La Fibrosi Cistica:
evoluzione da malattia fatale dell'infanzia a malattia cronica dell'adulto

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La Fibrosi Cistica

CF is the most common multiorgan genetic disease in the white population and leads to chronic lung disease, lung infection, bronchiectasis, and malnutrition secondary to pancreatic insufficiency.

Historically, CF was a disease with an early mortality, often before the patient reached adult age.

Caso clinico

G.V., ♂ 13.2.99

Secondogenita. Gravidanza normodecorsa, parto a termine (38 sett.).

Peso nascita: 2980 g. Apgar 1° : 7, 5° : 8

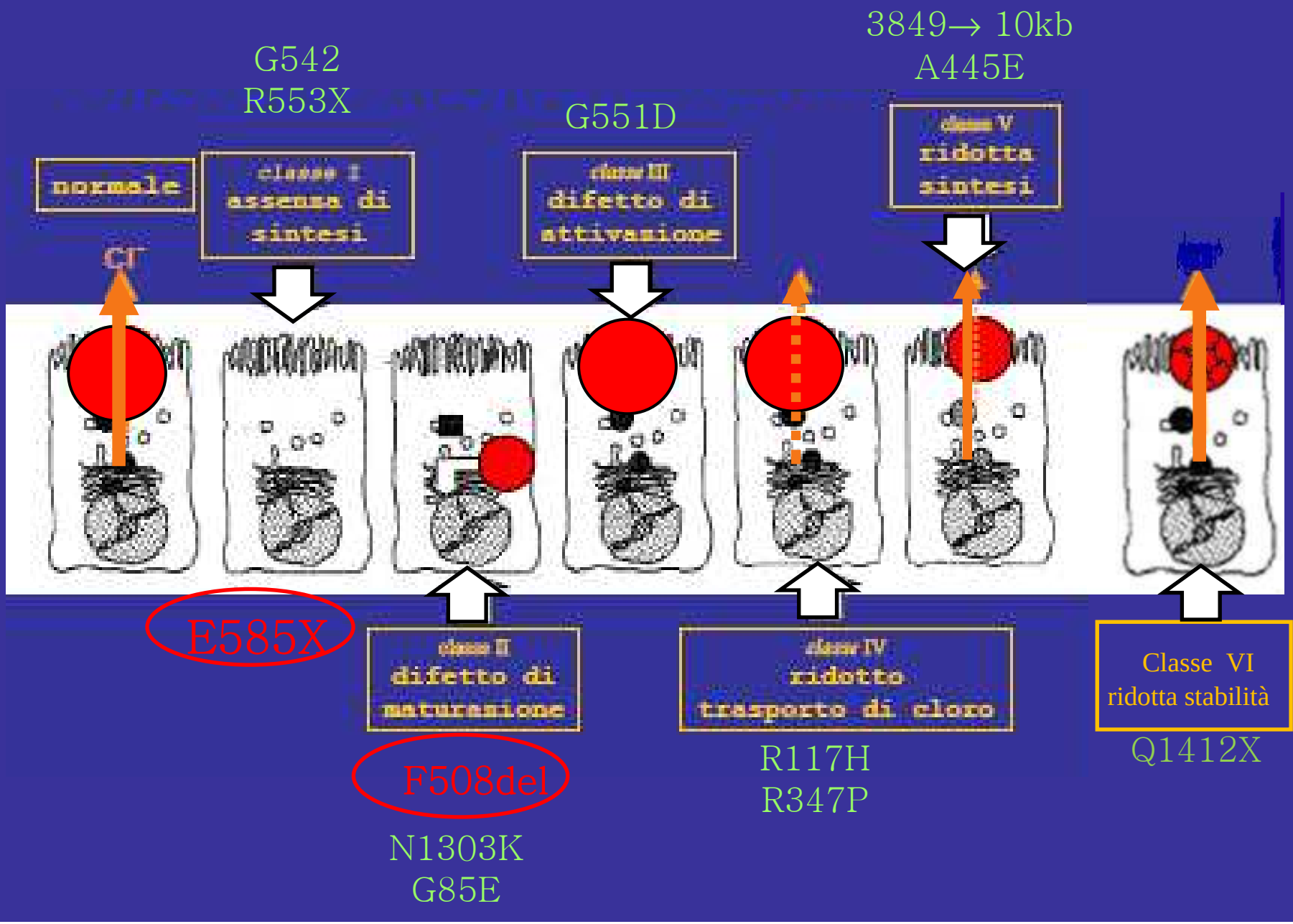
Dalla nascita alvo e crescita irregolare.

Diagnosi a 12 mesi durante un ricovero per bronchiolite.

Sweat test: Cl 109 mEq/L (v.n. > 60 mEq/L)

Genetica: F508 del/E585X

Classificazione delle mutazioni di CFTR



Insufficienza pancreatica → supplementazione enzimatica.

Persiste tosse catarrale e reperto broncostruttivo → broncodilatatore inal., steroide per os a cicli e antibiotico per os 15 gg/mese.

13 mesi : 1° isolamento di P. aeruginosa → tobra inal.

Dai 3 ai 6 anni : circa 2 ricoveri/anno per PEx. Sintomi persistenti.
Isolamento di nuovi microrganismi: Staf.aureus, Aspergillus, Achromobacter.
Terapia continuativa con **steroide** e azitro p.o.

8 anni: isolamento di Micobacterium abscessus (MABs).

9 anni: isolamento di Stenotrophomonas maltophilia.
Aumento markers di ABPA (no IgE spec.)

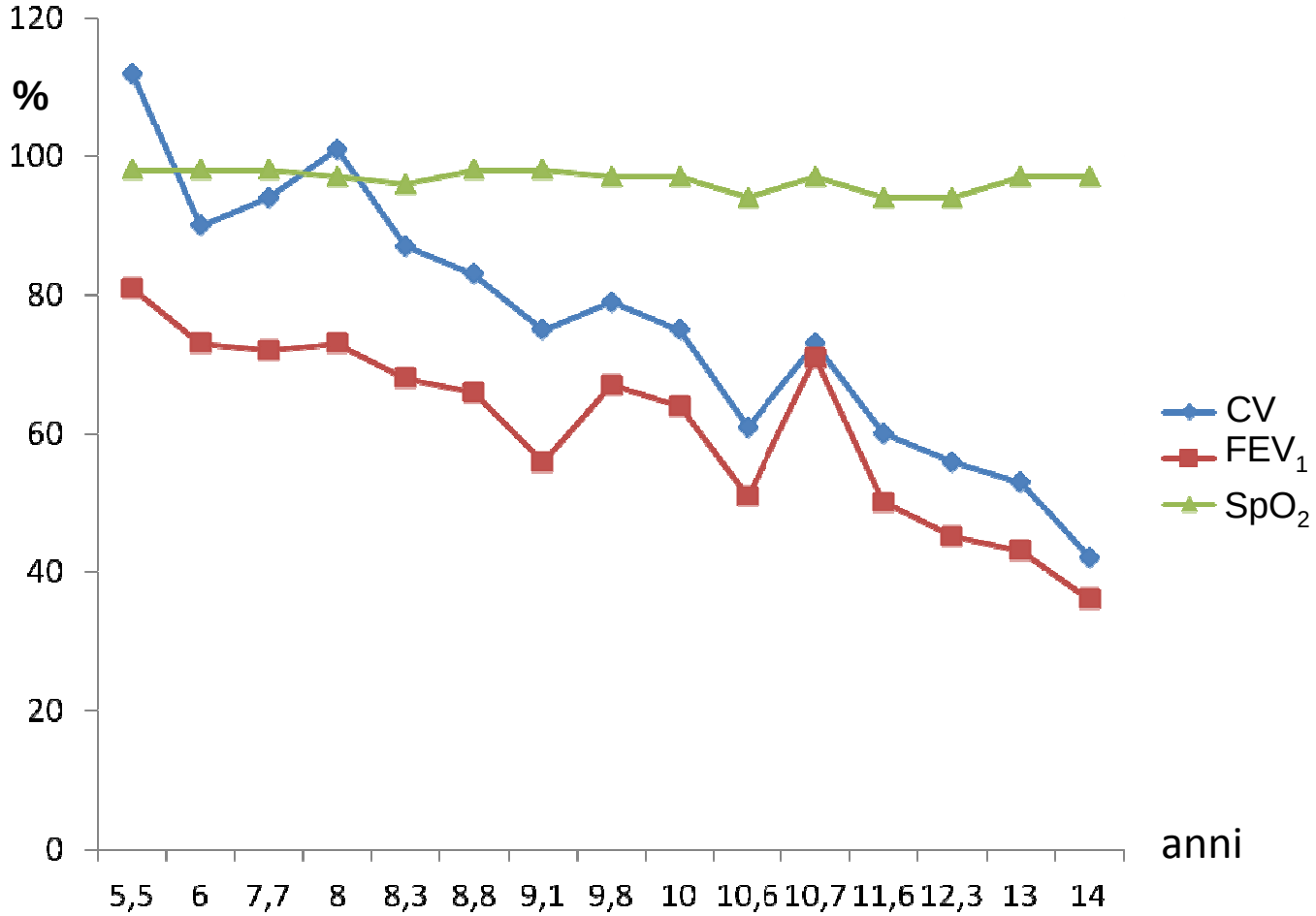
10 anni: inizia O2-terapia domiciliare e DNase inal.

