

## ***What is the European Cystic Fibrosis Registry?***

The European CF Registry (ECFR) was founded and run by the European Cystic Fibrosis Society (ECFS).

The purpose of the ECFR is to measure, survey and compare aspects of cystic fibrosis and its treatment in the participating countries, thereby encouraging new standards of dealing with the disease, to provide data for epidemiological research and to identify special patient groups suitable for multi-centre trials.

This information will facilitate long-term planning of health expenditure allocations and developing pan European support systems.

## ***The ECFR report of 2003 data (October 2006)***

This pilot report is a result of an attempt to merge data from different registries already functioning in Europe and collecting data on patients with CF.

The countries that contributed data were

Belgium	860	patients
Denmark	412	patients
France	4104	patients
Ireland	325	patients
Italy	4142	patients
Russia	547	patients
Sweden	362	patients

Total	10752	patients
-------	-------	----------

During the process of data merging several issues came up that need attention in the future, and which mean, that the data are not reliable for strict scientific analysis and comparison:

- Not all countries collect the essential data that we have agreed upon
- There are many missing data
- There are different definitions in different countries for the same variable
- Some values that were out of range (data cleaning)
- Some countries collected z-scores, some percentiles for weight and height
- Different prediction equations for pulmonary function
- Some countries have poor coverage of the total patient population

These are issues that we have to work with in order to make the registry fully functional and valuable to patients, clinicians and researchers. Therefore we are now planning a common registry using a common platform and with common definitions (see elsewhere on the ECFS homepage). Some countries might want to continue with their own registries, but for these a set of common definitions and reference values are essential.

We would very much like to thank the countries participating with data, as well as the countries that are committed to further cooperation, but were not able to deliver data from 2003.

Eitan Kerem

Laura Viviani

Hanne Vebert Olesen

# The European CF Registry

## Annual report

for the

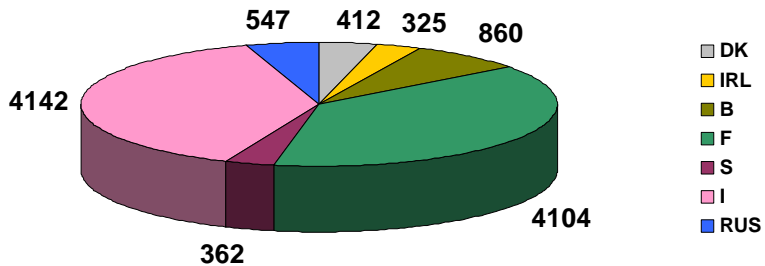
## 2003 data

October 2006



# Number of patients

Total 10257



For the combined results it is important to note that France and Italy contribute with 80% of the patients and thence have greater weight on means and medians

## Demographic data country level (2003)

	Patients in Registry 2003	Patients total (estimated)	% of patients represented	Participating centres	Neonatal screening since ?	% found by neonatal screening*
Belgium	860	1100	79	All	Pediatricians initiative	15
Denmark	412	415	>95	2/2	none	0
France	4104	5000	82	All	2002	17
Ireland	325	1600	20	All – started in 2003	No	0
Italy	4142	4500	92	29/38**	1991 (regional)	22.3
Russia	547	2000	27	Not all	2006	0
Sweden	362	500	72	3/4	none	0

\* Of the patients registered in 2003

\*\* all non-participating centres are supporting centres, so the patients are registered when they come to the larger centres

# Demographic parameters

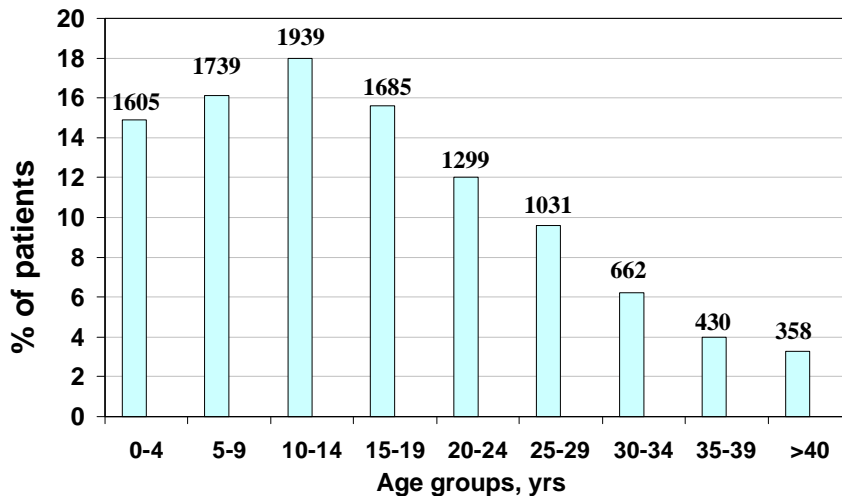
Mean current age, yrs N = 10748	17.0 ± 11.3 Median 15.3
Died during 2003	128 of 10752 (1.2%)
Male/Female % N = 10752	52.68/ 47.32
Sweat chloride concentration, mmol/L N = 7200	97.2 ± 25.8
% with pancreatic sufficiency	< 18 y - 939 of 5992 (15.7%) = 18 y - 901 of 4091 (22.02%)

N = number of patients with these parameters reported

## Current age (2003)

N=10748

Median - 15.3 yrs



# Age at diagnosis (yrs)

	n	Mean $\pm$ SD	Median	range
Males	5298	3.8 $\pm$ 7.4	0.5	0-60
Females	4761	4.1 $\pm$ 8.4	0.5	0-73
Both	10059	3.9 $\pm$ 7.9	0.5	0-73

