FRENCH CYSTIC FIBROSIS
Registry

2016

Annual data report

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Editorial

The French CF Registry (formerly National Cystic Fibrosis Observatory, initiated in 1992), has been accredited 10 years ago. This 2016 edition marks then a milestone.

Partnership with other databases - AFDPHE for neonatal screening, Muco-CFTR for validation of CFTR mutations, CépiDC-INSERM for deaths - has further improved its data quality and completeness. Consisting of both demographic and morbidity data, it is a crucial source of medical information.

What are the big trends over the last 10 years in the 2016 data ?

Demographic increase is a tremendous message of hope and reflects the constant improvement of the patients health status with the following characteristics:

- an increase in the total population of 37% with 6757 patients identified in 2016
- adults now represent 55% of the total population, the number of children remains stable in absolute value, but their relative proportion decreases
- the proportion of adults over 40 increases from 3.6% in 2006 to 11.3% in 2016.

The key therapeutic turning points of patient care are:

- lung transplantation has stabilized since 2010 (80 to 100 transplants per year) and today about 20% of adult patients are transplanted
- the CFTR modulators (ivacaftor authorized in 2012 targeting 2% of the CF patients, the lumacaftor/ivacaftor authorized in 2016 targeting more than 12% of the CF patients) highlight the Registry as an essential tool for the follow-up of these patients, who will be more and more numerous to benefit from innovative therapeutic advances in the near future.

The French CF Registry has become a recognized tool in 25 years in the fields of care and research. During the last few years, about fifty requests for statistical analysis were made per year. Registry data is used by CF centers, public and private research laboratories, and industrial partners. Projects, approaches, initiatives, in the fields of quality of life, social sciences and humanities, also rely on the data of the Registry.

The French CF Registry participates in the European Patient Registry (ECFSPR) and actively contributes to European and international projects. The French team is member of the ECFSPR Data quality group, the global project to harmonize data among registries, and participates in the CFTR2 project (Clinical and Functional Translation of CFTR).

What are the Registry's next steps?

- Data transparency improvement in partnership with the centers
- A specific report for transplanted patients
- At-a-glance version of the annual report
- A more efficient request tool

A simple survey at its onset, the Registry is now an unique epidemiological tool for predicting demographic changes in cystic fibrosis in France. As such, it has, and will have, an increasing importance in studies and the evolution of care. With the evolutions in use of individual data, the Registry is a major project for Vaincre la Mucoviscidose and the CF community.

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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 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 1,900 mutations have been identified, the most common (encountered in about 80% of patients) is the F508del mutation.

Before implementation of the systematic newborn screening program, the most common context for diagnosis was as follows: alerted by clinical symptoms (meconium ileus, steatorrhoea, bronchial obstruction, recurrent respiratory infections), the physician would carry out a sweat test. An elevated sweat chloride ions concentration would confirm the diagnosis, and this would be followed by molecular analysis of the *CFTR* gene and determination of the disease causing mutations.

Newborn screening has been systematic in France and the French overseas territories since 2002. This decision was taken by the Ministry of Health, which entrusted the task to the French association for screening and prevention of disabilities in children (*AFDPHE - Association Française pour le Dépistage et la Prévention des Handicaps de l'Enfant*). 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 up to 31/12/2014 then 29). 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 of the population with cystic fibrosis and the impact of therapeutics;
- 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 associations and other institutional partners in strategic decisions, in particular regarding fundings granted to centres in proportion to the number of patients;
- help research by facilitating pre-selection of patients eligible for clinical trials
- 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, the *Registre français de la mucovicidose*. This initiative was approved in July 2006 by the committee for protection of personal data in medical research (*Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé, CCTIRS*) and in March 2007 by the data protection agency (*Commission Nationale de l'Informatique et des Libertés, CNIL*). At the end of 2008 and then in 2011 and 2015, the registry was certified by the national committee of rare disease registries (*Comité National des Registres Maladies Rares*), an organ composed of the *Institut de Veille Sanitaire* (InVS), the *Institut National de la Santé et de la Recherche Médicale* (INSERM) and the national institute of cancer (Institut National des cancers, Inca).

Population and data

The population is composed of people with cystic fibrosis followed in the care centres participating in the registry in France (metropolitan France, Reunion Island and Guadeloupe). Data are collected once a year by means of a questionnaire transmitted using Web, paper questionnaires or exports from electronic patient files. The information requested refers to the preceding year and includes semi-anonymous patient identification, diagnosis, medical follow-up, treatments used, anthropometric data, respiratory function, bacteriological data, evolution of the condition and social and family situation. In thematic questionnaires are collected data on pregnancies, *Burkholderia Cepacia* complex and related, and inclusion in clinical trials.

Multi-sources data collection

Since 2010, data are no more exclusively collected from the CF centers. Other sources have been added in order to allow a better quality and exhaustivity of the diagnosis data (AFDPHE and molecular biology laboratories sources), death (CépiDc-Inserm) and transplantation data (Hôpital européen Georges-Pompidou (HEGP), Paris). Moreover, the online questionnaire has been simplified for social and transplantation data enabling more complete and accurate data collection.

Data use

Statistical analysis is performed on anonymized data. Unless otherwise indicated, the results presented hereafter relate to the population seen during the year 2016 and were produced by cross-sectional analysis of data. Data on patients seen during the year in at least two centres (said to have multiple accounts) were counted only once and allocated to the centre they visited most often during the year.

The French CF Registry also sends anonymised data to the European ECFS Patient Registry, in the aim of a broader use of the data with other countries.

Precautions before reading this report

The comparison of CF populations has to be careful and must take into account numerous bias such as newborn screening programme, transplantation strategy, socioeconomic aspects as well as the respect of guidelines, the use of different reference populations and the limits of the statistics regarding small numbers in age groups.

Missing data were considered as an absence of event, the calculated percentages may then be underestimated.

1. Demographics

Characteristics of the population

Figure 1.1. Evolution of the number of patients since 1992

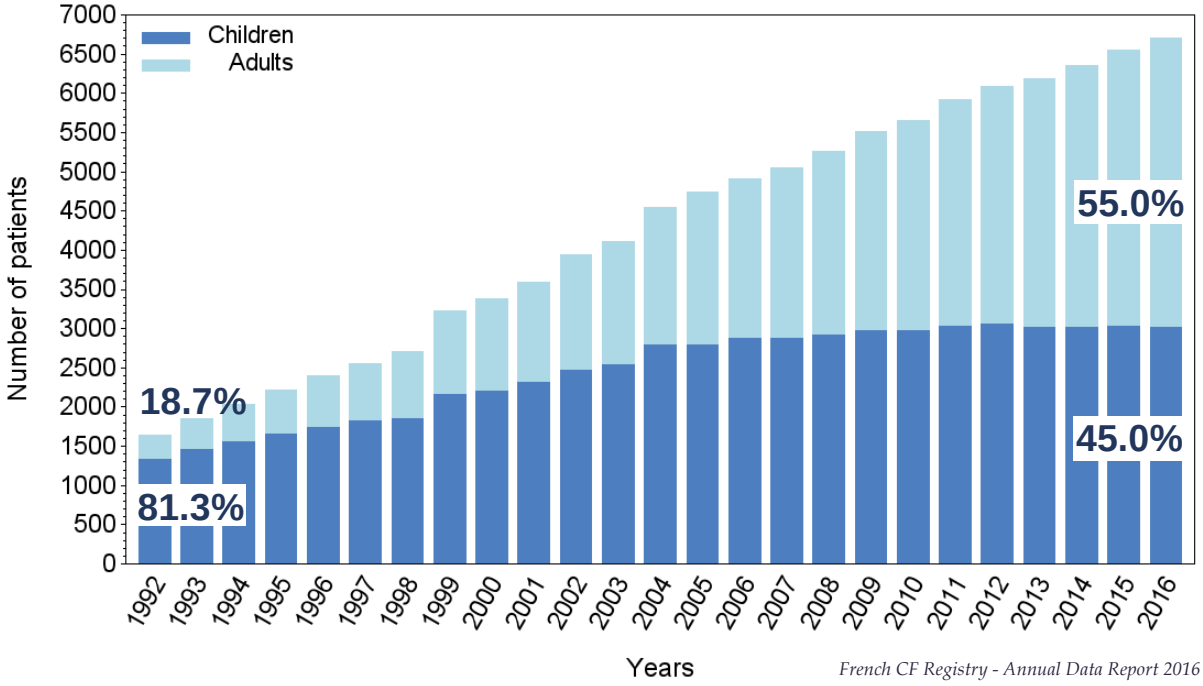

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Table 1.1. Annual evolution of the main indicators

	Years of follow-up										
Indicators	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
All patients*	4914	5067	5274	5531	5674	5966	6127	6232	6400	6589	6757
Patients seen during the year**	4903	5053	5263	5513	5660	5916	6086	6183	6351	6548	6707
Children	2870	2882	2912	2972	2973	3026	3055	3018	3013	3028	3020 (45.0 %)
Adults	2033	2171	2351	2541	2687	2890	3031	3165	3338	3520	3687 (55.0 %)
Over 40 years	175	202	247	308	341	399	454	512	587	670	755 (11.3 %)
Men	2547	2649	2744	2866	2916	3064	3148	3196	3283	3405	3513 (52.4 %)
Women	2356	2404	2519	2647	2744	2852	2938	2987	3068	3143	3194 (47.6 %)
Mean age (years)	16.8	17.1	17.6	18.1	18.5	19.1	19.6	20.2	20.8	21.3	21.9
Median age (years)	15.5	15.8	16.3	16.7	17	17.5	17.9	18.4	18.9	19.4	20
Minimum age (years)	0.1	0.1	0	0	0.1	0	0.1	0.1	0	0	0.1
Maximum age (years)	74.8	75.8	76.8	77.8	80	88	86.8	82.5	82.8	83.2	84.1

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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 data on survival.

Note: patients with an unconfirmed diagnosis were withdrawn from the report (98 in 2016).

1. Demographics

Characteristics of the population

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

Characteristics	2014		2015		**2016**	
	Men	Women	Men	Women	**Men**	**Women**
Patients seen during the year	3283	3068	3405	3143	3513	3194
Children	1533	1480	1559	1469	1565	1455
Adults	1750	1588	1846	1674	1948	1739
Mean age (years)	20.9	20.7	21.3	21.2	21.9	21.8
Median age (years)	19.2	18.8	19.6	19.2	20.2	19.7

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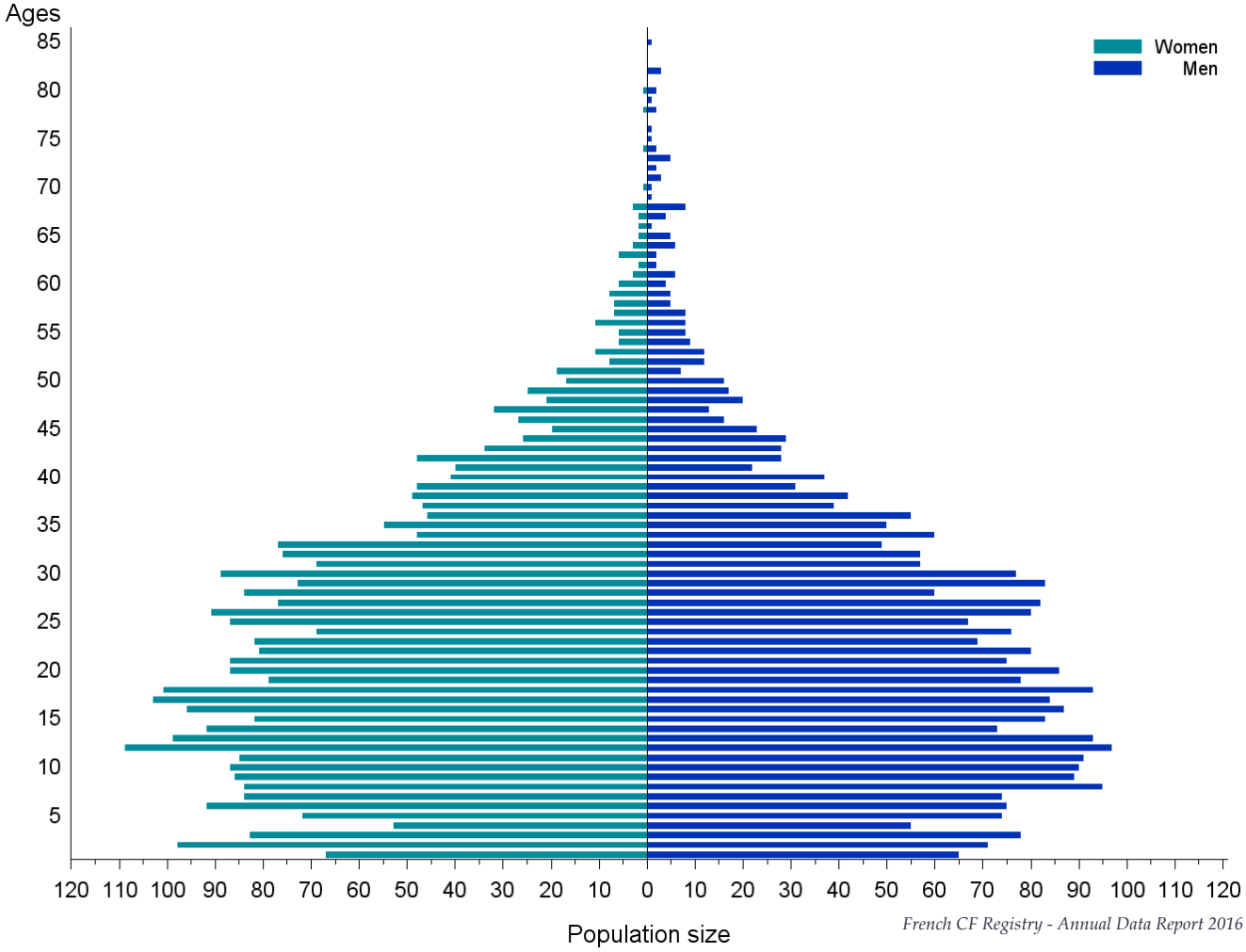
Figure 1.2. Population pyramid



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For the first year of life, the number of patients born in 2016 was 128 according to AFDPHE, and 112 seen in a CF center and collected in the Registry. Except for this age pyramide, only data of the 112 patients are used in this report (cf note p16).

The short bar corresponding to children born in 2013 has been validated with the AFDPHE 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	16	2040	30.4	127.5	0.1	48.9	10.3	10.5	9.3
Adult	12	2380	35.5	198.3	15.7	81.6	33.2	30.9	13.8
Paediatric/Adult	17	2171	32.4	127.7	0.1	84.1	20.6	18.1	19.2
Subtotal	45	6591	98.3	146.5	0.1	84.1	22.0	20.1	20.2
Other centres									
Paediatric	6	25 (b)	0.4	4.2	0.8	36.6	10.1	8.9	10.1
Paediatric/Adult	2	39 (c)	0.6	19.5	3.3	18.7	9.48	9.1	6.4
Other Centres	1	52 (d)	0.8	52.0	15.6	62.1	27.6	26.4	11.9
Subtotal	9	116	1.7	12.9	0.8	62.1	17.7	15.1	16.7
Total	54	6707	100	124.2	0.1	84.1	21.9	20.0	20.2

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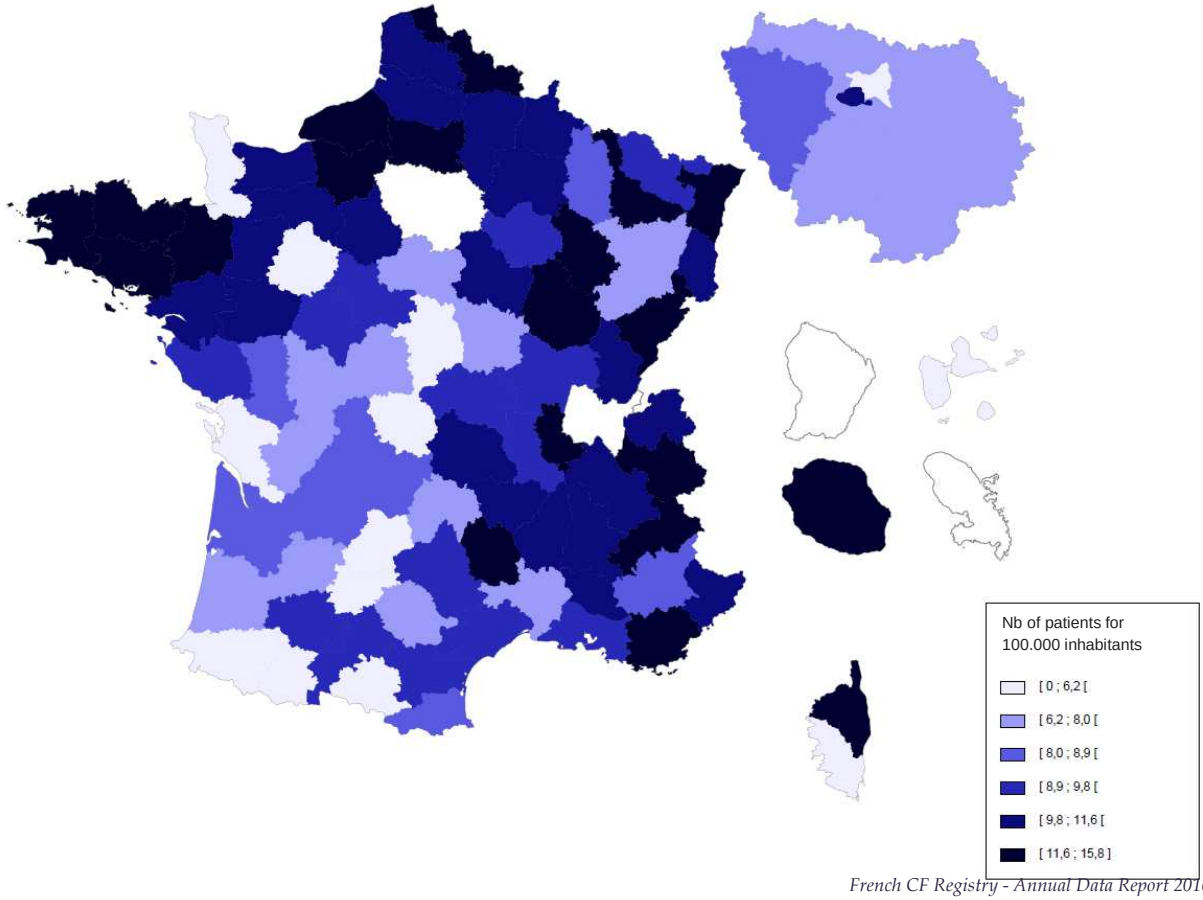
Notes : (a) After checking of patients in the multiple account category (cf page 6)
(b) Including 8 patients also seen by a CRCM.
(c) None of those patients were seen by a CRCM.
(d) Including 16 patients also seen by a CRCM

