13° FORUM ITALIANO SULLA FIBROSI CISTICA

Riscrivere il futuro insieme:
nuovi percorsi di vita e di cura.

BARI 15_16 NOV 2025 HOTEL PARCO DEI PRINCIPI

LIFC
Lega Italiana
Fibrosi Cistica

La Fibrosi Cistica: una malattia che invecchia!

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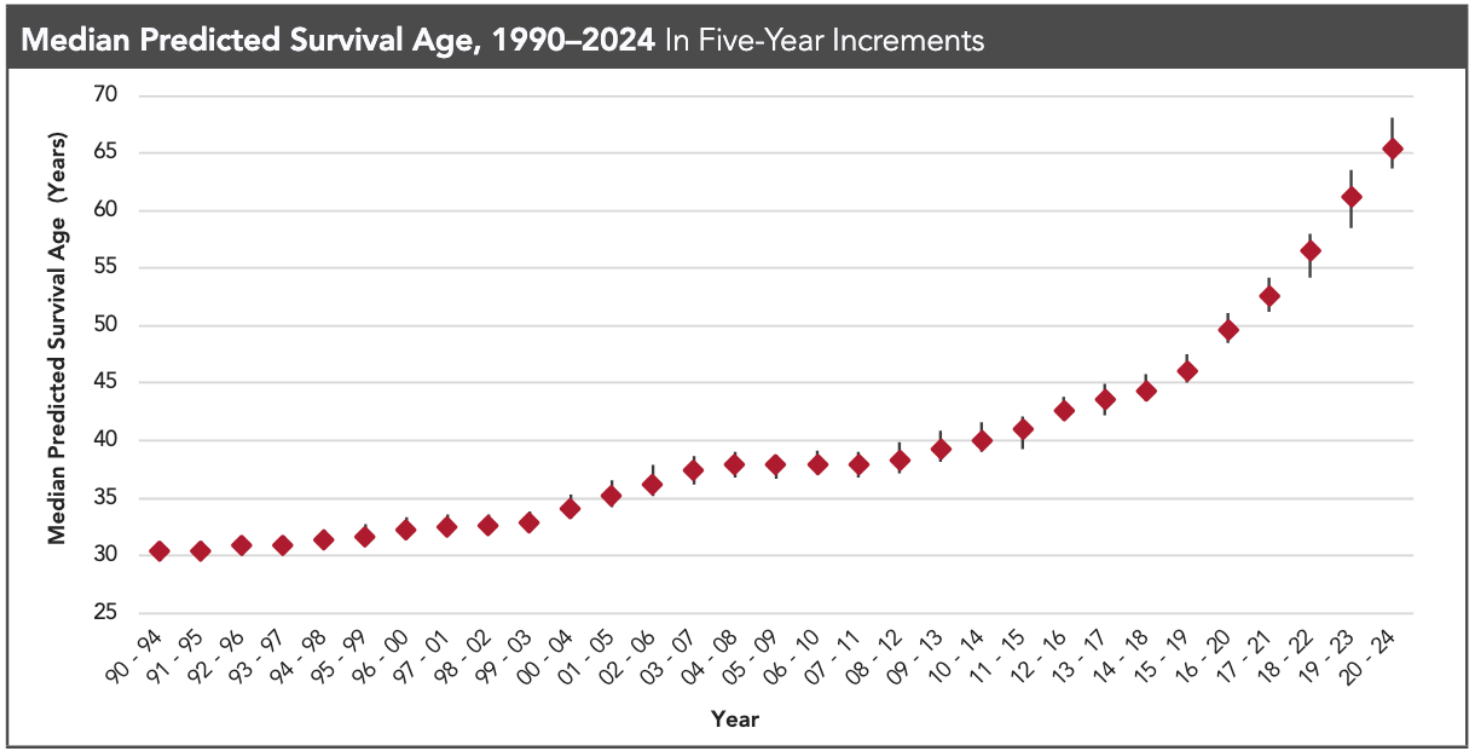
Nature 428: 116-8

Età media di sopravvivenza

65 anni

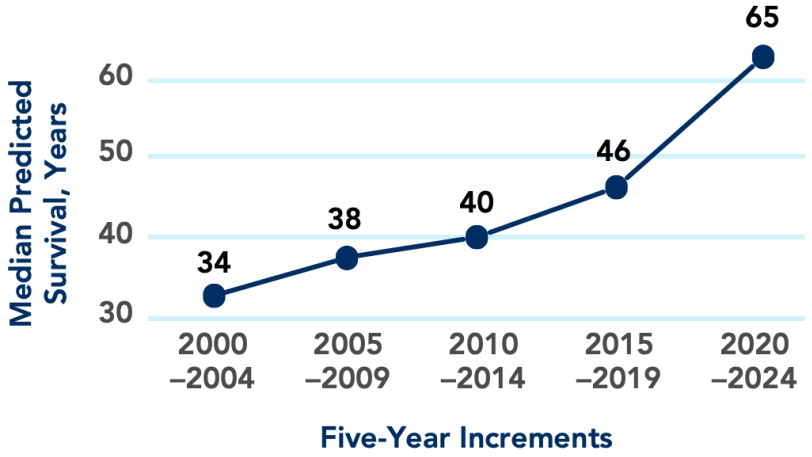
Median Predicted Survival Age, 1990–2024 In Five-Year Increments



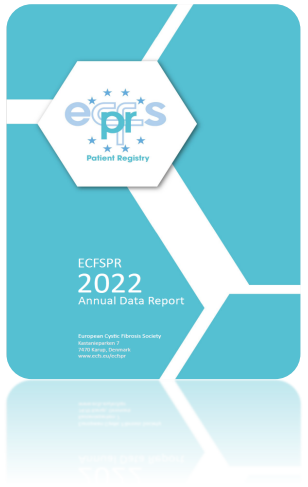
**Using the currently recommended method for calculating median predicted survival. For more information about the methodology, please see the Technical Supplement available at cff.org.*

Survival 65 YEARS | 2020–2024

Among people with CF born between 2020 and 2024, half are predicted to live to age 65 or beyond. However, this does not reflect individual variability. The median survival is lower — by possibly more than a decade — for those who are ineligible for CFTR modulators.

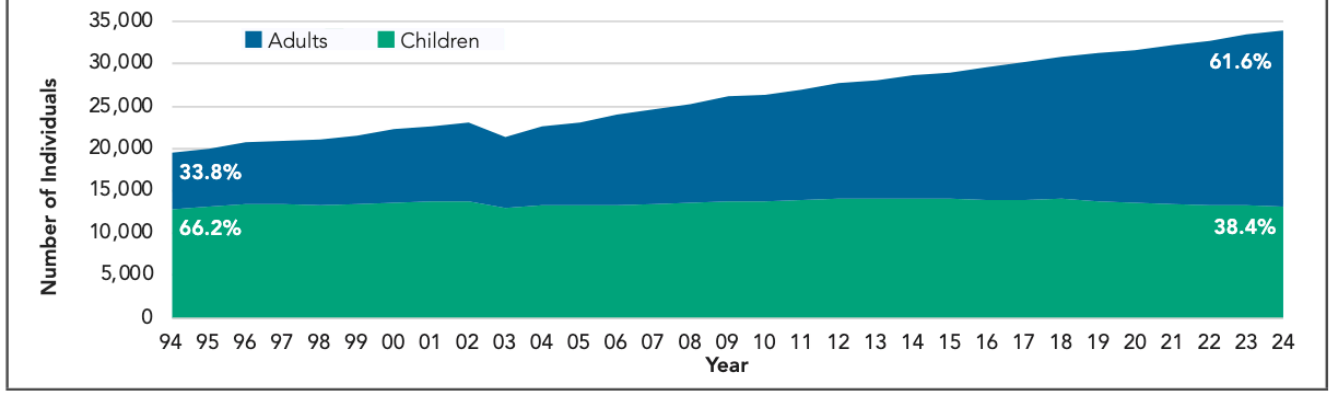


2024 CYSTIC FIBROSIS FOUNDATION Patient Registry Highlights



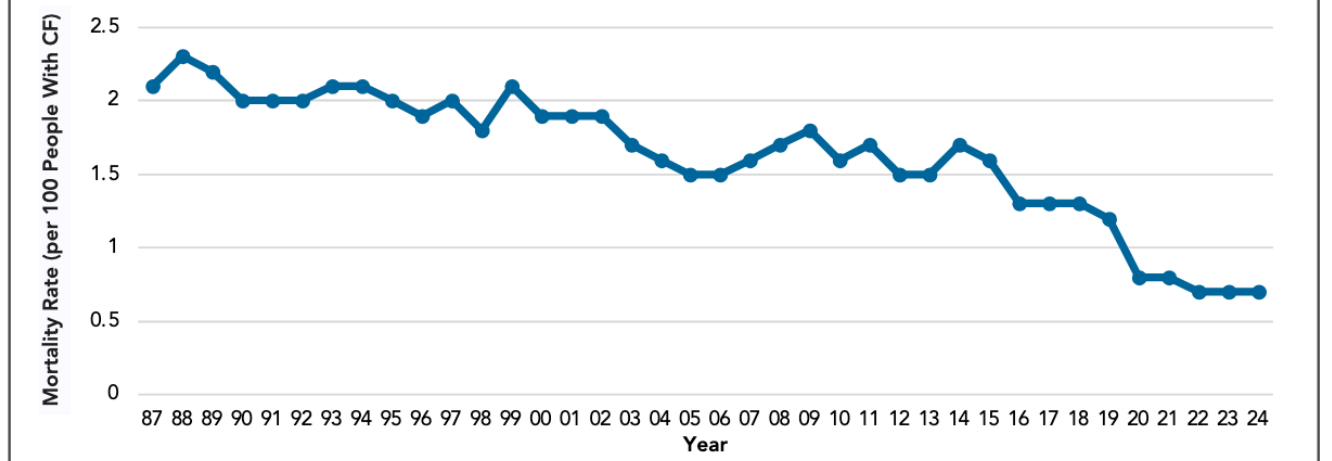
n	33989	54546	6182
Mean age	25,5	20,0	27,3
% adults	61,6	54,5	65,2