# Genotype Distribution

genotype (most frequent mutations)	Frequency	Percent	genotype (most frequent mutations)	Frequency	Percent
not reported	970	9.02	G85E\[\delta\]F508	42	0.39
[\delta]F508\[\delta\]F508	3903	36.30	3272-26A->G\[\delta\]F508	40	0.37
UN\[\delta\]F508	1104	10.27	G542X\G542X	38	0.35
G542X\[\delta\]F508	346	3.22	R347P\[\delta\]F508	38	0.35
N1303K\[\delta\]F508	342	3.18	1717-1G->AUN	35	0.33
UNUN	255	2.37	621+1G->T\[\delta\]F508	33	0.31
1717-1G->A\[\delta\]F508	158	1.47	D1152H\[\delta\]F508	30	0.28
2789+5G->A\[\delta\]F508	147	1.37	UNW1282X	30	0.28
W1282X\[\delta\]F508	101	0.94	1078delT\[\delta\]F508	29	0.27
N1303KUN	97	0.90	[\delta]F508\[\delta\]I507	29	0.27
R553X\[\delta\]F508	96	0.89	R334W\[\delta\]F508	28	0.26
G542XUN	93	0.86	S1251N\[\delta\]F508	28	0.26
G551D\[\delta\]F508	84	0.78	Y122X\[\delta\]F508	28	0.26
2183AA->G\[\delta\]F508	83	0.77	2183AA->GVUN	27	0.25
3849+10kbc->T\[\delta\]F508	83	0.77	R553XUN	25	0.23
R117H\[\delta\]F508	73	0.68	2789+5G->AUN	24	0.22
3659delC\[\delta\]F508	71	0.66	E60X\[\delta\]F508	21	0.20
R1162X\[\delta\]F508	68	0.63	G1244E\[\delta\]F508	21	0.20
394delTT\[\delta\]F508	57	0.53	G542X\N1303K	21	0.20
N1303K\N1303K	49	0.46	R347H\[\delta\]F508	20	0.19

## Mutations Distribution

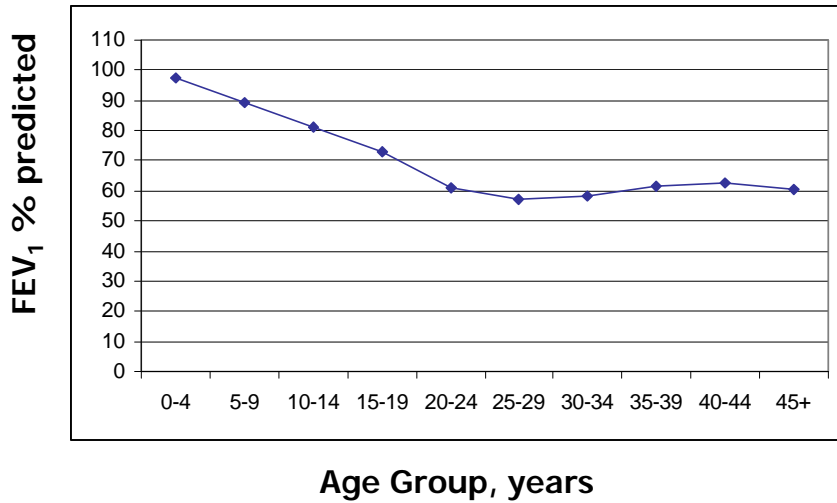
	Frequency	Percent	Cumulative Frequency	Cumulative Percent
<b>[delta]F508</b>	11888	60.76	11888	60.76
<b>Unknown</b>	2168	11.08	14056	71.85
<b>G542X</b>	681	3.48	14737	75.33
<b>N1303K</b>	675	3.45	15412	78.78
<b>1717-1G-&gt;A</b>	270	1.38	15682	80.16
<b>2789+5G-&gt;A</b>	262	1.34	15944	81.50
<b>W1282X</b>	217	1.11	16161	82.61
<b>2183AA-&gt;G</b>	202	1.03	16363	83.64
<b>R553X</b>	189	0.97	16552	84.60
<b>R1162X</b>	157	0.80	16709	85.41
<b>3849+10kbC-&gt;T</b>	135	0.69	16844	86.10
<b>G551D</b>	123	0.63	16967	86.73
<b>3659delC</b>	105	0.54	17072	87.26
<b>G85E</b>	104	0.53	17176	87.79
<b>R117H</b>	103	0.53	17279	88.32
<b>394delTT</b>	92	0.47	17371	88.79
<b>R347P</b>	91	0.47	17462	89.26
<b>Y122X</b>	62	0.32	17524	89.57
<b>621+1G-&gt;T</b>	57	0.29	17581	89.86
<b>3272-26A-&gt;G</b>	55	0.28	17636	90.15

## Genotype Summary

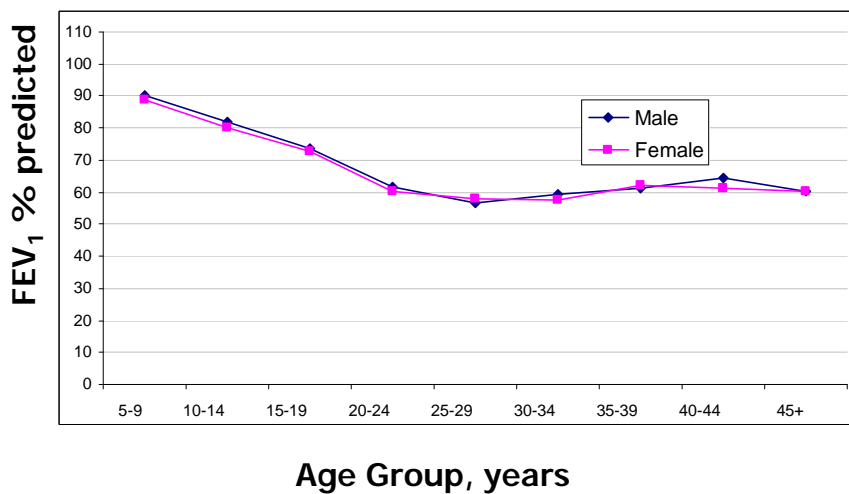
DF508 genotype		
N = 10752	Frequency	Percent
not reported	970	9.02
DF508/DF508	3903	36.30
DF508/other	4082	37.97
other/other	1797	16.71

