Una nuova Fibrosi Cistica comporta una nuova assistenza al paziente?

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Disclosures

I have accepted grants, speaking fees, consulting fees and conference invitations from:

- AstraZeneca
- Chiesi Farmaceutici
- GSK
- Grifols
- Laboratori Guidotti
- Insmed
- Janssen-Cilag
- Menarini Group
- Novartis
- OM Pharma
- Pfizer
- Sanofi
- Vertex Pharmaceuticals
- Viatris
- Zambon

Do all roads lead to adult care?

Images provided by speaker.

Epidemiology

- CF is the most common lethal inherited disease among the Caucasian population[1,2]
- Incidence in the EU: ~1 in 3,000 live births, with Ireland having the highest incidence of 1 in ~1,400 live births[3,4]
- Incidence varies according to ethnicity, with the lowest incidence rates among African American (1 in 15,000 to 20,000) and Asian populations[5,6]
- Data are missing for some regions of the world[7]
- The largest collection of epidemiological data for CF across Europe is the EU registry by the European Cystic Fibrosis Society (ECFS):[8] www.ecfs.eu

Incidence of CF across Europe

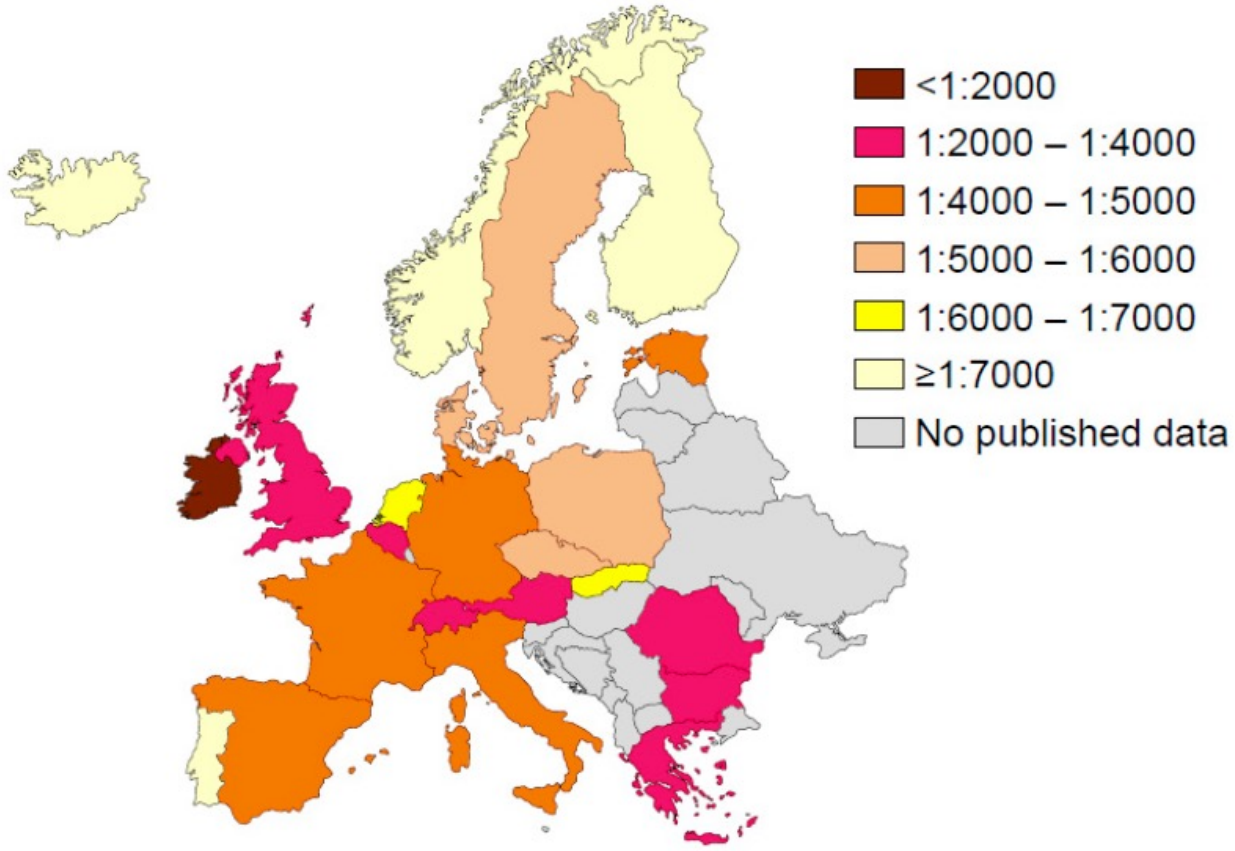


Figure from Scotet et al. 2020.[9]

CF, cystic fibrosis; EU, European Union; ECFS, European Cystic Fibrosis Society.

