FRENCH CYSTIC FIBROSIS REGISTRY

2017

Annual data report

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INSTITUT NATIONAL D'ÉTUDES DÉMOGRAPHIQUES

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VAINCRE LA MUCOVISCIDOSE

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Editorial

This report on the French Cystic Fibrosis Registry data collected in 2017 presents a detailed analysis of the situation of patients at the dawn of new therapeutic molecules accesses.
As for any rare disease, a Registry is an essential tool for physicians, researchers and strategy. Vaincre la Mucoviscidose confirms its decision to invest in it and has been managing it for more than 10 years, for the ultimate benefit of patients.

The Registry as an epidemiological tool

In the Registry were included 7114 patients in 2017, 56% of whom are adults. This new edition of the 2017 Annual data report contains an extra table on atypical forms in Annex 6.

The percentage of adult transplant recipients remains stable (21.7%). It increases in absolute number (843), leading to the development of a shared post-transplant follow-up between transplant and CF centres.

Among the 18-65 years old patients, 43% have a professional activity. Students represent 55% of the 18-25 years old patients and 43,6% of adults are in couple relationships.

The Registry, an essential clinical research tool for monitoring patients who benefit from new CFTR modulators

The number of patients benefiting from ivacaftor-lumacaftor (Orkambi®, Marketing Authorization in 2015) is increasing: it is prescribed for 16% of patients or almost 70% of eligible patients (12 years and over, homozygous F508del). The analysis of real-life data, in more than 800 patients who started this treatment in 2016, is underway as part of a study carried out under the aegis of the French Cystic Fibrosis Society.

Among the 2% of patients on ivacaftor (Kalydeco®, Marketing Authorization in 2012), those carrying a G551D mutation were the subject of an observational study full of lessons.

The Registry, a prospective tool

Soon, with more and more patients benefiting from innovative therapeutic advances and the initiation of CFTR modulators at early age, the future and management of patients will undergo profound transformations.

Crossing the Registry and the National Health Data System medico-administrative data will allow a better description of care and costs associated with cystic fibrosis in France.

Anticipating changes in care and being proactive by asking the public authorities for an adapted care offer, in a context of new financing methods for chronic diseases, is an important issue for the cystic fibrosis community.

The 2017 survey in brief

- a new data collection tool to facilitate data entry
- one file per patient and therefore the end of double entries for centers
- better historization and easier access to data
- the possibility of hosting new studies.

These changes are part of the deployment of the EpiMuco platform. This project aims to facilitate access, interoperability and reuse of health data collected in the context of clinical and epidemiological studies carried out on patients in France.

Acknowledgment

We would particularly like to thank the CF care teams. The 2017 data collection was all the more important as the annual survey questionnaire was enriched with many items. Without their investment, this almost exhaustive and quality Registry could not exist.

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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 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 and 2015, 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, Reunion Island and Guadeloupe). Data are collected once a year by means of an e-CRF, paper questionnaire 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.

Data use

Statistical analysis is performed on anonymized data. Unless otherwise indicated, the results presented hereafter relate to the population seen during the year 2017.

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

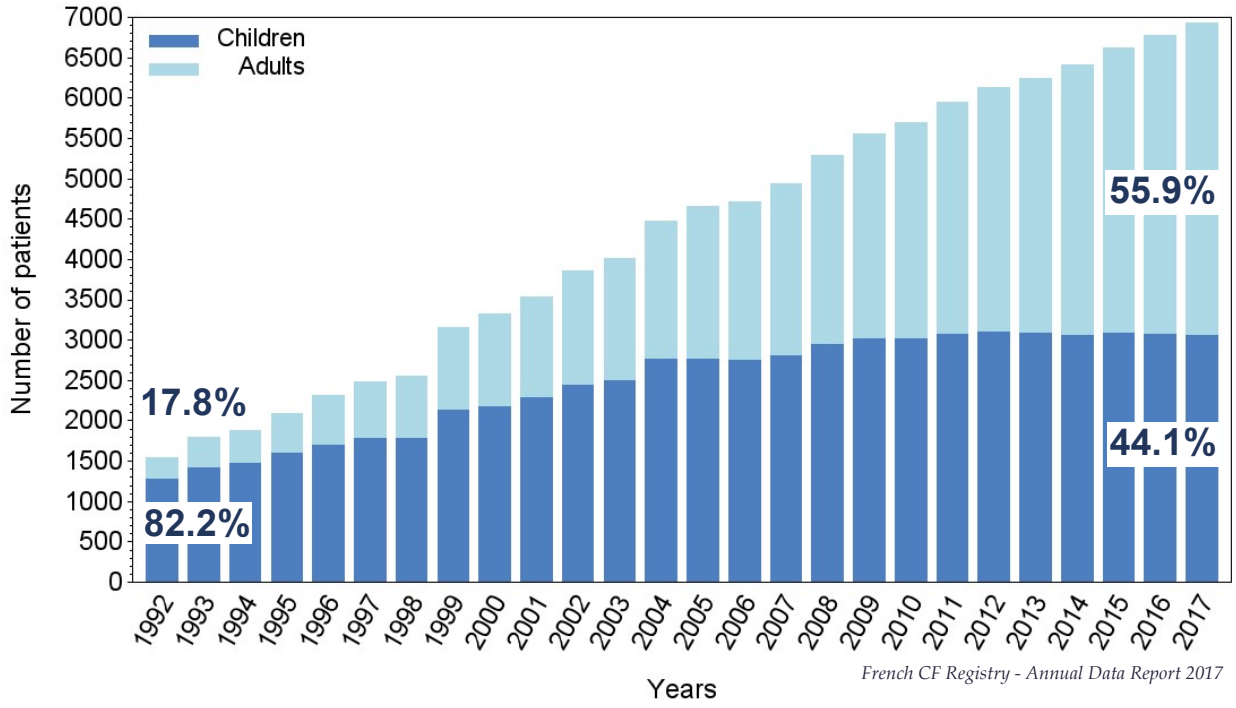

Table 1.1. Annual evolution of the main indicators

	Years of follow-up										
Indicators	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
All patients*	4949	5304	5568	5711	5966	6138	6251	6423	6628	6783	7114
Patients seen during the year**	4934	5293	5549	5702	5954	6126	6240	6409	6619	6776	6931
Children	2806	2942	3015	3015	3067	3106	3084	3065	3092	3075	3055 (44.1 %)
Adults	2128	2351	2534	2687	2887	3020	3156	3344	3527	3701	3876 (55.9 %)
Over 40 years	198	250	310	338	399	452	509	586	669	758	827 (11.9 %)
Men	2585	2760	2886	2937	3084	3166	3226	3314	3438	3543	3610 (52.1 %)
Women	2349	2533	2663	2765	2870	2960	3014	3095	3181	3233	3321 (47.9 %)
Mean age (years)	17.3	17.6	18.1	18.5	19.1	19.5	20.1	20.7	21.2	21.8	22.3
Median age (years)	16.0	16.2	16.5	16.9	17.4	17.8	18.2	18.9	19.3	19.9	20.3
Minimum age (years)	0.1	0.1	0	0.1	0	0.1	0.1	0.1	0	0.1	0.1
Maximum age (years)	75.8	76.8	77.8	80	88.0	86.8	82.4	82.8	83.2	84.1	85.1

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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.

Note: patients with unconfirmed or withdrawn diagnosis (N=30) were excluded from the analysis.

1. Demographics

Characteristics of the population

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

Characteristics	2015		2016		**2017**	
	Men	Women	Men	Women	**Men**	**Women**
Patients seen during the year	3438	3181	3543	3233	3610	3321
Children	1586	1506	1588	1487	1577	1478
Adults	1852	1675	1955	1746	2033	1843
Mean age (years)	21.2	21.1	21.9	21.8	22.3	22.4
Median age (years)	19.6	19.0	20.1	19.6	20.5	20.1

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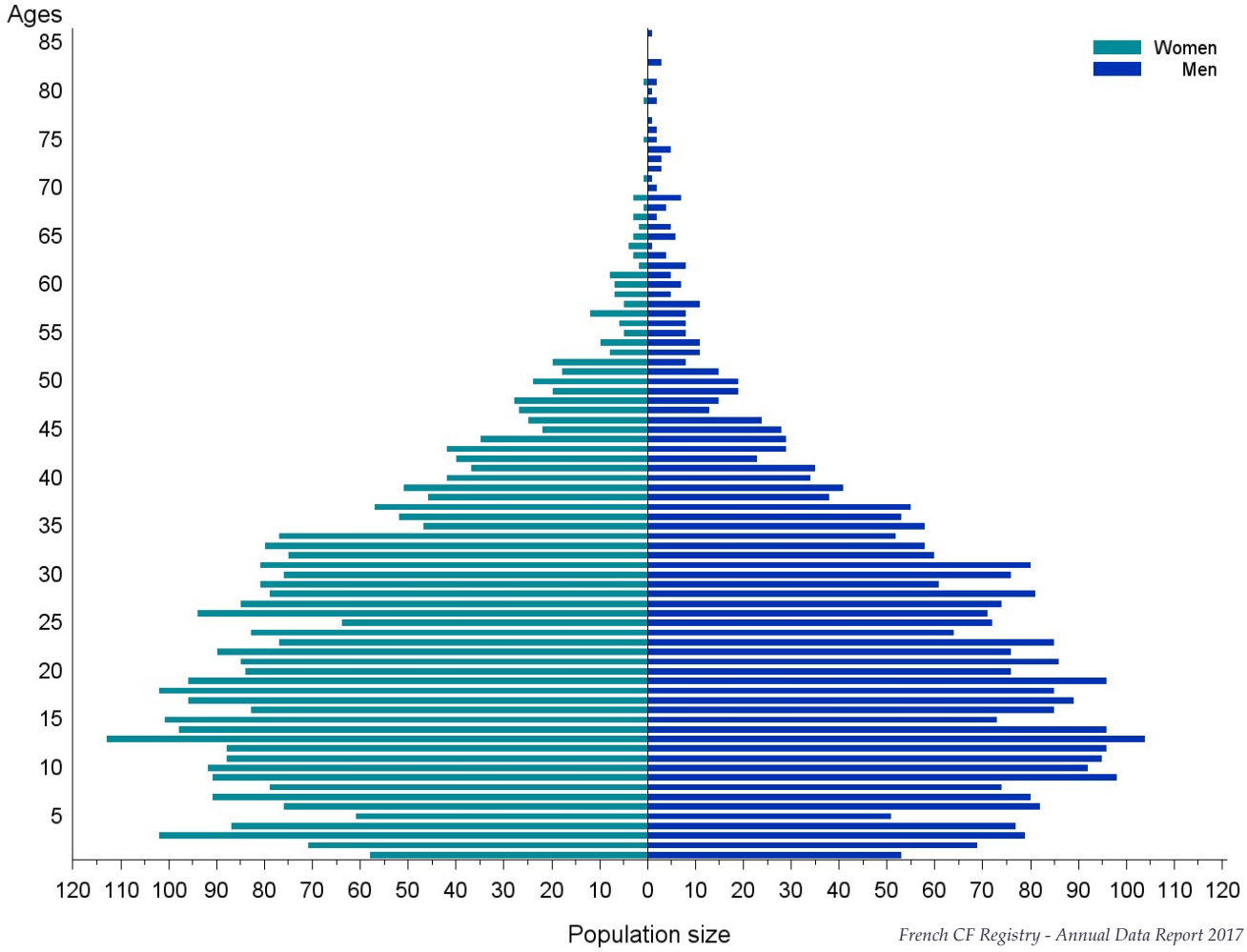
Figure 1.2. Population pyramid



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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

Types of centres	Nb	Patients' characteristics			Age of patients (years)				
		Nb (a)	%	Mean nb by centre	Min*	Max*	Mean	Median	Inter-quartile
CRCMs									
Paediatric	17	2131	30.7	125.4	0.1	61.9	10.1	10.3	8.8
Adult	14	2794	40.3	199.6	16.1	82.9	33.3	31.1	13.9
Paediatric/Adult	16	1918	27.7	119.9	0.1	85.1	20.2	17.6	18.4
Subtotal	47	6843	98.7	145.6	0.1	85.1	22.4	20.4	20.7
Other centres									
Paediatric	2	16 (b)	0.2	8.0	1.6	17.4	9.1	8.8	8.2
Paediatric/Adult	1	36	0.5	36.0	4.3	17.6	10.2	9.9	6.4
Other Centres	1	36 (c)	0.5	36.0	16.8	49.2	28.5	28.4	13.3
Subtotal	4	88	1.3	22.0	1.6	49.2	17.5	15.1	16.3
Total	51	6931	100	135.9	0.1	85.1	22.3	20.3	20.7

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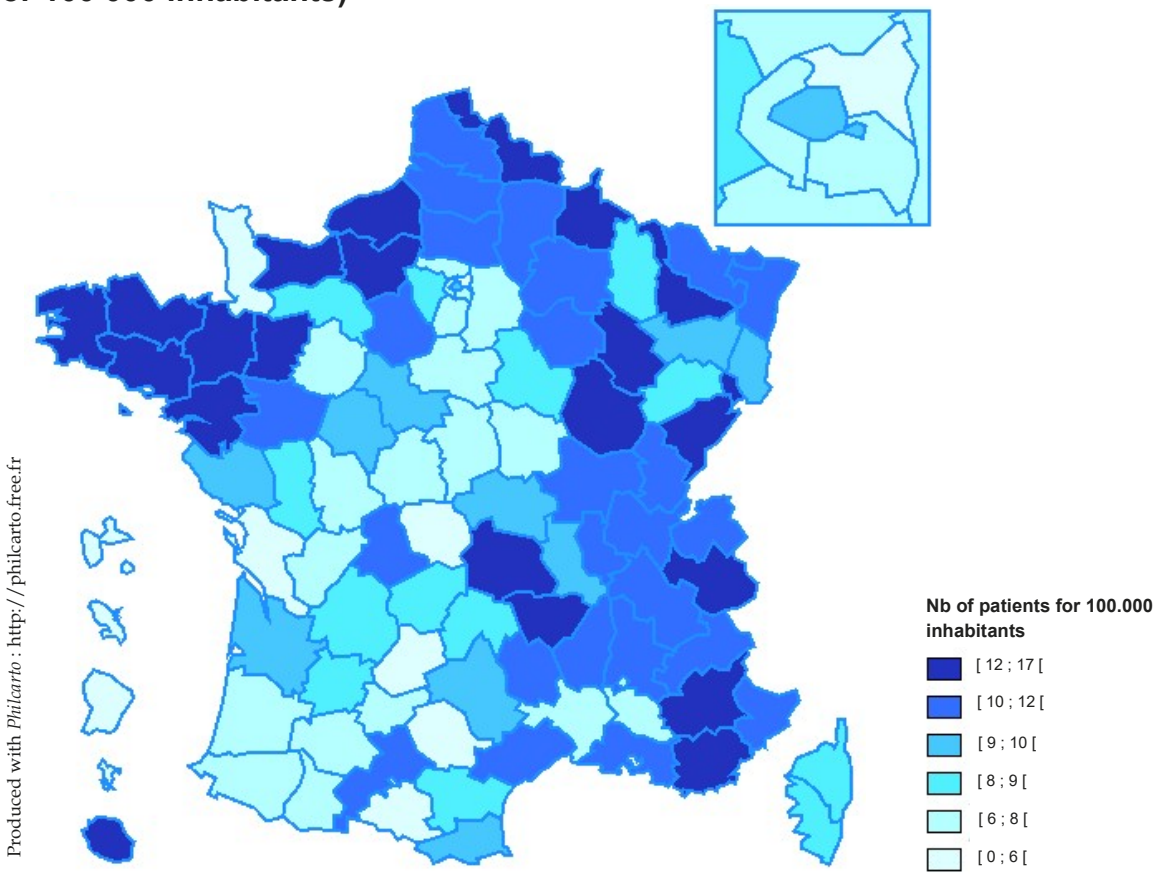
Notes : (a) Patients visiting at least 2 CF centres during the year were only counted in the one with the highest number of visits
(b) Including 1 patient also seen by a CF centre
(c) Including 8 patients also seen by a CF centre

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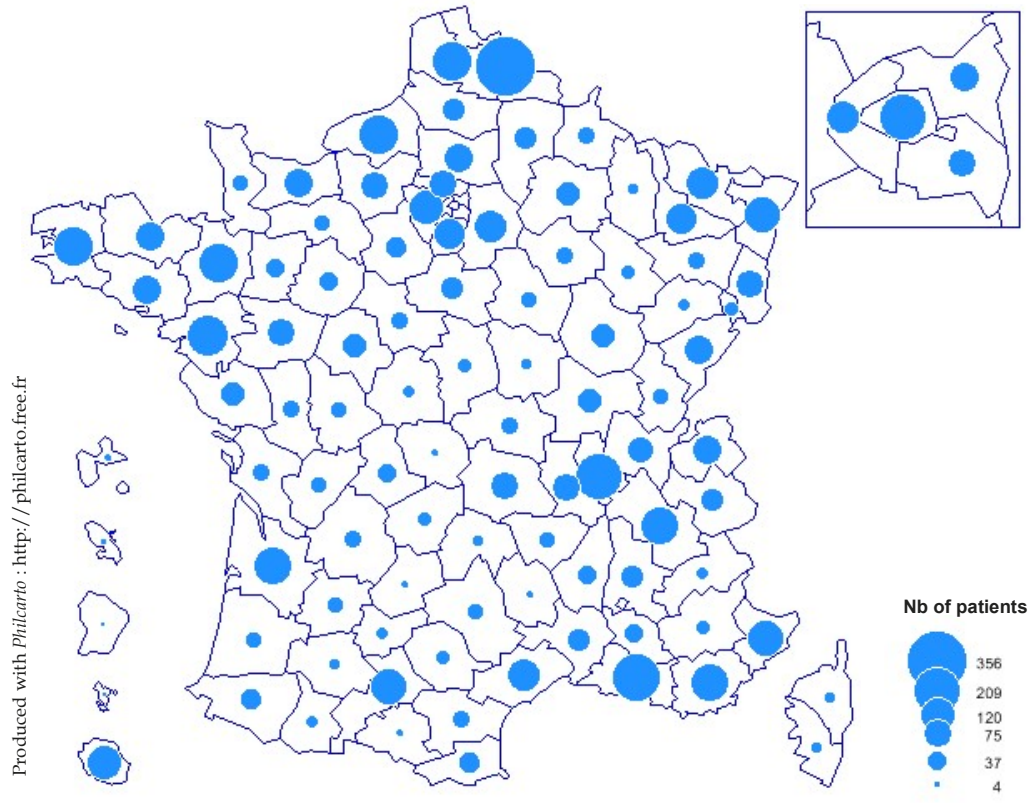
Map 1.2. Localisation of the patients by « département » of residence (absolute numbers)