* Cases when adult centres care children and 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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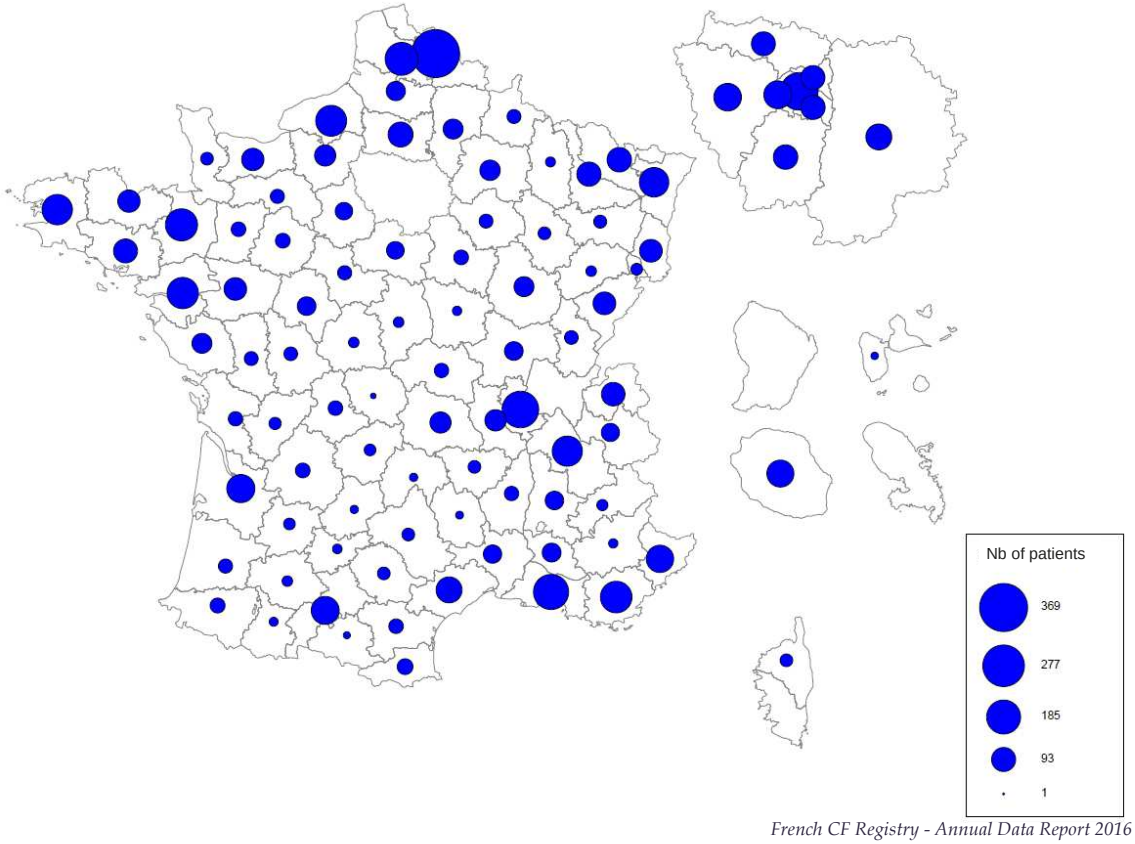
Map 1.2. Localisation of the patients by « département » of residence (absolute numbers)



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2. Mortality

Characteristics

Figure 2.1. Annual number of deaths since 1992

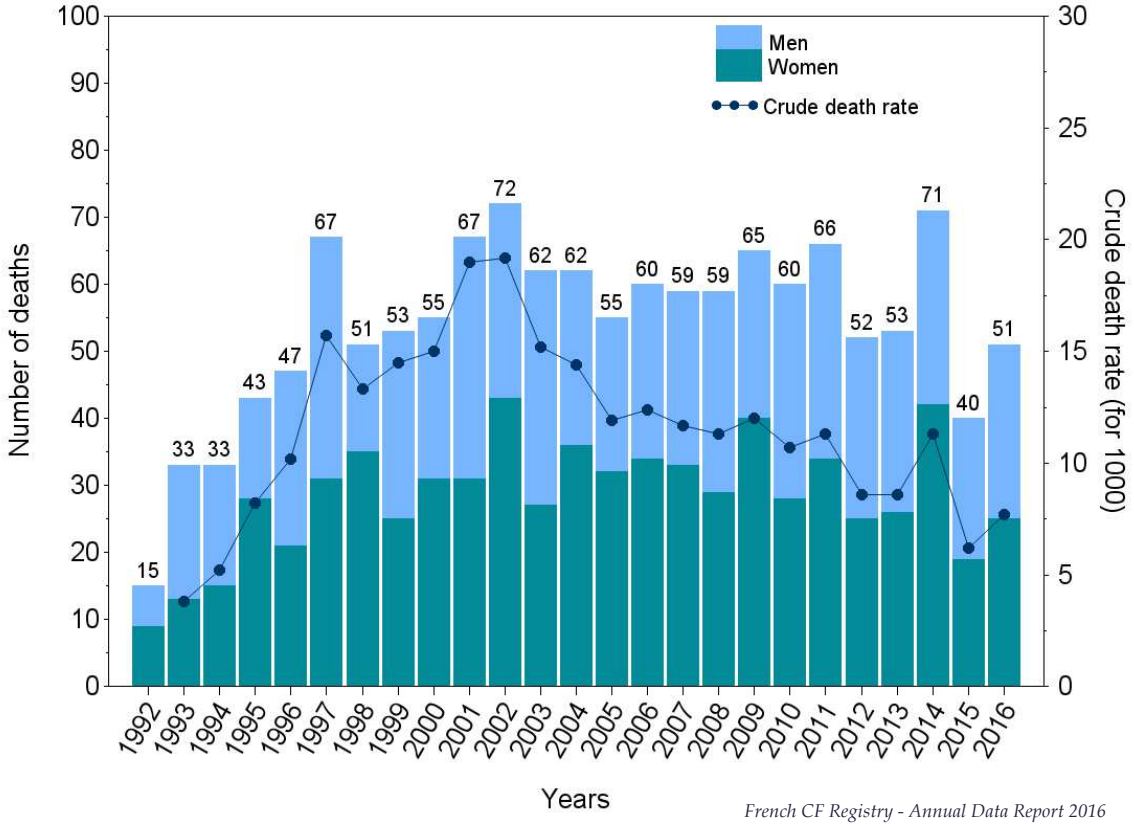

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Table 2.1. Mortality characteristics

	Years of follow-up										
Indicators	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Number of deaths	60	59	59	65	60	66	52	53	71	40	51
- including patients not seen during the year*	11	14	11	17	10	9	12	11	13	6	6
- including transplanted patients	19	29	27	33	31	35	27	30	43	21	37
Crude death rate (per 1000)	12.4	11.5	11.3	12.0	10.7	11.3	8.6	8.6	11.3	6.2	7.7
Mean age (years)	26.4	27.7	29.1	24.6	29.2	26.3	32.3	34.5	29.0	34.1	31.8
Median age (years)	24.0	26.2	27.9	23.3	27.6	24.8	27.8	30.7	27.1	30.6	28.0
Minimum age (years)	4.6	1.6	0.1	0.4	0.2	1.9	2.2	1.1	0.1	9.0	1.6
Maximum age (years)	76.3	70.0	66.1	73.4	68.9	55.5	88.4	82.5	71.2	83.2	76.0

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* Information of the death transmitted while the patient did not visit any centre during the year.

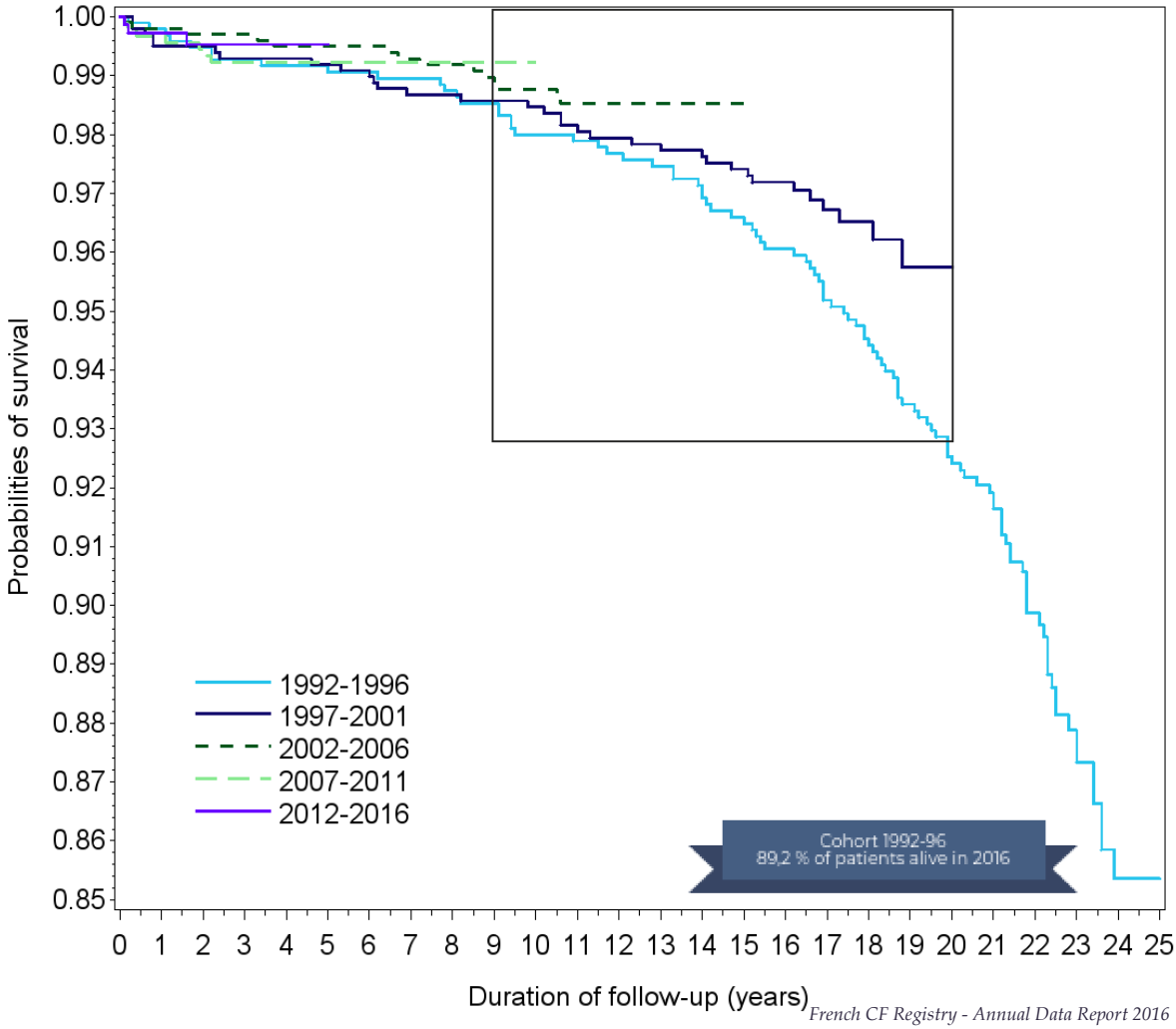
2. Mortality

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 2016 this cohort was followed during 25 years maximum): 959 patients, 103 deaths
- Births from 1997 to 2001 (maximum 20 years of follow up): 988 patients, 33 deaths
- Births from 2002 to 2006 (maximum 15 years of follow up): 1013 patients, 14 deaths
- Births from 2007 to 2011 (maximum 10 years of follow up): 915 patients, 7 deaths
- Births from 2012 to 2016 (maximum 5 years of follow up): 723 patients, 3 deaths



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 = 5.58, 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

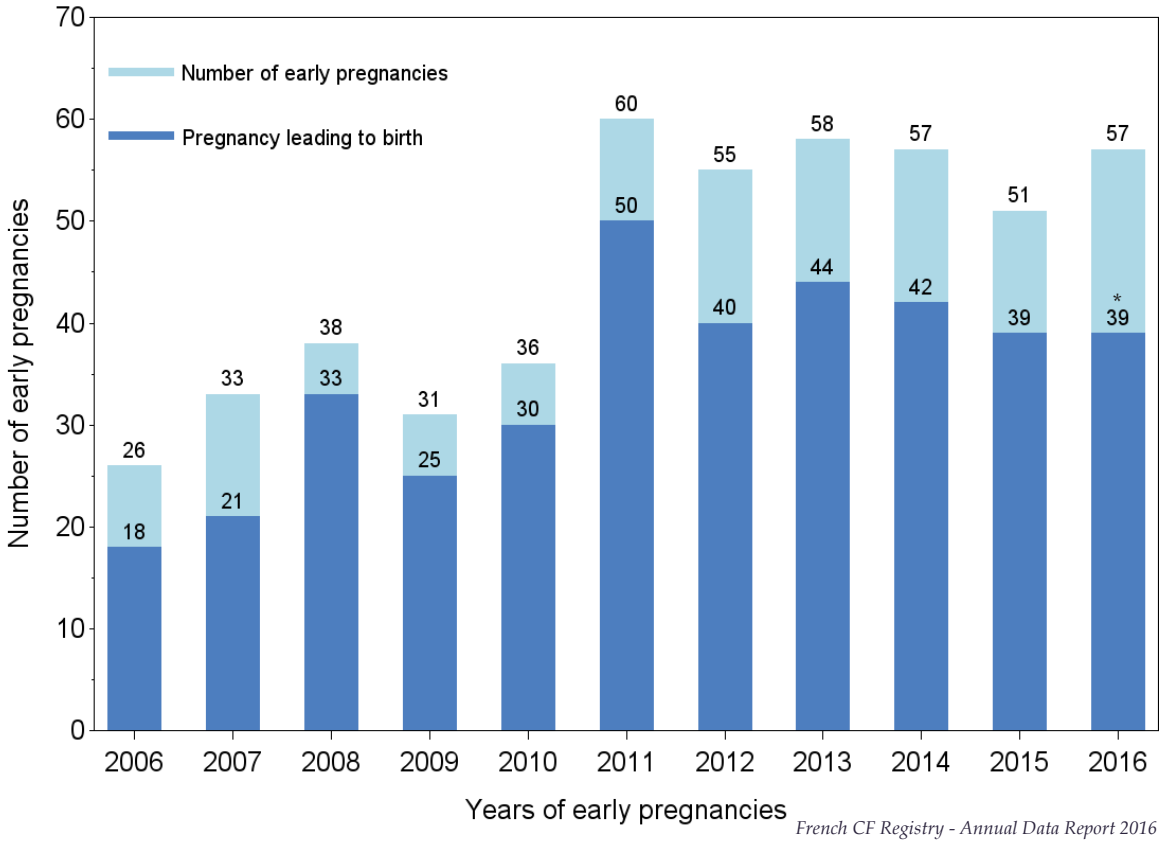


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Table 3.1. Early pregnancy characteristics

Characteristics	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Number of early pregnancies	26	33	38	31	36	60	55	58	57	51	57
Pregnancy rates in women aged 15 to 49 years (for 1000)	22.8	27.8	30.5	23.4	25.8	40.7	35.6	36	33.8	28.9	31.2
Mean age at 31st December of the year of early pregancy	27.4	27	27	27.3	28.8	28.4	28.2	28.5	28.6	30.6	28.3
Number of lung transplanted women starting a pregnancy	1	2	1	3	3	3	7	4	1	3	4

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3. Pregnancy – Paternity

Table 3.2. Paternities

Characteristics	N	Proportion (%)
Number of paternities, including:	43	
- Natural father	4	9.3
- Medically assisted reproduction, including:	33	76.7
+ Intracytoplasmic Sperm Injection / in vitro fertilization	30	90.9
+ Artificial insemination with sperm donor	1	3.0

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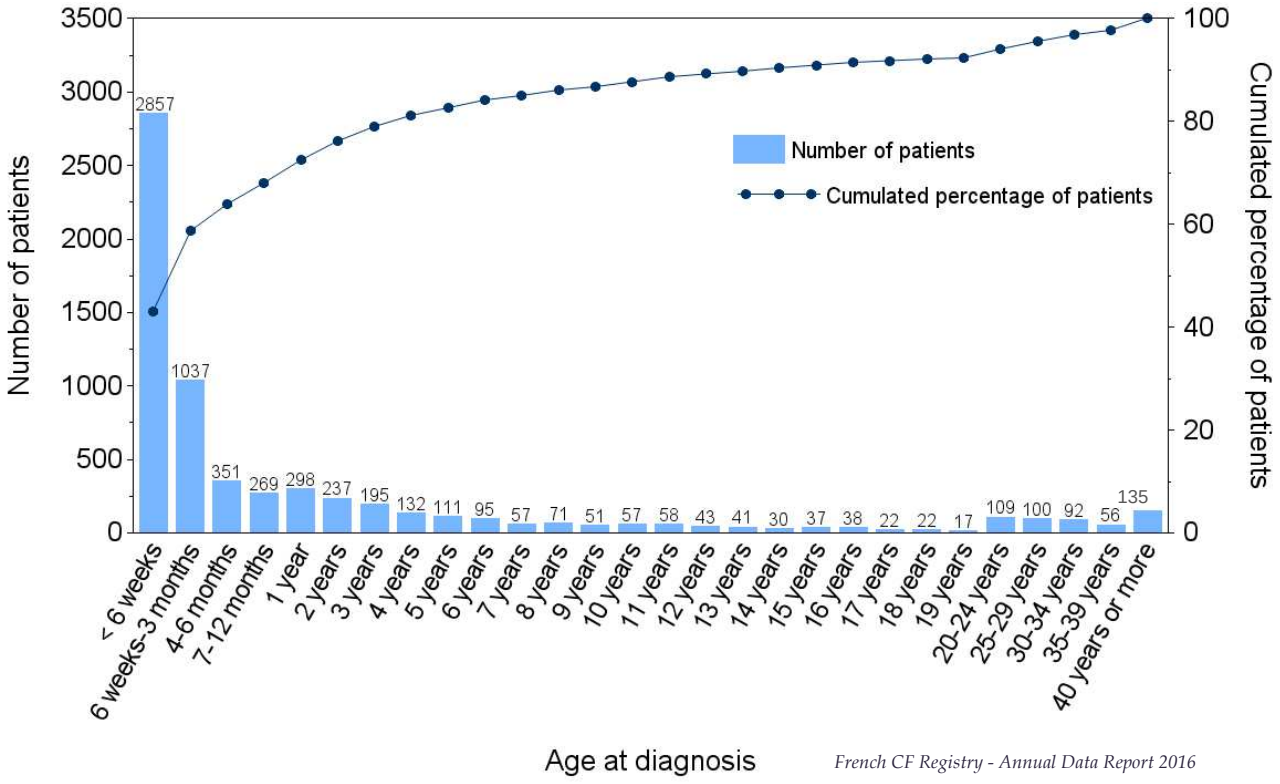
4. Diagnosis

Main characteristics

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

N = 6,633 (number of patients whose age at diagnosis is known).