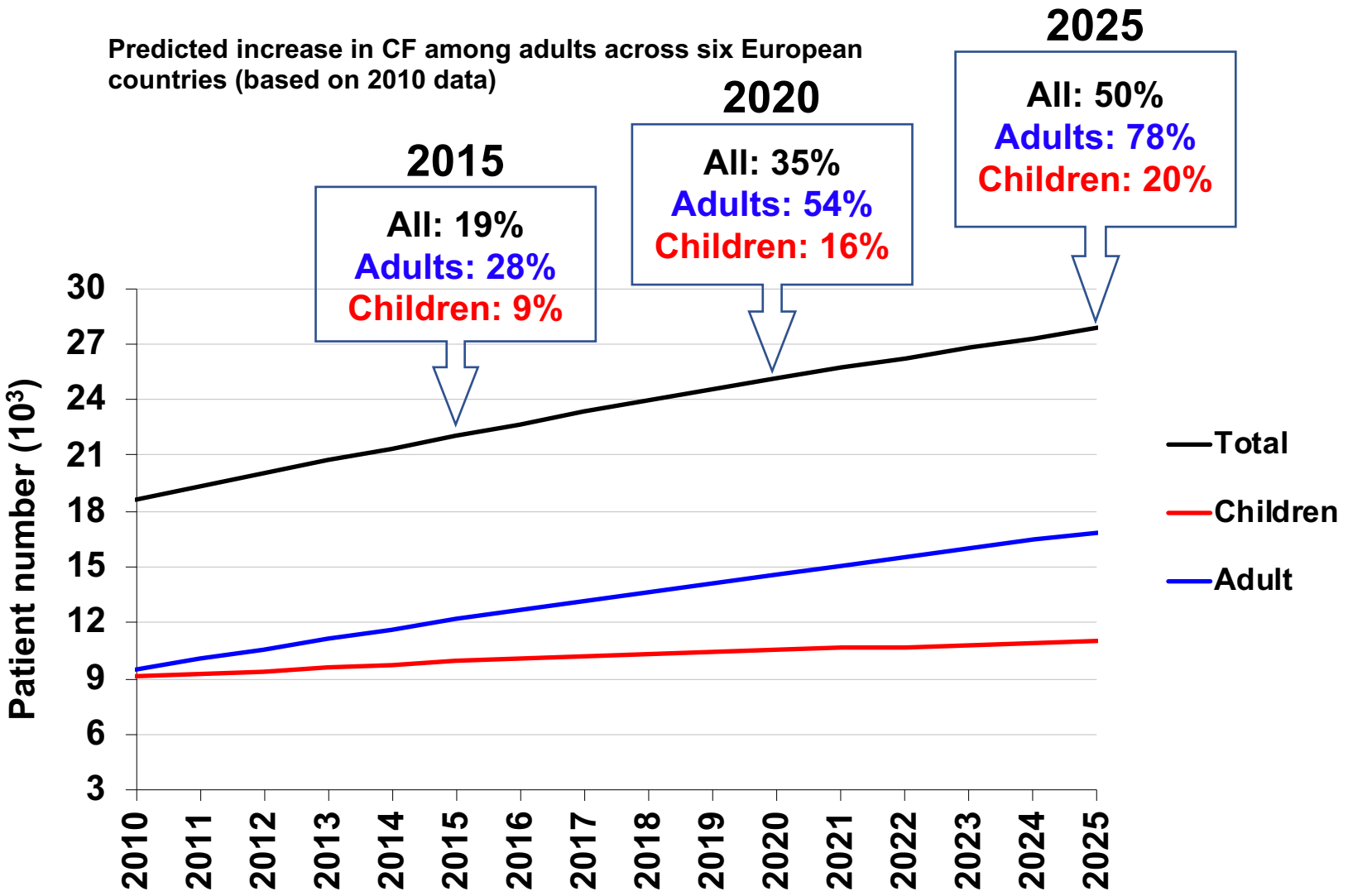
1. Cutting GR. Annu Rev Genomics Hum Genet. 2005;6:237–60; 2. Sibley CD, et al. Future Microbiol. 2006;1:53–61; 3. Kumar S, et al. Eur J Intern Med. 2014;25:803–7; 4. Farrell P, et al. Ir Med J. 2007;100:557–60; 6. Hangul M, et al. Balkan Med J. 2019;36:179–83; 7. Chen Q, et al. Anim Models Exp Med. 2021;4:220–32; 8. European Cystic Fibrosis Society. Introduction. Available from: https://www.ecfs.eu/ecfspr. Accessed September 2023; 9. Scotet V, et al. Int J Neonatal Screen. 2020;6:18.

Future trends in CF demography in Belgium, Czech Republic, Denmark, France, UK and The Netherlands

Group A countries contributed data to the ECFS Patient Registry, with ≥85% coverage of their national CF population and with longitudinal data for ≥4 years

The forecast for the number of adults and children with CF by 2015, 2020 and 2025 was predicted*

