



French Cystic Fibrosis Registry

Annual data report 2010

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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 1,600 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 (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 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 *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 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 15%). The 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 the test results are 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. The risk that the child has cystic fibrosis is, in this case, below 1%. 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).

On the pathological level, functional abnormalities occur in the digestive tract, the respiratory tract, the sweat glands and the 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 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

In 1992, the medical Council of the association *Vaincre la Mucoviscidose*, set up a national cystic fibrosis observatory, the *Observatoire national de la mucoviscidose* (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.

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 mucoviscidose*. 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)*.

The population is composed of people with cystic fibrosis followed in the care centres participating in the registry in France (metropolitan France and Reunion Island). 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. Statistical analysis is performed on anonymized data.

Unless otherwise indicated, the results presented hereafter relate to the population seen during the year 2010 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.

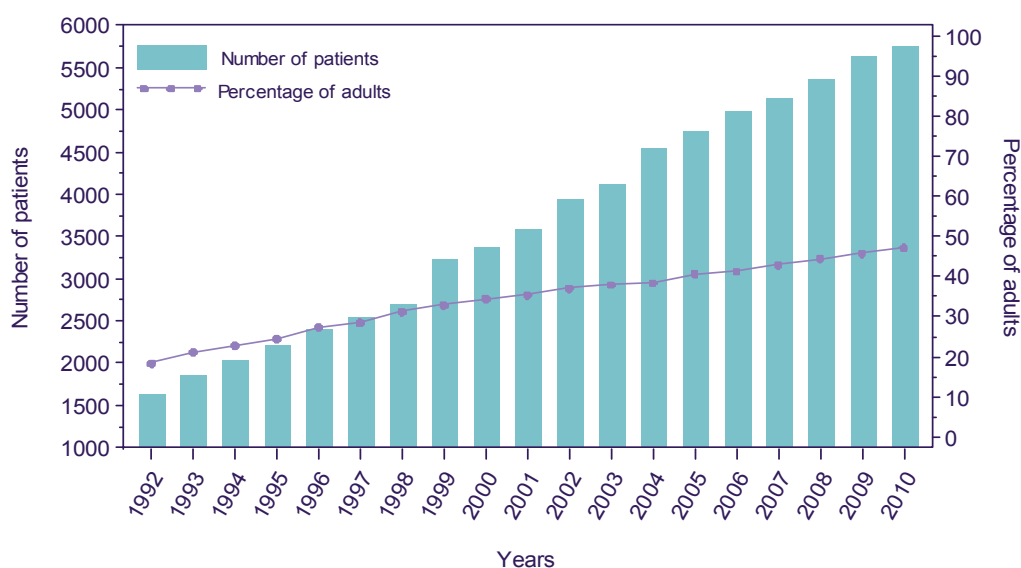
Read precautions before use

Comparisons between the indicators from different countries must be done with care, due to a number of bias coming from the implementation of newborn screening programs, transplantation frequency, socioeconomic status and a limited number of patients in some 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

Indicators	Years of follow-up									
	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
All patients*	3601	3941	4117	4549	4755	5003	5148	5379	5650	5792
Patients seen during the year**	3589	3936	4111	4544	4745	4994	5140	5357	5628	5758
Children	2317	2476	2550	2799	2812	2932	2935	2971	3049	3040
Adults	1272	1460	1561	1745	1933	2062	2205	2386	2579	2718
Over 40 years	90	119	124	160	175	196	226	272	329	358
Men	1875	2054	2157	2368	2497	2595	2686	2786	2916	2958
Women	1714	1882	1954	2176	2248	2399	2454	2571	2712	2800
Mean age (years)	15.2	15.6	15.8	16	16.3	16.4	16.8	17.3	17.7	18.1
Median age (years)	14	14	14	14	15	15	15	16	16	16
Minimum age (years)	0	0	0	0	0	0	0	0	0	0
Maximum age (years)	72	71	77	78	74	76	77	78	79	80

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

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

Demographics

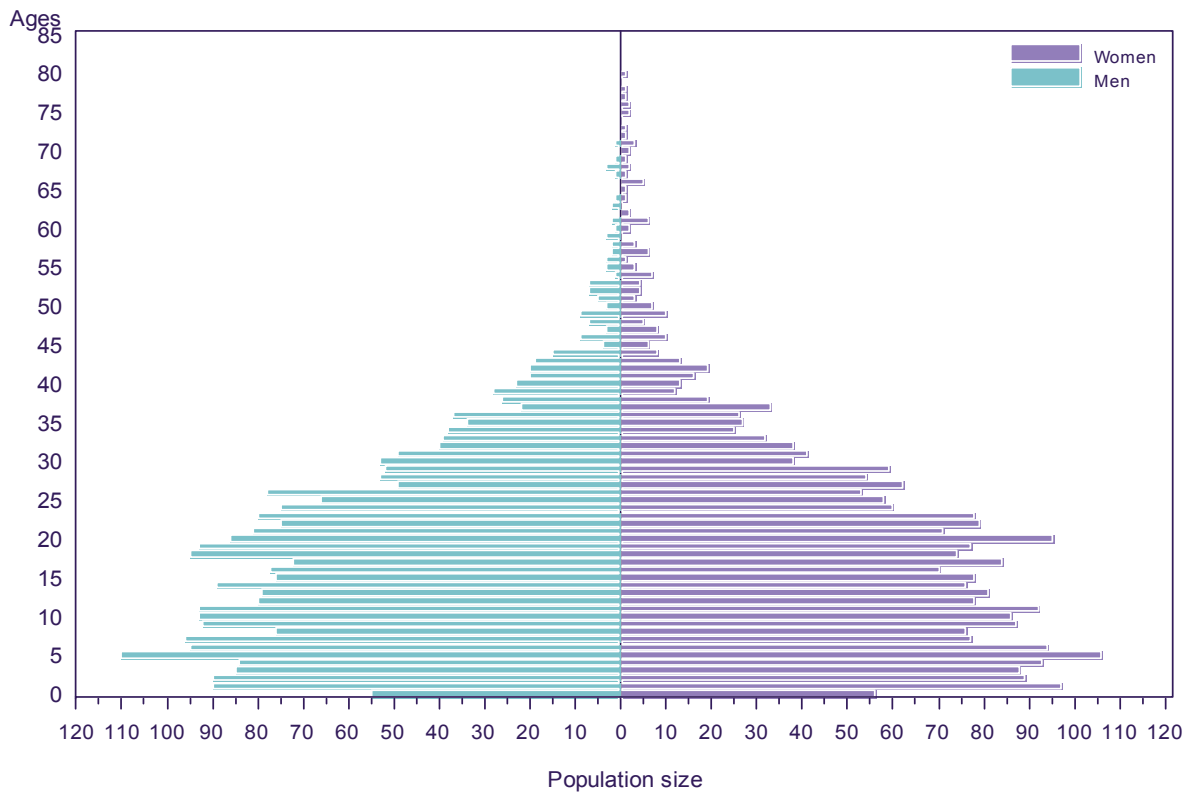
■ Characteristics of the population

Table 2. Characteristics of the population

Characteristics	2008		2009		2010	
	Men	Women	Men	Women	Men	Women
Patients seen during the year	2786	2571	2916	2712	2958	2800
Children	1539	1432	1553	1496	1532	1508
Adults	1247	1139	1363	1216	1426	1292
Mean age (years)	17.1	17.4	17.8	17.6	18.2	18
Median age (years)	16	16	17	16	17	16

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Figure 2. Population pyramid

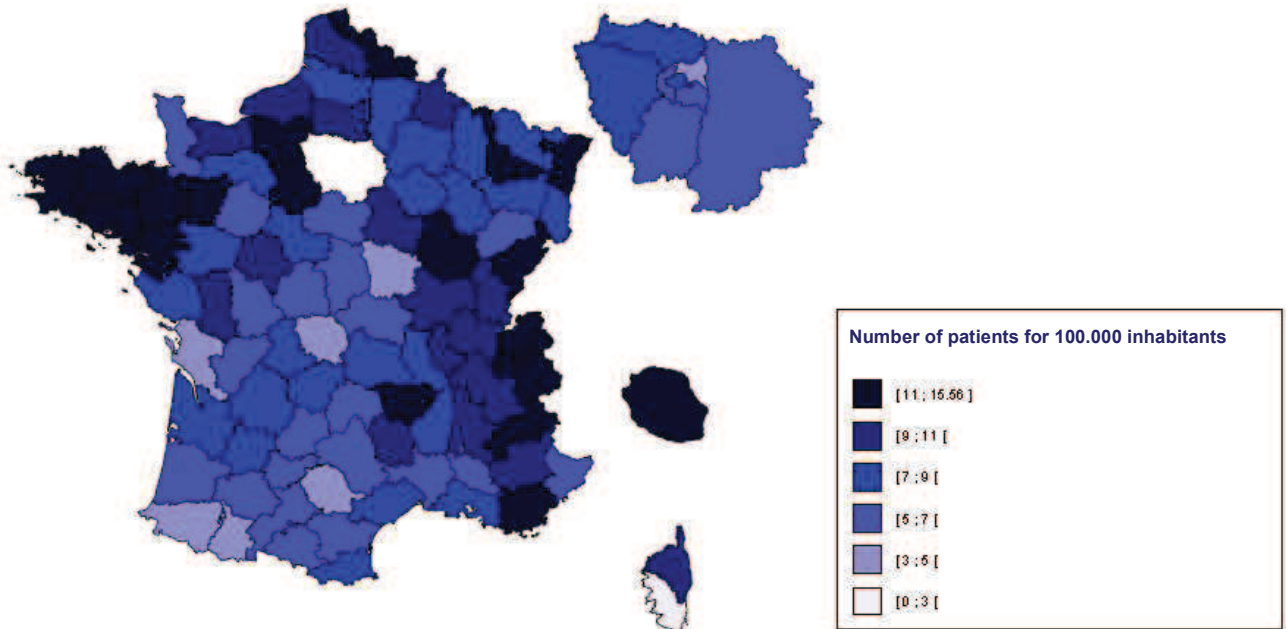


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A total of 111 patients are aged below 1 (0 year completed age). Entry into the registry is delayed the first year of life as a certain number of infants diagnosed through neonatal screening in a given year are not registered until the following year.

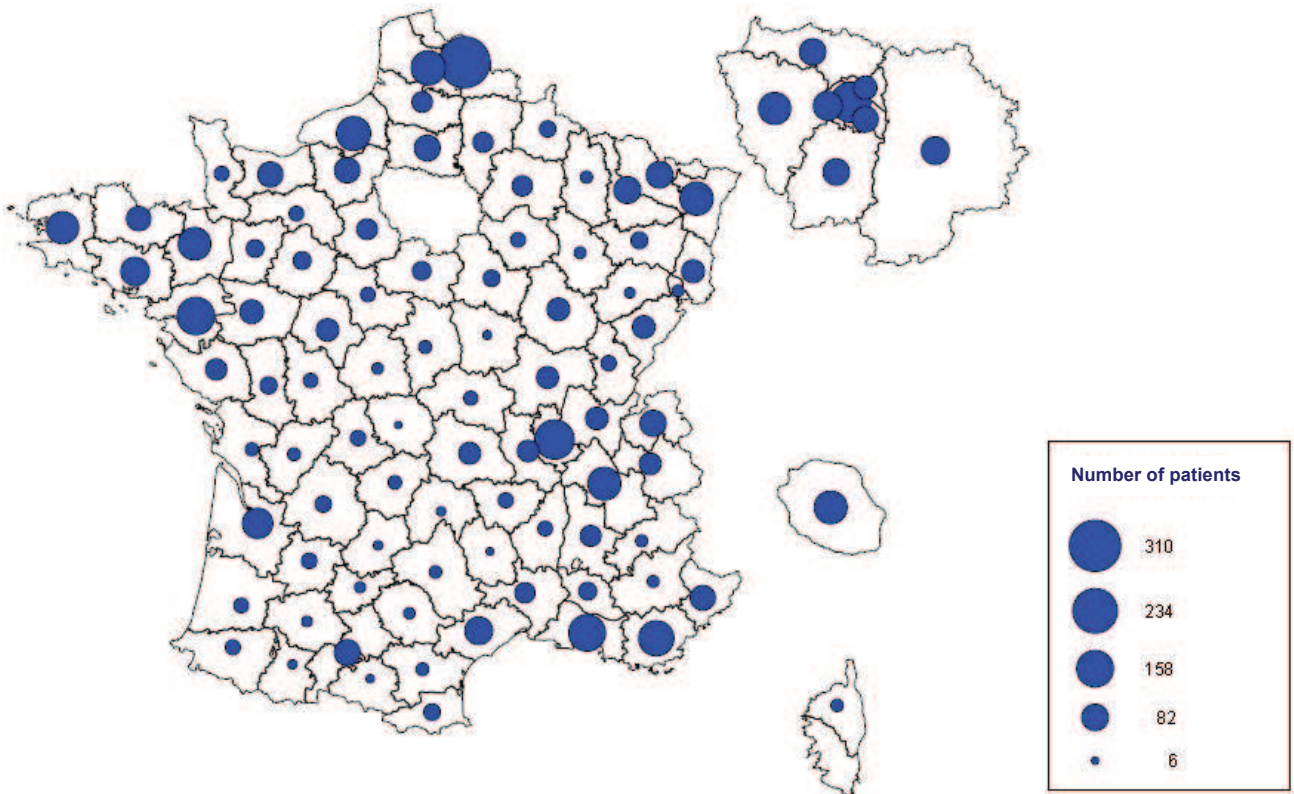
As an indicative reference, 14 children born in 2009 (of whom 7 in December) were diagnosed by neonatal screening in 2010. On the 2009 population pyramid, the number of patients aged 0, which stood at 162, could thus have been 162 + 14 = 176.

