5th WAidid CONGRESS

Milan 2024
28-30 November 2024
HOTEL NHOW MILAN

Outbreaks in healthcare settings

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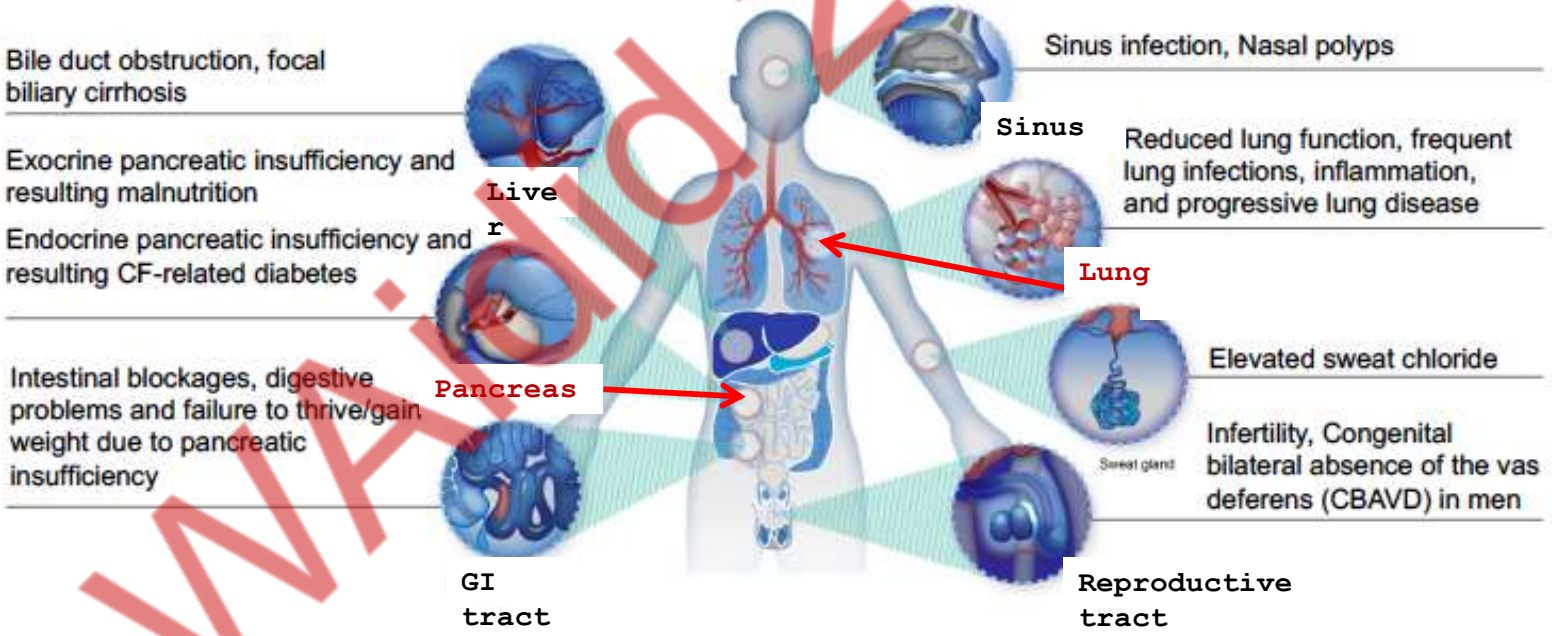
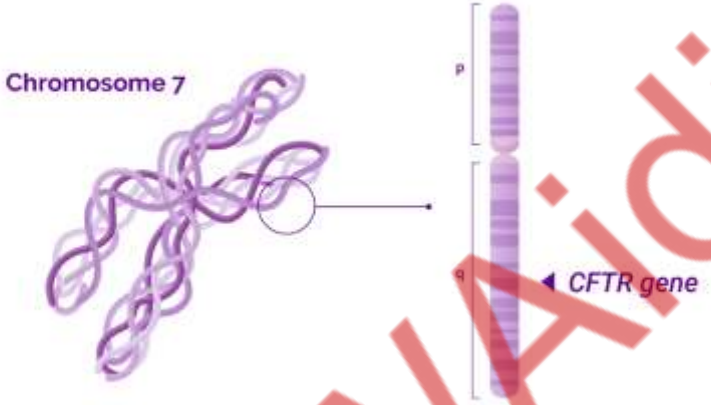
WAidid
World Association for Infectious Diseases and Immunological Disorders