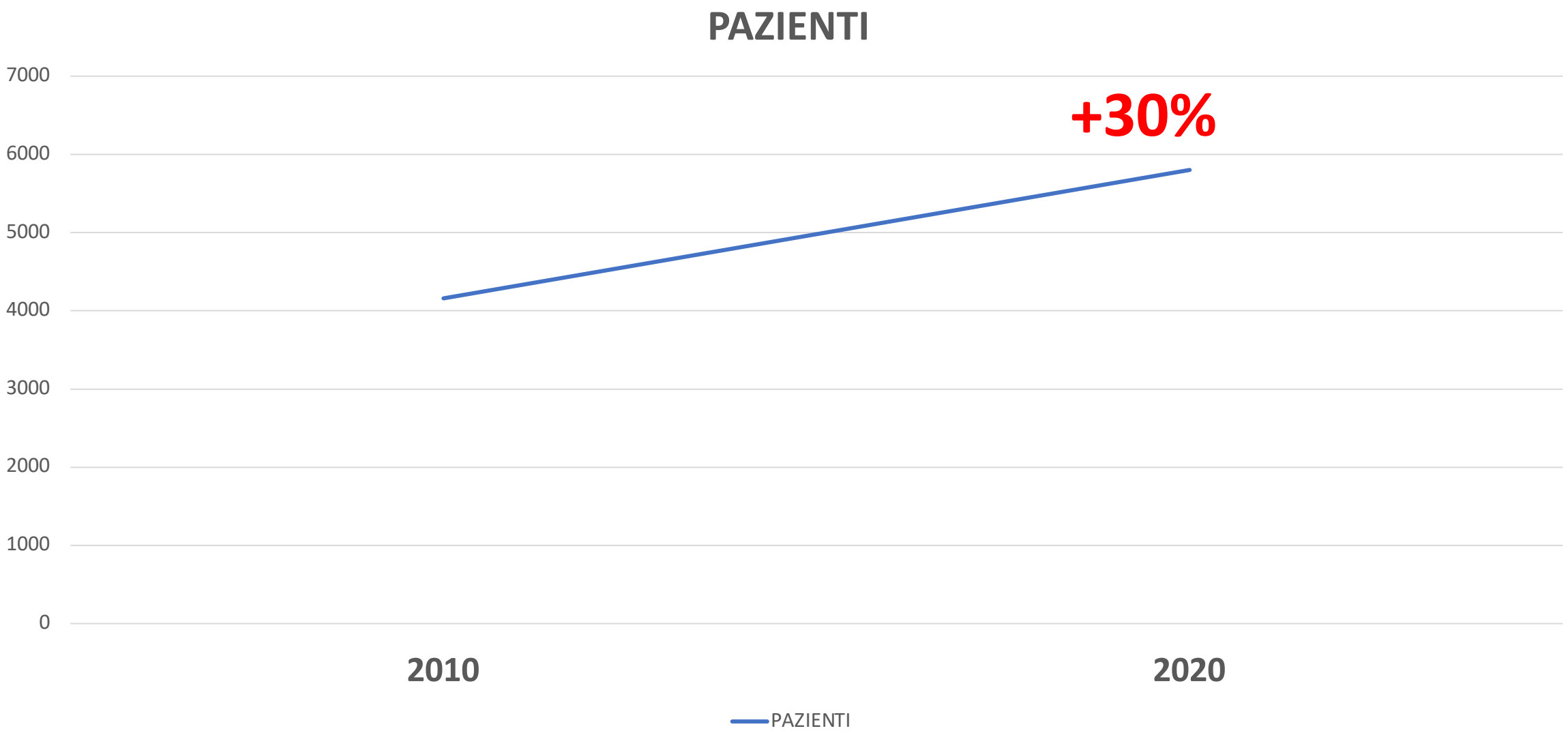
The predicted increase in CF among adults during the next decade indicates that more adult CF services throughout Europe are urgently required

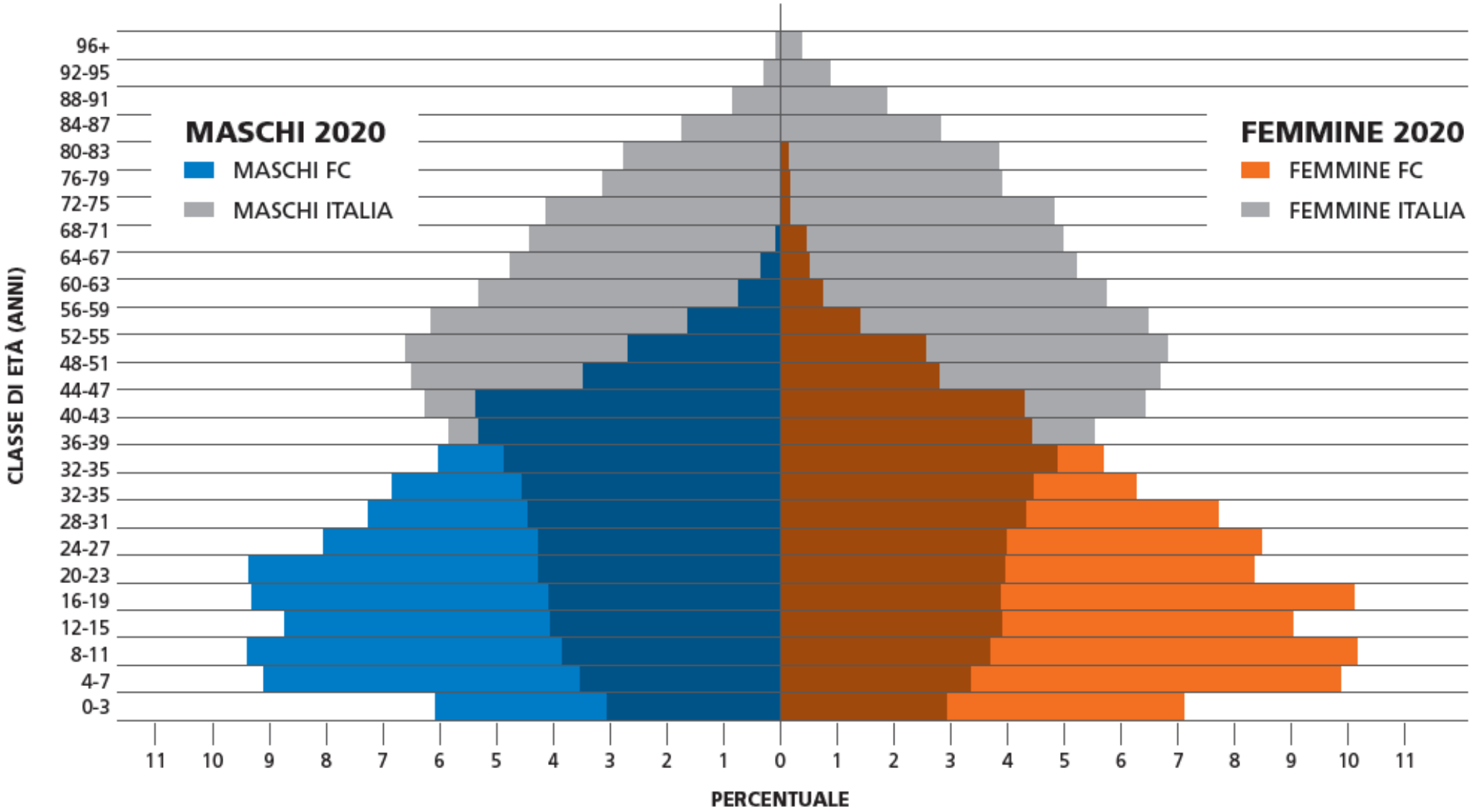


Graph created with data from Burgel et al. 2015.