4. Diagnosis

Main characteristics

Table 4.1. Diagnosis characteristics

Characteristics	2014	2015	**2016**
ALL PATIENTS			
Patients whose age at diagnosis is known - N (%) *	6307 (99.3 %)	6492 (99.1 %)	**6633 (98.9 %)**
Age at diagnosis			
- Median age (months)	2.2	2.1	**2.0**
- Mean age (years)	4.1	4.3	**4.3**
- Minimum age (years)	0	0	**0**
- Maximum age (years)	77	78	**78**
NEW PATIENTS DIAGNOSED DURING THE YEAR			
Number of patients			
New patients - N (%)	186 (2.9 %)	226 (3.5 %)	**177 (2.6 %)**
- Including 2016 newborn patients - N	126	145	**112**
Age at diagnosis			
- Median age (months)	1.3	1.3	**1.2**
- Mean age (years)	6.9	6.5	**7.0**
- Minimum age (years)	0	0	**0**
- Maximum age (years)	77	66	**70**
Context of diagnosis			
1. Screened positive newborns (NBS)	137	155	**134**
- including Prenatal diagnosis - N (%)	8 (5.8 %)	10 (6.5 %)	**10 (7.5 %)**
- including Meconium ileus - N (%)	19 (13.9 %)	22 (14.2 %)	**19 (14.2 %)**
2. Diagnosis on symptoms (NBS excluded)	49	71	**43**
- including Meconium ileus - N (%)	3 (6.1 %)	2 (2.8 %)	**2 (4.7 %)**
- including Symptoms (other than MI):- N (%)	46 (93.9 %)	69 (97.2 %)	**41 (95.3 %)**
- Mean age at diagnosis (years)	26.0	20.6	**28.0**

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* Data from AFDPHE were used to complete the Registry data when possible.

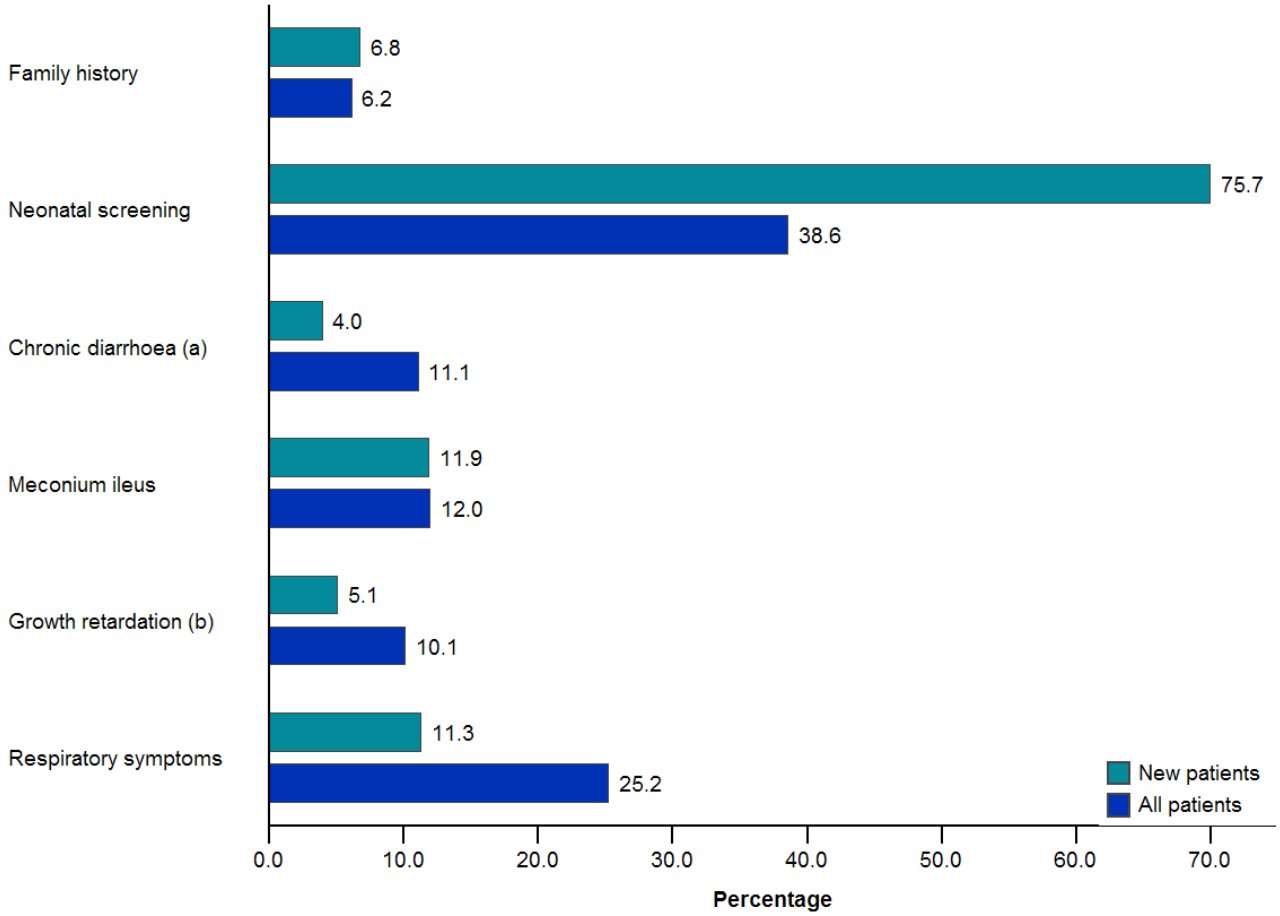
Among the 177 new patients, 112 were born in 2016. The method used to compile this report (patients seen in a care centre in 2016) means that infants born in 2016 and seen for the first time in 2017 are not included yet. For information purposes only, 25 newborns in 2015 were diagnosed in 2016 through neonatal screening. In the 2015 age pyramide, the number of patients aged 0 was 144 and should have been 144+25=169.

The number of patients diagnosed by neonatal screening (134) 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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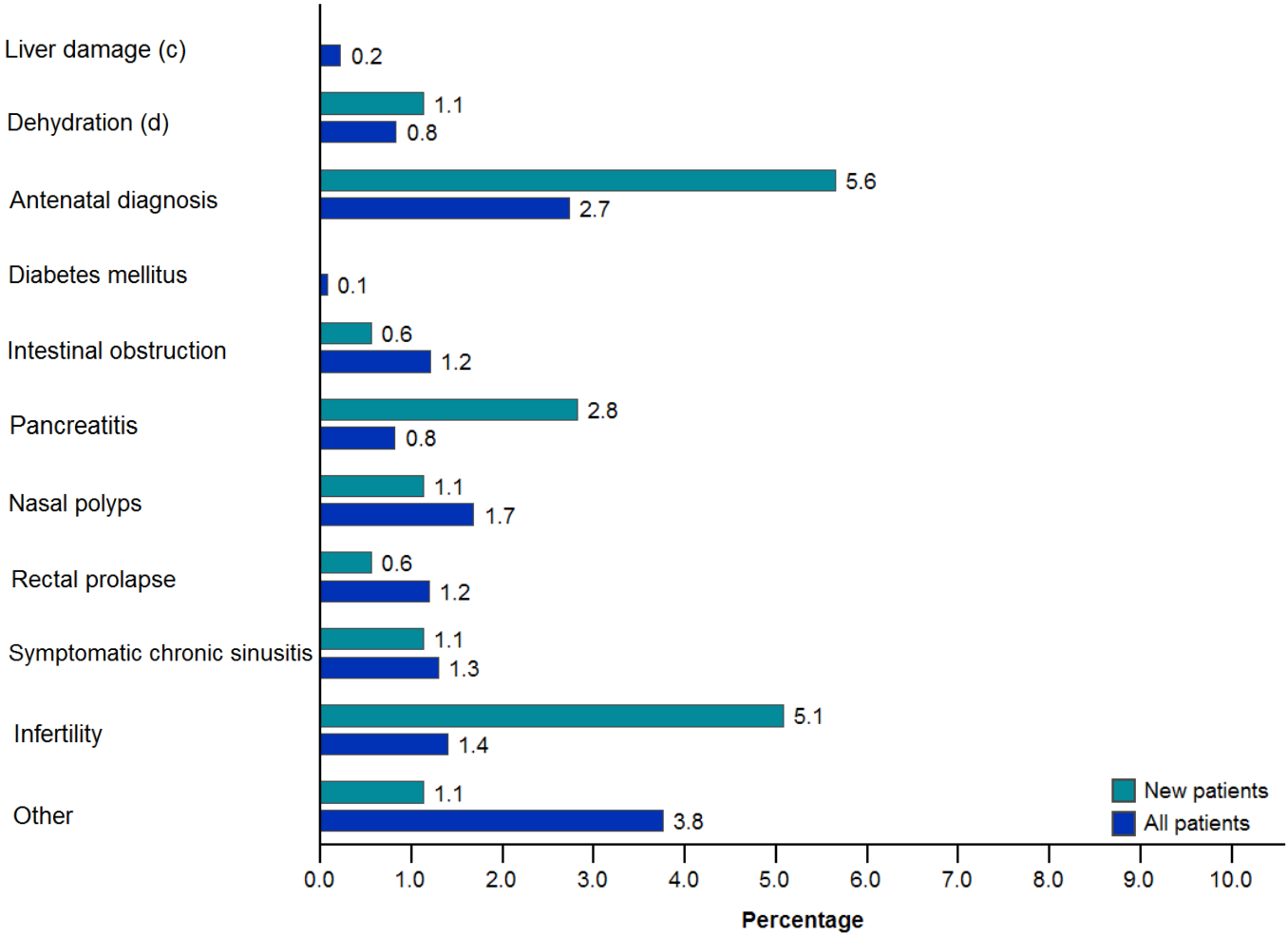
(a) Chronic diarrhoea / Steatorrhoea / Malabsorption
(b) Growth retardation / Malnutrition

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	5602	83.5
G542X	367	5.5
N1303K	285	4.2
2789+5G->A	171	2.5
1717-1G->A	140	2.1
R117H	131	2.0
R553X	120	1.8
G551D	112	1.7
W1282X	93	1.4
3849+10kbC->T	91	1.4
I507del	80	1.2
3272-26A->G	77	1.1
L206W	77	1.1
Y122X	76	1.1
711+1G->T	68	1.0
2183AA->G	67	1.0
D1152H	64	1.0
R347P	63	0.9
R1162X	58	0.9
3120+1G->A	52	0.8
R334W	46	0.7
G85E	45	0.7
3659delC	43	0.6
A455E	43	0.6
Y1092X	41	0.6
S945L	39	0.6
1078delT	38	0.6
R347H	37	0.6
1811+1.6kbA->G	35	0.5
394delTT	33	0.5
W846X	28	0.4
R1066C	27	0.4
621+1G->T	26	0.4
E60X	26	0.4
S1251N	26	0.4
E585X	19	0.3
1677delTA	18	0.3
Q220X	18	0.3
2711delT	17	0.3
G1244E	17	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	2817	42.0	20.7	19.8	62.1
F508del / Other	2713	40.5	22.1	19.7	79.7
Other/ Other	969	14.4	22.1	19	84.1
Subtotal (known genotypes)	6499	96.9	21.5	19.7	84.1
F508del / Missing	72	1.1	31	29.5	81.6
Other/ Missing	64	1.0	30.4	29.35	73
Missing/ Missing	72	1.1	38.4	35.25	81.2
Subtotal (partial genotypes / missing)	208	3.1	33.4	30.55	81.6
Total	6707	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	186	2.8	23.0	19.8	66.0
At least one nonsense mutation	1027	15.3	20.3	18.1	72.7
At least one R117H mutation	131	2.0	17.0	11.9	81.0

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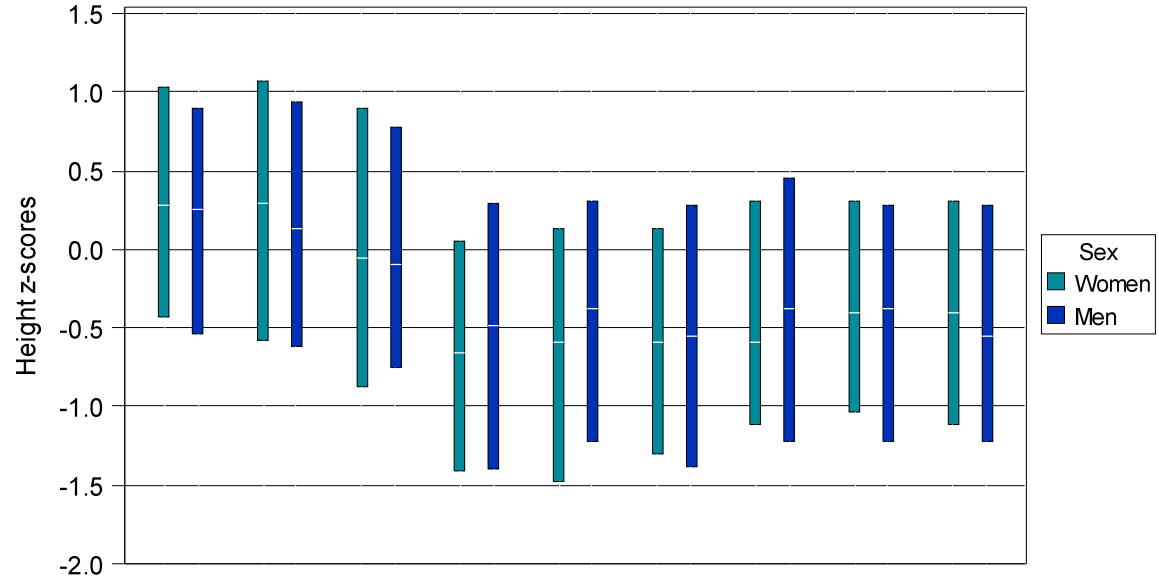
Gating mutations doesn't prevent the CFTR protein from reaching the cell membrane but alter choride transport.

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	0.27	0.24	0.01	-0.65	-0.64	-0.58	-0.48	-0.37	-0.37	-0.28
	Men	0.21	0.16	-0.00	-0.48	-0.49	-0.56	-0.47	-0.43	-0.43	-0.27
Median height z-score	Women	0.28	0.29	-0.06	-0.66	-0.59	-0.59	-0.59	-0.41	-0.41	-0.32
	Men	0.25	0.14	-0.09	-0.49	-0.38	-0.55	-0.38	-0.38	-0.55	-0.27

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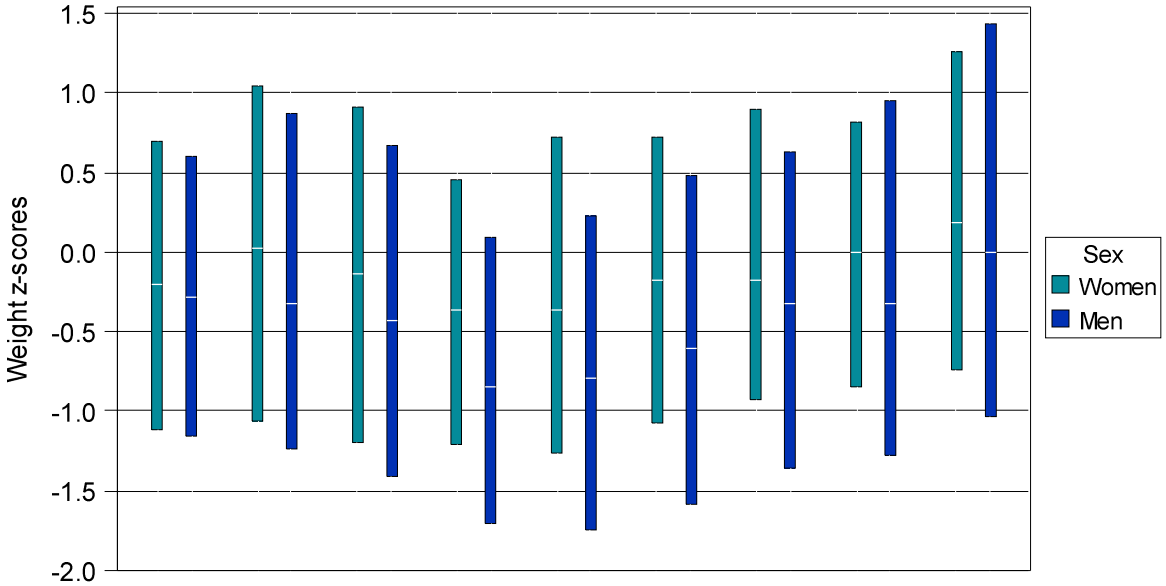
Figure 5.2. Weight z-scores*, by age group and sex



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	-0.14	0.10	-0.04	-0.30	-0.20	-0.11	-0.00	0.08	0.31	-0.05
	Men	-0.21	-0.15	-0.30	-0.69	-0.66	-0.46	-0.26	-0.17	0.18	-0.32
Median weight z-score	Women	-0.21	0.02	-0.13	-0.36	-0.36	-0.18	-0.18	0.00	0.18	-0.18
	Men	-0.28	-0.33	-0.43	-0.84	-0.79	-0.60	-0.32	-0.32	0.00	-0.48

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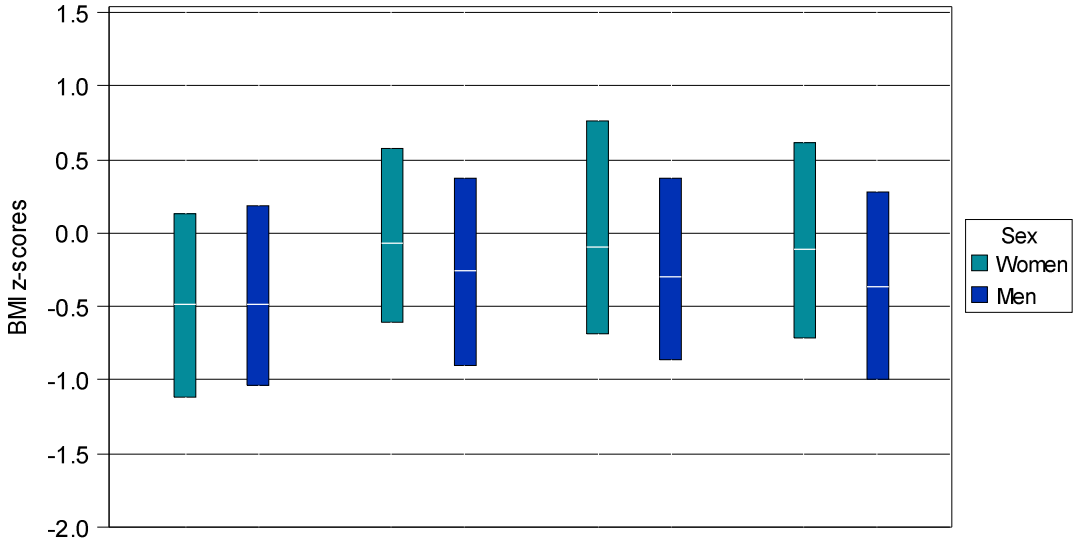
*See explicative note p 22.