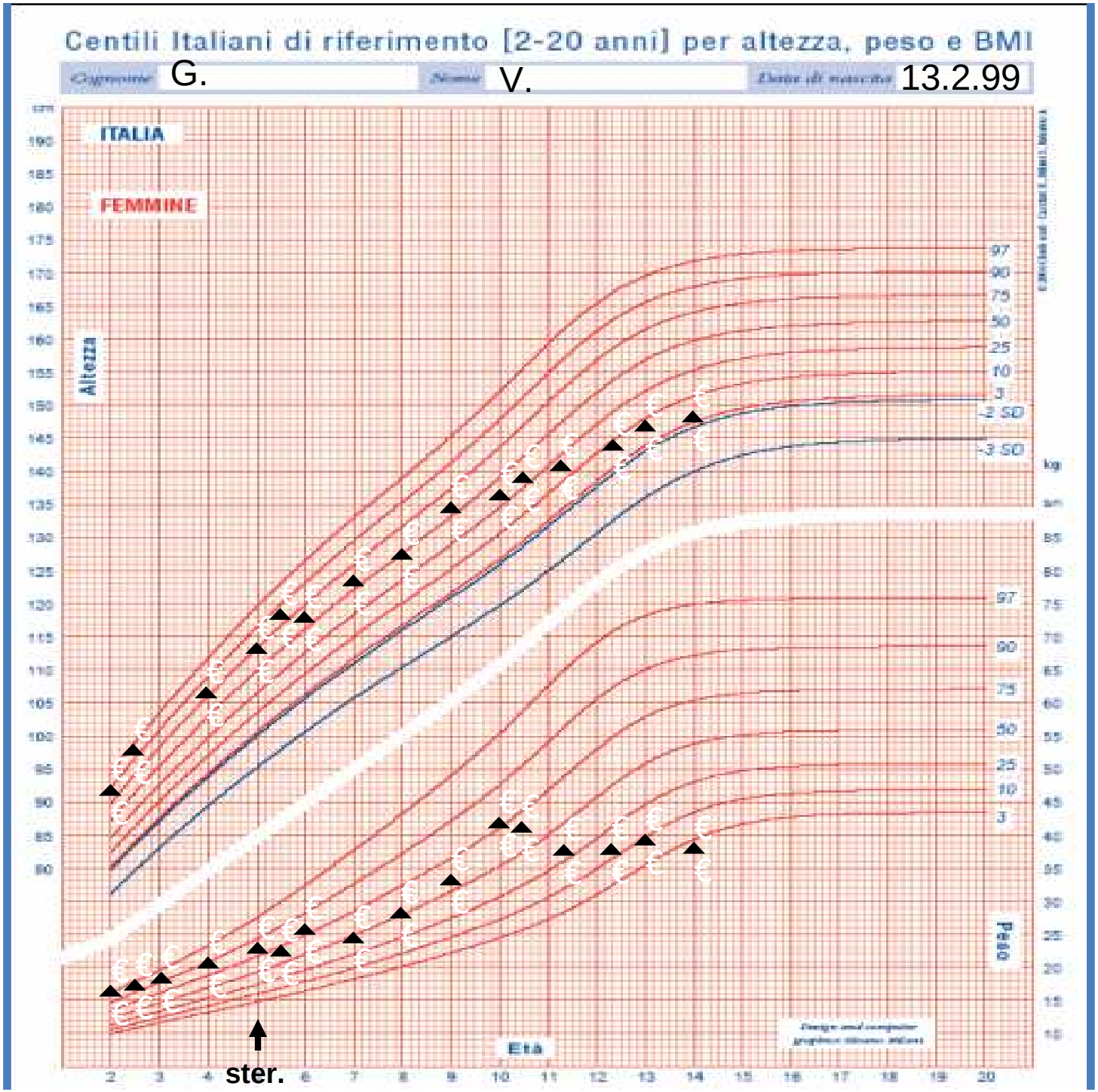
11 anni: cicli di Ig ev, sol. ipertonica inal. Impianto di port- a-cath.

13 anni: (2012) ricovero da agosto a dicembre per febbre ricorrente.
PNX dx. Rimosso port- a- cath.
Esordio di diabete → terapia insulinica.
Richiesta valutazione per TP.

14 anni: (2013) da febbraio ricovero per insufficienza respiratoria e febbre ricorrente. Re-impianto di port- a- cath.
Terapia continuativa anti-MABs : meropenem in infus continua ev
tigeciclina ev a g.alterni
amikacina inal.
cipro + voriconazolo po

