FRENCH CYSTIC FIBROSIS Registry

Annual data report 2013

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VAINCRE LA MUCOVISCIDOSE

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Editorial

2013… if the Registry has, during its first 20 years, reflected progresses in newborn screening and clinical care in CF, the recent years showed the first clinical applications of research in CFTR protein therapy. The Registry is a key instrument for numbering and identifying patients fulfilling the criteria for the first clinical trials and later for receiving authorized treatments. If such molecules are for the moment dedicated to a minority of patients, they pave the way, long considered as impassable, for action on the intimate cause of the disease in the cell, while up to now the treatments were mainly symptomatic.

At the light of those progresses, the Registry must face a double challenge and be, more than ever, an exhaustive and reliable database with high quality data, able to improve, and a tool for identification of patients fulfilling the inclusion criteria of clinical trials, for the implementation of new treatments and for the follow-up of patients under treatment.

This is why the objectives of the French CF Registry Steering Committee and the Medical Department team of Vaincre la Mucoviscidose, in collaboration with Ined (National institute for demographic studies), are to improve data quality, in particular diagnosis and genetic data (thanks to the partnership with the French association in charge of the newborn screening program – AFDPHE - and with the molecular biology laboratories), and increasing data collection as for inhaled antibiotics. An important review work on the Annual report by the Steering Committee enabled an improved presentation of the results: anthropometric (height, weight, BMI) and spirometric (FEV1%, FCV%) data are for the first time in this report presented in quartiles.

2013 is also symbolically the year of the transformation of a « children disease" into an "adult disease" as for the first time in the Registry, the number of adults exceeds the number of children. Beyond the positive meaning of those figures in terms of life expectancy, this demographic evolution is a turning point for Vaincre la Mucoviscidose as well as for the care and research community, meaning that new issues and new needs are emerging (parenthood, transplantation, ageing…) and the Registry will have to participate in their identification.

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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 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. The Ministry of Health entrusted this 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 algorithm includes immunoreactive trypsin (IRT) measurement in the blood at age 3 days and detection of *CFTR* mutations. 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 95-98% 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 coupled 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 treatment and monitoring ;

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

- although the IRT level is high, no mutation is found. A second blotting paper sample test is carried out at age 21 days. If a raised IRT level persists, 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.

On the pathological level, functional abnormalities occur in the respiratory and digestive tracts, the sweat glands and the genital tract. This wide range of abnormalities is associated with a broad spectrum of clinical expression, both regarding age at first symptoms apparition and their subsequent evolution. 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 management (physiotherapy, antibiotic treatment, oxygen therapy, lung transplant for end stage respiratory disease) and digestive and nutritional management (pancreatic enzyme supplements and a hypercaloric diet).

The French Cystic Fibrosis Data 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 in order to help parents and patients for their personal choices, patient organisations and institutional partners in their strategic choices, particularly for grants to CF centers on a prorated basis of the number of patients ;
- helping research through pre-identification of patients fulfilling the inclusion criteria of clinical trials
- faciliter la Recherche en particulier en permettant la pré-sélection des patients éligibles à des essais cliniques.

Covering the entire population of patients in France, has since been added to the initial objectives. The association 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, the registry was certified by the national committee of rare disease registries (*Comité National des Registres Maladies Rares*), an organ of the *Institut de Veille Sanitaire* (InVS) and of the *Institut National de la Santé et de la Recherche Médicale* (INSERM).

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:allowing a better quality and exhaustivity of the diagnosis data (AFDPHE and molecular biology laboratories sources), death and transplantation data. Moreover, the online questionnaire has been simplified 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 2013 and were produced by cross-sectional analysis of data. Data on patients seen during the year in at least two centres were processed differently. Patients in this category (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 Registry, in the aim of an 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.

Demographics

Characteristics of the population

Figure 1 - Number of patients seen during the year and % of adults, evolution since 1992

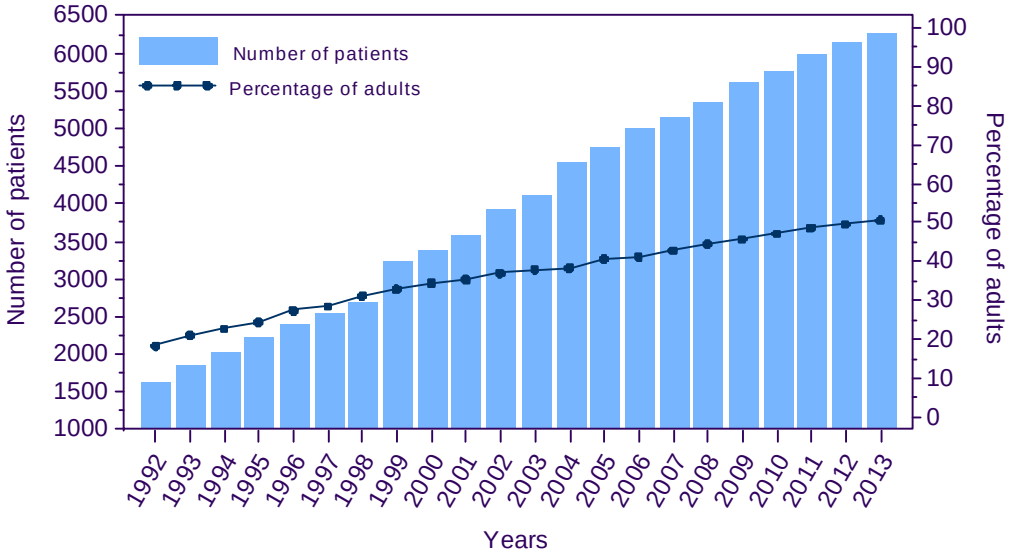

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Table 1. Annual evolution of the main indicators

	Years of follow-up									
Indicators	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
All patients*	4549	4755	5003	5148	5379	5650	5792	6046	6196	6329
Patients seen during the year**	4544	4745	4994	5140	5357	5628	5758	5993	6145	6275
Children	2799	2812	2932	2935	2971	3049	3040	3074	3099	3097 (49.4 %)
Adults	1745	1933	2062	2205	2386	2579	2718	2919	3046	3178 (50.6 %)
Over 40 years	160	175	196	226	272	329	358	415	469	521 (8.3 %)
Men	2368	2497	2595	2686	2786	2916	2958	3100	3171	3247 (51.7 %)
Women	2176	2248	2399	2454	2571	2712	2800	2893	2974	3028 (48.3 %)
Mean age (years)	16	16.3	16.4	16.8	17.3	17.7	18.1	18.7	19.2	19.7
Median age (years)	14	15	15	15	16	16	16	17	17	18
Minimum age (years)	0	0	0	0	0	0	0	0	0	0
Maximum age (years)	78	74	76	77	78	79	80	87	86	82

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

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

The number of patients in the Registry compares to 6,160 CF patients registered on December 31, 2013 under the general social security regime (for wage employees) which covers around 88% of the French population.

Demographics

Characteristics of the population

Table 2. Characteristics of the population, by sex and age

Characteristics	2011		2012		2013	
	Men	Women	Men	Women	Men	Women
Patients seen during the year	3100	2893	3171	2974	3247	3028
Children	1567	1507	1578	1521	1589	1508
Adults	1533	1386	1593	1453	1658	1520
Mean age (years)	18.7	18.6	19.2	19.1	19.7	19.7
Median age (years)	17	17	18	17	18	18

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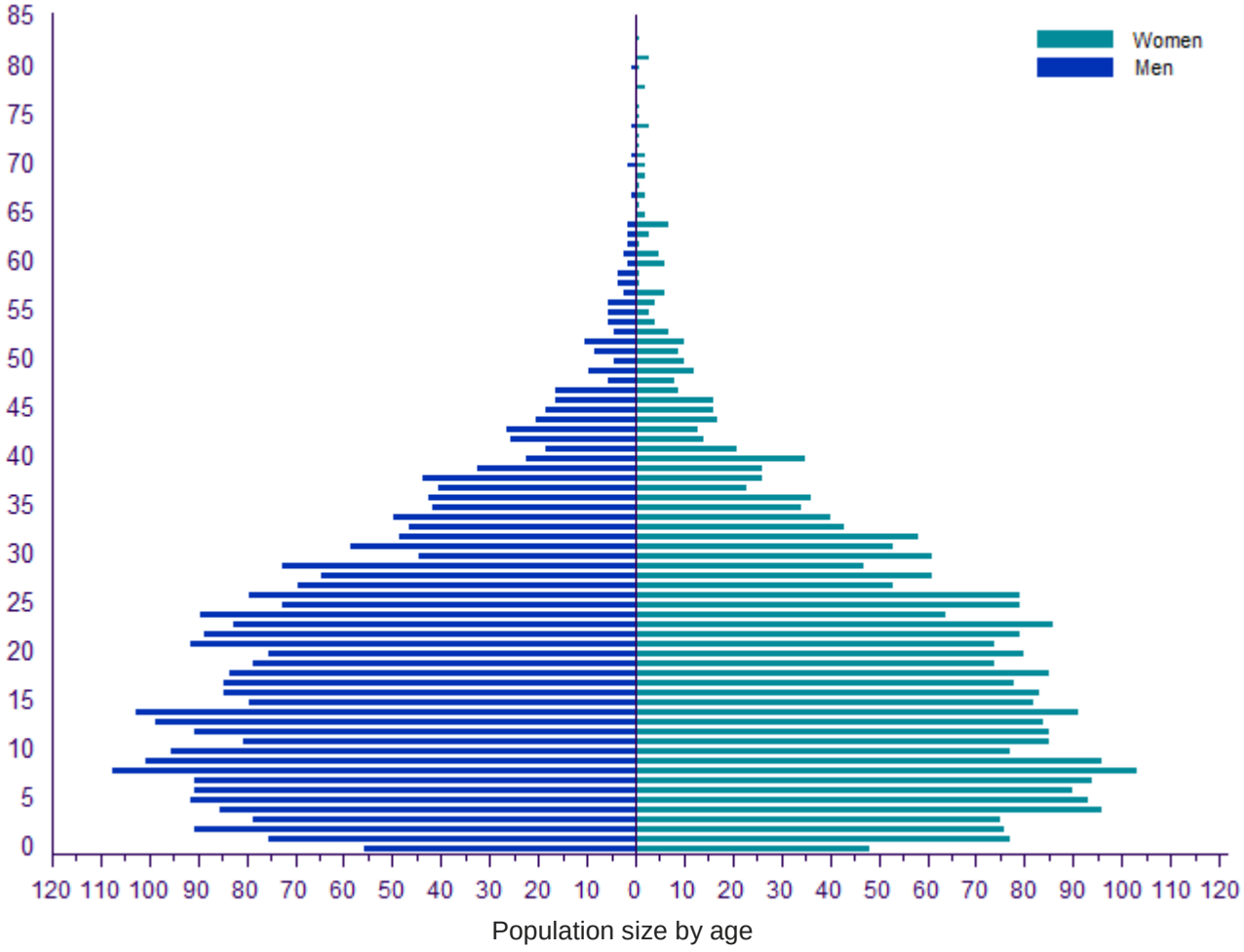
Figure 2. Population pyramid



For the first year of life, the number of patients born in 2013 was 105 according to AFDPHE, including 87 seen in a CF centre and collected in the Registry.

Except for this age pyramide, only data of the 87 patients are used in this report (cf note p15).

Demographics

Location by type of centre

Table 3. Patients' characteristics by type of centres

Types of centres	Nb	Patients' characteristics			Age of patients (years)				
		Nb (a)	%	Mean nb by centre	Min	Max	Mean	Median	Inter-quartile
Paediatric CRCMs	19	2222	35.4	116.9	0	62	10.1	10	10
Adult CRCMs	12	2007	32.0	167.3	15	81	31.4	29	12
Paediatric/Adult CRCMs	18	1958	31.2	108.8	0	82	18.5	16	18
Subtotal	49	6187	98.6	126.3	0	82	19.7	18	19
Paediatric local Centres	7	25 (b)	0.4	3.6	1	33	15.8	16	7
Adult local Centres	1	2 (c)	0.0	2.0	33	36	34.5	35	3
Paediatric/Adult local Centres	2	34 (d)	0.5	17.0	5	54	19.6	18	11
Other Centres	3	27 (e)	0.4	9.0	4	51	20.8	19	17
Subtotal	13	88	1.4	6.8	1	54	19.2	18	12
Total	62	6275	100	101.2	0	82	19.7	18	19

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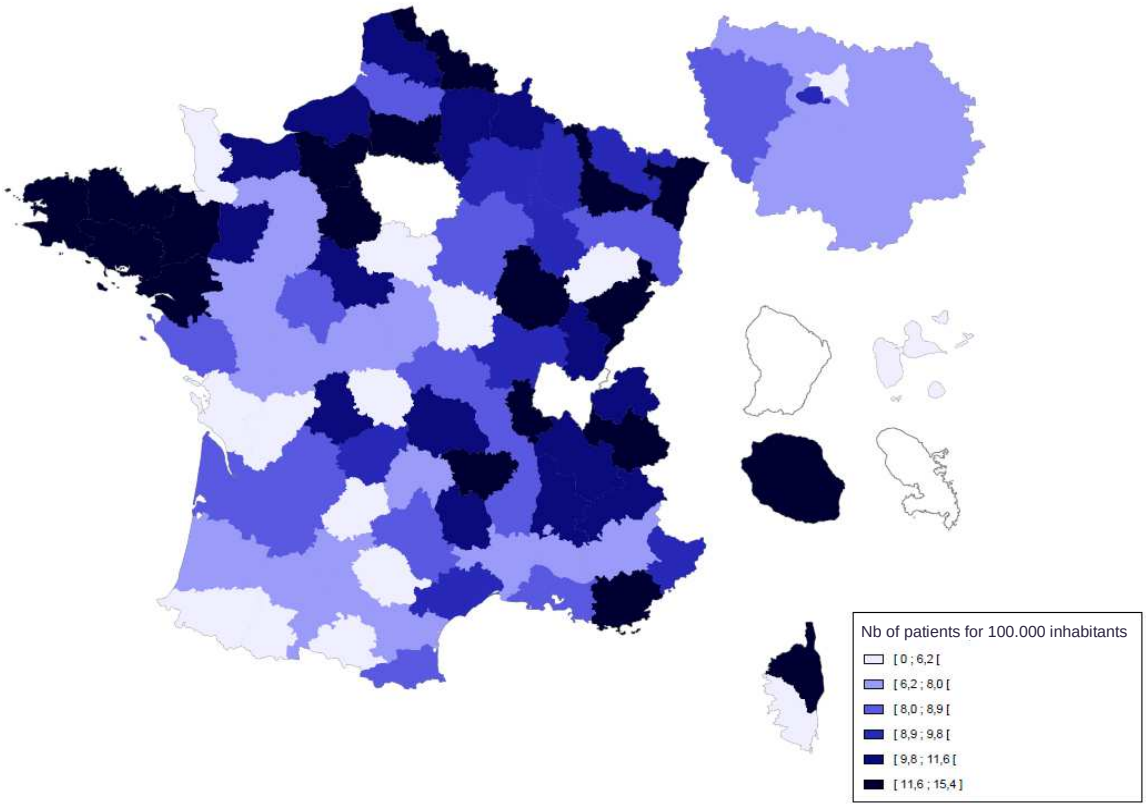
Notes : (a) After checking of patients in the multiple account category (cf page 5)
(b) Including 13 patients also seen by a CRCM.
(c) Including 2 patients also seen by a CRCM.
(d) Including 4 patients also seen by a CRCM
(e) Including 17 patients also seen by a CRCM.