Map 1. Prevalence of cystic fibrosis by « département » 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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Demographics

■ Location by type of centre

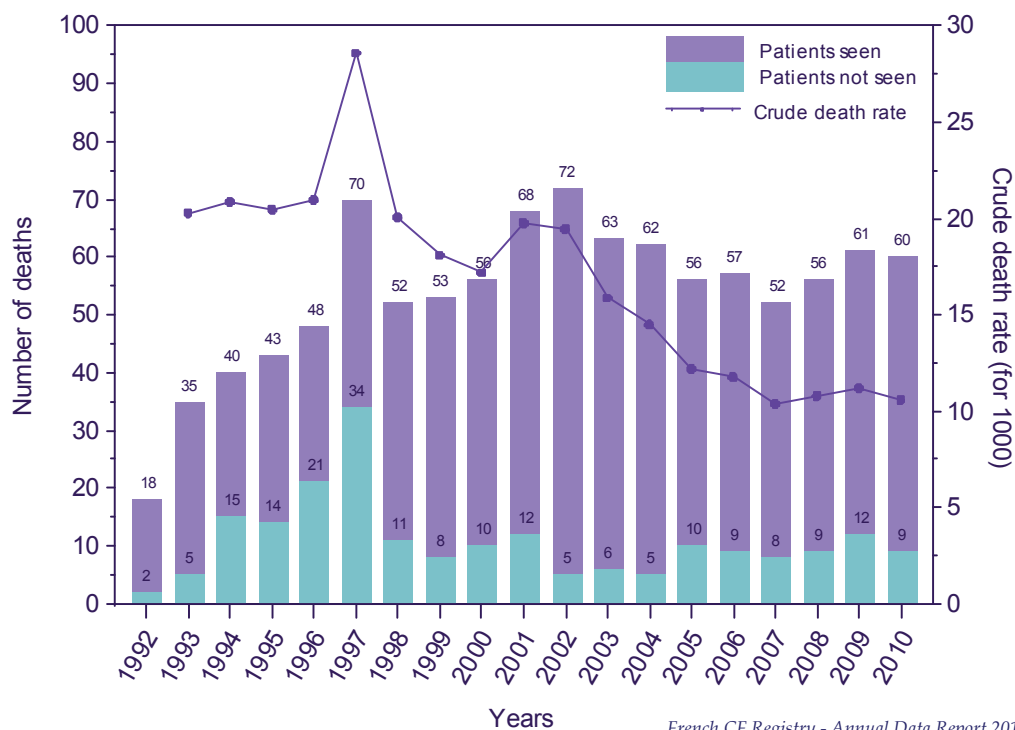
Table 3. Characteristics of the centres

Types of centres	Patients' characteristics				Age of patients (years)				
	Nb	Nb (a)	%	Mean	Min	Max	Mean	Median	Inter-quartile
Paediatric CRCMs*	19	2127	36.9	111.9	0	58	9.7	9.0	9.0
Adult CRCMs*	12	1641	28.5	136.8	14	78	30.1	28.0	12.0
Paediatric/Adult CRCMs*	18	1845	32.0	102.5	0	80	17.3	15.0	18.0
Subtotal	49	5613	97.5	114.5	0	80	18.2	17.0	18.0
Paediatric local Centres	10	117 (b)	2.0	11.7	1	62	15.0	14.0	13.0
Paediatric/Adult local Centres	1	16 (c)	0.3	16.0	8	36	19.8	16.5	16.5
Other Centres	4	12 (d)	0.2	3.0	6	36	16.1	14.5	7.5
Subtotal	15	145	2.5	9.7	1	62	15.6	14.0	12.0
Total	64	5758	100	90	0	80	18.1	16.0	18.0

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

Notes : (a) After checking of patients in the multiple account category (cf page 5)
 (b) Including 49 patients also seen by a CRCM.
 (c) Including 7 patients also seen by a CRCM.
 (d) Including 1 patients also seen by a CRCM.

Figure 3. Annual number of deaths since 1992

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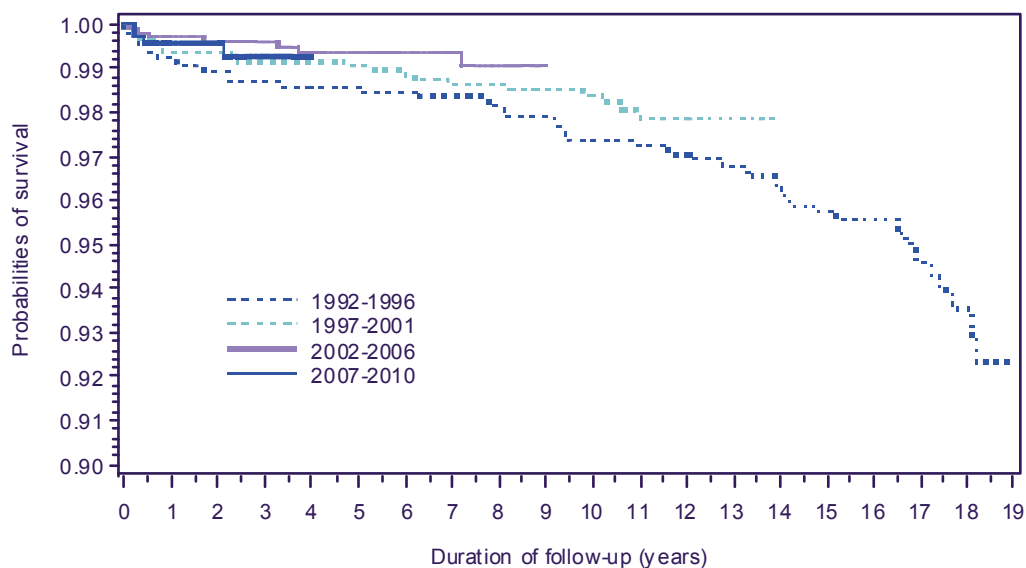
Table 4. Characteristics of mortality

Indicators	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Number of deaths	68	72	63	62	56	57	52	56	61	60
- including patients not seen during the year*	12	5	6	5	10	9	8	9	12	9
- including transplanted patients	10	17	6	10	9	14	22	22	26	27
Mean age (years)	23	22	24	22	24	25	27	28	25	29
Median age (years)	23	21	22	21	21	24	26	27	24	27
Minimum age (years)	0	0	6	0	0	4	10	0	0	0
Maximum age (years)	64	62	65	50	71	68	70	66	73	68

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

Figure 4. Survival curves by birth cohort (Kaplan-Meier method)



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Population : patients seen by participating centres and patients lost to follow-up.

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:

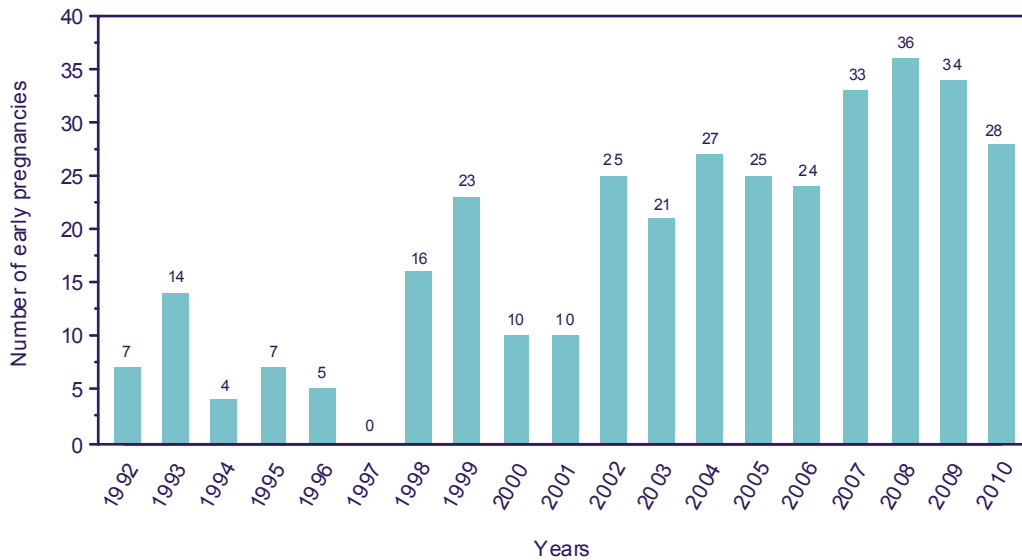
- Births from 1992 to 1996 (in 2010 this cohort was followed during 19 years maximum) : 922 patients, 48 deaths,
- Births from 1997 to 2001 (maximum 14 years of follow up) : 953 patients, 18 deaths,
- Births from 2002 to 2006 (maximum 9 years of follow up) : 997 patients, 7 deaths,
- Births from 2007 to 2010 (maximum 4 years of follow up) : 675 patients, 4 deaths.

There is no significant survival difference between those cohorts (Log-Rank test = 4,94, $p = 0,177$).

Survival analysis by genotype and sex are available on annex 2.

Pregnancy

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



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Table 5. Early pregnancy characteristics

Characteristics	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Number of early pregnancies	10.0	25.0	21.0	27.0	25.0	24.0	33.0	36.0	34.0	28.0
Pregnancy rates in women aged 15 to 49 years (for 1000)	14.2	31.6	24.4	28.6	23.9	21.5	28.2	29.1	25.8	20.1
Mean age at onset of pregnancy	21.2	26.7	27.0	27.5	25.4	25.8	28.6	27.0	28.4	29.2

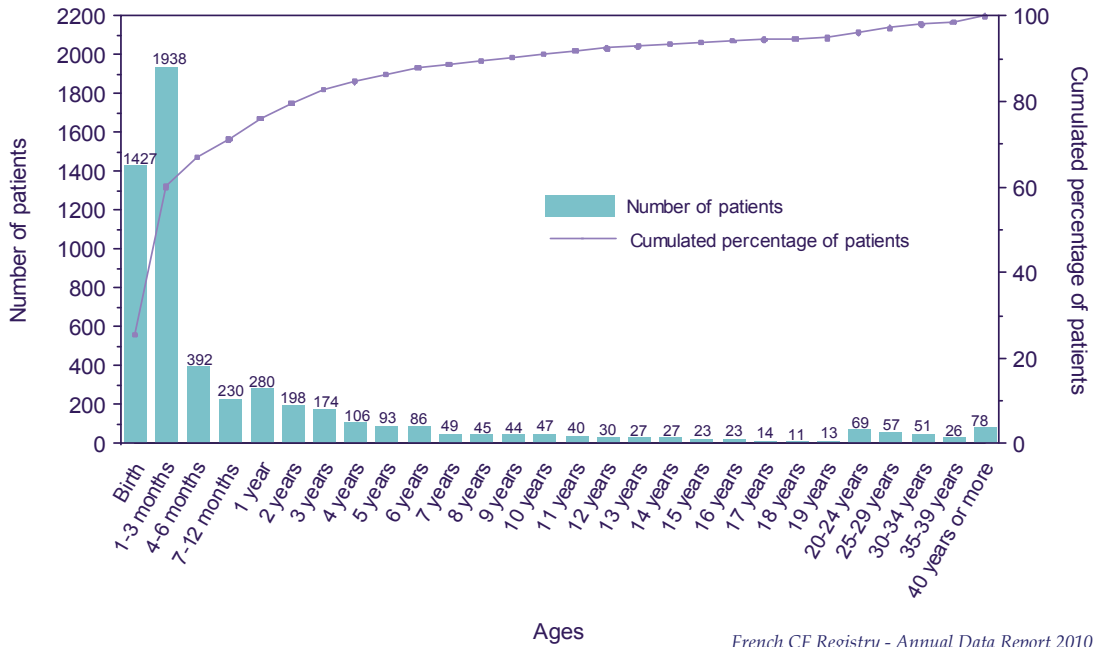
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Diagnosis

■ Main characteristics

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

N = 5 598 (number of patients whose age at diagnosis is known).



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Diagnosis

■ Main characteristics

Table 6. Diagnosis characteristics

Characteristics	2008	2009	2010
ALL PATIENTS			
Patients whose age at diagnosis is known - N (%)	5265 (98.3 %)	5503 (97.8 %)	5598 (97.2 %)
Mean age (months)	36.4	40.1	38.5
Median age (months)	2	2	2
Minimum age (years)	0	0	0
Maximum age (years)	74.8	74.8	74.8
NEW PATIENTS DIAGNOSED DURING THE YEAR			
Number of patients - age at diagnosis (a)			
New patients - N (%)	235 (4.4 %)	232 (4.1 %)	181 (3.1 %)
Mean age (months)	60.4	73.5	77.6
Median age (months)	1	1	2
Minimum age (years)	0	0	0
Maximum age (years)	58.8	72.1	69.1
Context of diagnosis			
Prenatal diagnosis - N (%)	5 (2.1 %)	4 (1.7 %)	8 (4.5 %)
Meconium ileus (MI) - N (%)	27 (11.5 %)	12 (5.2 %)	11 (5.6 %)
Neonatal screening - N (%)	158 (67.2 %)	155 (67.2 %)	112 (62.6 %)
Symptoms (excluding MI) - N (%)	60 (25.5 %)	69 (29.7 %)	56 (30.7 %)
Symptoms (excluding MI) - Mean age (years)	19.2	20.2	19.2

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Notes :

(a) Including family history and antenatal diagnosis.

(b) Patients diagnosed before the results of neonatal screening were excluded.