Andamento della funzionalità respiratoria




Centili Italiani di riferimento [2-20 anni] per altezza, peso e BMI
Cognome G.
Nome V.
Data di nascita 13.2.99
ITALIA
FEMMINE
Altezza
Peso
Età
97
90
75
50
25
10
3
-2 SD
-3 SD
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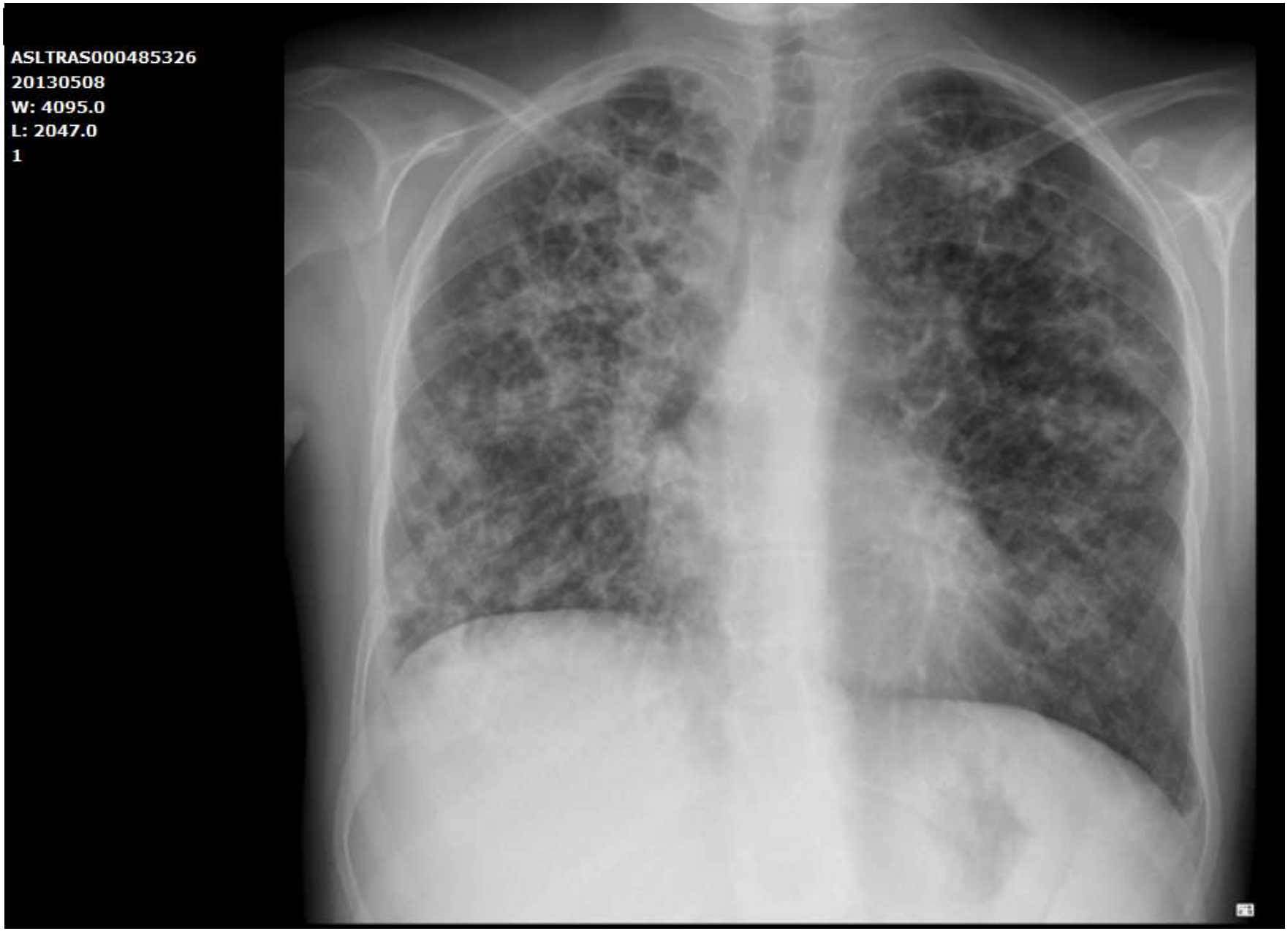
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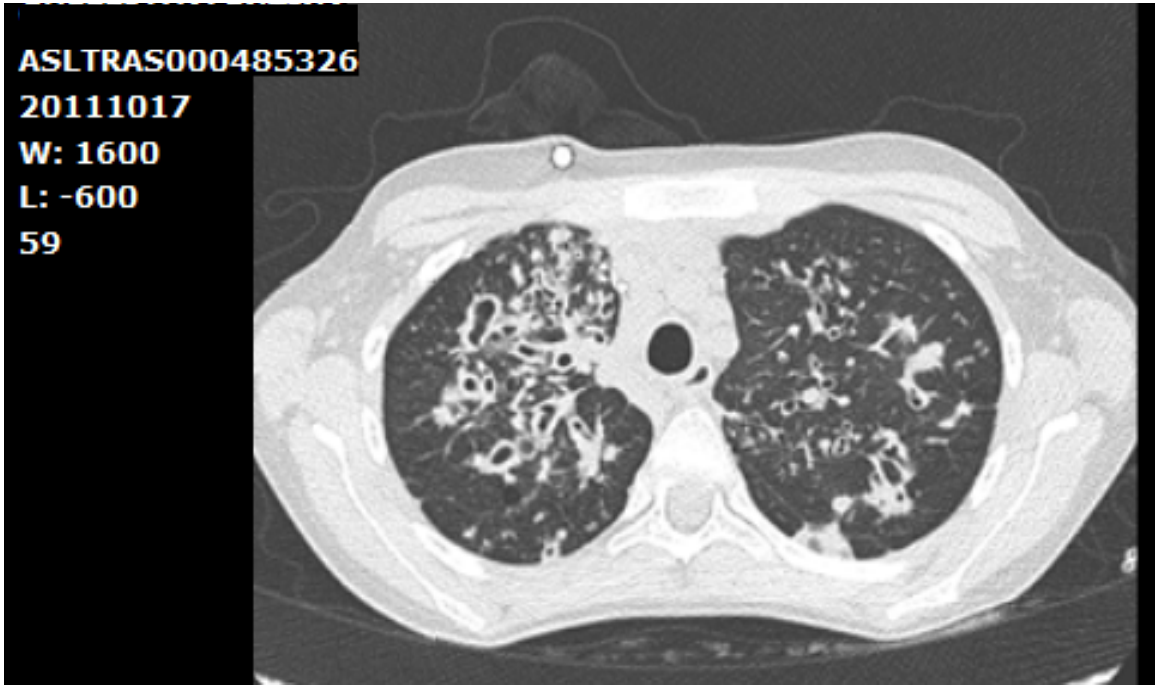
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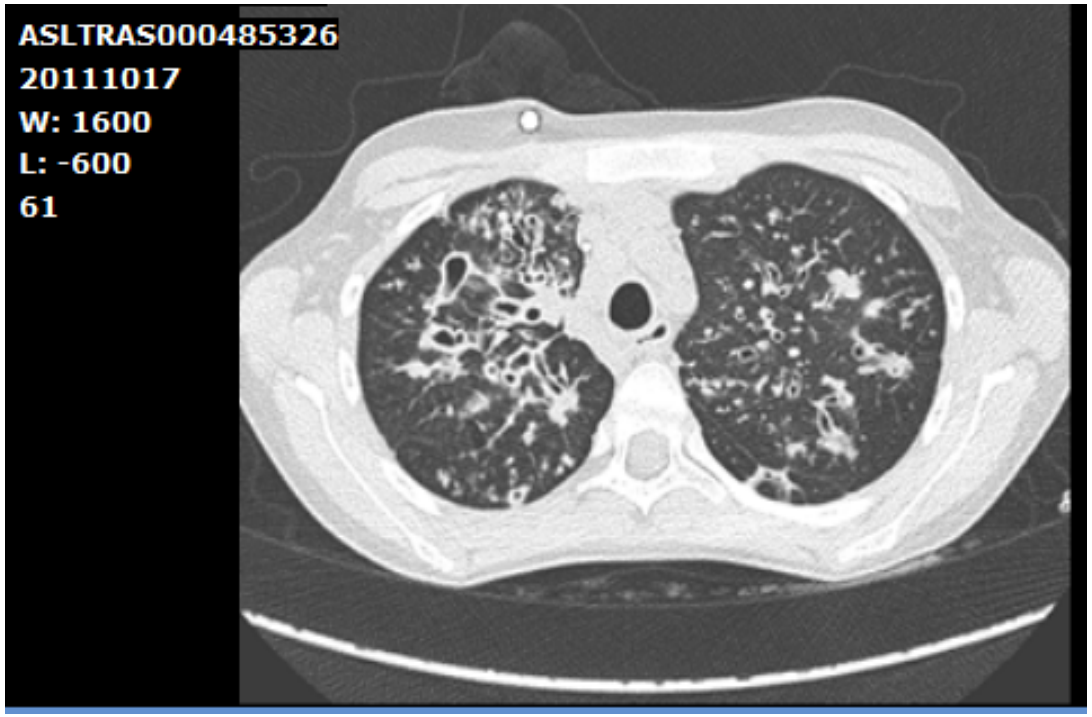
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CFF survival, US registry

