age group and sex



	Age groups (years)	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +	Total
Mean FEV_1	Women	99.4	93.3	85.0	74.9	76.5	73.4	73.1	71.8	80.6
	Men	95.1	92.9	88.1	77.9	71.5	70.7	68.7	72.5	79.6
	All patients	97.2	93.1	86.6	76.4	73.9	71.9	70.8	72.1	**80.1**
Median FEV_1	Women	100.1	95.3	88.5	77.9	76.9	73.7	73.9	71.0	83.7
	Men	98.0	94.9	91.3	82.1	73.4	73.4	67.4	74.7	83.3
	All patients	98.8	95.1	89.8	79.5	75.3	73.6	71.8	72.7	**83.5**

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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 (Knudson *et al*. Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis 1983*, 127, pp. 725-734).

*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.

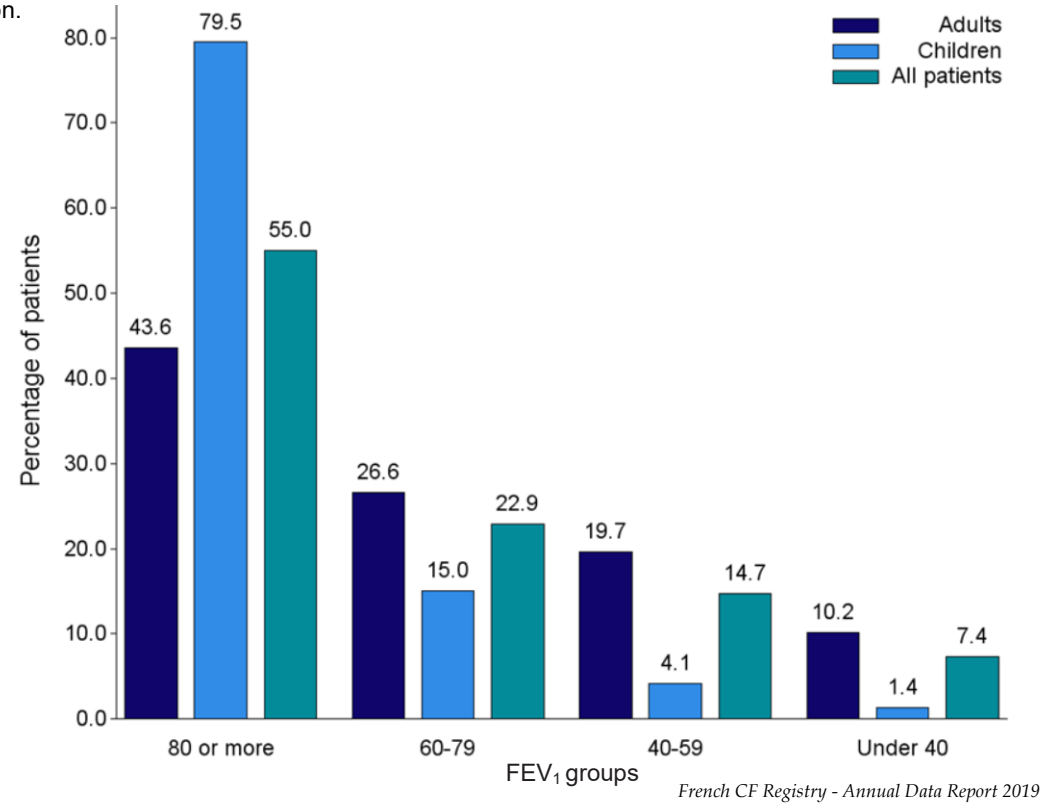
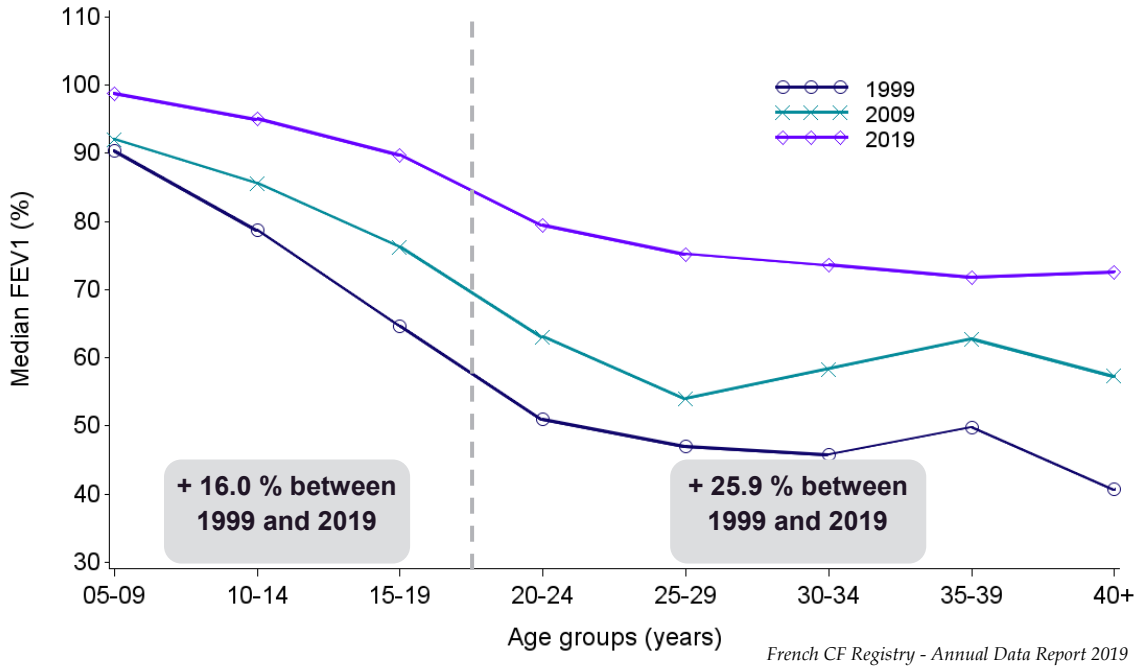


Figure 6.4. Median FEV_1 (% predicted) in 2019 compared with 1999 and 2009



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

The median FEV1 was 78.0 % for patients aged 6 to 19 years in 1999, and 94.0 % in 2019. It was 48.8 % in 1999 and 74.7 % in 2019 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	6150	*85.9 %*
Children	2898	*97.7 %*
Adults	3252	*77.6 %*

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In 2019, 85.9 % of the patients had at least one sputum culture. Among the patients without sputum culture (N=1010), 62.5 % 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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Patients with at least one sputum	**687**	**745**	**936**	**882**	**726**	**597**	**538**	**366**	**673**	**6150**	**85.9 %**
Normal culture	291	289	352	206	69	55	42	43	85	1432	20.0 %
Achromobacter xylosoxidans	13	31	69	85	95	69	62	29	44	497	6.9 %
Aspergillus	41	129	280	337	373	279	238	150	256	2083	29.1 %
Burkholderia cepacia, including:	2	13	19	20	27	30	18	12	17	158	2.2 %
- chronic B. cepacia	*.*	*4*	*6*	*11*	*17*	*26*	*11*	*6*	*10*	*91*	*1.3 %*
Haemophilus influenzae	180	265	186	153	135	93	85	53	67	1217	17.0 %
Atypical mycobacteria	5	13	26	43	37	47	32	16	43	262	3.7 %
Pneumococcus	49	59	22	6	4	6	8	8	12	174	2.4 %
Pseudomonas aeruginosa, including:	132	176	293	349	385	366	343	244	397	2685	37.5 %
- Chronic P. aeruginosa	*3*	*28*	*101*	*176*	*240*	*236*	*230*	*162*	*256*	*1432*	*20.0 %*
Staphylococcus, including:	482	573	777	726	583	441	377	214	356	4529	63.3 %
- MSSA	*471*	*557*	*760*	*696*	*534*	*404*	*321*	*193*	*307*	*4243*	*59.3 %*
- MRSA	*16*	*24*	*40*	*63*	*68*	*55*	*68*	*33*	*54*	*421*	*5.9 %*
Stenotrophomonas maltophilia	64	76	132	127	103	79	64	37	64	746	10.4 %

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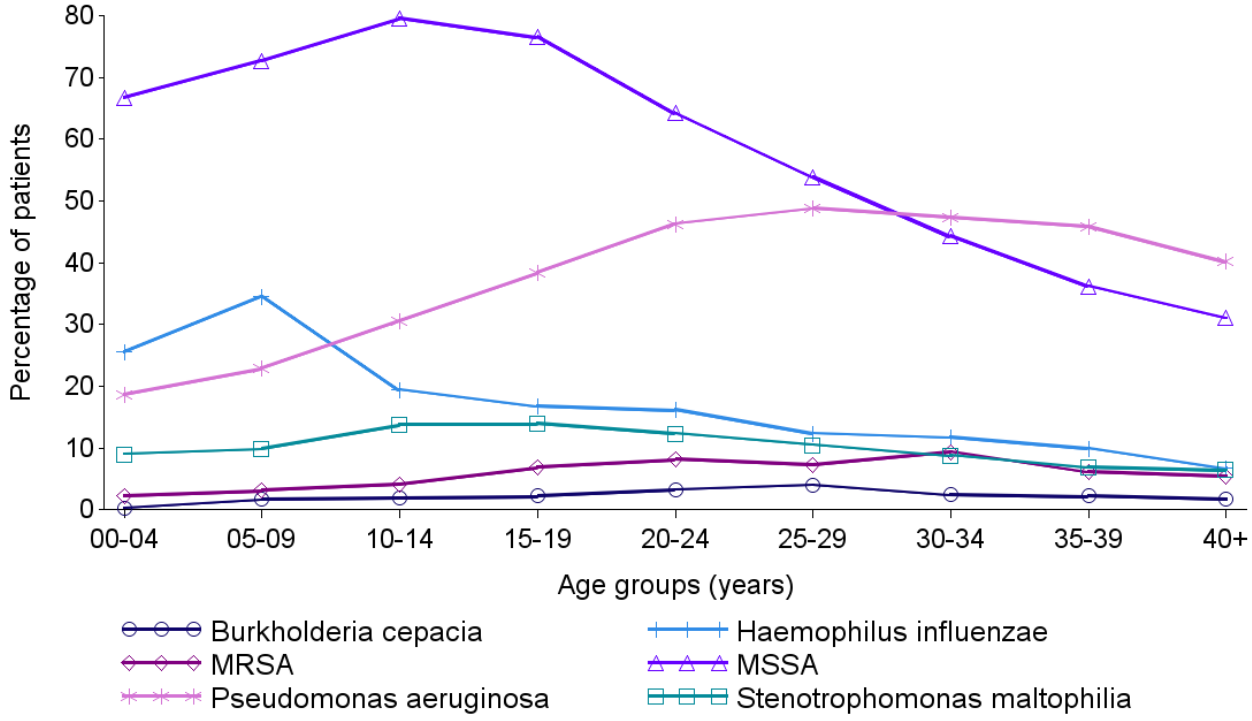
* Percentage with respect to the entire population.