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2. Mortality

Characteristics

Figure 2.1. Annual number of deaths since 1992

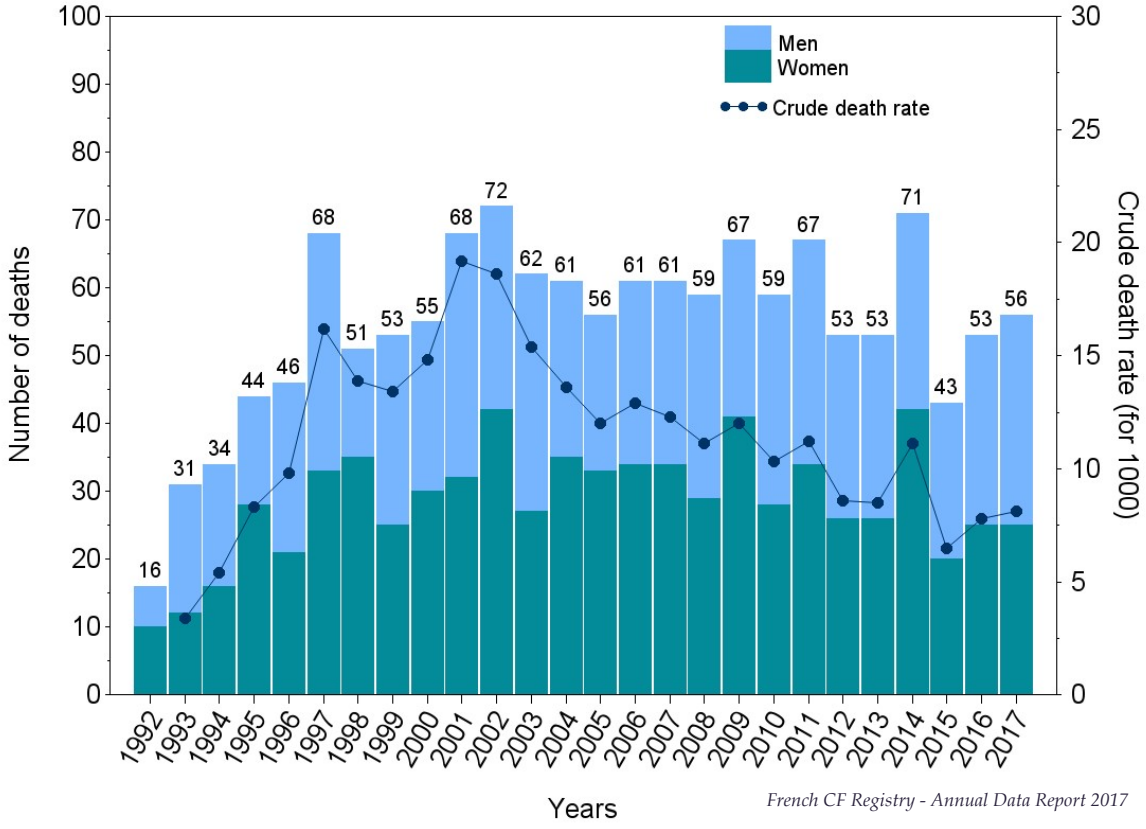

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Table 2.1. Mortality characteristics

	Years of follow-up										
Indicators	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Number of deaths	61	59	67	59	67	53	53	71	43	53	56*
- including transplanted patients	28	27	34	30	33	27	29	41	22	37	33
Crude death rate (per 1000)	12.3	11.1	12.0	10.3	11.2	8.6	8.5	11.1	6.5	7.8	8.1
Mean age (years)	27.3	29.1	23.5	29.3	26.4	32.3	34.0	29.0	34.1	31.9	35.0
Median age (years)	25.9	27.9	22.2	27.6	24.9	27.8	30.7	27.1	31.8	28.0	33.8
Minimum age (years)	1.6	0.1	0.1	0.2	1.9	2.2	0.1	0.1	9.0	1.6	5.9
Maximum age (years)	70.0	66.1	73.4	68.9	55.5	88.4	82.5	71.2	83.2	76.0	74.3

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* 9 out of the 56 were not seen by a CF center in 2017.

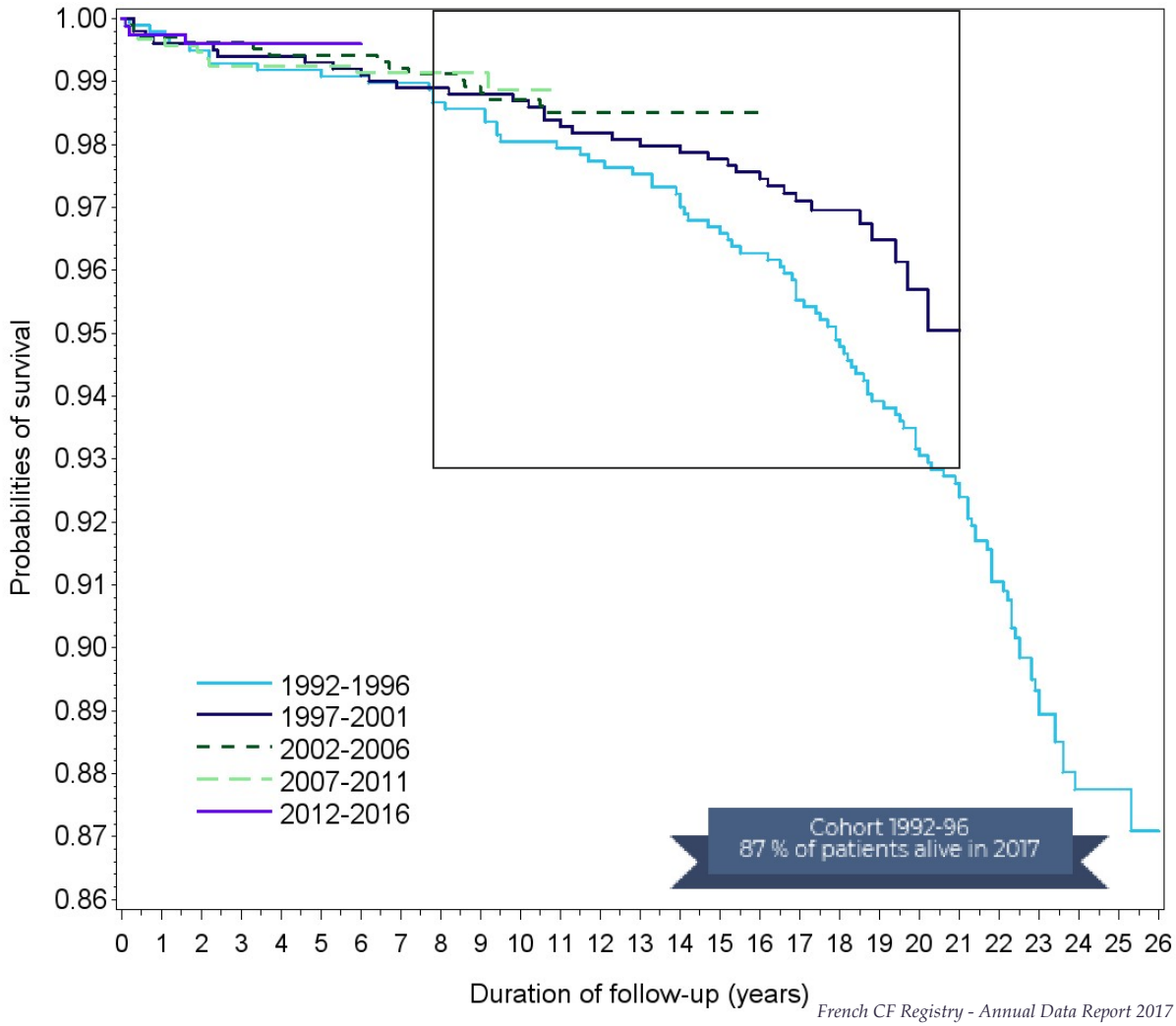
2. Mortality

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 2017 this cohort was followed during 26 years maximum): 982 patients, 102 deaths
- Births from 1997 to 2001 (maximum 21 years of follow up): 1004 patients, 34 deaths
- Births from 2002 to 2006 (maximum 16 years of follow up): 1042 patients, 15 deaths
- Births from 2007 to 2011 (maximum 11 years of follow up): 942 patients, 9 deaths
- Births from 2012 to 2016 (maximum 6 years of follow up): 783 patients, 3 deaths



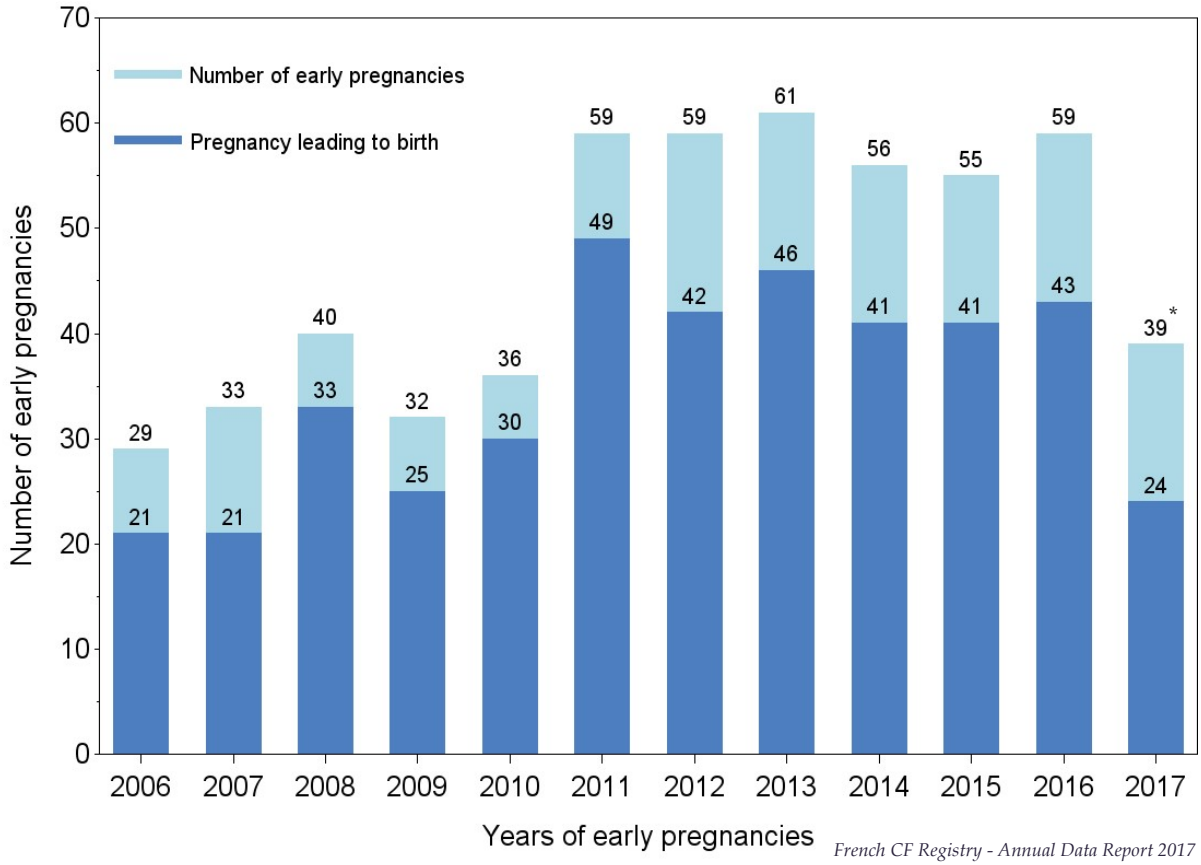
Until the age of 8, there is no difference in survival between the different birth cohorts.

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 = 5.18, p = 0.02).

Survival analysis by sex is available on annex 1.

3. Pregnancy – Paternity

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



Of the 39 early pregnancies in 2017, 24 resulted in a birth (in 2017 or 2018).

Table 3.1. Early pregnancy characteristics

Characteristics	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Number of early pregnancies	29	33	40	32	36	59	59	61	56	55	59	39
Pregnancy rates in women aged 15 to 49 years (for 1000)	26.1	28.5	32.3	24.2	25.9	40.1	38.2	37.8	33.2	31.1	32.2	20.6
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	30.2
Number of lung transplanted women starting a pregnancy	1	2	1	3	3	3	7	4	1	3	4	4

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3. Pregnancy – Paternity

Table 3.2. Paternities

Characteristics	N	Proportion (%)
Number of paternities, including:	24	
- Natural father	1	4.2
- Medically assisted reproduction, including:	22	91.7
+ Intracytoplasmic Sperm Injection / in vitro fertilization	21	95.5
+ Artificial insemination with sperm donor	1	4.5

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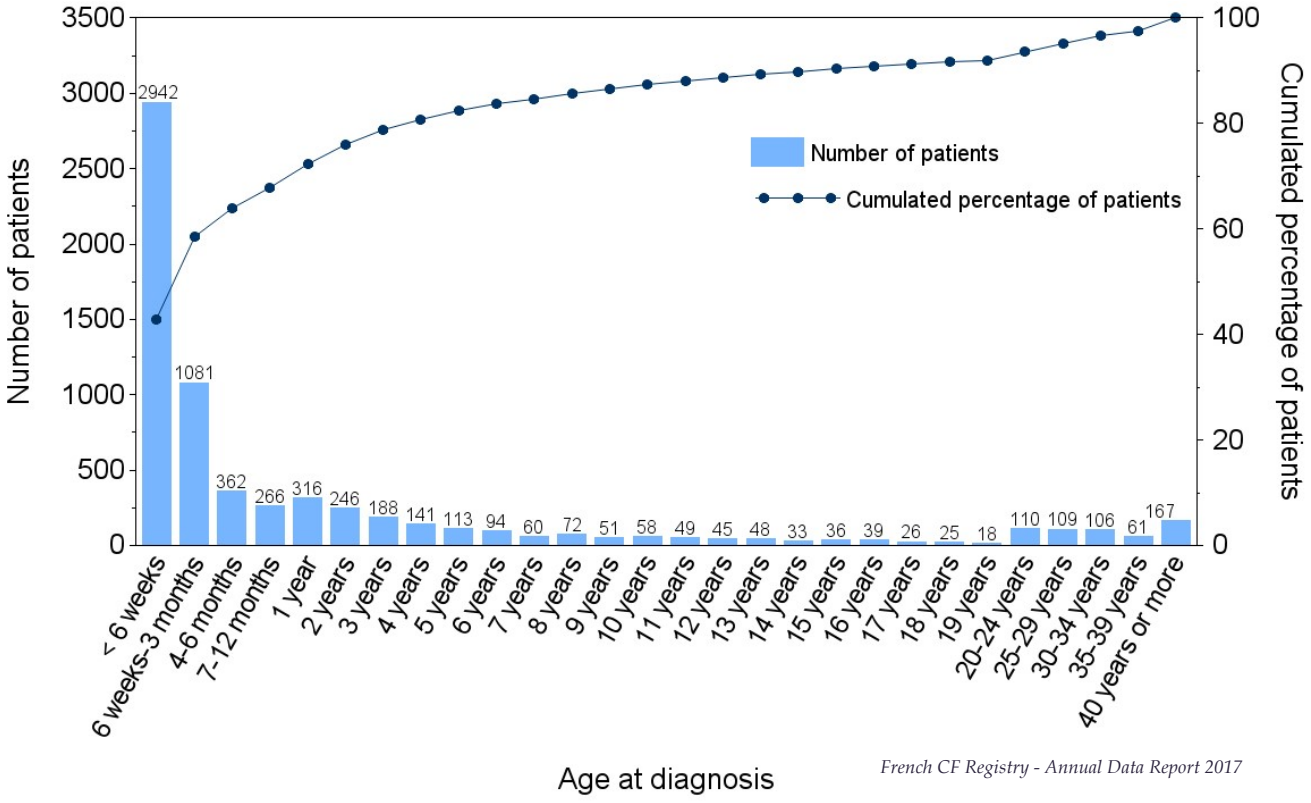
Note: precision on paternity was missing for one patient.

4. Diagnosis

Main characteristics

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

N = 6,862 (number of patients whose age at diagnosis is known).