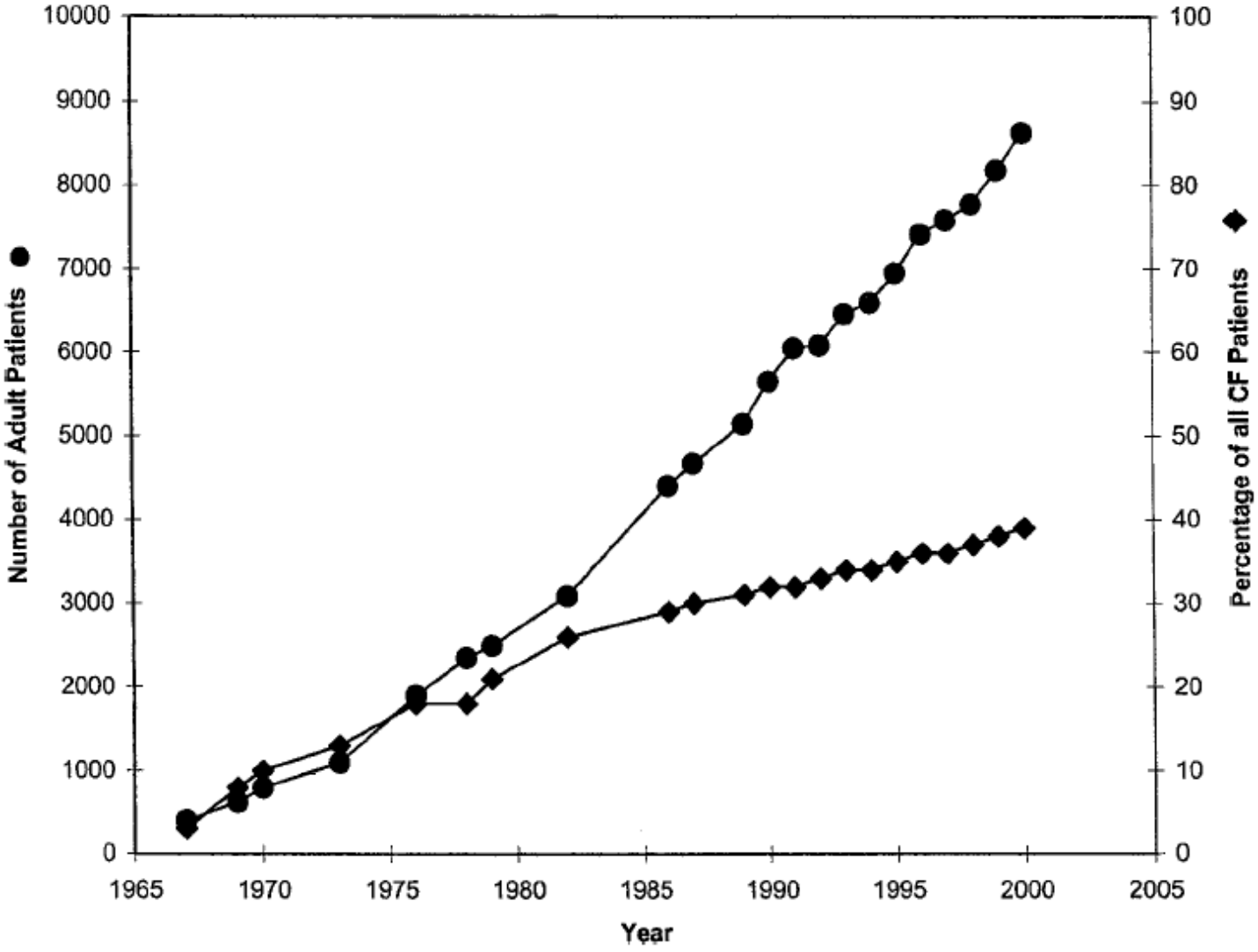
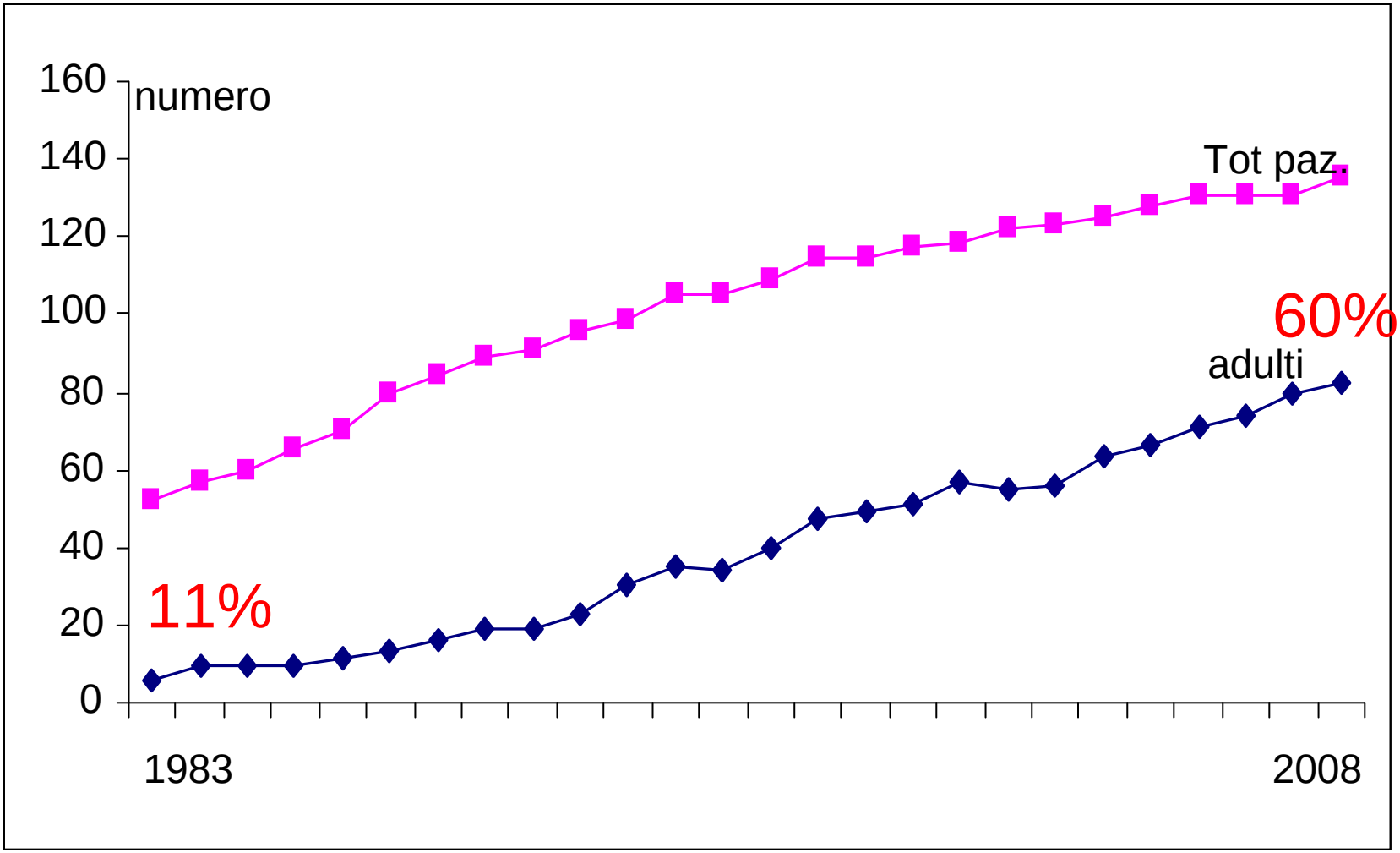