*Prediction based on 2010 data.
CF, cystic fibrosis; ECFS, European Cystic Fibrosis Society.
Burgel PR, et al. Eur Respir J. 2015;46:133–41.

REGISTRO ITALIANO FC





Fonte: Istat 2020

Figura 4. Piramide dell'età dei pazienti con fibrosi cistica *vs* popolazione italiana. Anno 2020.

Milestones in development of therapies targeting the underlying cause of CF

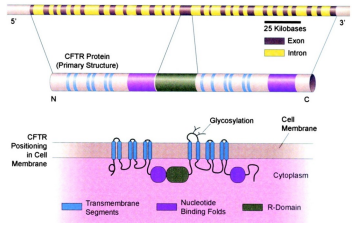


Image from Gibson et al. 2003.[1]

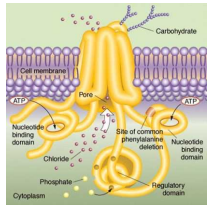


Image from Brouard et al. 2020.[2]

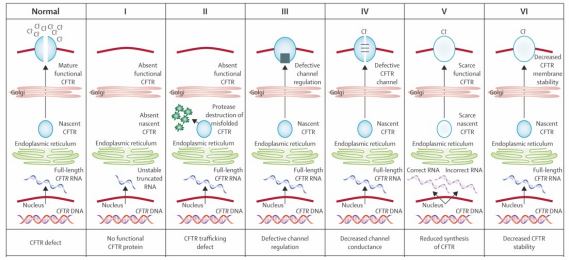
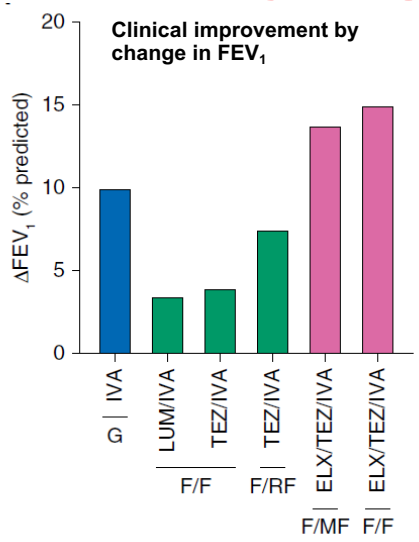
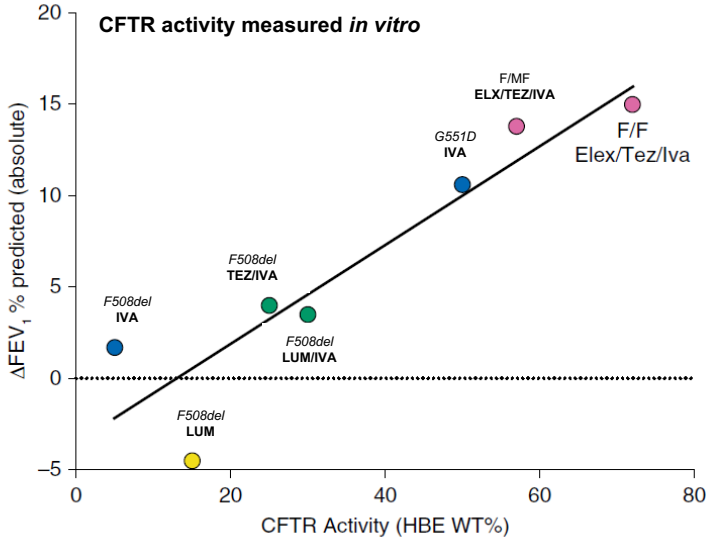


Image from Bell et al. 2020.[3]





Images from Mall et al. 2020.[4]

1989 — Discovery of the *CFTR* gene[5]

1993 — First gene therapy trials[6]

Late 1990s — First high throughput screens for small molecules[7,8]

2012 — IVA: first drug approved to treat the underlying cause of CF in patients with *G551D* (~5%) and nine other rare *CFTR* mutations[9,10]

2015 — LUM/IVA: first dual combination to treat patients homozygous for the most common *F508del* mutation (~45%)[11,12]

2018 — TEZ/IVA: second dual combination to treat patients homozygous for *F508del* and residual function mutations (~50%)[12–16]

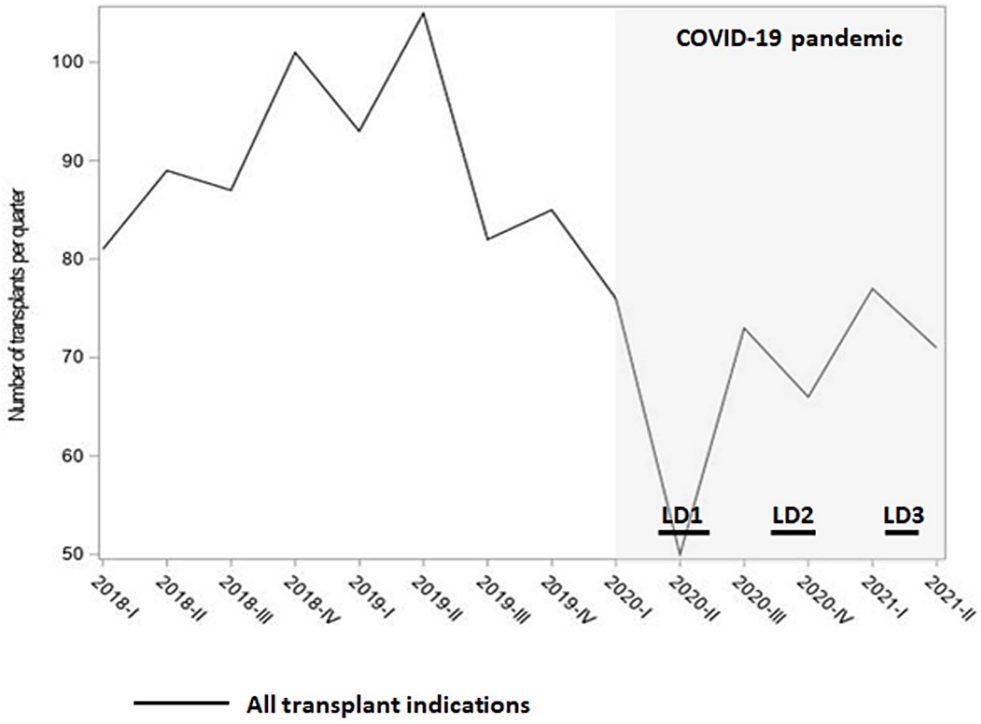
2020 — ELX/TEZ/IVA: first triple combination to treat patients with at least one *F508del* allele (~90%)[17–19]