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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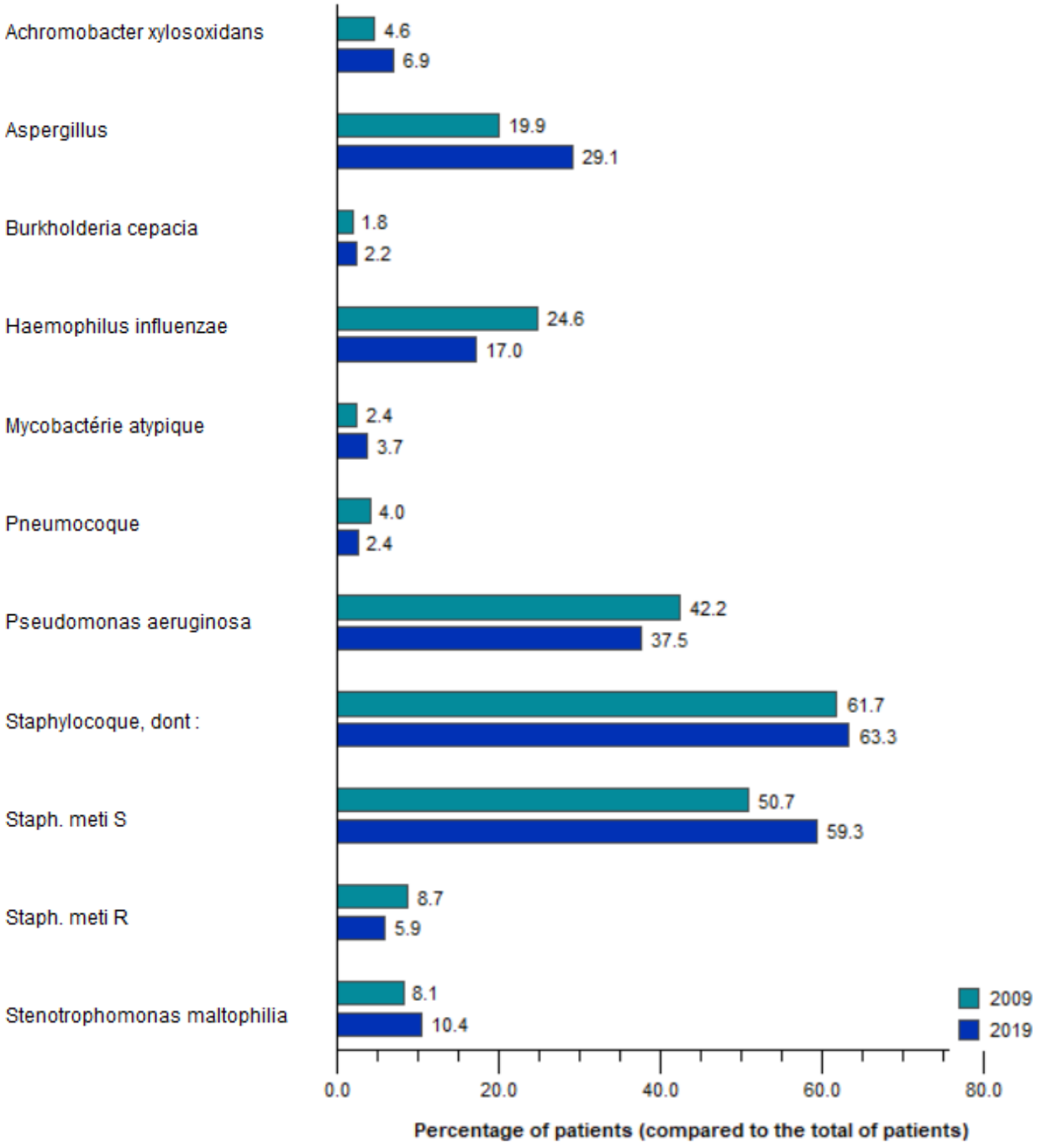
7. Microbiology

Figure 7.2. Comparison of germs in 2019 and in 2009



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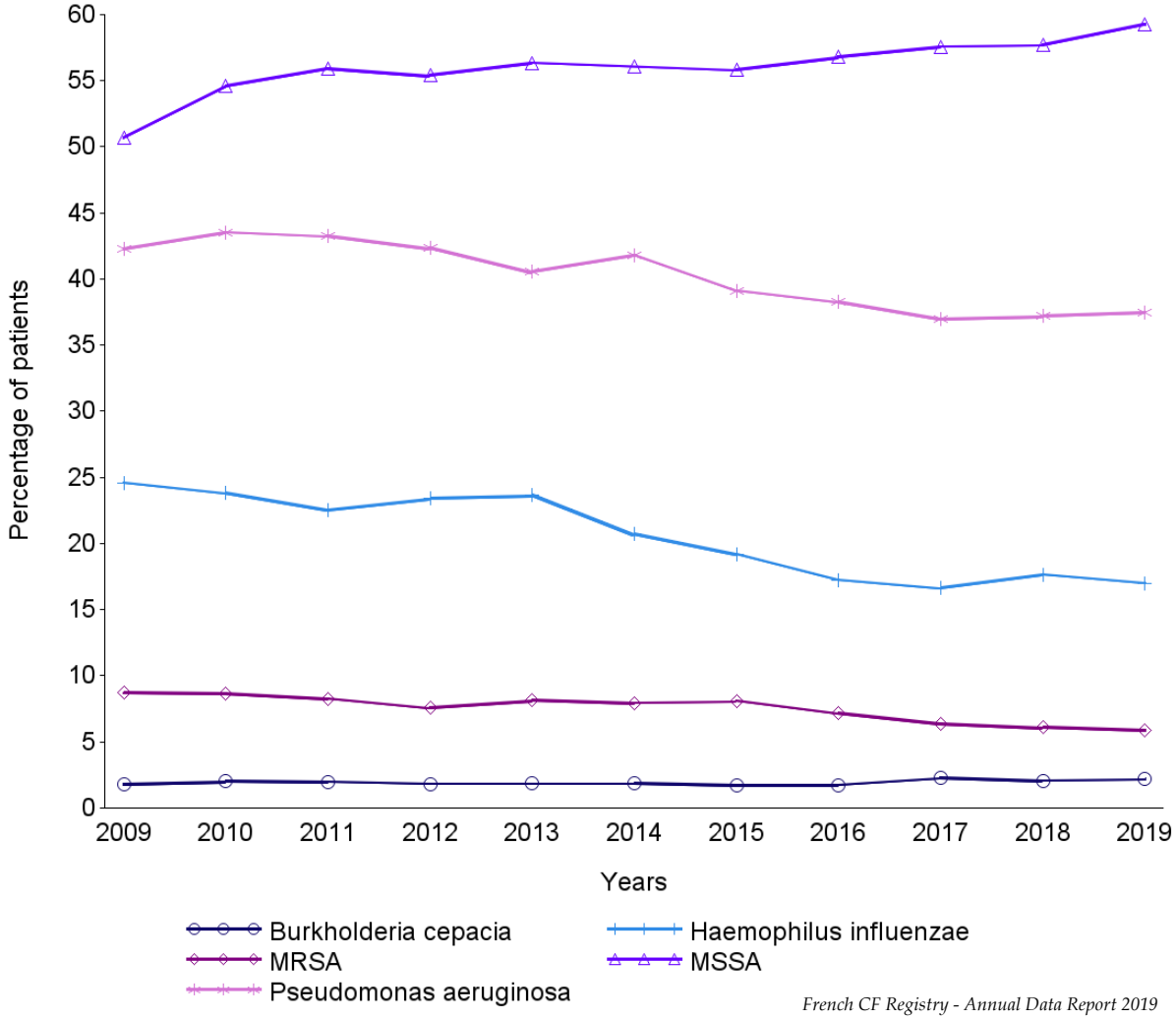
7. Microbiology

Figure 7.3. Evolution of respiratory germs since 2009



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8. Complications

Respiratory

Table 8.1. Respiratory complications

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Treated aspergillosis	6	28	75	108	113	86	75	46	83	620	8.7 %
Asthma	128	162	204	201	192	164	172	131	197	1551	21.7 %
Haemoptysis	1	2	20	58	78	84	70	43	53	409	5.7 %
Pneumothorax	1	1	3	8	7	6	.	2	5	33	0.5 %
Nasal polyps	20	102	179	194	203	174	144	105	208	1329	18.6 %

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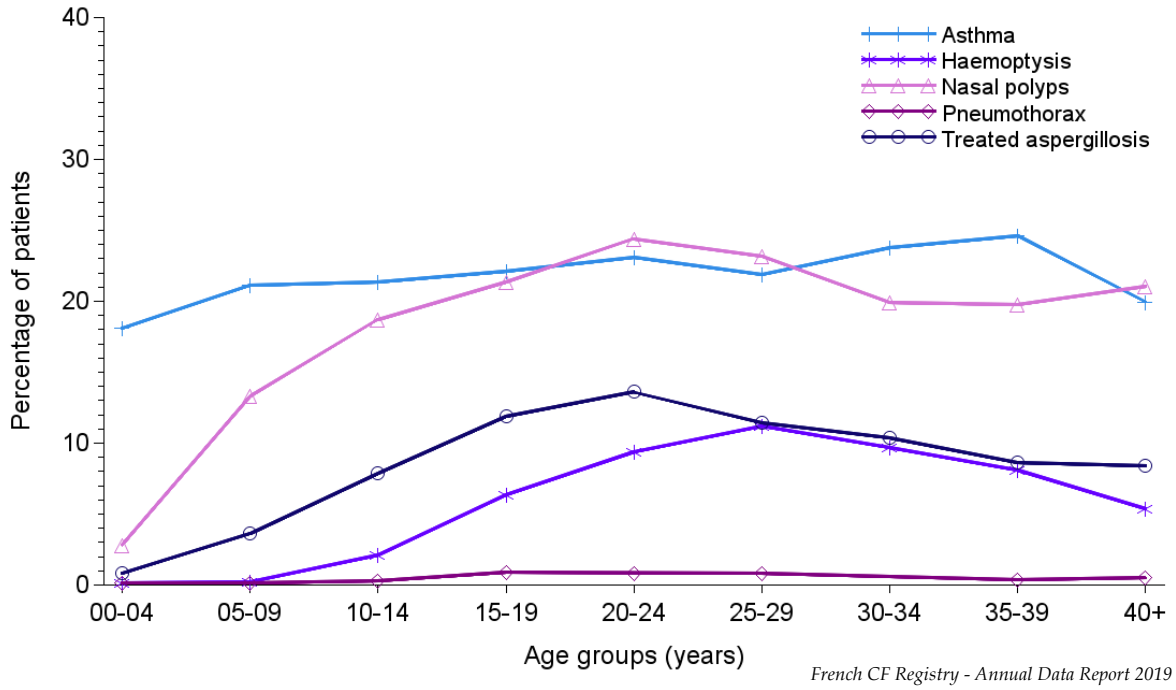
Figure 8.1. Respiratory complications