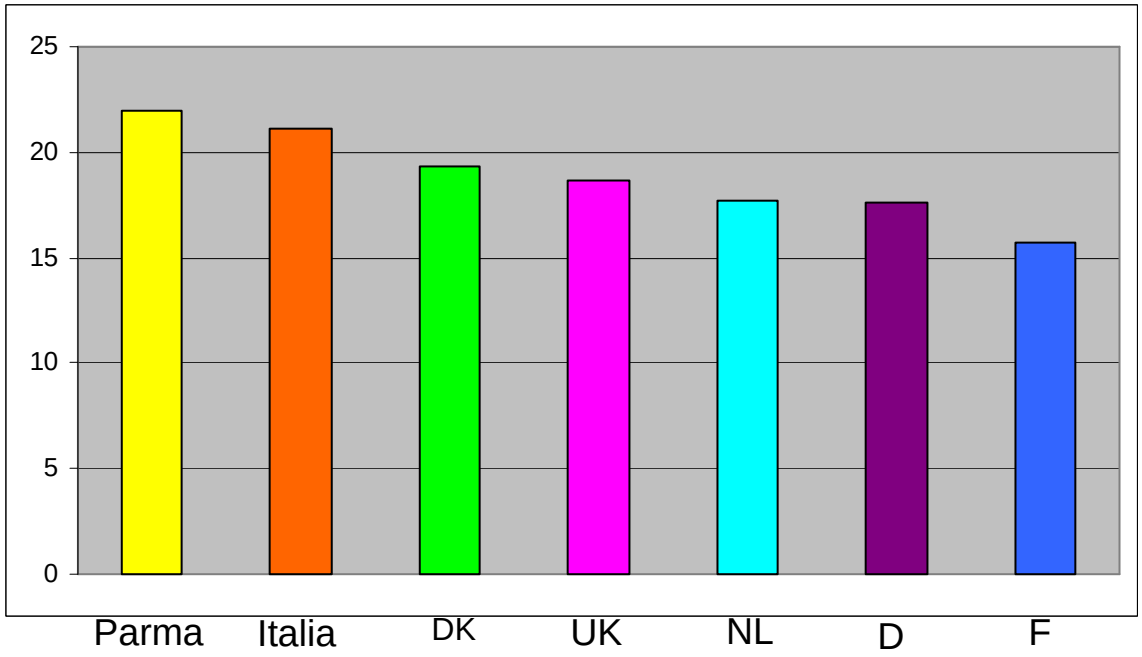
FIGURE 1. Adult CF patients, 1965 to 2000.

Centro FC Parma dal 1983 al 2008
N ° totale pazienti e n ° adulti.



Età mediana pazienti

	Parma	Italia	DK	UK	NL	D	F
Min-max.	0.1-56	0.2-69	0.5-59	0.1-76	0.0-68	0.1-67	0.1-78
% paz. > 18 a:	61	58	54	52	49	48	42



How to best deliver care to children with chronic illness: cystic fibrosis as a model

Robert Kaslovsky and Matthew Sadof

Current Opinion in Pediatrics 2010, 22:822–828

Transition of care

is an important aspect of managing the healthcare needs of patients dealing with chronic health issues, particularly those with conditions that manifest during childhood.

What is transition ?

Transfer

the responsibility of care is transferred from a pediatric care setting to an adult care setting, focused on the qualifications and training of the medical team.

Transition

a developmental process of skill-building in self-management (*supported by the health system*) that proceeds as the patient's and family's readiness progresses.

"the purposeful, planned preparation of pediatric patients (and their families) for **successful transfer** to an adult care setting "

Smoothing the transition from pediatric to adult care: lessons learned

Current Opinion in Pulmonary Medicine 2009, 15:611–614

Patrick A. Flume

The transition process should begin early in life

Evaluate the adolescent patient without the parent present

The adult team should participate in the care of the patient prior to the actual transfer: meeting the adult team prior to transfer can reduce anxiety

Transfer should occur at a defined time: makes it an actual goal.

Communication between programs is essential: a regular meeting between the pediatric and adult care teams promotes a common approach to CF care.

Transition document
CF team at Great Ormond Street Hospital, London

Table 4. Transition Program

Key Concepts	Content
Coordination	The coordinators in the transition program are the clinical nurse specialists. Their role is to identify all children approaching the age of transition, book transition clinic appointments, and ensure the families receive information about the process. Liaise with coordinators at the adult services.
Preparation	Transition is mentioned at annual review from early childhood; children and families therefore approach transition as an expectation. Psychosocial preparation begins at about 14 years of age and includes encouraging independence in health management and in relationships with the cystic fibrosis (CF) team, support for patients and parents in dealing with adolescent issues, staff acknowledgment of changing attitudes to the disease and management, provision of information about adult CF centers and adult health care services, including a schedule of likely timings and events.
Process	Transition commonly occurs at 16-17 years of age. Exceptions include the terminally ill, family stress, and siblings—the aim is to transfer siblings together if close enough in age. Children age 14 years and older are invited to transition clinics attended by the adult CF teams from targeted centers. Informal visits are encouraged to targeted adult centers. Discussion among patient, parents, and the teams from both the pediatric and adult centers continues until suitable choice of adult center is made. Great emphasis is made on the family to make the choice with guidance from professionals. A date is set for transfer; the pediatric team make a formal, multidisciplinary referral.
Outcome	After the first appointment at the adult center a final appointment occurs at the pediatric center to say goodbye. Liaison continues via the coordinators, although further contact with the patient and family is discouraged at the pediatric center.
Evaluation	The above protocol for transition is followed for each patient; the coordinator will audit each phase of the process, ensuring completion of the program.

S.Madge, M.Bryon, Journal of Pediatric Nursing, Vol17,No4(August),2002

Why adult care programs are necessary

"Ask any member of the CF team which physician they would call if they had a healthcare problem; it is highly unlikely they would ask for a pediatrician. Why should we expect any less for our adult patients ? "

PA Flume, 2009

Differences in the care of chronically ill adults and children

Adult-centered care	Child-centered care
Positive sense of future	Adulthood is unrealistic expectation
Patient-centered	Family-centered
Collaborative, empowering	Prescriptive, protective
Focused on present	Focused on future

Programma di transizione centro FC di Parma

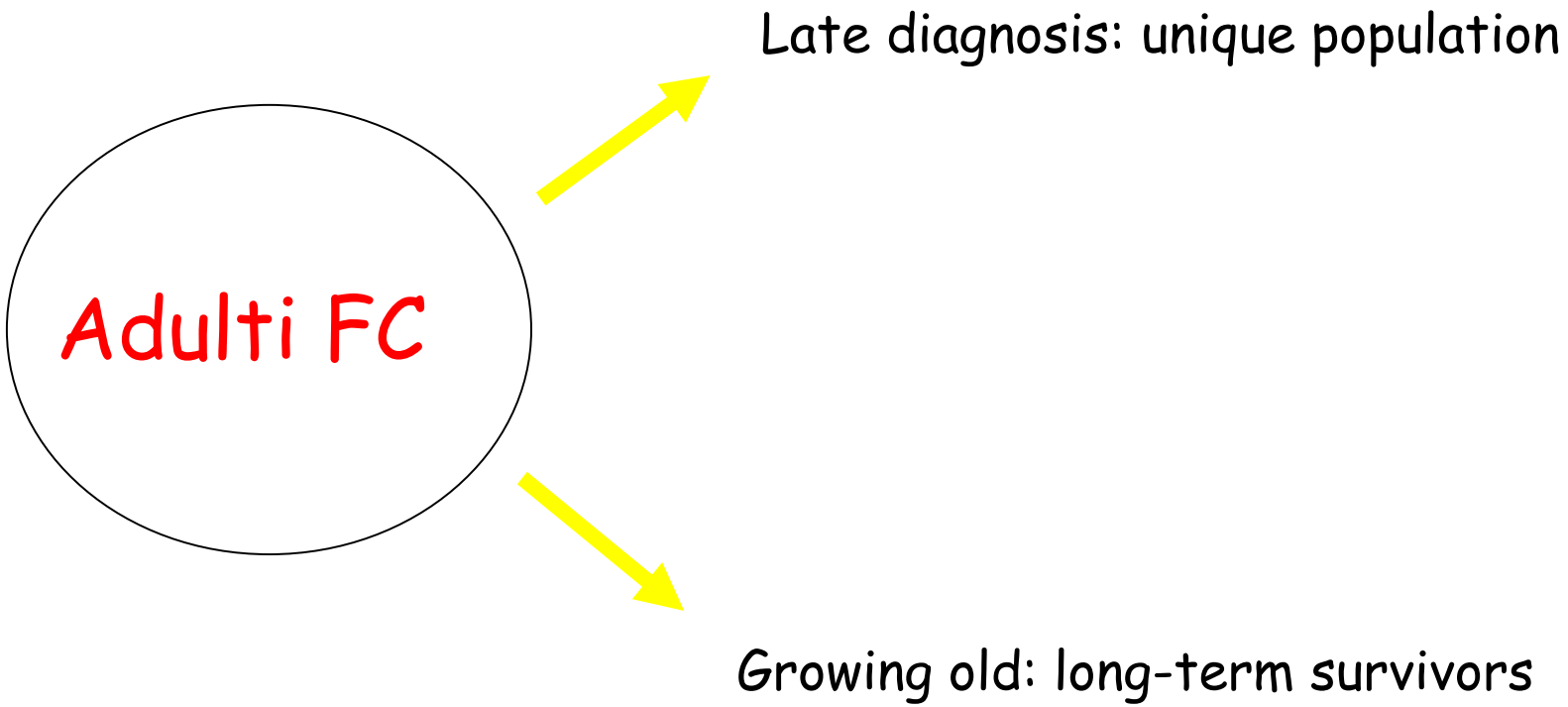
- inserimento nel team di uno pneumologo Dr. Francesco Longo, che dal 2007 segue i pazienti adulti sia in regime ambulatoriale che di ricovero