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	-0.41	0.06	0.10	0.01	-0.03
	Men	-0.39	-0.16	-0.14	-0.30	-0.24
Median BMI z-score	Women	-0.48	-0.08	-0.10	-0.11	-0.16
	Men	-0.49	-0.26	-0.30	-0.36	-0.33
BMI z-score >=0 (% of patients)	Women	29.3%	47.9%	47.6%	46.5%	43.8%
	Men	31.4%	39.6%	38.2%	35.8%	36.5%

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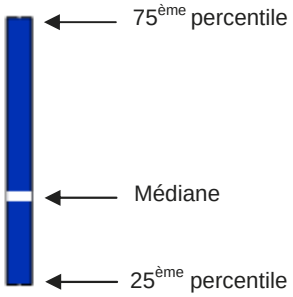
The z-score is a anthropometric reduced centered variable (Z = [measure-mean]/standard deviation), ajusted for gender and age; the mean and standard deviation are taken from the French reference population with the same gender and age as the patient. This index measures the difference with population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

- 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

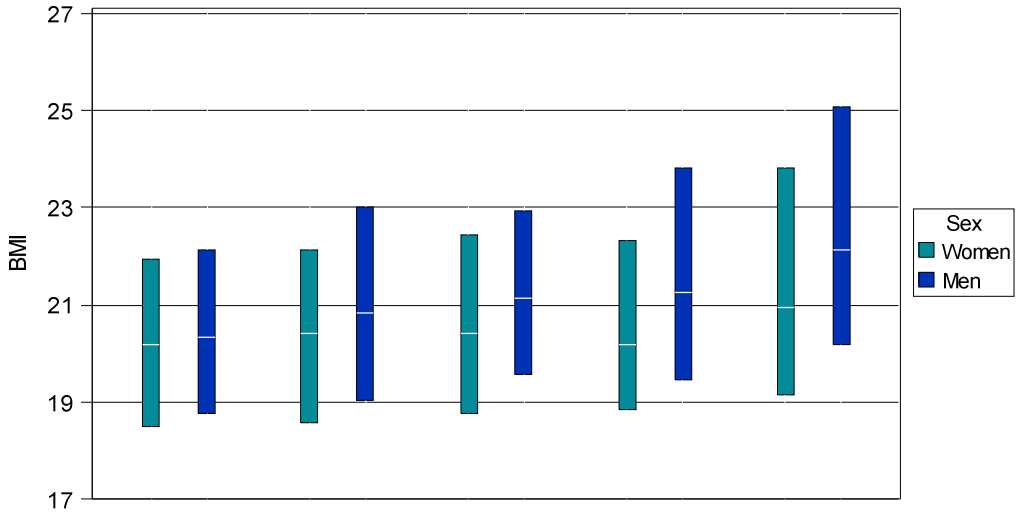
Those figures represent z-scores of anthropométrie and spirometry values.
For each age and sex group, median values are the white lines, extremes are the 25th and 75th percentiles.



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	20.7	21.1	20.9	22.2	21.1
	Men	20.6	21.2	21.4	21.7	22.8	21.5
Median BMI	Women	20.2	20.4	20.4	20.2	21.0	20.4
	Men	20.3	20.8	21.1	21.3	22.1	21.1
BMI ≥ 22 (% of patients)	Women	24.0%	26.4%	28.7%	27.5%	38.0%	28.9%
BMI ≥ 23 (% of patients)	Men	17.2%	25.4%	24.1%	32.0%	40.9%	27.7%
BMI < 18.5 (% of patients)	Women	25.1%	22.4%	19.5%	20.1%	17.8%	21.2%
	Men	22.3%	17.7%	15.9%	13.8%	11.1%	16.4%

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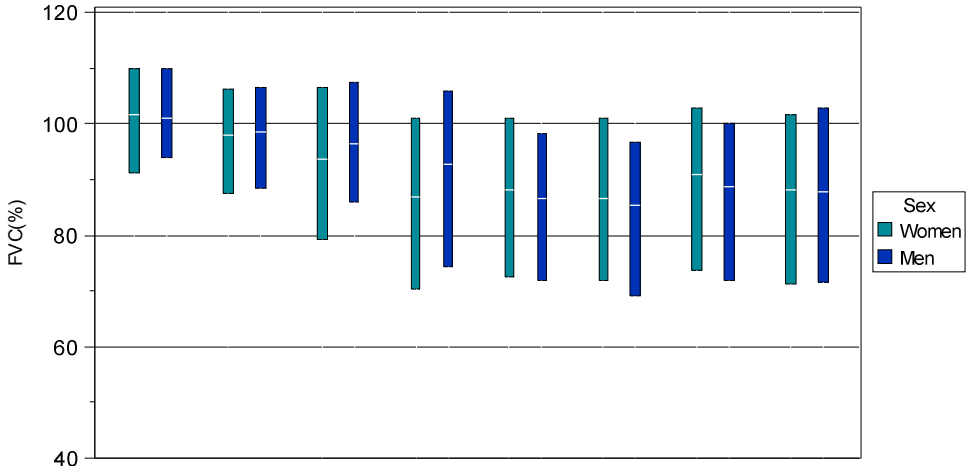
6. Spirometry

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	99.8	96.1	92.0	85.5	86.5	85.1	87.9	85.6	90.0
	Men	100.9	97.0	95.7	89.5	84.4	84.0	85.5	86.0	90.6
	All patients	100.3	96.5	93.9	87.6	85.4	84.5	86.6	85.8	**90.3**
Median FVC	Women	101.6	97.9	93.6	86.9	88.0	86.6	90.8	88.1	92.4
	Men	101.1	98.6	96.3	92.8	86.5	85.3	88.6	87.9	93.5
	All patients	101.4	98.3	95.4	89.9	87.3	85.8	89.4	87.9	**92.9**

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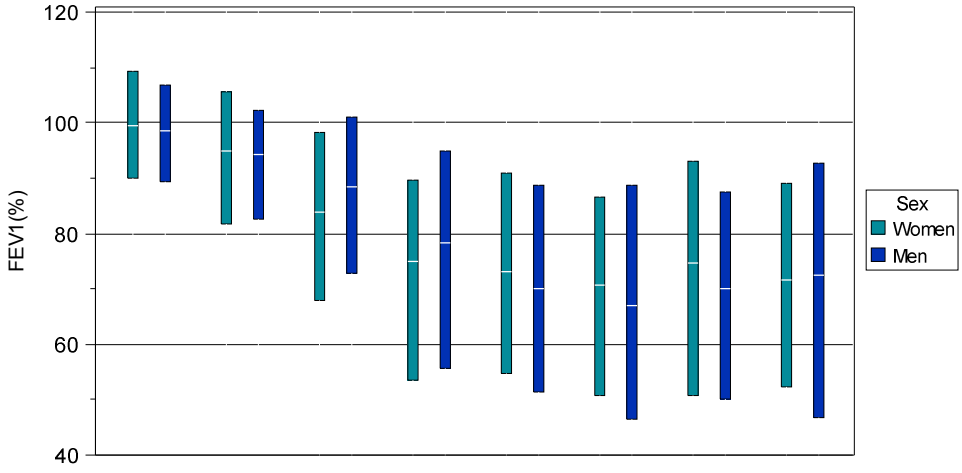
Figure 6.2. FEV_1 (% predicted)*, by age group and sex



	Age groups (years)	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +	Total
Mean FEV_1	Women	97.7	91.9	82.0	72.5	72.1	69.0	72.5	71.1	79.2
	Men	97.3	92.0	86.3	75.3	69.1	67.4	67.5	70.9	78.8
	All patients	97.5	92.0	84.2	74.0	70.6	68.1	69.9	71.0	**78.9**
Median FEV_1	Women	99.4	94.8	83.7	74.9	73.2	70.5	74.5	71.4	82.1
	Men	98.6	94.1	88.4	78.3	70.1	66.9	69.9	72.6	83.4
	All patients	99.0	94.3	86.8	76.7	72.0	69.2	71.8	72.3	**82.7**

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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.

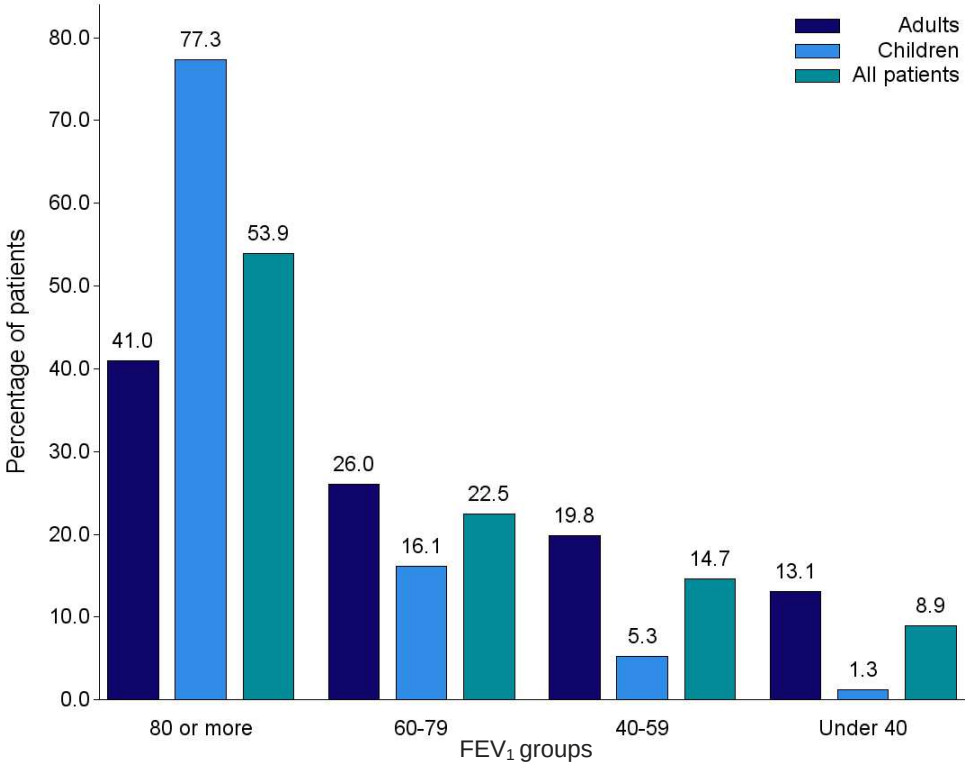
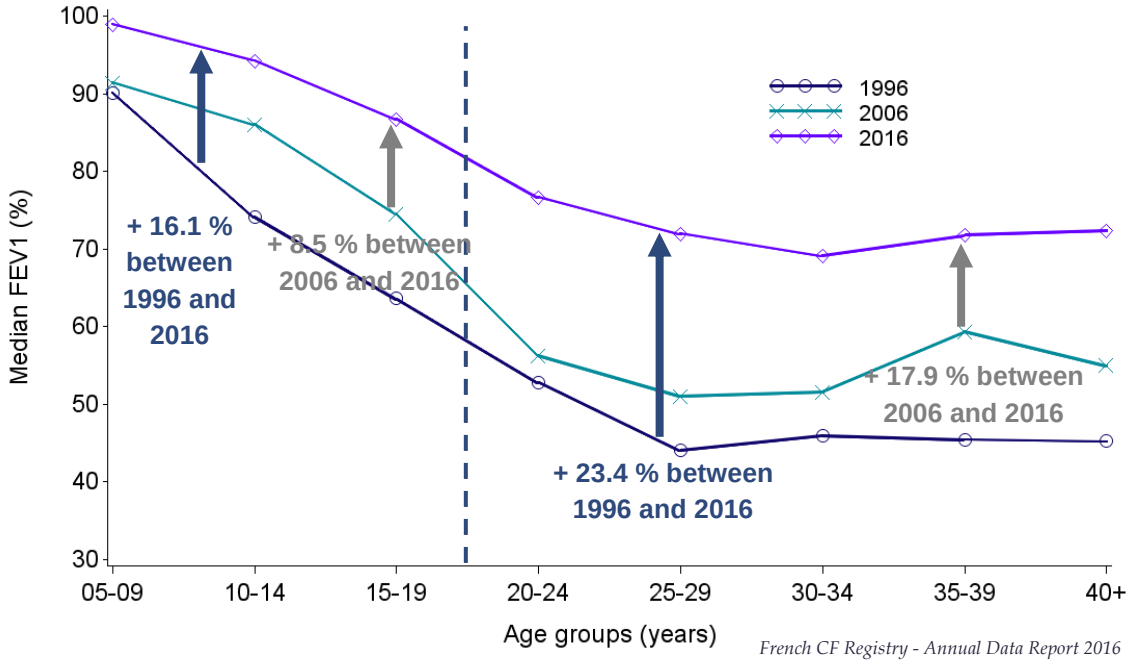


Figure 6.4. Median FEV_1 (% predicted) in 2016 compared with 1996 and 2006



The last FEV1 (%) value of the year was collected from 1992 to 2010, and the best value of the year since 2011. The median FEV1 was 77.1 % for patients aged 6 to 19 years in 1996, and 93.3 % in 2016. It was 48.9 % in 1996 and 72.4 % in 2016 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	5844	*87.1 %*
Children	2952	*97.7 %*
Adults	2892	*78.4 %*

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In 2016, 87.1 % of the patients had at least one sputum culture; this proportion slightly decreases as it was 88.1% in 2015 and 88.8 % in 2014. Among the patients without sputum culture (N=863), 61.0 % of them were transplanted.

Table 7.2. Distribution of the respiratory germs, by age group

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%*
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	.
Patients with at least one sputum	**671**	**838**	**886**	**862**	**665**	**636**	**443**	**304**	**539**	**5844**	**87.1 %**
Normal culture	425	471	415	289	90	59	59	39	97	1944	29.0 %
Achromobacter xylosoxidans	19	29	57	80	61	71	38	23	42	420	6.3 %
Aspergillus	38	115	243	329	255	219	151	103	175	1628	24.3 %
Burkholderia cepacia, including:	2	3	12	21	30	14	14	11	9	116	1.7 %
- chronic B. cepacia	*.*	*2*	*5*	*11*	*17*	*12*	*9*	*6*	*4*	*66*	*1.0 %*
Haemophilus influenzae	198	282	171	163	107	69	55	41	53	1139	17.0 %
Atypical mycobacteria	.	8	12	31	23	23	12	5	15	129	1.9 %
Pneumococcus	64	43	29	7	5	6	4	3	8	169	2.5 %
Pseudomonas aeruginosa, including:	107	163	273	367	379	449	288	208	318	2552	38.0 %
- Chronic P. aeruginosa	*3*	*18*	*75*	*179*	*248*	*307*	*215*	*154*	*228*	*1427*	*21.3 %*
- Multidrug resistant P. aeruginosa	*2*	*6*	*21*	*54*	*61*	*97*	*72*	*55*	*67*	*435*	*6.5 %*
Staphylococcus, including:	432	587	712	699	514	450	273	169	248	4084	60.9 %
- MSSA	*415*	*550*	*676*	*655*	*472*	*401*	*237*	*144*	*214*	*3764*	*56.1 %*
- MRSA	*17*	*33*	*60*	*88*	*66*	*78*	*49*	*32*	*43*	*466*	*6.9 %*
Stenotrophomonas maltophilia	65	73	110	148	101	86	46	32	45	706	10.5 %
Streptococcus (non *pneumoniae*)	26	39	17	14	12	4	4	7	11	134	2.0 %

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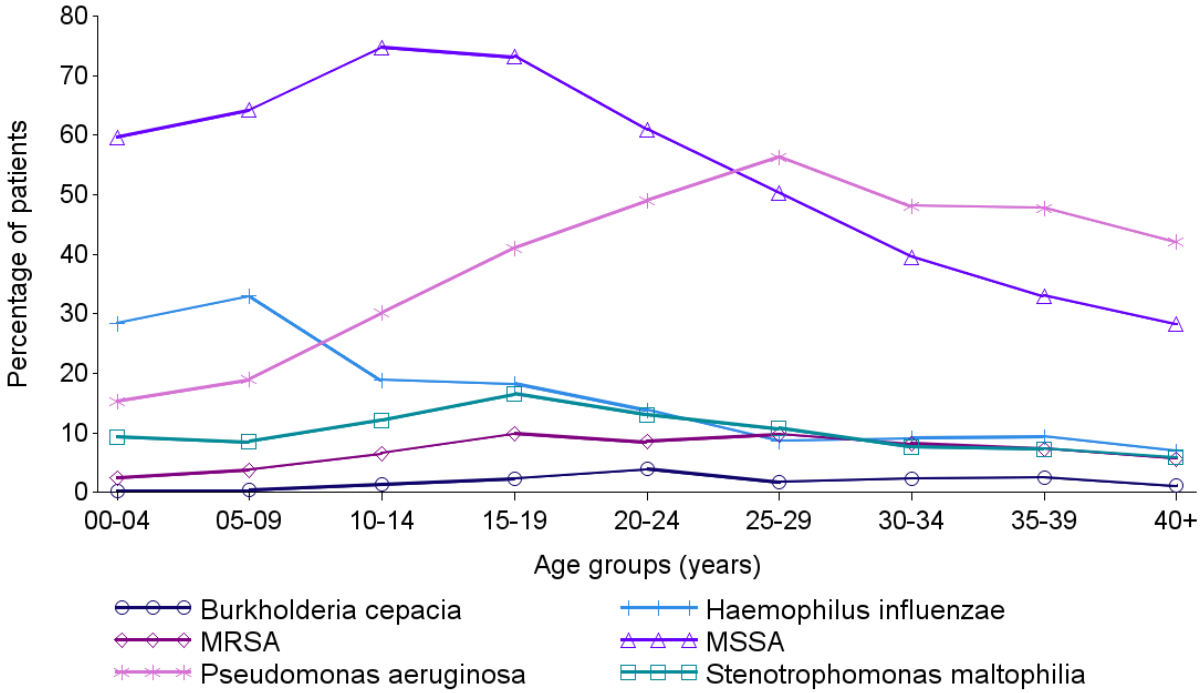
* Percentage with respect to the entire population.