CRCM (Centre de Ressources et de Compétences de la Mucoviscidose): CF centres

Demographics

Geographical location

Map 1. Prevalence of cystic fibrosis by « département » (area) of residence (number of patients for 100 000 inhabitants)



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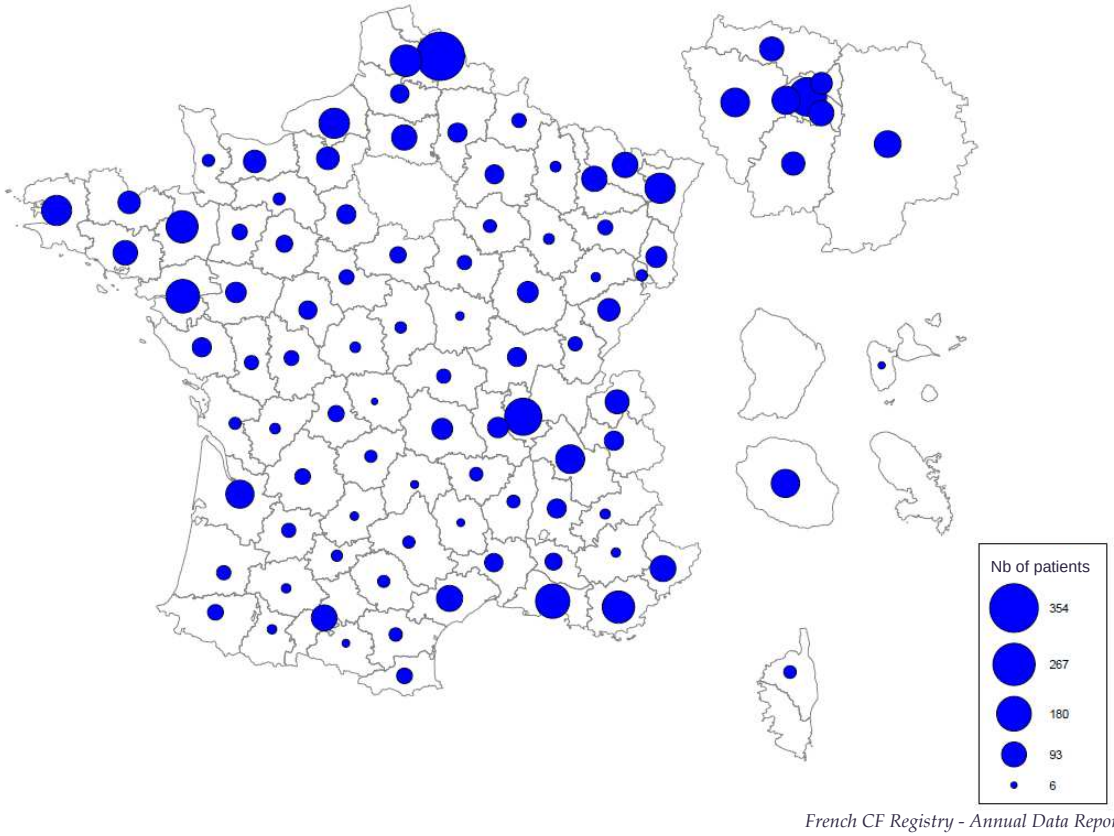
Map 2. Localisation of the patients by « département » of residence (absolute numbers)



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Mortality

Characteristics

Figure 3. Annual number of deaths since 1992

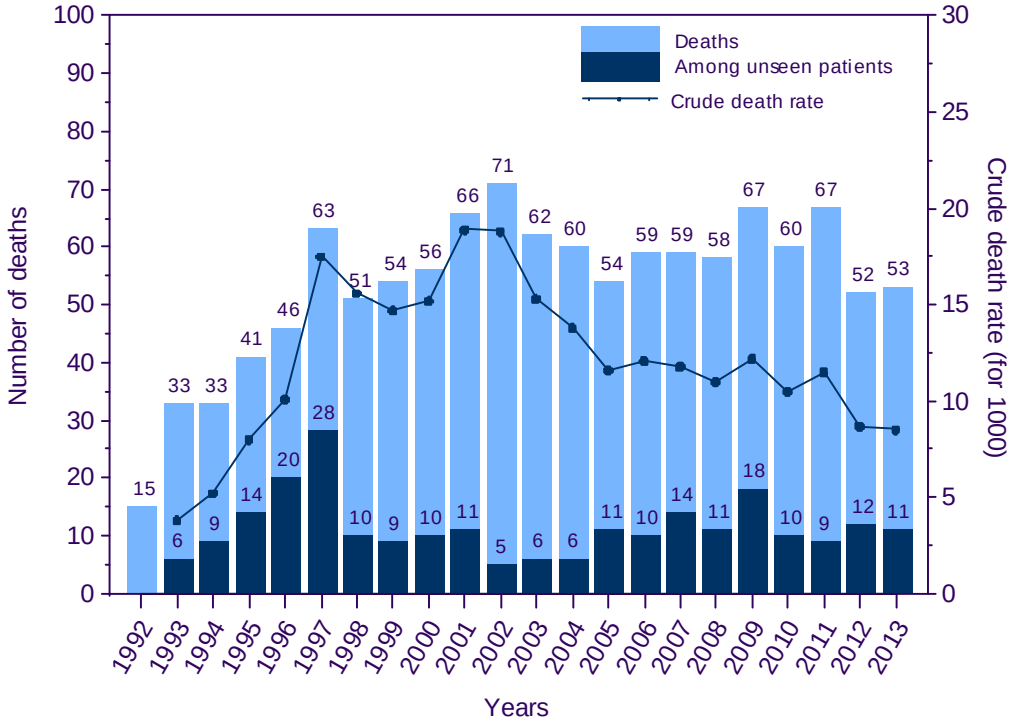

Table 4. Characteristics of mortality

Indicators	Years									
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Number of deaths	60	54	59	59	58	67	60	67	52	53
- including patients not seen during the year*	6	11	10	14	11	18	10	9	12	11
- including transplanted patients	9	9	15	24	26	31	28	34	27	28
Crude death rate (per 1000)	13.9	11.6	12.1	11.7	11.1	12.4	10.6	11.4	8.5	8.5
Mean age (years)	23	26	27	28	30	25	30	27	33	35
Median age (years)	22	24	24	27	29	24	28	26	29	31
Minimum age (years)	7	6	5	3	0	1	0	3	3	2
Maximum age (years)	51	72	76	70	67	74	70	56	89	83

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

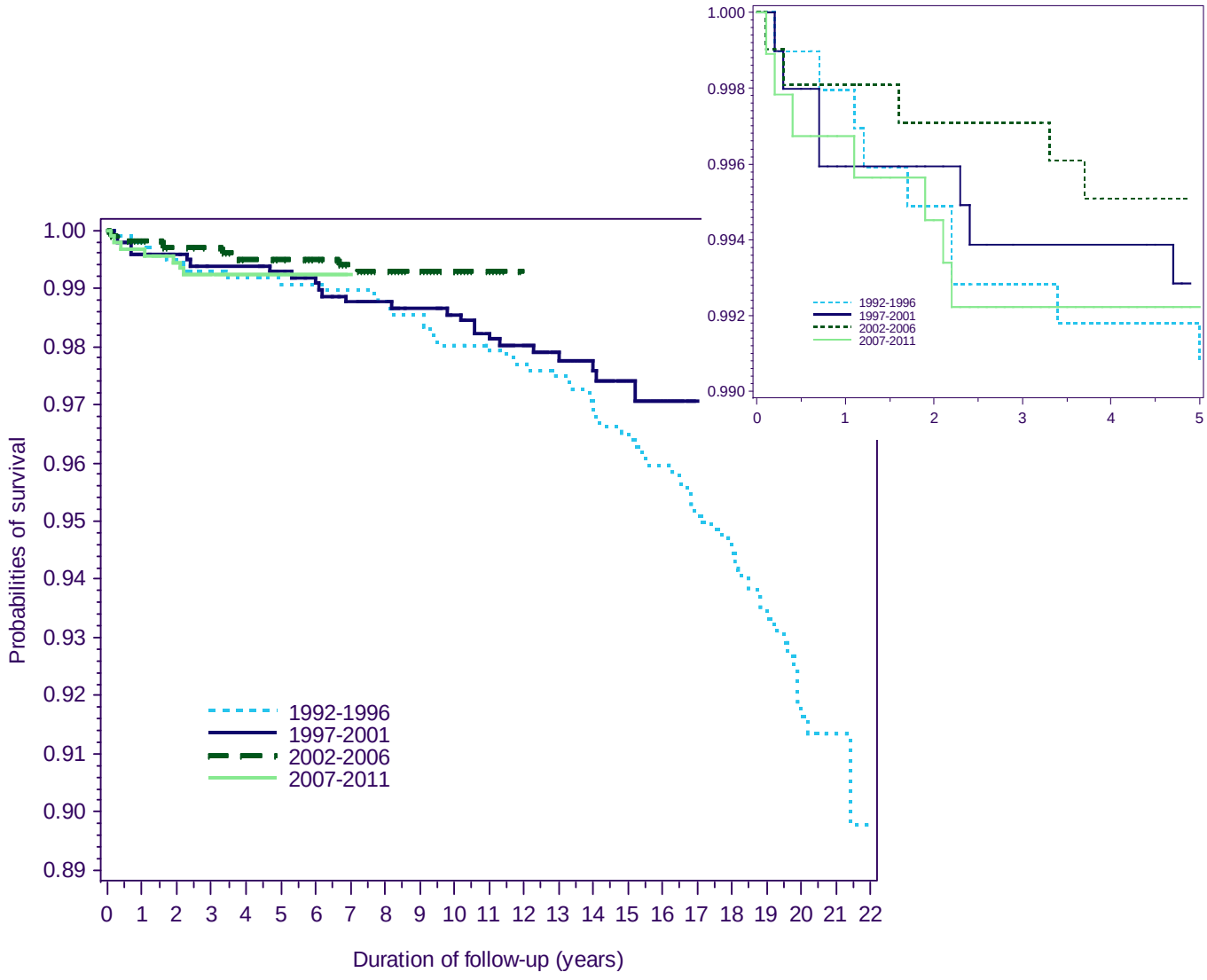
Mortality

Survival analysis

Figure 4. 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 4 birth cohorts; the numbers of patients and of deaths are:

- Births from 1992 to 1996 (in 2013 this cohort was followed during 22 years maximum) : 980 patients, 68 deaths
- Births from 1997 to 2001 (maximum 17 years of follow up) : 987 patients, 24 deaths
- Births from 2002 to 2006 (maximum 12 years of follow up) : 1040 patients, 8 deaths
- Births from 2007 to 2011 (maximum 7 years of follow up) : 919 patients, 7 deaths



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There is no significative survival difference between those cohorts (Log-Rank test = 5.73, p = 0,12).
Survival analysis by genotype and sex are available on annex 1.

* Deaths whatever the patient visited a CF centre or not during the year.

Pregnancy

Figure 5. Annual number of early pregnancies, evolution since 1992

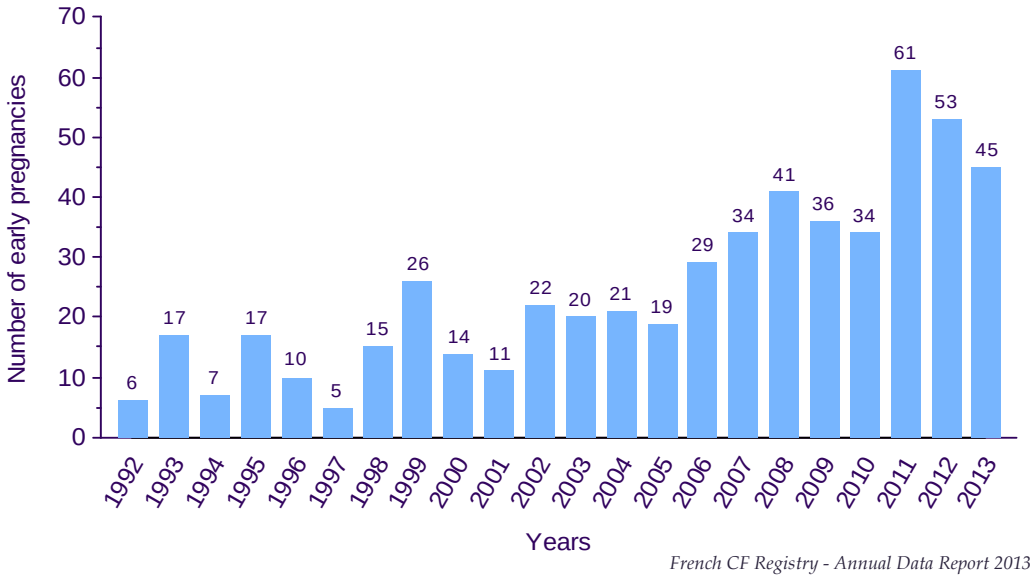

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Table 5. Early pregnancy characteristics

Characteristics	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Number of early pregnancies	21	19	29	34	41	36	34	61	53	45
Pregnancy rates in women aged 15 to 49 years (for 1000)	22.4	18.2	25.8	28.9	33.2	27.4	24.4	41.6	34.4	27.9
Mean age at 31st December of the year of early pregnancy	28.7	27.2	27.4	27.4	27.1	27.7	28.4	28.7	27.7	28.9

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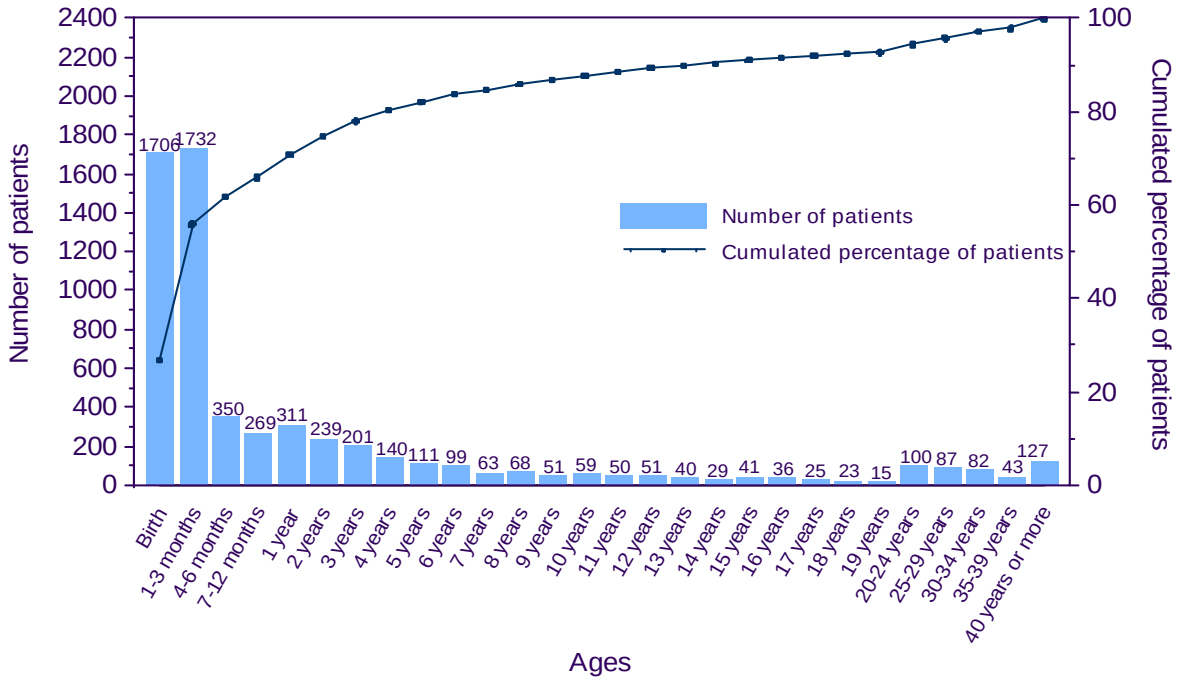
Diagnosis

Main characteristics

Figure 6. Number of patients and cumulative percentage of patients by age at diagnosis

N = 6148 (number of patients whose age at diagnosis is known).



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Diagnosis

Main characteristics

Table 6. Diagnosis characteristics

Characteristics	2011	2012	2013
ALL PATIENTS			
Patients whose age at diagnosis is known	5937 (99.1 %)	6032 (97.9 %)	6148 (97.3 %)
Age at diagnosis			
- Median age (months)	2.8	2.6	2.5
- Mean age (years)	4.2	4.2	4.3
- Minimum age (years)	0	0	0
- Maximum age (years)	86	79	79
NEW PATIENTS DIAGNOSED DURING THE YEAR			
Number of patients			
New patients - N (%)	215 (3.6 %)	188 (3.1 %)	165 (2.6%)
- Including newborn patients - N	133	119	87
Age at diagnosis (a)			
- Median age (months)	1.3	1.3	1.9
- Mean age (years)	6.9	5.5	9.1
- Minimum age (years)	0	0	0
- Maximum age (years)	69	72	72
Context of diagnosis			
1. Screened positive newborns (NBS)	131	124	90
- including Prenatal diagnosis - N (%)	4 (3 %)	2 (1.6 %)	2 (2.2 %)
- including Meconium ileus - N (%)	16 (12.2 %)	4 (3.2 %)	8 (8.9 %)
2. Diagnosis on symptoms (NBS excluded)	84	64	75
- including Meconium ileus - N (%)	10 (11.9 %)	9 (14 %)	7 (9.3 %)
- including Symptoms (other than MI):- N (%)	74 (88.1 %)	55 (86 %)	68 (90.7 %)
- Mean age at diagnosis (years)	17.8	16	19.9

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Note: (a) Including family history and antenatal diagnosis.

Among the 165 new patients, 87 were born in 2013. The method used to compile this report (patients seen in a care centre in 2013) means that infants born in 2013 and seen for the first time in 2014 are excluded (cf note page 8). For information purposes only, 20 newborns in 2012 were diagnosed in 2013 through NBS. In the 2012 age pyramide, the number of patients aged 0 was 119 and could have been 119 + 20 = 139.