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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Gallstones	4	5	19	16	19	34	41	29	38	205	2.9 %
Cirrhosis/Portal hypertension	6	10	46	47	50	31	24	18	26	258	3.6 %
Abnormal exocrine pancreatic function	558	597	771	732	690	637	594	450	676	5705	79.7 %
Intestinal obstruction	14	15	32	22	26	38	29	18	28	222	3.1 %
Acute pancreatitis	4	6	4	11	16	8	11	11	21	92	1.3 %
Treated gastro-oesophageal reflux disease	103	101	123	159	252	255	263	211	396	1863	26.0 %

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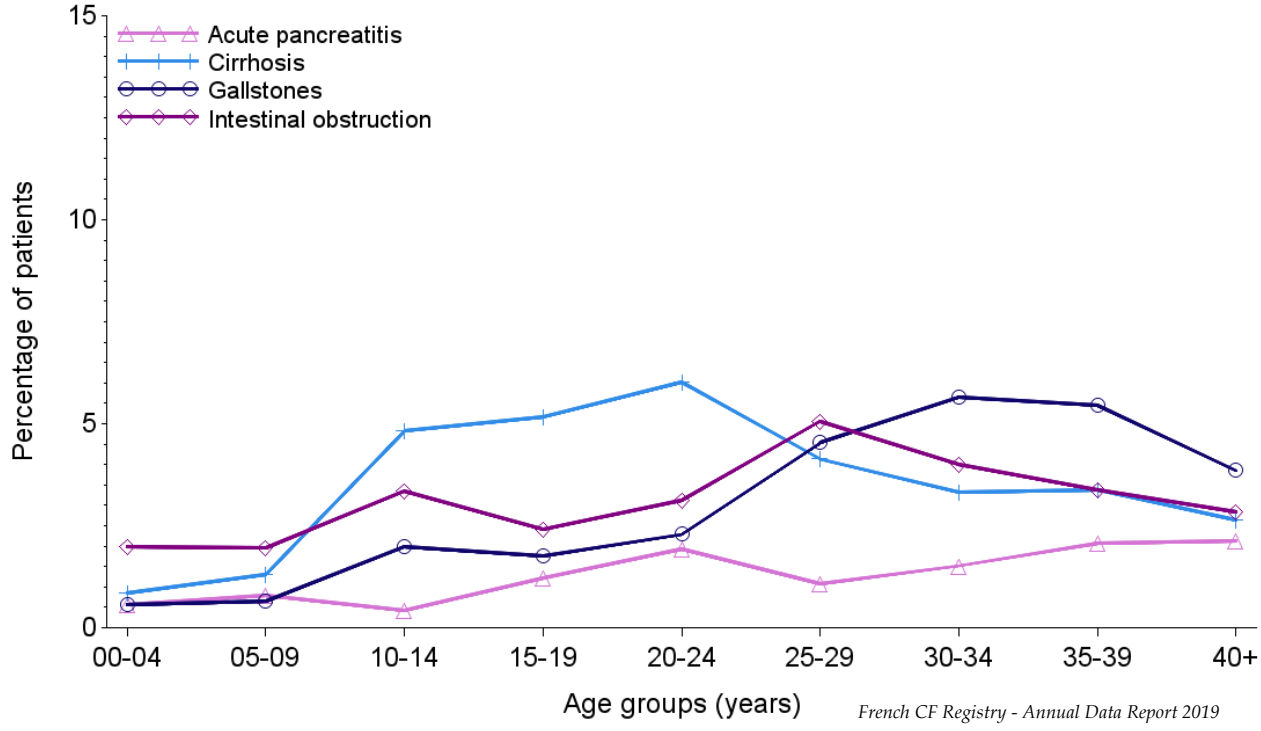
Figure 8.2. Gastro-intestinal complications

Percentage of age groups reporting complications.



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8. Complications

Diabetes mellitus

30.3% of adult patients are with diabetes mellitus

Table 8.3. Diabetes mellitus and degenerative complications of diabetes

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Total diabetes (ID and non ID diabetes)	1	8	88	144	196	214	247	210	333	1441	20.1 %
Non insulin-dependent diabetes	1	2	26	25	36	21	29	22	32	194	2.7 %
Insulin-dependent	.	6	62	120	162	193	219	191	303	1256	17.5 %
Degenerative complications of diabetes	.	.	.	.	3	11	19	17	26	76	1.1 %

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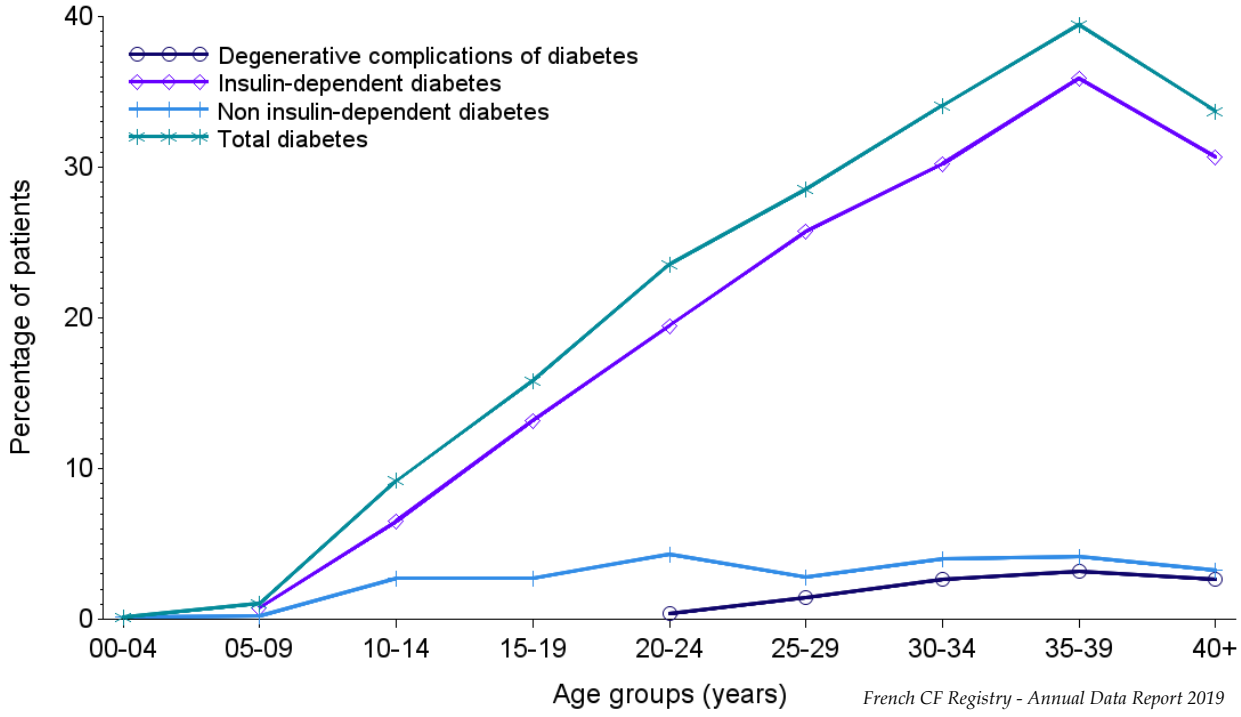
The line « Total diabetes » sums the number of patients having at least one type of diabetes. Among the 1441 patients, 9 patients presented with both types of diabetes during the year.

Figure 8.3. Diabetes mellitus and degenerative complications of diabetes

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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Arthropathy	.	4	11	15	14	24	26	33	68	195	2.7 %
Cancer	.	1	.	3	4	11	5	18	45	87	1.2 %
Depression (evaluated and followed)	.	7	28	40	68	91	82	79	163	558	7.8 %
Urinary incontinence	.	2	4	7	12	10	15	12	24	86	1.2 %
Terminal renal failure	.	.	.	.	2	3	7	7	13	32	0.4 %
Osteopenia/osteoporosis	.	1	23	52	139	165	161	160	328	1029	14.4 %
Deafness/Hypoacusia	4	4	8	14	47	112	124	96	188	597	8.3 %

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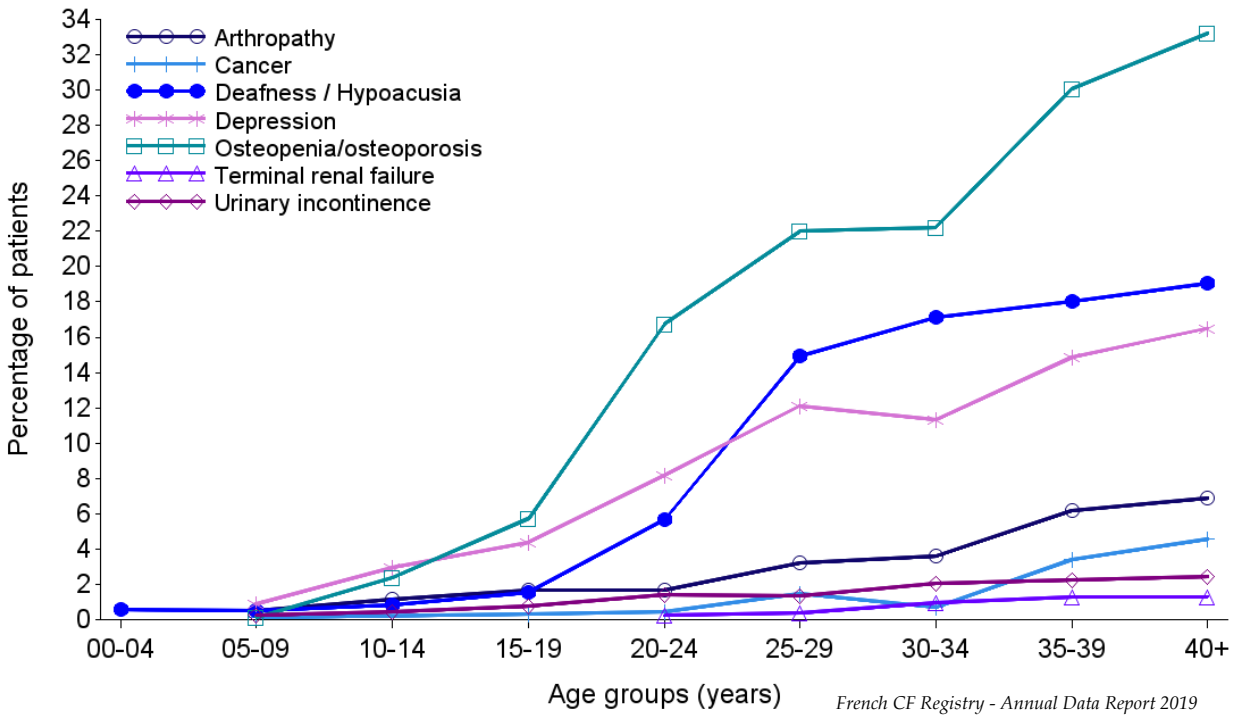
Figure 8.4. Other complications

Percentage of age groups reporting complications.