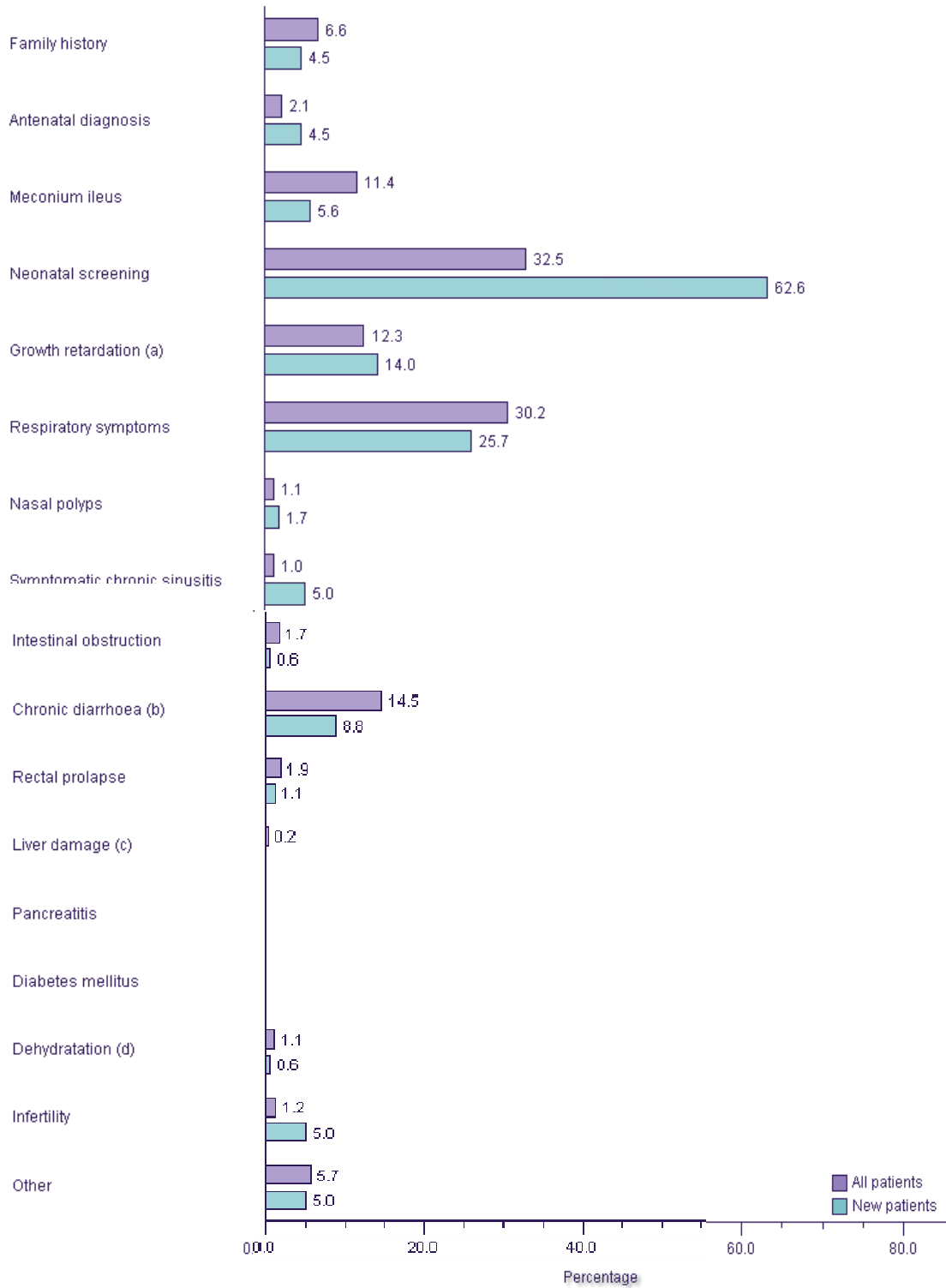
Among the 181 new patients, 111 were born in 2010. The method used to compile this report (patients seen in a care centre in 2010) means that infants born in 2010 and seen for the first time in 2011 are excluded (cf note page 7).

The number of patients diagnosed by neonatal screening (112) 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.

Diagnosis

■ Diagnosis signs

Figure 7. Diagnosis signs



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Notes :

Proportion of patients with respect to the total.

(a) Growth retardation / Malnutrition

(b) Chronic diarrhoea / Steatorrhoea / Malabsorption

(c) Liver damage / Jaundice / Portal hypertension

(d) Dehydration / Electrolyte imbalance

Table 7. Number and proportion of genotypes

Genotypes	Number of patients	%
F508del / F508del	2511	43.6
F508del / G542X	177	3.1
F508del / N1303K	135	2.3
F508del / 2789+5G->A	84	1.5
F508del / 1717-1G->A	85	1.5
F508del / R117H	81	1.4
F508del / R553X	65	1.1
F508del / G551D	57	1
F508del / 3849+10kbC->T	45	0.8
F508del / 3272-26A->G	45	0.8
F508del / W1282X	42	0.7
F508del / Y122X	40	0.7
F508del / R347P	37	0.6
F508del / [delta]I507	37	0.6
F508del / L206W	33	0.6
F508del / D1152H	29	0.5
F508del / 2183AA->G	29	0.5
F508del / A455E	27	0.5
F508del / R1162X	25	0.4
F508del / 1078delT	25	0.4
F508del / R347H	22	0.4
F508del / Y1092X	22	0.4
F508del / 3659delC	22	0.4
N1303K / N1303K	20	0.3
F508del / 5T	21	0.4
F508del / 711+1G->T	20	0.3
G542X / G542X	18	0.3
F508del / S1251N	18	0.3
F508del / 394delTT	17	0.3
F508del / E60X	17	0.3
F508del / R1066C	17	0.3
F508del / 1811+1.6kbA->G	16	0.3
F508del / S945L	16	0.3
F508del / W846X	16	0.3
F508del / 3120+1G->A	15	0.3
F508del / R334W	15	0.3
F508del / G85E	17	0.3
Y122X / Y122X	13	0.2
711+1G->T / 711+1G->T	12	0.2
F508del / 621+1G->T	10	0.2
F508del / I148T	11	0.2
F508del / Q220X	10	0.2
Other CFTR genotypes	1430	24.8
Subtotal (known genotypes)	5404	93.9
F508del / Missing	106	1.8
Other / Missing	65	1.1
Missing / Missing	183	3.2
Subtotal (partial genotypes / Missing)	354	6.1
Total	5758	100

Table 8. Age of patients by genotype

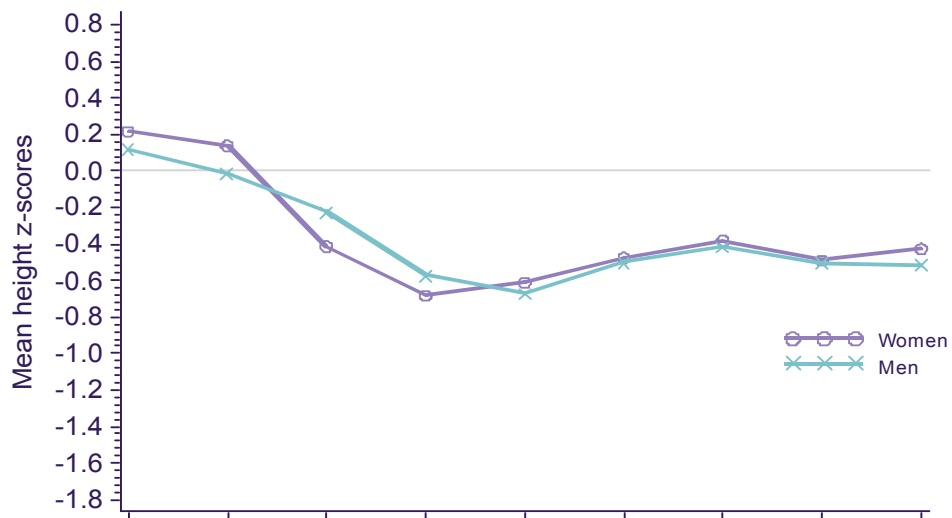
Genotypes	Number	%	Age (years)		
			Mean	Median	Max
F508del / F508del	2511	43.6	17.2	17	57
F508del / Other	2158	37.5	17.7	15	73
Other / Other	735	12.8	17.7	15	78
F508del / Missing	106	1.8	25.8	23	75
Other / Missing	65	1.1	25.4	23	80
Missing / Missing	183	3.2	29.2	26	76

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Anthropometry

■ Height and Weight

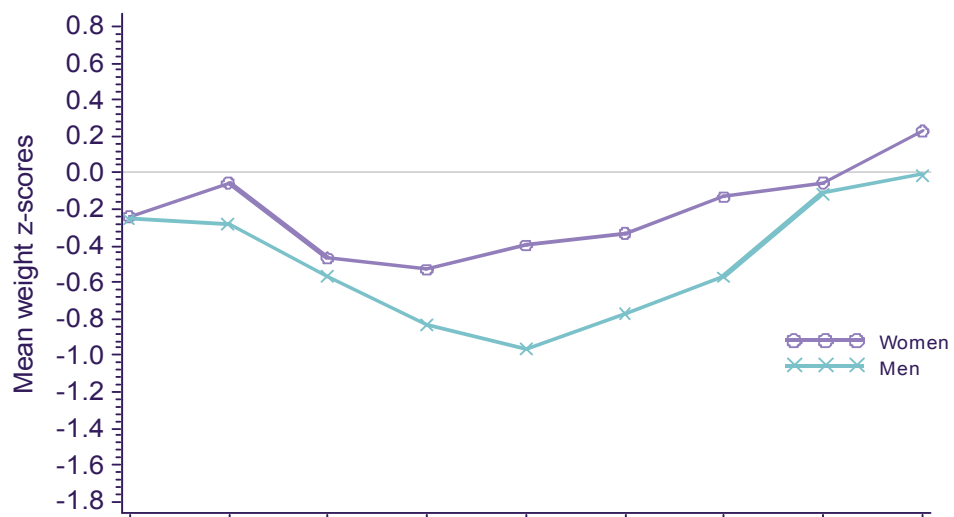
Figure 8. Mean height z-scores, by age and sex



Age groups (years)	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +
Women	0.22	0.14	-0.41	-0.68	-0.61	-0.48	-0.38	-0.49	-0.43
Men	0.12	-0.01	-0.23	-0.57	-0.67	-0.50	-0.42	-0.50	-0.51

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Figure 9. Mean weight z-scores, by age and sex



Age groups (years)	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +
Women	-0.24	-0.05	-0.47	-0.53	-0.40	-0.33	-0.13	-0.05	0.23
Men	-0.25	-0.28	-0.56	-0.83	-0.96	-0.77	-0.57	-0.11	-0.01

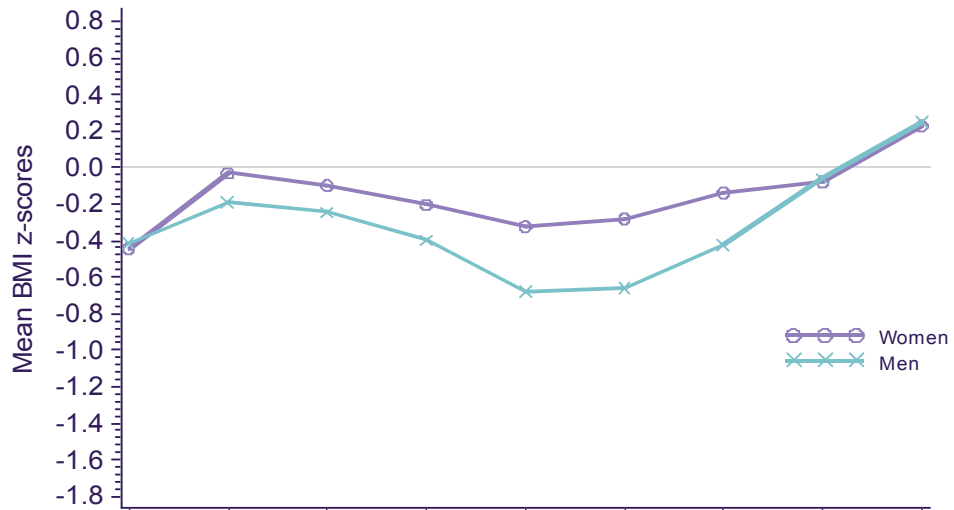
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Height and weight z-scores have been calculated with respect to the French reference population (Sempé M., 1997, *Auxologie – Méthode et séquences*, Méditations, Lyon, 205 p.).

Anthropometry

■ Body Mass Index (BMI)

Figure 10. Mean BMI z-scores, by age



Age groups (years)	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 +
Women	-0.44	-0.03	-0.10	-0.20	-0.32	-0.28	-0.14	-0.08	0.23
Men	-0.41	-0.19	-0.25	-0.40	-0.68	-0.66	-0.42	-0.06	0.25

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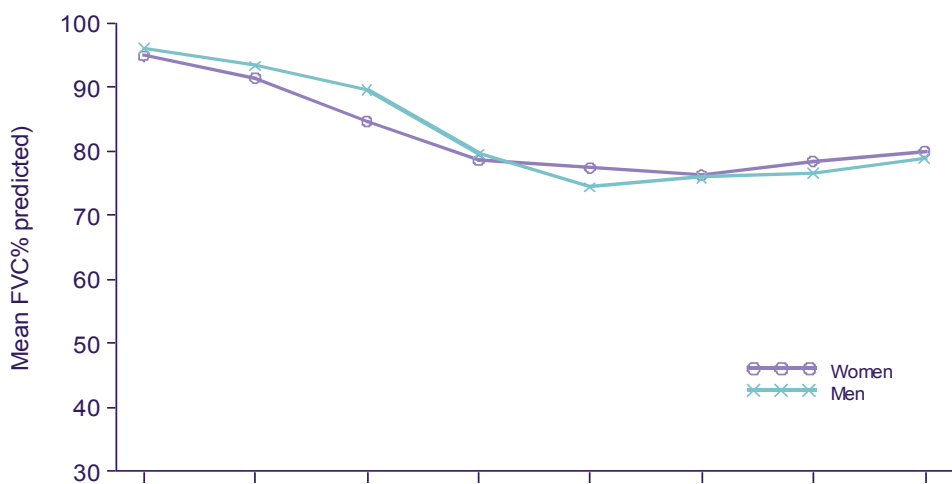
The z-score is an anthropometric reduced centered variable ($Z = \frac{\text{measure} - \text{mean}}{\text{standard deviation}}$), adjusted for sex and age; the mean and standard deviation are taken from the French reference population with the same sex and age as the patient. This index measures the difference with population norms and a negative score means growth retardation.