For differences between countries see slide 31

## FEV<sub>1</sub> % of predicted (mean) vs Age

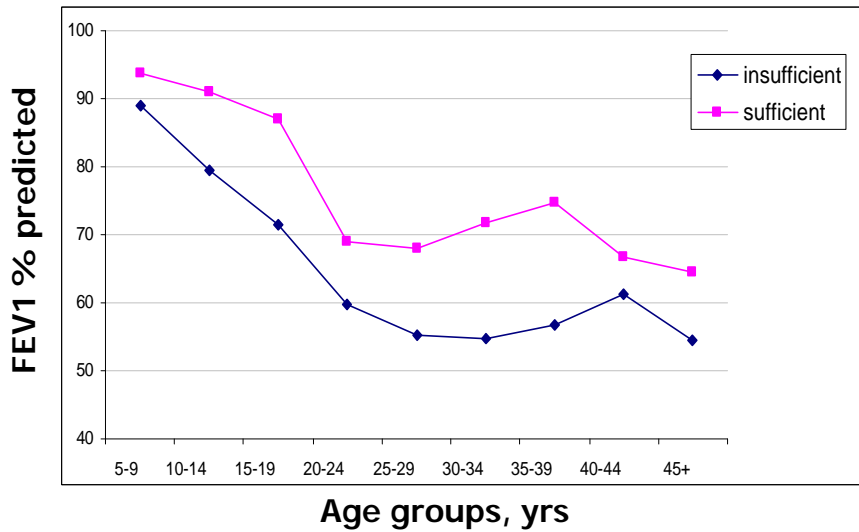


## FEV<sub>1</sub> % of predicted (mean) vs Age According to gender

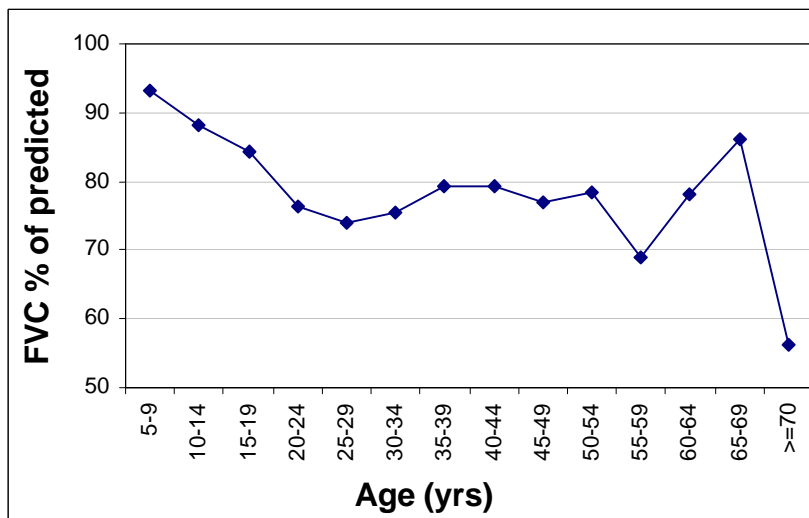




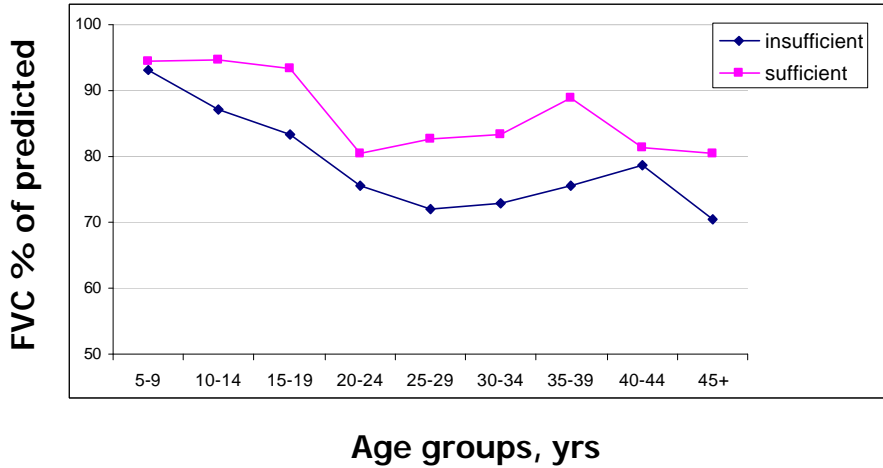
## Mean FEV<sub>1</sub> vs age according to pancreatic status