Number of Children and Adults With CF, 1994–2024

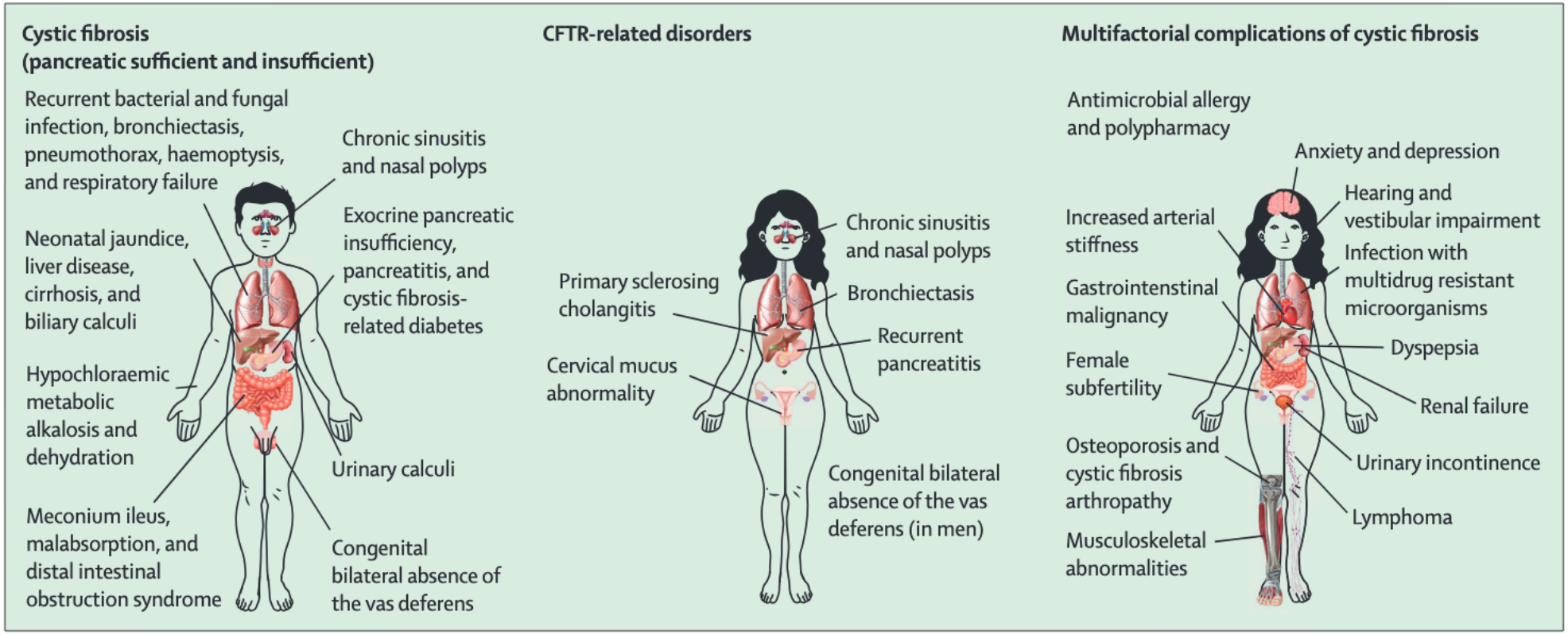


The decrease in the number of individuals reported in 2003 is due to a delay in obtaining informed consent forms before the close of the calendar year at some CF Care Centers.

Annual Mortality Rate (per 100 People With CF), 1987–2024



Una Malattia Complessa



Shteinberg M et al, Lancet 2021; 397: 2195–211

Orizzonti FC
Organo della Società Italiana per lo studio della Fibrosi Cistica

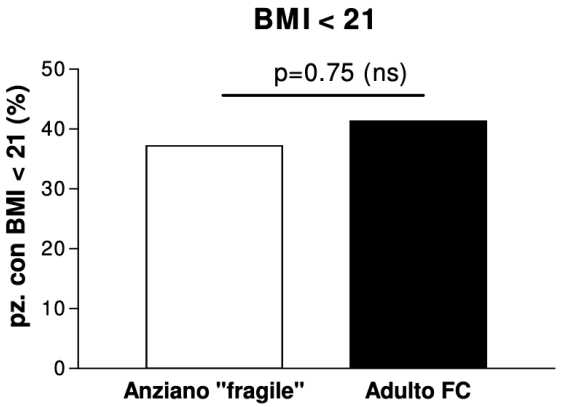
CONTRIBUTI ORIGINALI

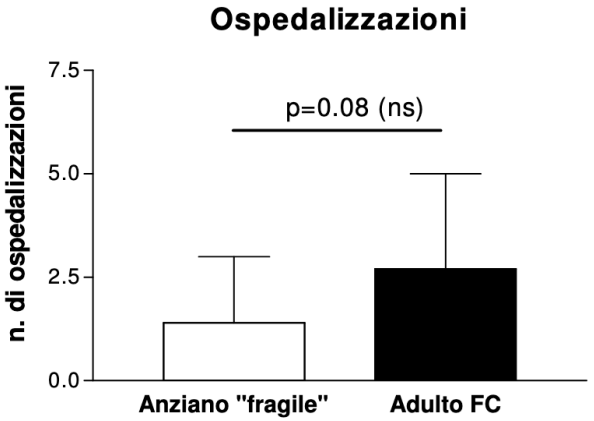
L'adulto affetto da fibrosi cistica: un paziente geriatrico in età adulta

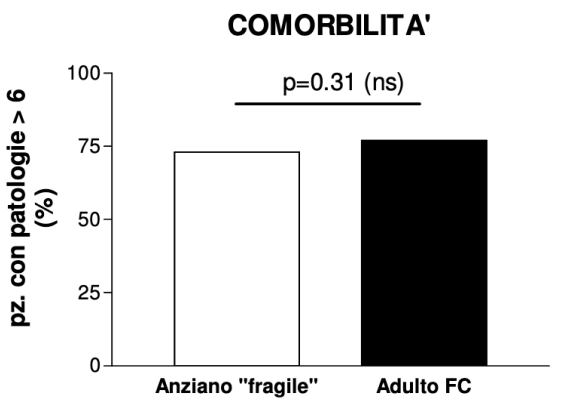
Tab.1. Caratteristiche dell'anziano fragile e degli adulti con FC

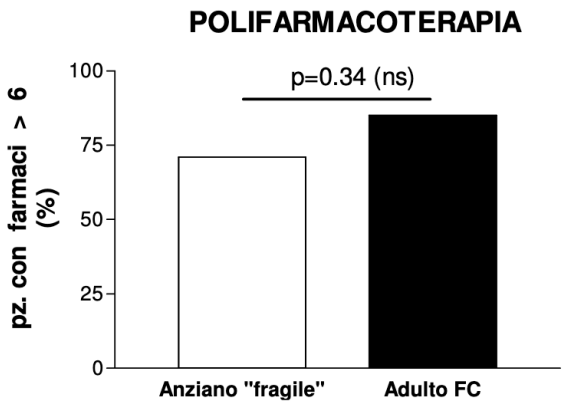
PARAMETRI	Anziano fragile (n=1640)	Adulto FC (n=89)	p
Età (anni)	84.9±8.0	26.8±6.1	0.001
Sesso femminile (%)	73.0	44.9	0.01
BMI < 21 (%)	37.2	41.3	(NS)
n. pazienti con > 4 patologie (%)	73.7	77.5	(NS)
n. pazienti con > 6 farmaci (%)	71.3	85.4	(NS)
n. pazienti con attività di base della vita quotidiana (BADL) perse > 4 (%)	86.6	75.3	(NS)
n. pazienti con attività strumentali della vita quotidiana perse (IADL) > 6 (%)	87.4	95.4	(NS)
Ospedalizzazioni/anno	1.4±1.6	2.7±2.3	(NS)

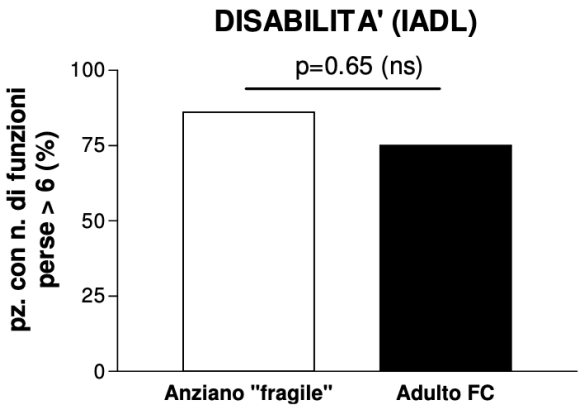
Orizzonti FC 2003

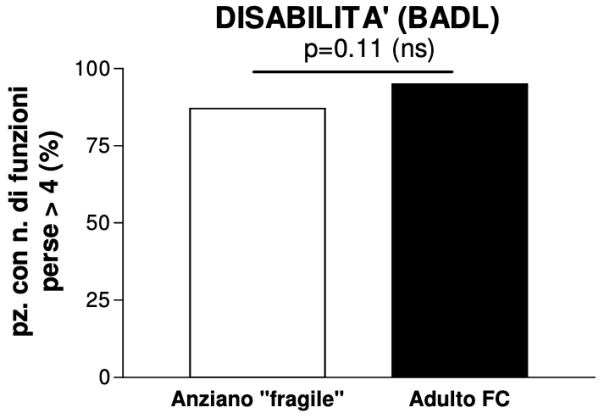












Orizzonti FC 2003

La **fragilità** è una **sindrome geriatrica multifattoriale**, uno stato clinico di particolare vulnerabilità allo sviluppo di dipendenza e dagli esiti negativi, dovuto al progressivo declino dell'omeostasi dei vari apparati che si verifica con l'invecchiamento.