- ricovero dei pazienti adulti in Clinica Pneumologica dal novembre 2009

- protocollo condiviso multidisciplinare di gestione e trattamento dei pazienti adulti affetti da FC in regime di ricovero ospedaliero

Ricoveri pazienti adulti 2011-2012

	2011	2012	variazione %
N° ricoveri	29	34	17
N° pazienti	20	28	40
N . Pazienti ≥ 2 ricoveri (%)	5 (17)	5 (15)	0 -2.5)
Età media (a,m)	26,7	26,6	- 0,4
Degenza media (gg)	23	17	- 29
N .impianto PICC (%)	9 (31)	19 (56)	111 (25)
N . NIV (%)	6 (21)	1 (3)	-83 (-18)
N .O_2ter. (%)	15 (52)	12 (35)	-20 (-16)


Adulti FC
Late diagnosis: unique population
Growing old: long-term survivors

Genetic and clinical features of patients with Cystic Fibrosis diagnosed after the age of 16 years.

Gan K-H, Geus WP, Bakker W, Lamers CBHW, Heijerman HGM

Thorax 1995;50:1301-1304

Among this group of 1423 adult patients with CF late diagnosed is caused mainly by delayed expression and mild progression of clinical symptoms.

Late diagnosis is associated with milder pulmonary disease, less pancreatic insufficiency, and different CF mutations.

Since mortality in CF depends on the progression of pulmonary disease, patients with a late diagnosis have a better prognosis than those diagnosed early.

Health Status and Sociodemographic Characteristics of Adults Receiving a Cystic Fibrosis Diagnosis After Age 18 Years*

Eileen Widerman, Lois Millner, William Sexauer and Stanley Fiel

Chest 2000, 118: 427

Late diagnosis was associated with fewer complications, fewer hospitalizations, less oxygen use, fewer courses of home IV treatment, and less enzyme use.

Psychosocially, those patients receiving late diagnoses were more likely to be college graduates, married, and employed full time.

Clinical Manifestations of Cystic Fibrosis Among Patients With Diagnosis in Adulthood*

Marita Gilljam, Lynda Ellis, Mary Corey, Julian Zielenski, Peter Durie and D. Elizabeth Tullis

Chest 2004;126;1215-1224

Table 1—*Proportion of Patients With CF Diagnosed in Adulthood and Childhood

	Adulthood†	Childhood
1960–1969	6 (2)	276 (98)
1970–1979	6 (2)	261 (98)
1980–1989	15 (6)	230 (94)
1990–2001	46 (18)	211 (82)

*Data are presented as No. of diagnoses (%).

†Age ≥ 18 years, or presenting to and receiving diagnosis in the adult clinic. A higher proportion of diagnoses were made in adult age after, compared to before, 1990 ($p < 0.0001$), even after excluding 11 adult patients derived from recent research studies ($p < 0.0001$).

Caratteristiche clinico-funzionali dei pazienti con diagnosi di CF in età adulta tra 1990-2001

sweat test + (% paz.)	**65**	
2 mutat. CFTR (% paz.)	33	
x FEV1 (% pred. , ± SD)	81 ± 26	
P symptoms (% paz.)	39	
P+ GI symptoms (% paz.)	22	} 100
Infertility (%paz.)	26	
Other symptoms (%paz.)	13	
Bronchiectasis (% paz.)	59	
P. aeruginosa (% paz.)	45	

Confronto delle caratteristiche cliniche dei pazienti diagnosticati in età adulta (AD) e in età pediatrica (C)

	AD	C	p
Diagnosi 1960-2001			
$\bar{x}$ sweat test (± SD) mmol/L	75 ± 26	100 ± 19	0.001
PS (% paz.)	73	13	0.001
P symptoms (% paz.)	87	64	0.002
GI symptoms (% paz.)	47	81	0.001
Diagnosi 1990-2001			
Δ F508/ Δ F508 (%paz.)	2	49	
Δ F508 eterozig. (%paz.)	63	39	

Conclusions

Patients with CF presenting in adulthood often have PS (73%), inconclusive sweat test results (1/3), and a high prevalence of mutations that are not commonly seen in CF diagnosed in childhood.

Patients with CF diagnosed in adulthood present with a wide spectrum of symptoms and severity of disease that does not resemble the characteristic features at presentation in childhood.

Furthermore, patients may come to the attention of several different disciplines, including andrologists, gastroenterologists, otolaryngologists, and respiratory physicians.

Late Diagnosis Defines a Unique Population of Long-term Survivors of Cystic Fibrosis

Fibrosis Center, National Jewish Medical and Research Center;
The Children's Hospital, Denver, Colorado

Am J Respir Crit Care Med Vol 171. pp 621–626, 2005

***CFTR* F508 homozygous individuals were more common in the Early Diagnosis (ED) group.**
The majority of Late Diagnosis (LD) patients were female,had a significantly lower prevalence of pancreatic insufficiency and CF-related diabetes, and better lung function.
Fewer patients were infected with *Pseudomonas aeruginosa*.

Our findings indicate that patients diagnosed as adults differ distinctly from survivors of long-term CF diagnosed as children.

Growing old with cystic fibrosis — The characteristics of long-term survivors of cystic fibrosis

Nicholas J. Simmonds [a,*], Paul Cullinan [b], Margaret E. Hodson [a]

Respiratory Medicine (2009) 103, 629–635

A case series (n.112) of patients from Royal Brompton Hospital London who had reached their 40th birthday without transplantation.

Results

median age: 43.1 years (range 40 -71.1); 57% men.
68% diagnosed before 16 years of age.
30% were DF508/DF508.
82% pancreatic insufficiency
76% colonisation with Pseudomonas aeruginosa

They required less than one hospital admission a year; lung function and BMI were relatively well preserved. Many were married and working.

Conclusions

We describe one of the largest surveys to date of CF patients aged more than 40 years.

The full spectrum of disease is represented in this population and, importantly, 30% are DF508 homozygous.

CASO CLINICO

S.V., F, DoB: 17.7.75

DIAGNOSI: 06/05/1981, età di 5 anni e 10 mesi.

Motivo della diagnosi:
sintomi (alvo irregolare e steatorrea, scarso accrescimento, ricorrenti bronchiti)
Sweat test : Cl 124 mEq/L (VN < 60 mEq/L)

Profilo genetico: eterozigote composta per le mutazioni F508del ed E585X

Insufficienza pancreatica.

DIABETE dall'età di 10 anni in terapia con Insulina

MICROBIOLOGIA: infezione cronica da Pseudomonas aeruginosa , spesso isolamento di Aspergillus.