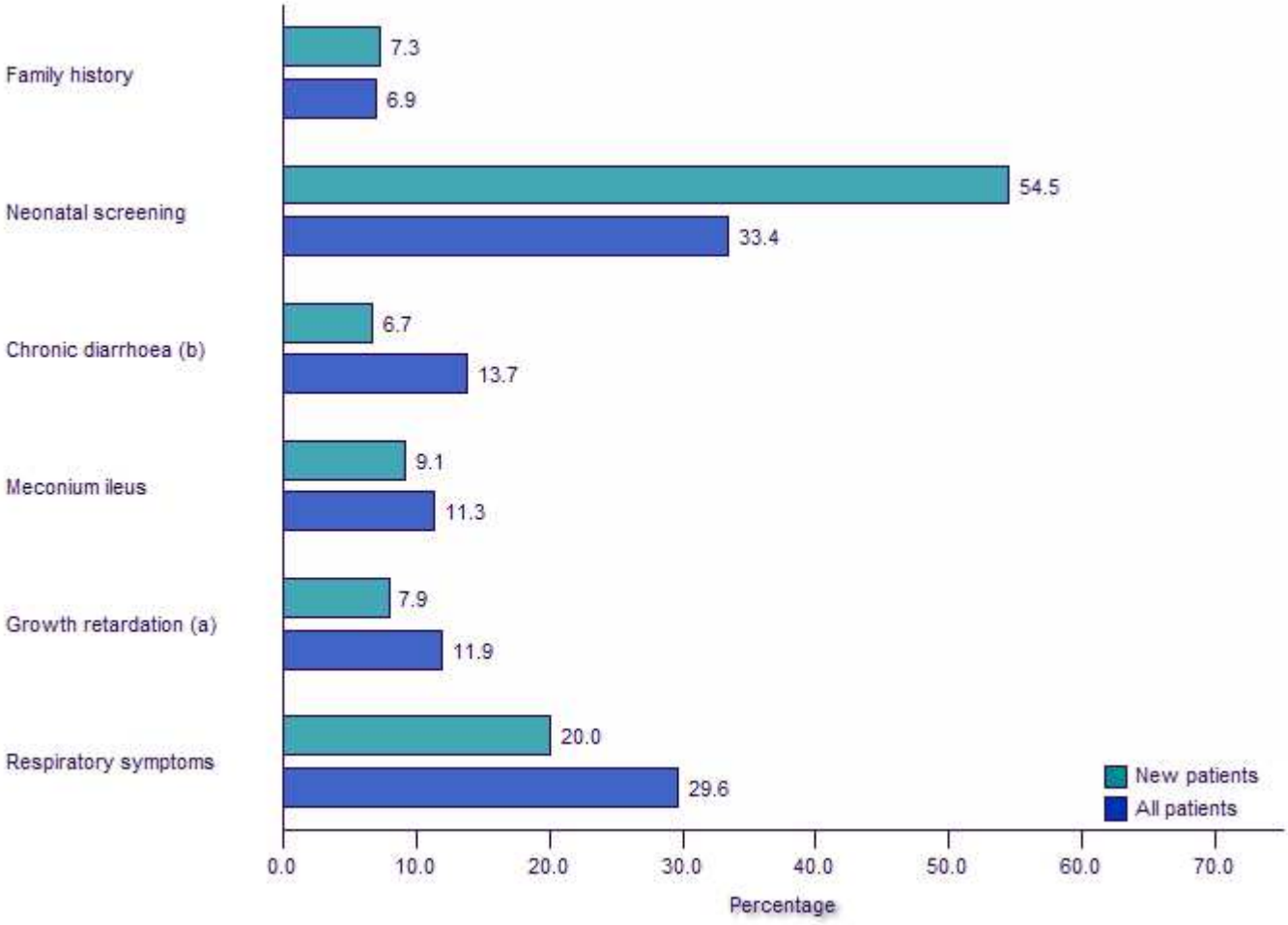
The number of patients diagnosed by neonatal screening (90) given in this report is not the total for France, but represents the patients for whom screening resulted in diagnosis. Patients diagnosed with CF before the screening result was known, (e.g. through meconium ileus), are not included in the total of 90.

For comparison and for the 2013 data, the number of new patients considered as having a (CF) long duration disease by the general social security regime (for wage employees) was 340 (round figure) and the number of newborns screened according to AFDPHE was 105.

Diagnosis

Diagnosis context

Figure 7a. Symptoms leading to diagnosis (most frequent ones)



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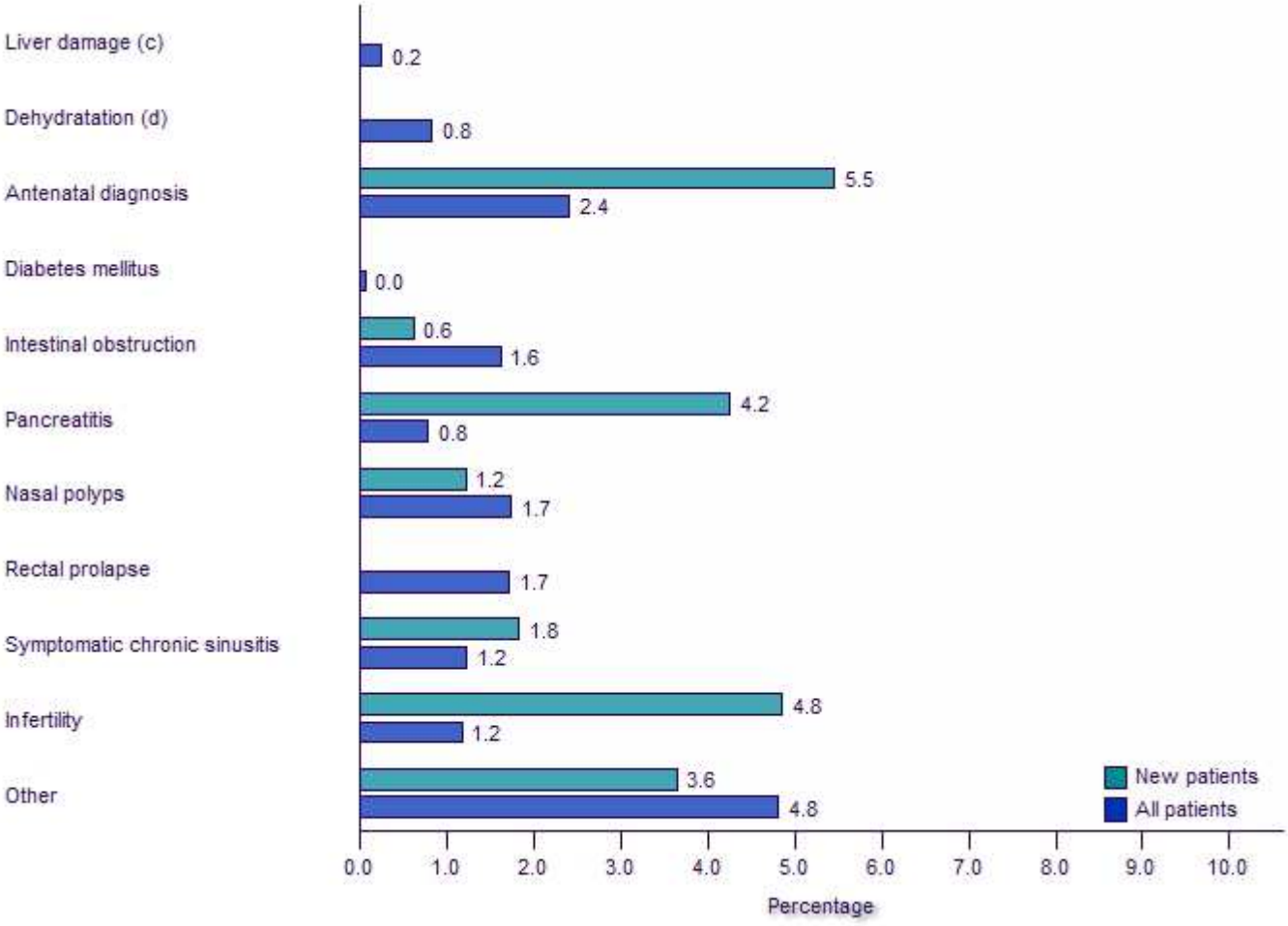
(a) Growth retardation / Malnutrition
(b) Chronic diarrhoea / Steatorrhoea / Malabsorption

Diagnosis

Diagnosis context

Figure 7b. Symptoms leading to diagnosis (less frequent ones)



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

Diagnosis

Genotypes

Table 7. Number and proportion of the most frequent genotypes

Genotypes	Number of patients	%
F508del / F508del	2660	42.4 %
F508del / G542X	196	3.1 %
F508del / N1303K	144	2.3 %
F508del / 2789+5G->A	108	1.7 %
F508del / 1717-1G->A	101	1.6 %
F508del / R117H	93	1.5 %
F508del / R553X	65	1.0 %
F508del / G551D	63	1.0 %
F508del / 3849+10kbC->T	51	0.8 %
F508del / 3272-26A->G	53	0.8 %
F508del / W1282X	40	0.6 %
F508del / Y122X	45	0.7 %
F508del / [delta]I507	44	0.7 %
F508del / L206W	46	0.7 %
F508del / R347P	39	0.6 %
F508del / D1152H	36	0.6 %
F508del / 2183AA->G	36	0.6 %
F508del / 5T	23	0.4 %
F508del / R1162X	29	0.5 %
F508del / A455E	31	0.5 %
F508del / 1078delT	22	0.4 %
F508del / R347H	24	0.4 %
F508del / Y1092X	26	0.4 %
F508del / R334W	20	0.3 %
F508del / 3659delC	22	0.4 %
N1303K / N1303K	21	0.3 %
F508del / 711+1G->T	23	0.4 %
G542X / G542X	20	0.3 %
F508del / S945L	21	0.3 %
F508del / 394delTT	18	0.3 %
F508del / E60X	19	0.3 %
F508del / S1251N	17	0.3 %
F508del / W846X	19	0.3 %
F508del / G85E	23	0.4 %
F508del / R1066C	14	0.2 %
F508del / 1811+1.6kbA->G	19	0.3 %
F508del / 3120+1G->A	21	0.3 %
Y122X / Y122X	13	0.2 %
711+1G->T / 711+1G->T	14	0.2 %
F508del / 621+1G->T	12	0.2 %
F508del / I148T	8	0.1 %
F508del / Q220X	9	0.1 %
Other CFTR genotypes	1626	25.9 %
Subtotal (known genotypes)	5934	94.6 %
F508del / Missing	129	2.1 %
Other / Missing	93	1.5 %
Missing / Missing	119	1.9 %
Subtotal (partial genotypes / Missing)	341	5.4 %
Total	6275	100.0 %

Diagnosis

Genotypes

Table 8. Age of patients by genotype

Genotypes	Patients		Age (years)		
	Number	%	Mean	Median	Max
F508del / F508del	2660	42.4	18.8	18	60
F508del / Other	2442	38.9	19.6	17	76
Other / Other	832	13.3	19.4	17	82
F508del / Missing	129	2.1	27	23	78
Other / Missing	93	1.5	25.6	25	81
Missing / Missing	119	1.9	29.7	25	80

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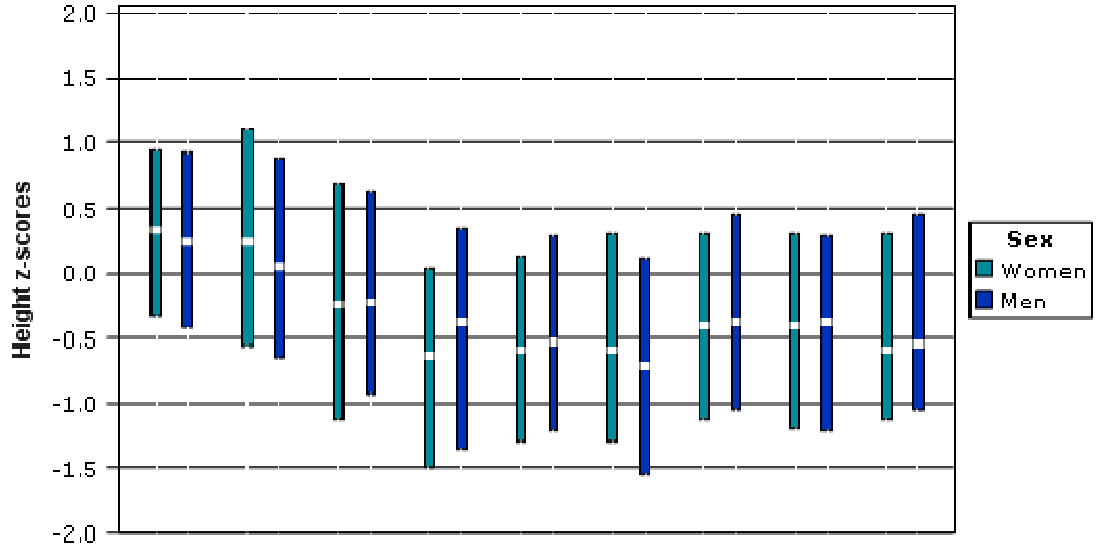
Anthropometry

Height and Weight

Figure 8. Height z-scores, by gender and age group



Age groups (years)		00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +
Mean	Men	0.29	0.10	-0.16	-0.50	-0.52	-0.66	-0.34	-0.44	-0.36
	Women	0.26	0.30	-0.22	-0.70	-0.64	-0.51	-0.42	-0.41	-0.39
Median	Men	0.23	0.06	-0.22	-0.38	-0.53	-0.72	-0.38	-0.38	-0.55
	Women	0.33	0.25	-0.24	-0.63	-0.59	-0.59	-0.41	-0.41	-0.59

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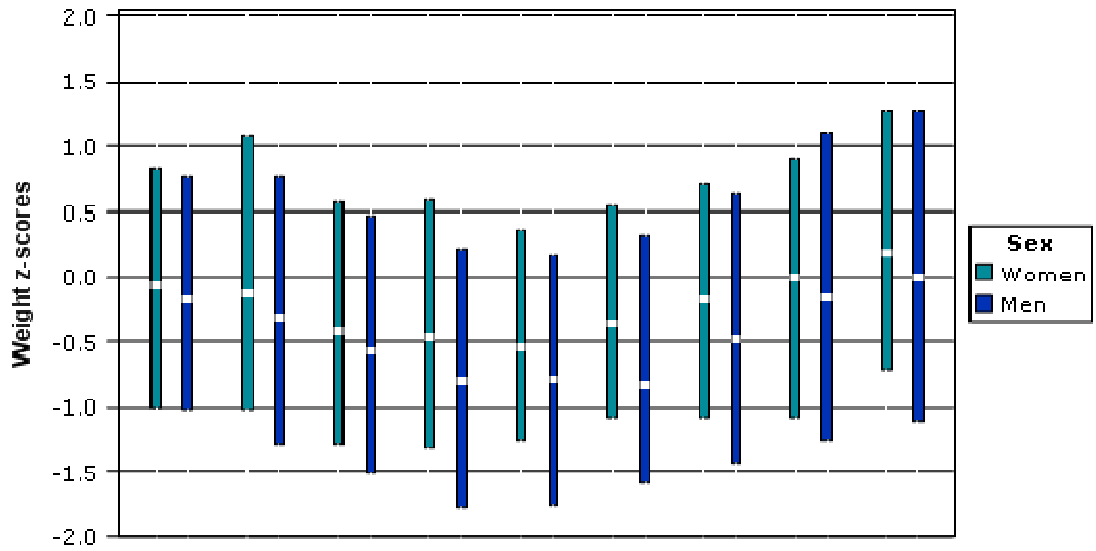
Figure 9. Weight z-scores, by gender and age group



Age groups (years)		00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +
Mean	Men	-0.07	-0.20	-0.46	-0.67	-0.70	-0.69	-0.35	-0.07	0.14
	Women	-0.04	0.08	-0.30	-0.35	-0.40	-0.24	-0.04	-0.03	0.35
Median	Men	-0.18	-0.31	-0.58	-0.80	-0.79	-0.83	-0.48	-0.16	0
	Women	-0.07	-0.13	-0.42	-0.47	-0.54	-0.36	-0.18	0	0.18

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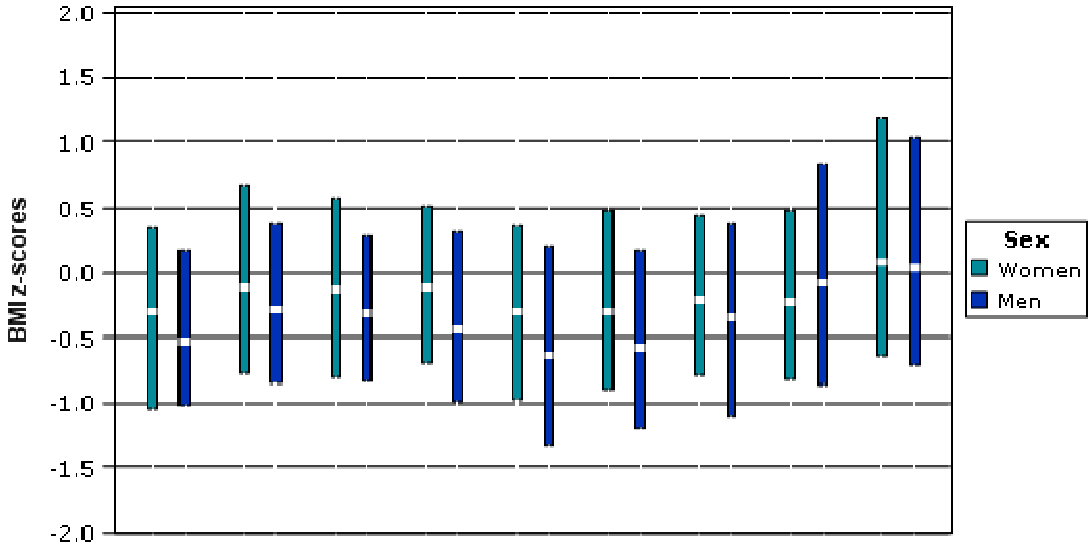
Anthropometry