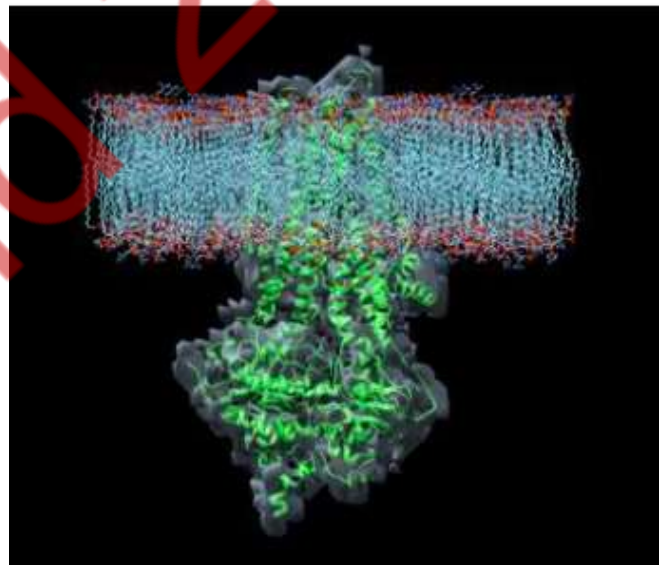
Cystic Fibrosis is a life-shortening genetic disease