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4. Diagnosis

Main characteristics

Table 4.1. Diagnosis characteristics

Characteristics	**2017**
ALL PATIENTS	
Patients whose age at diagnosis is known - N (%) *	6862 (99 %)
Age at diagnosis	
- Median age (months)	2.0
- Mean age (years)	4.5
- Minimum age (years)	0
- Maximum age (years)	79
NEW PATIENTS DIAGNOSED DURING THE YEAR	
Number of patients	
New patients - N (%)	180 (2.6 %)
- Including 2016 newborn patients - N	111
Age at diagnosis	
- Median age (months)	1.5
- Mean age (years)	8.3
- Minimum age (years)	0
- Maximum age (years)	72
Context of diagnosis	
1. Screened positive newborns (NBS)	**116**
- including Prenatal diagnosis - N (%)	5 (4.3 %)
- including Meconium ileus - N (%)	14 (12.1 %)
2. Diagnosis on symptoms (NBS excluded)	**64**
- including Meconium ileus - N (%)	3 (4.7 %)
- including Symptoms (other than MI):- N (%)	61 (95.3 %)
- Mean age at diagnosis (years)	22.9

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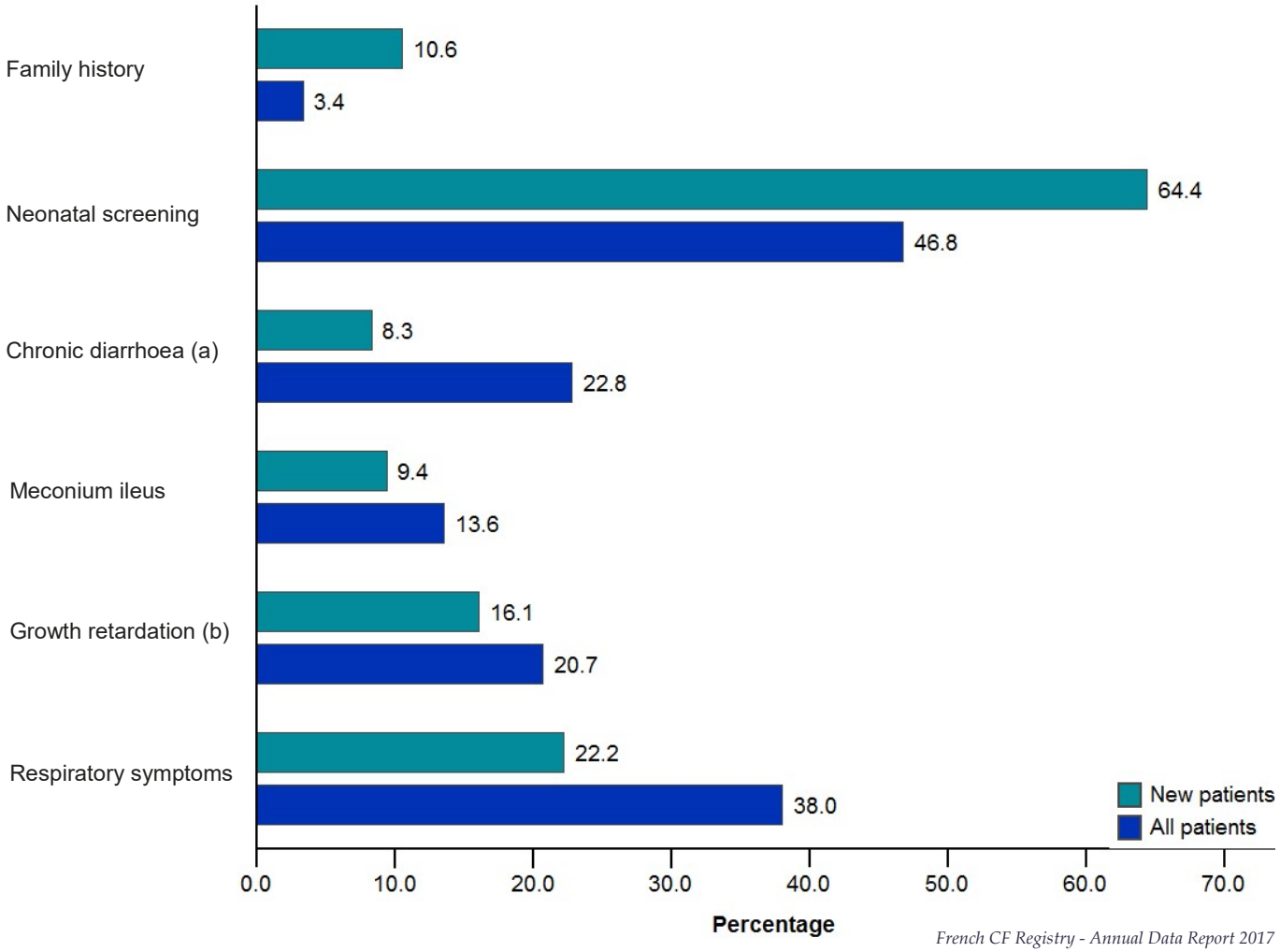
Among the 180 new patients, 111 were born in 2017. The method used to compile this report (patients seen in a care centre in 2017) means that infants born in 2017 and seen for the first time in 2018 are not included yet. For information purposes only, 12 newborns in 2016 were diagnosed in 2017 through neonatal screening. In the 2016 age pyramide, the number of patients aged 0 was 112 and should have been 112+12=124.

The number of patients diagnosed by neonatal screening (116) 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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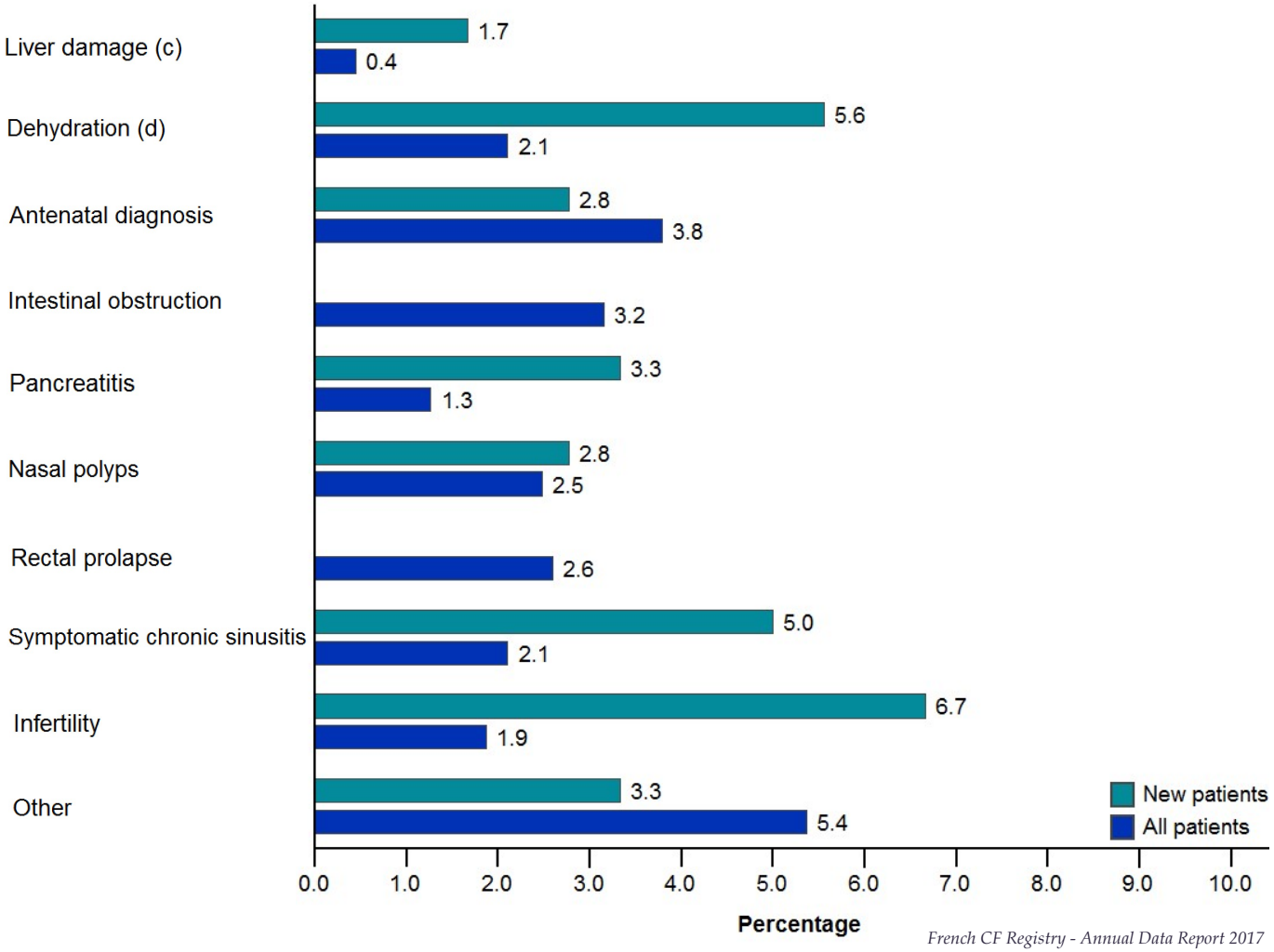
(a) Chronic diarrhoea / Steatorrhoea / Malabsorption
(b) Growth retardation / Malnutrition

4. Diagnosis

Diagnosis signs

Figure 4.3. Diagnosis signs (less frequent ones)



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(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	5777	83.4
G542X	383	5.5
N1303K	295	4.3
2789+5G->A	175	2.5
R117H	150	2.2
1717-1G->A	145	2.1
R553X	126	1.8
G551D	116	1.7
W1282X	99	1.4
3849+10kbC->T	95	1.4
L206W	87	1.3
I507del	83	1.2
3272-26A->G	80	1.2
D1152H	79	1.1
Y122X	76	1.1
711+1G->T	73	1.1
2183AA->G	71	1.0
R347P	68	1.0
R1162X	60	0.9
3120+1G->A	56	0.8
Y1092X	50	0.7
R334W	47	0.7
G85E	46	0.7
3659delC	44	0.6
A455E	43	0.6
R347H	41	0.6
S945L	41	0.6
1078delT	38	0.5
1811+1.6kbA->G	36	0.5
394delTT	33	0.5
R1066C	33	0.5
E60X	31	0.4
W846X	31	0.4
621+1G->T	29	0.4
S1251N	27	0.4
1677delTA	21	0.3
L997F	21	0.3
R74W	21	0.3
E585X	20	0.3
Q220X	20	0.3

* 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	2872	41.4	21.2	20.3	63.1
F508del / Other	2859	41.2	22.4	20	82.9
Other/ Other	1020	14.7	22.7	19.4	85.1
Subtotal (non missing genotypes)	6751	97.4	22	20	85.1
F508del / Missing	46	0.7	38.1	36.9	82.6
Other/ Missing	57	0.8	31.4	31.4	74
Missing/ Missing	77	1.1	38	34.7	82.2
Subtotal (partial genotypes / missing)	180	2.6	35.9	33.7	82.6
Total	6931	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	195	2.8	23.4	20.2	67
At least one nonsense mutation	1077	15.5	20.8	18.8	73.7
At least one R117H mutation	150	2.2	16.3	12.4	74.3

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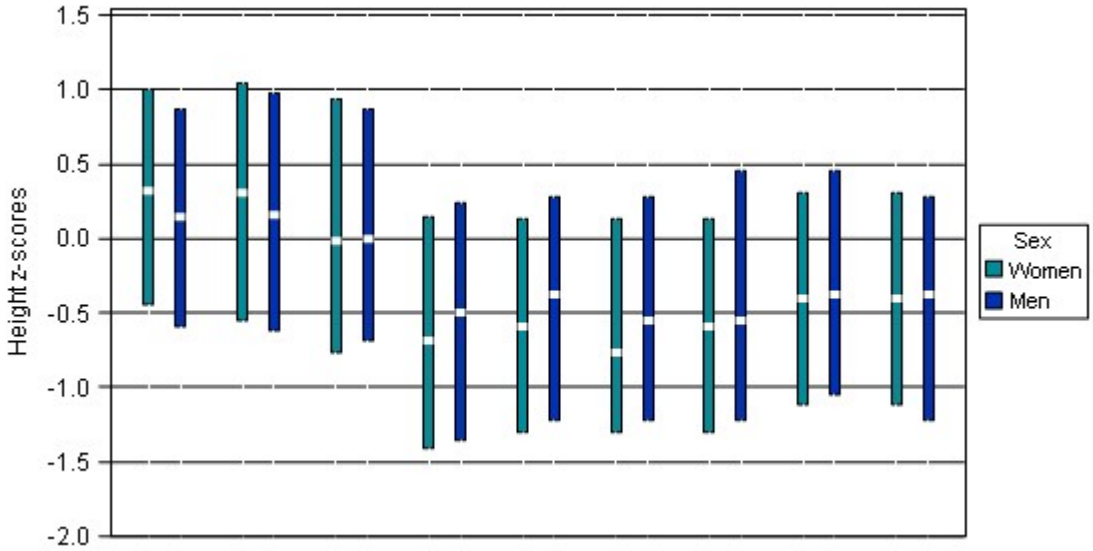
Gating mutations doesn't prevent the CFTR protein from reaching the cell membrane but alter choride transport.

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	0.26	0.28	0.06	-0.66	-0.64	-0.60	-0.52	-0.40	-0.39	-0.28
	Men	0.18	0.20	0.06	-0.47	-0.49	-0.47	-0.48	-0.35	-0.43	-0.24
Median height z-score	Women	0.32	0.30	-0.02	-0.69	-0.59	-0.77	-0.59	-0.41	-0.41	-0.32
	Men	0.15	0.16	0.00	-0.50	-0.38	-0.55	-0.55	-0.38	-0.38	-0.25

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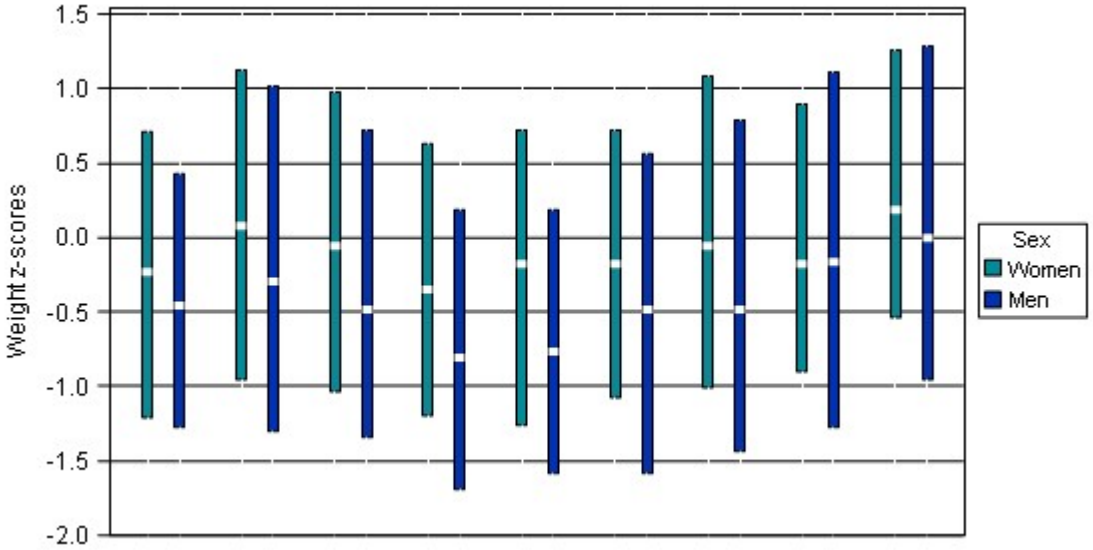
Figure 5.2. Weight z-scores*, by age group and sex



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	-0.22	0.14	0.05	-0.25	-0.15	-0.13	0.07	0.01	0.40	-0.01
	Men	-0.34	-0.15	-0.25	-0.67	-0.57	-0.42	-0.21	-0.07	0.23	-0.29
Median weight z-score	Women	-0.24	0.09	-0.06	-0.35	-0.18	-0.18	-0.05	-0.18	0.18	-0.10
	Men	-0.46	-0.30	-0.49	-0.81	-0.77	-0.48	-0.48	-0.16	0.00	-0.48

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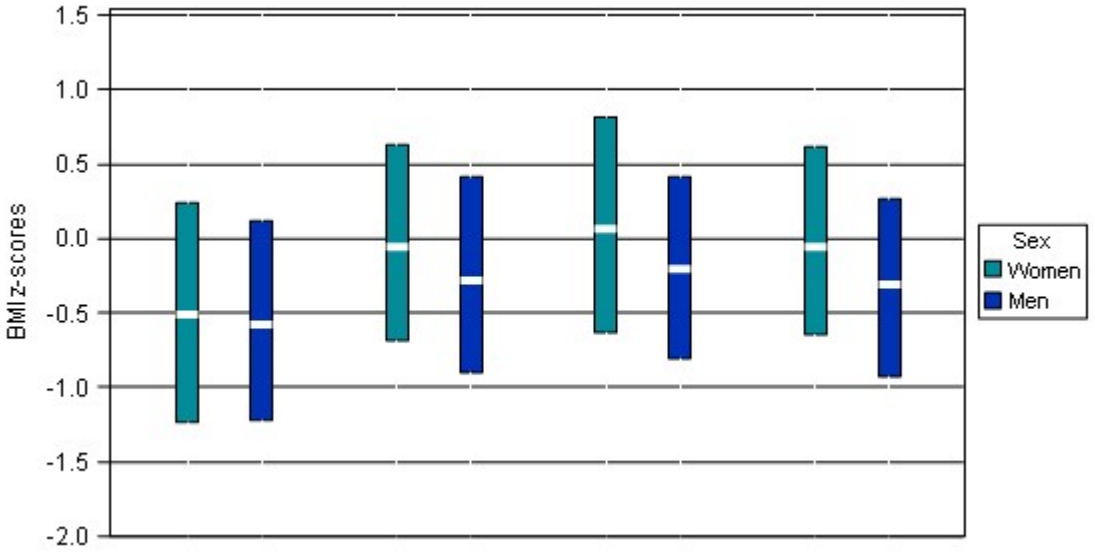
*See explicative note p 22.