ΔFEV$_1$, change in forced expiratory volume in one second; CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductance regulator; ELX, elexacaftor; F/F, homozygous for CFTR mutation; F/MF, minimal function CFTR mutation; F/RF, residual function CFTR mutation; HBE, human bronchial epithelial; IVA, ivacaftor; LUM, lumacaftor; TEZ, tezacaftor; WT, wild type.

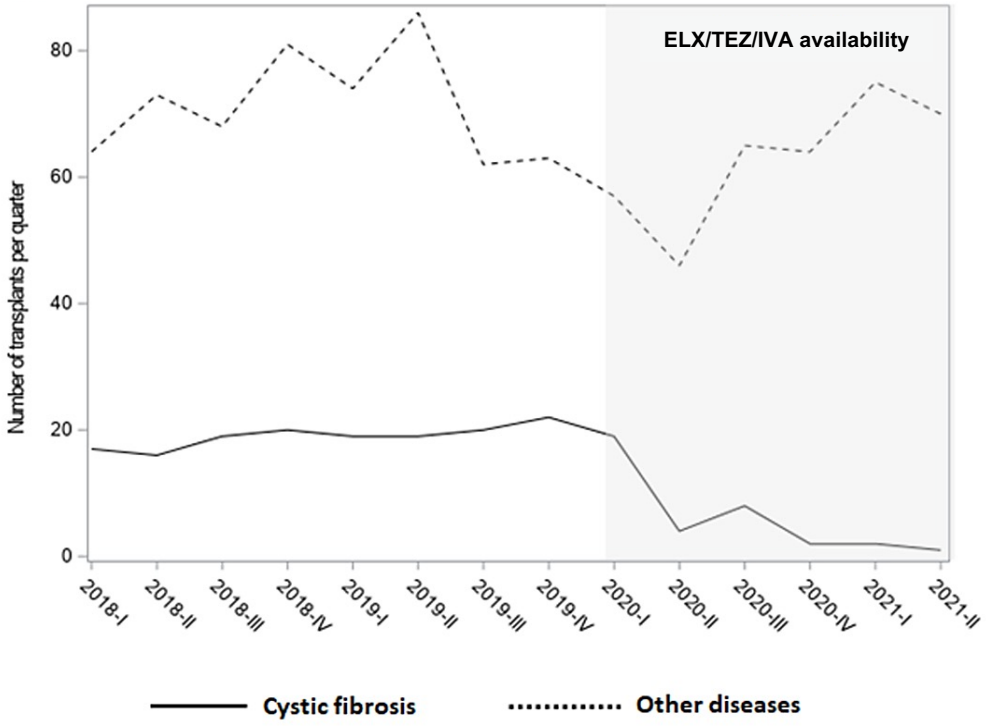
1. Gibson RL, et al. Am J Respir Crit Care Med. 2003;168:918–51; 2. Brouard C. Inférence de réseaux d'interaction protéine-protéine par apprentissage statistique. Available at: https://theses.hal.science/tel-00845692/file/These.pdf. Accessed September 2023; 3. Bell SC, et al. Lancet Respir Med. 2020;8:65–124; 4. Mall MA, et al. Am J Respir Crit Care Med. 2020;201:1193–20; 5. Férec C. Med Sci (Paris). 2021;37:618–24; 6. Davies JC and Alton EWFW. Proc Am Thorac Soc. 2010;7:408–14; 7. Mayr LM and Botanic D. Curr Opin Pharmacol. 2009;9:580–8; 8. Coussens NP, et al. Pharmacol Rev. 2017;69:479–96; 9. Ramsey BW, et al. N Engl J Med. 2011;365:1663–72; 10. Kalydeco®. Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/kalydeco-epar-product-information_en.pdf. Accessed September 2023; 11. Orkambi®. Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/orkambi-epar-product-information_en.pdf. Accessed September 2023; 12. Wainwright CE, et al. N Engl J Med. 2015;373:220–31; 13. Taylor-Cousar JL, et al. N Engl J Med. 2017;377:2013–23; 14. Rowe SM, et al. N Engl J Med. 2017;377:2024–35; 15. Symkevi®. Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/symkevi-epar-product-information_en.pdf. Accessed September 2023; 16. Sawicki GS, et al. Pulm Ther. 2022;8:385–95; 17. Middleton P, et al. N Engl J Med. 2019;381:1809–19; 18. Kaftrio®. Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/kaftrio-epar-product-information_en.pdf. Accessed September 2023; 19. Heijerman HGM, et al. Lancet. 2019;394:1940–8.