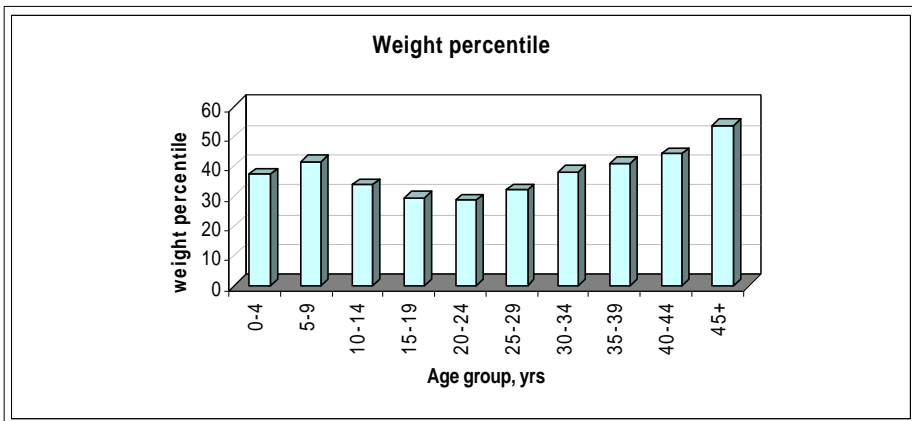
## FVC vs Age



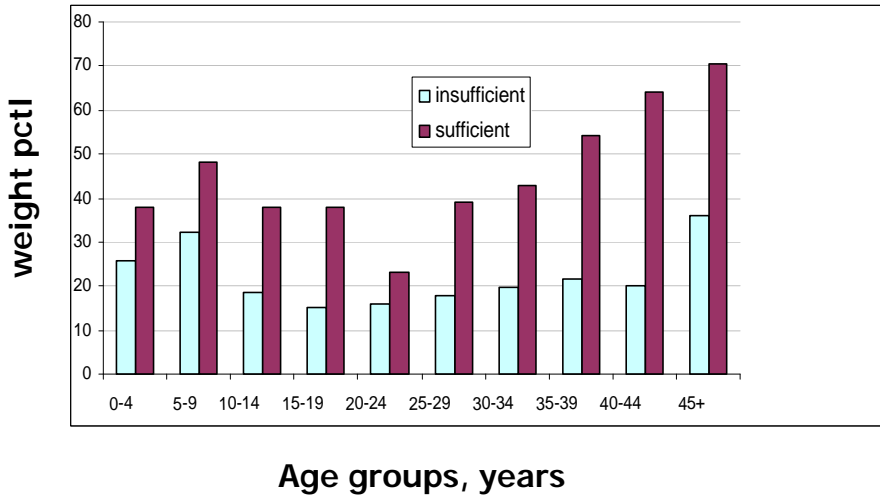
## Mean FVC % vs age for pancreatic status



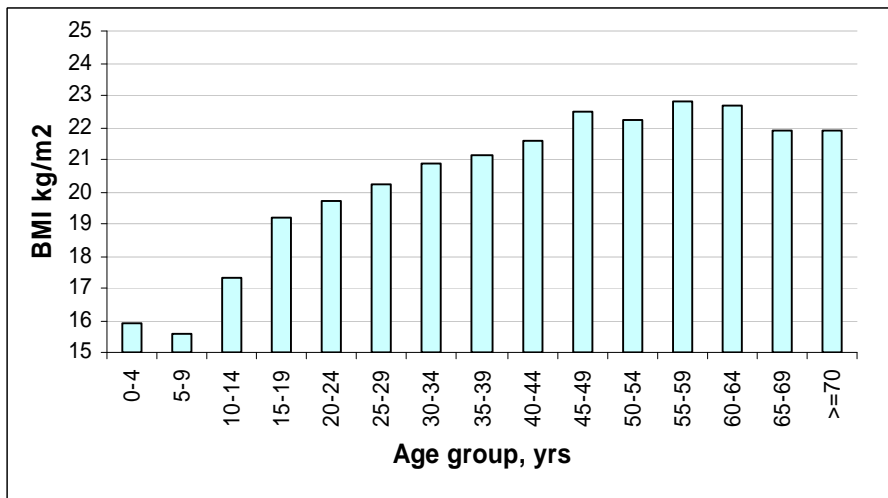
## Weight percentile (mean) vs age



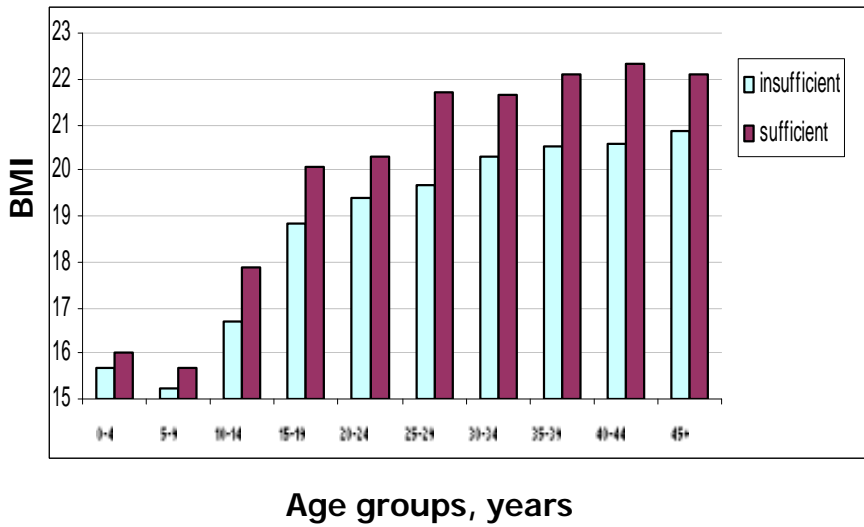
### Median weight percentiles vs age for pancreatic status n=5294 (4395 PI, 899 PS)