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	-0.44	0.05	0.17	0.04	-0.01
	Men	-0.54	-0.16	-0.11	-0.28	-0.26
Median BMI z-score	Women	-0.51	-0.06	0.07	-0.05	-0.13
	Men	-0.58	-0.29	-0.20	-0.32	-0.32
BMI z-score >=0 (% of patients)	Women	30.2	49.5	53.3	49.1	46.9
	Men	29.3	38.6	39.7	33.8	35.7

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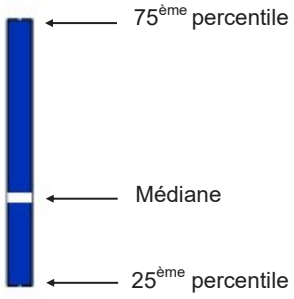
The z-score is a anthropometric reduced centered variable (Z = [measure-mean]/standard deviation), ajusted for gender and age; the mean and standard deviation are taken from the French reference population with the same gender and age as the patient. This index measures the difference with population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

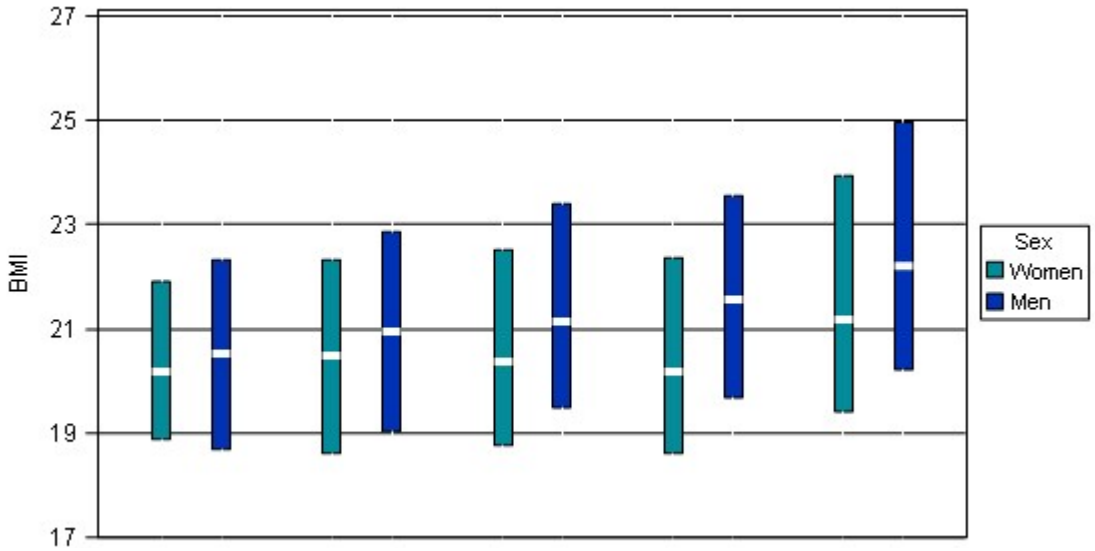
Those figures represent z-scores of anthropométrie and spirometry values.
For each age and sex group, median values are the white lines, extremes are the 25th and 75th percentiles.



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	20.6	20.8	21.2	20.9	22.3	21.2
	Men	20.8	21.1	21.6	21.8	22.7	21.6
Median BMI	Women	20.2	20.5	20.4	20.2	21.2	20.6
	Men	20.5	21.0	21.1	21.6	22.2	21.2
BMI ≥ 22 (% of patients)	Women	23.6	28.3	30.0	27.7	40.2	30.2
BMI ≥ 23 (% of patients)	Men	19.5	23.5	29.0	31.3	41.6	28.9
BMI < 18.5 (% of patients)	Women	20.7	23.1	21.7	23.2	14.8	20.3
	Men	22.6	19.4	14.5	13.4	10.0	16.2

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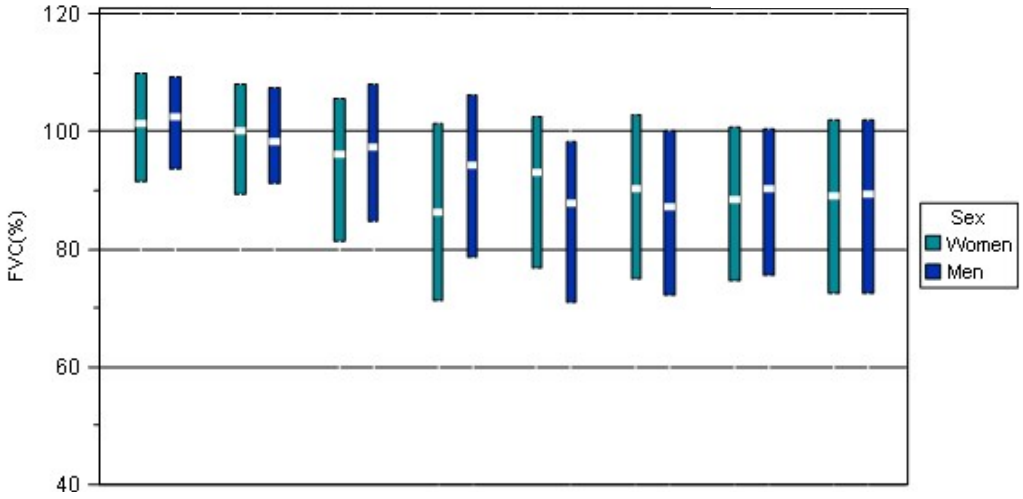
6. Spirometry

95.6% 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	100.1	98.0	93.4	85.6	88.9	88.2	87.4	87.0	91.2
	Men	101.2	98.4	95.6	91.2	85.2	85.1	87.5	86.6	91.5
	All patients	100.7	98.2	94.6	88.4	86.9	86.6	87.4	86.8	**91.3**
Median FVC	Women	101.3	100.0	96.1	86.4	93.0	90.2	88.6	89.1	94.0
	Men	102.5	98.3	97.2	94.2	87.9	87.3	90.3	89.4	94.3
	All patients	102.0	99.1	96.8	90.8	89.8	88.6	89.5	89.3	**94.2**

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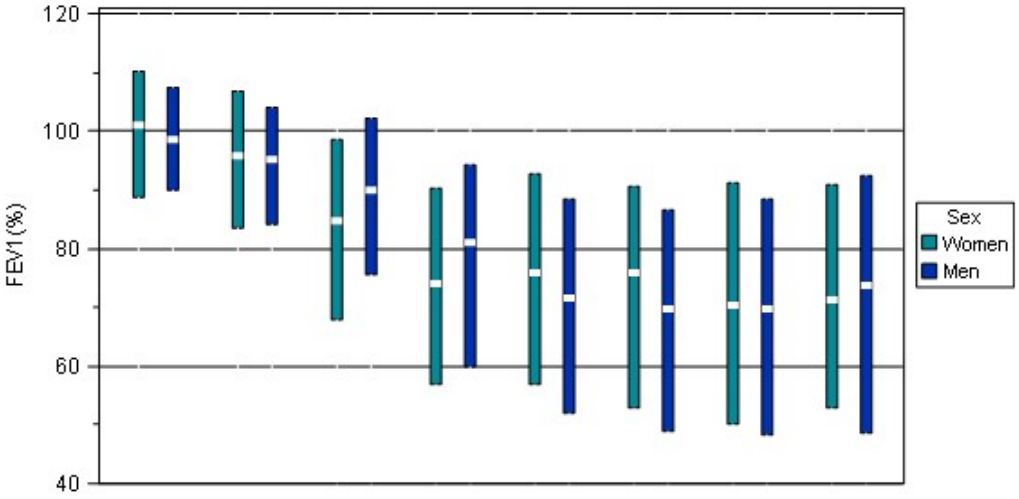
Figure 6.2. FEV_1 (% predicted)*, by age group and sex



	Age groups (years)	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +	Total
Mean FEV_1	Women	98.4	93.6	82.9	73.5	74.4	72.7	70.9	71.8	80.1
	Men	98.0	93.3	86.9	77.1	70.3	68.8	69.0	70.7	79.7
	All patients	98.2	93.4	85.0	75.4	72.2	70.6	69.9	71.2	**79.9**
Median FEV_1	Women	100.8	95.7	84.8	74.1	75.9	75.8	70.3	71.3	82.8
	Men	98.7	95.3	89.9	81.0	71.5	69.8	69.8	73.6	83.9
	All patients	99.4	95.6	87.6	78.4	73.8	73.1	69.9	72.3	**83.3**

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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 appendix 2 for additional information on spirometry and transplantation.
*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.

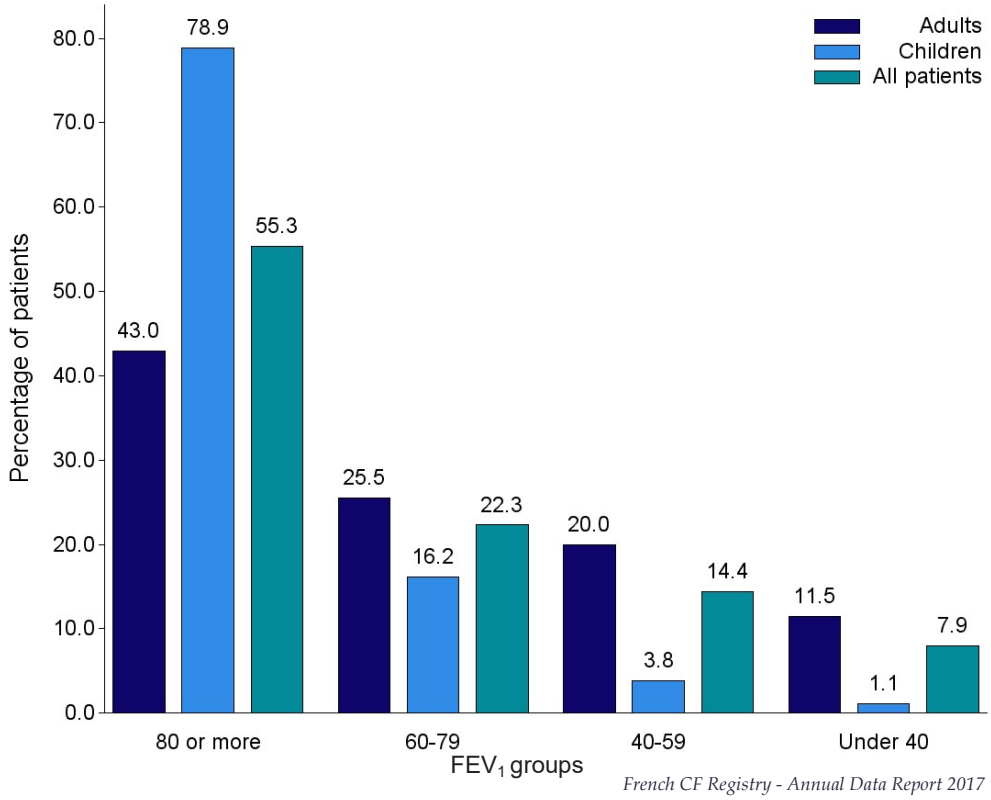
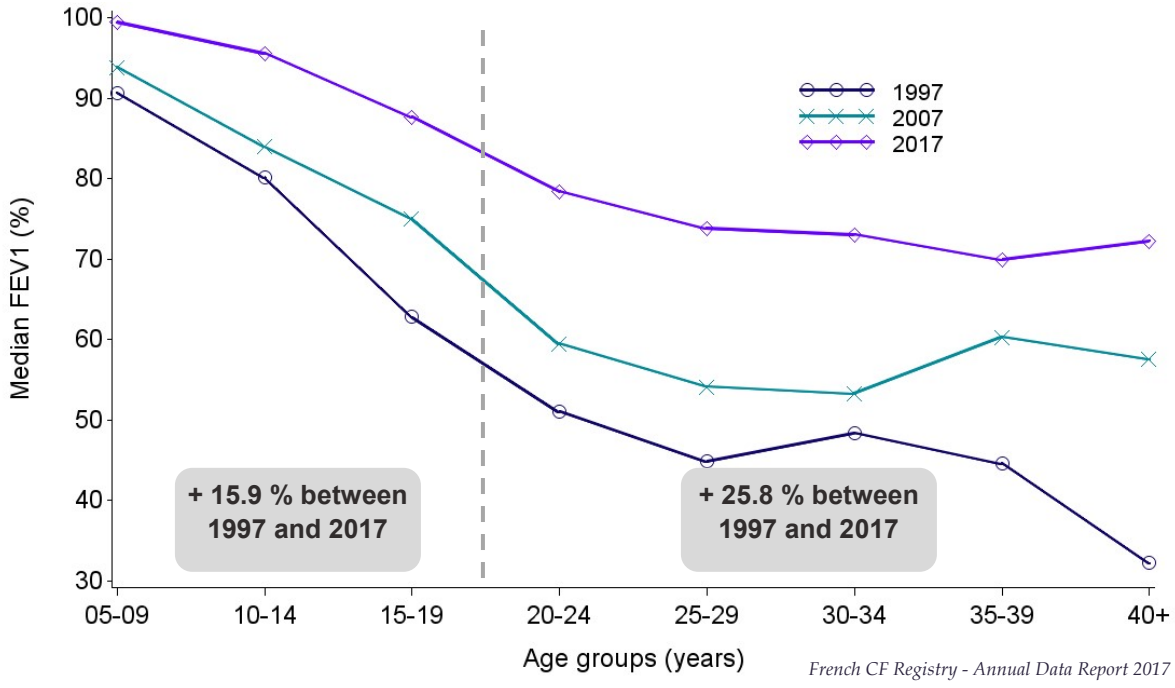


Figure 6.4. Median FEV_1 (% predicted) in 2017 compared with 1997 and 2007



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

The median FEV1 was 78.6 % for patients aged 6 to 19 years in 1997, and 94.5 % in 2017. It was 47.8 % in 1997 and 73.6 % in 2017 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	6057	*87.4 %*
Children	2979	*97.5 %*
Adults	3078	*79.4 %*

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In 2017, 87.4 % of the patients had at least one sputum culture. Among the patients without sputum culture (N=874), 62.4 % 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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Patients with at least one sputum	**681**	**832**	**932**	**858**	**693**	**639**	**505**	**332**	**585**	**6057**	**87.4 %**
Normal culture	254	309	268	182	140	145	110	81	154	1643	23.7 %
Achromobacter xylosoxidans	14	27	65	88	68	71	56	27	42	458	6.6 %
Aspergillus	44	143	241	338	343	298	199	147	235	1988	28.7 %
Burkholderia cepacia, including:	4	12	13	28	34	21	17	11	16	156	2.3 %
- chronic B. cepacia	*.*	*2*	*4*	*18*	*23*	*19*	*8*	*4*	*9*	*87*	*1.3 %*
Haemophilus influenzae	180	270	191	141	101	95	64	44	63	1149	16.6 %
Atypical mycobacteria	1	6	15	32	37	38	18	14	22	183	2.6 %
Pneumococcus	55	49	27	12	4	4	7	10	10	178	2.6 %
Pseudomonas aeruginosa, including:	118	159	258	349	379	400	328	220	338	2549	36.8 %
- Chronic P. aeruginosa	*5*	*20*	*99*	*175*	*237*	*267*	*230*	*158*	*231*	*1422*	*20.5 %*
Staphylococcus, including:	433	609	758	690	542	433	328	192	286	4271	61.6 %
- MSSA	*416*	*593*	*725*	*650*	*492*	*388*	*286*	*163*	*249*	*3962*	*57.2 %*
- MRSA	*16*	*20*	*56*	*70*	*65*	*66*	*64*	*37*	*44*	*438*	*6.3 %*
Stenotrophomonas maltophilia	69	72	136	121	120	83	51	29	53	734	10.6 %

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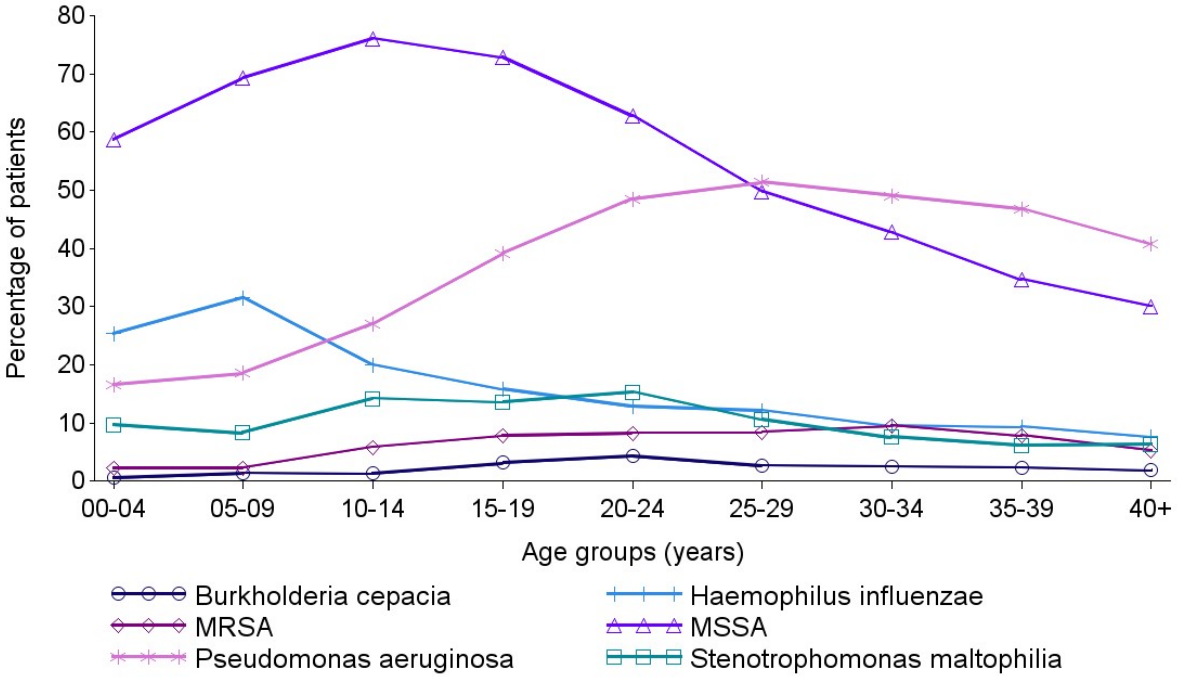
* Percentage with respect to the entire population.