Body Mass Index (BMI)

Figure 10. BMI z-scores, by gender and age group



Age groups (years)		00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +
Mean	Men	-0.39	-0.16	-0.18	-0.31	-0.53	-0.48	-0.32	-0.02	0.22
	Women	-0.31	0.03	-0.06	-0.05	-0.22	-0.15	-0.05	-0.10	0.28
Median	Men	-0.53	-0.29	-0.32	-0.43	-0.63	-0.58	-0.35	-0.08	0.04
	Women	-0.30	-0.12	-0.13	-0.11	-0.30	-0.31	-0.21	-0.22	0.08

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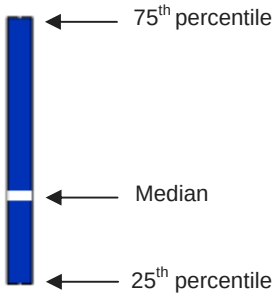
The z-score is a anthropometric reduced centered variable (Z = [measure-mean]/standard deviation), ajusted for gender and age; the mean and standard deviation are taken from the French reference population with the same gender and age as the patient. This index measures the difference with population 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 8 to 12 (pages 20, 21 et 22)

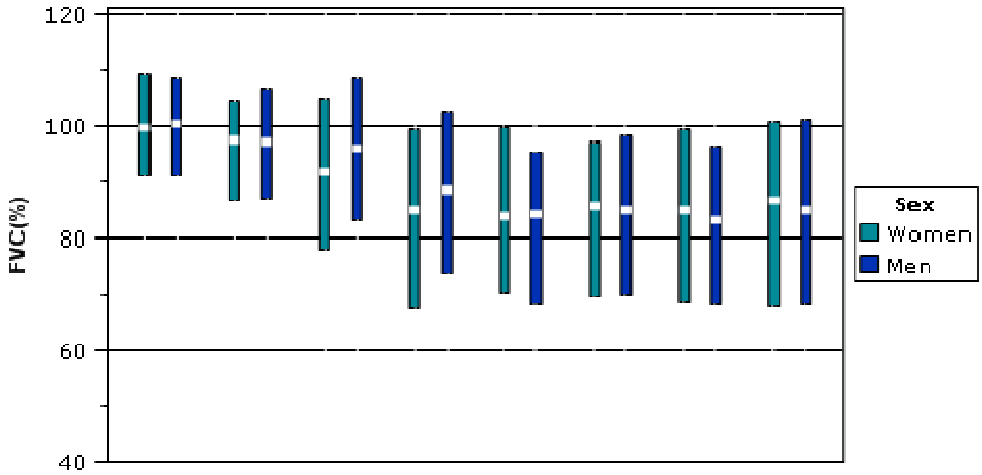
Those figures represent z-scores of anthropométrie and spirometry values.
For each age and sex group, median values are the white lines, extremes are the 25th and 75th percentiles.



Spirometry

In 2013, 95.2 % of the patients aged 6 or more had at least one spirometry (94.6 % in 2011 and 2012).

Figure 11. FVC (% predicted), by gender and age group



	Age groups (years)	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +	Total
Mean	Men	99.3	96.0	94.6	87.0	81.8	83.2	82.0	84.0	89.6
	Women	99.6	95.1	91.1	82.8	83.6	83.1	82.4	84.0	88.6
	All patients	99.4	95.6	92.8	85.0	82.6	83.1	82.2	84.0	**89.2**
Median	Men	100.5	97.0	96.2	88.7	84.4	84.8	83.3	85.0	92.3
	Women	99.7	97.6	91.7	85.0	83.9	85.7	85.1	86.9	91.3
	All patients	100.2	97.4	94.4	87.1	84.4	85.3	84.7	86.2	**91.8**

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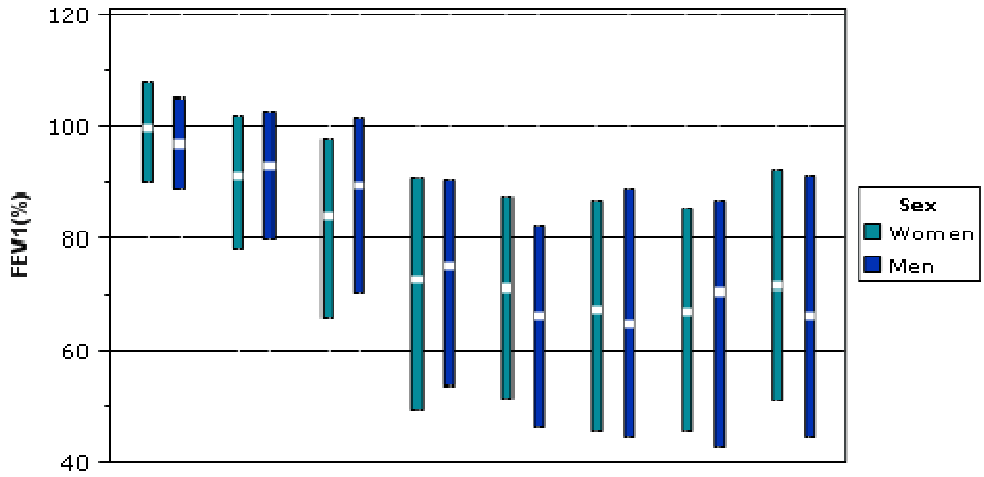
Figure 12. FEV_1 (% predicted), by gender and age group



	Age groups (years)	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +	Total
Mean	Men	95.5	90.0	85.2	72.1	65.0	66.1	66.1	67.9	78.0
	Women	97.6	88.8	80.8	70.3	69.6	67.7	67.0	71.1	78.3
	All patients	96.5	89.4	83.0	71.2	67.2	66.9	66.5	69.5	**78.1**
Median	Men	96.9	92.8	89.2	75.0	66.0	64.7	70.3	66.2	82.0
	Women	99.6	91.2	83.8	72.4	70.9	67.1	66.8	71.3	81.6
	All patients	98.1	92.1	86.4	73.3	68.7	66.0	68.8	68.4	**81.4**

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The pulmonary function tests need an active participation of the patient, difficult to obtain before 6 years of age.

The forced vital capacity (FCV) and the forced expiratory volume in the first second (FEV1) are given in % predicted (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).

A complementary analysis comparing transplanted patients to the whole population is represented in annex 2.

Spirometry

Figure 13. FEV_1 (% predicted) classes

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

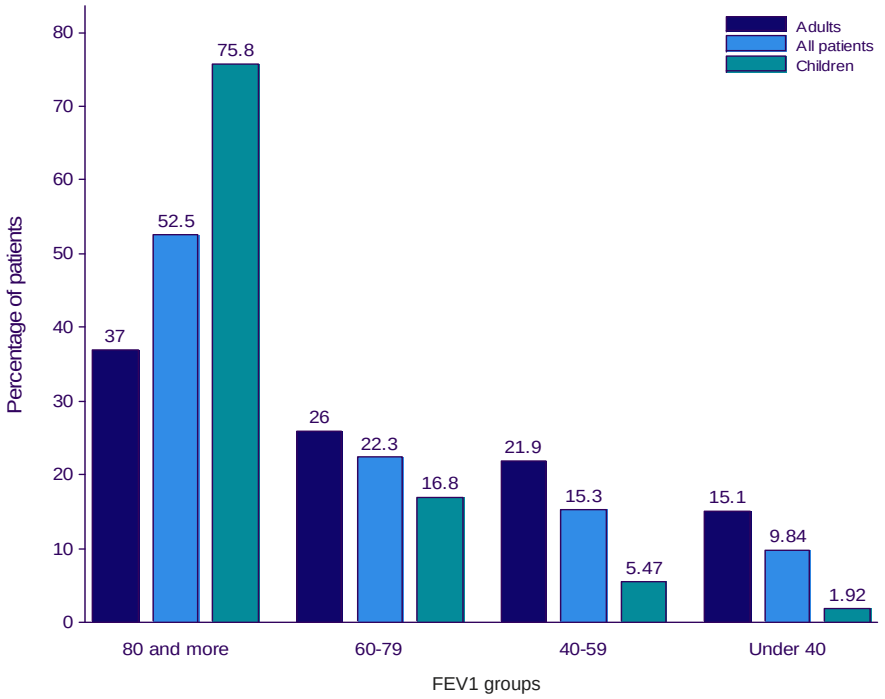

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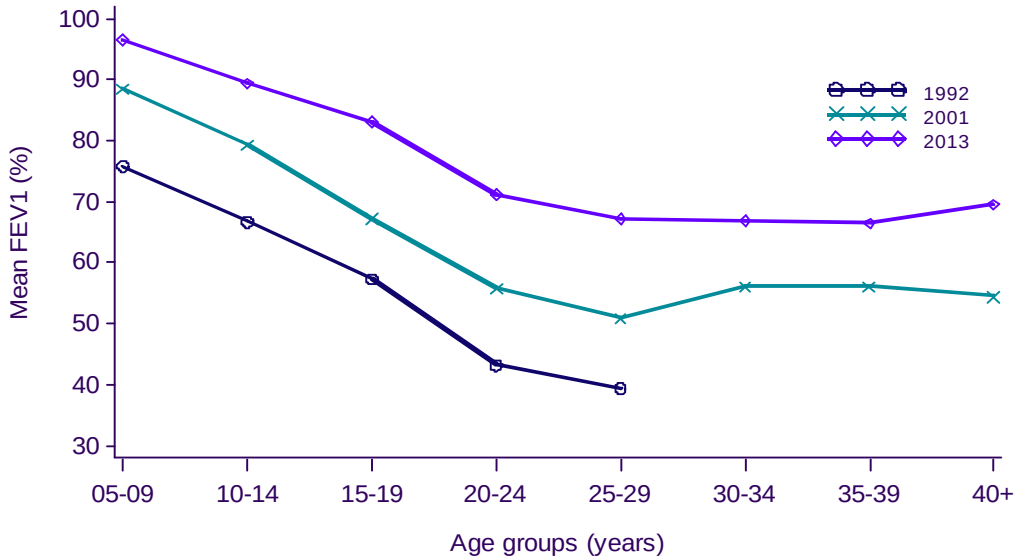
Figure 14. Mean FEV_1 (% predicted)* in 2013 compared with 1992 and 2001, by age



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* In 1992 and 2001 was collected the last FEV1 of the year. In 2013, it was the best value of the year.

Microbiology

Table 9. Sputum cultures

Patients with at least one sputum	N	*Proportion (%)*
All patients	5673	*90.4 %*
Children	3028	*97.8 %*
Adults	2645	*83.2 %*

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In 2013, 90.4% of the patients had at least one sputum culture; this proportion remains steady as it was 91.2% % in 2012 and 91.7 % in 2011. Among the patients without sputum culture (N=602), 56 % of them were transplanted.

Table 10. 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	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*	.
Patients with at least one sputum	**719**	**937**	**880**	**785**	**728**	**568**	**392**	**263**	**401**	**5673**	**90.4 %**
Normal culture	443	512	320	221	98	78	51	45	85	1853	29.5 %
Achromobacter xylosoxidans	13	40	59	68	62	43	32	13	25	355	5.7 %
Aspergillus	17	111	230	272	280	217	126	80	121	1454	23.2 %
Burkholderia cepacia	3	9	14	22	28	17	11	11	3	118	1.9 %
Haemophilus influenzae	304	401	271	163	124	64	45	28	55	1455	23.2 %
Atypical mycobacteria	.	5	15	32	32	31	13	7	17	152	2.4 %
Pneumococcus	67	68	20	10	8	3	2	6	8	192	3.1 %
Pseudomonas aeruginosa, including:	120	208	291	364	438	382	283	180	228	2494	39.7 %
- Chronic P. aeruginosa	*2*	*37*	*115*	*188*	*277*	*253*	*180*	*124*	*147*	*1323*	*21.1 %*
- Multidrug resistant P. aeruginosa	*1*	*5*	*22*	*38*	*83*	*93*	*66*	*39*	*58*	*405*	*6.5 %*
Staphylococcus, including:	438	688	732	627	519	368	222	121	180	3895	62.1 %
- MSSA	*412*	*658*	*667*	*577*	*454*	*294*	*180*	*92*	*142*	*3476*	*55.4 %*
- MRSA	*22*	*43*	*91*	*88*	*70*	*77*	*36*	*28*	*30*	*485*	*7.7 %*
Stenotrophomonas maltophilia	66	80	122	137	100	67	33	22	34	661	10.5 %
Streptococcus (non pneumoniae)	23	51	29	24	71	61	42	22	37	360	5.7 %

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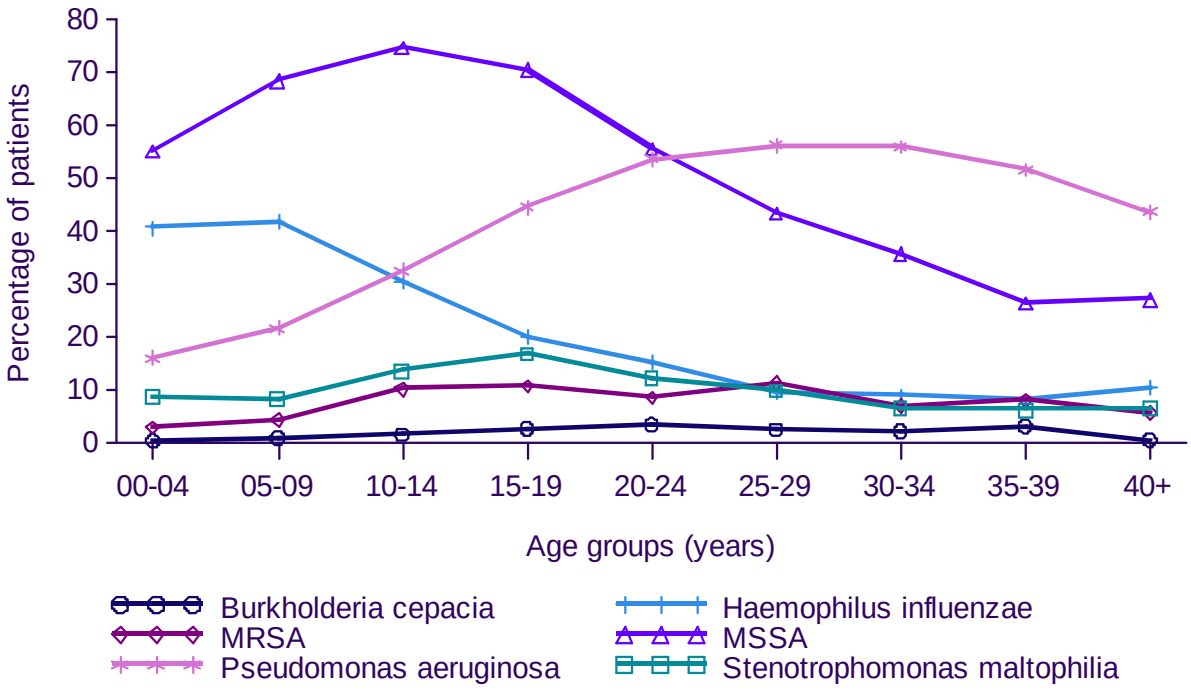
* Percentage with respect to the entire population.

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.