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).

Spirometry

In 2010, 92,4 % of the patients aged 6 or more had at least one spirometry (88,9 % in 2009 and 90,9 % in 2008).

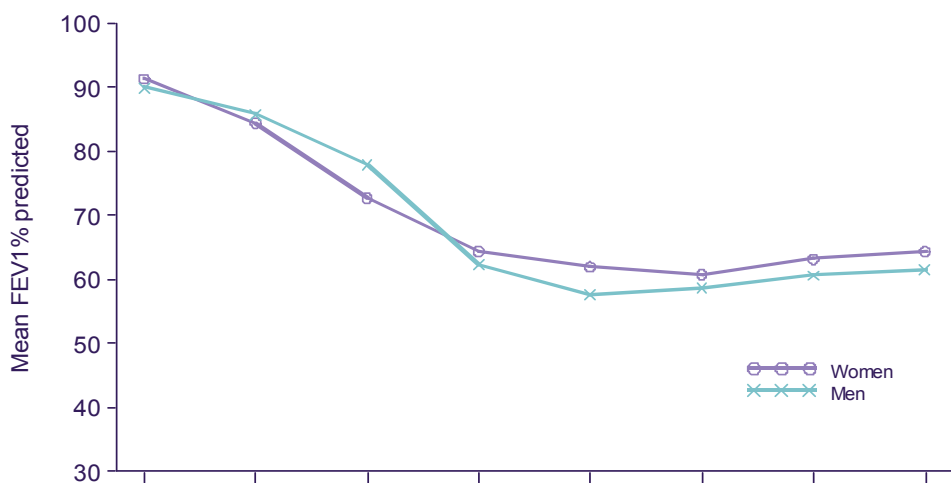
Figure 11. Mean FVC (% predicted), by age



Age groups (years)	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +	05-80
Women	95.0	91.5	84.8	78.6	77.5	76.3	78.5	80.0	84.0
Men	96.2	93.4	89.6	79.6	74.4	76.0	76.7	79.0	85.0
All patients	95.6	92.5	87.3	79.2	75.9	76.1	77.5	79.5	84.5

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Figure 12. Mean FEV₁ (% predicted), by age



Age groups (years)	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +	05-80
Women	91.4	84.5	72.7	64.4	62.0	60.8	63.2	64.4	72.6
Men	90.0	85.9	77.9	62.4	57.7	58.8	60.7	61.6	72.1
All patients	90.6	85.2	75.4	63.4	59.8	59.7	61.8	63.0	72.3

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The pulmonary function tests need an active participation of the patient, difficult to obtain before 6 years of age. The forced vital capacity (FCV) and the forced expiratory volume in the first second (FEV₁) are given in % predicted (Knudson *et al.* Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis* 1983, 127, pp. 725-734).

See appendix 1 for additional information on spirometry and transplantation.



Figure 13. FEV₁ (% predicted) classes

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

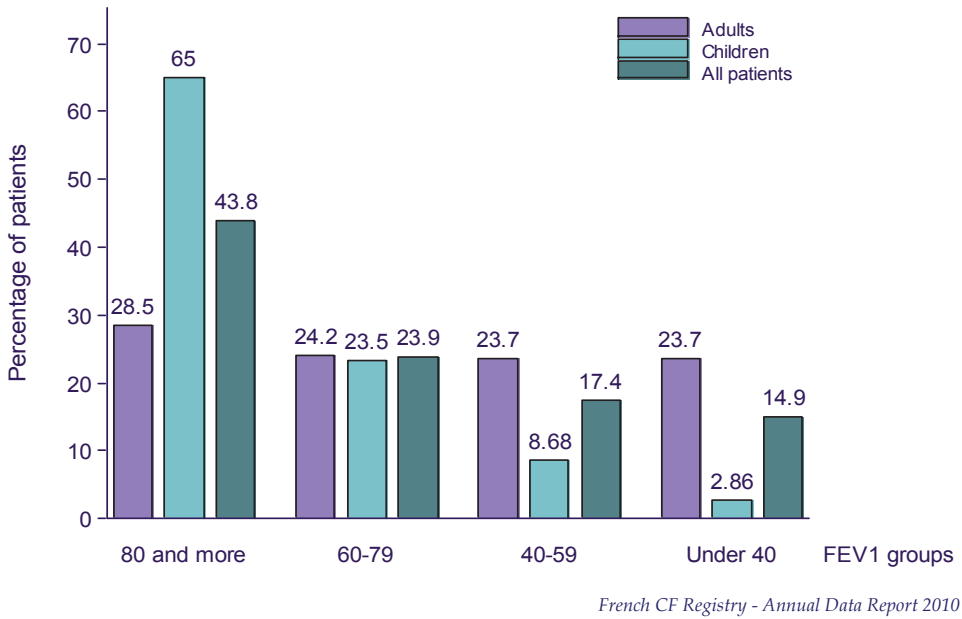


Figure 14. FEV₁ (% predicted) in 2010 compared with 2001, by age



Table 9. Sputum cultures

Patients with at least one sputum	N	Proportion (%)
All patients	5354	93.0 %
Children	2950	97.0 %
Adults	2404	88.4 %

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In 2010, 93 % of the patients had at least one sputum culture; this proportion remains steady as it was 92,4 % in 2009 and 92,6 % in 2008. Among the patients without sputum culture (N=404), 46,5 % of them were transplanted.

Table 10. Distribution of the germs

	Age groups (years)									Total	%*
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	.
Patients with at least one sputum	790	886	828	770	726	527	330	210	287	5354	92.9 %
Normal culture	385	396	281	194	109	75	46	30	52	1568	27.2 %
Achromobacter xylosoxidans	8	31	34	44	56	34	20	12	17	256	4.4 %
Aspergillus	29	115	224	247	235	165	91	41	62	1209	21.0 %
Burkholderia cepacia	.	8	13	27	19	25	13	7	3	115	2.0 %
Haemophilus influenzae	276	371	257	194	94	59	36	22	38	1347	23.4 %
Atypical mycobacteria	6	11	16	29	36	23	10	6	14	151	2.6 %
Pneumococcus	82	55	41	13	3	8	4	5	11	222	3.9 %
Pseudomonas aeruginosa, including:	165	226	309	402	469	350	232	143	172	2468	42.9 %
- Chronic P. aeruginosa	16	41	102	204	340	253	173	107	119	1355	23.5 %
- Multidrug resistant P. aeruginosa	4	10	35	75	122	110	76	52	53	537	9.3 %
Staphylococcus, including:	464	644	674	591	506	329	183	99	111	3601	62.5 %
- MSSA	419	568	587	490	416	274	146	82	101	3083	53.5 %
- MRSA	15	68	71	76	95	66	38	20	14	463	8.0 %
Stenotrophomonas maltophilia	60	74	73	96	77	47	24	14	26	491	8.5 %
Streptococcus (non pneumoniae)	45	53	23	38	41	35	18	13	15	281	4.9 %

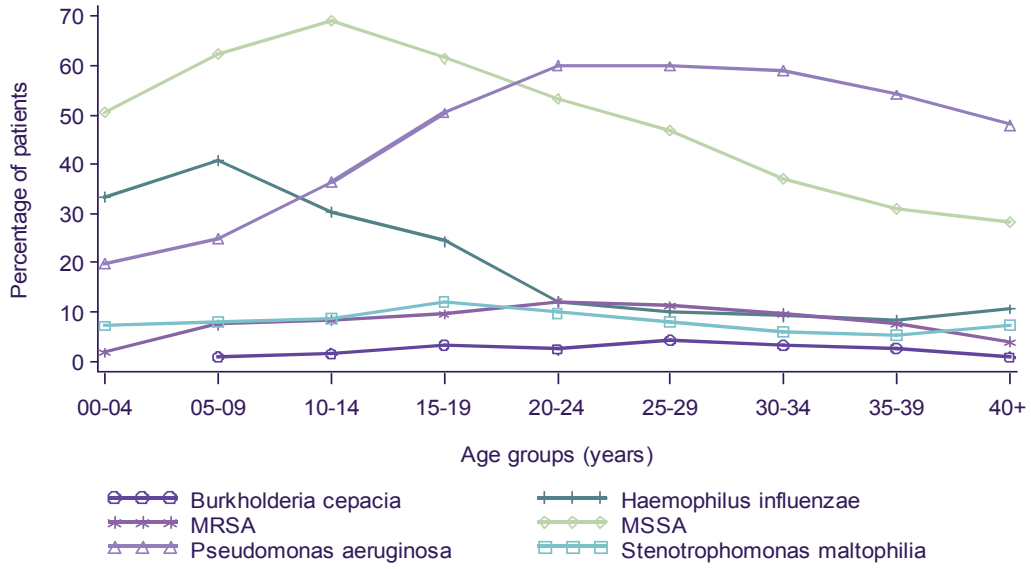
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* Percentage with respect to the entire population.

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).

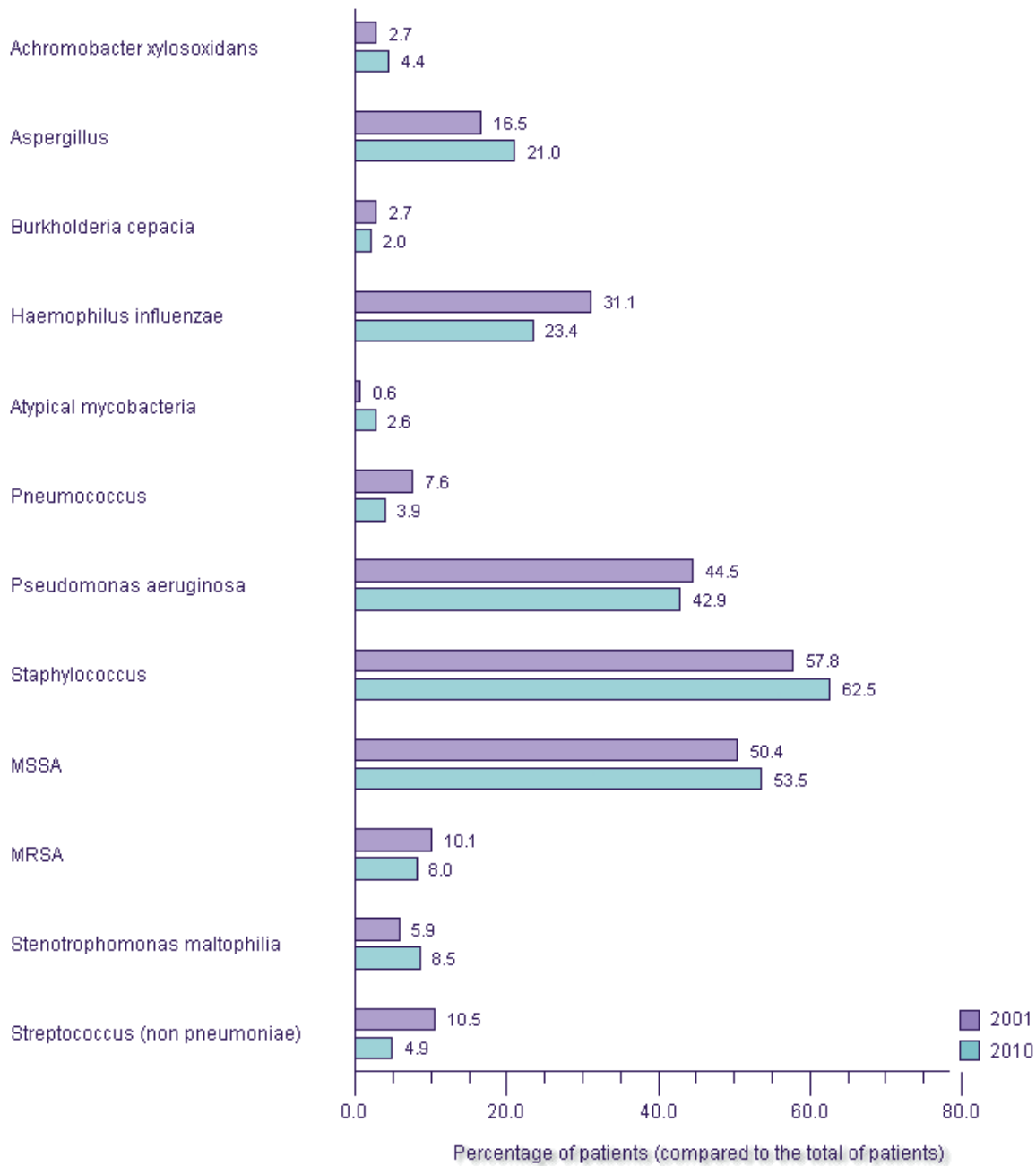
Multi-resistant colonization: resistant to all the antibiotics in at least two antibiotic classes.