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).
Multi-resistant colonization: resistant to all the antibiotics in at least two antibiotic classes.

7. Microbiology

Figure 7.1. Clinically important bacteria, by age group



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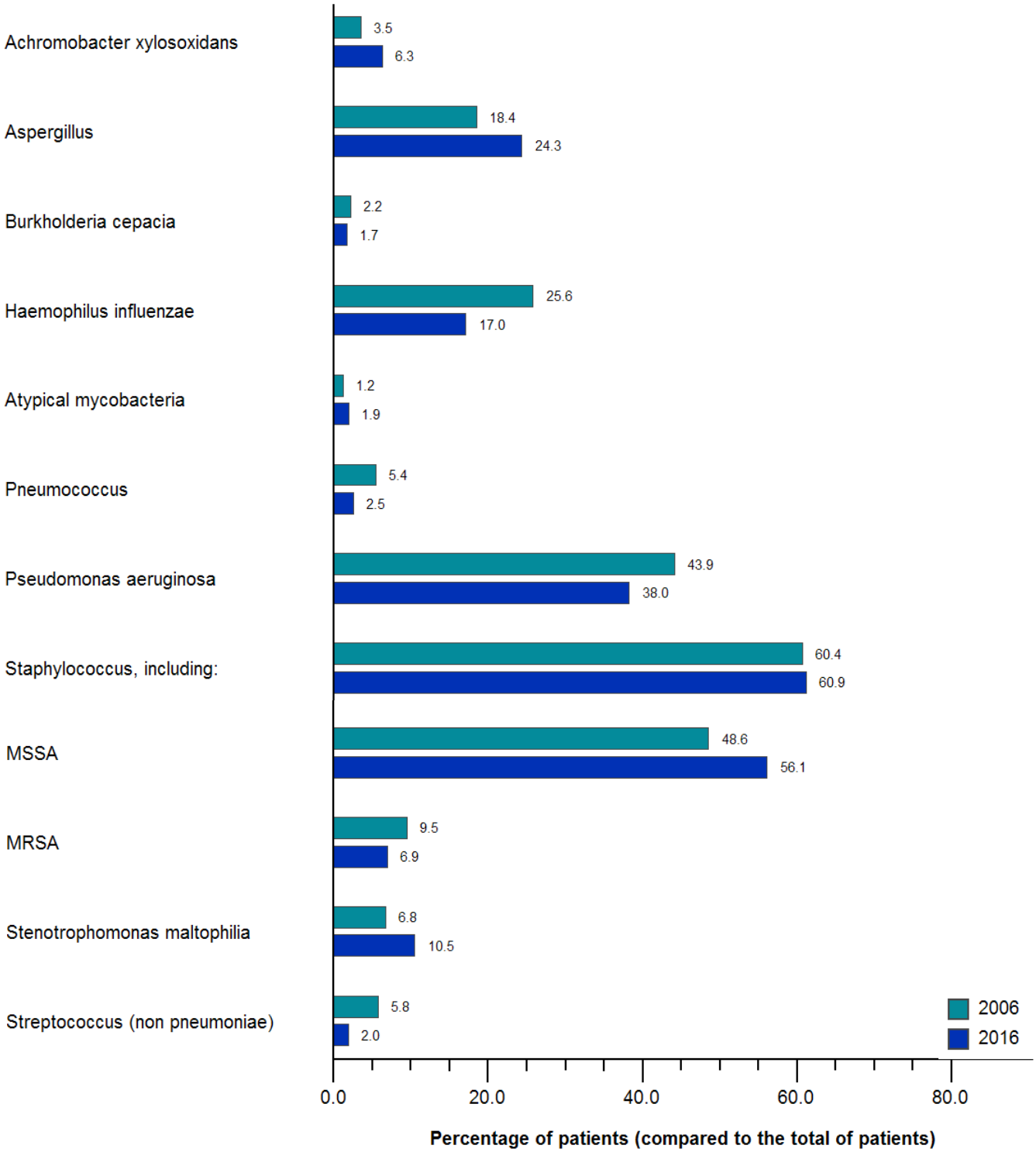
7. Microbiology

Figure 7.2. Comparison of germs in 2015 and in 2006



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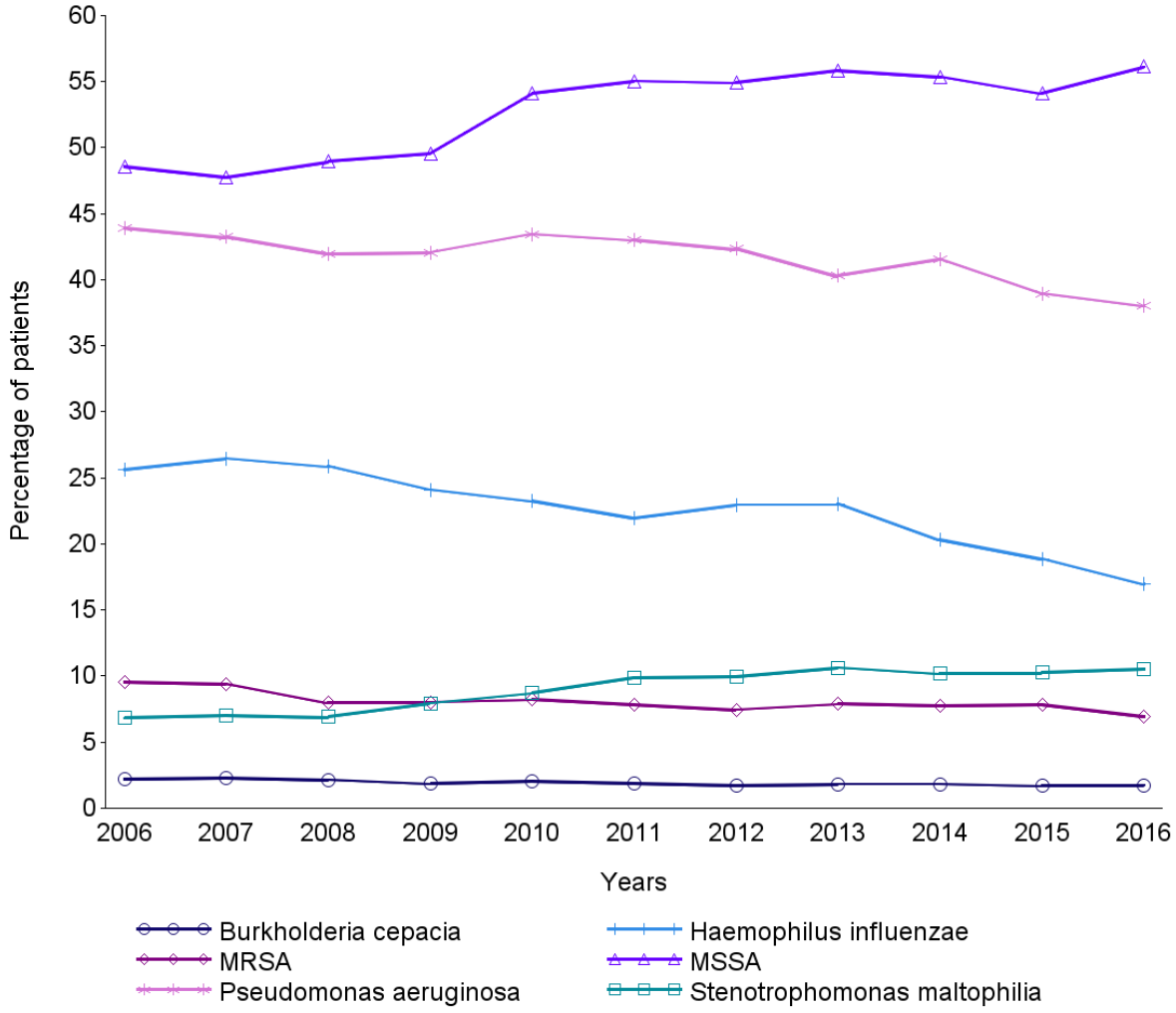
7. Microbiology

Figure 7.3. Evolution of respiratory germs since 2006



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8. Complications

Respiratory

Table 8.1. Respiratory complications, by age group

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Treated aspergillosis	2	48	84	117	132	93	68	35	61	640	9.5 %
Asthma	95	175	227	176	121	130	88	58	114	1184	17.7 %
Haemoptysis	.	2	15	55	81	86	55	24	36	354	5.3 %
Pneumothorax	.	.	1	6	8	14	4	8	6	47	0.7 %
Nasal polyps	7	90	139	183	131	134	106	72	123	985	14.7 %

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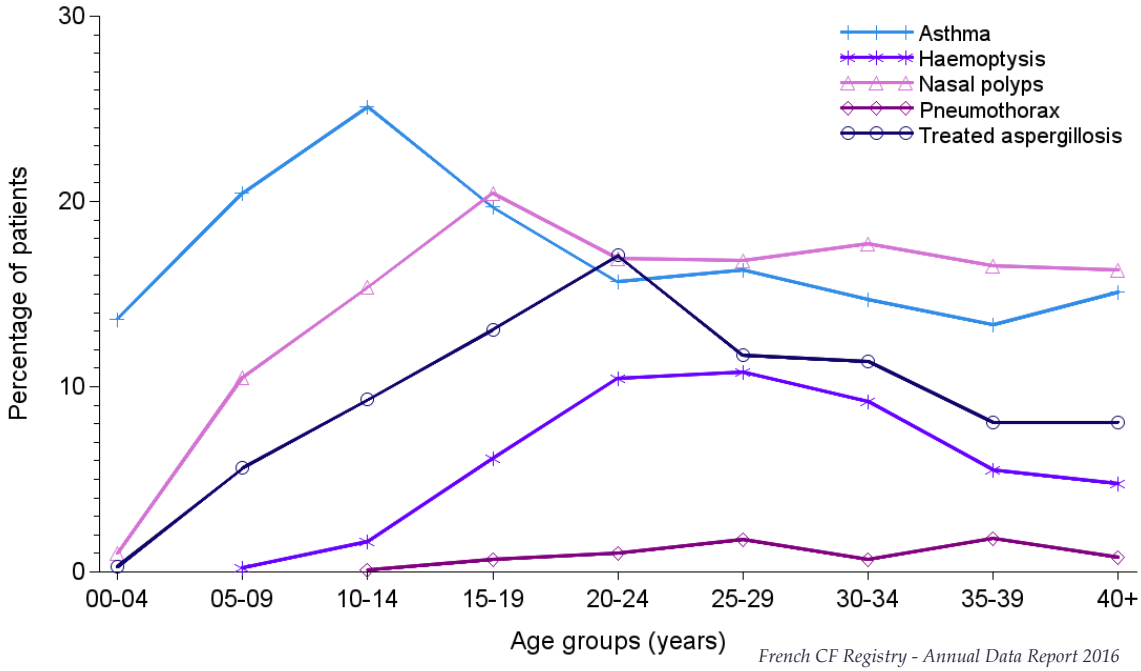
Figure 8.1. Respiratory complications, by age group

Percentage of age groups reporting complications.



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8. Complications

Gastro-intestinal

Table 8.2. Gastro-intestinal complications, by age group

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Gallstones	4	10	15	14	18	34	29	18	26	168	2.5 %
Cirrhosis/Portal hypertension	1	11	37	67	43	38	30	16	19	262	3.9 %
Elevated liver enzymes	45	49	76	85	60	72	47	27	35	496	7.4 %
Abnormal exocrine pancrea-tic function	554	690	730	769	654	687	513	355	488	5440	81.1 %
Intestinal obstruction	14	18	23	31	33	39	31	25	17	231	3.4 %
Acute pancreatitis	1	6	3	10	17	13	13	7	12	82	1.2 %
Treated gastro-oesophageal reflux disease	92	77	95	124	169	214	150	101	235	1257	18.7 %

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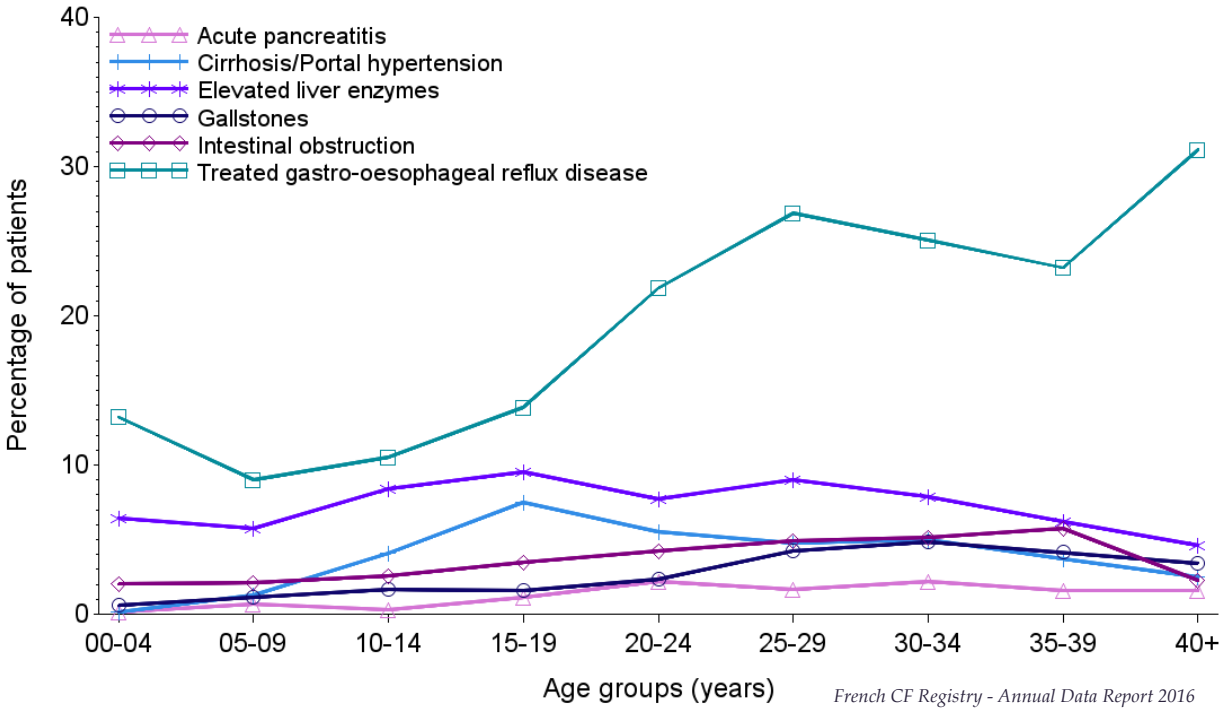
Figure 8.2. Gastro-intestinal complications, by age group

Percentage of age groups reporting complications.



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8. Complications

Diabetes mellitus

31% of adult patients are with diabetes mellitus

Table 8.3. Diabetes mellitus and degenerative

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Total diabetes (ID and non ID diabetes)	2	19	51	136	194	238	214	172	255	1281	19.1 %
Non insulin-dependent diabetes	2	2	6	17	29	44	27	32	44	203	3.0 %
Insulin-dependent diabetes	.	17	46	119	167	202	188	141	213	1093	16.3 %
Degenerative complications of diabetes	.	.	.	.	2	9	16	12	14	53	0.8 %

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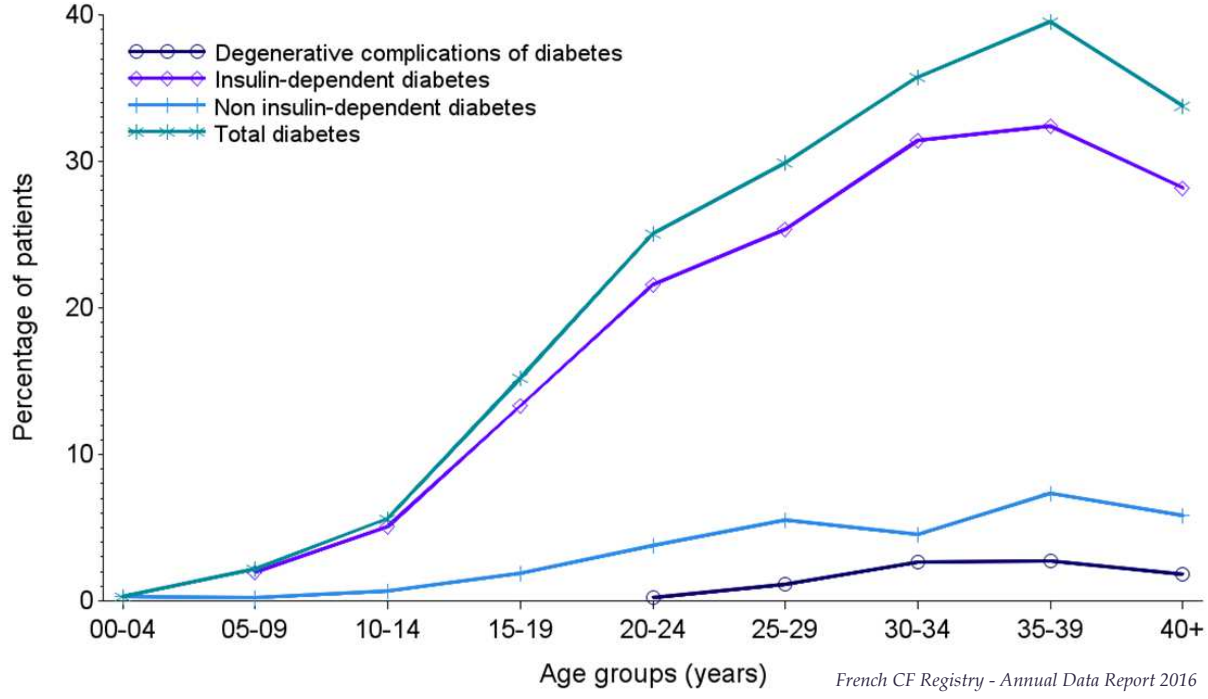
The line « Total diabetes » sums the number of patients having at least one type of diabetes. Among the 1281 patients, 15 patients presented with both types of diabetes during the year.