Journal of *Clinical Medicine*

MDPI

Article

Cystic Fibrosis in Adults: A Paradigm of Frailty Syndrome? An Observational Study

Paola Iacotucci [1], Vincenzo Carnovale [2,*], Lorenza Ferrillo [2], Jolanda Somma [2], Marialuisa Bocchino [1], Marcella D'Ippolito [2], Alessandro Sanduzzi Zamparelli [1], Giuseppe Rengo [2], Nicola Ferrara [2], Valeria Conti [3] and Graziamaria Corbi [2]

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LIFC Lega Italiana Fibrosi Cistica

- Valutare le principali caratteristiche cliniche e anamnestiche dei pazienti adulti con FC e valutare l'associazione della fragilità con la classificazione di genotipizzazione della FC
- 139 pazienti FC(46% F)
- Spirometria per la funzione respiratoria, da ADL e IADL per lo stato funzionale e dallo Studio delle Fratture Osteoporotiche (SOF) Index per la fragilità.

Variables	Robust (n = 84)	Pre-Frail/Frail (n = 55)	p
Age, years, mean ± SD	32.38 ± 11.48	33.67 ± 10.12	0.498
Gender, M/W, n (%)	52/32 (61.90/38.10)	23/32 (41.82/58.18)	**0.020**
BMI, kg/m^2, mean ± SD	24.82 ± 3.76	22.57 ± 4.03	**0.001**
Smokers, n (%)	6 (7.14)	1 (1.82)	0.160
FEV_1, L, mean ± SD	3.28 ± 0.98	1.55 ± 0.75	**<0.001**
FEV_1, %, mean ± SD	84.93 ± 23.95	46.98 ± 22.65	**<0.001**
FVC, L, mean ± SD	4.26 ± 1.07	2.43 ± 0.86	**<0.001**
FVC, %, mean ± SD	94.95 ± 16.09	61.71 ± 20.45	**<0.001**
MMEF, %, mean ± SD	74.37 ± 32.43	29.33 ± 27.65	**<0.001**
Main Genotypes			0.116
DELTAF508/DELTAF508, n (%)	10 (12.05)	17 (30.91)	
DELTAF508/5T-12TG, n (%)	10 (12.05)	1 (1.82)	
DELTAF508/N1303K, n (%)	1 (0.72)	4 (2.90)	
N° pulmonary exacerbations per year, mean ± SD	0.58 ± 1.06	2.56 ± 2.51	**<0.001**
Cycles of IV antibiotic therapy, mean ± SD	0.08 ± 0.28	0.58 ± 1.32	**<0.001**
Cycles of oral antibiotic therapy, mean ± SD	0.50 ± 0.91	1.93 ± 1.87	**<0.001**
N° of hospitalizations per year, mean ± SD	0.11 ± 0.35	0.47 ± 0.88	**<0.001**
BADL lost, mean ± SD	0.00 ± 0.00	0.24 ± 0.77	**0.006**
IADL lost, mean ± SD	0.00 ± 0.00	0.65 ± 1.82	**0.001**
N° of drugs, mean ± SD	4.49 ± 3.80	8.60 ± 3.10	**<0.001**
N° of CF-related diseases, mean ± SD	2.65 ± 2.57	5.67 ± 2.64	**<0.001**
N° of non-CF-related diseases, mean ± SD	0.35 ± 0.67	0.42 ± 0.74	0.547
N° of total diseases, mean ± SD	3.00 ± 2.57	6.09 ± 2.80	**<0.001**

Robust vs. Pre-Frail/Frail	β	95% Conf. Interval Low High	*p*
Gender			
Women	−0.092	−0.236 0.051	0.205
BMI, kg/m^2	−0.010	−0.027 0.007	0.261
FEV_1, L	−0.221	−0.297 −0.145	**<0.001**
Number of pulmonary exacerbations per year	0.075	0.024 0.125	**0.004**
Cycles of IV antibiotic therapy	−0.003	−0.149 0.142	0.966
Number of hospitalizations per year	−0.122	−0.326 0.082	0.239
BADL lost	−0.088	−0.293 0.117	0.399
IADL lost	0.073	−0.004 0.150	0.063
Number of drugs	−0.010	−0.040 0.019	0.483
Number of CF-related diseases	0.021	−0.018 0.060	0.287
Number of non-CF-related diseases	0.030	−0.062 0.121	0.525

- Il gruppo pre-fragile/fragile era più frequentemente costituito da donne (p = 0,020), aveva un BMI più basso (p = 0,001), una funzione respiratoria peggiore, un numero più elevato di esacerbazioni polmonari/anno, cicli di terapia antibiotica e ospedalizzazione rispetto ai pazienti robusti. I soggetti pre-fragili/fragili usavano più farmaci ed erano affetti da più malattie correlate alla FC (tutti p < 0,001)
- **Il miglior predittore dello stato pre-fragile/fragile era un basso livello di FEV1.**

I pazienti con FC mostrano somiglianze con i soggetti anziani pre-fragili, suggerendo che la FC potrebbe essere considerata un'espressione precoce di questa sindrome geriatrica. Questo risultato è interessante perché potrebbe aiutare a definire meglio la possibile progressione della FC, ma nel complesso, suggerisce anche l'utilità di impiegare alcuni degli strumenti utilizzati nella gestione e nella terapia dei soggetti fragili per identificare i soggetti con FC più gravi.

life

MDPI

Review

Advances in the Cystic Fibrosis Drug Development Pipeline

Christine Esposito [1,*], Martin Kamper [1], Jessica Trentacoste [1,*], Susan Galvin [2], Halie Pfister [3] and Janice Wang [1,3]

CFTR Modulators	mRNA-Based Therapies	Gene-Based Therapies
Ivacaftor [1]	Aminoglycoside read-through nonsense mutation (ELX-02) [2]	CFTR Gene Transfer Vectors: • Recombinant adeno-associated viral vectors (rAAV) (4D-710) [2] • Liposomal vector (pGM169/GL67A) [2] • Lentiviral vector [3]
Lumacaftor/Ivacaftor [1]	Depletion of termination factor, eRF1 (SRI-37240) [3]	
Tezacaftor/Ivacaftor [1]	Inhaled CFTR mRNA (MRT5005 [2] VX-522 [2] ARCT-032 [2] ReCode [3])	
Elexacaftor/Tezacaftor/Ivacaftor [1]	Short-interfering RNAs (siRNAs) [3]	Zinc-finger nucleases (ZFN) [3]
Deuticaftor (VX561) [2]		Transcription activator-like effector nucleases (TALENS) [3]
Vanzacaftor (VX-121)/tezacaftor/ Deuticaftor [2]		Clustered Regularly Interspersed Palindromic Repeats (CRISPR)/CRISPR-associated nuclease 9 (CAS9) [3]
Navocaftor (ABBV-3067), galicaftor (ABBV-2222) and ABBV-576 [2] *		