Figure 15. Clinically important bacteria



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Figure 16. Comparison of germs in 2010 and in 2001



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Complications

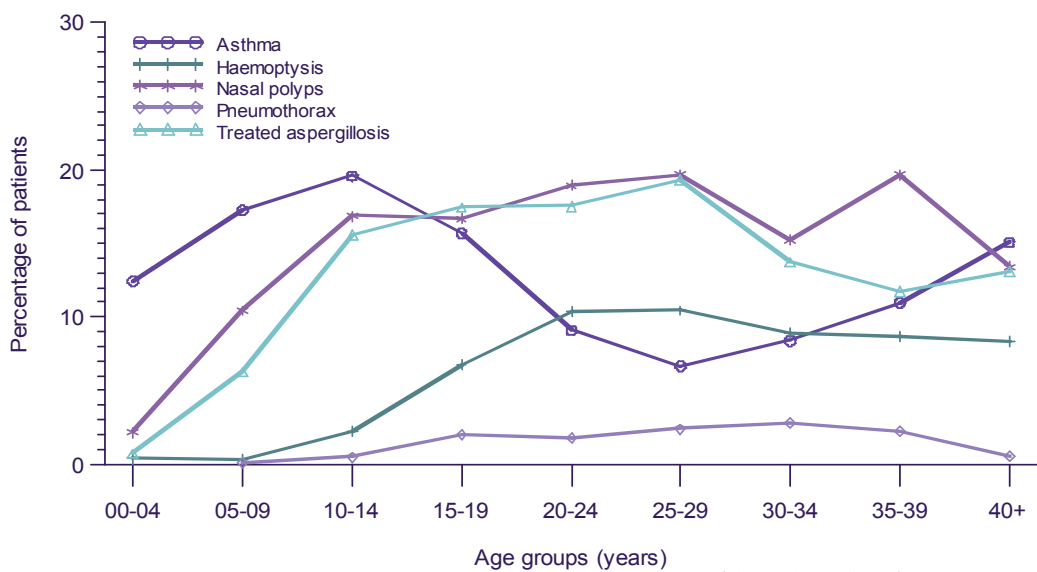
■ Respiratory

Table 11. Respiratory complications

	Age groups (years)									Total	%
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	.
Treated aspergillosis	6	57	132	139	137	113	54	31	47	716	12.4 %
Asthma	103	157	166	125	71	39	33	29	54	777	13.5 %
Haemoptysis	3	3	19	54	81	61	35	23	30	309	5.4 %
Pneumothorax	.	1	4	16	14	14	11	6	2	68	1.2 %
Nasal polyps	18	95	143	133	148	115	60	52	48	812	14.1 %

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Figure 17. Respiratory complications



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Complications

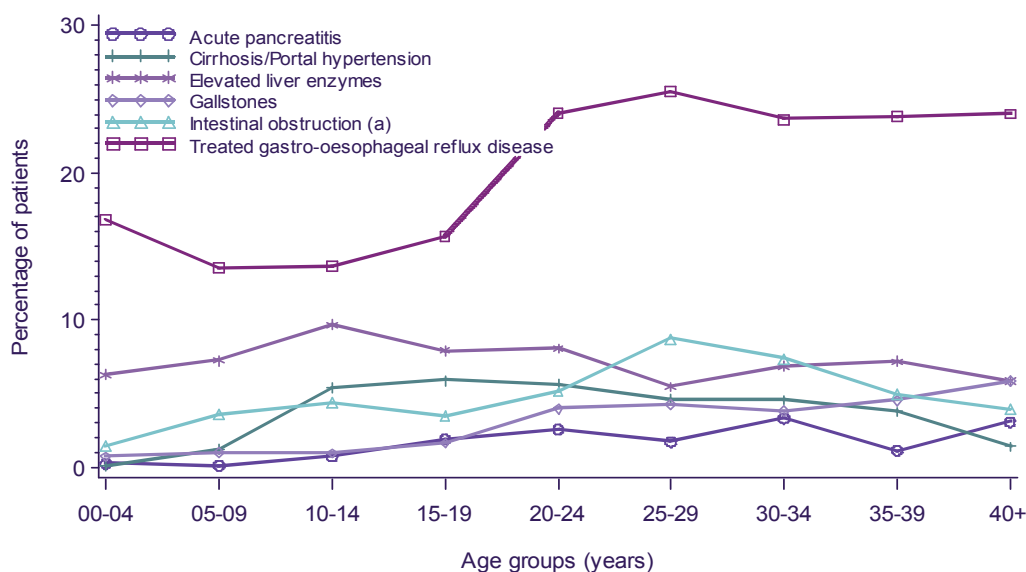
Gastro-intestinal

Table 12. Gastro-intestinal complications

	Age groups (years)									Total	%
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	.
Gallstones	6	9	8	13	31	25	15	12	21	140	2.4 %
Cirrhosis/Portal hypertension	1	11	46	47	44	27	18	10	5	209	3.6 %
Elevated liver enzymes	52	66	82	63	63	32	27	19	21	425	7.4 %
Acute pancreatitis	2	1	6	15	20	10	13	3	11	81	1.4 %
Treated gastro-oesophageal reflux disease	139	123	116	125	188	149	93	63	86	1082	18.8 %
Intestinal obstruction (a)	12	33	37	28	40	51	29	13	14	257	4.5 %

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Figure 18. Gastro-intestinal complications



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Note :
(a) Other than meconium ileus.

Complications

Diabetes mellitus

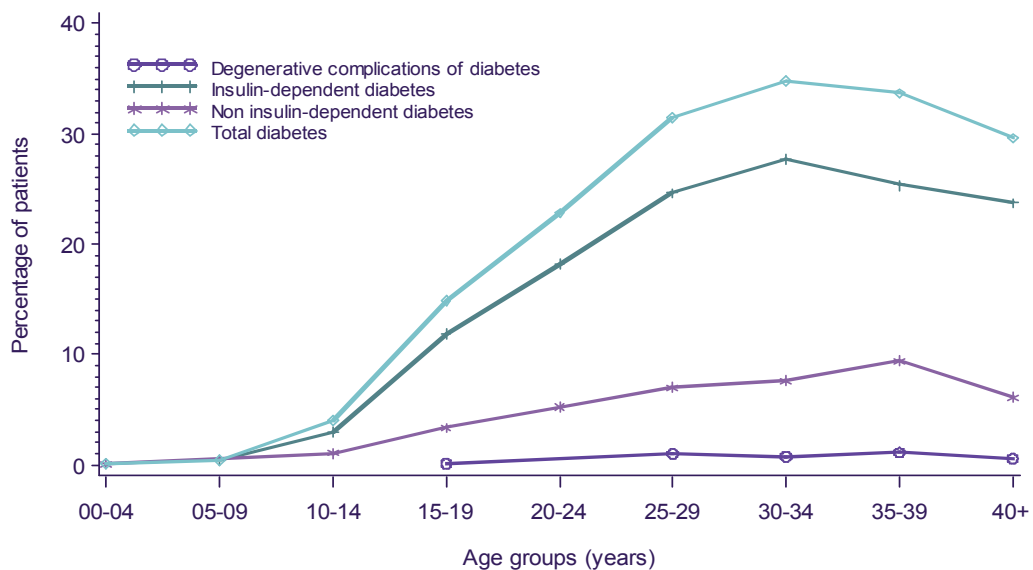
Table 13. Diabetes mellitus and degenerative complications of diabetes

	Age groups (years)									Total	%
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	.
Degenerative complications of diabetes	.	.	.	1	.	6	3	3	2	15	0.3 %
Non insulin-dependent diabetes	1	.	9	27	41	41	30	25	22	196	3.4 %
Insulin-dependent diabetes	.	4	25	95	142	144	109	67	85	671	11.7 %
Total diabetes	1	4	34	119	178	184	137	89	106	852	14.8 %

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The line « Total diabetes » sums the number of patients having at least one type of diabetes. Among the 852 patients, 15 patients presented with both types of diabetes during the year.

Figure 19. Diabetes mellitus and degenerative complications of diabetes



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Complications

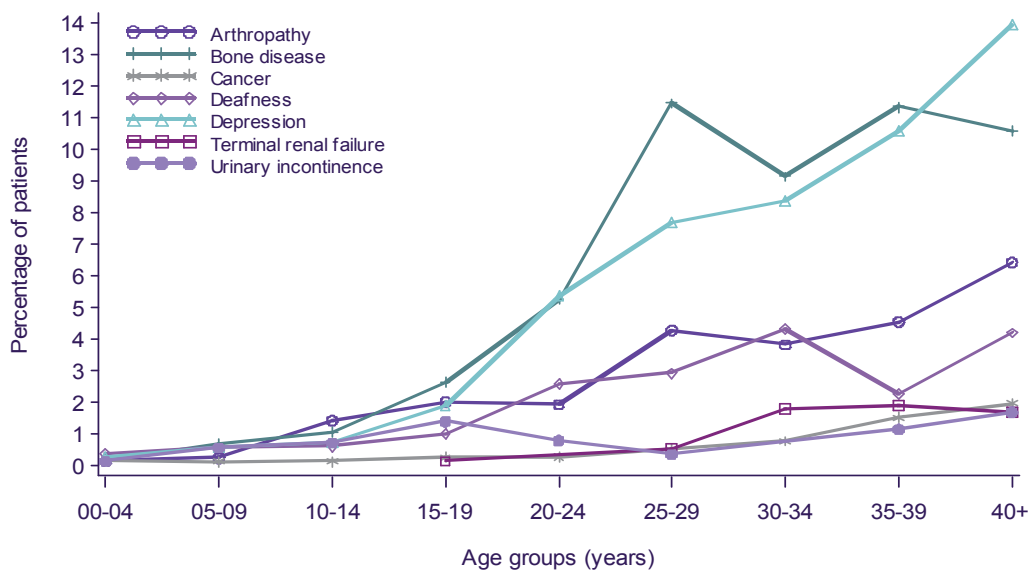
■ Other complications

Table 14. Other complications

	Age groups (years)									Total	%
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	.
Arthropathy	1	2	12	16	15	25	15	12	23	121	2.1 %
Cancer	1	1	1	2	2	3	3	4	7	24	0.4 %
Depression	2	5	6	15	42	45	33	28	50	226	3.9 %
Urinary incontinence	1	5	6	11	6	2	.	3	6	40	0.7 %
Terminal renal failure	.	.	.	1	.	3	7	5	6	22	0.4 %
Bone disease	1	6	9	21	41	67	36	30	38	249	4.3 %
Deafness	3	5	5	8	20	17	17	6	15	96	1.7 %

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Figure 20. Other complications



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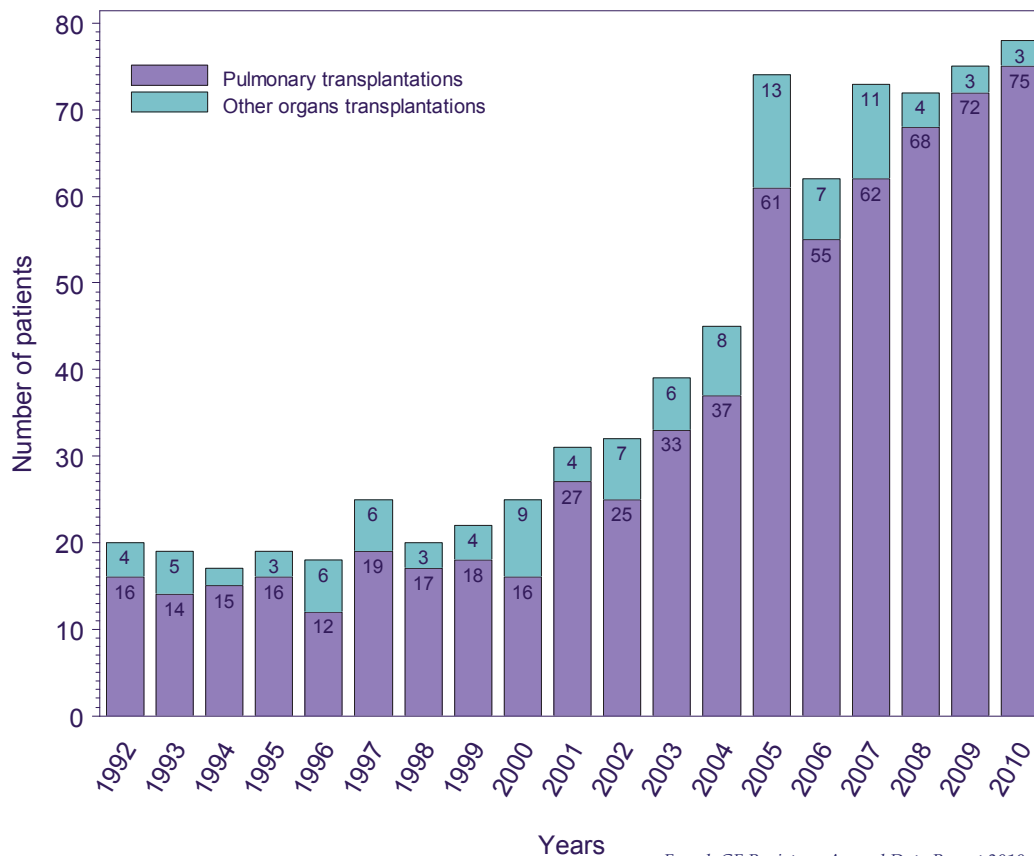
Transplantations

Tableau 15. Characteristics of the transplantations

Characteristics	All patients	Patients
WAITING LIST	All waiting patients	Listed in 2010
Nb of patients	136	75
Mean age (years)	27.3	26.9
Extremes of age (years)	10-57	10-57
Deaths on waiting list	1	1
TRANSPLANTATION	All transplanted	Transplanted in 2010
Nb of patients	440	78
- incl. patients with heart-lung transplants - N (%)	30 (6.8 %)	2 (2.6 %)
- incl. patients with bilateral lung transplants - N (%)	388 (88 %)	75 (97.4 %)
- incl. patients with liver transplants - N (%)	34 (7.7 %)	1 (1.3 %)
- incl. patients with kidney transplants - N (%)	28 (6.3 %)	2 (2.6 %)
- incl. patients with other organs - N (%)	12 (2.7 %)	
Mean age (years)	30.7	27.3
Extremes of age (years)	11-57	11-49
Post-transplantation deaths	27	8

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Figure 21. Annual number of patients transplanted, since 1992



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Inpatient and outpatient visits