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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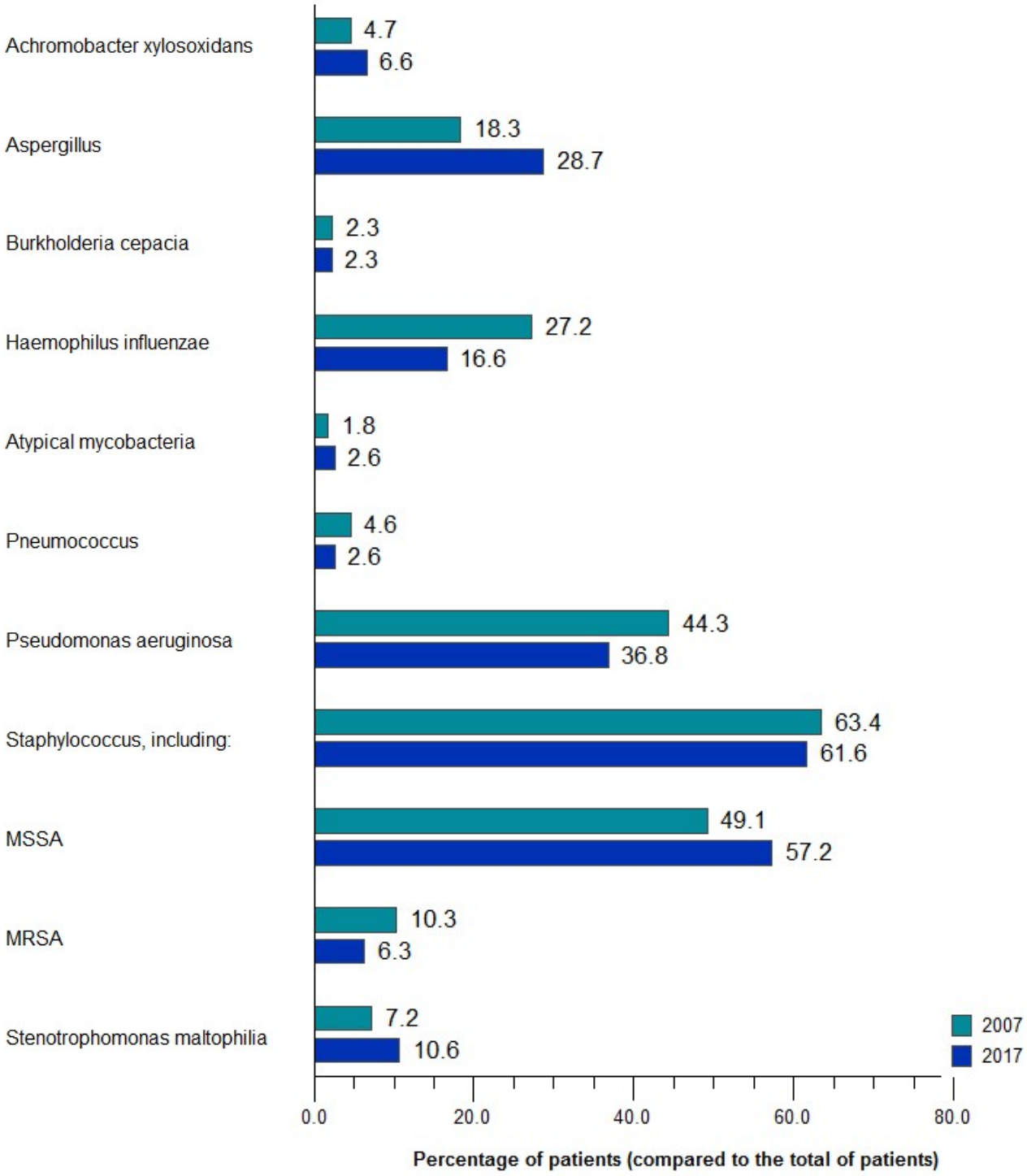
7. Microbiology

Figure 7.2. Comparison of germs in 2017 and in 2007



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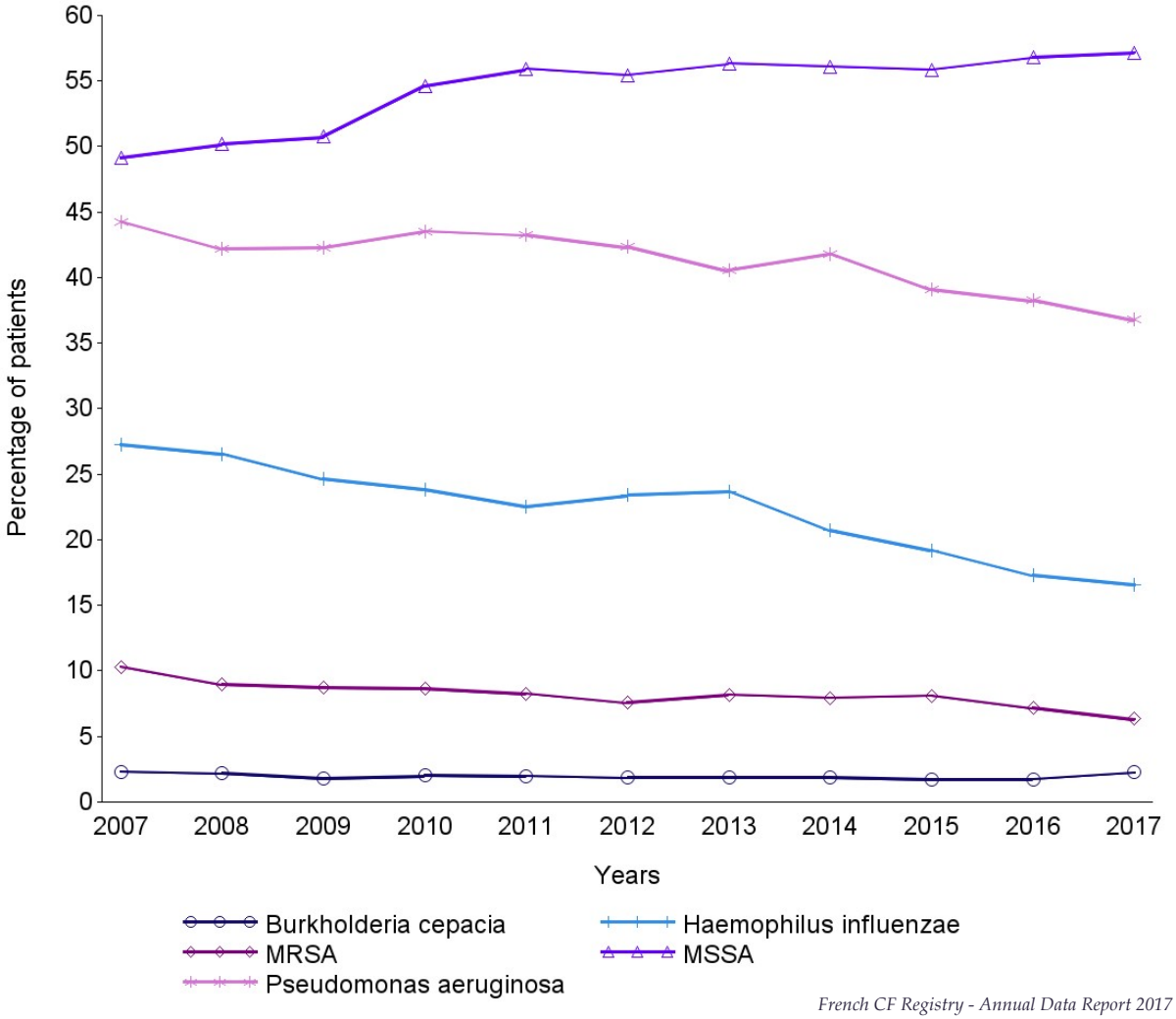
7. Microbiology

Figure 7.3. Evolution of respiratory germs since 2007



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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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Treated aspergillosis	3	30	83	107	131	106	65	48	88	661	9.5 %
Asthma	123	174	254	220	230	196	182	111	199	1689	24.4 %
Haemoptysis	2	4	17	63	81	118	74	32	60	451	6.5 %
Pneumothorax	2	2	2	12	10	15	3	9	3	58	0.8 %
Nasal polyps	16	95	173	223	189	192	143	96	171	1298	18.7 %

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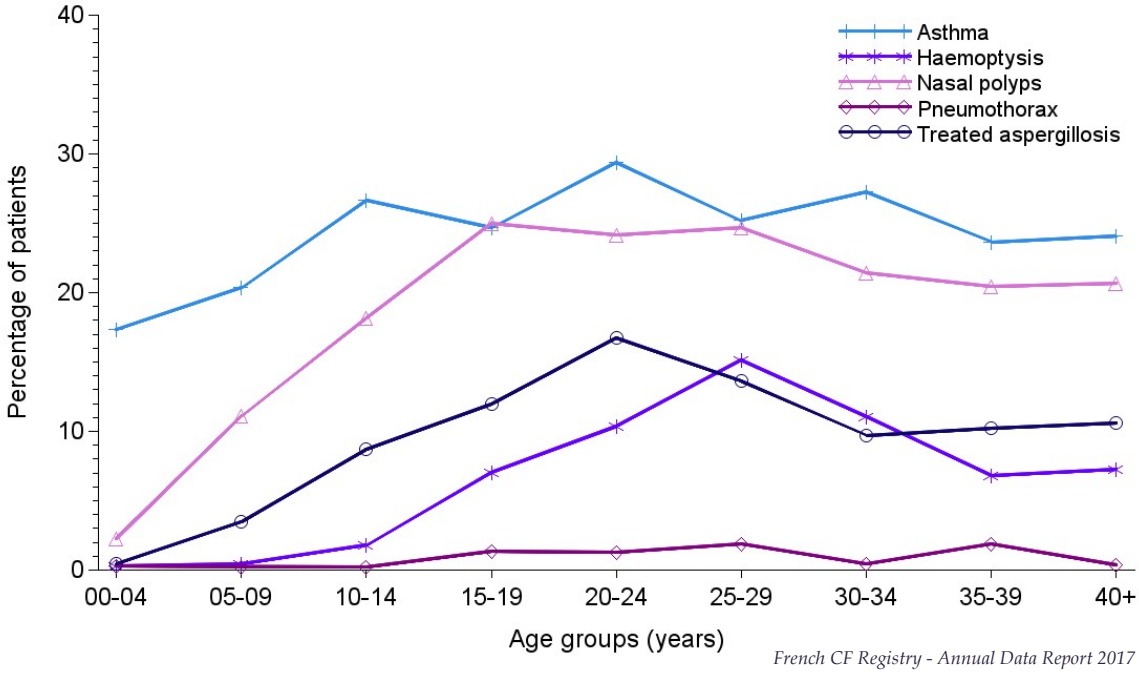
Figure 8.1. Respiratory complications

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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Gallstones	7	6	17	21	22	40	42	28	45	228	3.3 %
Cirrhosis/Portal hypertension	2	8	46	60	36	37	38	10	24	261	3.8 %
Abnormal exocrine pancreatic function	551	676	757	747	673	662	565	389	543	5563	80.3 %
Intestinal obstruction	14	15	28	27	33	37	34	24	40	252	3.6 %
Acute pancreatitis	.	5	4	11	13	12	18	10	18	91	1.3 %
Treated gastro-oesophageal reflux disease	114	119	151	201	276	301	286	199	360	2007	29.0 %

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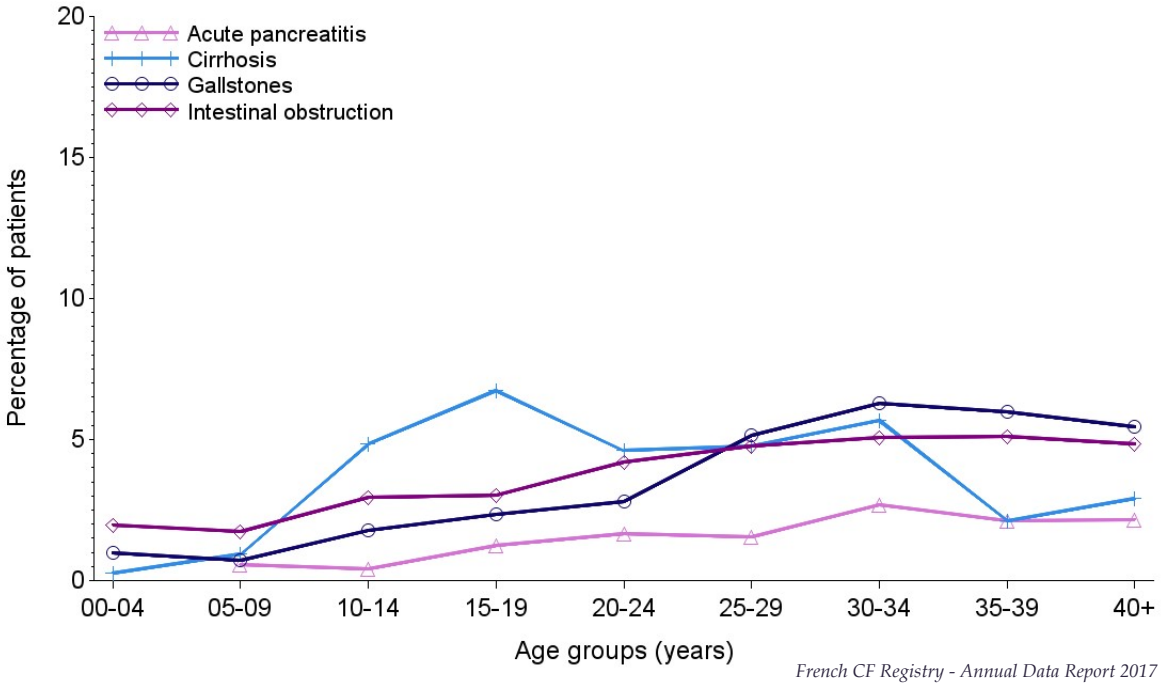
Figure 8.2. Gastro-intestinal complications

Percentage of age groups reporting complications.



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8. Complications

Diabetes mellitus

29.8% 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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Total diabetes (ID and non ID diabetes)	4	13	76	142	186	230	230	175	273	1329	19.2 %
Non insulin-dependent diabetes	3	3	20	30	21	28	26	23	26	180	2.6 %
Insulin-dependent	1	11	57	115	167	204	210	156	251	1172	16.9 %
Degenerative complications of diabetes	.	.	1	.	2	12	20	11	25	71	1.0 %

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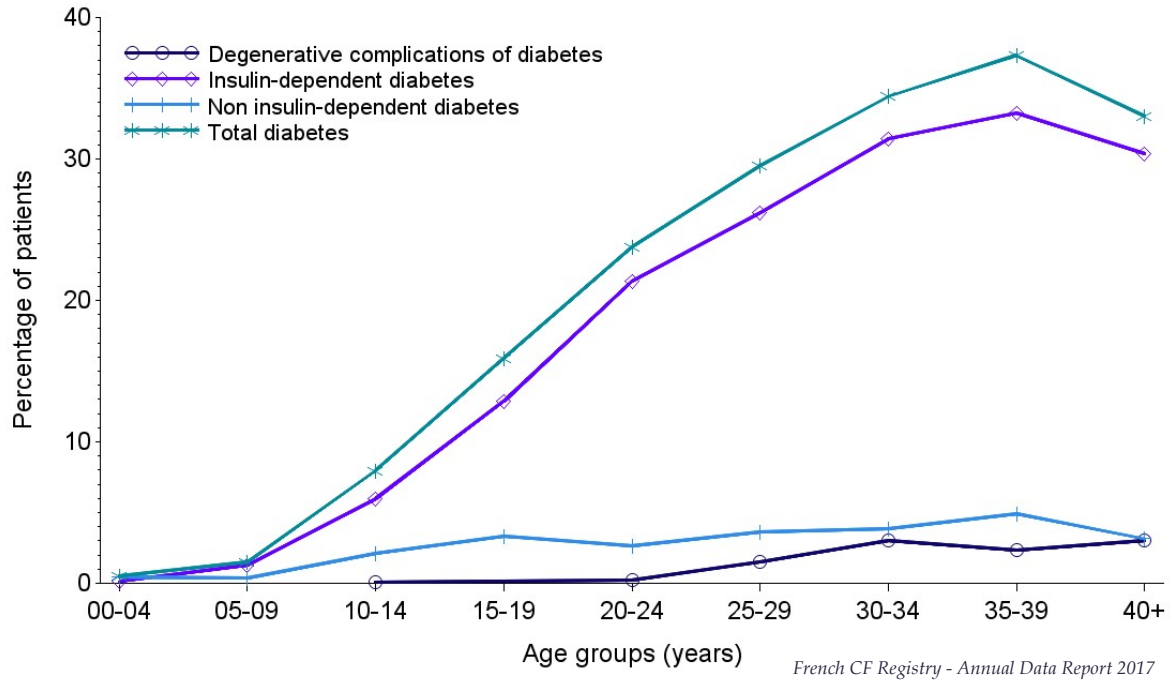
The line « Total diabetes » sums the number of patients having at least one type of diabetes. Among the 1329 patients, 23 patients presented with both types of diabetes during the year.

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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Arthropathy	.	2	11	17	29	29	27	27	52	194	2.8 %
Cancer	.	1	.	2	8	7	11	8	32	69	1.0 %
Depression (evaluated and followed)	5	13	23	42	72	91	80	71	151	548	7.9 %
Urinary incontinence	.	5	1	6	15	16	12	16	26	97	1.4 %
Terminal renal failure	.	1	.	.	3	4	8	7	11	34	0.5 %
Osteopenia/osteoporosis	.	6	32	68	123	179	171	151	264	994	14.3 %
Deafness/Hypoacusia	5	10	8	28	88	128	129	93	163	652	9.4 %

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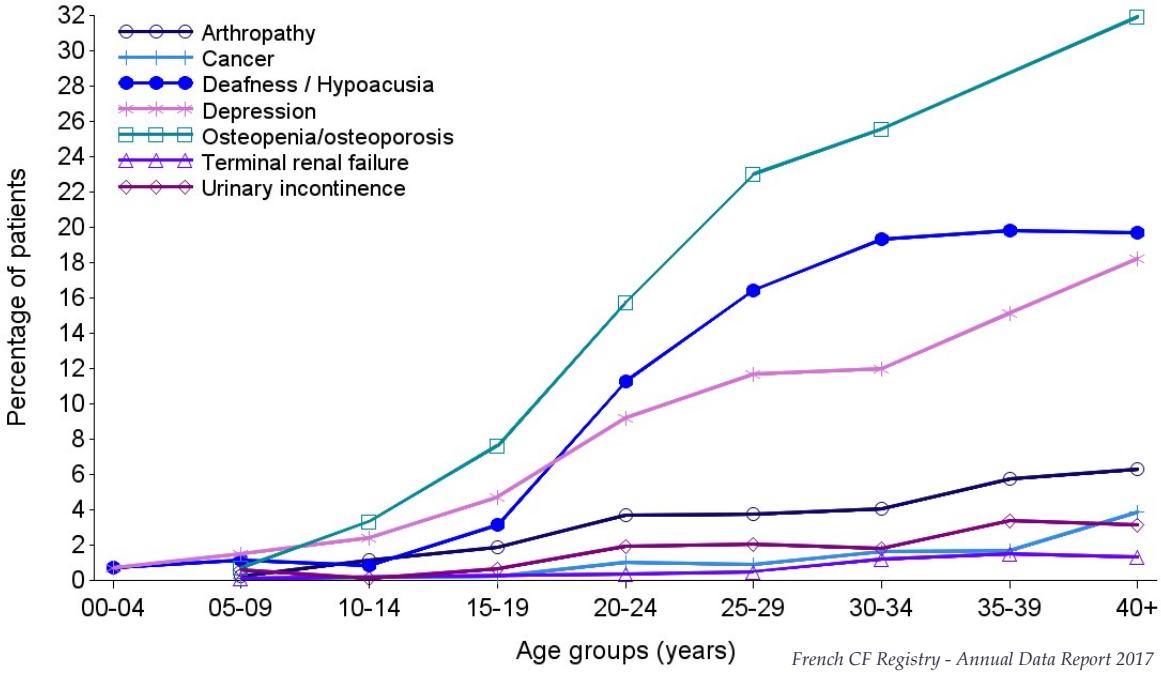
Figure 8.4. Other complications

Percentage of age groups reporting complications.