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9. Transplantation

21.5% 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 2019.

	All years	2019
WAITING LIST	All waiting patients	Listed in 2019
Nb of patients	**139**	**91**
Mean age (years) and standard deviation (SD)	30.9 ± 10.0	29.7 ± 9.49
Extremes of age (years)	2.08-67.8	2.08-57.8
Deaths on waiting list	4	0
TRANSPLANTATION	All transplanted*	Transplanted in 2019
Nb of patients	**923**	**93**
Single organ transplant:		
- bilateral lung - N (%)	870 (94.3 %)	78 (83.9 %)
- liver - N (%)	28 (3.0 %)	1 (1.1 %)
- kidney - N (%)	66 (7.2 %)	11 (11.8 %)
- bilobar lung transplantation, N(%)	1 (0.1 %)	
- single lung - N (%)	9 (1.0 %)	
- pancreatic islets, N(%)	1 (0.1 %)	
- bone marrow - N (%)	1 (0.1 %)	
Multiple organ transplant:		
- heart-lung - N (%)	24 (2.6 %)	
- heart-lung / liver - N (%)	2 (0.2 %)	
- bilateral lung / liver - N (%)	24 (2.6 %)	1 (1.1 %)
- bilateral lung / kidney - N (%)	5 (0.5 %)	1 (1.1 %)
- bilateral lung / islet of Langerhans - N (%)	9 (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 %)	1 (1.1 %)
Mean age (years)	36.4	30.7
SD	10.3	9.97
Extremes of age (years)	2.08-70.3	2.08-67.8
Post-transplantation deaths	21	3

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

9. Transplantation

Figure 9.1. Annual number of transplanted patients, since 1992

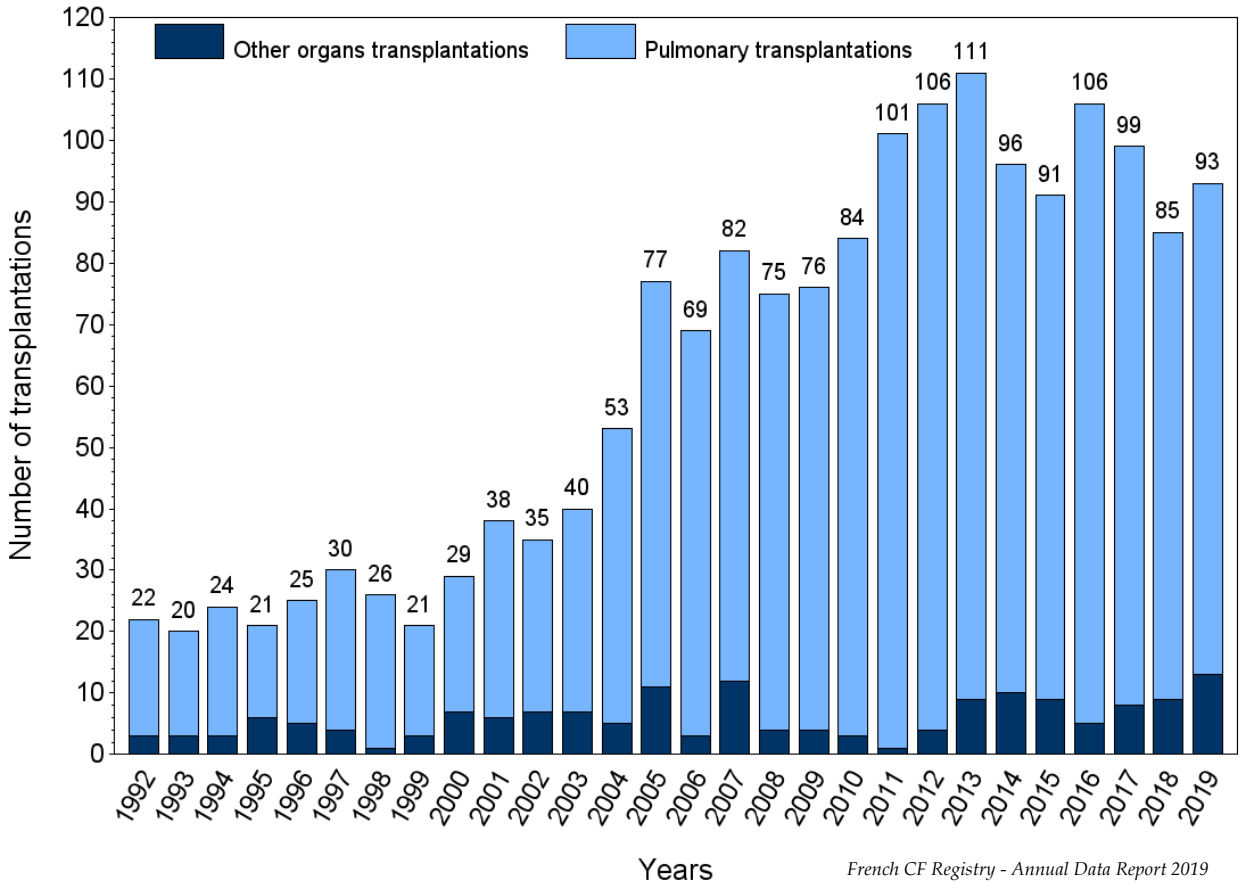

Table 9.2. Annual number of transplanted patients, since 1992

	Years													
Transplant type	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Pulmonary*	19	17	21	15	20	26	25	18	22	32	28	33	48	66
Other organs	3	3	3	6	5	4	1	3	7	6	7	7	5	11

	Years													
Greffes	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Pulmonaires *	66	70	71	72	81	100	102	102	86	82	101	91	76	80
Autres organes	3	12	4	4	3	1	4	9	10	9	5	8	9	13

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

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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*
< 4 visits per year	118	157	183	196	242	206	209	172	391	1874
≥ 4 visits per years	588	609	772	713	589	544	515	360	596	5286
Outpatient visits										
Number of patients with at least one outpatient visit	*445*	*459*	*582*	*574*	*598*	*529*	*501*	*370*	*676*	*4734*
Median number of visits	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Mean number of visits	3.7	3.3	3.5	3.7	3.9	3.9	3.7	3.8	3.4	3.7
One-day hospitalizations										
Number of patients with at least one one-day visit	*612*	*714*	*908*	*838*	*679*	*612*	*596*	*415*	*758*	*6132*
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	3.8	3.0	3.3	3.3	2.9	2.8	2.9	2.8	2.7	3.1
Inpatient visits										
Number of patients with at least one inpatient visit	*164*	*106*	*220*	*249*	*251*	*254*	*224*	*196*	*300*	*1964*
Median number of visits	1.0	1.0	1.0	2.0	2.0	2.0	1.5	1.0	1.0	1.0
Mean number of visits	1.5	1.8	1.9	2.7	2.5	3.0	2.4	2.6	2.5	2.4
Median duration (days)	10.0	7.0	8.0	9.0	10.0	12.0	11.0	8.5	8.0	9.0
Mean duration (days)	17.6	15.3	15.4	24.4	22.1	22.3	17.9	17.2	19.2	19.5

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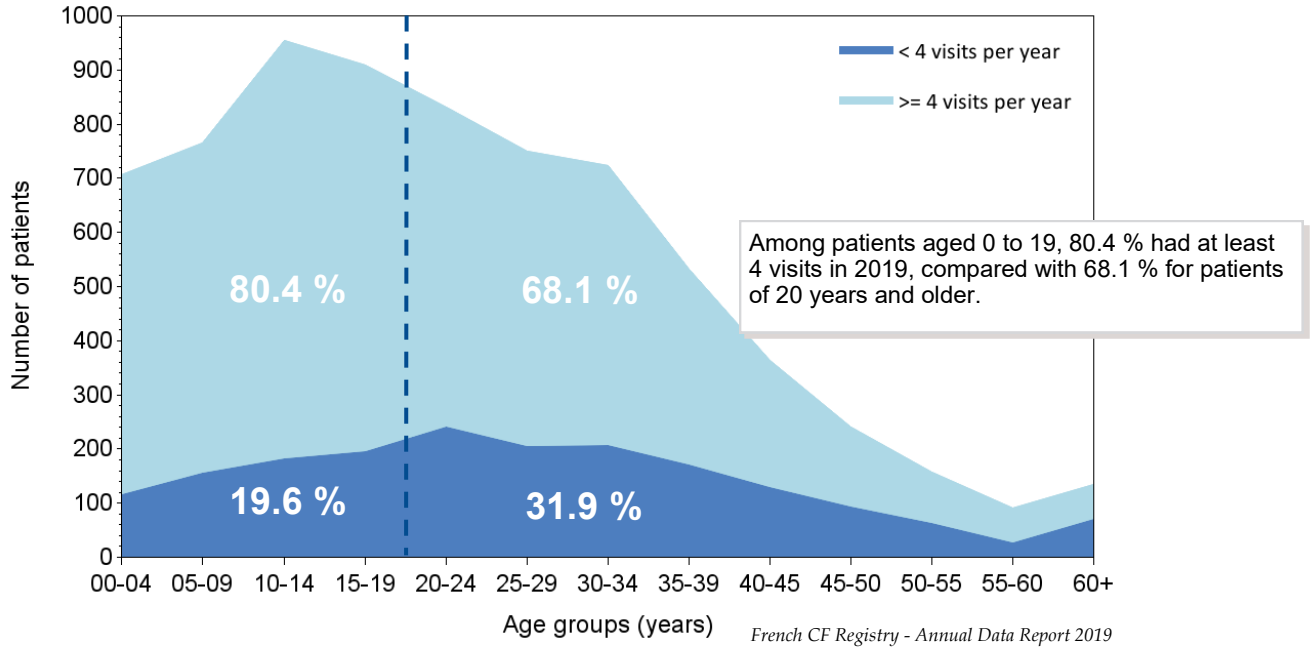
Figure 10.1. Number of visits



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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).