Median predicted age of survival in 2018 was 52 years

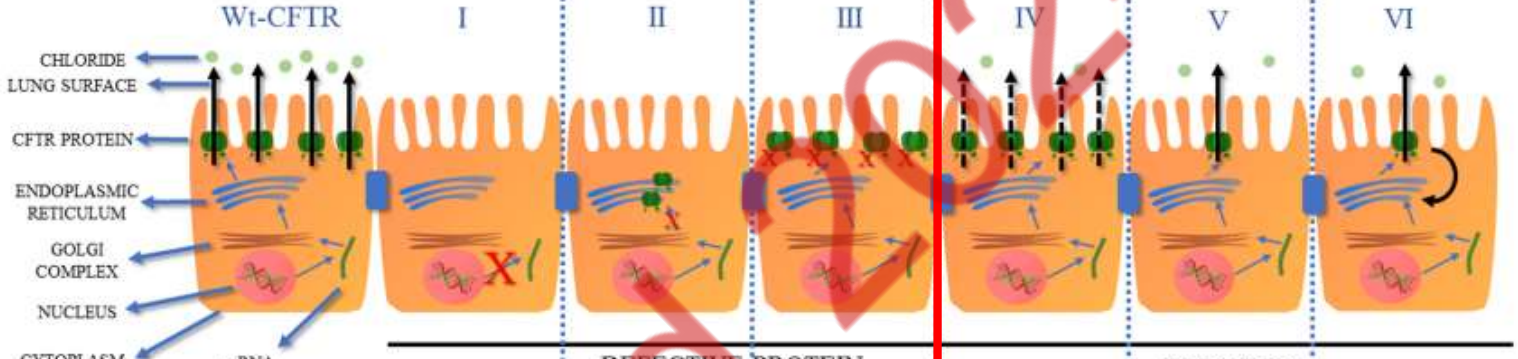


Cystic Fibrosis Transmembrane conductance Regula





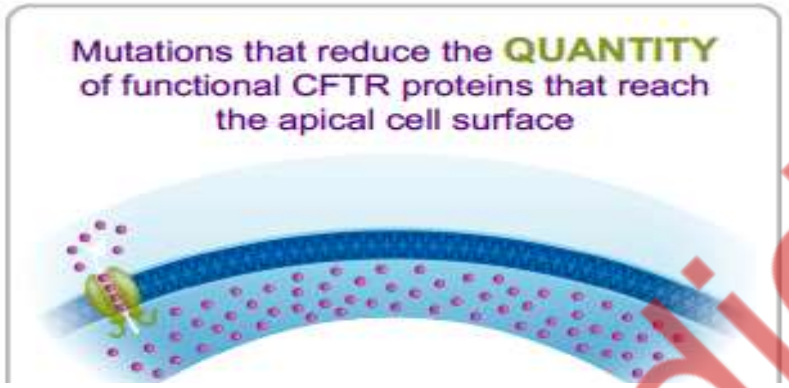
cff.org

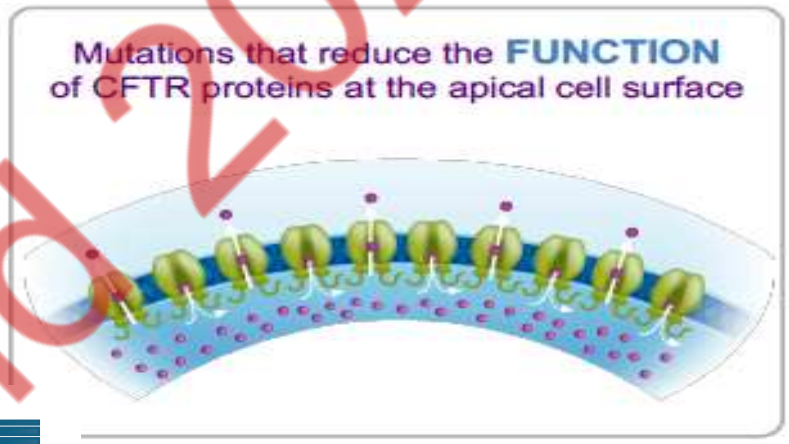


	DEFECTIVE PROTEIN			REDUCED		
	PRODUCTION	PROCESSING	REGULATION	CONDUCTANCE	AMOUNT OF FUNCTIONING PROTEIN	CELL SURFACE STABILITY
	IA / IB					
CFTR defect	No mRNA / No protein	No traffic	Impaired gating	Decreased conductance	Less protein	Less stable
Mutation examples	Dele2,3(21 kb), 1717-1G→A / Gly542X, Trp1282X	F508del, Asn1303Lys, Ala561Glu	Gly551Asp, Ser549Arg, Gly1349Asp	Arg117His, Arg334Trp, Ala455Glu	3272-26A→G, 3849+10 kg C→T	c.120del23, rPhe580del
Corrective therapy	Unrescuable / Rescue synthesis	Rescue traffic	Restore channel activity	Restore channel activity	Correct splicing	Promote stability
Drugs (approved)	Read-throug agents (Ataluren, amynoglicosydes)	Correctors (+Potentiators) Lumacaftor (+Ivacaftor)	Potentiators (Ivacaftor)	Potentiators (Ivacaftor)	Splicing modulators amplifiers	Stabilizers HGF (hepatocyte growth factor)
Clinical features (global aspect)	MORE SEVERE DISEASE			LESS SEVERE DISEASE		

Marson FAL Front Pharmacol 2017

Cystic Fibrosis Conductance Regulator (CFTR) protein





- CFTR channels conduct bicarbonate in addition to chloride ions.

MacDonald KD et al. *Paediatr Drugs* 2007;9:1–10

Reduction of Chloride transport outside the epithelia

- Gram-negative organisms
- **Opportunistic** pathogens ubiquitously distributed in nature
- **Biofilms** that can protect from both host defenses and antibiotics
- Expression of virulence factors regulated in a cell **density-dependent** manner

CF Trust UK 2023

Pseudomonas aeruginosa, PA

- Transmission between patients of an antibiotic-resistant strain of PA was first documented in the CF center in Copenhagen in 1986 (Pedersen SS 1986)

- In 1996 a beta-lactam resistant clone of PA was responsible for an outbreak in a CF center in Liverpool called the "*Liverpool Epidemic Strain*" (Al-Aloul M 2004)

Clinical Trial > Pediatrics. 1997 Nov;100(5):E2. doi: 10.1542/peds.100.5.e2.