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9. Transplantation

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 2017.

	All years	2017
WAITING LIST	All waiting patients	Listed in 2017
Nb of patients	**151**	**95**
Mean age (years) and standard deviation (SD)	31.8 ± 11.4	31.8 ± 9.8
Extremes of age (years)	3.5-68.3	12.5-68.3
Deaths on waiting list	3	2
TRANSPLANTATION	All transplanted*	Transplanted in 2017
Nb of patients	**865**	**98**
Single organ transplant:		
- bilateral lung - N (%)	801 (92.6 %)	84 (85.7 %)
- liver - N (%)	28 (3.2 %)	1 (1.0 %)
- kidney - N (%)	52 (6.0 %)	8 (8.2 %)
- single lung - N (%)	10 (1.2 %)	2 (2.0 %)
- bilobar lung transplantation, N(%)	1 (0.1 %)	
- pancreatic islets, N(%)	2 (0.2 %)	1 (1.0 %)
- bone marrow - N (%)	1 (0.1 %)	
Multiple organ transplant:		
- heart-lung - N (%)	30 (3.5 %)	
- heart-lung / liver - N (%)	2 (0.2 %)	
- bilateral lung / liver - N (%)	24 (2.8 %)	3 (3.1 %)
- bilateral lung / kidney - N (%)	4 (0.5 %)	
- bilateral lung / islet of Langerhans - N (%)	8 (0.9 %)	
- liver / single lung - N (%)	1 (0.1 %)	
- liver / kidney - N (%)	1 (0.1 %)	
- liver / pancreas - N (%)	1 (0.1 %)	
- kidney / pancreas - N (%)	3 (0.3 %)	
Mean age (years)	35.1	30.5
SD	9.94	10.9
Extremes of age (years)	3.5-68.3	3.5-68.3
Post-transplantation deaths	33	9

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

9. Transplantation

Figure 9.1. Annual number of transplanted patients, since 1992

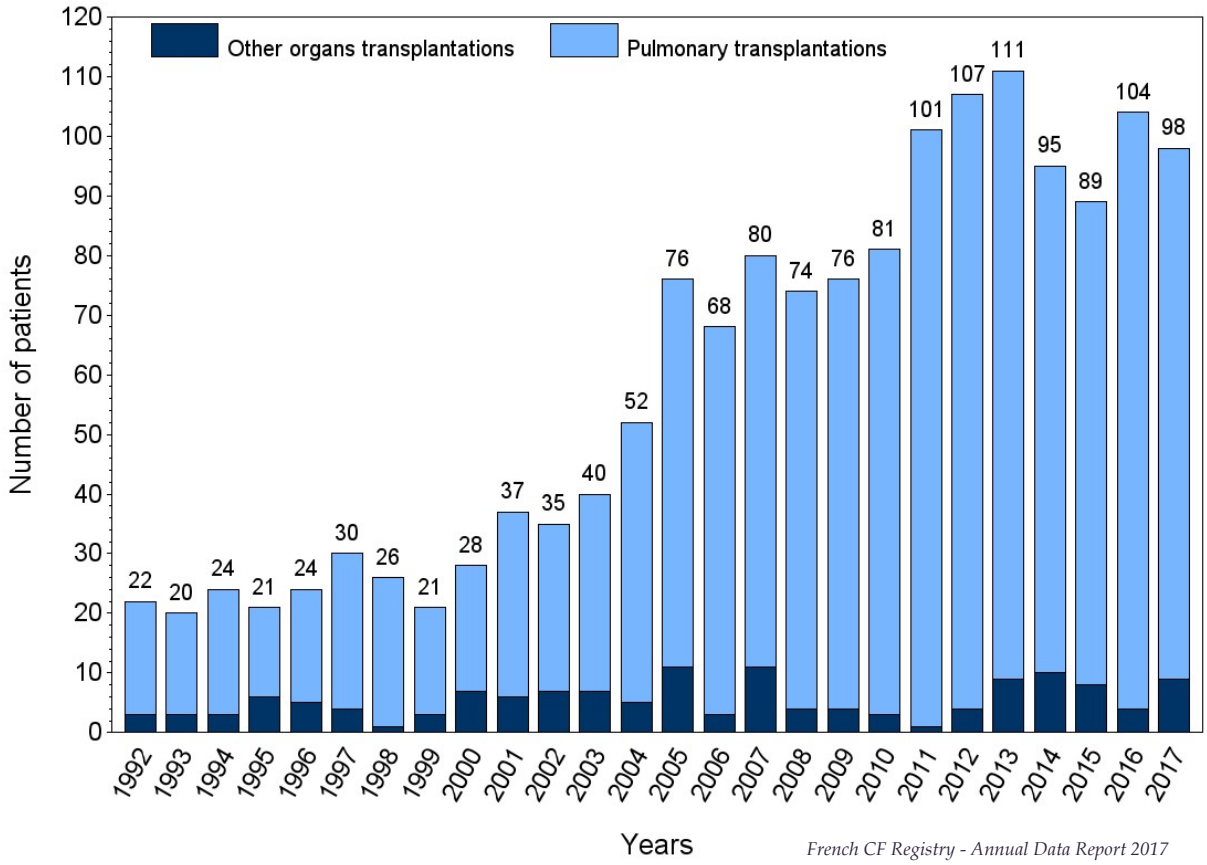

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Table 9.2. Annual number of transplanted patients, since 1992

	Years												
Transplant type	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Pulmonary*	19	17	21	15	19	26	25	18	21	31	28	33	47
Other organs	3	3	3	6	5	4	1	3	7	6	7	7	5

	Years												
Transplant type	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Pulmonary*	65	65	69	70	72	78	100	103	102	85	81	100	89
Other organs	11	3	11	4	4	3	1	4	9	10	8	4	9

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* single lung, 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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*
< 4 visits per year	139	192	205	173	200	177	181	139	308	1714 (24.7 %)
≥ 4 visits per years	569	663	747	719	582	601	487	330	519	5217 (75.3 %)
Outpatient visits										
Number of patients with at least one outpatient visit	*472*	*534*	*614*	*572*	*569*	*562*	*479*	*346*	*582*	*4730*
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	3.9	3.2	3.4	3.7	4.2	4.1	3.8	3.7	3.6	3.7
One-day hospitalizations										
Number of patients with at least one one-day visit	*606*	*799*	*901*	*822*	*657*	*644*	*547*	*373*	*617*	*5966*
Median number of visits	3.0	3.0	3.0	3.0	2.0	2.0	2.0	2.0	2.0	2.0
Mean number of visits	3.3	2.9	3.1	3.4	2.9	3.0	3.0	3.1	2.7	3.1
Inpatient visits										
Number of patients with at least one inpatient visit	*163*	*132*	*202*	*268*	*235*	*277*	*232*	*148*	*264*	*1921*
Median number of visits	1.0	1.0	1.0	2.0	2.0	2.0	1.0	1.0	2.0	1.0
Mean number of visits	1.9	1.7	2.0	2.3	2.6	2.7	2.3	2.4	2.5	2.3
Median duration (days)	8.0	5.0	7.0	11.0	13.0	11.0	9.0	10.0	12.0	9.0
Mean duration (days)	17.0	10.2	15.2	19.3	24.7	21.0	20.2	18.2	24.4	19.7

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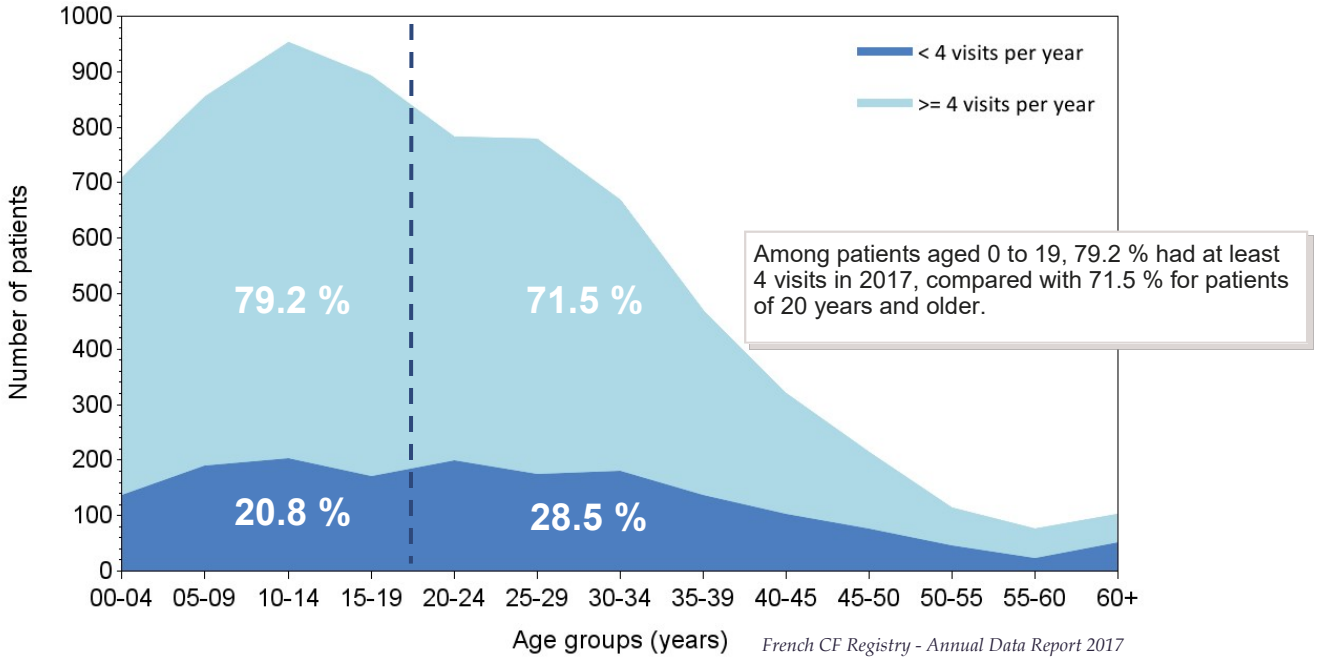
Figure 10.1. Number of visits



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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	708	855	952	892	782	778	668	469	827	6931
Nb of patients with at least one course	67	97	198	308	311	341	283	176	256	2037 (29.4 %)
- and with TIVAD*	9	26	66	128	139	153	117	81	96	815 (11.8 %)
Nb of courses	89	171	392	648	873	872	722	426	625	4818
Nb of days of courses including:	1099	2500	6847	9425	13958	13166	11358	6886	9448	74687
- at hospital	827	1005	2134	3796	3349	3214	3200	1642	3208	22375
- at home	272	1512	4599	5648	9832	9886	8035	4846	6092	50722
TIVAD* (with and without course)	10	26	69	136	143	157	122	84	102	849 (12.2 %)

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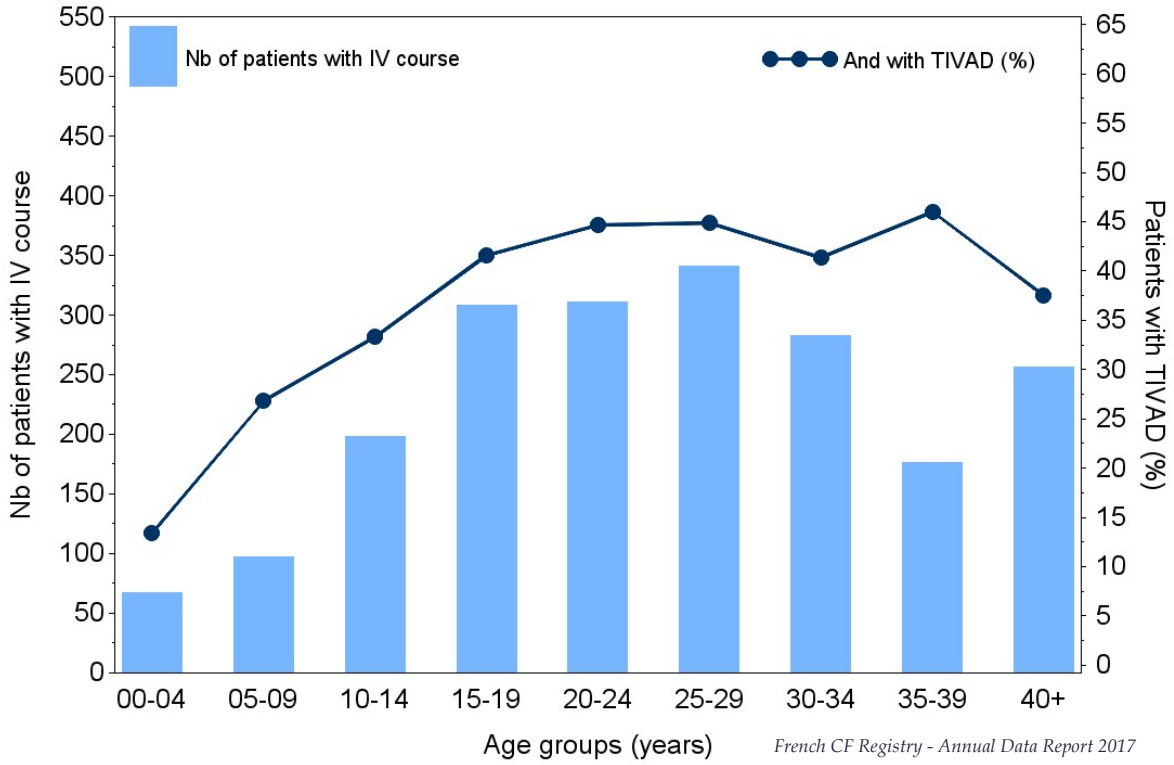
Figure 11.1. Patients with at least one IV antibiotic course and a TIVAD *



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* TIVAD: Totally Implantable Vascular Access Device

11. Therapeutic management

Antibiotic courses

Table 11.2. Repartition 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	1.8	2.0	2.1	2.8	2.6	2.6	2.4	2.5	2.4
SD	0.7	1.3	1.4	1.6	2.8	2.1	2.7	2.1	2.7	2.2
Median number of courses	1.0	1.0	1.0	2.0	2.0	2.0	2.0	2.0	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	2.5	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Day of courses										
Mean duration of courses (days)	16.4	26.3	34.9	31.8	45.5	39.8	41.2	39.3	38.7	37.6
SD	11.1	21.7	40.1	27.1	52.5	38.9	48.5	41.1	39.8	41.0
Median duration of courses (days)	14.0	15.0	15.0	21.0	28.0	28.0	28.0	28.0	28.0	28.0
1st quartile (Q1)	11.0	14.0	14.0	14.0	14.0	14.0	15.0	14.0	14.0	14.0
3rd quartile (Q3)	15.0	30.0	44.5	42.0	47.0	47.0	45.0	45.0	49.0	44.0

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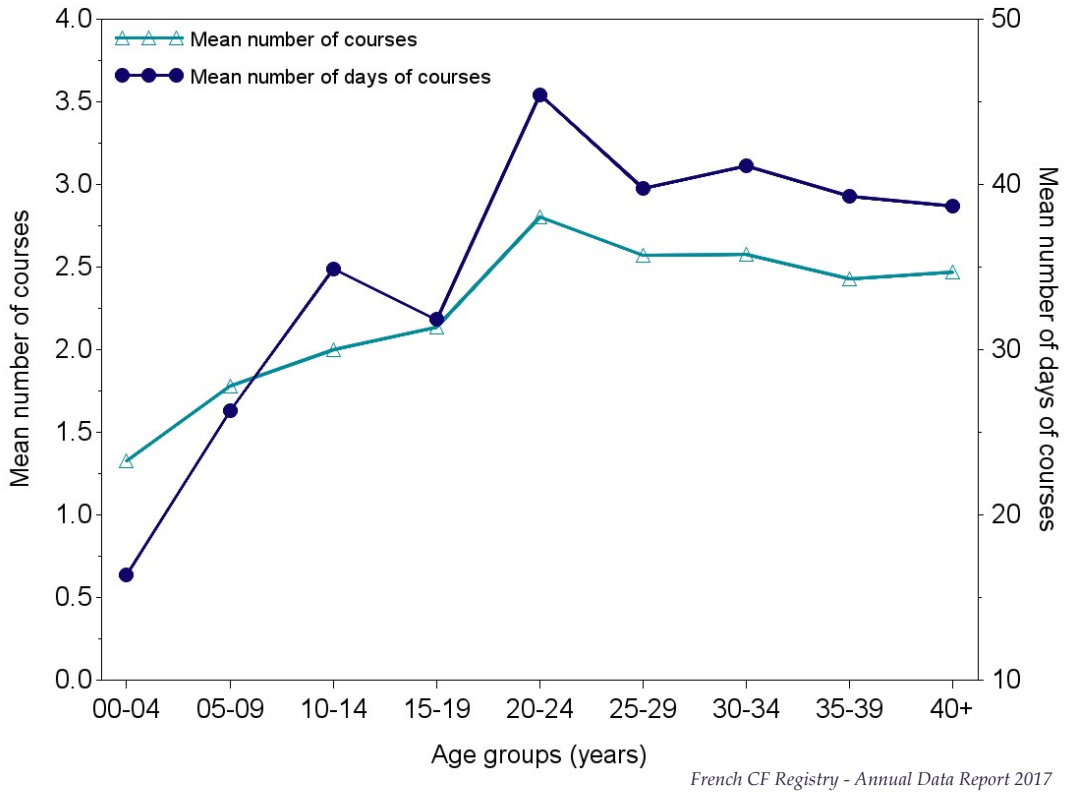
Figure 11.2. Mean number of courses and of days of courses