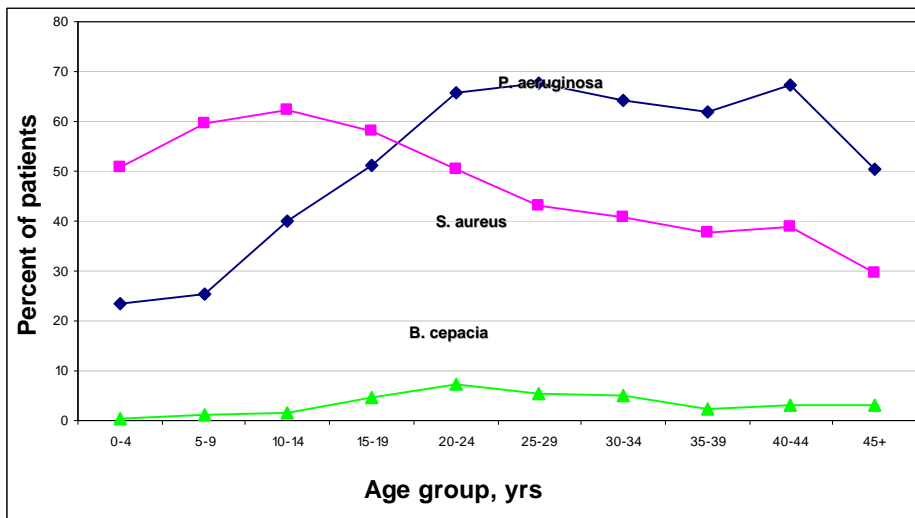
### BMI (mean) vs Age



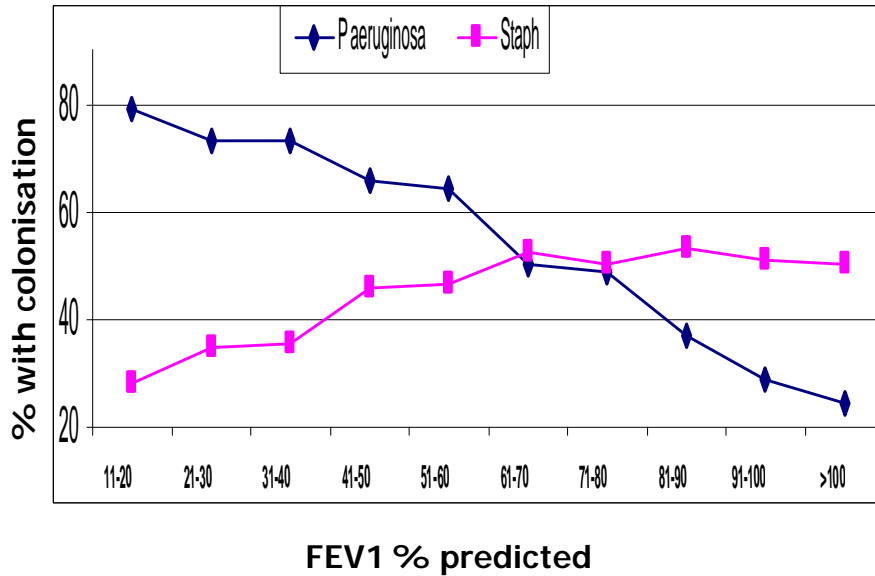
### Median BMI vs age for pancreatic status; n=6087 (5148 PI, 939 PS)



### Respiratory infections vs age - 2003



## Bacterial colonization vs Mean FEV<sub>1</sub>



## Treatment - 2003

Inhaled antibiotics		
N = 10752	n	%
Continuous	1891	17.6
Intermittent	546	5.1
Not treated	2741	25.5
Not reported	5574	51.8

## Treatment - 2003

Pulmozyme		
N = 10752	n	%
Treated	3028	28.16
Not treated	2561	23.82
not reported	5163	48.02

## Treatments - 2003

	No report	Treated	Treated % of reported	Treated, % of total patients
Inhaled steroids	5574	1995	42.6%	18.5%
Oral Steroids	9880	313	83.0%	2.9%
Inhaled bronchodilators	5574	2748	58.6%	26%
Urso	8312	1037	53.3%	9.6%
Oxygen	3145	410	5.8%	3.8%

## CF related Complications CFRD

	not reported	IGGT	IGGT % (1) (2)	Insulin	Insulin % (1) (2)
<18	2982	31	0.5 0.9	97	1.5 2.9
>=18	2385	75	1.7 3.7	439	10 21.8