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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*
Nb of patients with at least one course	78	98	207	276	329	322	278	207	288	2083
- and with TIVAD*	6	29	69	100	128	149	129	99	131	840
Nb of courses	90	171	448	637	739	777	652	429	625	4568
Nb of days of courses including:	1463	2557	6858	9893	12077	12388	10460	6325	9416	71437
- at hospital	1055	1288	2429	3419	2951	3146	1983	1489	2726	20486
- at home	383	1269	4457	6431	8629	8595	8039	4798	6477	49078
TIVAD* (with and without course)	6	29	72	108	139	160	149	112	156	931

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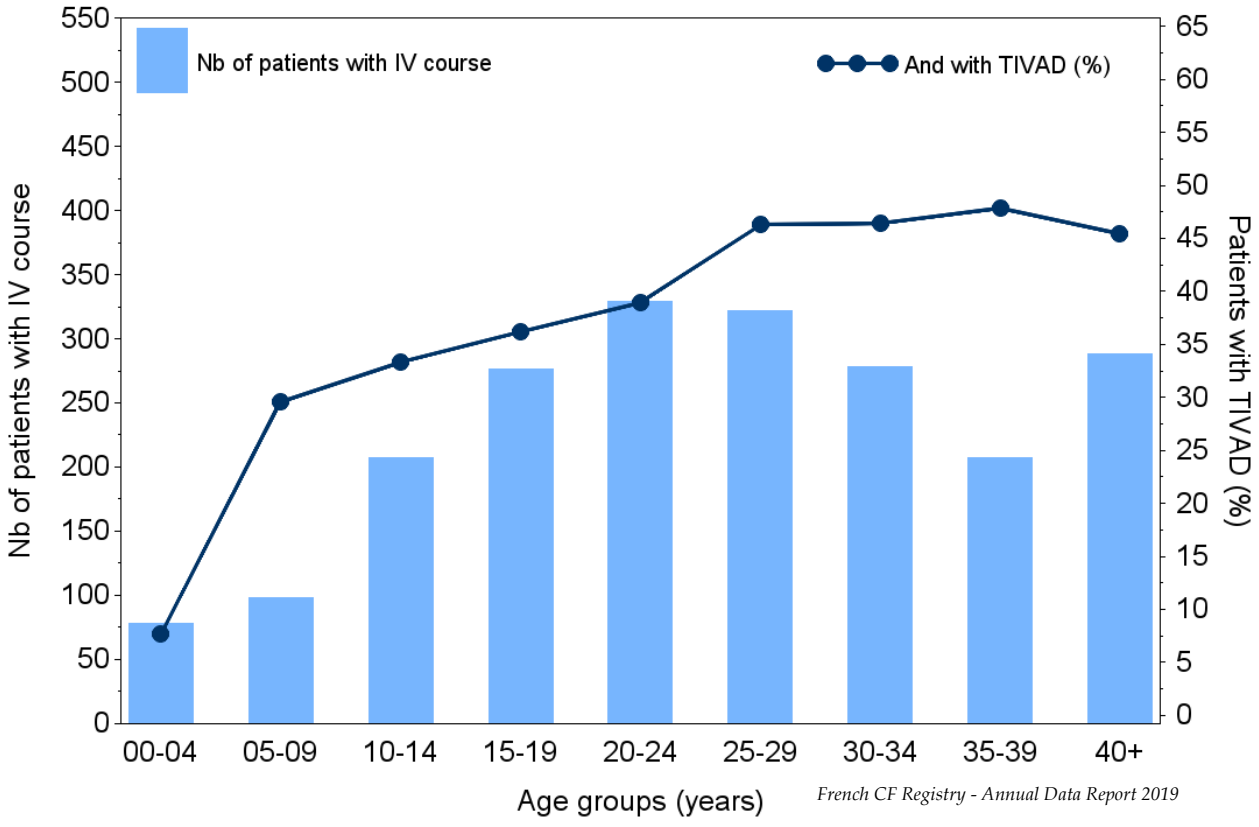
Figure 11.1. Patients with at least one IV antibiotic course and a TIVAD *



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* TIVAD: Totally Implantable Vascular Access Device

11. Therapeutic management

IV antibiotic courses

Table 11.2. Repartition of IV antibiotic 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	1.2	1.7	2.2	2.3	2.3	2.5	2.4	2.1	2.2	2.2
SD	0.5	1.3	1.7	1.7	1.8	2.0	2.0	1.6	1.7	1.8
Median number of courses	1.0	1.0	2.0	2.0	2.0	2.0	2.0	1.0	2.0	2.0
1st quartile (Q1)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
3rd quartile (Q3)	1.0	2.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Day of courses										
Mean duration of courses (days)	19.3	26.1	33.5	36.6	38.1	40.1	38.9	31.9	34.1	35.4
SD	25.6	22.3	33.0	30.5	41.4	42.5	42.1	33.0	29.0	36.1
Median duration of courses (days)	14.0	15.0	22.0	28.0	28.0	28.0	28.0	17.0	28.0	26.0
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)	15.0	30.0	42.0	45.0	43.0	45.0	48.0	37.0	42.0	43.0

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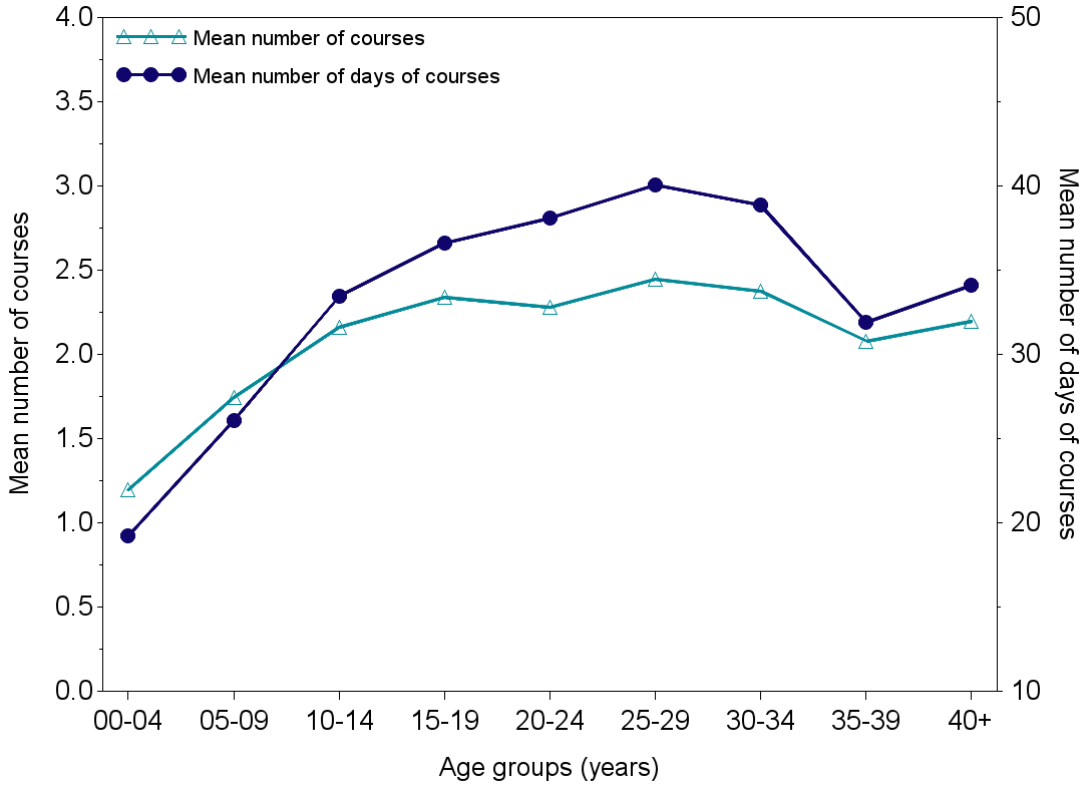
Figure 11.2. Mean number of courses and of days of IV antibiotic courses *



* Among patients having received at least one IV antibiotic course.

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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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Aerosol therapy*	374	596	829	795	735	624	582	410	744	5689	79.5 %
Azithromycin	74	161	271	298	335	348	342	280	470	2579	36.0 %
Oxygen therapy	1	2	14	29	50	52	46	36	95	325	4.5 %
Oral corticosteroids	7	13	29	44	104	148	162	152	285	944	13.2 %
Nasal ventilation	1	21	37	49	35	45	38	30	75	331	4.6 %

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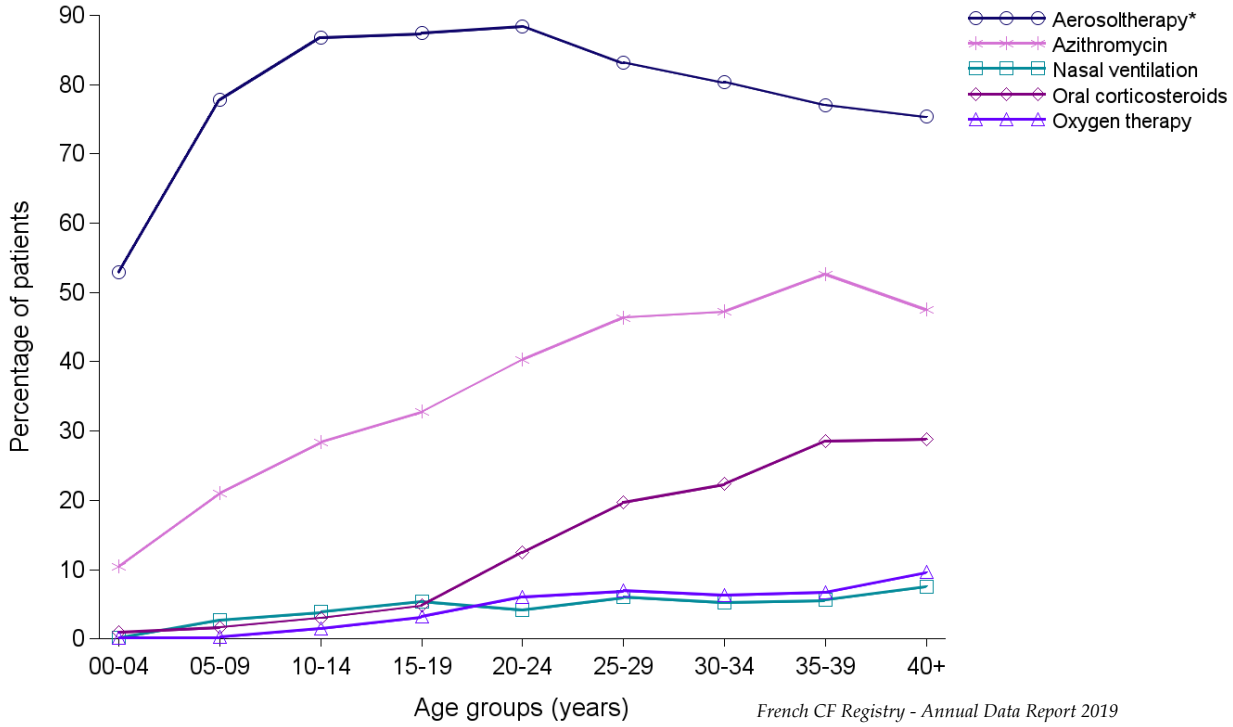
Figure 11.3. Respiratory therapeutics (≥ 3 months)