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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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Aerosol therapy*	352	683	823	799	687	640	523	372	608	5487	79.2 %
Azithromycin	52	173	277	302	304	347	320	227	353	2355	34.0 %
Oxygen therapy	2	2	11	35	46	57	49	37	75	314	4.5 %
Oral corticosteroids	11	30	45	60	99	152	173	152	225	947	13.7 %
Nasal ventilation	.	6	23	36	32	36	37	26	65	261	3.8 %

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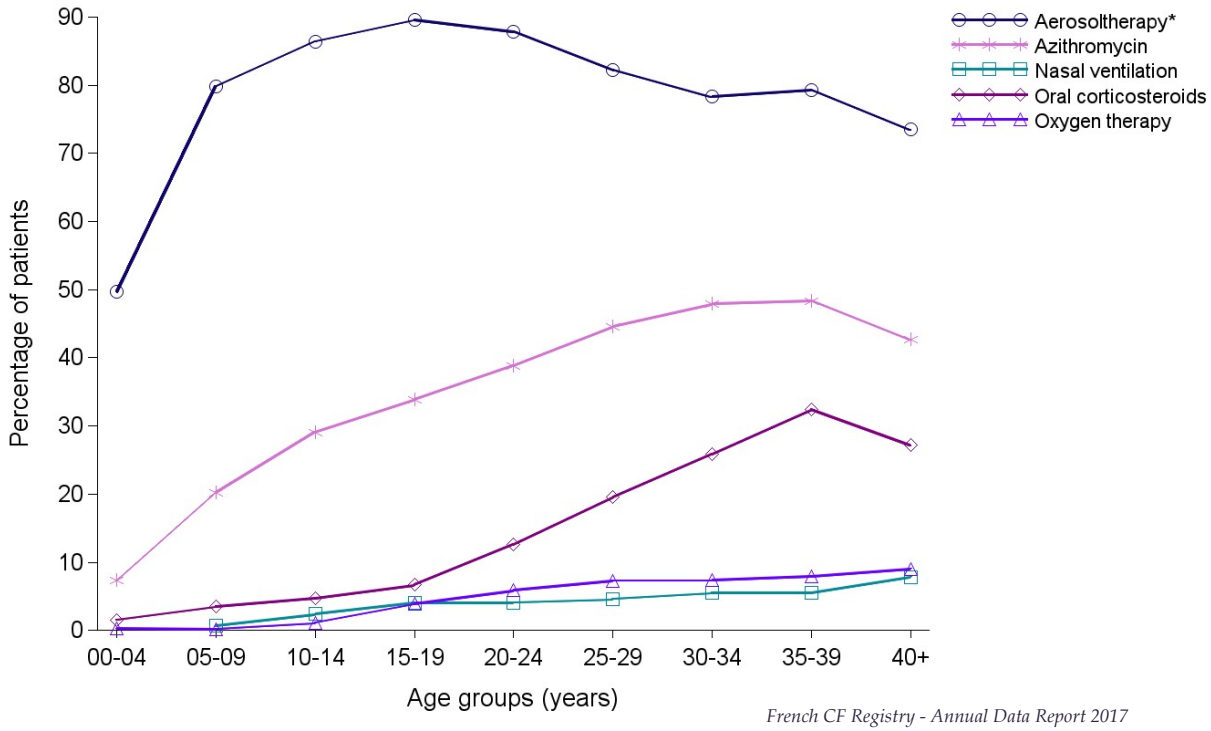
Figure 11.3. Respiratory therapeutics (≥ 3 months)



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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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Ivacaftor	6	24	24	20	11	15	11	7	20	138	2.0 %
Lumacaftor + Ivacaftor	.	1	170	280	192	177	142	78	59	1099	15.9 %

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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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Patients under aerosol therapy*	**352**	**683**	**823**	**799**	**687**	**640**	**523**	**372**	**608**	**5487**	**79.2 %**
Inhaled antibiotics, including:	114	190	317	422	428	410	338	238	313	2770	40.0 %
- Tobramycin	*46*	*91*	*150*	*239*	*197*	*175*	*119*	*85*	*79*	*1181*	*17.0 %*
- Colistin	*43*	*76*	*167*	*236*	*218*	*230*	*180*	*125*	*188*	*1463*	*21.1 %*
- Aztreonam	*.*	*5*	*11*	*18*	*20*	*27*	*37*	*25*	*20*	*163*	*2.4 %*
Inhaled bronchodilators	237	427	621	598	547	481	407	287	483	4088	59.0 %
Inhaled corticosteroids	127	257	426	412	338	288	236	175	301	2560	36.9 %
Inhaled hypertonic saline	67	121	180	171	74	54	56	32	56	811	11.7 %
RhDNase	84	468	619	564	389	328	222	129	218	3021	43.6 %

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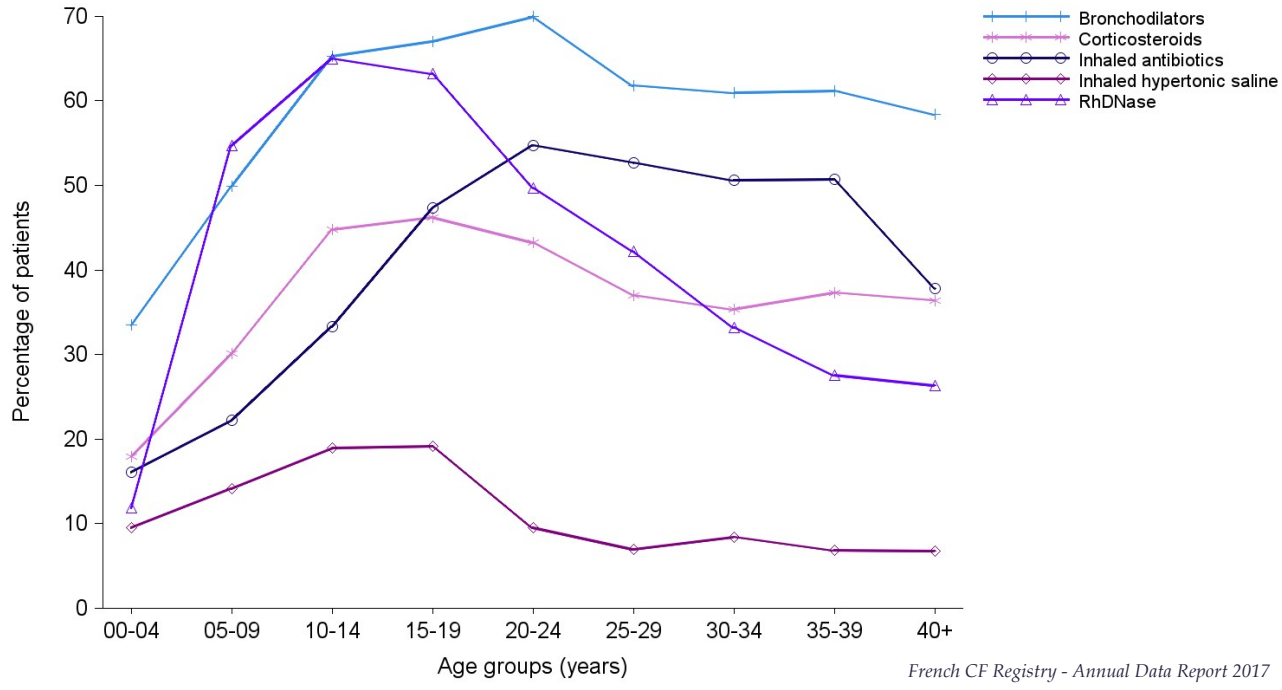
* By nebulization, spray or powder

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	*708*	*855*	*952*	*892*	*782*	*778*	*668*	*469*	*827*	*6931*	
Ursodeoxycholic acid	46	118	234	283	226	213	199	108	132	1559	22.5 %
Acid blockers	224	252	364	391	403	430	388	268	473	3193	46.1 %
Pancreatic enzymes	547	674	755	751	674	674	567	390	541	5573	80.4 %
Supplemental tube feeding	46	37	72	82	45	42	17	10	16	367	5.3 %
Oral supplemental feeding	164	255	313	297	284	308	223	148	177	2169	31.3 %
Fat-soluble vitamins	643	789	884	826	710	677	569	393	614	6105	88.1 %

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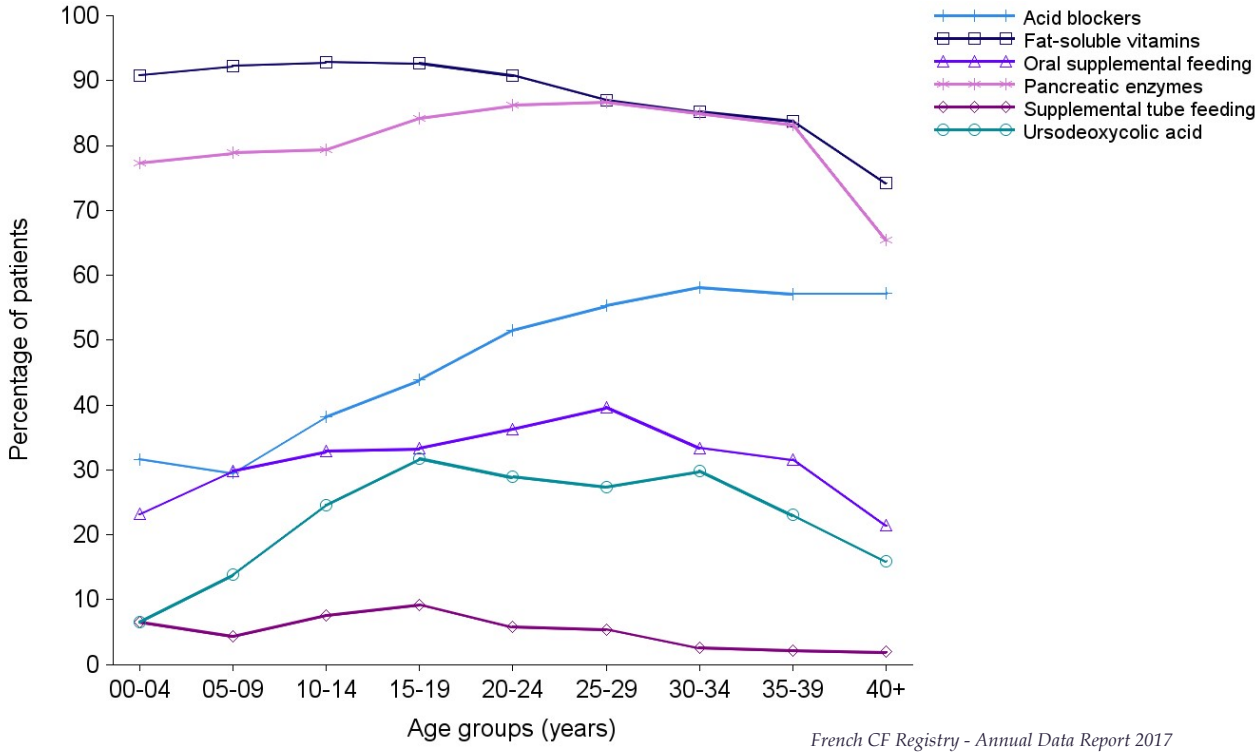
Figure 11.5. Hepatic, digestive and nutritional treatments (≥ 3 months)



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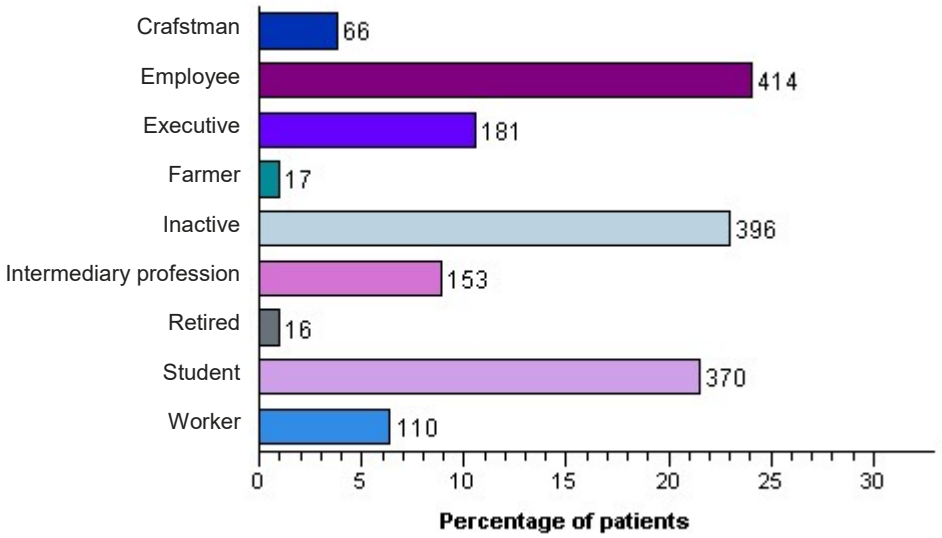
12. Social data

Employment

Figure 12.1. Employment of men ≥ 18 years

N = 1723 (number of men with a known employment situation, corresponding to 84.8 % of adults men).



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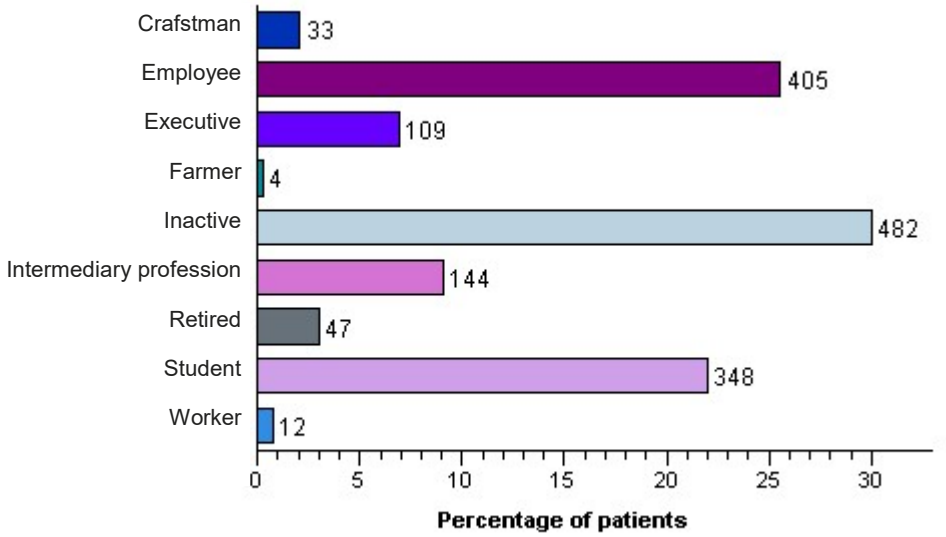
Among men aged 18 to 65, 46.5 % are workers.

Among men aged 18 to 25, 55.4 % are studiants.

Figure 12.2. Employment of women ≥ 18 years

N = 1584 (number of women with a known employment situation, corresponding to 86.0 % of adults women).



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Among women aged 18 to 65, 39.1 % are workers.

Among women aged 18 to 25, 54.4% are studiants.

12. Social data

Marital status

Figure 12.3. Family status of men ≥ 18 years

Number of men with a known family status: 1701 (83.7 % of adult men).

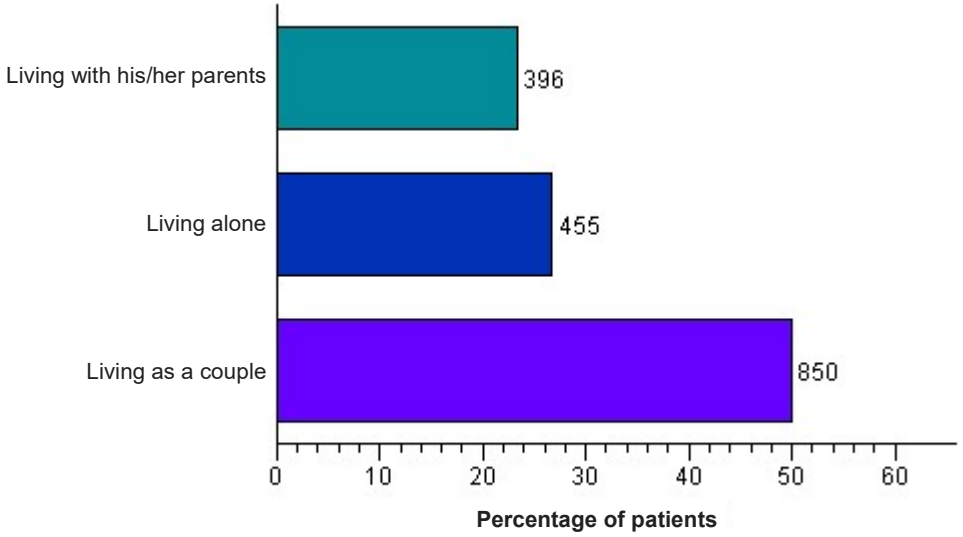

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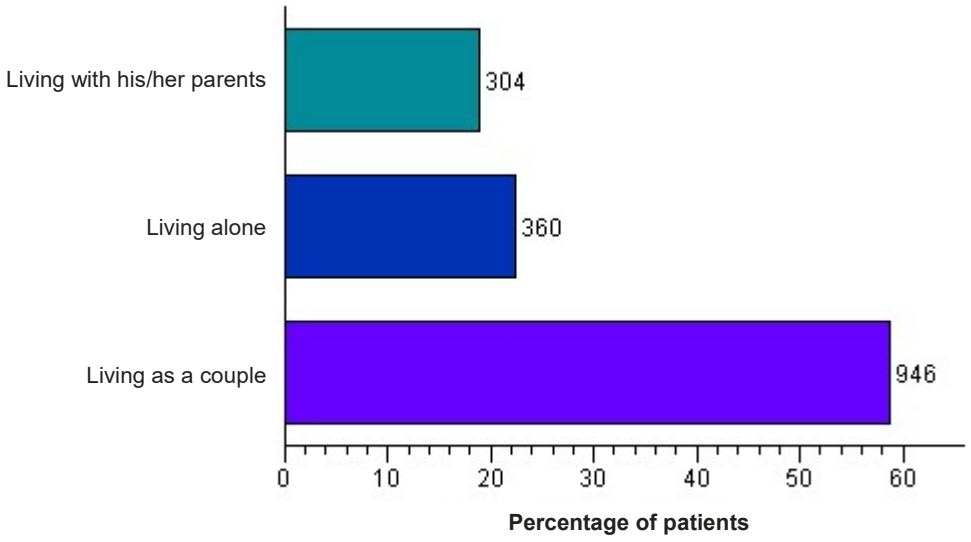
Figure 12.4. Family status of women ≥ 18 years

Number of women with a known family status: 1610 (87.4 % of adult women).