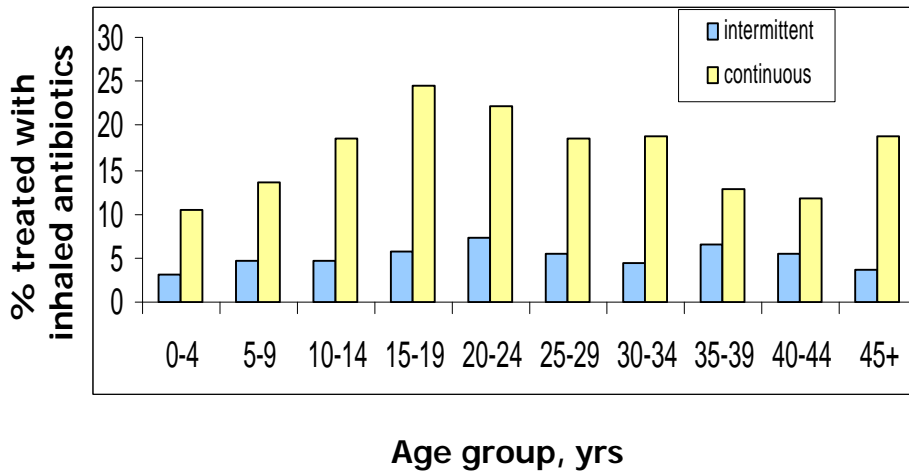
(1) % of total patients

(2) % of reported

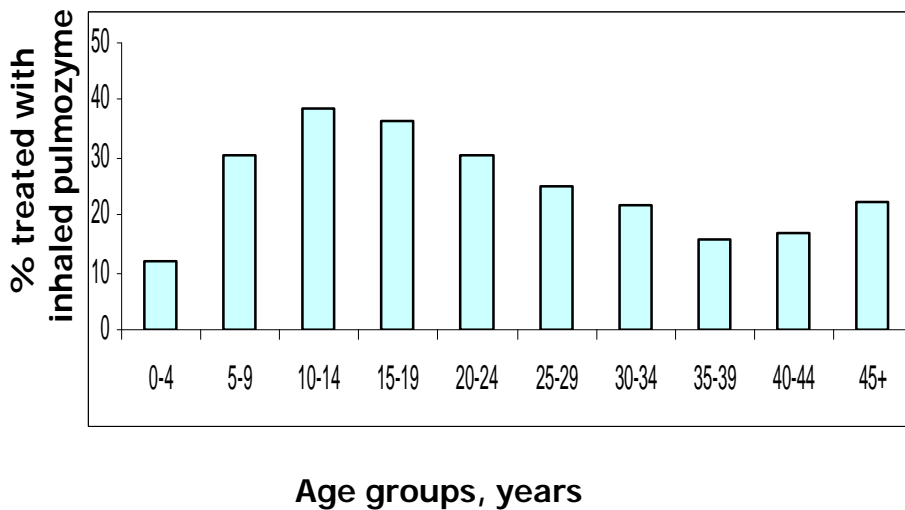
## CF related Complications

complication	age	not reported	n	% (tot pts)	% (reported)
ABPA	<18	1627	226	3.6	5.3
	>=18	1518	322	7.4	11.2
DIOS	<18	1690	87	1.4	1.9
	>=18	1578	111	2.5	3.9
liver cirrhosis	<18	901	304	4.8	5.6
	>=18	763	233	5.3	6.4
nasal polyps	<18	1686	258	4.1	5.5
	>=18	1582	264	6.0	9.4
malignancy	<18	2519	9		
	>=18	2142	10		

### Percent of inhaled antibiotics according to age groups (n= 5178)



### Percent of inhaled pulmozyme according to age groups (n=5589)

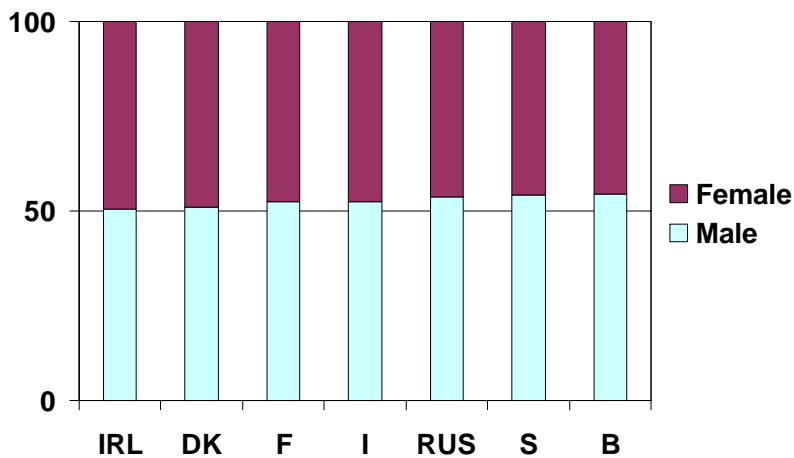




# On a country level

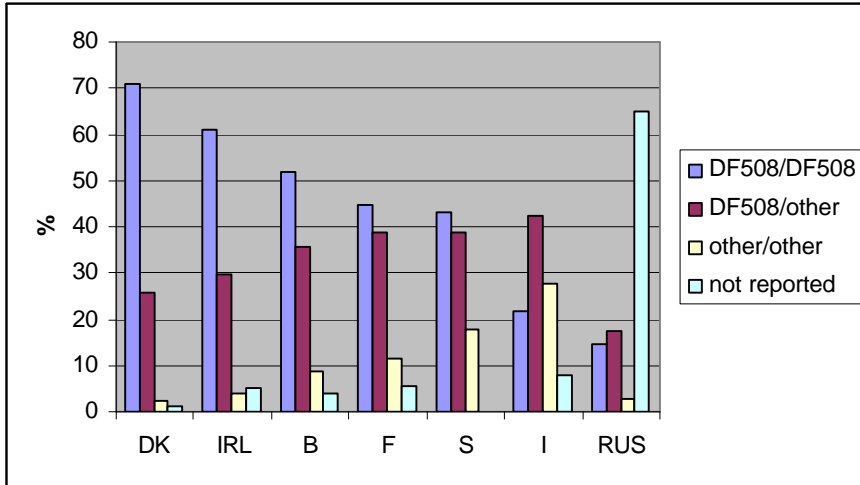
Results split on the 7 participating countries