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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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Ivacaftor	5	19	27	26	21	17	12	12	32	171	2.4 %
Lumacaftor + Ivacaftor	2	9	193	283	239	172	140	87	82	1207	16.9 %

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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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Patients under aerosol therapy*	**374**	**596**	**829**	**795**	**735**	**624**	**582**	**410**	**744**	**5689**	**79.5 %**
Inhaled antibiotics, including:	122	185	305	377	408	386	349	259	395	2786	38.9 %
- Tobramycin	*43*	*80*	*151*	*186*	*193*	*154*	*140*	*84*	*110*	*1141*	*15.9 %*
- Colistin	*37*	*75*	*161*	*197*	*218*	*209*	*199*	*162*	*235*	*1493*	*20.9 %*
- Aztreonam	*1*	*1*	*8*	*16*	*31*	*31*	*36*	*31*	*44*	*199*	*2.8 %*
Inhaled bronchodilators	248	396	591	591	575	479	454	326	587	4247	59.3 %
Inhaled corticosteroids	122	248	373	413	364	283	263	192	339	2597	36.3 %
Inhaled hypertonic saline	66	119	173	172	103	56	57	47	55	848	11.8 %
RhDNase	77	375	565	518	382	282	244	141	242	2826	39.5 %

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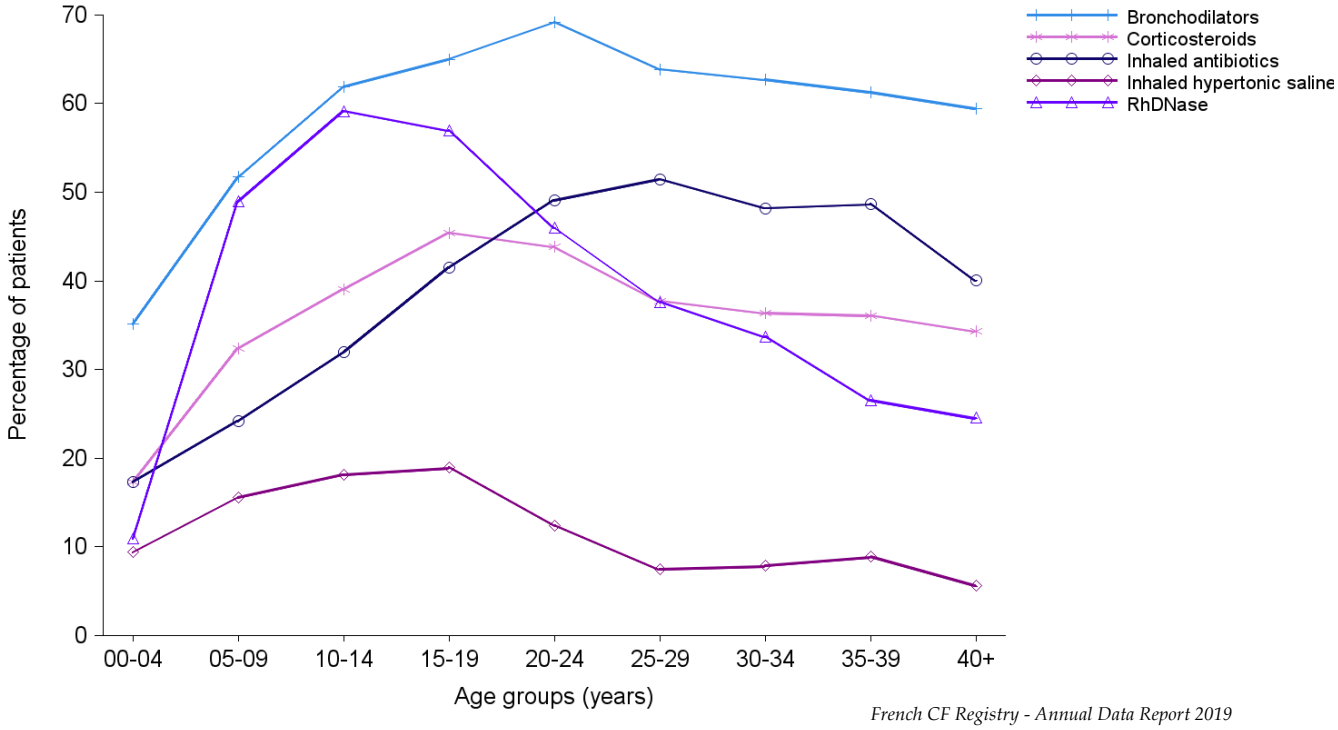
* By nebulization, spray or powder

Figure 11.4. Aerosoltherapy treatments (≥ 3 months)



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11. Therapeutic management

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	*706*	*766*	*955*	*909*	*831*	*750*	*724*	*532*	*987*	*7160*	
Ursodeoxycholic acid	44	114	235	286	260	208	223	131	177	1678	23.4 %
Acid blockers	180	212	295	358	422	401	387	294	553	3102	43.3 %
Pancreatic enzymes	558	595	762	735	703	640	604	455	675	5727	80.0 %
Supplemental tube feeding	52	46	67	69	52	30	20	13	23	372	5.2 %
Oral supplemental feeding	150	238	352	303	311	298	251	209	250	2362	33.0 %
Fat-soluble vitamins	639	699	878	829	761	673	611	464	770	6324	88.3 %

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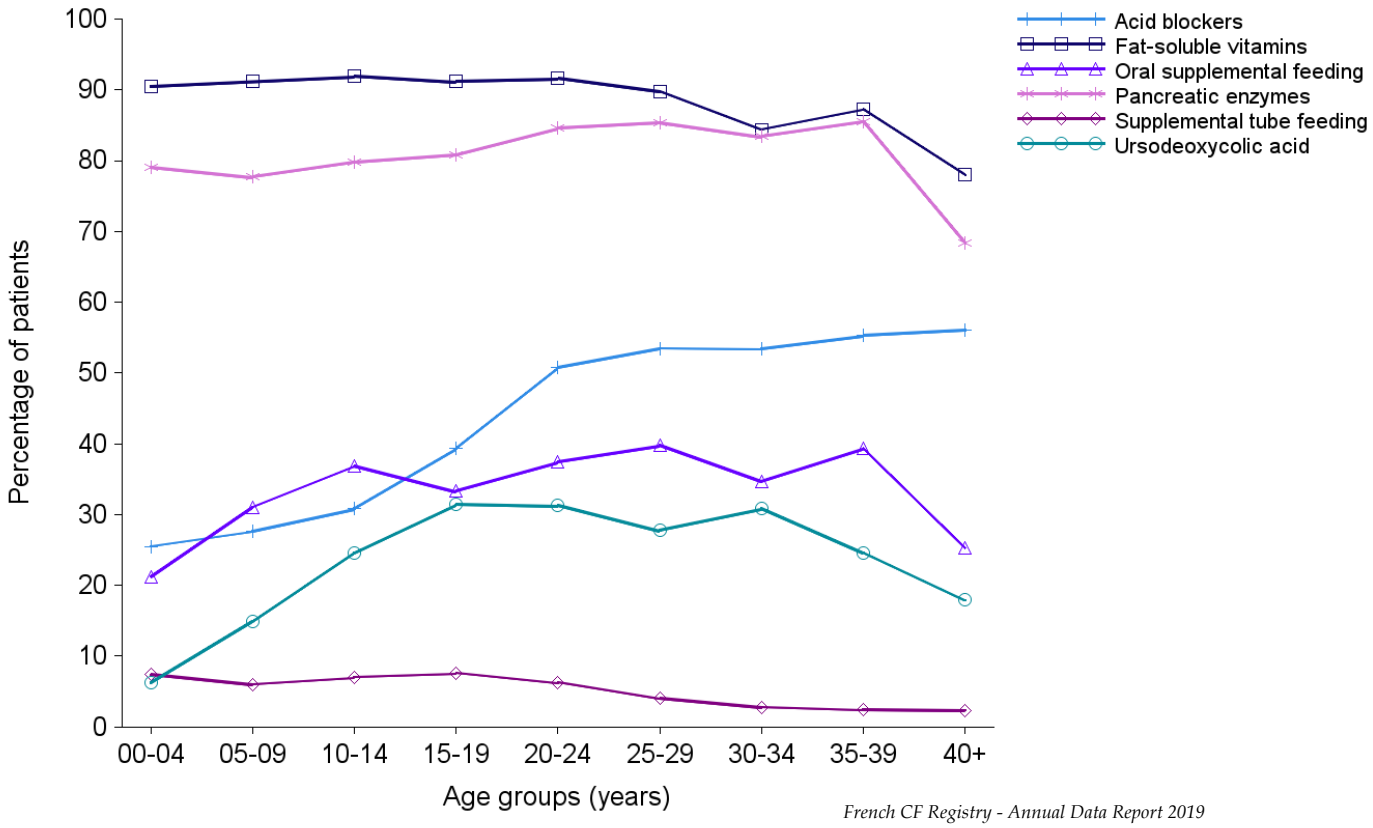
Figure 11.5. Hepatic, digestive and nutritional treatments (≥ 3 months)



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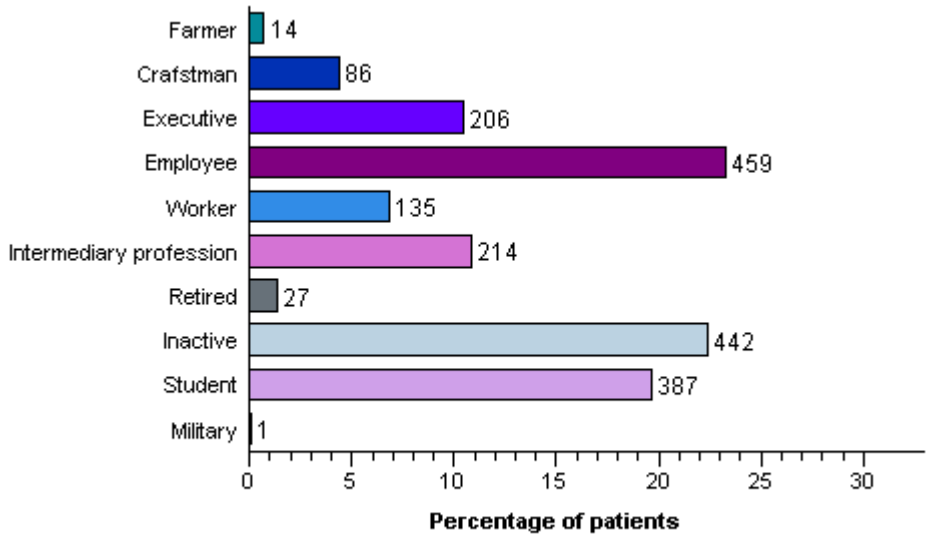
12. Social data

Employment

Figure 12.1. Employment of men ≥ 18 years

N = 1971 (number of men with a known employment situation, corresponding to 88.9 % of adults men).