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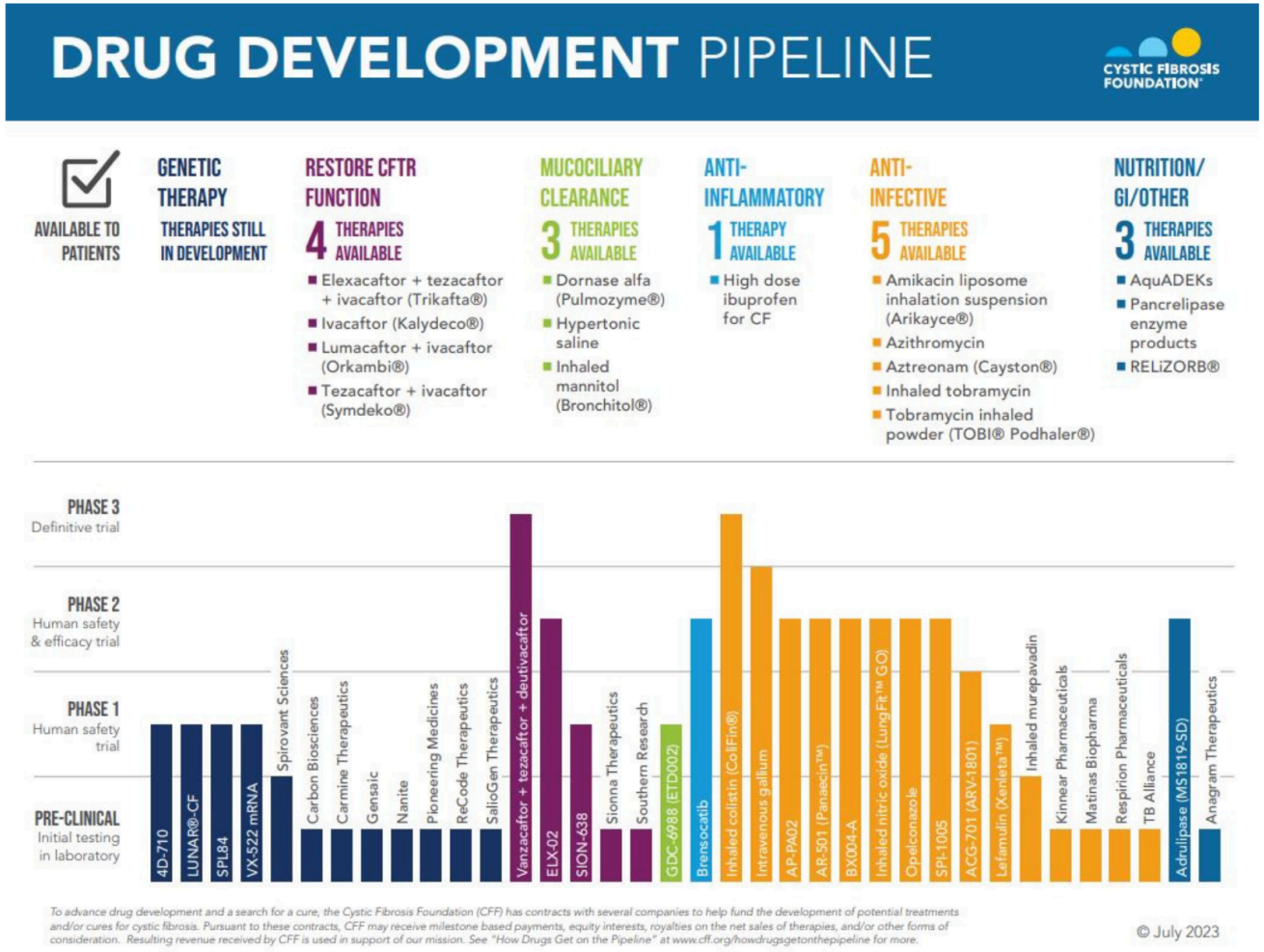


CFTR modulator therapy: transforming the landscape of clinical care in cystic fibrosis

Jennifer L Taylor-Cousar, Paul D Robinson, Michal Shteinberg, Damian G Downey

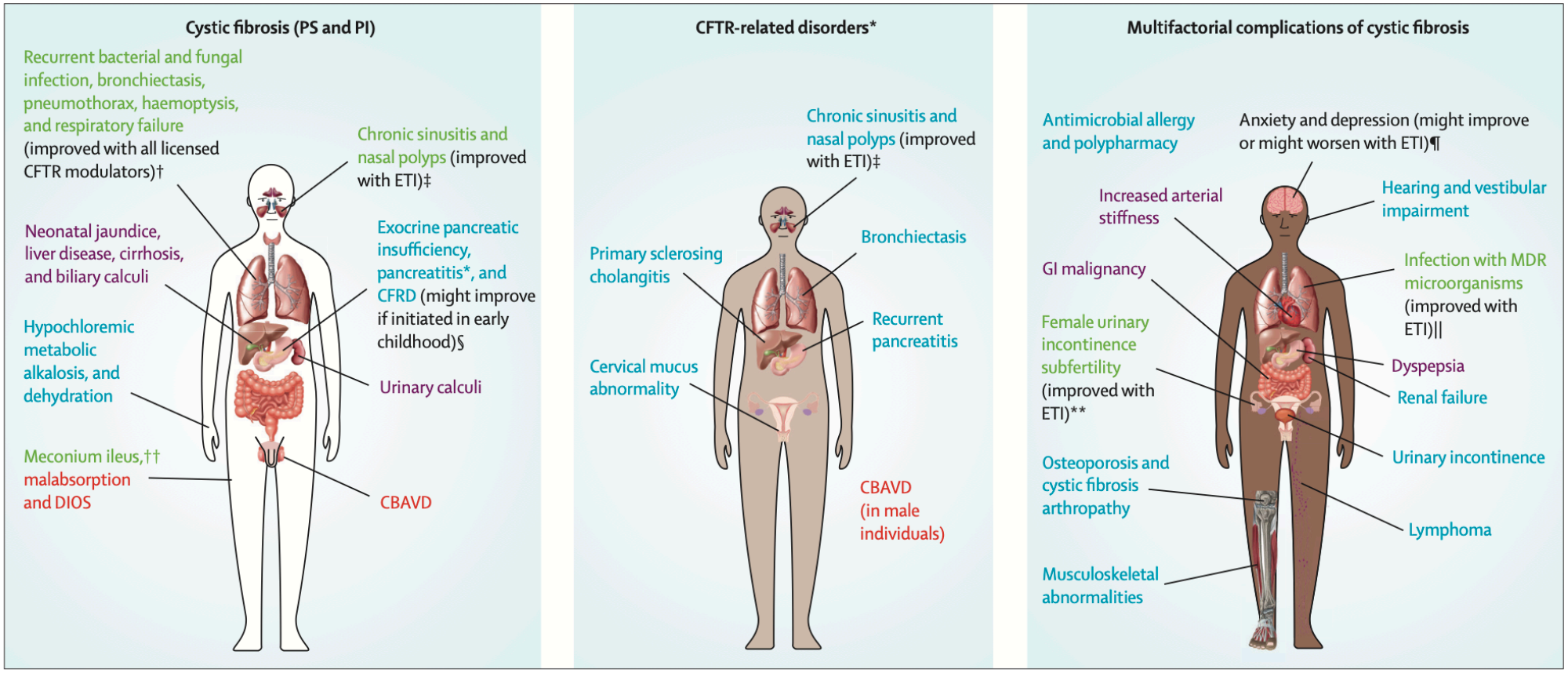
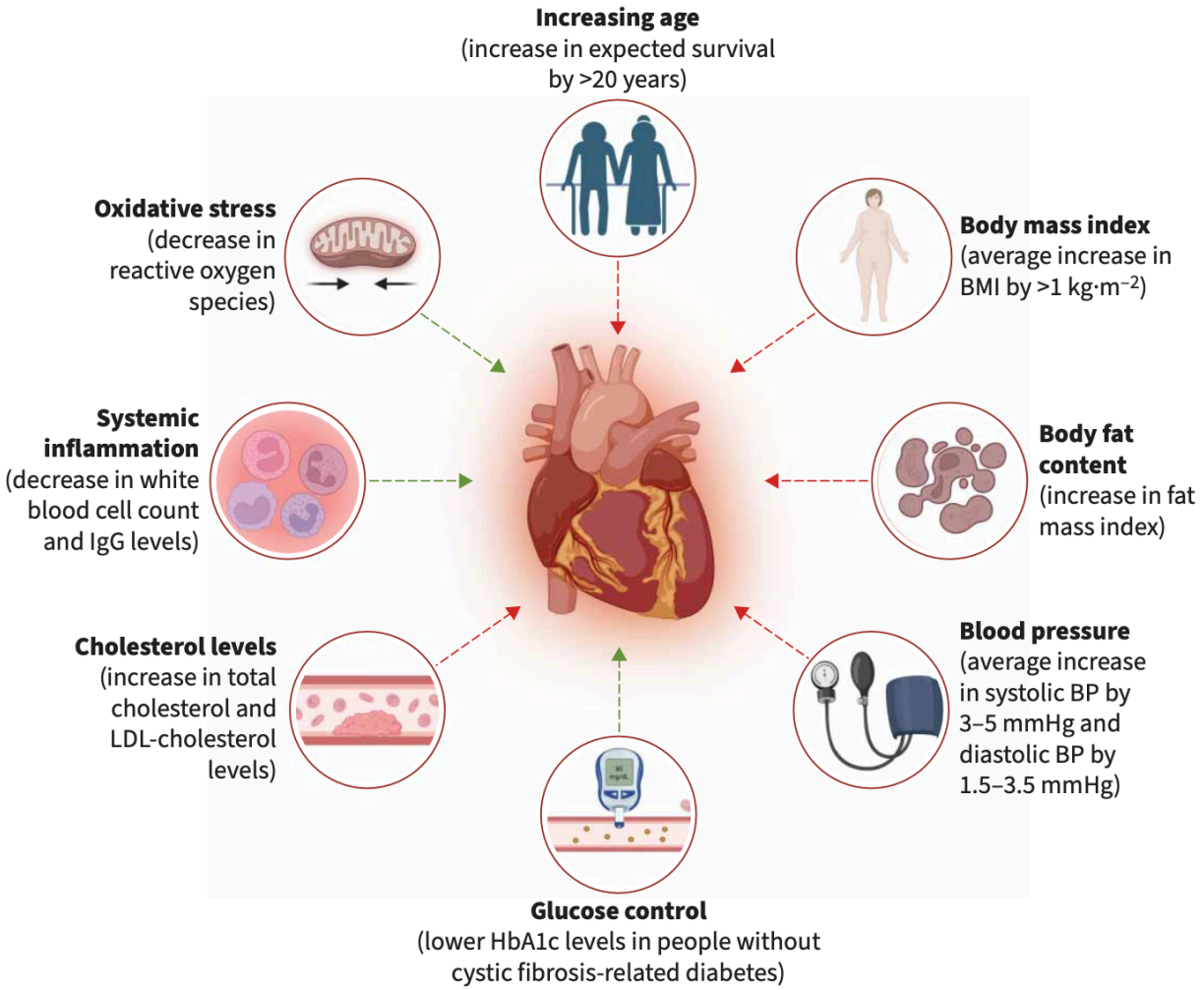