## Gender distribution by country

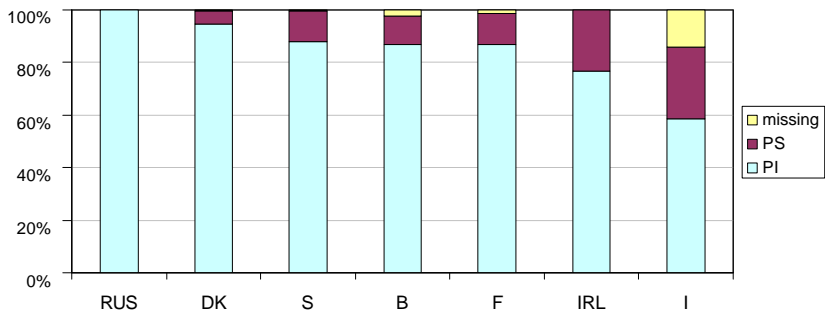


P = 0.82 for all. IRL vs B: p=0.21

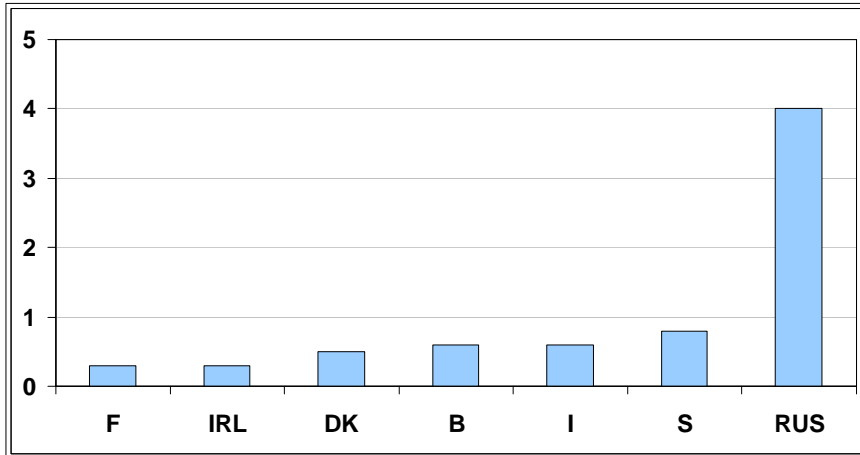
# Genotypes



# Pancreatic insufficiency

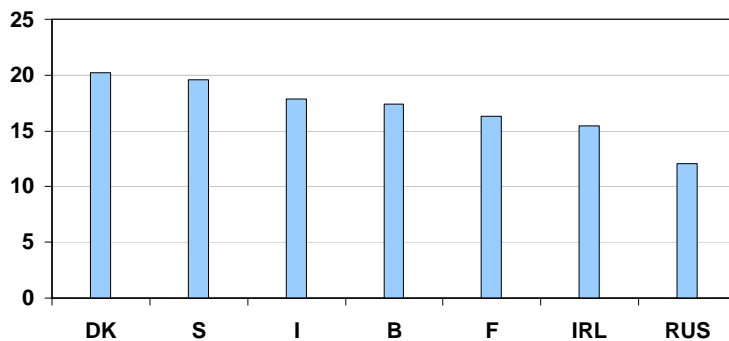


## Median age at diagnosis (yrs)



Some of this might reflect the policy of newborn screening (see slide 3), as well as the access to genetic diagnosis

## Mean age by 12.31.03

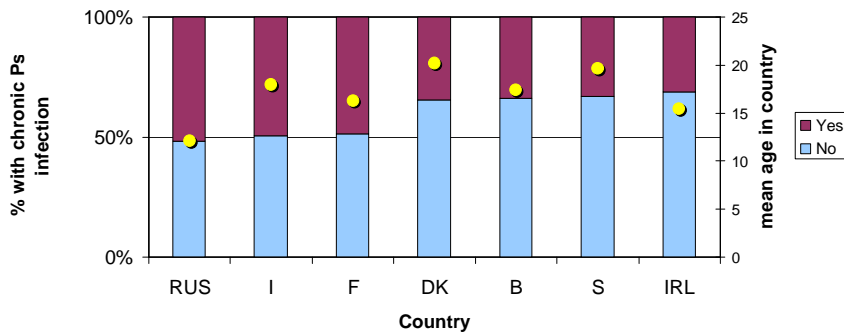


# Mortality in 2003

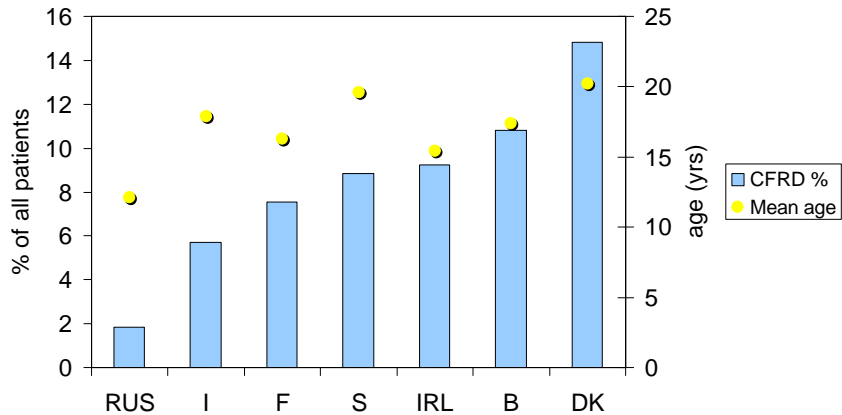
	B	DK	F	IRL	I	S	RUS	Total
Total patients	860	412	4104	325	4142	362	547	10742
Deaths	13	5	56	4	43	2	0	115
Mortality %	1.51	1.23	1.38	1.25	1.05	0.56	0	1.08

This is of course a snapshot and includes only one years observation period, making statistic comparison irrelevant

# Chronic pseudomonas infection



# CFRD with insulin



Some countries report both IGGT and IDDM as CFRD

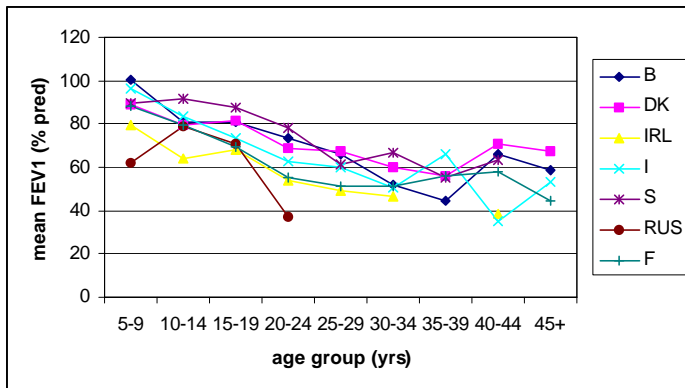
# Lung transplantation dF508 homozygotes

	no	yes- before 03	yes- during 03	% Lung TX
<b>IRL</b>	198	0	0	0
<b>RUS</b>	80	0	0	0
<b>S</b>	155	1	0	0.64
<b>I</b>	878	19	1	2.23
<b>B</b>	429	13	3	3.60
<b>F</b>	1538	62	0	3.88
<b>DK</b>	268	19	5	8.22