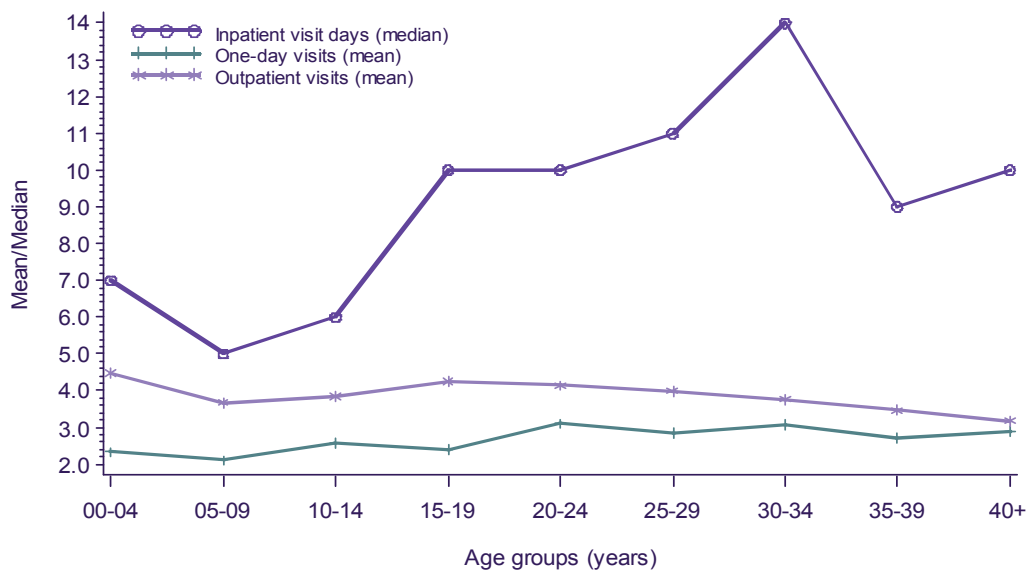
Table 16. Characteristics of the visits

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40+	
All patients	827	909	847	796	780	584	393	264	358	5758
< 4 visits* per year	162	215	158	174	240	176	132	104	140	1501
>= 4 visits* per year	665	694	689	622	540	408	261	160	218	4257
Outpatient visits
Median	4.0	3.0	4.0	4.0	3.0	3.0	3.0	3.0	3.0	3.0
Mean	4.5	3.7	3.9	4.3	4.1	4.0	3.8	3.5	3.2	3.9
One-day visits
Median	1.0	1.0	1.0	1.0	1.0	1.0	2.0	1.0	2.0	1.1
Mean	2.3	2.1	2.6	2.4	3.1	2.8	3.1	2.7	2.9	2.7
Inpatient visits
Median	1.0	1.0	1.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0
Mean	1.7	1.6	1.8	2.3	2.4	2.4	2.3	2.0	1.9	2.0
Days (median)	7.0	5.0	6.0	10	10	11	14	9.0	10	10
Days (mean)	15	9.8	15	19	19	21	22	24	18	18

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* Outpatient, One-day and Inpatient visits.

Figure 22. Visits



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Therapeutic management

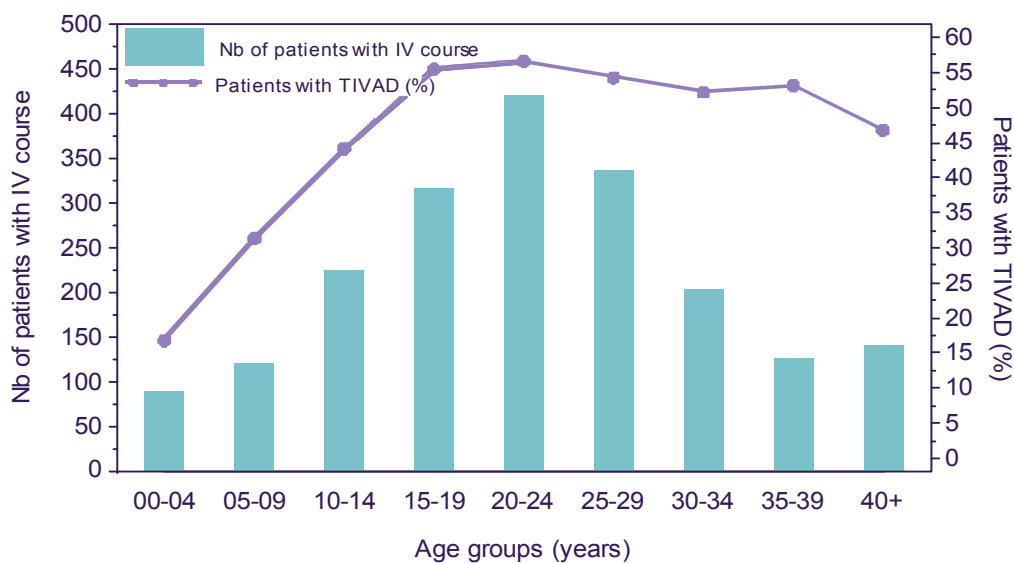
■ IV antibiotic courses – TIVAD

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 ou +	
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758
Nb of patients with at least 1 course	89	121	224	317	422	337	203	126	141	1980
Nb of courses	113	211	470	755	1083	817	457	270	328	4504
Nb of days of courses incl:	1490	2927	6223	11439	15911	11422	6997	4066	4387	64862
- at hospital	798	960	1495	2639	2838	2322	1394	1219	1242	14907
- at home	692	1806	4771	8775	12940	8454	5474	2728	3106	48746
TIVAD*	18	45	114	198	268	217	127	87	79	1153

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Figure 23. Patients with at least one IV antibiotic course and a TIVAD*



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* TIVAD: Totally Implantable Vascular Access Device

Therapeutic management

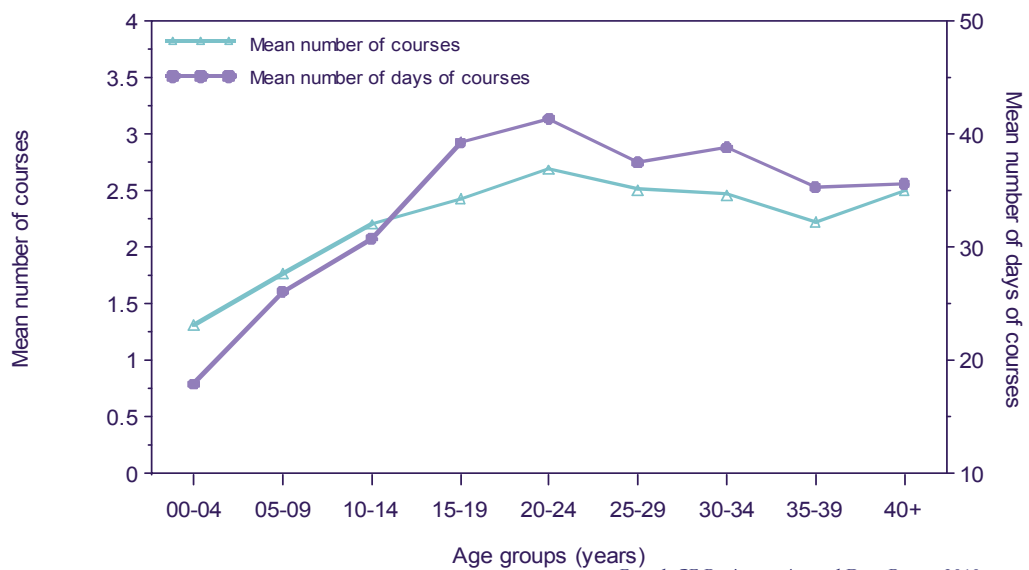
- Antibiotic courses

Table 18. Répartition of courses

	Age groups (years)									Total
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +	
Mean number of courses	1.3	1.8	2.2	2.4	2.7	2.5	2.5	2.2	2.5	2.4
Mean number of days of courses	18.0	26.1	30.8	39.3	41.4	37.6	38.9	35.4	35.7	36.2

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Figure 24. Mean number of courses and of days of courses



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Therapeutic management

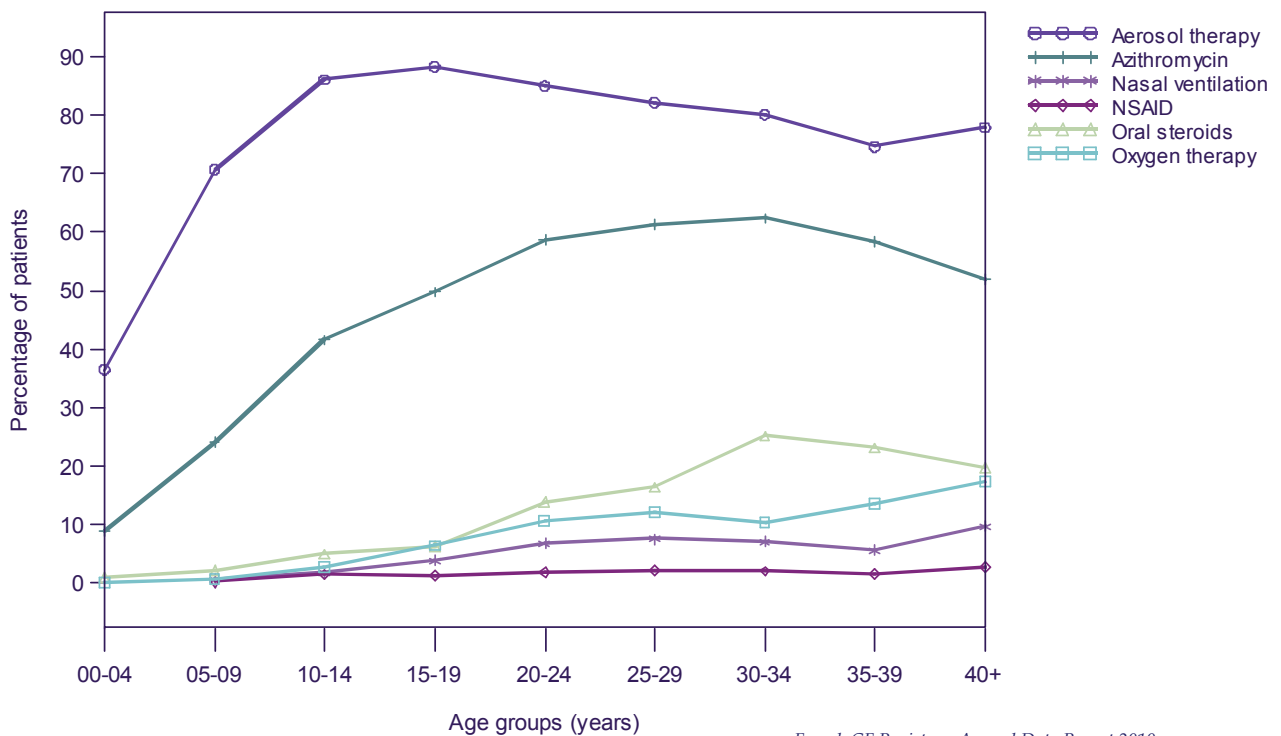
■ Respiratory

Table 19. Respiratory therapeutics

	Age groups (years)									Total	%
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	
Aerosol therapy	302	643	729	703	663	480	315	197	279	4311	74.9 %
NSAID		2	12	10	14	13	8	4	10	73	1.3 %
Azithromycin	74	220	352	396	458	358	245	154	186	2443	42.4 %
Oxygen therapy	1	6	23	51	83	71	41	36	62	374	6.5 %
Oral steroids	9	19	42	50	109	96	99	61	71	556	9.7 %
Nasal ventilation		6	15	31	53	44	28	15	35	227	3.9 %

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Figure 25. Respiratory therapeutics



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Therapeutic management

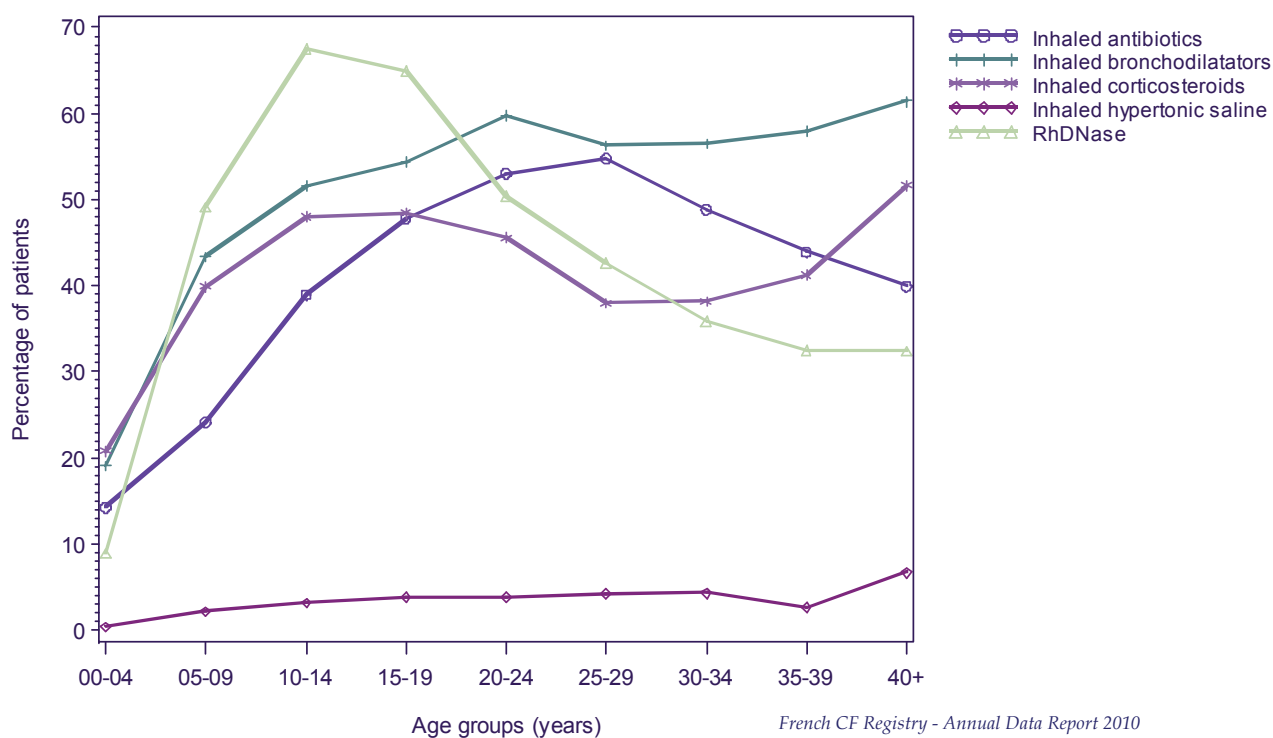
Aerosoltherapy

Table 20. Aerosoltherapy treatments

	Age groups (years)									Total	%
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	
Patients under aerosol therapy	302	643	729	703	663	480	315	197	279	4311	74.9 %
Inhaled antibiotics	118	220	330	381	414	320	192	116	143	2234	38.8 %
Inhaled bronchodilators	158	394	437	433	466	329	222	153	220	2812	48.8 %
Inhaled corticosteroids	172	363	407	386	356	222	150	109	185	2350	40.8 %
Inhaled hypertonic saline	3	20	27	31	30	25	17	7	24	184	3.2 %
RhDNase	74	447	572	517	393	249	141	86	116	2595	45.1 %