Grafico trend FEV1(% PRED)

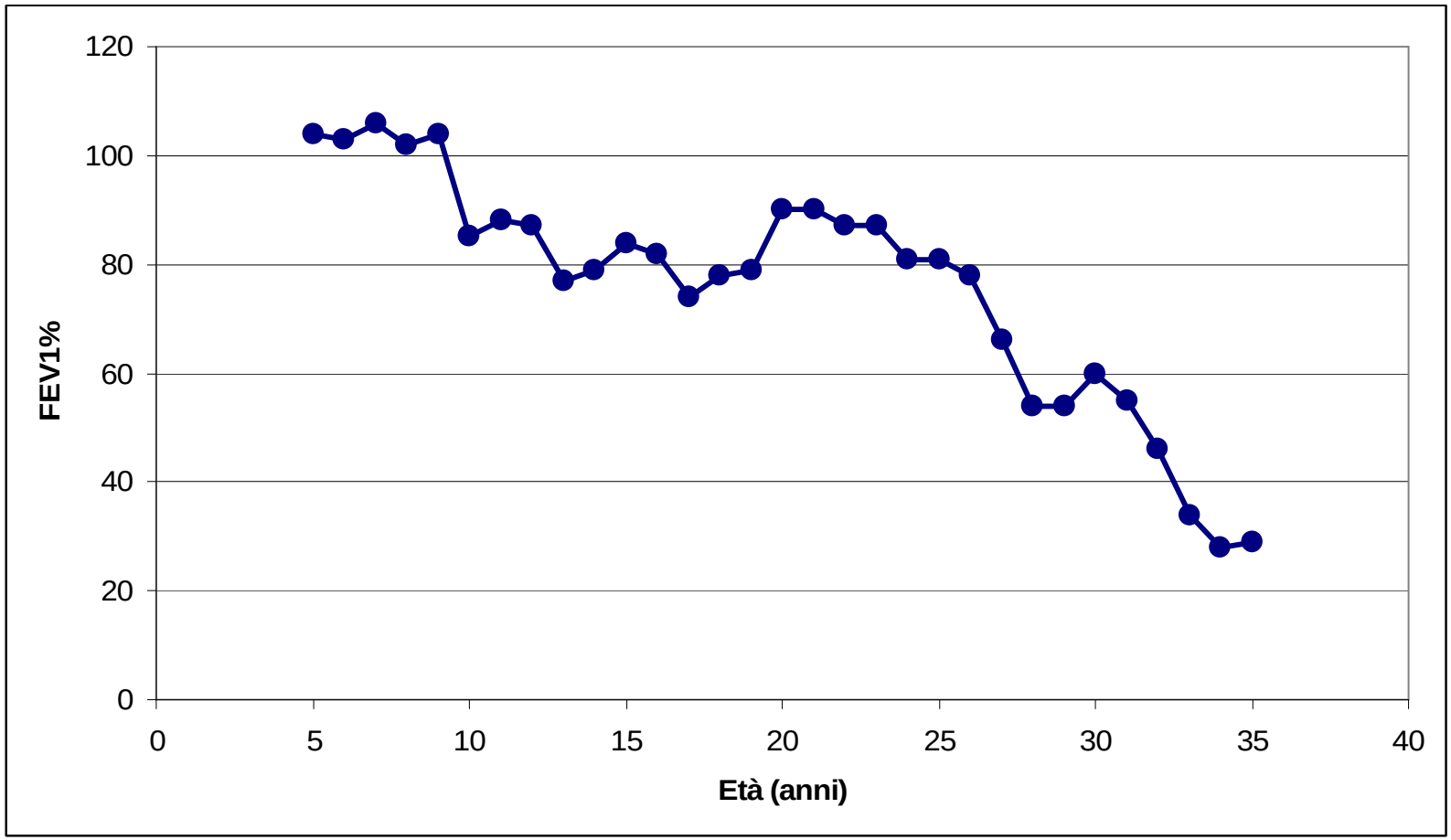
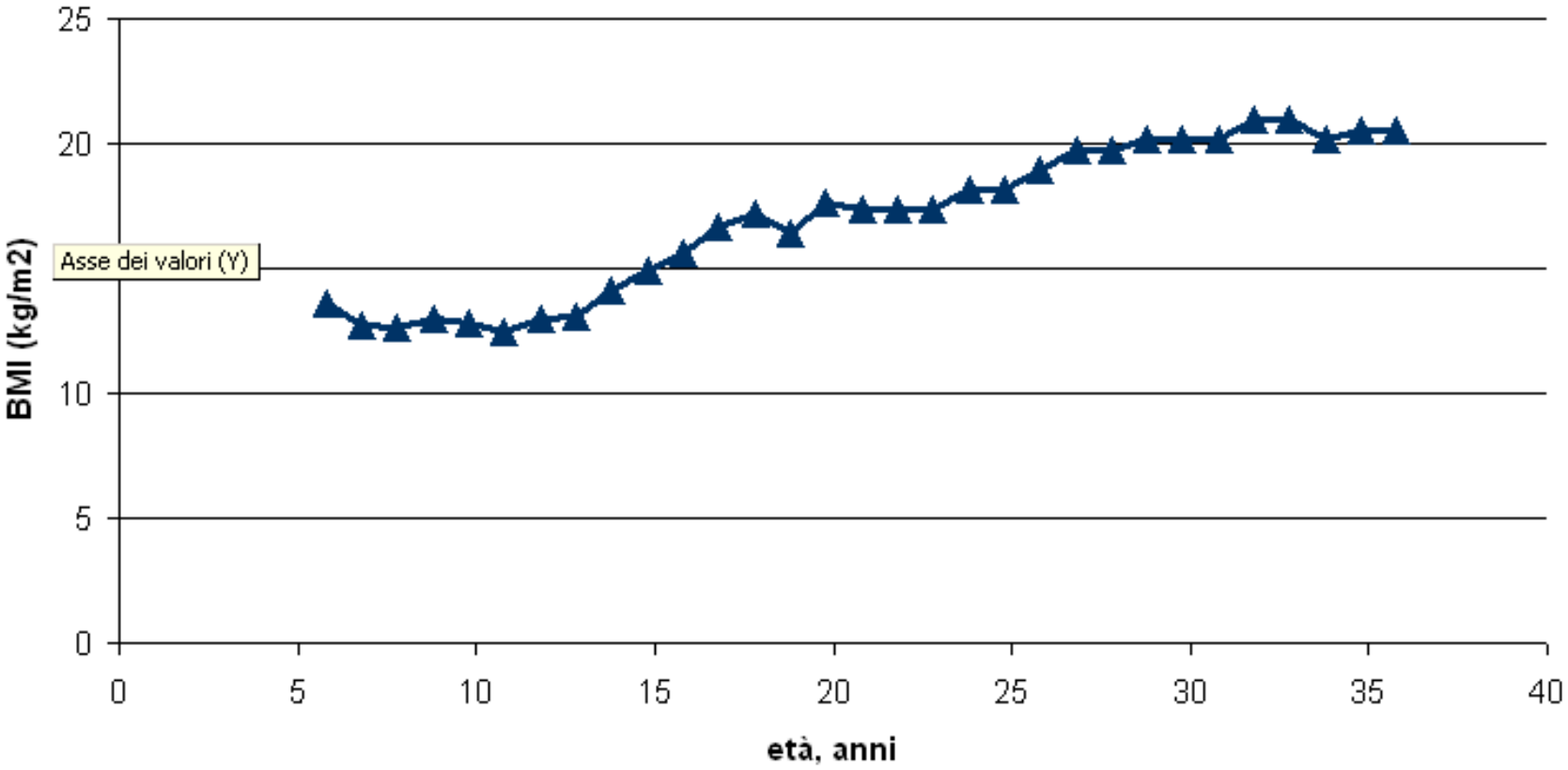


Grafico trend BMI (kg/m2)