Microbiology

Figure 15. Clinically important bacteria, by age group



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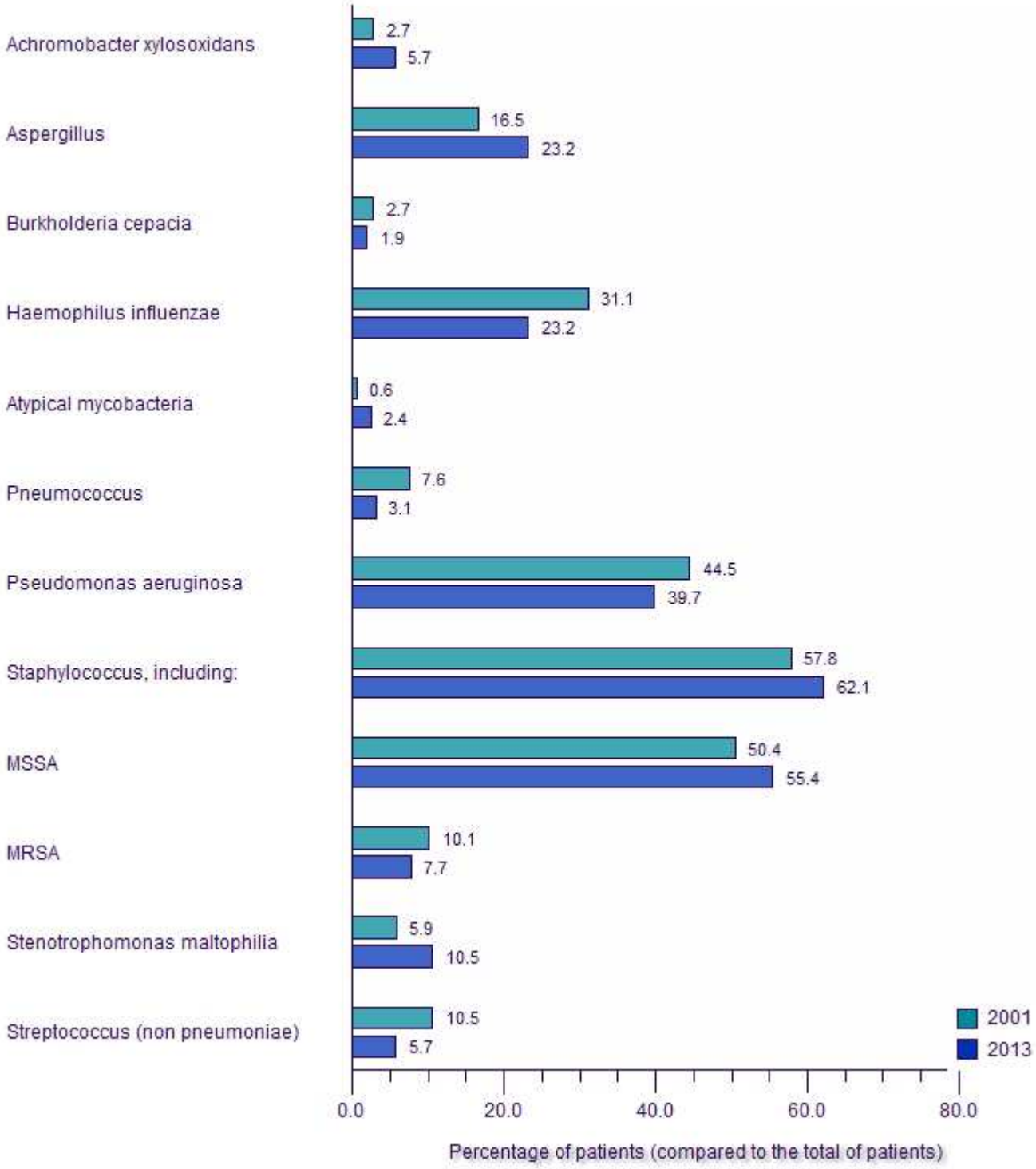
Microbiology

Figure 16. Comparison of germs in 2013 and in 2001



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Complications

Respiratory

Table 11. 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	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*	.
Treated aspergillosis	3	50	117	122	132	74	49	29	45	621	9.9 %
Asthma	95	219	190	138	107	78	42	35	67	971	15.5 %
Haemoptysis	.	3	18	48	70	50	36	21	28	274	4.4 %
Pneumothorax	.	.	.	11	14	9	7	5	5	51	0.8 %
Nasal polyps	18	104	144	130	144	98	64	58	66	826	13.2 %

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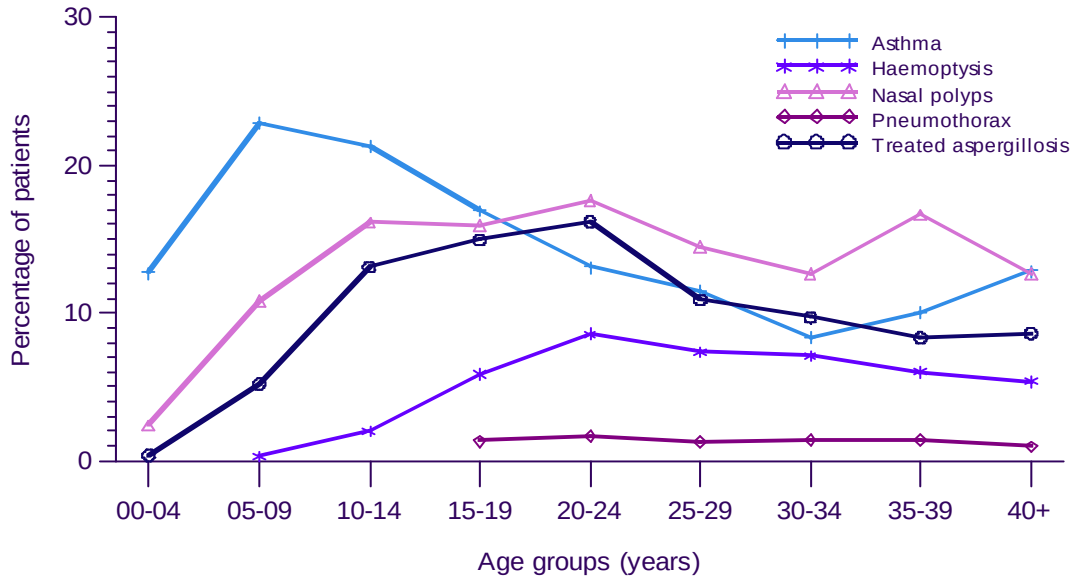
Figure 17. Respiratory complications, by age group

Percentage of age groups reporting complications



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Complications

Gastro–intestinal and hepatic

Table 12. Gastro-intestinal and hepatic complications

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*	.
Gallstones	3	13	11	11	26	36	21	20	26	167	2.7 %
Cirrhosis/Portal hypertension	2	18	37	70	53	34	22	12	14	262	4.2 %
Elevated liver enzymes	28	56	69	92	56	42	21	17	21	402	6.4 %
Abnormal exocrine pancreatic function	575	772	748	694	708	599	428	285	320	5129	81.7 %
Intestinal obstruction	11	13	21	32	39	49	18	17	22	222	3.5 %
Acute pancreatitis	.	.	5	6	19	8	8	9	14	69	1.1 %
Treated gastro-oesophageal reflux disease	82	61	106	97	165	166	117	83	127	1004	16.0 %

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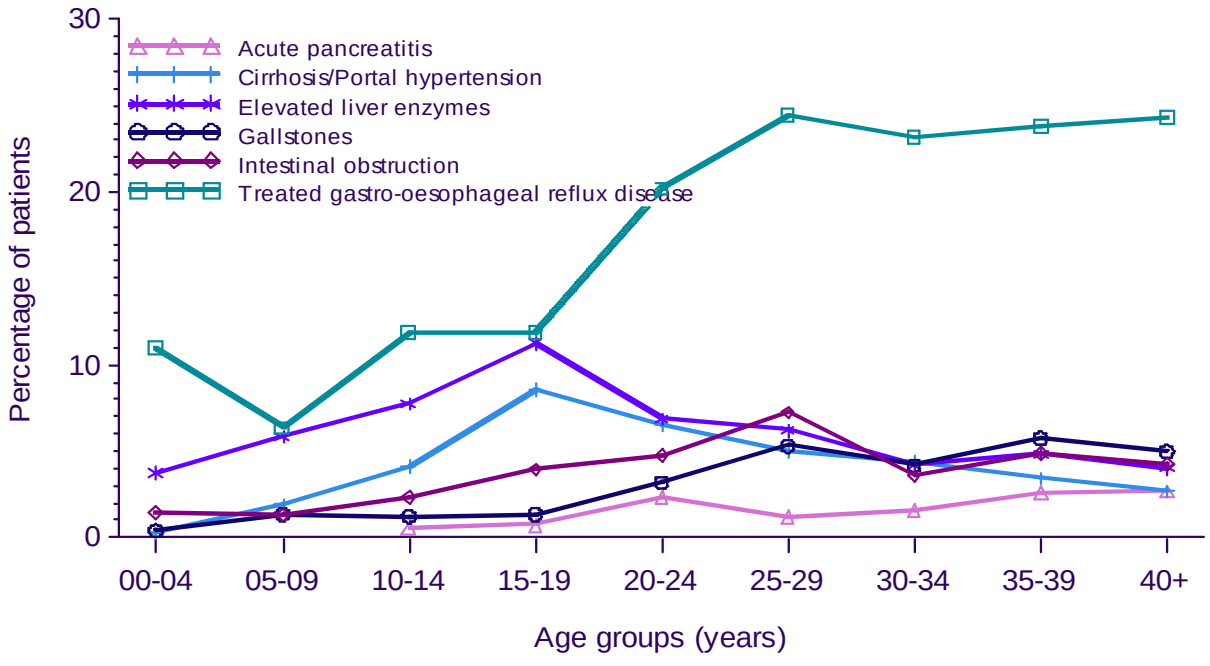
Figure 18. Gastro-intestinal and hepatic complications, by age group

Percentage of age groups reporting complications



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Complications

Diabetes mellitus

Table 13. 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	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*	.
Total diabetes *	2	12	42	129	195	212	174	142	158	1066	17.0 %
Non insulin-dependent diabetes	.	3	10	29	44	40	29	31	35	221	3.5 %
Insulin-dependent diabetes	2	9	32	104	154	178	148	113	125	865	13.8 %
Degenerative complications of diabetes	.	.	1	.	4	5	12	7	6	35	0.6 %

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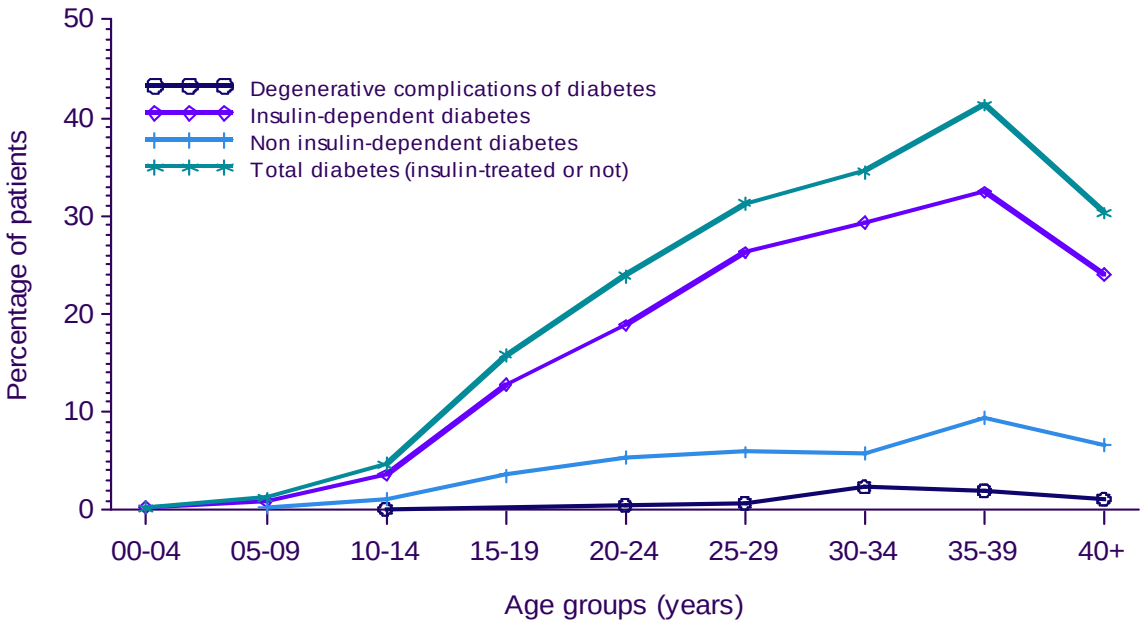
* The line « Total diabetes » sums the number of patients having at least one type of diabetes (insulin-dependent and non insulin-dependent diabetes). Among the 1066 patients, 20 patients presented with both types of diabetes during the year.

Figure 19. Diabetes mellitus and degenerative complications of diabetes, by age group

Percentage of age groups reporting complications



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Complications

Other complications

Table 14. 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	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*	.
Arthropathy	.	6	10	15	16	19	14	10	29	119	1.9 %
Cancer	.	1	.	2	4	2	7	5	15	36	0.6 %
Depression (evaluated and followed)	.	1	4	17	26	28	28	19	46	169	2.7 %
Urinary incontinence	.	4	3	7	7	8	7	5	9	50	0.8 %
Terminal renal failure	.	.	.	2	1	4	9	8	14	38	0.6 %
Bone disease	.	4	14	23	35	56	35	44	70	281	4.5 %
Deafness/Hypoacusia	1	4	13	14	29	43	39	25	40	208	3.3 %

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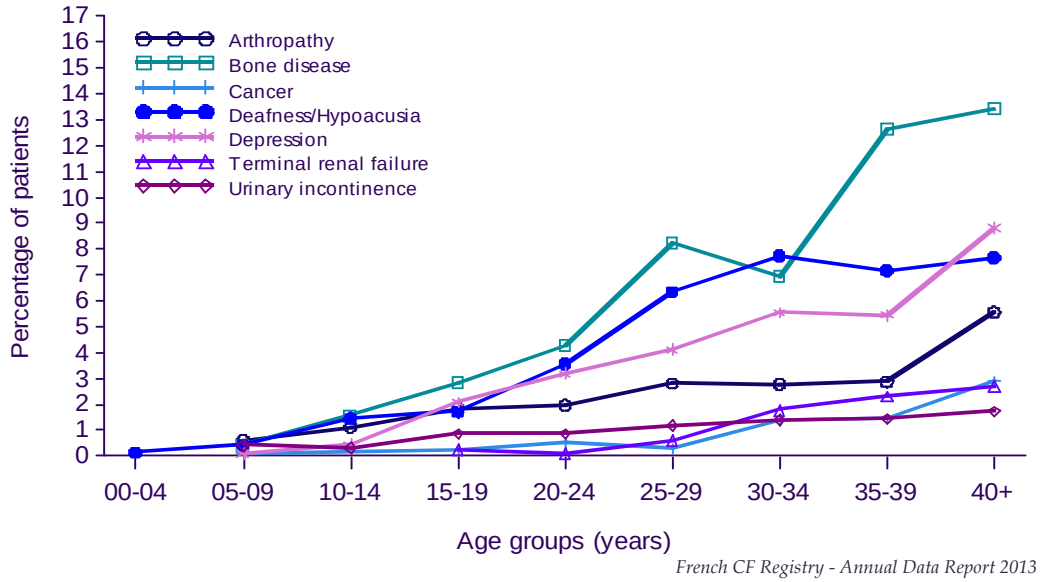
Figure 20. Other complications, by age group

Percentage of age groups reporting complications



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Organ transplant

Tableau 15. Characteristics of the patients on waiting list and of transplant recipients

	All years	In 2013
WAITING LIST	All waiting patients	Listed in 2013
Nb of patients	**152**	**101**
Mean age (years)	27.9	27.7
Extremes of age (years)	8.4-61.5	8.4-61.5
Deaths on waiting list	2	2
TRANSPLANTATION	All transplanted*	Transplanted in 2013
Nb of patients	**638**	**101**
Transplant type:		
- bilateral lung - N (%)	571 (89.5 %)	85 (84.2 %)
- liver - N (%)	19 (3.0 %)	1 (1.0 %)
- kidney - N (%)	31 (4.9 %)	4 (4.0 %)
- other organs - N (%)	9 (1.4 %)	2 (2.0 %)
Combined transplantations:		
- heart-lung - N (%)	30 (4.7 %)	1 (1.0 %)
- heart-lung / liver - N (%)	2 (0.3 %)	
- bilateral lung / liver - N (%)	19 (3.0 %)	6 (5.9 %)
- bilateral lung / kidney - N (%)	4 (0.6 %)	1 (1.0 %)
- liver / kidney - N (%)	2 (0.3 %)	
- other combined transplant - N (%)	6 (0.9 %)	1 (1.0 %)
Mean age (years)	32.5	28.5
Extremes of age (years)	8-61.8	8.4-61.5
Post-transplantation deaths in 2013	24	8

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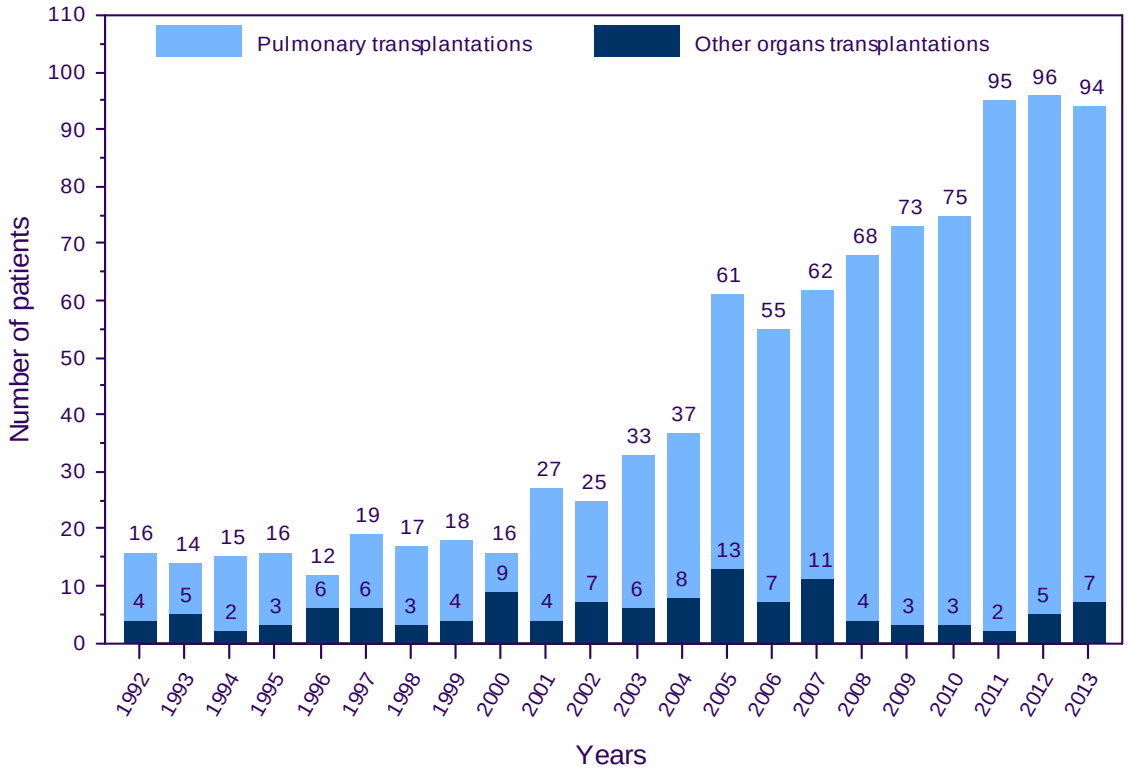
* 48 patients underwent two or more organ transplants.