Figure 8.3. Diabetes mellitus and degenerative complications of diabetes, by age group

Percentage of age groups reporting complications.



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8. Complications

Other complications

Table 8.4. Other complications, by age group

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Arthropathy	.	3	8	10	14	18	25	11	26	115	1.7 %
Cancer	.	.	.	2	3	5	7	5	27	49	0.7 %
Depression (evaluated and followed)	.	.	7	10	20	34	36	26	62	195	2.9 %
Urinary incontinence	.	3	4	6	8	9	6	11	12	59	0.9 %
Terminal renal failure	1	.	.	3	2	8	10	15	21	60	0.9 %
Bone disease	.	2	16	33	61	87	64	46	121	430	6.4 %
Deafness/Hypoacusia	2	9	11	19	33	57	51	47	76	305	4.5 %

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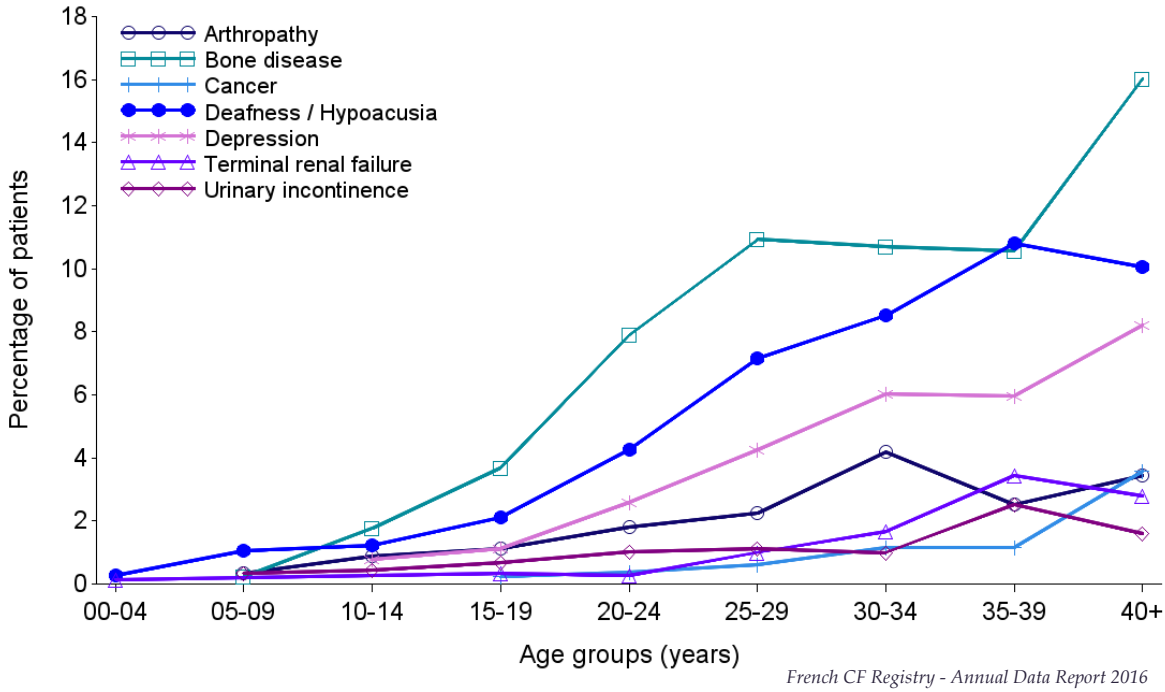
Figure 8.4. Other complications, by age group

Percentage of age groups reporting complications.



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9. Transplantation

Were included in this table all the patients seen and/or dead in 2016.

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

	All years	2016
WAITING LIST	All waiting patients	Listed in 2016
Nb of patients	**148**	**96**
Mean age (years) and standard deviation (SD)	29.9 ± 10.7	30.8 ± 10.3
Extremes of age (years)	8.2-61.7	9.4-61.7
Deaths on waiting list	3	1
TRANSPLANTATION	All transplanted*	Transplanted in 2016
Nb of patients	**807**	**101**
Transplant type:		
- bilateral lung - N (%)	748 (92.7 %)	89 (88.1 %)
- liver - N (%)	24 (3.0 %)	
- kidney - N (%)	44 (5.5 %)	3 (3.0 %)
- monopulmonary - N (%)	6 (0.7 %)	1 (1.0 %)
- other organ - N (%)**	1 (0.1 %)	
Combined transplantations:		
- heart / lung - N (%)	30 (3.7 %)	2 (2.0 %)
- heart / lung / liver - N (%)	2 (0.2 %)	
- bilateral lung / liver - N (%)	23 (2.9 %)	5 (5.0 %)
- bilateral lung / kidney - N (%)	4 (0.5 %)	
- liver / kidney - N (%)	1 (0.1 %)	
- bilateral lung / Islets of Langerhans - N (%)	7 (0.9 %)	1 (1.0 %)
- other combined transplant - N (%)***	5 (0.6 %)	
Mean age (years)	34.7	31.5
SD	9.68	9.38
Extremes of age (years)	11-64.8	12.8-61.7
Post-transplantation deaths	37	11

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

** 1 bone marrow transplantation.

*** 3 kidney / pancreas, 1 liver / pancreas and 1 liver / monopulmonary transplantations.

9. Transplantation

Figure 9.1. Annual number of transplanted patients, since 1992

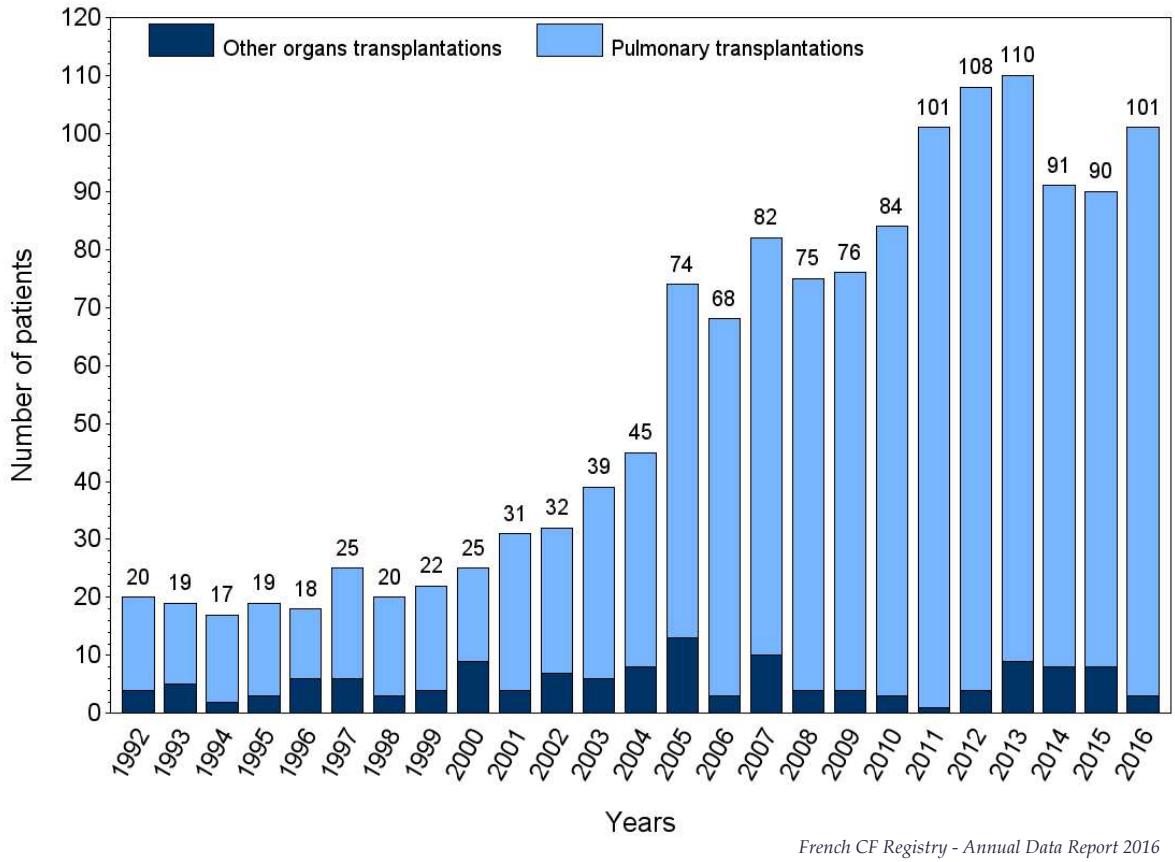

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Table 9.2. Annual number of transplanted patients, since 1992

	Years												
Transplant type	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Pulmonary*	16	14	15	16	12	19	17	18	16	27	25	33	37
Other organs	4	5	2	3	6	6	3	4	9	4	7	6	8

	Years											
Transplant type	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Pulmonary*	61	65	72	71	72	81	100	104	101	83	82	98
Other organs	13	3	10	4	4	3	1	4	9	8	8	3

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* monopulmonary, bilateral lung or heart -lung (alone or combined with another organ).

10. Outpatient and inpatient visits

Table 10.1. Characteristics of the visits, by age group

	Age groups (years)									
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*
< 4 visits per year	110	187	198	159	216	192	184	139	304	1689
≥ 4 visits per years	586	669	706	735	557	604	414	296	451	5018
Outpatient visits										
Number of patients with at least one outpatient visit	*484*	*551*	*595*	*589*	*585*	*590*	*436*	*311*	*538*	*4679*
Median number of visits	3	3	3	3	3	3	3	3	3	3
Mean number of visits	3.8	3.4	3.5	3.6	4.0	3.8	3.4	3.4	3.1	3.6
One-day hospitalizations										
Number of patients with at least one one-day visit	*628*	*794*	*844*	*806*	*643*	*673*	*499*	*359*	*593*	*5839*
Median number of visits	3	2	3	3	2	2	2	2	2	2
Mean number of visits	3.5	2.8	3.4	3.5	2.8	2.8	2.9	2.9	2.6	3.1
Inpatient visits										
Number of patients with at least one inpatient visit	*152*	*138*	*205*	*279*	*242*	*309*	*223*	*139*	*241*	*1928*
Median number of visits	1	1	1	1	2	1	2	1	1	1
Mean number of visits	1.7	1.8	1.9	2.3	2.6	2.3	2.2	2.3	2.2	2.2
Median duration (days)	9	6.5	9	10	12.5	8	9	8	8	9
Mean duration (days)	17.2	12.2	16.3	19.8	23.3	17.6	19.2	20.0	22.4	19.0

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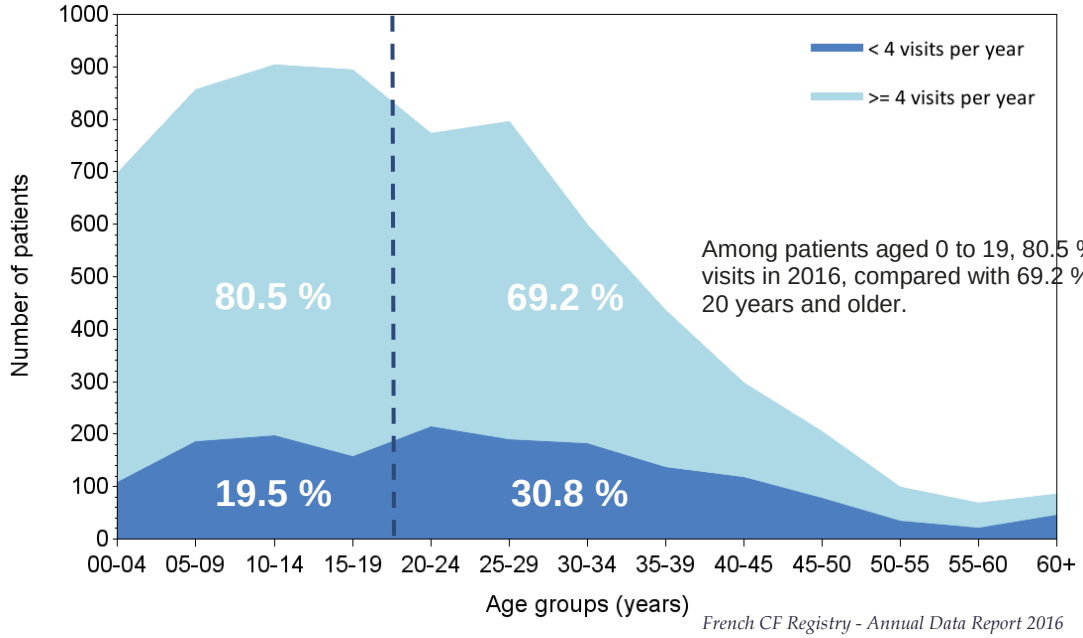
Figure 10.1. Number of visits, by age group



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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, by age group

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*
Nb of patients with at least one course	55	107	197	301	348	376	260	168	264	2076 (31.0 %)
- and with TIVAD*	6	28	67	127	171	198	134	83	120	934 (13.9 %)
Nb of courses	65	194	401	625	884	943	625	408	541	4686
Nb of days of courses including:	820	2675	6574	10220	13730	14384	10750	6572	8930	74655
- at hospital	547	1198	1743	3520	3188	3310	2285	1504	2724	20019
- at home	258	1487	4452	6040	10379	10647	7652	4958	5953	51826
TIVAD* (with and without course)	9	33	80	154	207	253	177	121	177	1211 (18.1 %)

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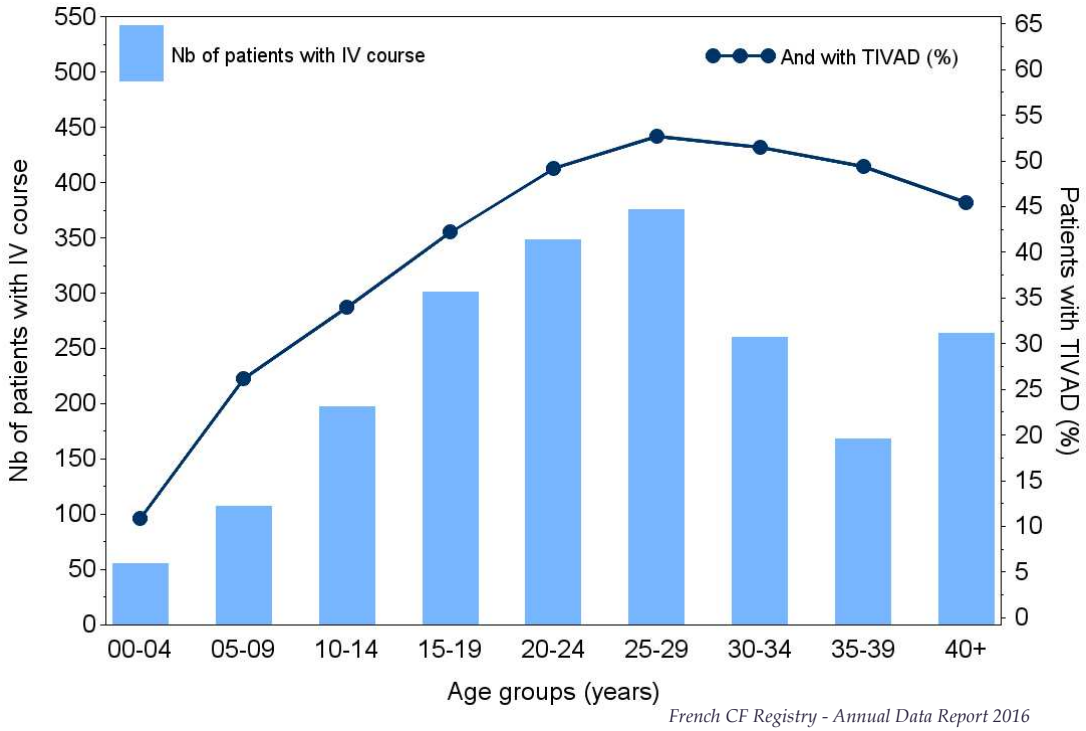
Figure 11.1. Patients with at least one IV antibiotic course and a TIVAD*, by age group



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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	1.2	1.8	2.1	2.2	2.6	2.6	2.5	2.5	2.2	2.3
SD	0.6	1.1	1.3	1.6	2.3	2.0	2.5	2.2	1.7	2.0
Median number of courses	1	1	2	2	2	2	2	2	2	2
1st quartile (Q1)	1	1	1	1	1	1	1	1	1	1
3rd quartile (Q3)	1	2	3	3	3	3	3	3	3	3
Day of courses										
Mean duration of courses (days)	15.5	25.2	34.2	36.1	41.0	39.4	43.5	40.3	36.0	37.5
SD	10.2	16.7	34.7	38.7	39.4	36.1	50.3	41.3	38.0	38.8
Median duration of courses (days)	14	15	28	28	30	28	28	28	27.5	28.0
1st quartile (Q1)	14	14	15	14	15	14	15	15	14	14.0
3rd quartile (Q3)	15	30	44.5	43	47	48	53	52	45	45.0