# Liver transplantation dF508 homozygotes

	no	yes-before 03	yes-during 03	% Liver TX
RUS	80	0	0	0
IRL	198	0	0	0
DK	291	1	0	0.34
I	894	4	0	0.45
F	1538	7	0	0.45
B	439	4	1	1.13
S	154	1	1	1.28

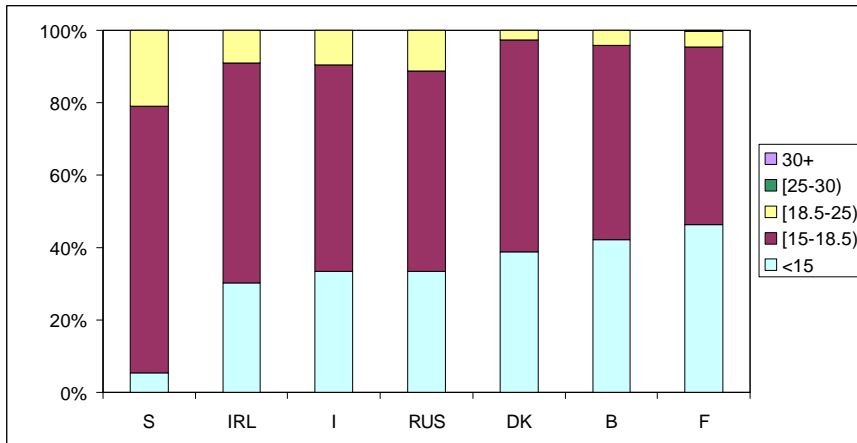
## Mean FEV1 in age groups – deltaF508 homozygotes



	Number of patients in each agegroup									
	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45+	
B	55	81	63	61	34	21	19	5	1	
DK	23	49	42	31	32	26	13	10	4	
IRL	28	29	31	23	12	7	0	2		
I	33	51	35	24	20	15	4	1	1	
S	19	33	22	17	13	12	9	3		
RUS	6	11	5	2						
F	196	325	293	226	146	77	39	9	6	

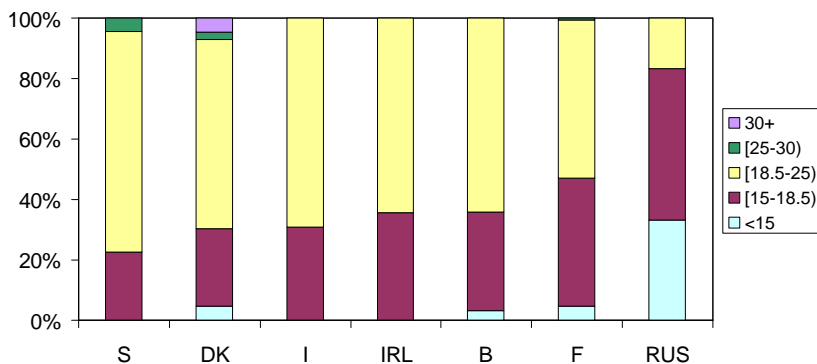
Please note that – apart from France – the number of patients in each group is small

## Median BMI 5-9 y-old dF508 homozygotes



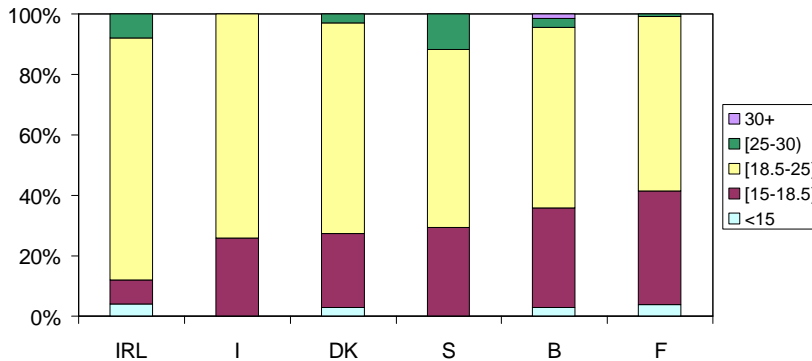
Normal median BMI 15,5 to 16 in this age group (Karlberg, Acta Pædiatr 2001, 90:1427-1434)

## Median BMI 15-19 y-old dF508 homozygotes



Normal median BMI 15,5 to 16 in this age group (Karlberg, Acta Pædiatr 2001, 90:1427-1434)

## Median BMI 20-24 y-old dF508 homozygotes



Normal median BMI should be 21-23 in this age group. BMI lower than 18.5 is underweight (1997 WHO Expert Consultation on Obesity).

## Conclusions

- Data merging is possible
- There is no standardization of data entry
- There is no consensus on definitions
- There are **many** missing data

SO....

We need a common registry with common definitions, and clinical value that will make the clinicians use it



## Thanks to ....

- Sophie Ravilly, France
- Linda Foley, Ireland
- Claude Sevens, Belgium
- Anders Lindblad, Sweden
- Natalia Kashirskaya and Tatiana Kapustina, Russia
- And the national registries of all 7 countries for the contribution