Major decrease in lung transplantation for patients with CF in France: COVID-19 vs ELX/TEZ/IVA

Lung transplantation in France from 2018 to 2021 during the COVID-19 pandemic (all transplant indications)



Lung transplantation in France from 2018 to 2021 based on ELX/TEZ/IVA availability (CF vs other pulmonary disease)



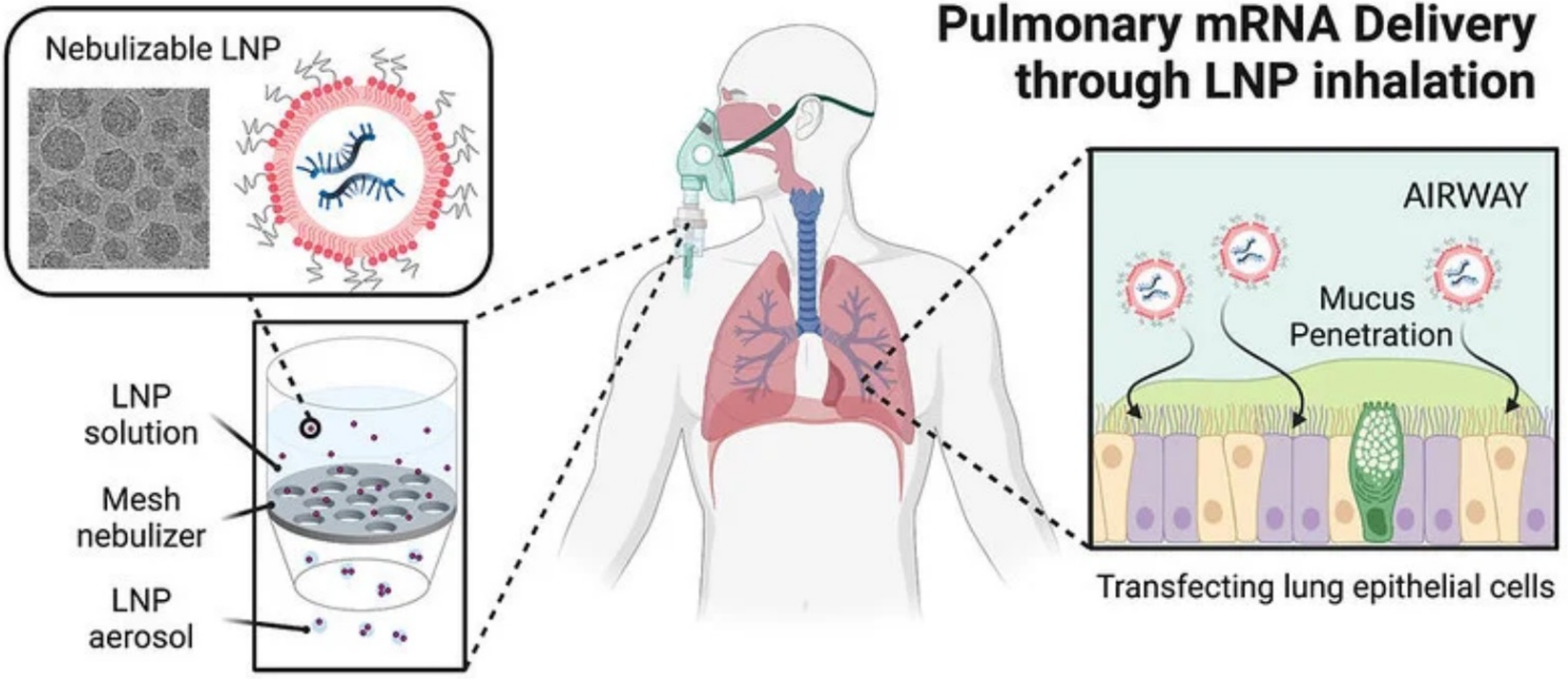
Graphs from Martin et al. 2022.

- Effects of ELX/TEZ/IVA were studied in patients with CF with advanced pulmonary disease (n=245)
- Patients with advanced CF pulmonary disease showed a reduction in the need for lung transplantation over the first months following the availability of ELX/TEZ/IVA
- Overall, patients on ELX/TEZ/IVA showed rapid improvement in lung function and BMI, with an acceptable safety profile

BMI, body mass index; COVID-19, coronavirus disease 2019; CF, cystic fibrosis; ELX, elexacaftor; IVA, ivacaftor; LD, lockdown; TEZ, tezacaftor.

Martin C, et al. Am J Respir Crit Care Med. 2022;205:584–6.