Transplantations

Figure 21. Annual number of transplanted patients, since 1992



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Inpatient and outpatient visits

Table 16. Characteristics of hospital visits

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	
All patients	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*
< 4 visits* per year	151	221	169	171	246	213	160	121	212	1664
>= 4 visits* per year	595	737	722	644	569	464	344	227	309	4611
Outpatient visits										
Median	3	3	3	3	3	3	3	3	2	3
Mean	3.5	3.3	3.4	3.8	3.7	3.6	3.7	3.3	3.1	3.5
One-day visits										
Median	3	3	3	3	2	2	2	2	2	2
Mean	3.4	3	3.5	3.4	2.9	3.2	3.1	2.9	2.8	3.2
Inpatient visits										
Median	1	1	1	2	1	1	2	2	1	1
Mean	1.7	1.6	1.9	2.3	2.4	2.3	2.4	2.6	1.9	2.1
Days (median)	8	6	6	9	11	11	9	12	10	9
Days (mean)	15.8	10.9	12.7	17.4	23.3	19.2	17.7	24.6	18.6	17.9

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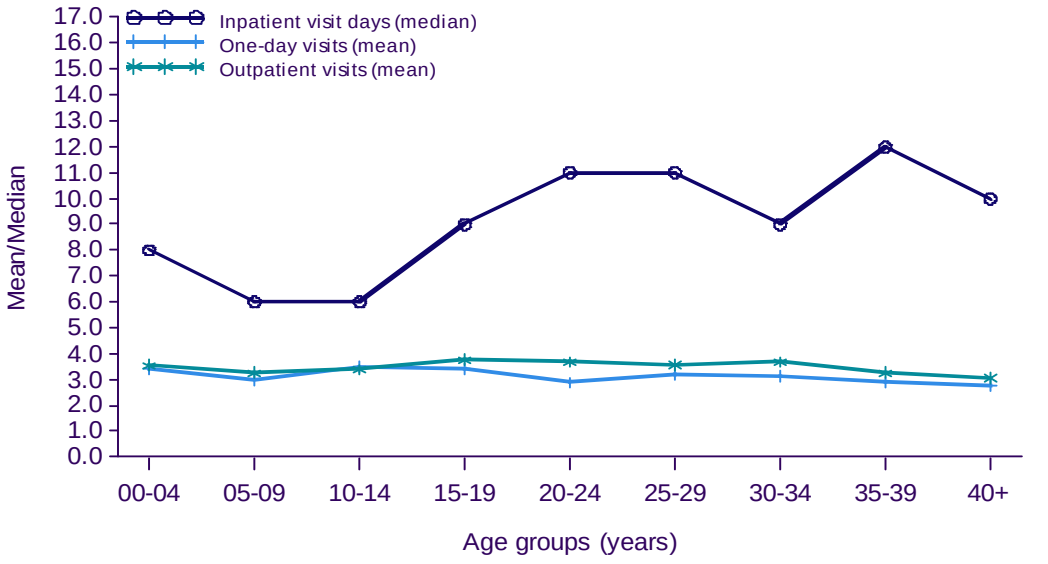
* Outpatient, One-day and Inpatient visits.

Figure 22. Hospital visits, by age group



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Therapeutic management

IV antibiotic courses – TIVAD

Table 17. Patients with 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	746	958	891	815	815	677	504	348	521	6 275
Nb of patients with at least 1 course	55	137	232	306	398	335	224	138	186	2 011
- and with TIVAD*	5	37	85	131	226	177	129	80	84	954
Nb of courses	73	248	486	689	1 043	780	529	292	361	4 501
Nb of days of courses incl:	914	3 445	7 963	10 949	14 349	12 096	8 412	4 524	6 209	68 861
- at hospital	651	1 355	2 544	2 799	3 614	2 559	1 539	1 057	1 497	17 615
- at home	263	2 132	5 338	7 604	10 459	9 215	6 898	3 406	3 724	49 039
TIVAD* (with and without course)	7	47	107	150	270	228	169	100	119	1 197

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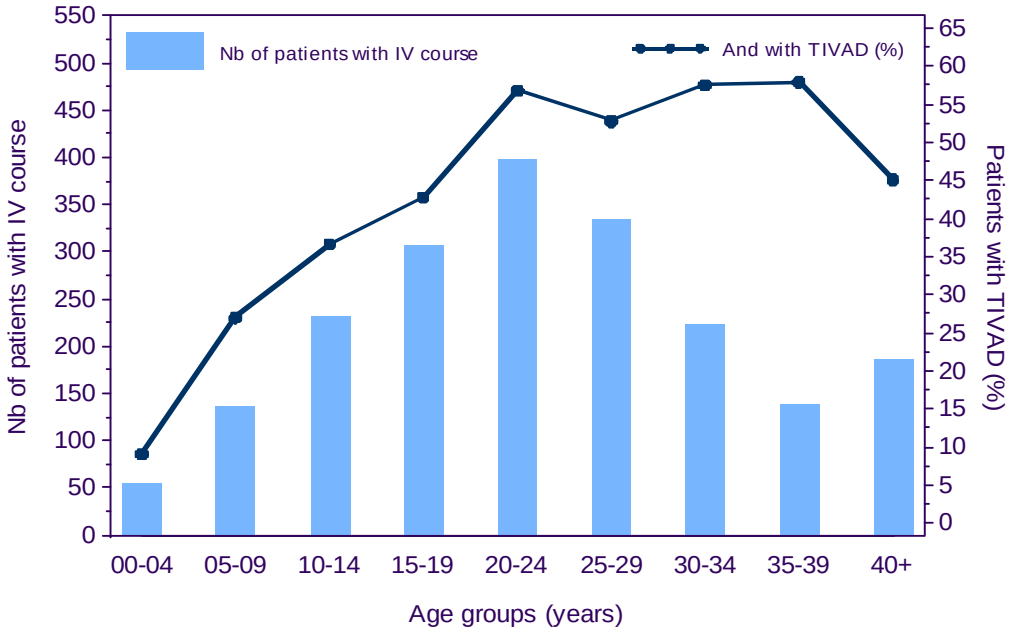
Figure 23. Patients with at least one IV antibiotic course and a TIVAD*, by age group



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* TIVAD: Totally Implantable Vascular Access Device

Therapeutic management

IV antibiotic courses

Table 18. Repartition of IV antibiotic courses

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	
Courses										
Mean	1.3	1.8	2.2	2.3	2.7	2.4	2.5	2.3	2.0	2.3
Standard deviation	0.7	1.7	1.8	1.6	4.9	2.2	1.7	1.5	1.3	2.7
Median	1	1	2	2	2	2	2	2	2	2
Days of courses										
Mean	17.2	26.5	35.7	37.8	39.3	38.6	39.9	36.2	34.5	36.4
Standard deviation	9.8	22.9	36.7	37.6	38.4	41	34.2	31.2	42.5	36.9
Median	15	15	28	28	30	28	28.5	28	26	28

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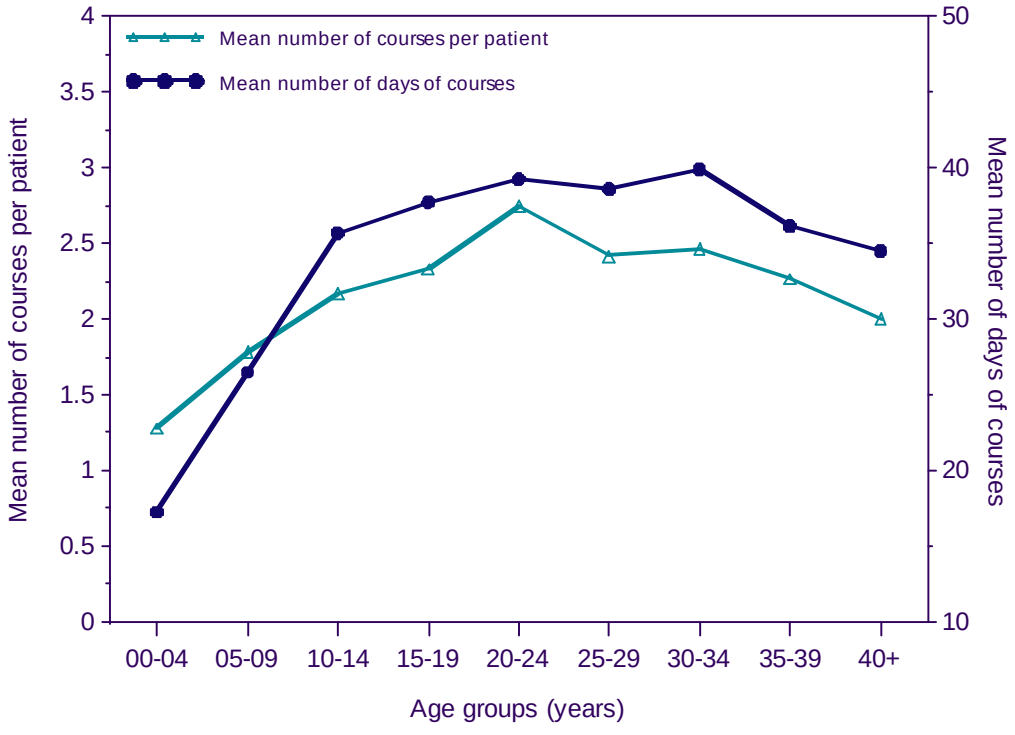
Figure 24. Mean number of IV antibiotic courses and of days of courses, by age group



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Therapeutic management

Respiratory

Table 19. Respiratory therapeutics

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*	.
Aerosol therapy*	348	738	772	714	675	533	374	255	371	4780	76.2 %
NSAID	11	25	50	54	30	19	20	5	22	236	3.8 %
Azithromycin	73	247	392	406	450	396	286	205	250	2705	43.1 %
Oxygen therapy	2	8	18	31	55	47	37	35	54	287	4.6 %
Oral steroids	11	35	75	98	118	145	135	93	128	838	13.4 %
Nasal ventilation	1	5	21	26	41	31	20	20	42	207	3.3 %

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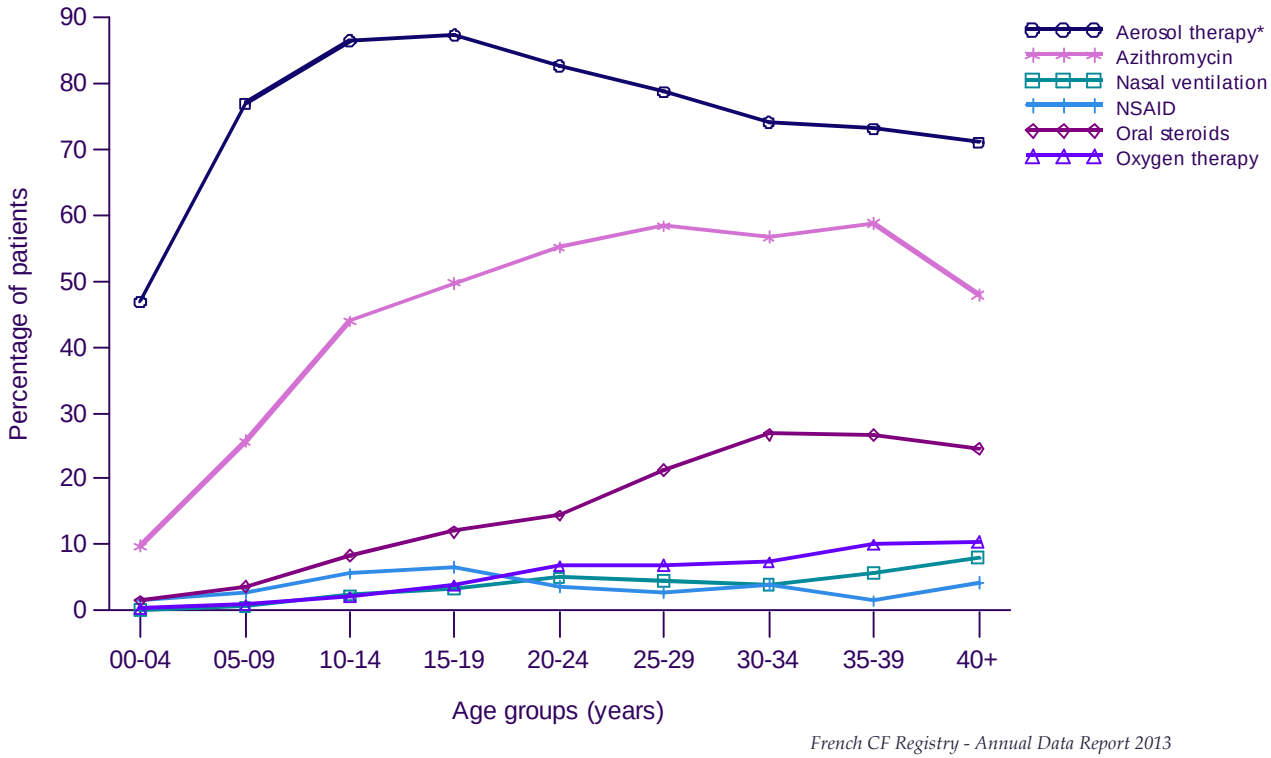
NSAID: Non-steroidal anti-inflammatory drugs.