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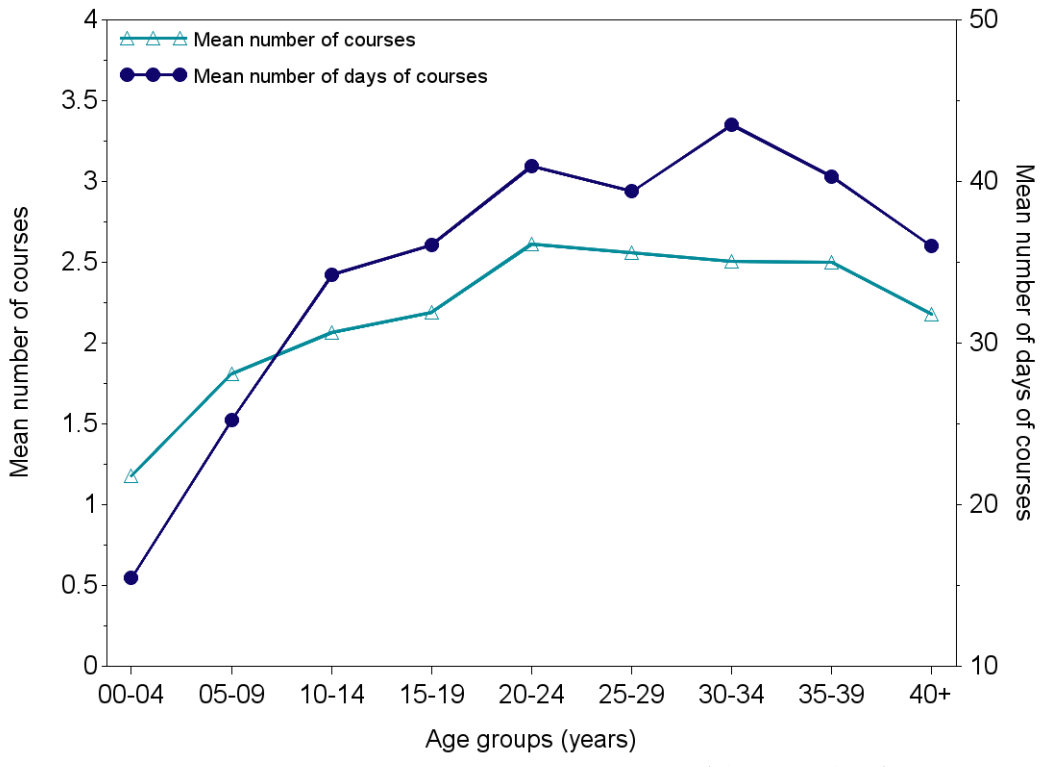
Figure 11.2. Mean number of courses and of days of courses, by age group



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11. Therapeutic management

Respiratory /CFTR gene modulators

Table 11.3. Respiratory therapeutics, by age group

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Aerosol therapy*	314	668	778	789	649	621	450	312	518	5099	76.0 %
NSAID	8	29	42	48	50	49	33	29	41	329	4.9 %
Azithromycin	67	217	343	418	392	443	349	243	393	2865	42.7 %
Oxygen therapy	.	4	17	33	46	53	55	29	74	311	4.6 %
Oral corticosteroids	11	36	55	85	116	152	169	133	200	957	14.3 %
Nasal ventilation	1	9	22	39	29	40	44	21	66	271	4.0 %

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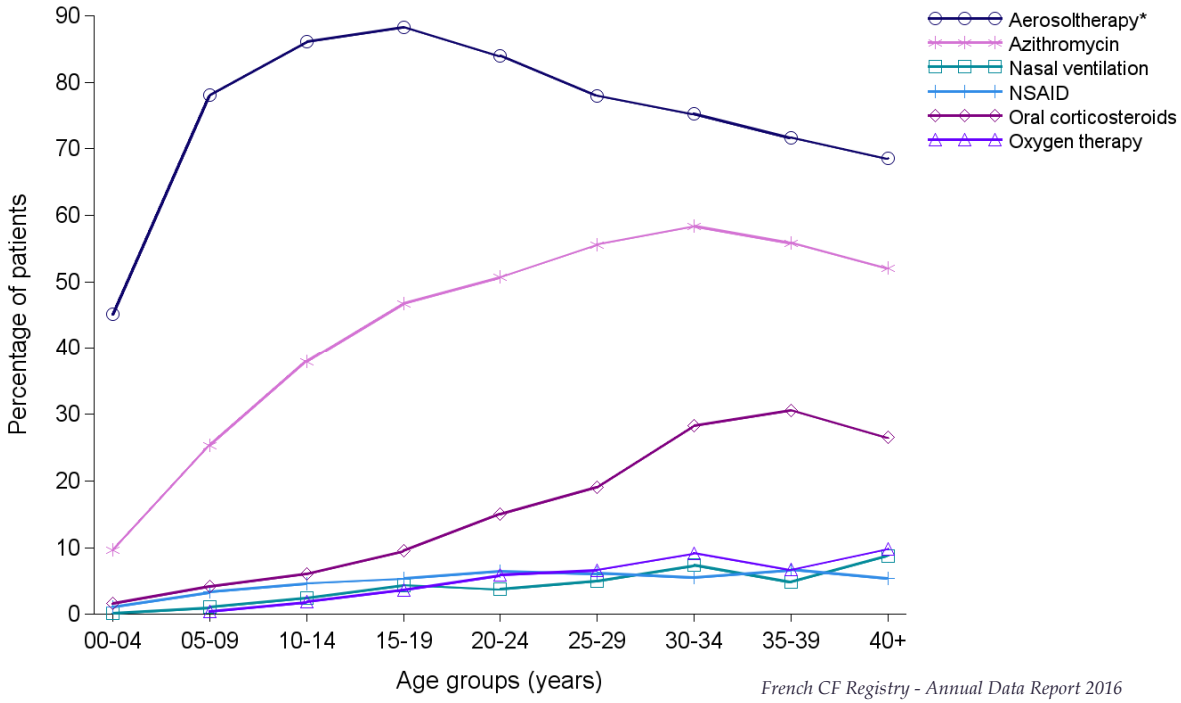
Figure 11.3. Respiratory therapeutics, by age group



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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	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Ivacaftor	.	20	23	24	11	14	10	6	24	132	2.0 %
Lumacaftor + Ivacaftor	.	2	128	233	144	138	102	50	48	845	12.6 %

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11. Therapeutic management

Aerosoltherapy

Table 11.5. Aerosoltherapy treatments, by age group

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Patients under aerosol therapy*	**314**	**668**	**778**	**789**	**649**	**621**	**450**	**312**	**518**	**5099**	**76.0 %**
Inhaled antibiotics, including:	103	188	335	415	398	394	289	192	268	2582	38.5 %
- Tobramycin	*61*	*112*	*189*	*247*	*207*	*204*	*131*	*74*	*88*	*1313*	*19.6 %*
- Colistin	*54*	*100*	*194*	*249*	*241*	*249*	*179*	*110*	*187*	*1563*	*23.3 %*
- Aztreonam	*3*	*8*	*14*	*14*	*29*	*36*	*39*	*26*	*30*	*199*	*3.0 %*
Inhaled bronchodilators	205	403	522	548	431	451	328	246	405	3539	52.8 %
Inhaled corticosteroids	177	332	436	425	311	301	226	157	301	2666	39.7 %
Inhaled hypertonic saline	46	90	138	145	49	46	37	16	34	601	9.0 %
RhDNase	82	503	637	596	438	370	226	147	220	3219	48.0 %

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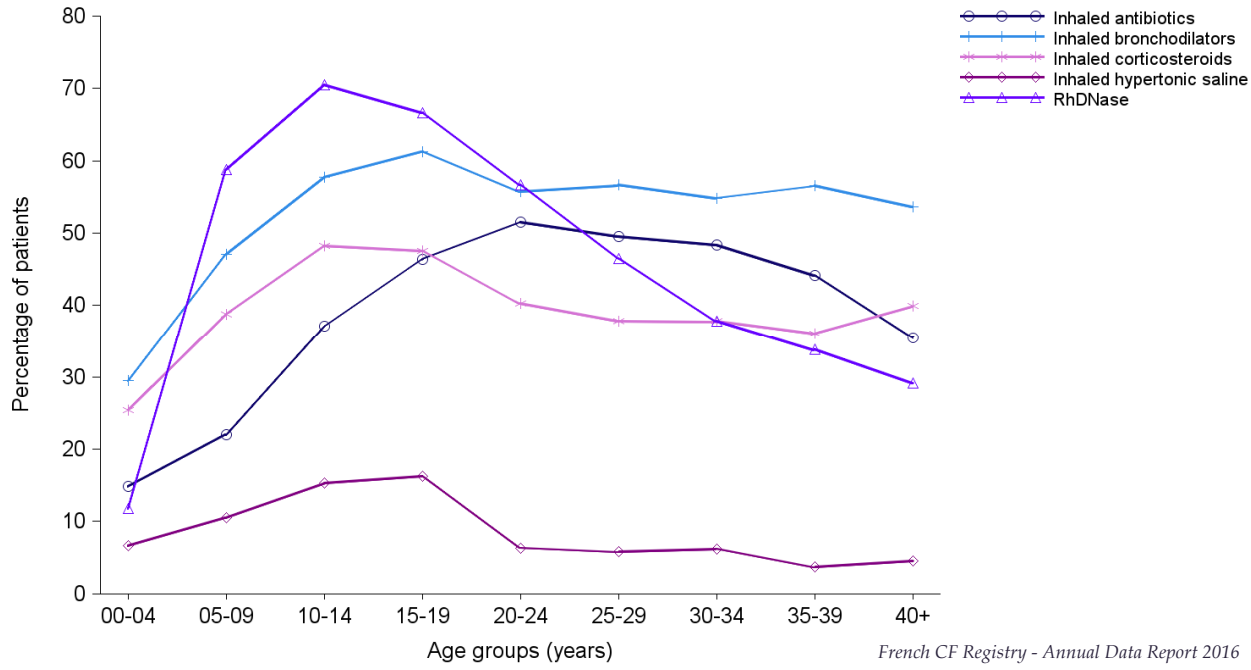
* By nebulization, spray or powder

Figure 11.4. Aerosoltherapy treatments, by age group



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11. Therapeutic management

Digestive and nutritional

Table 11.6. Hepatic, digestive and nutritional treatments, by age group

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*696*	*856*	*904*	*894*	*773*	*796*	*598*	*435*	*755*	*6707*	
Ursodeoxycholic acid	87	193	301	365	296	311	202	123	164	2042	30.4 %
Acid blockers	234	292	371	447	401	432	333	229	415	3154	47.0 %
Pancreatic enzymes	557	695	735	776	666	701	514	359	492	5495	81.9 %
Supplemental tube feeding	33	29	68	80	49	37	13	11	15	335	5.0 %
Oral supplemental feeding	166	280	315	289	287	282	194	144	164	2121	31.6 %
Fat-soluble vitamins	643	808	857	844	708	697	544	386	586	6073	90.5 %

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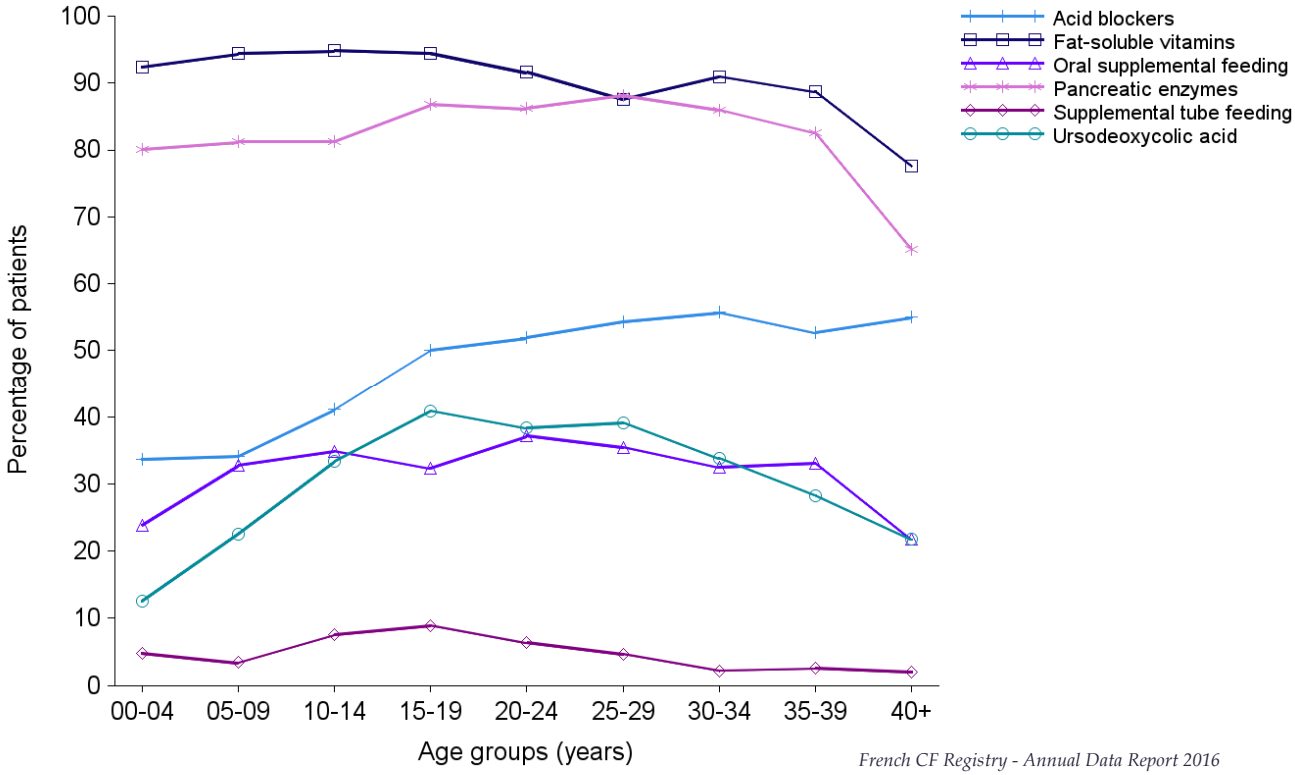
Figure 11.5. Hepatic, digestive and nutritional treatments, by age group



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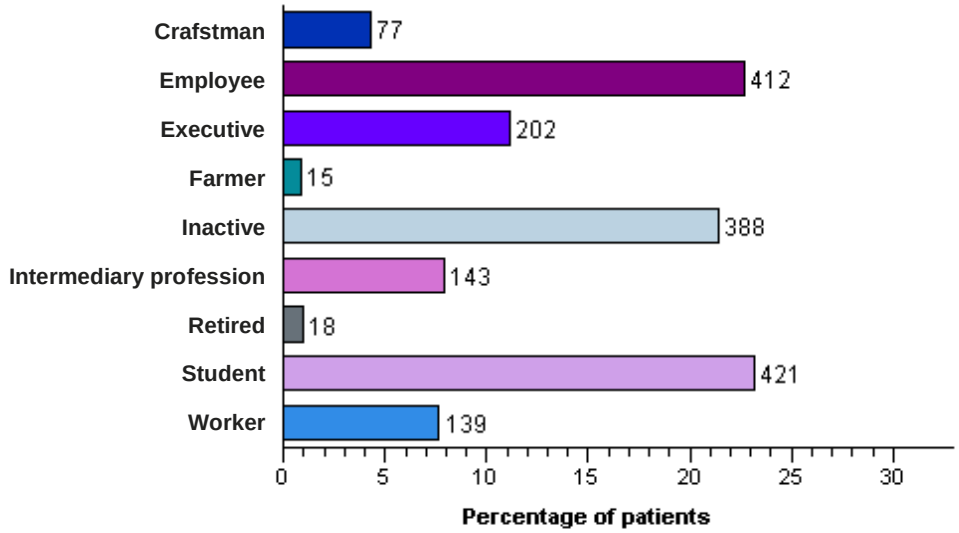
12. Social data

Employment

Figure 12.1. Employment of men ≥ 18 years

N = 1816 (number of men with a known employment situation, corresponding to 93.2 % of adults men).



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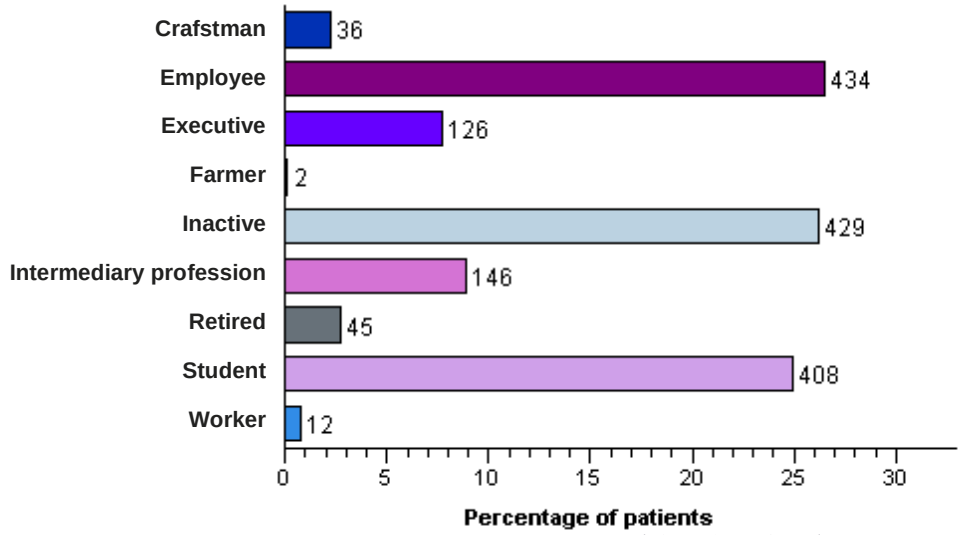
Among men aged 18 to 65, 49.0 % are working.

Among men aged 18 to 25, 58.8 % are studying.

Figure 12.2. Employment of women ≥ 18 years

N = 1638 (number of women with a known employment situation, corresponding to 94.2 % of adults women).



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Among women aged 18 to 65, 44.4 % are working.

Among women aged 18 to 25, 61.3 % are studying.

12. Social data

Marital status

Figure 12.3. Marital status of men ≥ 18 years

N = 1785 (number of men with a known marital status, corresponding to 91.6 % of adults men).