Figure 1: **Known and potential effect of CFTR modulation on cystic fibrosis and CFTR-related disease manifestations**

Lancet 2023; 402: 1171–84



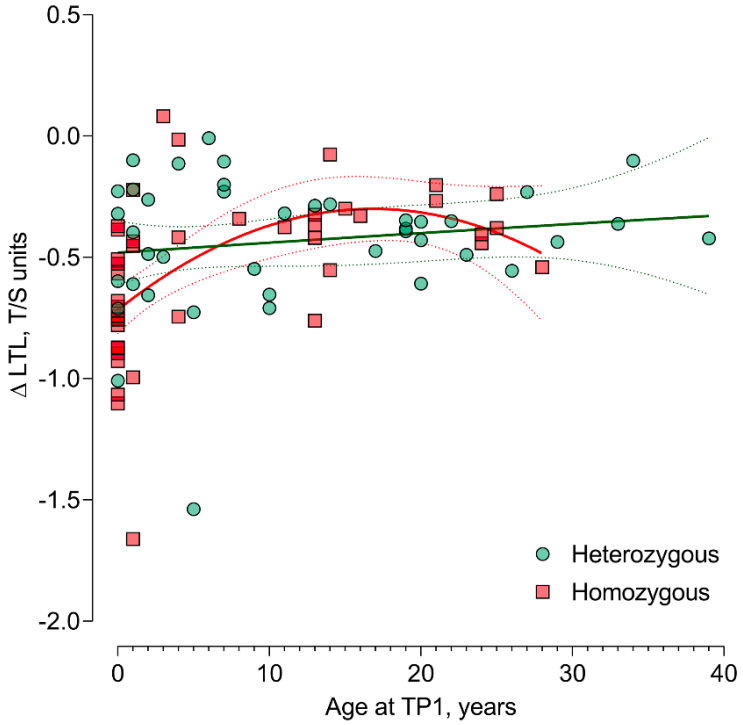
Hebestreit & Thornton Eur Respir J 2023; 62: 2301253

www.aging-us.com AGING 2024, Vol. 16, No. 16

Research Paper

Leukocyte telomere length and attrition in association with disease severity in cystic fibrosis patients

Dries S. Martens[1,*], Elise J. Lammertyn[2,*], Pieter C. Goeminne[3], Kristine Colpaert[4], Marijke Proesmans[5], Bart M. Vanaudenaerde[2], Tim S. Nawrot[1,6], Lieven J. Dupont[2,4]



Difference in age-dependent leukocyte telomere length change from timepoint 1 to timepoint 2 in ΔF508 homozygous vs. heterozygous

L'**invecchiamento** è un processo biologico complesso caratterizzato dal progressivo indebolimento di quasi tutte le funzioni fisiologiche con conseguente aumento della mortalità tempo-dipendente.

La **senescenza**, meccanismo alla base dell'invecchiamento, comprende un processo che impone un arresto proliferativo permanente sulle cellule invecchiate che hanno accumulato danni cronicamente nel corso degli anni fino a raggiungere una soglia di stress cellulare. I possibili induttori della senescenza cellulare includono lo **stress ossidativo, il danno al DNA e l'accorciamento dei telomeri**. I **telomeri** sono tratti di DNA ripetitivi che coprono le estremità dei cromosomi, proteggendoli dalla riparazione e dalla degradazione non programmata del DNA.

La gravità della malattia nei pazienti con FC influenza negativamente la lunghezza dei Telomeri dei Leucociti (LTL), con effetti leggermente più pronunciati negli uomini e negli omozigoti per ΔF508, con conseguente aumento del tasso di invecchiamento che influisce sulle altre funzioni corporee e li rende più inclini a malattie legate all'età.

Questi effetti sono probabilmente già stabiliti durante l'infanzia, sottolineando la necessità di una diagnosi precoce della FC e di una terapia appropriata fin dalla più tenera età.

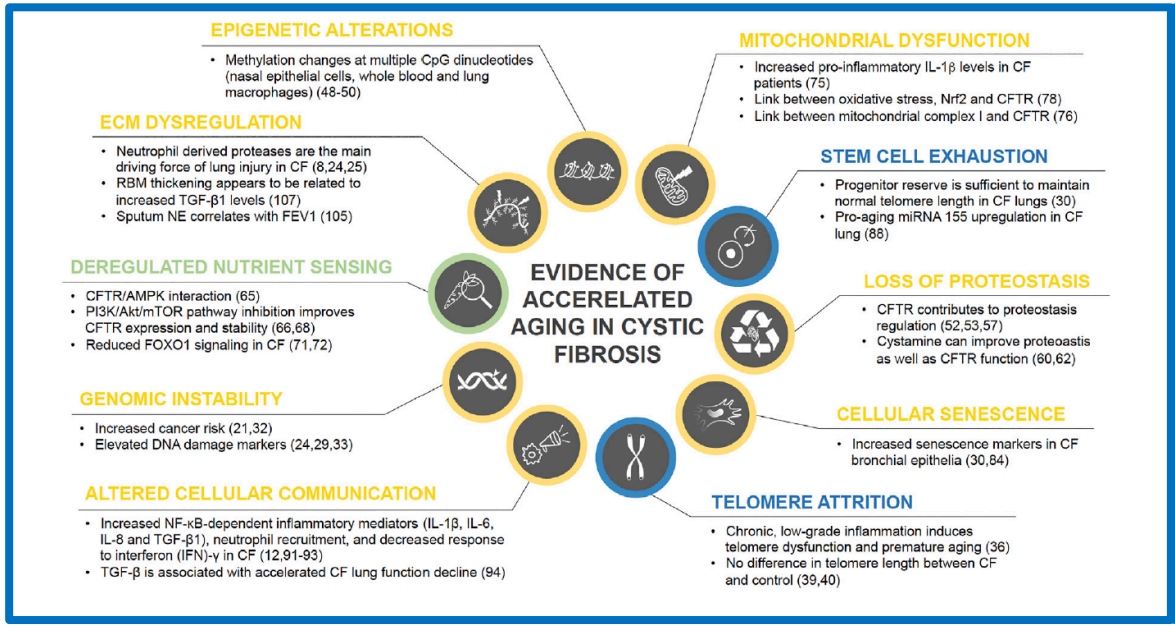
frontiers in Pharmacology

MINI REVIEW
published: 15 April 2021
doi: 10.3389/fphar.2021.601438

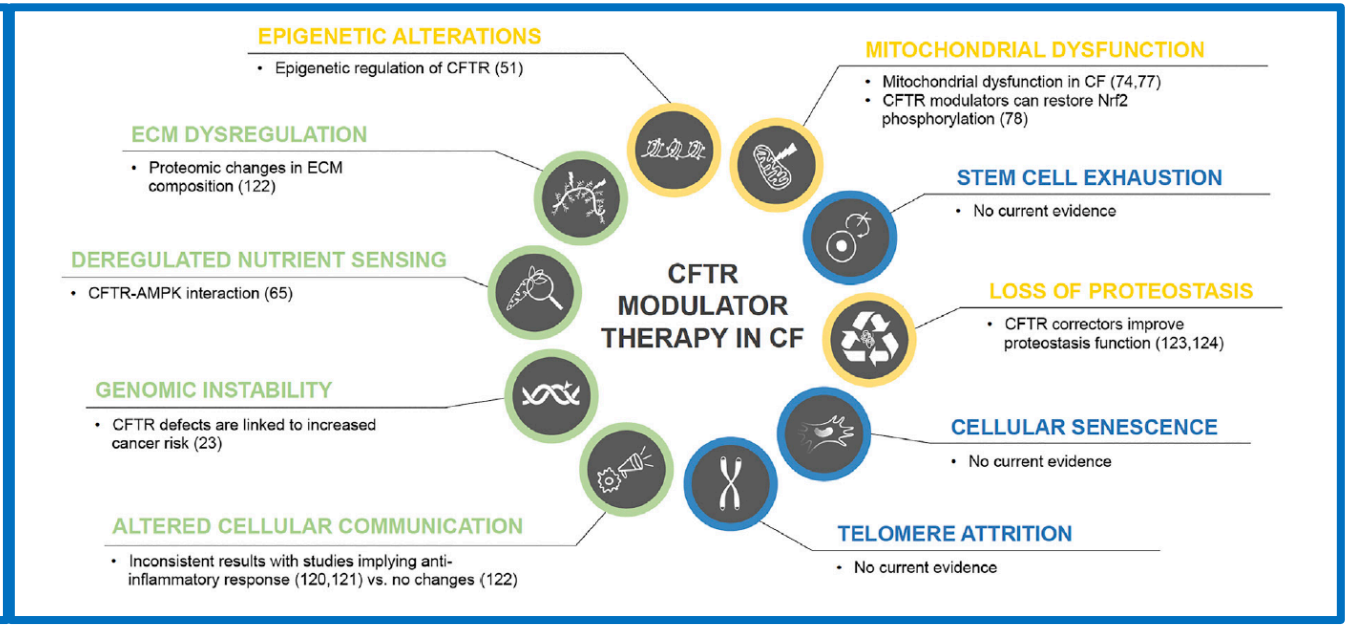
Cystic Fibrosis Lung Disease in the Aging Population

*Lisa Künzi [1,2], Molly Easter [1], Meghan June Hirsch [1] and Stefanie Krick [1,3,4]**

Current state of evidence on accelerated aging processes in CF.