Figure 25. Respiratory therapeutics, by age group



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* By nebulization, spray or powder

Therapeutic management

Aerosoltherapy

Table 20. Aerosoltherapy treatments

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*794*	*949*	*868*	*795*	*816*	*655*	*479*	*320*	*469*	*6145*	.
Patients under aerosol therapy*	348	738	772	714	675	533	374	255	371	4780	76.2 %
Inhaled antibiotics:	122	223	337	396	397	347	241	164	195	2422	38.6 %
- *Tobramycin*	72	125	236	249	243	204	117	69	64	1379	22.0 %
- *Colistin*	73	126	191	230	217	186	124	94	126	1367	21.8 %
- Aztreonam	.	3	10	14	23	33	23	5	22	133	2.1 %
Inhaled bronchodilatators	194	423	506	465	457	380	270	189	272	3156	50.3 %
Inhaled corticosteroids	181	392	439	377	327	261	173	128	210	2488	39.6 %
Inhaled hypertonic saline	23	36	55	47	31	25	25	17	23	282	4.5 %
RhDNase	103	561	618	535	410	286	171	107	146	2937	46.8 %

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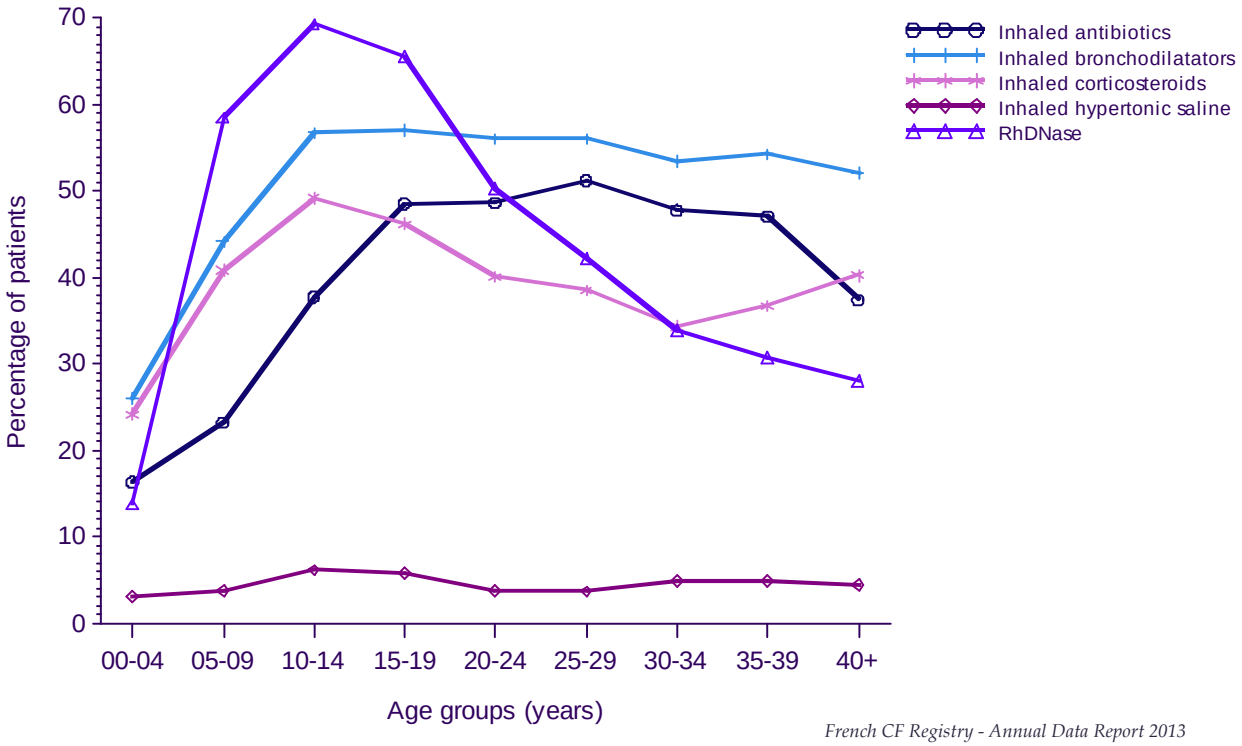
* By nebulization, spray or powder

Figure 26. Aerosoltherapy treatments, by age group



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Therapeutic management

Digestive and nutritional/ CFTR gene modulator

Table 21. Hepatic, digestive and nutritional treatments CFTR gene modulator

	Age groups (years)										
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	Total	%
All patients	*746*	*958*	*891*	*815*	*815*	*677*	*504*	*348*	*521*	*6275*	
Hepatic, digestive and nutritional treatments											
Ursodeoxycholic acid	122	250	357	347	319	273	163	99	112	2042	32.5 %
Anti-acids	258	340	380	388	397	370	261	198	258	2850	45.4 %
Pancreatic enzymes	580	772	750	700	708	601	429	285	314	5139	81.9 %
Tube supplemental feeding	25	34	75	68	55	33	20	10	10	330	5.3 %
Oral supplemental feeding	166	273	347	274	277	248	171	93	107	1956	31.2 %
Fat-soluble vitamins	678	902	840	756	725	604	444	292	367	5608	89.4 %
CFTR gene modulator											
Ivacaftor	.	11	13	16	12	8	7	4	9	80	1.3 %

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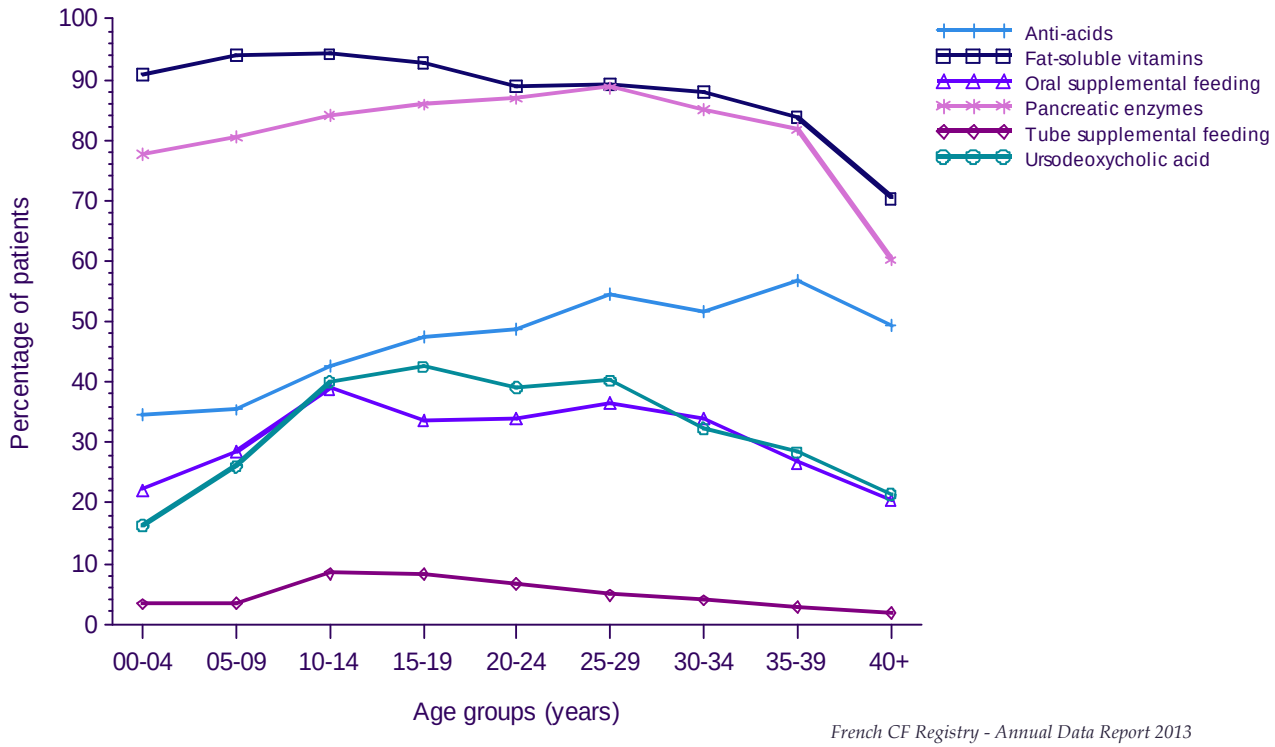
Figure 27. Hepatic, digestive and nutritional treatments, by age group



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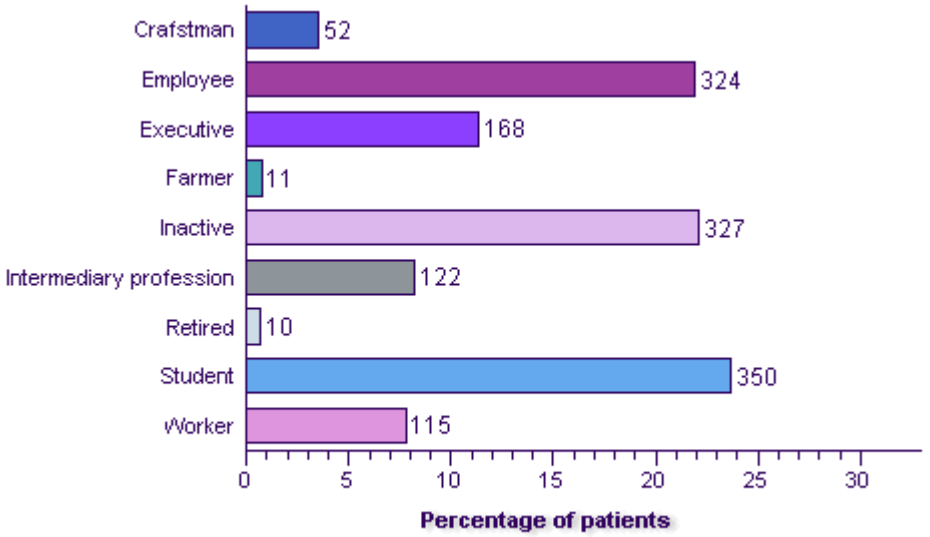
Social data

Employment

Figure 28. Employment of men ≥ 18 years

N = 1479 (number of men with a known employment situation, corresponding to 89.2 % of adults men).



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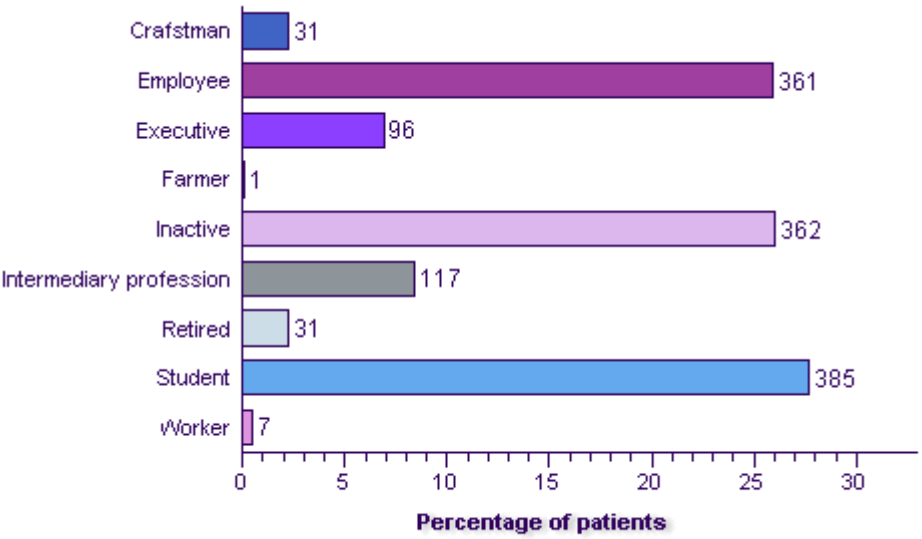
There are 47.9 % of students among men from 18 to 25 years old.

Figure 29. Figure 29. Employment of women ≥ 18 years

N = 1391 (number of women with a known employment situation, corresponding to 91.5 % of adults women).



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There are 55.8 % of students among women from 18 to 25 years old.

Social data

Marital status

Figure 30. Marital status of men ≥ 18 years

N = 1492 (number of men with a known marital status, corresponding to 90 % of adults men).

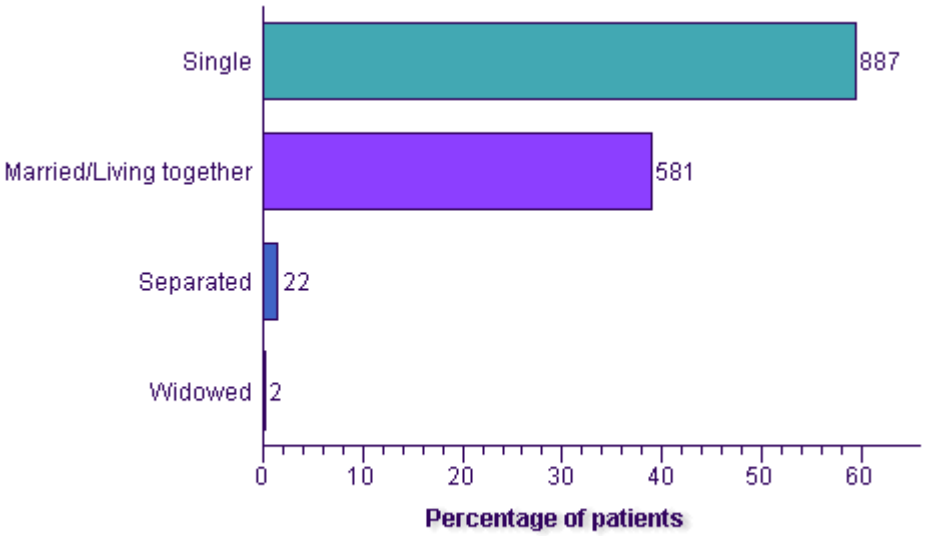

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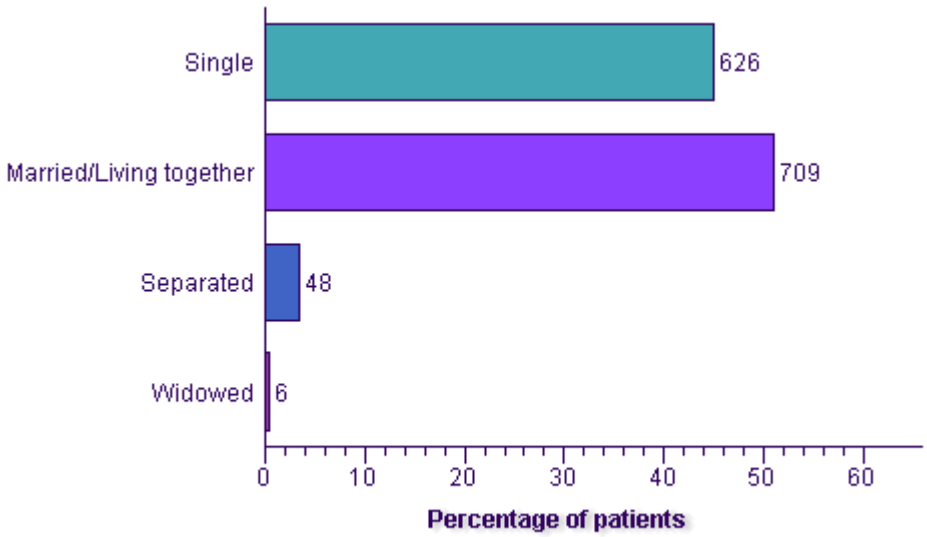
Figure 31. Marital status of women ≥ 18 years

N = 1389 (number of women with a known marital status, corresponding to 91.4 % of adults women).



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Annex 1 (1/2)

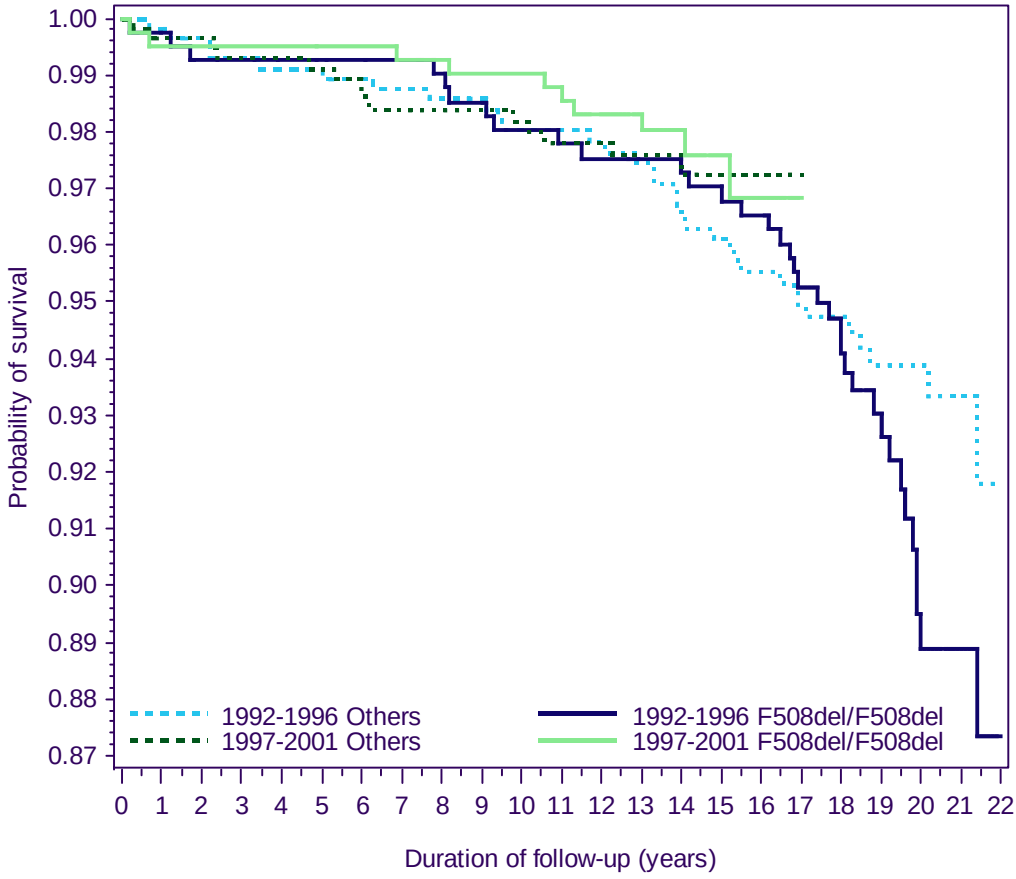
- Complement on survival analysis – stratification by genotype

Figure 32. Survival curves by birth cohort and genotype (Kaplan-Meier method)

The survival analysis (fig. 4) was completed for the oldest birth cohorts, stratified according to the **genotype**:

- Births from 1992 to 1996:
  - F508del/F508del : 413 patients, 35 deaths
  - other genotypes : 567 patients, 33 deaths

- Births from 1997 to 2001:
  - F508del/F508del : 421 patients, 10 deaths
  - other genotypes : 566 patients, 14 deaths



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There is no significative survival difference between those cohorts (Log-Rank test = 3.24, p = 0,35).