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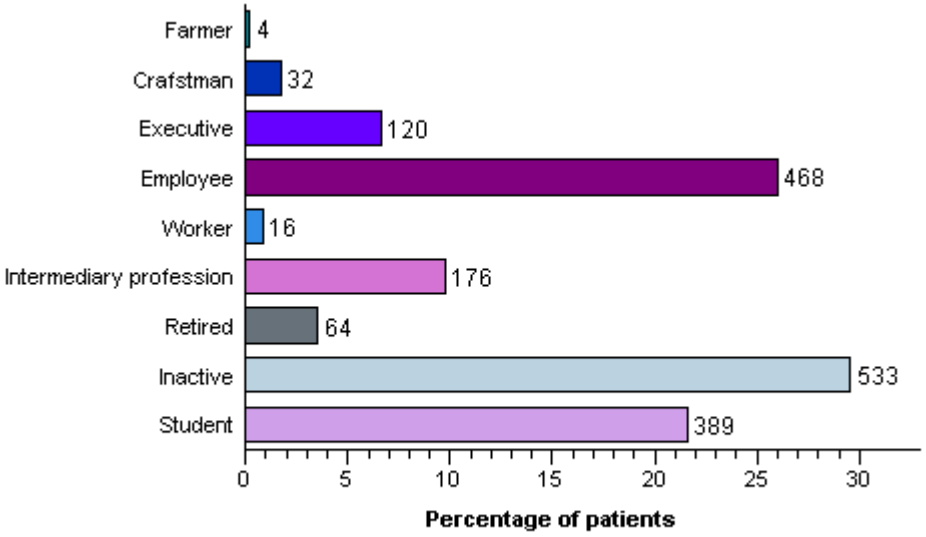
Among men aged 18 to 65, 50.6 % are workers.

Among men aged 18 to 25, 53.5 % are studiants.

Figure 12.2. Employment of women ≥ 18 years

N = 1802 (number of women with a known employment situation, corresponding to 91.2 % of adults women).



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Among women aged 18 to 65, 42.4 % are workers.

Among women aged 18 to 25, 56.6 % are studiants.

12. Social data

Marital status

Figure 12.3. Family status of men ≥ 18 years

Number of men with a known family status: 2059 (92.9 % of adult men).

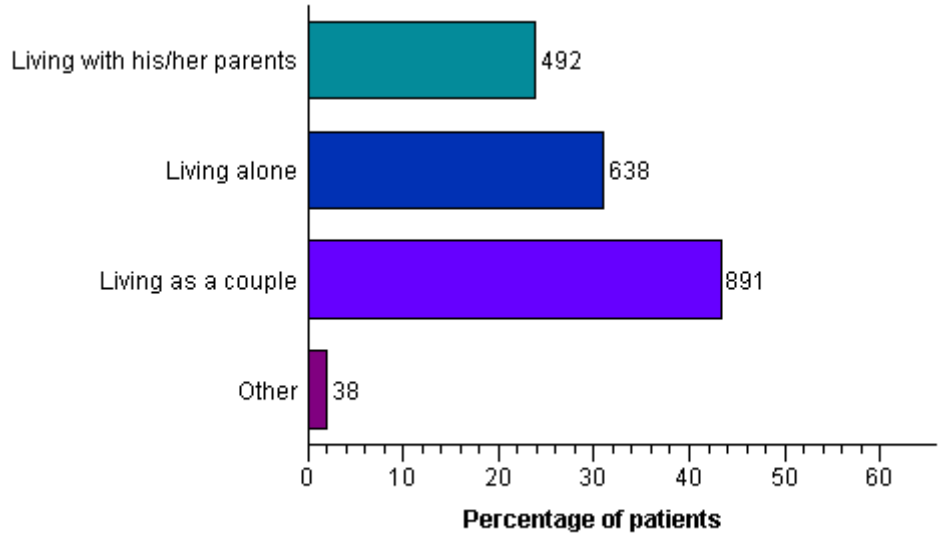

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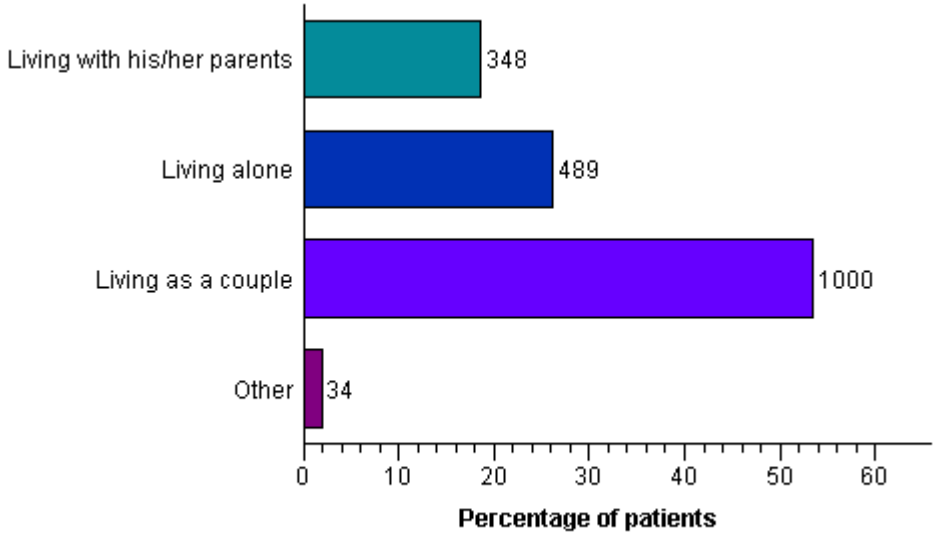
Figure 12.4. Family status of women ≥ 18 years

Number of women with a known family status: 1871 (94.7 % of adult women).



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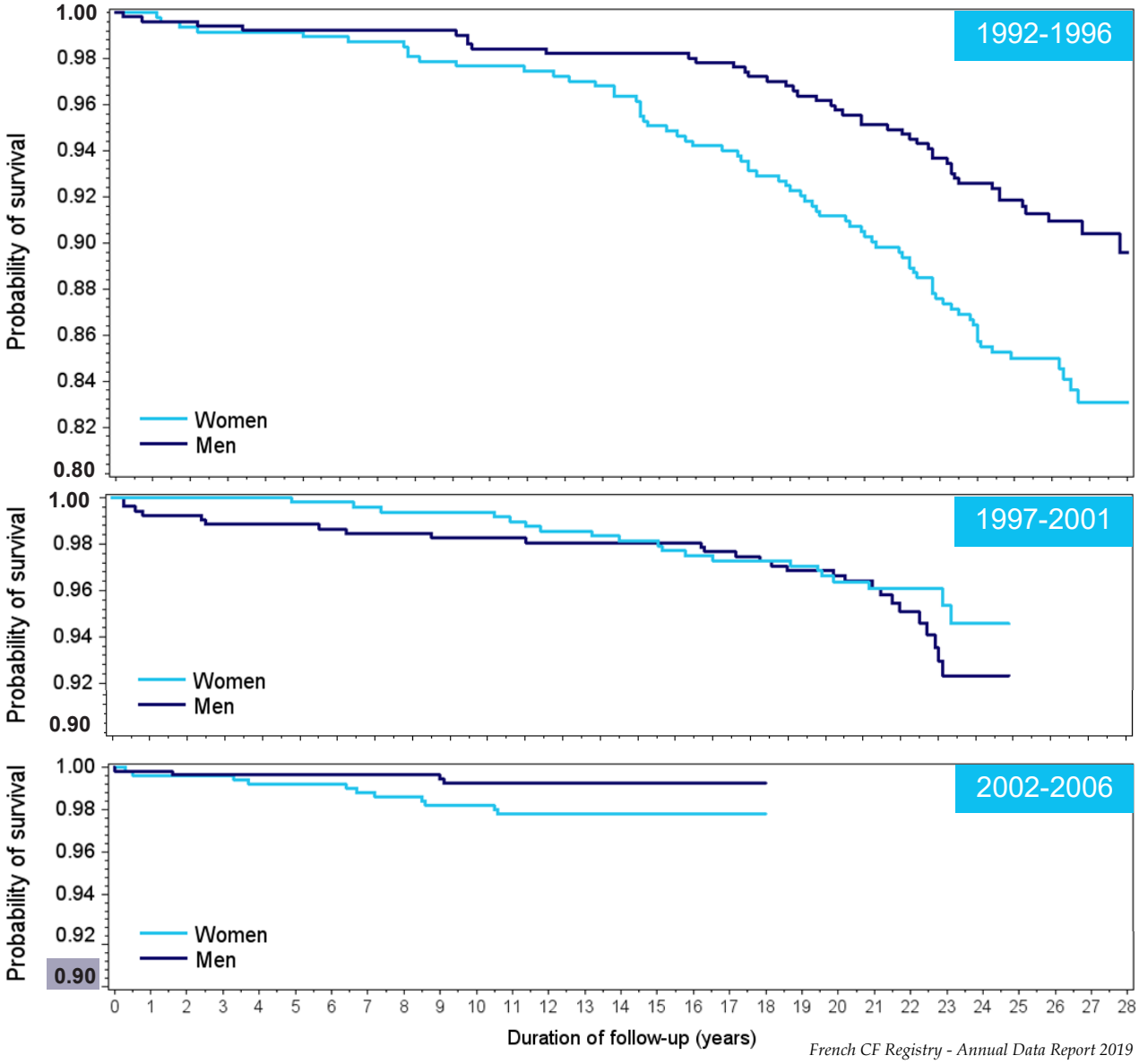
Annex 1

- 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	512	44	474	72
1997-2001	519	27	497	20
2002-2006	553	4	512	11