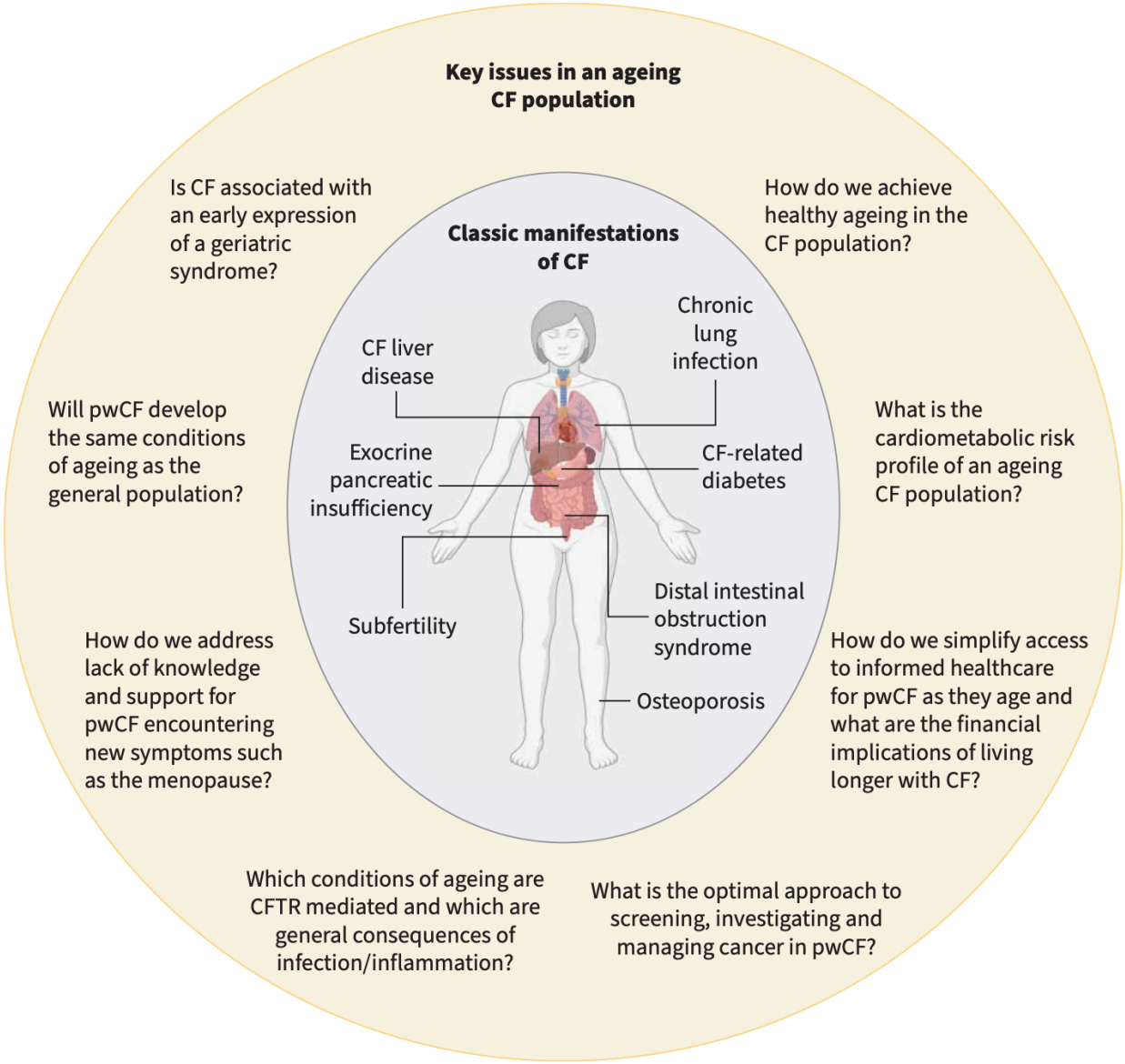
CFTR modulator therapy in CF and potential effects on the hallmarks of aging



- Increasing evidence suggests that accelerated aging processes are involved in CF lung pathology
- accelerated aging in CF patients is not only a consequence of chronic lung inflammation, but aging associated processes are also driving disease progression

- CFTR correctors also have been shown to act as proteostasis regulators and there is evidence that CFTR modulators can regulate mitochondrial dysfunction and epigenetic alterations.

Kunzi L. et al Frontiers in Pharmacology


Key issues in an ageing CF population
Is CF associated with an early expression of a geriatric syndrome?
How do we achieve healthy ageing in the CF population?
Classic manifestations of CF
Chronic lung infection
CF liver disease
Will pwCF develop the same conditions of ageing as the general population?
Exocrine pancreatic insufficiency
CF-related diabetes
What is the cardiometabolic risk profile of an ageing CF population?
Subfertility
Distal intestinal obstruction syndrome
How do we address lack of knowledge and support for pwCF encountering new symptoms such as the menopause?
Osteoporosis
How do we simplify access to informed healthcare for pwCF as they age and what are the financial implications of living longer with CF?
Which conditions of ageing are CFTR mediated and which are general consequences of infection/inflammation?
What is the optimal approach to screening, investigating and managing cancer in pwCF?

frontiers | Frontiers in Medicine

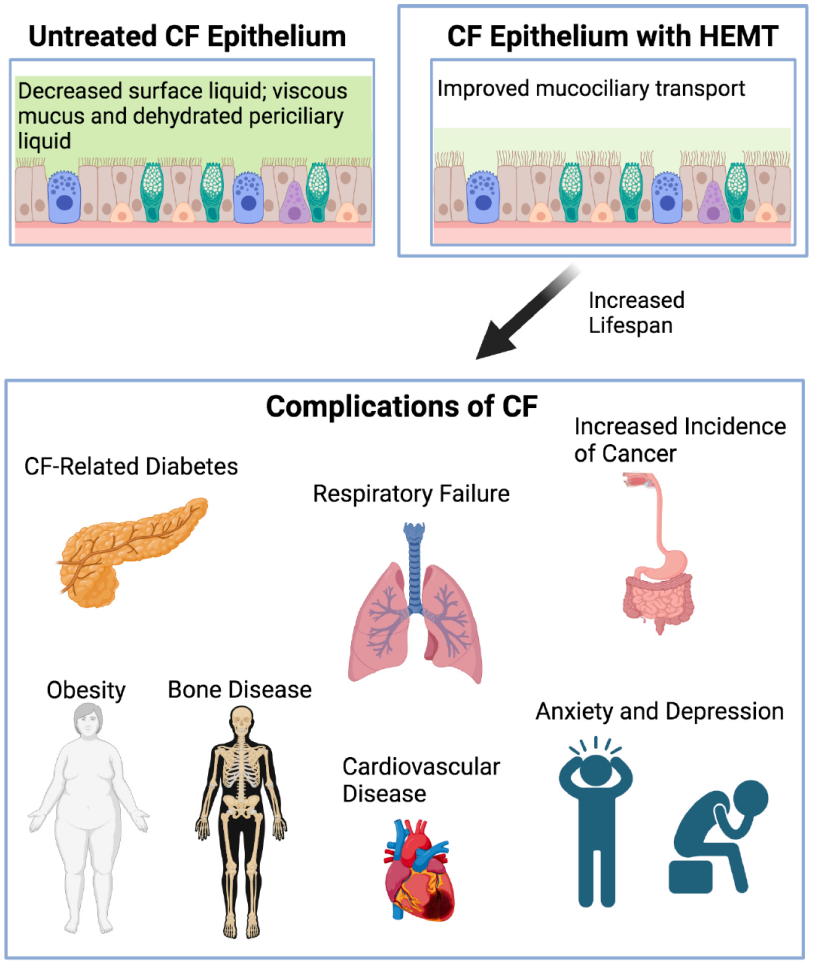
TYPE Mini Review
PUBLISHED 08 January 2024
DOI 10.3389/fmed.2023.1340388

What the future holds: cystic fibrosis and aging

Sydney Blankenship[1], Aaron R. Landis[1], Emily Harrison Williams[1], Jacelyn E. Peabody Lever[1], Bryan Garcia[1], George Solomon[1] and Stefanie Krick[1,2]*

Lo sviluppo di terapie modulatorie della CFTR ha cambiato il panorama della FC e ha portato a un aumento dell'aspettativa di vita per la pwCF.