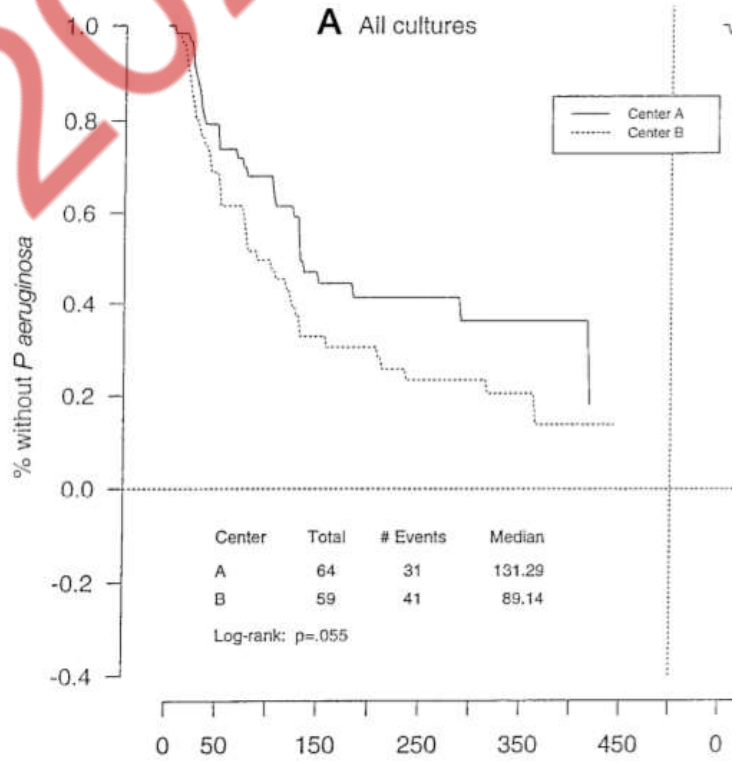
Acquisition of Pseudomonas aeruginosa in children with cystic fibrosis

P M Farrell [1], G Shen, M Splaingard, C E Colby, A Laxova, M F

Center A: infants diagnosed with CF were **segregated** from adults.

Center B: infants diagnosed with CF were **integrated** with older CF patients in the regular CF clinics, they used a common waiting room throughout the study, and the center was small.

The median time from diagnosis by newborn screening to PA acquisition was **289 weeks** in the center which employed segregation vs **52 weeks** in the center which did not.



N= 3323, 1-5 yrs.

Prognostic factor, 1990		Risk of death, 1991-98 Hazard ratio relative to baseline category (95% CI)[2]	*P*-value	*P. aeruginosa*-positive in 1998 Odds ratio relative to baseline category (95% CI)[2]	*P*-value	Hospitalized for acute exacerb Odds ratio relative to baseline categroy (95% CI)[2]	*P*-value
P. aeruginosa status	Positive	2.6 (1.6, 4.1)	<0.001	3.3 (2.6, 4.2)	<0.001	2.2 (1.7, 2.7)	<0.001
	No culture	1.6 (1.0, 2.7)		1.0 (0.9, 1.2)		1.1 (0.9, 1.4)	
Gender	Female	1.3 (0.9, 1.9)	0.12	1.2 (1.0, 1.4)	0.06	1.4 (1.2, 1.7)	<0.001
CF hospitalizations	Any	4.1 (2.8, 6.1)	<0.001			2.5 (2.0, 3.1)	<0.001
Respiratory symptoms[3]	Yes					1.3 (1.1, 1.6)	<0.01
Weight percentile	≤5	3.9 (2.1, 7.3)	<0.001				
	5–15	2.4 (1.2, 4.8)					
	15–50	1.5 (0.8, 2.9)					
Age at diagnosis	≤6 months					1.6 (1.1, 2.3)	0.02
	6–24 months					1.3 (0.9, 1.9)	
Age (1990)	1	0.5 (0.3, 1.0)	0.33	0.6 (0.5, 0.8)	<0.001	0.5 (0.4, 0.7)	<0.001
	2	0.8 (0.5, 1.5)		0.7 (0.6, 0.9)		0.6 (0.5, 0.8)	
	3	1.0 (0.6, 1.7)		1.0 (0.7, 1.2)		0.7 (0.5, 0.9)	
	4	1.0 (0.6, 1.7)		1.1 (0.9, 1.4)		0.8 (0.6, 1.1)	
Baseline rate		0.005%[4]		55.0%[5]		13.0%[5]	