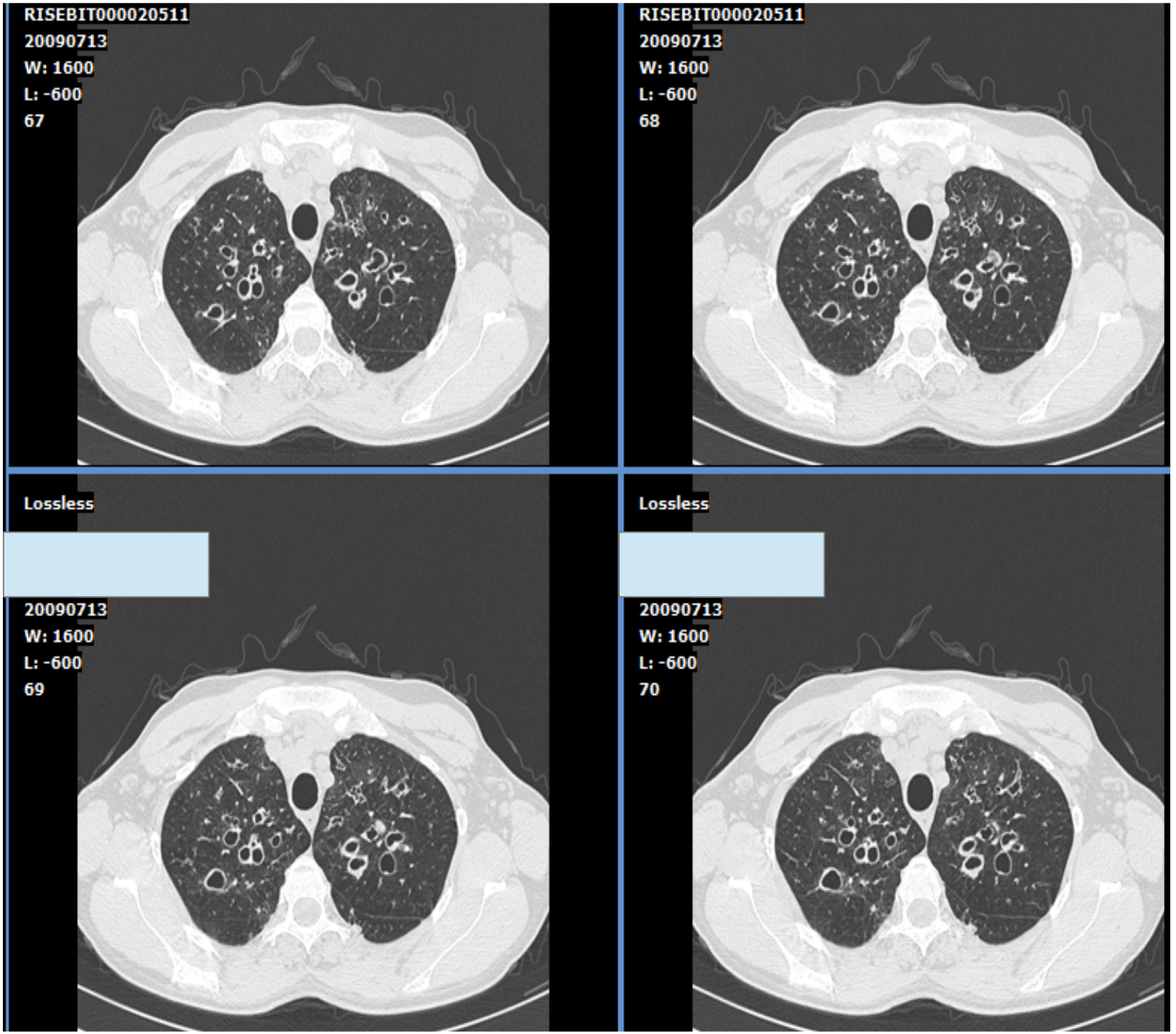
Dal luglio 2008 (31 anni) in Ossigeno- terapia domiciliare continuativa.

Agosto 2009:inserita in lista di TP presso Policlinico Umberto I Roma

Gennaio 2010: prolungato ricovero per broncopolmonite basale sx e insufficienza respiratoria $\rightarrow$ dimessa con NIV (Bi-PAP) a domicilio di notte + programma riallenamento allo sforzo

Nel 2010 impianto di catetere venoso centrale tipo port-a-cath

TRAPIANTO BIPOLMONARE il 22/10/2011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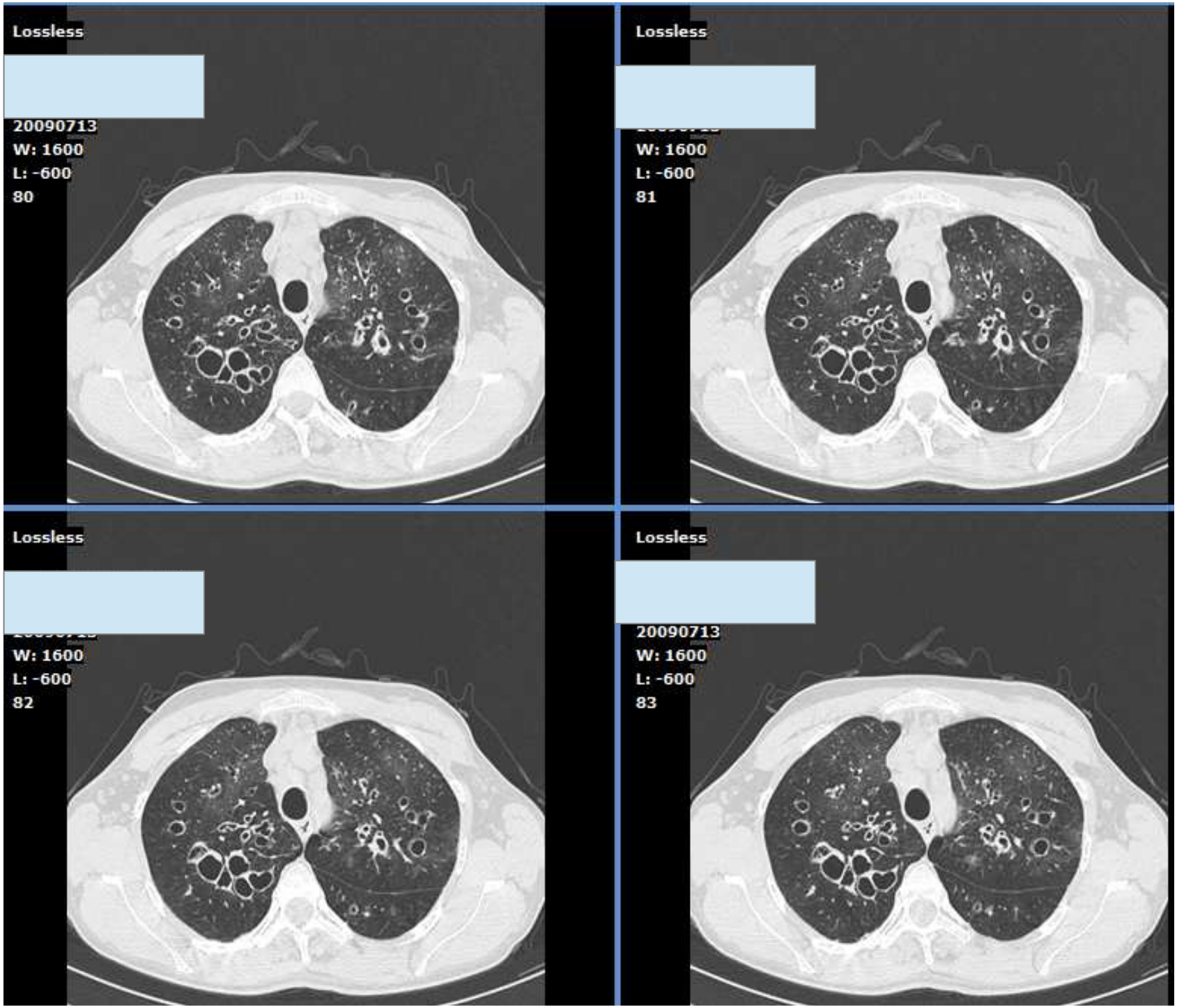
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Conclusioni

•I sempre più frequenti casi di FC nell'adulto rendono necessario un programma terapeutico di transizione che coinvolga pediatri e pneumologi

•Gli adulti FC appartengono a due categorie clinicamente distinte di pazienti: le diagnosi tardive e i *long survivors*

•Le diagnosi tardive hanno meno sintomi e minor compromissione funzionale e possono giungere all'attenzione di diversi specialisti

•I *long survivors* sono pazienti particolarmente impegnativi che di frequente richiedono O2-terapia e NIV e rientrano nei criteri per il trapianto polmonare