NEW STRATEGIES FOR NOT-ELIGIBLES



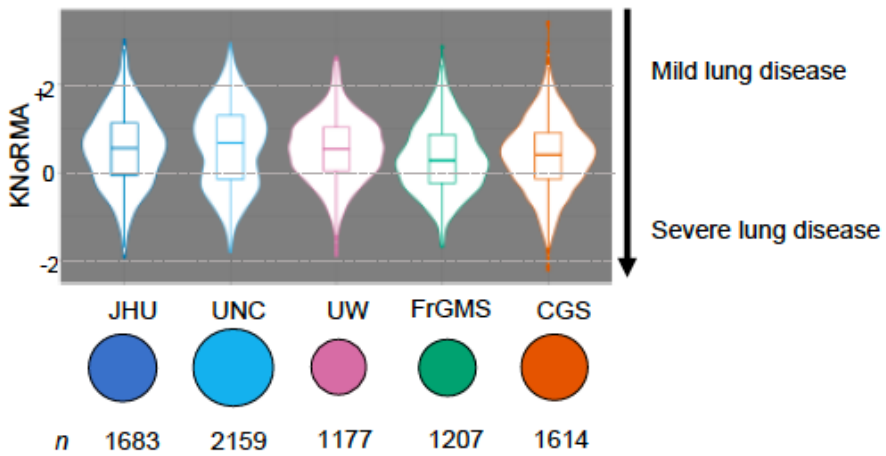
https://apps.cff.org/trials/pipeline/

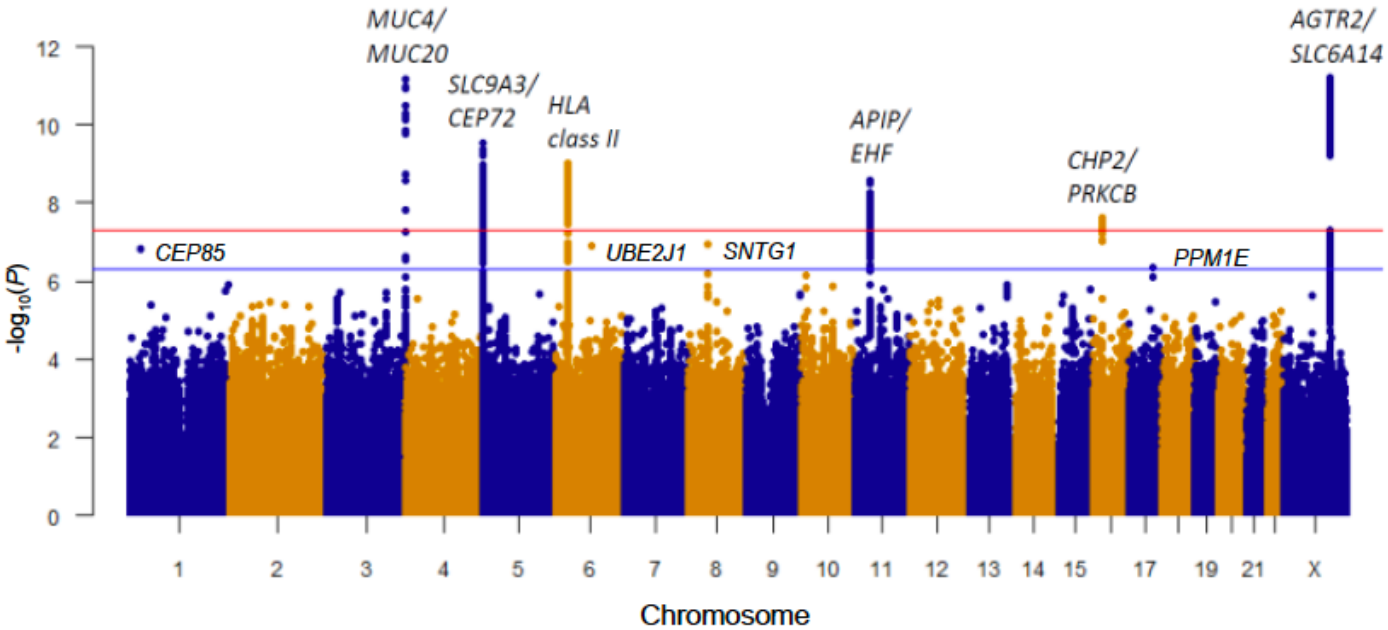
	ARE ALL PEOPLE WITH CF ELIGIBLE?	DOSING SCHEDULE	DELIVERY MODE	POTENTIAL CHALLENGES	IS PERMANENT CURE?
mRNA delivery	✓	 Maybe weekly	 Lungs (at first)	Any cell that takes it up will make protein	✗
Gene delivery (transfer)	✓	 Maybe monthly	 Lungs (at first)	Any cell that takes it up will make protein	✗
Gene editing	✓	 Unknown	 Systemic	Can edit DNA outside of CFTR gene	✓

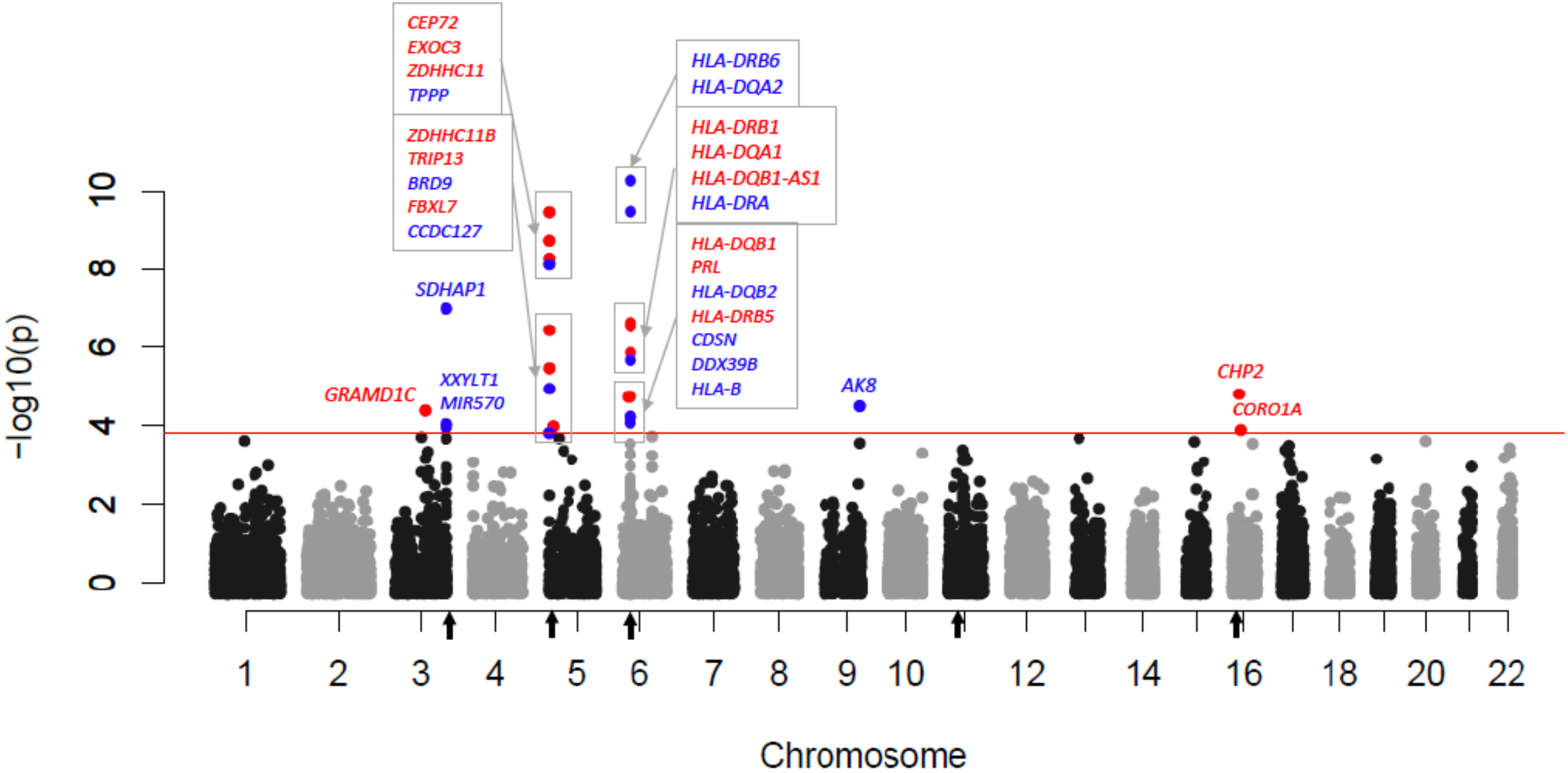
Genetic modifiers of cystic fibrosis lung disease severity: whole genome analysis of 7,840 patients