AIM: to determine prognostic **indicators of 8-year mortality and morbidity** in young children with CF.

Lower FEV1 and weight percentile at follow-up.

Emerson J 2022

Burkholderia cepacea

- *B. cenocepacia* and *B. multivorans*
- Distinct **lipopolysaccharide** implicated in resistance to antibiotics
- **Secretion** of a number of factors, such as catalases, proteases and siderophores, which can help to evade the host's defenses

Responsible of **outbreaks** in hospital and in the CF community

***Burkholderia cepacea* syndrome**

Acute, **necrotizing pneumonia** with elevated mortality rate, characterized by high fever, bacteremia, and rapidly progressive

Comparative Study > Nat Med. 1995 Jul;1(7):661-6. doi: 10.1038/nm0795-661.

The emergence of a highly transmissible lineage of cbl+ Pseudomonas (Burkholderia) cepacia causing CF centre epidemics in North America and Britain

Original Paper

Investigation of Burkholderia cepacia Nosocomial Outbreak with High Fatality in Patients Suffering from Diseases other than Cystic Fibrosis

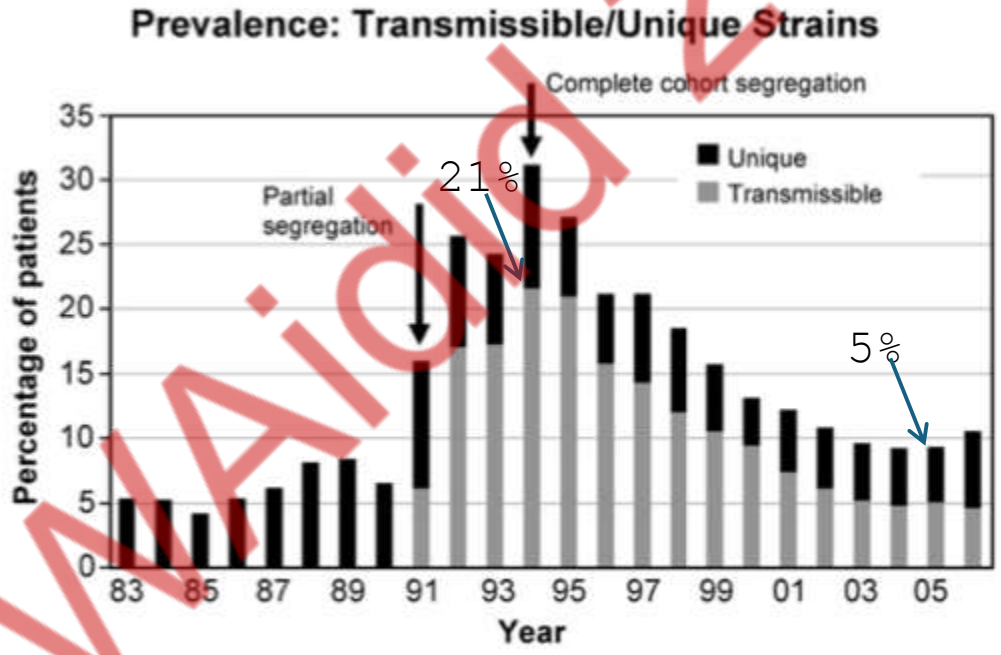
Asem A Shehabi ✉, Waleed Abu-al-soud, Azmi Mahafzah, Najwa Khuri-bulos, Ilham Abu Khader,

J Infect Dis. 1999 May ; 179(5): 1197–1205. doi:10.1086/314699.