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Figure 26. Aerosoltherapy treatments



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Therapeutic management

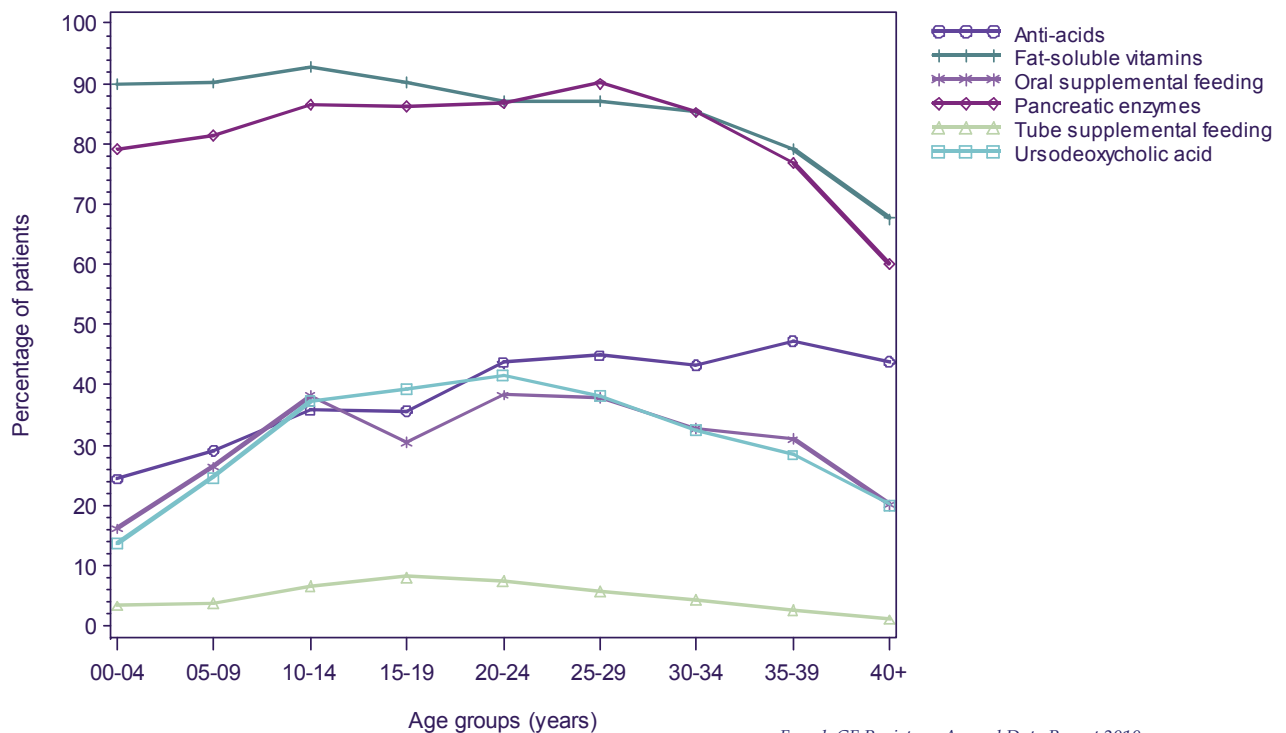
Digestive and nutritional

Table 21. Digestive and nutritional treatments

	Age groups (years)									Total	%
	00-04	05-09	10-14	15-19	20-24	25-29	30-34	35-39	40 ou +		
<i>All patients</i>	827	909	847	796	780	584	393	264	358	5758	
Ursodeoxycholic acid	114	224	316	313	325	223	128	75	72	1790	31.1 %
Anti-acids	202	265	303	284	341	262	170	125	157	2109	36.6 %
Pancreatic enzymes	654	740	733	687	676	526	335	203	215	4769	82.8 %
Tube supplemental feeding	28	35	56	65	58	34	17	7	4	304	5.3 %
Oral supplemental feeding	134	240	324	243	299	221	129	82	72	1744	30.3 %
Fat-soluble vitamins	744	819	786	718	679	509	335	209	242	5041	87.5 %

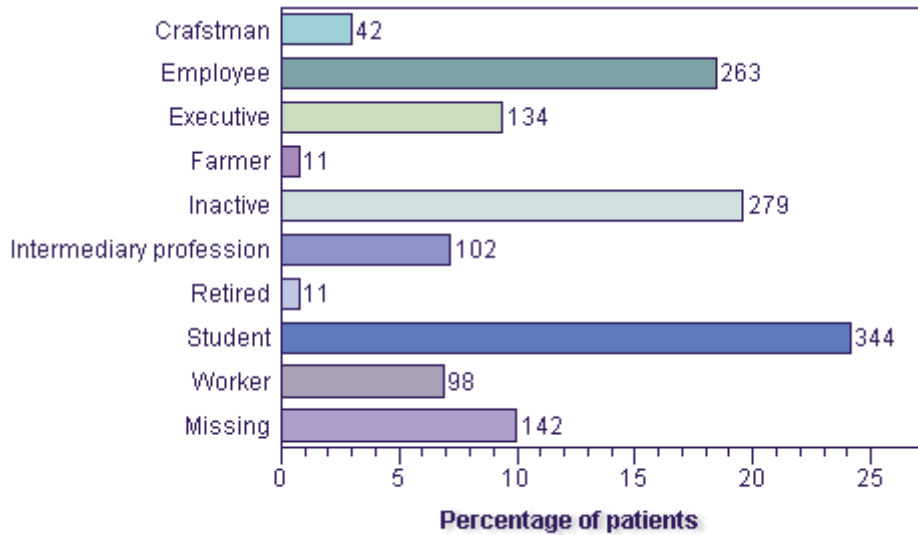
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Figure 27. Digestive and nutritional treatments



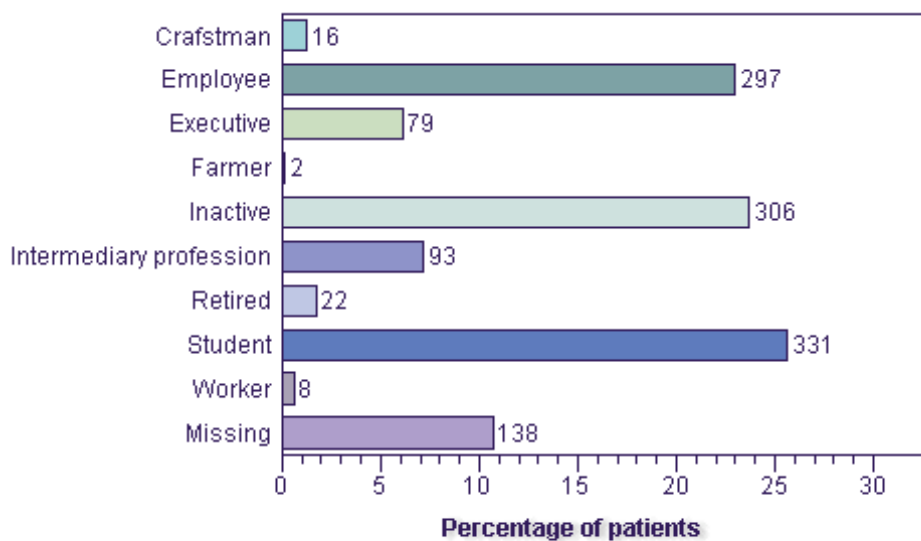
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Figure 28. Employment of men ≥ 18 years in 2010



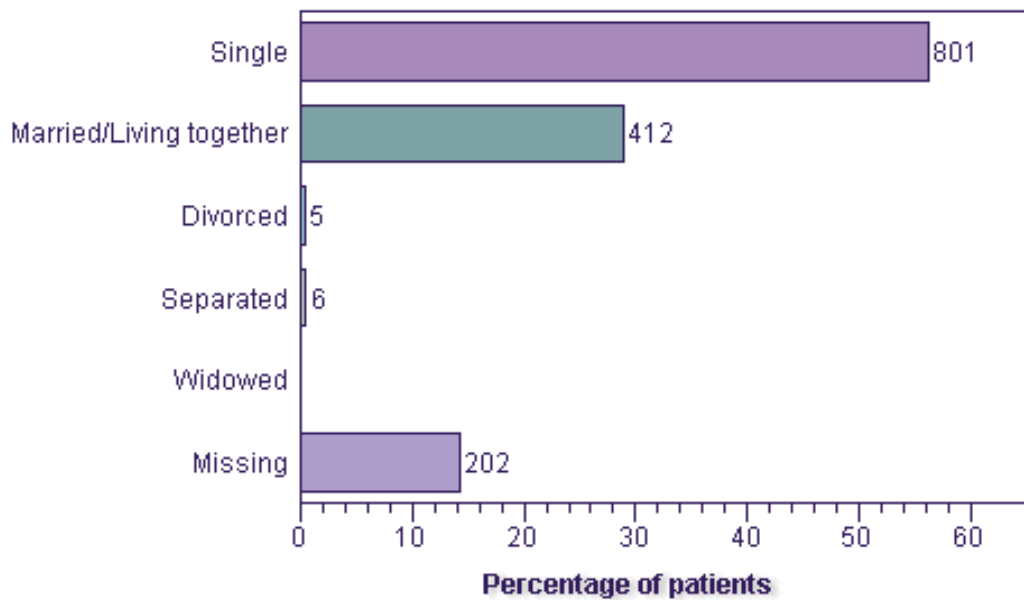
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Figure 29. Employment of women ≥ 18 years in 2010



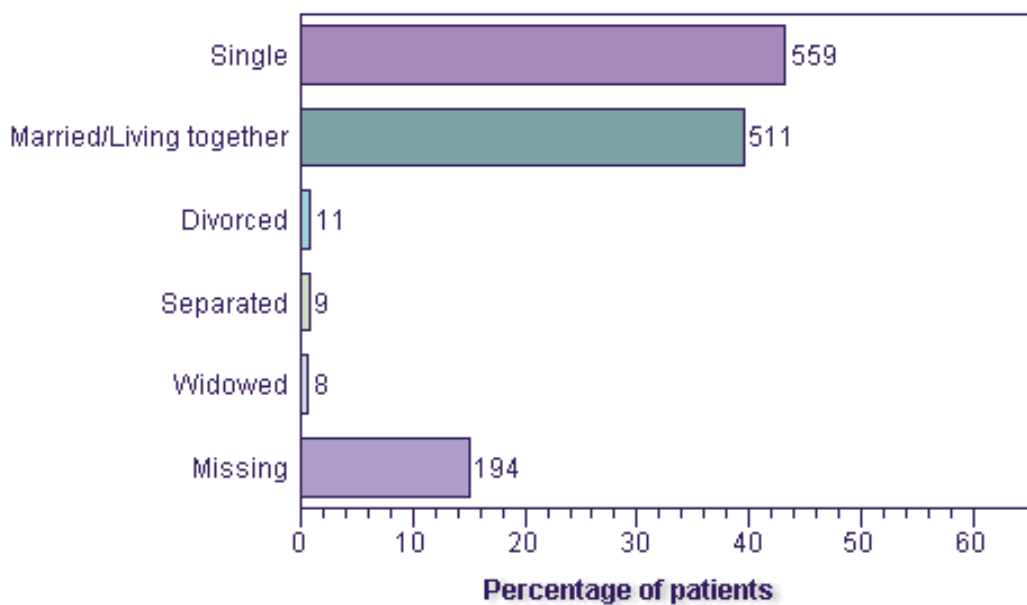
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Figure 30. Marital status of men ≥ 18 years in 2010



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Figure 31. Marital status of women ≥ 18 years in 2010



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Annex 1

Spirometry and transplantation

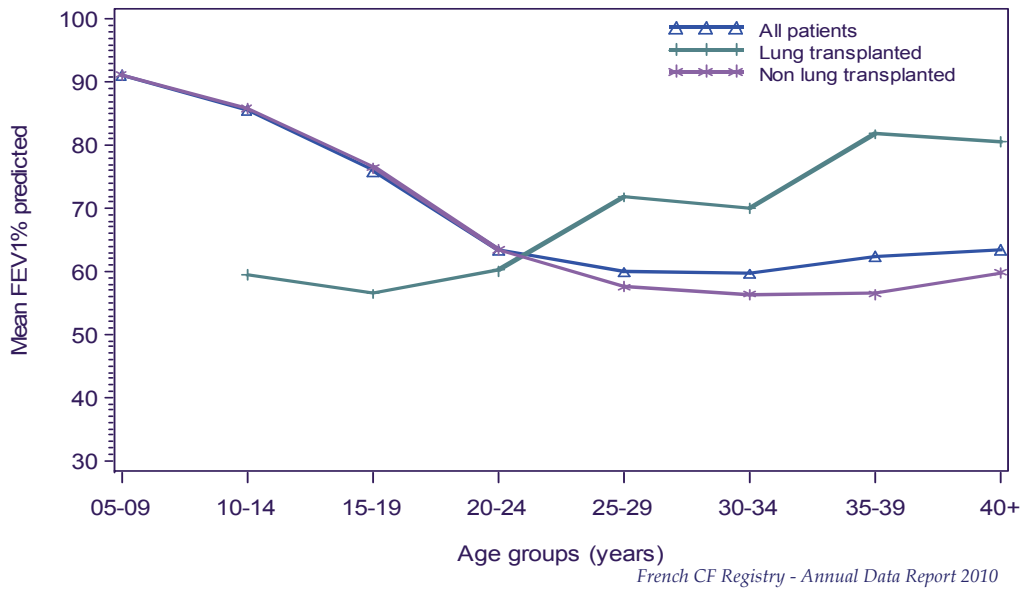
To provide a more comprehensive picture, further comparisons were made using the curves of FEV₁ by age in 2010:

FEV₁ (% predicted) of all patients was compared to that of patients who had or had not received a heart-lung or bilateral lung transplant.