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

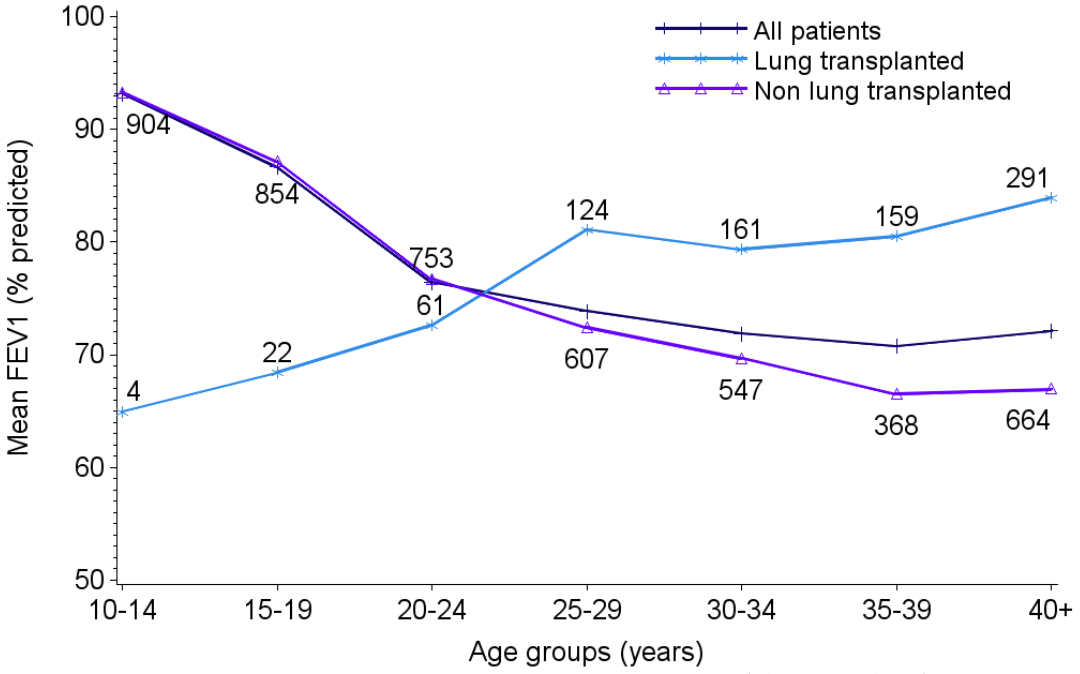
Spirometry and transplantation

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: 124 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: 607 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	67
Bordeaux	170
Grenoble	124
Lille	187
Lyon	258
Marseille	135
Nancy	140
Nantes	112
Paris Necker	187
Paris Robert Debré	161
Paris Trousseau	51
Rennes St Brieuc	122
Saint Denis de la Réunion	61
Strasbourg	109
Toulouse	121
Tours	125
Versailles	66
Adults CF care centres	
Besançon	77
Bordeaux	137
Grenoble	94
Lille	228
Lyon	402
Marseille	263
Nancy	92
Nantes	255
Paris Cochin	576
Rennes	131
Strasbourg	161
Suresnes Foch	543
Toulouse	197
Tours	88
Paediatric and Adults CF care centres	
Amiens	103
Angers-Le Mans	135
Caen	123
Clermont-Ferrand	139
Créteil	119
Dijon	130
Dunkerque	87
Giens	203
Limoges	70
Montpellier	226
Nice	107
Reims	142
Roscoff	170
Rouen	220
Saint Pierre de la Réunion	82
Vannes-Lorient	93

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	18
Montluçon	1
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 2019 were excluded from those statistics.

Annex 4 (1/2)

Table A4.1. Summary of data

	2017	2018	2019
Patients seen during the year and centres participating to the registry			
- Patients registered* (N):	7076	7181	7280
- Patients seen during the year in a centre** (N):	6933	7073	7160
- Centres (N) :			
Paediatric CRCMs:	17	17	17
Adult CRCMs:	14	14	14
Paediatric and Adult CRCMs:	16	16	16
Other centres:	4	4	3
Demographics			
- Male patients (%):	52.2	52.0	52.2
- Age of patients, in years (mean):	22.3	22.9	23.4
- Age of patients, in years (median):	20.3	20.9	21.3
- Age of patients. in years (min-max):	0.1-85.1	0.1-86.1	0.1-84.6
- Patients aged 18 years and over (%):	55.8	57.4	58.6
- Early pregnancies in the year (N):	49	56	50
- Pregnancy rates in women aged 15 to 49 years (for 1000):	25.9	28.9	25.2
- Age at 31st December of the year of early pregancy (mean):	29.9	29.9	29.5
- Deaths (N):	56	57	41
- Crude death rate (for 1 000):	8.1	8.1	5.7
- Age at death, in years (mean):	35.0	33.6	34.7
- Age at death, in years (median):	33.8	31.0	34.0
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	2.1	2	2
- New patients diagnosed during the year (N):	186	176	163
- Age at diagnosis of the new patients, in years (median):	1.7	1.2	1.1
- Age at diagnosis of the new patients, in years (min-max):	0-72	0-81	0-76
- Full genotypes identified (%):	97.9	97.9	97.8
F508del / F508del:	41.4	40.9	41
F508del / Other:	41.6	41.5	41.6
Other / Other:	14.9	15.4	15.2
F508del / Missing:	0.5	0.5	0.6
Other / Missing:	0.7	0.7	0.7
Missing / Missing:	0.9	0.9	0.8
Anthropometry			
- Patients aged 17 years and less, Height z-score (mean):	0.05	0.02	0.04
Weight z-score (mean):	-0.5	-0.51	-0.49
- Patients aged 18 years and over, Height z-score (mean):	-0.18	-0.19	-0.21
Weight z-score (mean):	-0.13	-0.12	-0.11

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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

	2017	2018	2019
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - Knudson (mean):	92.9	93.3	93
- Patients aged 18 years and over, FEV_1 (% predicted) - Knudson (mean):	73.1	74.4	74.1
Microbiology			
- Patients with at least one sputum during the year (%):	87.6	86	85.9
H. influenzae:	16.6	17.6	17
MSSA:	57.6	57.7	59.3
MRSA:	6.3	6.1	5.9
P. aeruginosa:	37	37.2	37.5
S. maltophilia:	10.7	10.3	10.4
B. cepacia:	2.3	2.1	2.2
Aspergillus:	29.5	27.7	29.1
Achromobacter xylosoxidans:	6.7	6.7	6.9
Complications and transplantations			
- Aspergillus (%) :	9.6	8.6	8.7
- Abnormal exocrine pancreatic function (%) :	80.3	80.3	79.7
- Treated gastro-oesophageal reflux (%) :	28.9	27.3	26
- Osteopenia/osteoporosis (%) :	14.3	15.1	14.4
- Haemoptysis (%):	6.5	5.3	5.7
- Cirrhosis / portal hypertension (%):	3.8	3.3	3.6
- Insulin-dependent and non insulin-dependant diabetes (%):	19.1	19.7	20.1
- Transplanted patients (N):	865	892	923
Including patients transplanted during the year:	99	84	93
- Patients on waiting list (N):	150	131	139
Including patients listed during the year:	99	84	91
Deaths on waiting list:	3	2	4
Therapeutic management			
- IV courses (%):	29.4	29	29.1
- Oxygenotherapy (%):	4.6	4.9	4.5
- Nasal ventilation (%):	3.9	4.6	4.6
- Azithromycin (%):	33.9	33.7	36
- Inhaled antibiotics (%):	40.2	37.7	38.9
- Bronchodilators (%):	59.1	59	59.3
- RhDNase (%):	43.9	43.4	39.5
- Corticosteroids (%):	37	37.4	36.3
- Pancreatic enzymes (%):	80.6	80	80

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Annex 5

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

	Transplanted patients	Non transplanted patients	2019 data
- Patients seen during the year in a centre* (N):	921	6239	7160
Demographics			
- Age of patients, in years (mean):	36.4	21.5	23.4
- Age of patients, in years (median):	35.5	19	21.3
- Patients aged 18 years and over (%):	97.8	52.8	58.6
- Early pregnancies during the year (N):	10	40	50
- Deaths (N):	21	20	41
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	5.4	1.8	2
- Full genotypes identified (%):	97.3	97.9	97.8
F508del / F508del:	49.5	39.7	41
F508del / Other:	37.4	42.3	41.6
Other / Other:	10.4	15.9	15.2
F508del / Missing:	0.7	0.6	0.6
Other / Missing:	0.7	0.8	0.7
Missing / Missing:	1.4	0.8	0.8
Anthropometry and spirometry			
- Patients aged 17 years and less, Height z-score (mean):	-1.01	0.04	0.04
Weight z-score (mean):	-1.6	-0.2	-0.21
BMI z-score (mean):	-0.89	-0.15	-0.15
- Patients aged 18 years and over, Height z-score (mean):	-0.72	-0.43	-0.49
Weight z-score (mean):	-0.67	0.05	-0.11
BMI (mean):	20.2	21.7	21.4
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - Knudson (mean):	74.9	93.2	93
- Patients aged 18 years and over, FEV_1 (% predicted) - Knudson (mean):	81	72.2	74.1
Complications			
- Treated aspergillosis (%)	6.1	9	8.7
- Abnormal exocrine pancreatic function (%) :	92.1	77.8	79.7
- Treated gastro-oesophageal reflux disease (%) :	58	21.3	26
- Osteopenia/osteoporosis (%) :	42	10.3	14.4
- Haemoptysis (%):	3.6	6	5.7
- Cirrhosis / portal hypertension (%):	2.9	3.7	3.6
- Insulin-dependent and non insulin-dependant diabetes (%):	61.8	14	20.1
Therapeutic management			
- Pancreatic enzymes (%) :	93.3	78	80
- Oral steroids (%) :	74.5	4.1	13.2

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** The difference between the number of transplanted patients page 34 (923) and the number of patients shown in this table (921) are the patients who died and were not seen in 2019.*

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	2019 data
- Patients seen during the year in a centre* (N):	6492	435	7160
Demographics			
- Age of patients, in years (mean):	23	24.6	23.4
- Age of patients, in years (median):	20.9	16.7	21.3
- Patients aged 18 years and over (%):	58.2	46.4	58.6
- Early pregnancies during the year (N):	46	2	50
- Deaths (N):	34	2	41
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	1.8	35.6	2
- Full genotypes identified (%):	98.7	86.9	97.8
F508del / F508del:	43.9	0.2	41
F508del / Other:	40.6	60.2	41.6
Other / Other:	14.2	26.4	15.2
F508del / Missing:	0.4	2.3	0.6
Other / Missing:	0.4	5.3	0.7
Missing / Missing:	0.5	5.5	0.8
Anthropometry and spirometry			
- Patients aged 17 years and less, Height z-score (mean):	0	0.44	0.04
Weight z-score (mean):	-0.26	0.47	-0.21
BMI z-score (mean):	-0.18	0.17	-0.15
- Patients aged 18 years and over, Height z-score (mean):	-0.53	0.15	-0.49
Weight z-score (mean):	-0.17	0.93	-0.11
BMI (mean):	21.2	23.7	21.4
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - Knudson (mean):	92.3	102	93
- Patients aged 18 years and over, FEV_1 (% predicted) - Knudson (mean):	73.3	87.9	74.1
Complications			
- Treated aspergillosis (%)	9	3.9	8.7
- Abnormal exocrine pancreatic function (%) :	84.7	11.7	79.7
- Treated gastro-oesophageal reflux disease (%) :	27.2	9.9	26
- Osteopenia/osteoporosis (%) :	14.8	4.1	14.4
- Haemoptysis (%):	5.9	0.7	5.7
- Cirrhosis / portal hypertension (%):	3.9	0.2	3.6
- Insulin-dependent and non insulin-dependant diabetes (%):	21.2	1.4	20.1
Therapeutic management			
- Pancreatic enzymes (%) :	84.9	12.6	80
- Oral steroids (%) :	13.7	1.8	13.2

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** Diagnosis type is missing for 233 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.

VAINCRE LA MUCOVISCIDOSE

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