An Epidemic of *Burkholderia cepacia* Transmitted between Patients with and without Cystic Fibrosis

ELSEVIER
Journal of Cystic Fibrosis 7 (2008) 368–372
Journal of Cystic Fibrosis
www.elsevier.com/locate/jcf

The changing epidemiology of *Burkholderia* species infection at an adult cystic fibrosis centre



France MW 2008

WAidid CONGRESS
children
MDPI
28-30 November 2024 Milan 2024

Article

Multidrug-Resistant Bacteria in Children and Adolescents with Cystic Fibrosis

Valentina Fainardi [1], Cosimo Neglia [1], Maria Muscarà [1], Cinzia Spaggiari [1], Marco Tornesello [1], Roberto Grandinetti [1], Alberto Argentiero [1], Adriana Calderaro [2], Susanna Esposito [1,*] and Giovanna Pisi [1]

Table 1. Characteristics and pulmonary function tests at time of data collection in patients with CF colonized by MDR bacteria and in control group.

	Patients Colonized with MDR Bacteria (n = 7)	Matched Controls (n = 14)
Age (years)	14.2 ± 1.8	14.3 ± 3.9
Genotype (F/F, n)	2/7	2/14
BMI (kg/m^2)	16.9 ± 1.6	19.9 ± 3.4 *
FEV_1 pp %	76.5 ± 27.0	88.7± 21.3
FVC pp	88.1 ± 26.2	92.8 ± 14.7
FEV_1/FVC	75.7 ± 9.6	82.6 ± 10.1 **
Pex	2 ± 1.6	0.3 ± 0.7 **

Data are expressed as mean ± SD. BMI, body mass index; FEV_1, forced expiratory flow in 1 s; FVC, forced vital capacity; pp, percent of predicted; F/F, homozygous F508 del; Pex, pulmonary exacerbations. * t = 4.29, $p < 0.001$; ** t = 2.19, $p < 0.03$.

Sources of infection

Acquisition can occur through:

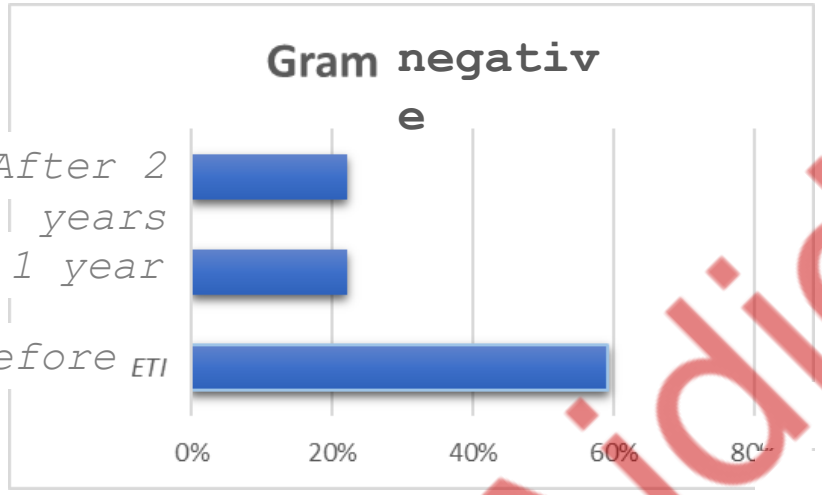
- From the **environmental** reservoirs (soil and water)
- **Person-to-person** transmission
  - airborne transmission during coughing and nebulization
  - contaminated hands of patients or health professionals → can be transmitted by shaking hands for up to 180 min (Bryant JM 2016)
- From the **healthcare** environment
  - contaminated nebulizers (Doring G 1996)
  - respiratory filters are effective at preventing the