In una popolazione FC che invecchia emergeranno nuove comorbidità che prima non erano così prevalenti, come la disfunzione cognitiva, le malattie cardiovascolari e le complicanze legate all'obesità



Blankenship et al. Frontiers in Medicine 2024

Complicazioni legate all'invecchiamento

Complications of CF, 2024

	Age < 18 (%)	Age ≥ 18 (%)	All (%)
Number of Individuals (n)	**13,060**	**19,432**	**32,492**
Percentage with no complications	25.1	4.1	12.5
Percentage with complications not reported[A]	1.1	2.3	1.8
Cystic Fibrosis-Related Diabetes			
Cystic fibrosis-related diabetes (CFRD)[B]	4.2	29.3	19.2
Hepatobiliary			
Gallstones	0.1	0.3	0.3
Liver disease, cirrhosis[C]	1.1	3.8	2.7
Liver disease, non-cirrhosis	3.0	3.9	3.5
Acute hepatitis	0.1	0.1	0.1
Hepatic steatosis	0.6	1.2	0.9
Liver disease, other	2.2	1.7	1.9
Bone/Joints			
Arthritis/arthropathy	0.1	5.8	3.5
Bone fracture	0.4	0.1	0.2
Osteopenia	0.8	19.4	11.8
Osteoporosis	0.2	8.3	5.0

Table continues on the next page

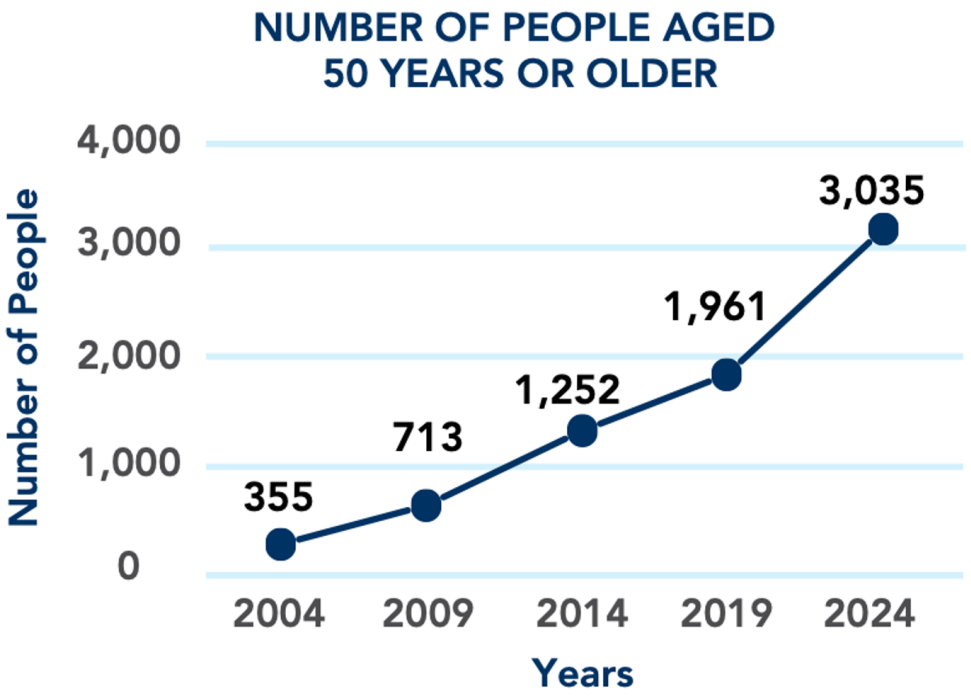
Complications of CF, 2024 *continued*

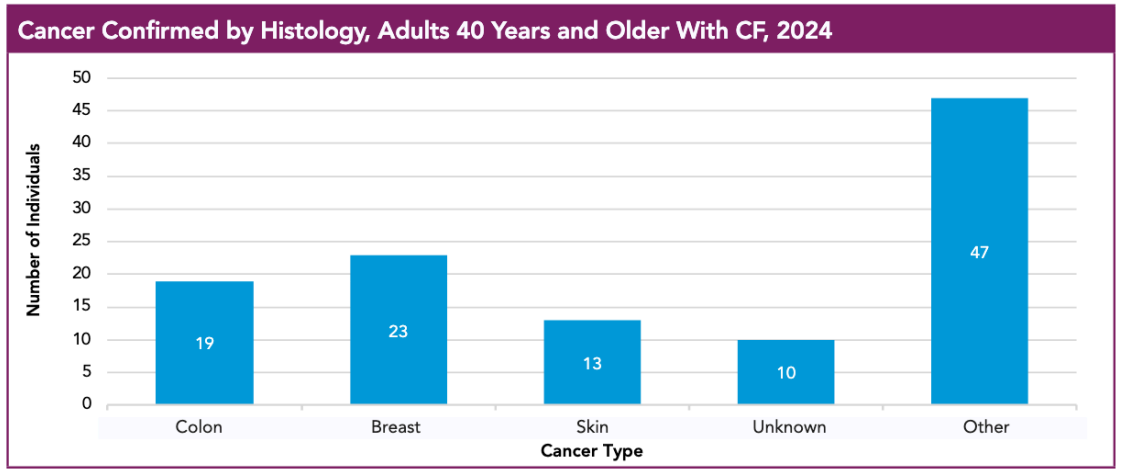
	Age < 18 (%)	Age ≥ 18 (%)	All (%)
Pulmonary			
Allergic bronchopulmonary aspergillosis (ABPA)	1.1	6.2	4.1
Asthma	22.6	34.8	29.9
Hemoptysis	0.2	2.6	1.6
Hemoptysis, massive	<0.1	0.3	0.2
Pneumothorax requiring chest tube	<0.1	0.1	0.1
GI			
Distal intestinal obstruction syndrome (DIOS)	1.5	1.3	1.4
Fibrosing colonopathy/colonic stricture	<0.1	<0.1	<0.1
Gastroesophageal reflux disease (GERD)	24.5	42.2	35.0
History of intestinal or colon surgery	6.5	3.4	4.6
Pancreatitis	0.3	1.0	0.7
Rectal prolapse	0.3	0.1	0.2
Clostridium difficile (C. diff) colitis	<0.1	0.1	0.1

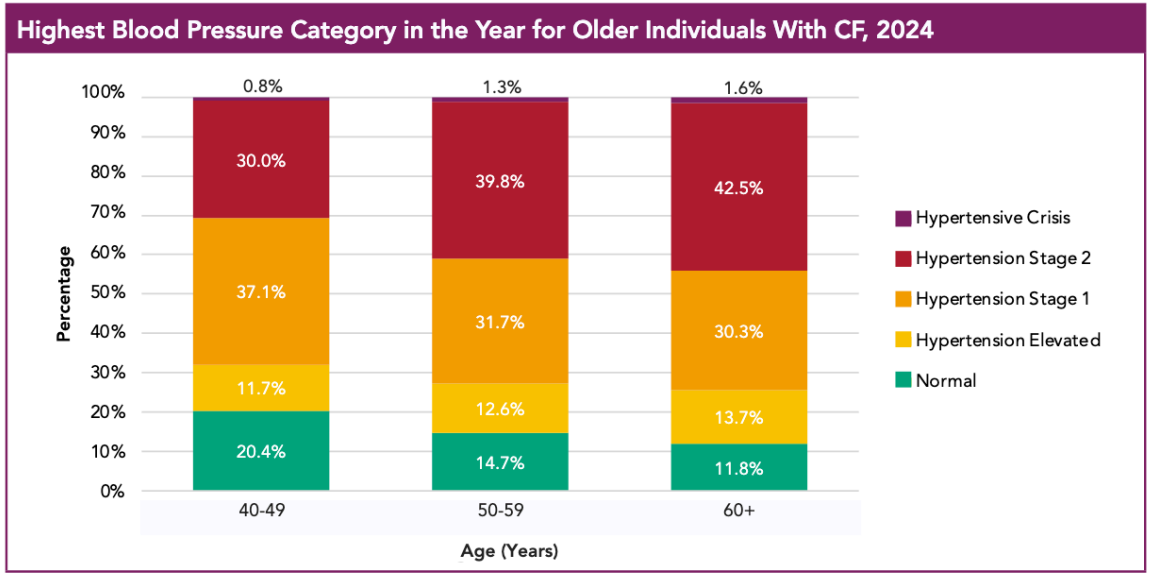
Complications of CF, 2024 *continued*

	Age < 18 (%)	Age ≥ 18 (%)	All (%)
Mental Health[D]			
Anxiety disorder	14.4	31.9	28.4
Depression	9.2	30.2	25.9
Other Complications			
Cancer confirmed by histology	<0.1	0.7	0.4
Hearing loss	1.1	3.8	2.7
Hypertension	0.6	8.7	5.4
Kidney stones	0.1	1.3	0.8
Nasal polyps requiring surgery	2.0	2.0	2.0
Renal failure requiring dialysis[E]	<0.1	0.1	0.1
Sinus disease	14.3	50.2	35.6

AGING IN CF







2024 CYSTIC FIBROSIS FOUNDATION Patient Registry Highlights

[Chest Infections CHEST Reviews]

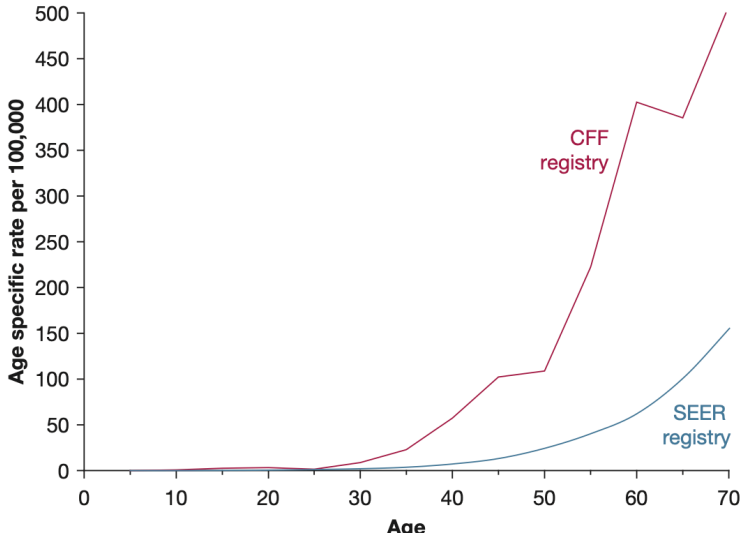
CHEST

Cancer in Cystic Fibrosis: A Narrative Review of Prevalence, Risk Factors, Screening, and Treatment Challenges

Adult Cystic Fibrosis Series

Patrick Maisonneuve, Dipl.Eng; and Albert B. Lowenfels, MD

Check for updates



- For nontransplanted patients, colonoscopy should begin at 40 years of age, with rescreening at 5-year intervals.
- The screening interval should be shortened to 3 years if adenomatous polyps are discovered.
- For transplanted patients, screening should start at 30 years of age, or within 2 years of the transplant operation.
- Before colonoscopy, it is essential for patients with CF to undergo a special, more intensive bowel preparation than normally used for those without CF.