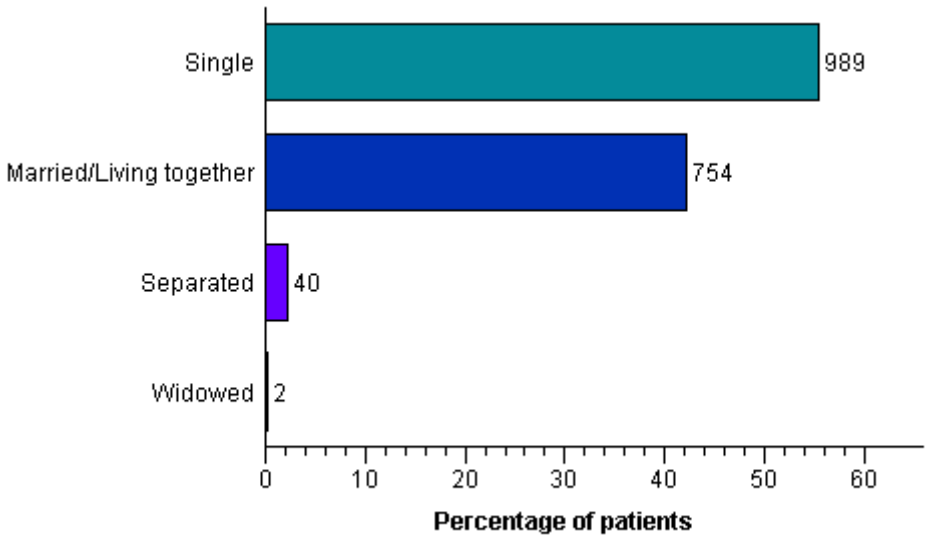

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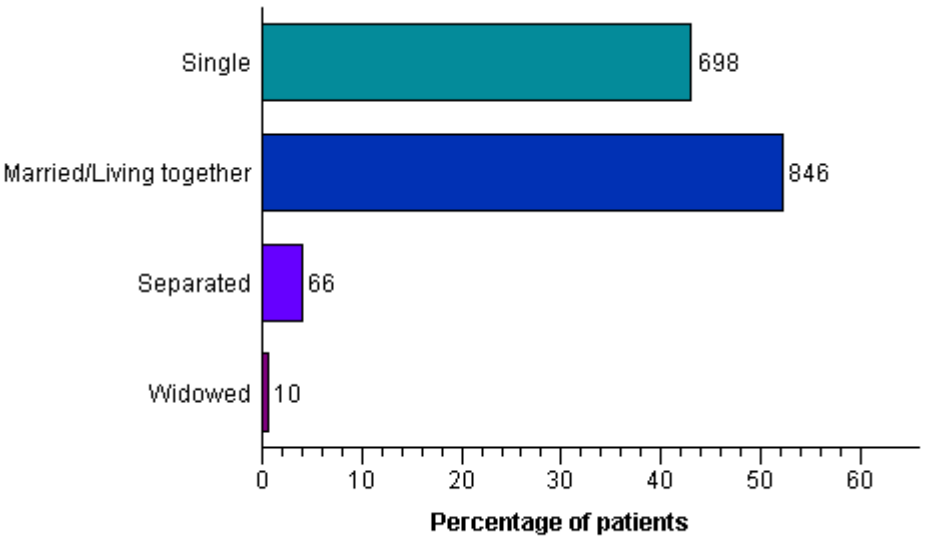
Figure 12.4. Marital status of women ≥ 18 years

N = 1620 (number of women with a known marital status, corresponding to 93.2 % of adults women).



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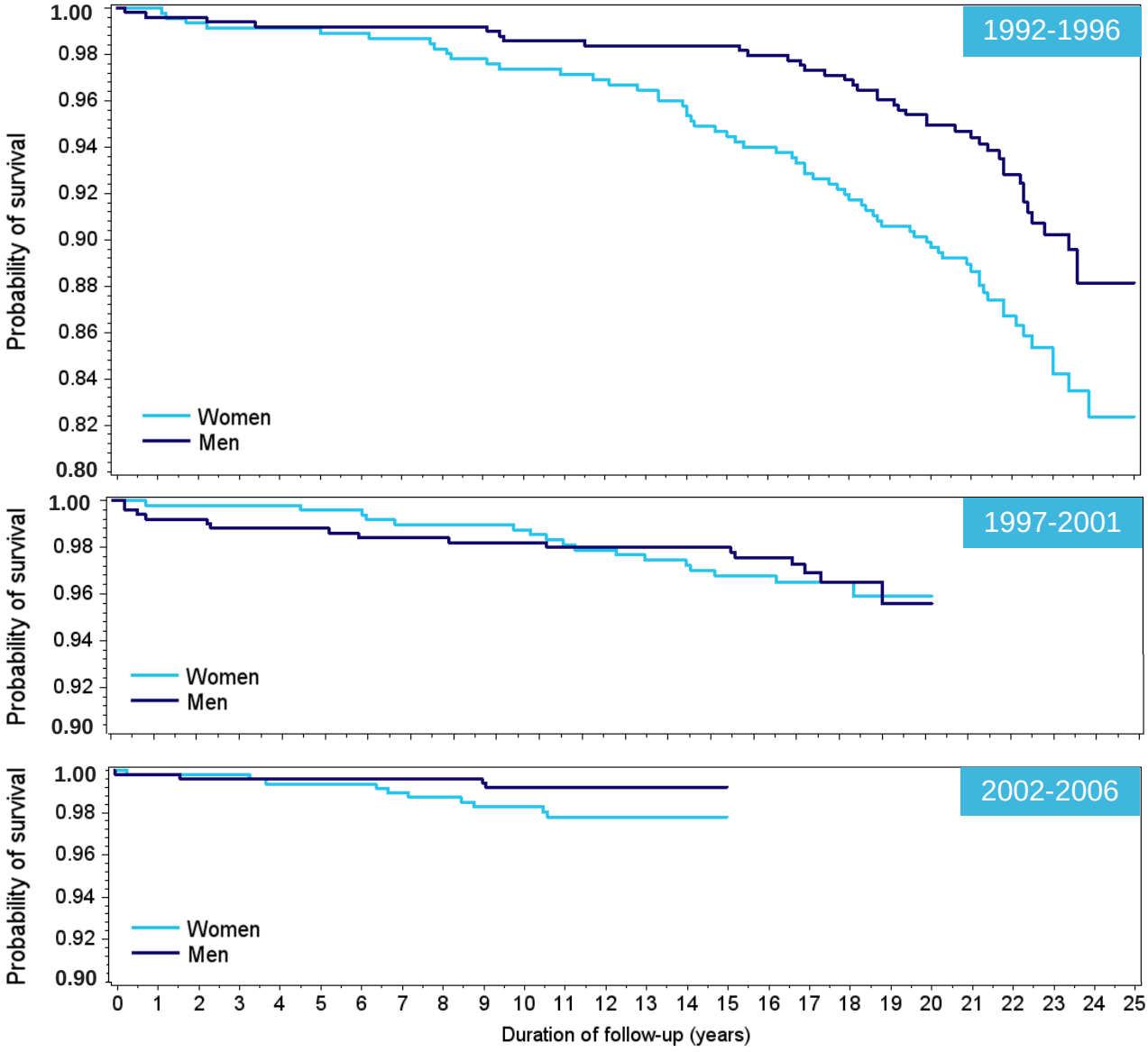
Annex 1

- 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	499	40	460	63
1997-2001	501	16	487	17
2002-2006	526	4	487	10



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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 15 years.

Annex 2

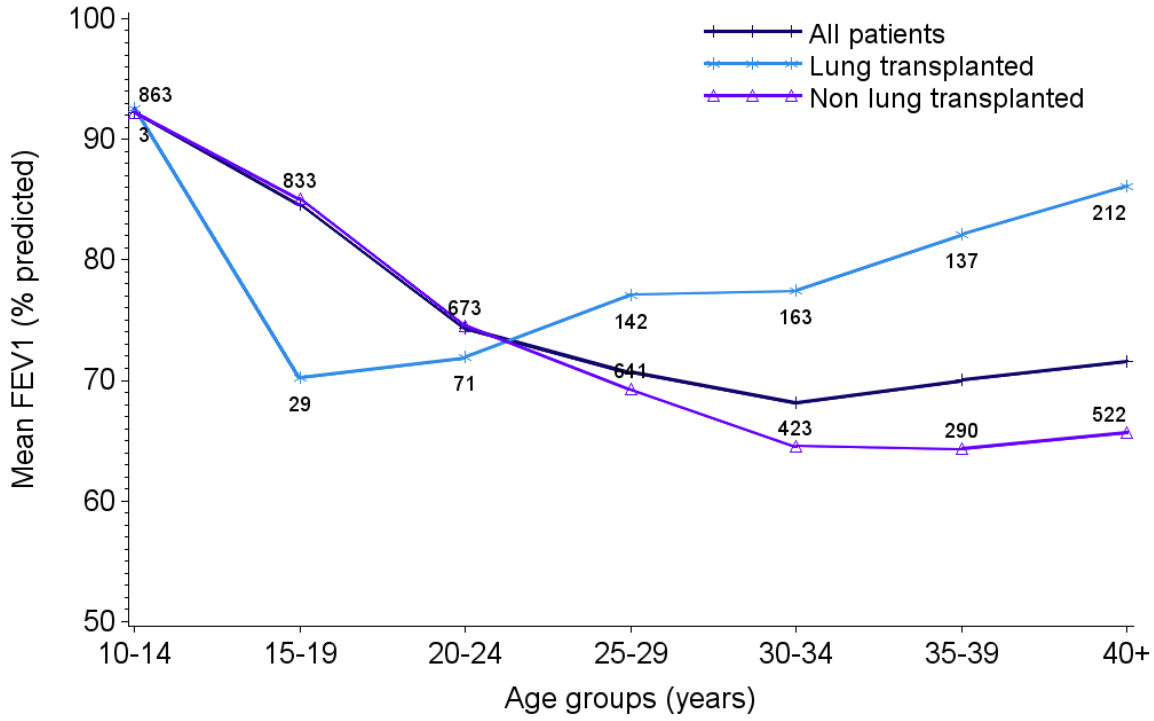
Spirometry and transplantation

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, by age group



Curve « Lung transplant recipients »:

- The values **above** the curve represent the number of lung transplant recipients with a FEV1 value (eg: 142 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: 641 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	
AMIENS Picardie CHU Sud	100
BORDEAUX Groupe Pellegrin Hôpital d'Enfants	151
GRENOBLE Hôpital de la Tronche Pédiatrie	116
LILLE Hôpital Jeanne de Flandres Pédiatrie	177
LYON Hôpital Mère-Enfant / Groupt Hosp. Est	273
MARSEILLE Hôpital La Timone Pédiatrie	131
NANCY Hôpital d'enfants	122
NANTES Hôpital Mère-Enfant	107
PARIS Hôpital Armand Trousseau	68
PARIS Hôpital Necker	203
PARIS Hôpital Robert Debré	168
RENNES-ST BRIEUC Pédiatrie	133
ST DENIS DE LA REUNION Hôpital d'Enfants	45
TOULOUSE Hôpital des Enfants	132
TOURS Hôpital de Clocheville Pédiatrie	135
VERSAILLES Hôpital Mignot Pédiatrie	63
Adults CF care centres	
BORDEAUX-PESSAC Groupe Sud Hospitalier	143
GRENOBLE Hopital de la Tronche Pneumologie	106
LILLE Hôpital Calmette Pneumologie	240
LYON SUD Centre Hospitalier	354
MARSEILLE CHU Nord	243
NANCY Hôpital de Brabois Pneumologie	94
NANTES Hôpital Laënnec	226
PARIS Hôpital Cochin	434
RENNES Hôpital Pontchaillou Pneumologie	102
SURESNES Hôpital Foch	458
TOULOUSE Hôpital Larrey Pneumologie	173
TOURS Hôpital Bretonneau Pneumologie	70
Paediatric and Adults CF care centres	
ANGERS - LE MANS	131
BESANCON	137
CAEN	112
CLERMONT FERRAND	114
CRETEIL	126
DIJON	121
DUNKERQUE	82
GIENS	214
LIMOGES	65
MONTPELLIER	212
NICE	101
REIMS	138
ROSCOFF	154
ROUEN	209
ST PIERRE DE LA REUNION	78
STRASBOURG	266
VANNES-LORIENT	91

Annex 3 (2/2)

Participating centres

Table A3.2. List of the participating centres (CF care centres excepted)

Centres	Number of patients*
Paediatric local centres	
BREST Hôpital Augustin Morvan	2
COLMAR CHG Louis Pasteur Pédiatrie	1
DAX Centre Hospitalier	12
LE HAVRE Hôpital Flaubert	22
MONTLUCON Centre Hospitalier	5
POINTE A PITRE CHU	5
Paediatric and Adults local centres	
BRIVE	1
LENS	40
Other centres	
PARIS Hôp. Européen G.Pompidou	59

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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 2016 were excluded from those statistics.

Annex 4 (1/2)

Table A4.1. Summary of data

	2014	2015	2016
Patients seen during the year and centres participating to the registry			
- Patients registered* (N):	6400	6589	6757
- Patients seen during the year in a centre** (N):	6351	6548	6707
- Centres (N) :			
Paediatric CRCMs:	16	16	16
Adult CRCMs:	12	12	12
Paediatric and Adult CRCMs:	17	17	17
Other centres:	16	12	9
Demographics			
- Male patients (%):	51.7	52.0	52.4
- Age of patients, in years (mean):	20.8	21.3	21.9
- Age of patients, in years (median):	18.9	19.4	20
- Age of patients. in years (min-max):	0-83	0-83	0-84
- Patients aged 18 years and over (%):	52.6	53.8	55.0
- Age of patients, in years (mean):	57	51	56
- Age of patients, in years (median):	33.8	28.9	30.7
- Age of patients. in years (min-max):	28.8	30.6	27.9
- Deaths (N):	71	40	51
Including death of patients not seen during the year:	13	6	6
- Crude death rate (for 1 000):	11.3	6.2	7.7
- Age at death, in years (mean):	29.0	34.1	31.8
- Age at death, in years (median):	27.1	30.6	28.0
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	2.2	2.1	2.0
- New patients diagnosed during the year (N):	186	226	177
Including by neonatal screening:	124	137	134
- Age at diagnosis of the new patients, in years (median):	1.3	1.3	1.2
- Age at diagnosis of the new patients, in years (min-max):	0-77	0-66	0-70
- Full genotypes identified (%):	96.8	96.7	96.9
F508del / F508del:	42.6	41.9	42.0
F508del / Other:	40.1	40.3	40.5
Other / Other:	14.2	14.6	14.4
F508del / Missing:	1.2	1.1	1.1
Other / Missing:	1.0	0.9	1.0
Missing / Missing:	1.0	1.2	1.1
Anthropometry			
- Height z-score, patients aged 17 years and less (mean):	-0.03	-0.01	0
- Height z-score, patients aged 18 years and over (mean):	-0.51	-0.49	-0.5
- Weight z-score, patients aged 17 years and less (mean):	-0.24	-0.23	-0.21
- Weight z-score, patients aged 18 years and over (mean):	-0.22	-0.21	-0.18

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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

	2014	2015	2016
Spirometry			
- FEV_1 (% predicted) - Knudson, patients aged 17 years and less (mean):	90.9	90.9	91.9
- FEV_1 (% predicted) - Knudson, patients aged 18 years and over (mean):	70.2	71.2	71.8
Microbiology			
- Patients with at least one sputum during the year (%):	88.9	88.1	87.1
H. influenzae:	20.3	18.9	17.0
MSSA:	55.4	54.1	56.1
MRSA:	7.7	7.8	6.9
P. aeruginosa:	41.6	39.0	38.0
S. maltophilia:	10.2	10.3	10.5
B. cepacia:	1.8	1.7	1.7
Aspergillus:	24.7	22.2	24.3
Achromobacter xylosoxidans:	5.6	6.3	6.3
Complications and transplantations			
- Aspergillus (%) :	10.3	9.6	9.5
- Abnormal exocrine pancreatic function (%) :	83.2	80.6	81.1
- Treated gastro-oesophageal reflux (%) :	16.7	17.7	18.7
- Bone disease (%) :	5.7	5.9	6.4
- Haemoptysis (%):	5.0	4.8	5.3
- Cirrhosis / portal hypertension (%):	4.3	3.9	3.9
- Insulin-dependent and non insulin-dependant diabetes (%):	18.2	18.2	19.1
- Transplanted patients (N):	772	725	807
Including patients transplanted during the year:	88	87	101
- Patients on waiting list (N):	132	141	148
Including patients listed during the year:	52	78	96
Deaths on waiting list:	5	3	3
Therapeutic management			
- IV courses (%):	32.1	31.4	31.0
- Oxygenotherapy (%):	4.7	4.9	4.6
- Nasal ventilation (%):	3.7	3.8	4.0
- Azithromycin (%):	44.3	43.0	42.7
- Inhaled antibiotics (%):	40.7	38.3	38.5
- rhDNase (%):	50.2	51.5	48.0
- Inhaled bronchodilatators (%):	48.9	48.7	52.8
- Inhaled corticosteroids (%):	39.3	40.5	39.7
- Pancreatic enzymes (%):	83.0	81.9	81.9

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Annex 5

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

	Transplanted patients	Non transplanted patients	2016 data
- Patients seen during the year in a centre* (N):	803	5904	6707
Demographics			
- Age of patients, in years (mean):	34.7	20.1	21.9
- Age of patients, in years (median):	33.7	17.7	20.0
- Patients aged 18 years and over (%):	97.3	49.2	55.0
- Early pregnancies during the year (N):	5	51	56
- Deaths (N):	37	14	51
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	5.7	1.9	2.0
- Full genotypes identified (%):	96.5	97.0	96.9
F508del / F508del:	52.8	40.5	42.0
F508del / Other:	33.7	41.4	40.5
Other / Other:	10.0	15.1	14.4
F508del / Missing:	1.2	1.1	1.1
Other / Missing:	0.6	1.0	1.0
Missing / Missing:	1.6	1.0	1.1
Anthropometry and spirometry			
- Height z-score, patients aged 17 years and less (mean):	-1.48	0.02	0
- Height z-score, patients aged 18 years and over (mean):	-0.7	-0.44	-0.5
- Weight z-score, patients aged 17 years and less (mean):	-1.83	-0.19	-0.21
- Weight z-score, patients aged 18 years and over (mean):	-0.71	-0.03	-0.18
- BMI z-score, patients aged 17 years and less (mean):	-0.93	-0.13	-0.14
- BMI, patients aged 18 years and over (mean):	20.1	21.5	21.2
Spirometry			
- FEV_1 (% predicted) - Knudson, patients aged 17 years and less (mean):	80.8	92.0	91.9
- FEV_1 (% predicted) - Knudson, patients aged 18 years and over (mean):	79.0	69.9	71.8
Complications			
- Treated aspergillosis (%)	8.1	9.7	9.5
- Abnormal exocrine pancreatic function (%) :	93.3	79.5	81.1
- Treated gastro-oesophageal reflux disease (%) :	35.1	16.5	18.7
- Bone disease (%) :	15.7	5.1	6.4
- Haemoptysis (%):	2.4	5.7	5.3
- Cirrhosis / portal hypertension (%):	4.0	3.9	3.9
- Insulin-dependent and non insulin-dependant diabetes (%):	63.5	13.1	19.1
Therapeutic management			
- Pancreatic enzymes (%) :	94.6	80.2	81.9
- Oral steroids (%) :	73.2	6.3	14.3

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** The difference between the number of transplanted patients page 34 (807) and the number of patients shown in this table (803) are the patients who died and were not seen in 2016.*

FRENCH CYSTIC FIBROSIS

Registry

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