The curves of the whole population and of non-transplanted patients are identical up to age 20-24. After that, FEV₁ (% predicted) of non-transplanted patients drops more sharply than that of the total population, with a difference of almost 7 percentage points at ages 35-39. Among older patients (aged 40 or above) an upward trend is observed for both patient categories, suggesting a selection effect of patients with the mildest forms of CF at these ages.

For patients who had received a lung transplant, for whom the average FEV₁ (% predicted) is available only from ages 10-14, the values are increasing from ages 25-29 up to above 70% of the predicted values.

Figure 32. Mean FEV₁ (% predicted) and transplantation



Annex 2

■ Complement on survival analysis

Two additional survival analysis were performed with the oldest birth cohorts, stratified according to:

1) **genotype (figure 33) :**

- Births from 1992 to 1996: *F508del/F508del* : 406 patients, 17 deaths; *other genotypes*: 516 patients, 31 deaths
- Births from 1997 to 2001: *F508del/F508del* : 415 patients, 7 deaths; *other genotypes*: 538 patients, 11 deaths

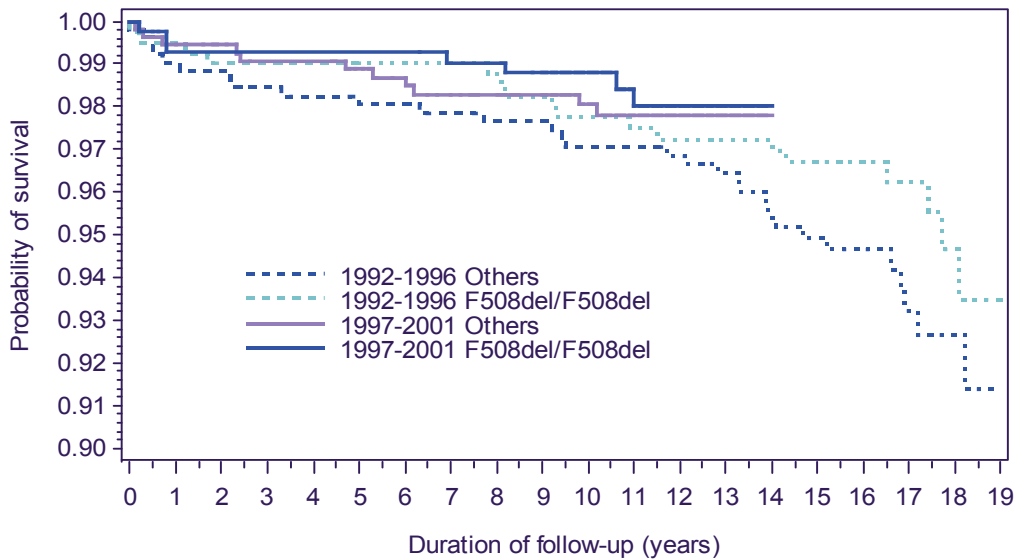
There is no significative survival difference between those cohorts (Log-Rank test = 4,16, p = 0,244).

2) **sex (figure 34) :**

- Births from 1992 to 1996: *men*: 475 patients, 16 deaths; *women*: 447 patients, 32 deaths
- Births from 1997 to 2001: *men*: 482 patients, 11 deaths; *women*: 471 patients, 7 deaths

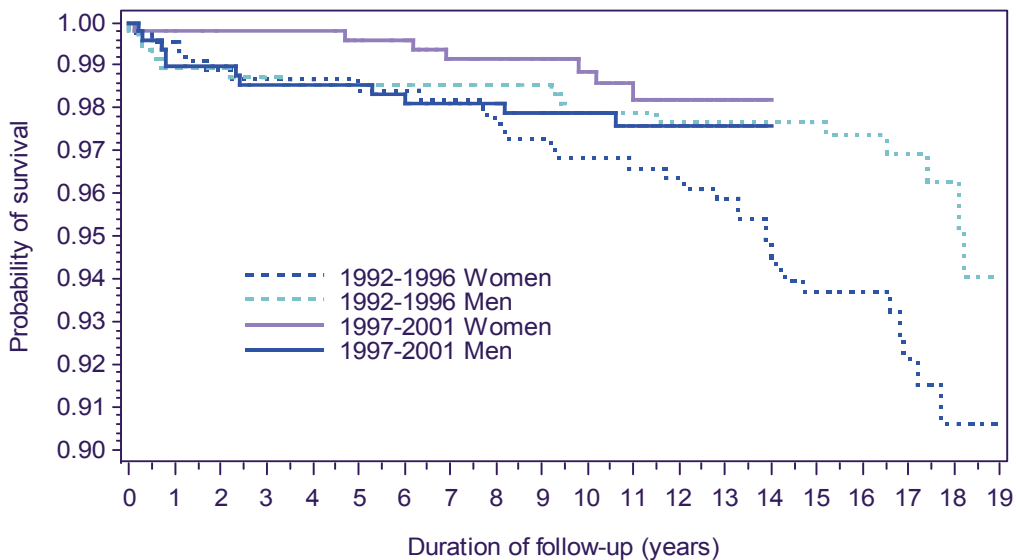
There is a significative survival difference in the 1992-1996 cohorts, men vs women (Log-Rank test = 6,80, p = 0,009) but no difference in the 1997-2001 cohorts.

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



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Figure 34. Survival curves by birth cohort and sex (Kaplan-Meier method)



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Population : patients seen by participating centres and patients lost to follow-up.

Annex 3

■ Participating centres

Table 22. List of the participating CRCMs

CRCMs	Number of patients*
Paediatric CRCMs	
AMIENS Hôpital Nord	82
BORDEAUX Groupe Pellegrin Hôpital d'Enfants	150
GRENOBLE Hôpital de la Tronche Pédiatrie	109
LE HAVRE Hôpital Flaubert	27
LILLE Hôpital Jeanne de Flandres Pédiatrie	189
LISIEUX Centre Hospitalier Robert Bisson	21
LYON Hôpital Mère-Enfant / Groupé Hosp. Est	306
MARSEILLE Hôpital La Timone Pédiatrie	111
NANCY Hôpital d'enfants	136
NANTES Hôpital Mère-Enfant	96
NICE CHU-LENVAL	39
PARIS Hôpital Armand Trousseau	106
PARIS Hôpital Necker	197
PARIS Hôpital Robert Debré	156
RENNES Hôpital Sud Pédiatrie	123
ST DENIS DE LA REUNION Hôpital d'Enfants	65
TOULOUSE Hôpital des Enfants	121
TOURS Hôpital de Clocheville Pédiatrie	123
VERSAILLES Hôpital Mignot Pédiatrie	74
Adult CRCMs	
BORDEAUX-PESSAC Groupe Sud Hospitalier	75
GRENOBLE Hôpital de la Tronche Pneumologie	103
LILLE Hôpital Calmette Pneumologie	148
LYON SUD Centre Hospitalier	227
MARSEILLE Hôpital Sainte Marguerite Pôle Thorax	142
NANCY Hôpital de Brabois Pneumologie	104
NANTES Hôpital Laënnec	168
PARIS Hôpital Cochin	353
RENNES Hôpital Pontchaillou Pneumologie	83
SURESNES Hôpital Foch	271
TOULOUSE Hôpital Larrey Pneumologie	121
TOURS Hôpital Bretonneau Pneumologie	50
Paediatric and Adult CRCMs	
ANGERS - LE MANS	118
BESANCON Adultes et Pédiatrie	106
CAEN Adultes et Pédiatrie	116
CLERMONT-FERRAND Adultes et Pédiatrie	94
CRETEIL Centre Hospitalier Intercommunal	84
DIJON Hôpital d'Enfants du Bocage	111
DUNKERQUE Centre Hospitalier	62
GIENS Hôpital Renée Sabran	224
LENS Centre Hospitalier	44
LIMOGES Hôpital Mère/Enfant	52
MONTPELLIER Hôpital Arnaud de Villeneuve	174
POITIERS Hôpital La Milétrie	35
REIMS American Memorial Hospital	111
ROSCOFF Centre de Perharidy	159
ROUEN Adultes et Pédiatrie	146
ST PIERRE DE LA REUNION Groupe Hosp. Sud	58
STRASBOURG Adultes et Pédiatrie	213
VANNES-LORIENT	78

Annex 3

■ Participating centres

Table 23. List of the participating centres (CRCMs excepted)

Centres	Number of patients*
Paediatric local centres	
BREST Hôpital Augustin Morvan	8
COLMAR CHG Louis Pasteur Pédiatrie	8
DAX Centre Hospitalier	13
ELBEUF Hôpital des Feugrais	14
MONTLUCON Centre Hospitalier	10
MULHOUSE Centre Hospitalier Pédiatrie	14
ST BRIEUC Centre Hospitalier Yves Le Foll	40
ST ETIENNE Hôpital Nord	3
ST TROJAN LES BAINS Centre Hélio Marin	7
Adult local centres	
MULHOUSE Centre Hospitalier Pneumologie	4
Paediatric and Adult local centres	
BRIVE Centre Hospitalier	17
ST NAZAIRE Centre Hospitalier	23
Other centres	
DIEULEFIT Centre Médical/Climatique Bellevue	2
MONTARGIS Centre Hospitalier	1
ST QUENTIN Centre Hospitalier Général	1

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* Number of patients who visited the centre during the year. Patients followed by a centre who did not visit it in 2010 were excluded from those statistics.



Annex 4

Table 24. Summary of data (1/2)

	2010	2009
Patients seen during the year and centres participating to the registry		
- Patients registered* (N):	5792	5 650
- Patients seen during the year in a centre** (N):	5758	5 628
- Centres (N) :	64	64
Paediatric CRCMs***:	19	19
Adult CRCMs***:	12	12
Paediatric and Adult CRCMs***:	18	18
Other centres:	15	15
Demographics		
- Male patients (%) :	51,4	51,8
- Age of patients, in years (mean):	18,1	17,7
- Age of patients, in years (median):	16,0	16,0
- Age of patients, in years (extrêmes):	0 – 80	0 – 79
- Patients aged 18 years and over (%):	47,2	45,8
- Early pregnancies during the year (N):	28	34
- Pregnancy rates in women aged 15 to 49 ans (for 1 000):	20,1	25,8
- Age of patients at onset of pregnancy, in years (mean):	29,0	28,4
- Deaths (N):	60	61
Including death of patients not seen during the year:	9	12
- Crude death rate (for 1 000):	10,6	11,2
- Age at death, in years (mean):	29,0	25,5
- Age at death, in years (median):	27,0	24,0
Diagnosis and genetics		
- Age at diagnosis, in months (median) :	2,0	2,0
- New patients diagnosed during the year (N):	181	230
Including by neonatal screening:	112	146
- Age at diagnosis of the new patients, in years (min-max):	0 – 69	0 – 72
- Full genotypes identified (%):	93,9	93,9
F508del / F508del:	43,6	43,6
F508del / Other:	37,5	37,2
Other / Other:	12,8	13,1
F508del / Missing:	1,8	2,0
Other / Missing:	1,1	1,2
Missing / Missing:	3,2	2,9
Anthropometry and spirometry		
- Height z-score, patients aged 17 years and less (mean):	- 0,13	- 0,16
- Height z-score, patients aged 18 years and over (mean):	- 0,53	- 0,54
- Weight z-score, patients aged 17 years and less (mean):	- 0,37	- 0,39
- Weight z-score, patients aged 18 years and over (mean):	- 0,46	- 0,46
- FEV ₁ (% predicted) - Knudson, patients aged 17 years and less (mean):	85,4	84,31
- FEV ₁ (% predicted) - Knudson, patients aged 18 years and over (mean):	62,9	62,26



Annex 4

Table 24. Summary of data (2/2)

	2010	2009
Microbiology		
- Patients with at least one sputum during the year (%):	93,0	92,4
<i>H. influenzae</i> :	23,4	24,1
MSSA:	53,5	48,9
MRSA:	8	7,9
<i>P. aeruginosa</i> :	42,9	41,4
<i>S. maltophilia</i> :	8,5	7,8
<i>B. cepacia</i> :	2	1,9
<i>Aspergillus</i> :	21	19,2
Complications and transplantations		
- Haemoptysis (%):	5,4	5,3
- Cirrhosis / portal hypertension (%):	3,6	3,6
- Insulin-dependent and non insulin-dependant diabetes (%):	14,8	14,1
- Transplanted patients (N):	440	400
Including patients transplanted during the year:	78	74
- Patients on waiting list (N):	136	161
Including patients listed during the year:	75	65
Deaths on waiting list:	1	3
Therapeutic management		
- IV courses (%):	34,4	35,3
- Oxygenotherapy (%):	6,5	6,3
- Nasal ventilation (%):	3,9	4,1
- Azithromycin (%):	42,4	40,6
- Inhaled antibiotics (%):	38,8	35,9
- rhDNase (%):	45,1	43,4
- Inhaled bronchodilators (%):	48,8	49,1
- Inhaled corticosteroids (%):	40,8	40,5
- Pancreatic enzymes (%):	82,8	82,7

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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.

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

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