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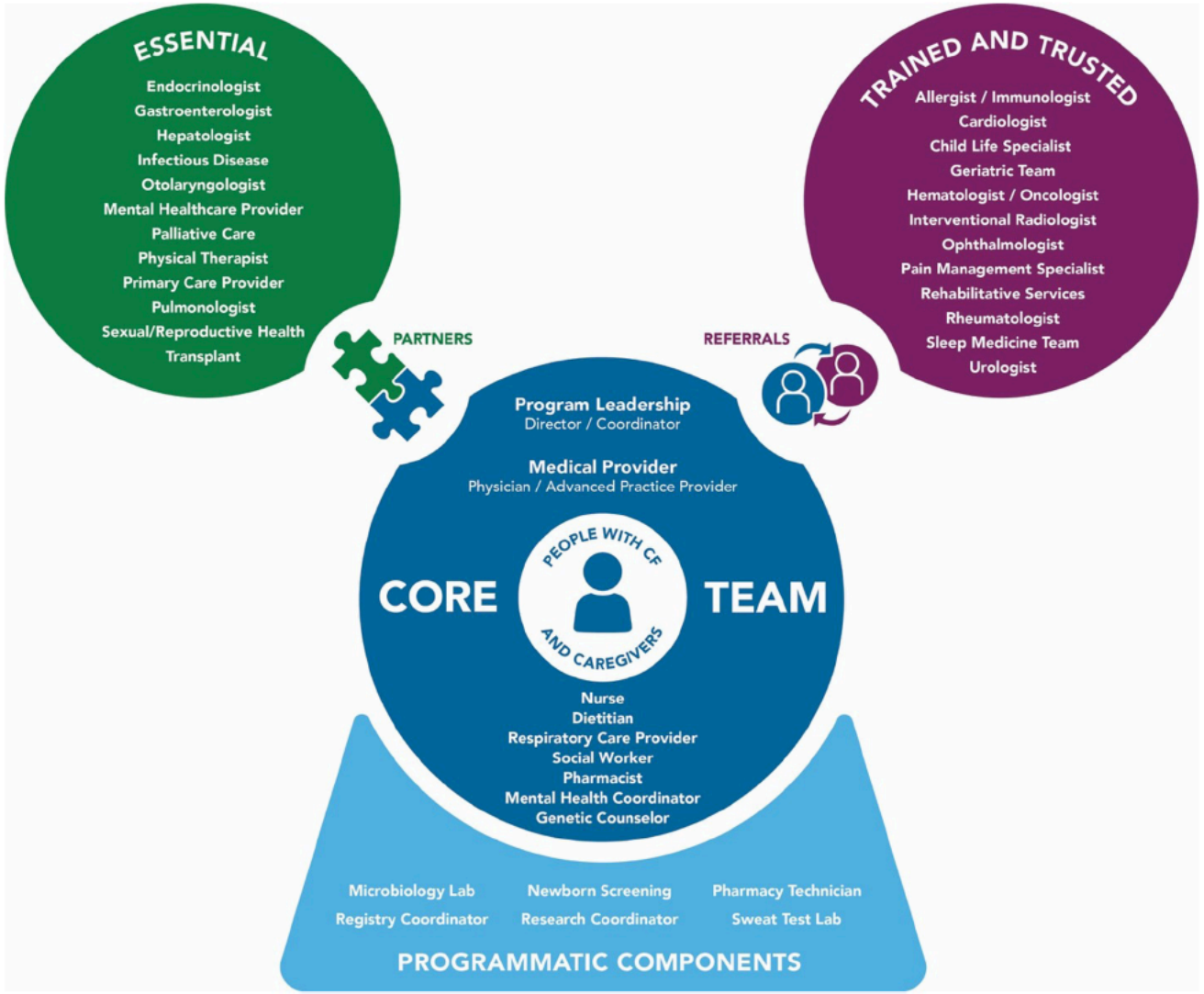
journal homepage: www.elsevier.com/locate/jcf

Review

Cystic fibrosis foundation position paper: Redefining the cystic fibrosis care team



PLANNING FOR A LONGER LIFE

Percorsi diagnostici-terapeutici-follow up personalizzati per i vari pazienti nei vari aspetti della loro vita;
Gestire nei vari momenti della vita aspetti quali **fertilità e gravidanze**

Nuovi percorsi terapeutici:
Grande numero di farmaci in fase di sperimentazione clinica
Garantire accesso per tutti i pazienti alle nuove terapie e capire come le useremo, quando le useremo e quali combinazioni funzioneranno meglio: personalizzazione delle terapie
Trial clinic, Trial Clinical Network che coinvolgano la CF community
Uso sempre maggiore dei registri di malattia

Paziente FC che invecchia:
Impostare programmi di screening e monitoraggio per le nuove comorbidità
Implementare il team multidisciplinare coinvolgendo specialisti (ginecologi, oncologi…)

Gramegna A. et al Standards for the care of people with cystic fibrosis (CF); Planning for alonger life JCF 2024

Table 1
Statements resulting from the Delphi consensus process (>94 % agreement achieved for all statements).

1	The CF team should support people with CF through their life journey, recognising key stress points such as changing school, gaining employment and living independently.
2	The CF team should acknowledge and respect the differing values and beliefs of people with CF.
3	The CF team should work with the family to introduce the concept of subfertility to young people with CF in a sensitive manner.
4	The CF team should provide clear, age-appropriate information about assisted reproductive technologies.
5	For women with CF who wish to conceive, the CF team should promote optimisation of pre-conceptional health including lung function, nutritional and metabolic status.
6	Pregnant women with CF should undergo regular monitoring by the CF and obstetric teams including screening for gestational diabetes and re-assessment of chronic supportive care.
7	The decision to continue or discontinue CFTR modulator therapy during and after pregnancy should be made in partnership between the CF team and the person with CF.
8	More research and high-quality evidence are needed to characterise maternal and foetal outcomes following CFTR modulator therapy use during pregnancy and breastfeeding.
9	The CF team should work in close partnership with primary care to ensure that people with CF have appropriate support and screening as they grow older.
10	CF teams should be aware of issues of incontinence (even from an early age) and provide support appropriately.
11	The CF team should evaluate for musculoskeletal problems and postural changes to facilitate early and appropriate management.
12	The CF community should work towards minimising global inequities, through collaboration, agreed standards of care and improved access to therapies.
13	The CF team should be aware of and take measures to tackle the inequalities in health outcomes experienced by people with CF from a less well-resourced backgrounds.
14	The CF community should endeavour to act on a micro and macro scale to minimise the impact of providing complex healthcare on the planet, without compromising quality of care.
15	Access to research participation should be equitable.
16	People with CF, from all backgrounds and ages, should be involved in the prioritisation and design of clinical studies, from an early stage.
17	The role of clinical trial networks is to facilitate the delivery of a wide portfolio of commercially sponsored and investigator-led studies, across multiple sites and/or countries.
18	CF registries are instrumental to guide policy and funding, improve quality of care and facilitate research for the benefit of the CF community.

REVIEW

Evolving cystic fibrosis care models in the modulator era

Isaac Martin[a], *Felix Ratjen*[a] *and Patrick Flume*[b]

Table 1. Recommendations for adapting to a new model of care

Recommendation	Rationale
Do not equate CFTR modulator use with clinical stability	Variability in response and persistence of inflammation/infection
Separate de-escalation from visit frequency	Therapy withdrawal may necessitate closer follow-up
Use objective metrics to guide care	FEV_1, cultures, PROMs support individualized decisions
Validate new models prospectively	Trials like HERO-2 and CF STORM are essential
Maintain flexibility through hybrid models	Tailor in-person and remote elements based on risk
Centre equity in redesign	Guard against digital divide and modulator ineligibility

- Il modello di cura della FC dovrebbe adattarsi per tenere conto dell'eterogeneità clinica della risposta alla terapia con modulatori, con **definizioni individualizzate di stabilità**.
- La **riduzione delle terapie croniche** deve essere distinta dalla stabilità clinica e richiede un monitoraggio strutturato.
- Il monitoraggio remoto e la telemedicina offrono nuove opportunità di erogazione delle cure;
- Alcune complicanze extra-polmonari (ad esempio, CFRD, CFLD, infezione persistente) si verificano ancora in corso di terapia con modulatori, giustificando un monitoraggio continuo.
- I modelli di cura rivisti dovrebbero mantenere il supporto multidisciplinare e dare priorità alla gestione condivisa del paziente, soprattutto durante le transizioni.

La Fibrosi Cistica: una malattia che invecchia!

Grazie per l'attenzione!

Dr. Vincenzo Carnovale
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