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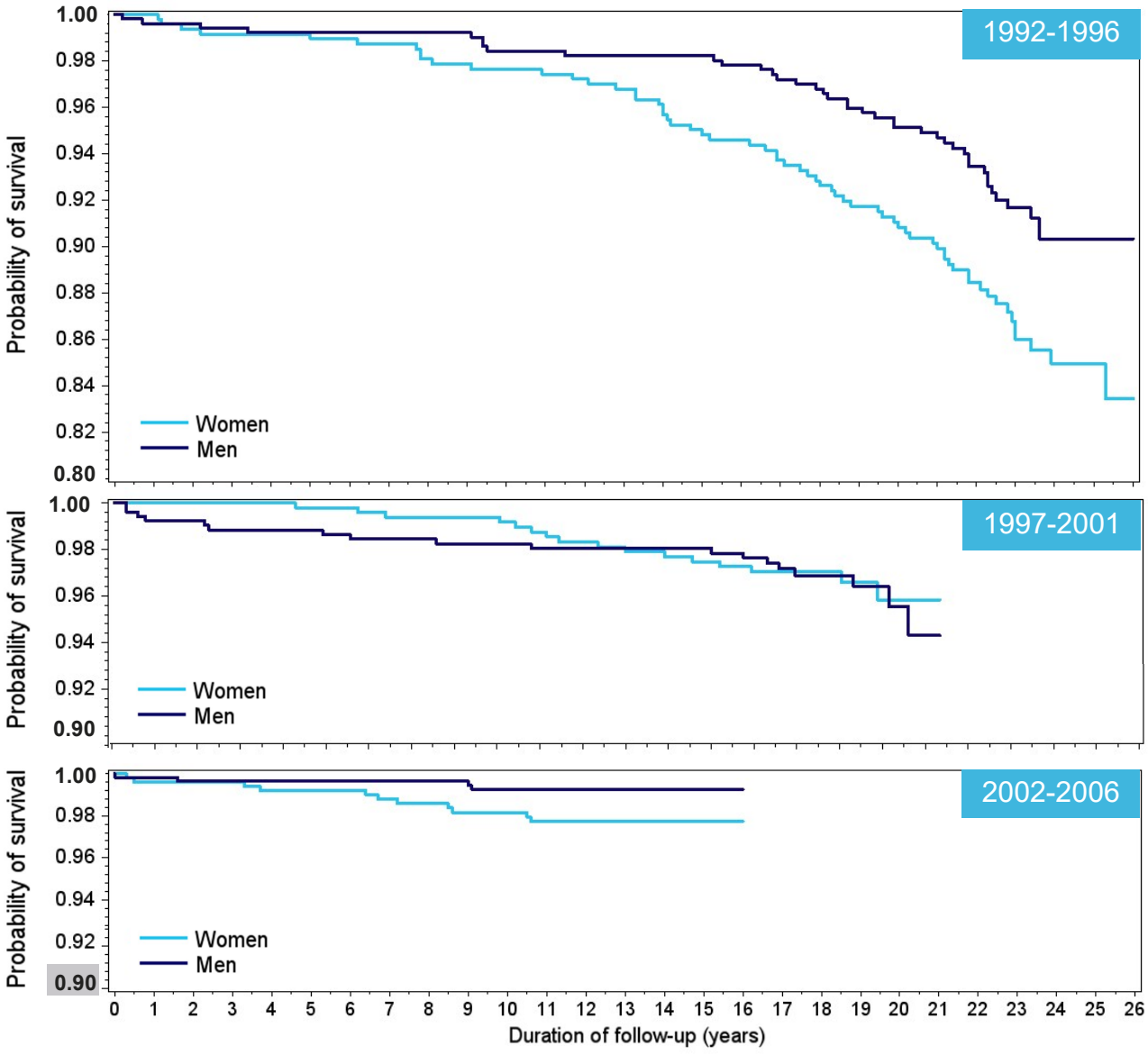
Annex 1

- 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	472	40	408	62
1997-2001	495	18	475	16
2002-2006	536	4	491	11



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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 16 years.

Annex 2

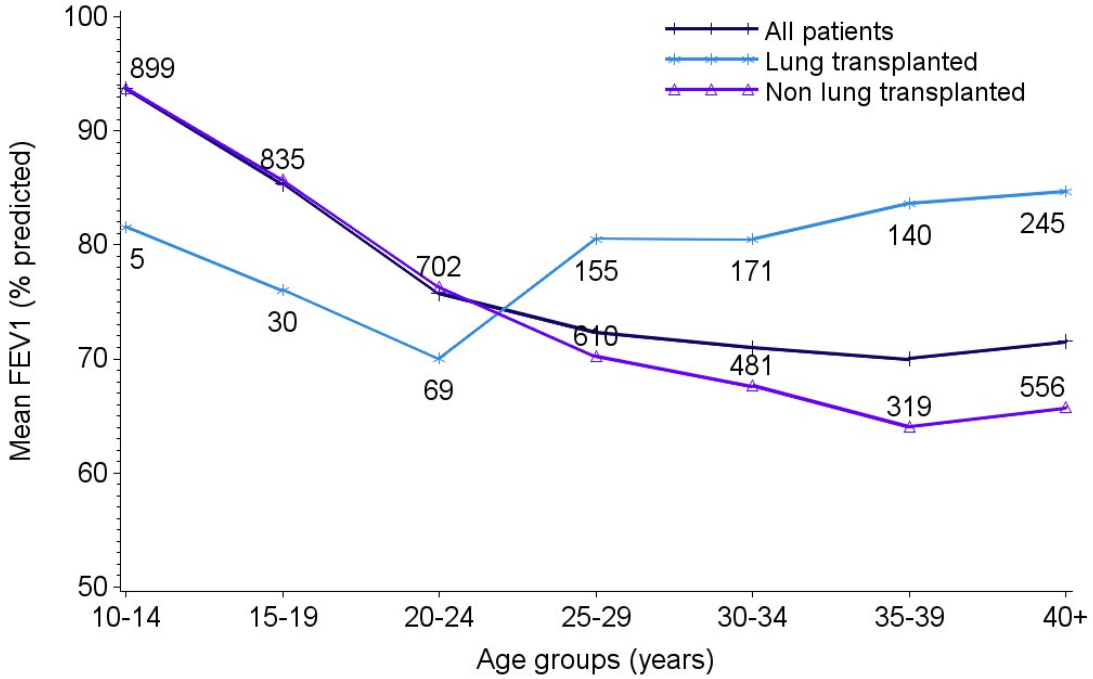
Spirometry and transplantation

This complementary analysis compares by age group the whole CF population to: 1) double lung or heart-lung transplant recipients and, 2) to 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. Among transplanted patients, the explanatory factors for this increase are probably different.

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



Curve « Lung transplant recipients »:
- The values **below** the curve represent the number of lung transplant recipients with a FEV1 value (eg: 155 patients in the 25-29 age group).
- No pulmonary transplantation has been reported in patients under 10.

Curve « Non lung transplant recipients »:
- The values **above** the curve represent the number of non lung transplant recipients with a FEV1 value (eg: 610 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	70
Bordeaux	161
Grenoble	113
Lille	175
Lyon	282
Marseille	144
Nancy	141
Nantes	106
Paris Necker	214
Paris Robert Debré	168
Paris Trousseau	67
Rennes St Brieuc	131
Saint Denis de la Réunion	57
Strasbourg	117
Toulouse	131
Tours	126
Versailles	65
Adults CF care centres	
Besançon	68
Bordeaux	143
Grenoble	96
Lille	225
Lyon	373
Marseille	247
Nancy	97
Nantes	235
Paris Cochin	469
Rennes	110
Strasbourg	152
Suresnes Foch	490
Toulouse	193
Tours	83
Paediatric and Adults CF care centres	
Amiens	97
Angers-Le Mans	138
Caen	115
Clermont-Ferrand	117
Créteil	125
Dijon	125
Dunkerque	85
Giens	209
Limoges	64
Montpellier	220
Nice	111
Reims	135
Roscoff	163
Rouen	220
Saint Pierre de la Réunion	74
Vannes-Lorient	84

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	2
Le Havre	21
Montluçon	3
Pointe à Pitre	6
Paediatric and Adults local centres	
Lens	37
Other centres	
Paris HEGP Transplantation	62

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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 2017 were excluded from those statistics.

Annex 4 (1/2)

Table A4.1. Summary of data

	2015	2016	2017
Patients seen during the year and centres participating to the registry			
- Patients registered* (N):	6628	6783	7114
- Patients seen during the year in a centre** (N):	6619	6776	6931
- Centres (N) :			
Paediatric CRCMs:	16	16	17
Adult CRCMs:	12	12	14
Paediatric and Adult CRCMs:	17	17	16
Other centres:	12	9	4
Demographics			
- Male patients (%):	51.9	52.3	52.1
- Age of patients, in years (mean):	21.2	21.8	22.3
- Age of patients, in years (median):	19.3	19.9	20.3
- Age of patients. in years (min-max):	0-83.2	0.1-84.1	0.1-85.1
- Patients aged 18 years and over (%):	53.3	54.6	55.9
- Early pregnancies in the year (N):	55	59	39
- Pregnancy rates in women aged 15 to 49 years (for 1000):	31.1	32.2	20.6
- Age at 31st December of the year of early pregancy (mean):	30.9	28.2	30.2
- Deaths (N):	43	53	56
- Crude death rate (for 1 000):	6.5	7.8	8.1
- Age at death, in years (mean):	34.1	31.9	35.0
- Age at death, in years (median):	31.8	28.0	33.8
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	2.2	2.1	2.0
- New patients diagnosed during the year (N):	254	189	180
- Age at diagnosis of the new patients, in years (median):	1.5	1.3	1.5
- Age at diagnosis of the new patients, in years (min-max):	0-69	0-72	0-72
- Full genotypes identified (%):	97.3	97.6	97.4
F508del / F508del:	41.6	41.6	41.4
F508del / Other:	41.1	41.4	41.2
Other / Other:	14.6	14.5	14.7
F508del / Missing:	0.6	0.6	0.7
Other / Missing:	0.8	0.8	0.8
Missing / Missing:	1.3	1.1	1.1
Anthropometry			
- Patients aged 17 years and less, Height z-score (mean):	0	0.01	0.05
Weight z-score (mean):	-0.21	-0.19	-0.18
- Patients aged 18 years and over, Height z-score (mean):	-0.49	-0.5	-0.5
Weight z-score (mean):	-0.21	-0.18	-0.13

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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

	2015	2016	2017
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - Knudson (mean):	91.1	92.1	92.9
- Patients aged 18 years and over, FEV_1 (% predicted) - Knudson (mean):	71.3	72.3	73.1
Microbiology			
- Patients with at least one sputum during the year (%):	88.3	87.4	87.4
H. influenzae:	19.2	17.3	16.6
MSSA:	55.9	56.8	57.2
MRSA:	8.1	7.2	6.3
P. aeruginosa:	39.1	38.3	36.8
S. maltophilia:	10.3	10.6	10.6
B. cepacia:	1.7	1.7	2.3
Aspergillus:	22.8	24.5	28.7
Achromobacter xylosoxidans:	6.3	6.3	6.6
Complications and transplantations			
- Aspergillus (%) :	10	9.9	9.5
- Abnormal exocrine pancreatic function (%) :	80.3	80.6	80.3
- Treated gastro-oesophageal reflux (%) :	18.7	19.7	29
- Osteopenia/osteoporosis (%) :	6.5	7	14.3
- Haemoptysis (%):	5.2	5.7	6.5
- Cirrhosis / portal hypertension (%):	4.1	4.1	3.8
- Insulin-dependent and non insulin-dependant diabetes (%):	18.4	19.3	19.2
- Transplanted patients (N):	743	810	865
Including patients transplanted during the year:	88	103	98
- Patients on waiting list (N):	152	156	151
Including patients listed during the year:	102	93	95
Deaths on waiting list:	2	7	3
Therapeutic management			
- IV courses (%):	30.9	30.5	29.4
- Oxygenotherapy (%):	5.3	4.9	4.5
- Nasal ventilation (%):	4.0	4.4	3.8
- Azithromycin (%):	43.4	43.2	34
- Pancreatic enzymes (%):	81.1	81.2	80.4

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Annex 5

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

	Transplanted patients	Non transplanted patients	2017 data
- Patients seen during the year in a centre* (N):	859	6072	6931
Demographics			
- Age of patients, in years (mean):	35.1	20.5	22.3
- Age of patients, in years (median):	34.2	18	20.3
- Patients aged 18 years and over (%):	97.4	50	55.9
- Early pregnancies during the year (N):	4	35	39
- Deaths (N):	33	23	56
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	5	1.9	2
- Full genotypes identified (%):	97.3	97.4	97.4
F508del / F508del:	51.3	40	41.4
F508del / Other:	36.1	42	41.2
Other / Other:	9.9	15.4	14.7
F508del / Missing:	0.6	0.7	0.7
Other / Missing:	0.5	0.9	0.8
Missing / Missing:	1.6	1	1.1
Anthropometry and spirometry			
- Patients aged 17 years and less, Height z-score (mean):	-1.03	0.05	0.05
Weight z-score (mean):	-1.52	-0.17	-0.18
BMI z-score (mean):	-0.79	-0.12	-0.13
- Patients aged 18 years and over, Height z-score (mean):	-0.69	-0.44	-0.5
Weight z-score (mean):	-0.65	0.01	-0.13
BMI (mean):	20.2	21.6	21.3
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - Knudson (mean):	72.7	93.1	92.9
- Patients aged 18 years and over, FEV_1 (% predicted) - Knudson (mean):	80.7	71	73.1
Complications			
- Treated aspergillosis (%)	7.3	9.8	9.5
- Abnormal exocrine pancreatic function (%) :	92.5	78.5	80.3
- Treated gastro-oesophageal reflux disease (%) :	67.4	23.5	29
- Osteopenia/osteoporosis (%) :	47.1	9.7	14.3
- Haemoptysis (%):	3.4	6.9	6.5
- Cirrhosis / portal hypertension (%):	2.8	3.9	3.8
- Insulin-dependent and non insulin-dependant diabetes (%):	60.4	13.3	19.2
Therapeutic management			
- Pancreatic enzymes (%) :	92.1	78.8	80.4
- Oral steroids (%) :	76	4.8	13.7

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** The difference between the number of transplanted patients page 34 (865) and the number of patients shown in this table (859) are the patients who died and were not seen in 2017.*

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	All
- Patients seen during the year in a centre* (N):	5767	398	6931
Demographics			
- Age of patients, in years (mean):	21	23.7	22.3
- Age of patients, in years (median):	18.7	16.9	20.3
- Patients aged 18 years and over (%):	52.3	48.2	55.9
- Early pregnancies during the year (N):	32	0	39
- Deaths (N):	43	1	56
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	1.7	37.8	2
- Full genotypes identified (%):	98.3	87.2	97.4
F508del / F508del:	45.1	1.8	41.4
F508del / Other:	40.1	58.8	41.2
Other / Other:	13.1	26.6	14.7
F508del / Missing:	0.6	2	0.7
Other / Missing:	0.6	4.3	0.8
Missing / Missing:	0.6	6.5	1.1
Anthropometry and spirometry			
- Patients aged 17 years and less, Height z-score (mean):	0.01	0.6	0.05
Weight z-score (mean):	-0.23	0.49	-0.18
BMI z-score (mean):	-0.16	0.2	-0.13
- Patients aged 18 years and over, Height z-score (mean):	-0.56	0.16	-0.5
Weight z-score (mean):	-0.22	0.87	-0.13
BMI (mean):	21.1	23.6	21.3
Spirometry			
- Patients aged 17 years and less, FEV_1 (% predicted) - Knudson (mean):	92.4	100.8	92.9
- Patients aged 18 years and over, FEV_1 (% predicted) - Knudson (mean):	73.2	86.6	73.1
Complications			
- Treated aspergillosis (%)	9.6	3.8	9.5
- Abnormal exocrine pancreatic function (%) :	85.8	10.6	80.3
- Treated gastro-oesophageal reflux disease (%) :	30.7	11.8	29
- Osteopenia/osteoporosis (%) :	12.7	4.3	14.3
- Haemoptysis (%):	6	1.5	6.5
- Cirrhosis / portal hypertension (%):	4	0.5	3.8
- Insulin-dependent and non insulin-dependant diabetes (%):	20.3	2	19.2
Therapeutic management			
- Pancreatic enzymes (%) :	85.7	12.1	80.4
- Oral steroids (%) :	14.7	3.3	13.7

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** Diagnosis type is missing for 766 patients.*

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