Annex 1 (2/2)

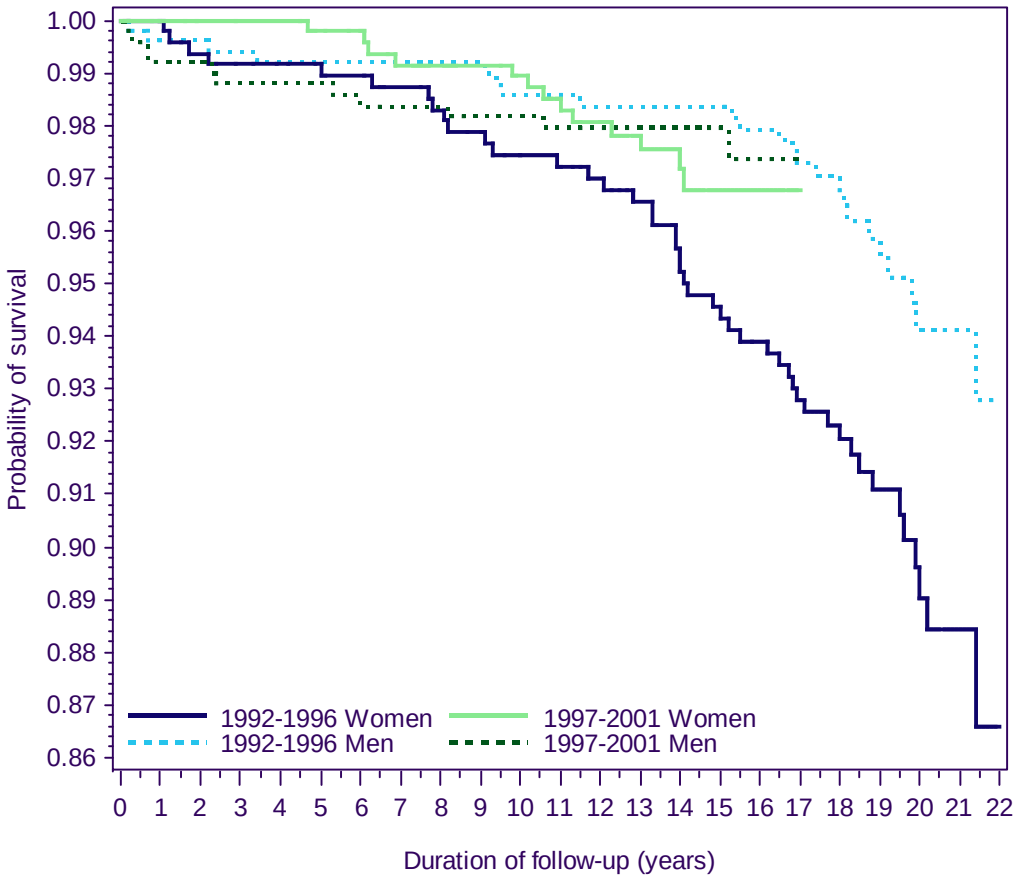
- Complement on survival analysis – stratification by sex

Figure 33. Survival curves by birth cohort and gender (Kaplan-Meier method)

The survival analysis (fig. 4) was completed for the oldest birth cohorts, stratified according to the **gender**:

- Births from 1992 to 1996:
  - men : 501 patients, 23 deaths
  - women : 479 patients, 45 deaths

- Births from 1997 to 2001:
  - men : 500 patients, 11 deaths
  - women : 486 patients, 13 deaths



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There is a significant survival difference in the 1992-1996 cohorts, men vs women (Log-Rank test = 8.86, p = 0,03) but no difference in the 1997-2001 cohorts.

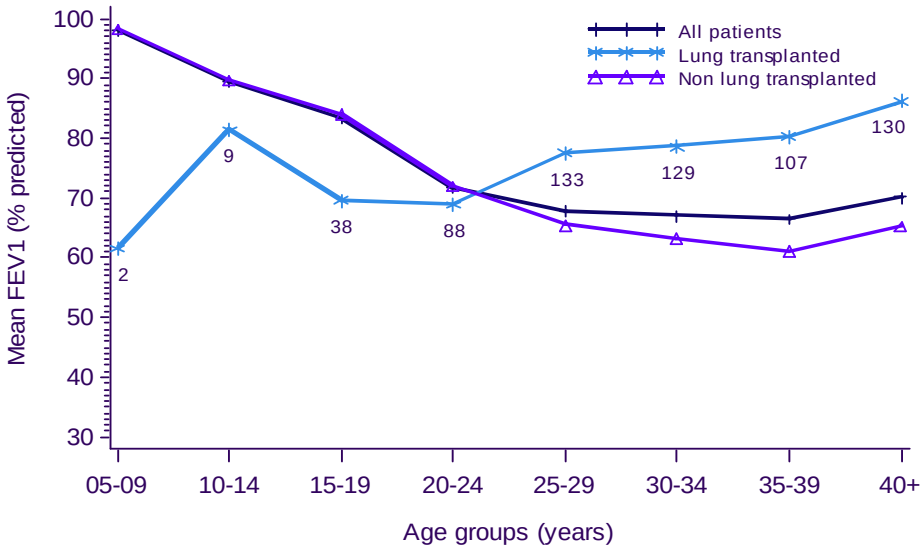
Annex 2

Spirometry and transplantation

To provide a more comprehensive picture, further comparisons were made using curves of FEV_1 by age: mean FEV_1 (% predicted) of all patients was compared to the one of patients who had or had not received a heart-lung or bilateral lung transplant (figure 34).

The curves of the whole population and of non-transplanted patients are identical up to age 20-24. Above 25 years, mean FEV_1 (% predicted) of non-transplanted patients drops more sharply than that of the total population, with a difference of almost 5 percentage points at ages 35-39. Among older patients (aged 40 or above) an slightly upward trend is observed for both patient categories, suggesting a selection effect of patients with the mildest forms of CF at these ages.

Figure 34. Mean FEV_1 (% predicted) and transplantation, by age group



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« Lung transplanted » curve :

- Values are the number of lung transplanted patients in each age group.

Annexe 3 (1/2)

- Participating centres

Table 22. List of the participating CF centres

CRCMs	Number of patients*
Paediatric CF centres	
AMIENS Picardie CHU Sud	91
BORDEAUX Groupe Pellegrin Hôpital d'Enfants	165
GRENOBLE Hôpital de la Tronche Pédiatrie	119
LE HAVRE Hôpital Flaubert	26
LILLE Hôpital Jeanne de Flandres Pédiatrie	186
LISIEUX Centre Hospitalier Robert Bisson	22
LYON Hôpital Mère-Enfant / Groupt Hosp. Est	299
MARSEILLE Hôpital La Timone Pédiatrie	124
NANCY Hôpital d'enfants	133
NANTES Hôpital Mère-Enfant	103
NICE CHU Lenval - Hôpital Pasteur	96
PARIS Hôpital Armand Trousseau	78
PARIS Hôpital Necker	190
PARIS Hôpital Robert Debré	165
RENNES - ST BRIEUC Pédiatrie	143
ST DENIS DE LA REUNION Hôpital d'Enfants	46
TOULOUSE Hôpital des Enfants	129
TOURS Hôpital de Clocheville Pédiatrie	121
VERSAILLES Hôpital Mignot Pédiatrie	67
Adults CF centres	
BORDEAUX-PESSAC Groupe Sud Hospitalier	97
GRENOBLE Hôpital de la Tronche Pneumologie	80
LILLE Hôpital Calmette Pneumologie	196
LYON SUD Centre Hospitalier	293
MARSEILLE CHU Nord	199
NANCY Hôpital de Brabois Pneumologie	100
NANTES Hôpital Laënnec	196
PARIS Hôpital Cochin	387
RENNES Hôpital Pontchaillou Pneumologie	97
SURESNES Hôpital Foch	382
TOULOUSE Hôpital Larrey Pneumologie	158
TOURS Hôpital Bretonneau Pneumologie	52
Paediatric and Adults CF centres	
ANGERS - LE MANS	120
BESANCON	120
CAEN	88
CLERMONT FERRAND CHU d'Estaing	99
CRETEIL Centre Hospitalier Intercommunal	104
DIJON Hôpital d'Enfants du Bocage	120
DUNKERQUE Centre Hospitalier	66
GIENS Hôpital Renée Sabran	220
LENS Centre Hospitalier	42
LIMOGES Hôpital Mère/Enfant	61
MONTPELLIER Hôpital Arnaud de Villeneuve	198
POITIERS Hôpital La Milétrie	41
REIMS American Memorial Hospital	125
ROSCOFF Centre de Perharidy	139
ROUEN	169
ST PIERRE DE LA REUNION Groupe Hosp. Sud	75
STRASBOURG	244
VANNES-LORIENT	83

Annex 3 (2/2)

Participating centres

Table 23. List of the participating centres (non accredited CF centres)

Centres	Number of patients*
Paediatric local centres	
BREST Hôpital Augustin Morvan	6
COLMAR CHG Louis Pasteur Pédiatrie	4
DAX Centre Hospitalier	11
MONTLUCON Centre Hospitalier	9
MULHOUSE Centre Hospitalier Pédiatrie	14
ST ETIENNE Hôpital Nord	2
ST TROJAN LES BAINS Centre Hélio Marin	1
Adult local centres	
MULHOUSE Centre Hospitalier Pneumologie	4
Paediatric and Adult local centres	
BRIVE Centre Hospitalier	13
ST NAZAIRE Centre Hospitalier	23
Other centres	
DIEULEFIT Centre Médical/Climatique Bellevue	1
PARIS Hôpital Européen G.Pompidou	26
POINTE A PITRE CHU	8

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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 2013 were excluded from those statistics.

Annex 4 (1/2)

Table 24. Data summary

	2011	2012	2013
Patients seen during the year and centres participating to the registry			
- Patients registered* (N):	6046	6196	6329
- Patients seen during the year in a centre** (N):	5993	6145	6275
- Centres (N) :	65	63	62
Paediatric CRCMs	19	19	19
Adult CRCMs	12	12	12
Paediatric and Adult CRCMs	18	18	18
Other centres:	16	14	13
Demographics			
- Male patients (%) :	51,7	51,6	51,7
- Age of patients, in years (mean):	18,7	19,2	19,7
- Age of patients, in years (median):	17	17	18
- Age of patients. in years (min-max):	0 – 87	0 – 86	0 – 82
- Patients aged 18 years and over (%):	48,7	49,6	50,6
- Early pregnancies during the year (N):	61	53	45
- Pregnancy rates in women aged 15 to 49 ans (for 1 000):	41,6	34,4	27,9
- Age of patients at onset of pregnancy, in years (mean):	28,7	27,7	28,9
- Deaths (N):	67	52	53
Including death of patients not seen during the year:	9	12	11
- Crude death rate (for 1 000):	11,4	8,5	8,5
- Age at death, in years (mean):	26,4	33	35
- Age at death, in years (median):	25	29	31
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	2.8	2.6	2.5
- New patients diagnosed during the year (N):	215	188	165
Including by neonatal screening:	131	124	90
- Age at diagnosis of the new patients, in years (median):	1.3	1.3	1.9
- Age at diagnosis of the new patients, in years (min-max):	0 – 69	0 – 72	0 – 72
- Full genotypes identified (%):	94,9	94,6	94,6
F508del / F508del:	43,3	42,3	42,4
F508del / Other:	38	38,9	38,9
Other / Other:	13,1	13,4	13,3
F508del / Missing:	1,9	1,7	2,1
Other / Missing:	1,2	0,9	1,5
Missing / Missing:	2,5	2,8	1,9
Anthropometry and spirometry			
- Height z-score, patients aged 17 years and less (mean):	-0,08	-0,10	-0,03
- Height z-score, patients aged 18 years and over (mean):	-0,52	-0,51	-0,50
- Weight z-score, patients aged 17 years and less (mean):	-0,33	-0,30	-0,23
- Weight z-score, patients aged 18 years and over (mean):	-0,41	-0,34	-0,30

* 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 24. Data summary

	2011	2012	2013
Spirometry			
- FEV_1 (% predicted) - Knudson, patients aged 17 years and less (mean):	89,7	90,6	90,9
- FEV_1 (% predicted) - Knudson, patients aged 18 years and over (mean):	67,3	68,6	69,6
Microbiology			
- Patients with at least one sputum during the year (%):	91,7	91,2	90,4
H. influenzae:	22,1	22,9	23,2
MSSA:	54,7	54,4	55,4
MRSA:	7,7	7,4	7,7
P. aeruginosa:	42,6	41,8	39,7
S. maltophilia:	9,7	9,9	10,5
B. cepacia:	1,9	1,7	1,9
Aspergillus:	22,6	23,8	23,2
Complications			
- Treated aspergillosis (%) :	12,6	11,3	9,9
- Abnormal exocrine pancreatic function (%) :	82,9	82,3	81,7
- Treated gastro-oesophageal reflux disease (%) :	17	16,4	16
- Bone disease (%) :	5,7	5,2	4,5
- Haemoptysis (%):	5,0	4,6	4,4
- Cirrhosis / portal hypertension (%):	4,1	4,3	4,2
- Insulin-dependent and non insulin-dependant diabetes (%):	15,2	15,8	17
Therapeutic management			
- Pancreatic enzymes (%):	83,2	82,6	81,9
- IV courses (%):	34,6	33,5	32
- Oxygenotherapy (%):	5,9	5,3	4,6
- Nasal ventilation (%):	4,8	4,1	3,3
- Azithromycin (%):	42,1	43,1	43,1
- Inhaled antibiotics (%):	37,3	38,9	38,6
- rhDNase (%):	46,9	46,3	46,8
- Inhaled bronchodilatators (%):	49	50,5	50,3
- Inhaled corticosteroids (%):	39,2	39,6	39,6
- Transplanted patients (N):	529	573	638
Including patients transplanted during the year:	97	101	100
- Patients on waiting list (N):	177	153	152
Including patients listed during the year:	98	96	102
Deaths on waiting list:	0	3	2

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Annex 5

Table 25. Data summary: Transplanted versus non-transplanted patients

	Transplanted	Non-transplanted	Registre 2013
Patients seen during the year and centres participating to the Registry			
- Patients seen during the year in a centre (N):	638	5637	6275
Demographics			
- Age of patients, in years (mean):	32,5	18,3	19,7
- Age of patients, in years (median):	31,5	16	18
- Patients aged 18 years and over (%):	95,8	45,5	50,6
- Early pregnancies during the year (N):	6	39	45
- Deaths (N):	28	25	53
Diagnosis and genetics			
- Age at diagnosis, in months (median) :	7,2	2,2	2,5
- Full genotypes identified (%):	94,8	94,5	94,6
F508del / F508del:	55,8	40,8	42,4
F508del / Other:	29,9	39,9	38,9
Other / Other:	9,1	13,8	13,3
F508del / Missing:	1,7	2,1	2,1
Other / Missing:	1,4	1,5	1,5
Missing / Missing:	2	1,9	1,9
Anthropometry			
- Height z-score, patients aged 17 years and less (mean):	-1,62	-0,02	-0,03
- Height z-score, patients aged 18 years and over (mean):	-0,72	-0,45	-0,50
- Weight z-score, patients aged 17 years and less (mean):	-1,72	-0,22	-0,23
- Weight z-score, patients aged 18 years and over (mean):	-0,81	-0,17	-0,30
- BMI z-score, patients aged 17 years and less (mean):	-0,67	-0,16	-0,16
- BMI z-score, patients aged 18 years and over (mean):	-0,55	-0,10	-0,19
Spirometry			
- FEV_1 (% predicted) - Knudson, patients aged 17 years and less (mean):	69,6	91,2	90,9
- FEV_1 (% predicted) - Knudson, patients aged 18 years and over (mean):	78,1	67,6	69,6
Complications			
- Treated aspergillosis (%) :	6,1	10,3	9,9
- Abnormal exocrine pancreatic function (%) :	92,9	80,5	81,7
- Treated gastro-oesophageal reflux disease (%) :	32	14,2	16
- Bone disease (%) :	11,6	3,7	4,5
- Haemoptysis (%):	2,5	4,6	4,4
- Cirrhosis / portal hypertension (%):	5,3	4,0	4,2
- Insulin-dependent and non insulin-dependant diabetes (%):	62,1	11,9	17
Therapeutic management			
- Pancreatic enzymes (%):	95	80,4	81,9
- Oral steroids (%) :	72,6	6,7	13,4

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