Rowbotham NJ 2019

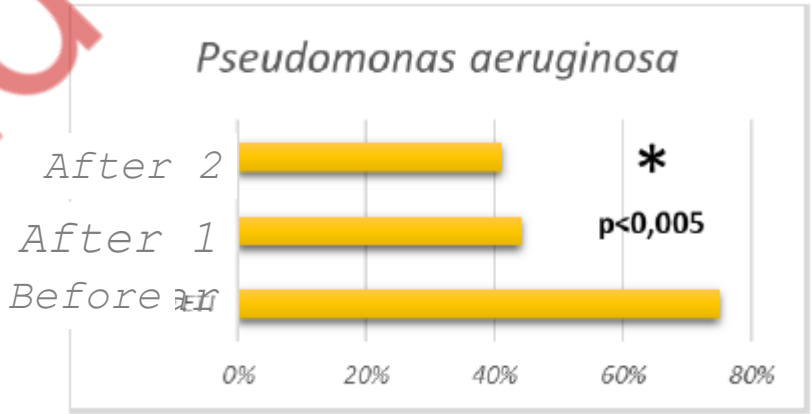
Burkholderia prevalence

ECFS registry 2022

Effect of CFTR modulators on MDR bacteria



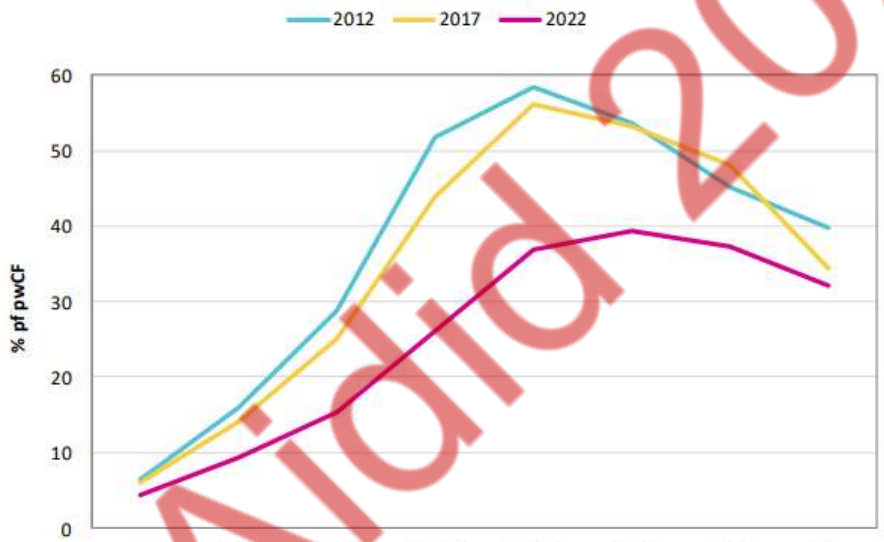
ETI: Elexacaftor-Tezacaftor-Ivacaftor



Unpublished

Figure 5.8 *The prevalence of Pseudomonas aeruginosa infection has decreased in the CF population in Europe since increased availability of CFTR modulators.*

Prevalence of chronic *Pseudomonas aeruginosa* infection in people with CF, by age group, in 2012, 2017 and 2022.



age	0-5	6-11	12-17	18-29	30-39	40-49	50-59	60+
2022	7806	8285	7761	11322	6416	3309	1588	653
2017	8336	7682	6780	10404	4882	2366	912	357
2012	5396	4880	4838	7387	2841	1285	370	163

ECFS registry 2022

Infection prevention and control (the pat

- Personal hygiene methods such as handwashing and hand sanitizer.
- **Cohort segregation** of CF patients (based on carrier status of organisms) → different days and different rooms of examination.
- **Individual segregation** of CF patients (single rooms when admitted, space and better provision of hygienic precautions, disposable equipment to visit the patient).
- Avoid waiting area
- Limitation of social events.

Infection prevention and control (the ope

- Wearing personal **protective equipment** such as gloves, gowns, and masks by both patients and health-care workers.
- Cleaning and **disinfection** of areas and equipment.
- **Education** of patients and staff.
- Bacterial culture of sputum or swab every 3 months to monitor the patient.
- **Telehealth** to reduce face to face contact and cross-infection risk.