Yi-Hui Zhou, PhD,[1, 2,*] Paul J. Gallins, MS,[1] Rhonda G. Pace, BS,[3] Hong Dang, PhD,[3] Melis A. Aksit, PhD,[4] Elizabeth E. Blue, PhD,[5, 6] Kati J. Buckingham, BS,[7] Joseph M. Collaco, MD, MS, PhD,[8] Anna V. Faino, MS,[9] William W. Gordon, MS,[7] Kurt N. Hetrick, MS,[10] Hua Ling, PhD,[10] Weifang Liu, BA,[11] Frankline M. Onchiri, PhD,[9] Kymberleigh Pagel, PhD,[12] Elizabeth W. Pugh, PhD,[10] Karen S. Raraigh, MGC, CGC,[4] Margaret Rosenfeld, MD, MPH,[13, 14] Quan Sun, BS,[11] Jia Wen, PhD,[15] Yun Li, PhD,[11, 15, 16] Harriet Corvol, PhD,[17, 18] Lisa J. Strug, PhD,[19, 20, 21, 22, 23] Michael J. Bamshad, MD,[5, 7, 24] Scott M. Blackman, MD, PhD,[4, 25] Garry R. Cutting, MD,[4] Ronald L. Gibson, MD, PhD,[13, 14] Wanda K. O'Neal, PhD,[3,27] Fred A. Wright, PhD,[1, 2, 26,27] Michael R. Knowles, MD[3,27,*] on behalf of the Cystic Fibrosis Genome Project

AJRCCM Articles in Press. Published March 15, 2023 as 10.1164/rccm.202209-1653OC







Red colored text corresponds to increased expression associated with improved lung function and blue colored text corresponds to increased expression associated with decreased lung function. Regions of significant genome-wide phenotype-genotype association are marked with black arrows on the X axis.

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Panel: **Ongoing studies that aim to achieve treatment for all patients and address outstanding research questions[2]**

Genetic therapy

4D-710: this study will test the safety and tolerability of 4D-710, an investigational gene therapy, in adults with CF who are not eligible for, or are unable to, tolerate CFTR modulator therapy (NCT05248230).

VX-522: VX-522 is an inhaled messenger RNA (mRNA) therapy. The aim of the therapy is to deliver a full-length copy of CFTR mRNA to lung cells using a lipid nanoparticle. Lung cells would then use the mRNA to create functional CFTR protein. This type of therapy could work for any person with cystic fibrosis, regardless of their CFTR mutations (NCT05668741).

Restoring the CFTR protein

Vanzacaftor—tezacaftor—deutivacaftor: vanzacaftor—tezacaftor—deutivacaftor is a combination therapy that combines three CFTR modulators, which would allow it to be taken once a day. A phase 2 study to test the safety and effectiveness of vanzacaftor—tezacaftor—deutivacaftor in adults with cystic fibrosis has been completed (NCT03912233, NCT05033080, and NCT05422222).

ELX-02: ELX-02 is a compound designed to restore CFTR function in people with cystic fibrosis who have nonsense mutations and is intended to allow lung cells to override these premature stop signals and make full-length, functional CFTR protein (NCT04135495).

Anti-inflammatory

Brensocatib: brensocatib is an oral drug designed to block the function of enzymes, such as neutrophil elastase, that have an essential role in inflammation. A phase 2 study to test the safety of brensocatib in adults with cystic fibrosis is underway (NCT05090904).

LAU-7b: LAU-7b is an oral compound and is a form of the retinoid fenretinide. Retinoids are a group of compounds related to vitamin A. Fenretinide might help reduce the inflammatory response in the lungs of people with cystic fibrosis. A phase 2 study will test the safety and effectiveness (NCT03265288).

Anti-infective

Intravenous gallium (IGNITE): gallium is a molecule that disrupts iron-dependent biological processes and has been shown to kill antibiotic-resistant strains of *Pseudomonas aeruginosa* in laboratory research. A phase 2 study to test the safety and effectiveness of intravenous gallium in controlling *P aeruginosa* in people with cystic fibrosis has been completed (NCT02354859).

AP-PA02: AP-PA02 is a type of phage therapy designed to fight *P aeruginosa* infections in people with cystic fibrosis. Bacteriophages are specialised viruses that kill very specific bacterial strains. A phase 1b/2 trial to test the safety and tolerability of AP-PA02 in adults with cystic fibrosis is underway (NCT04596319).

Factors affecting response to CFTRm

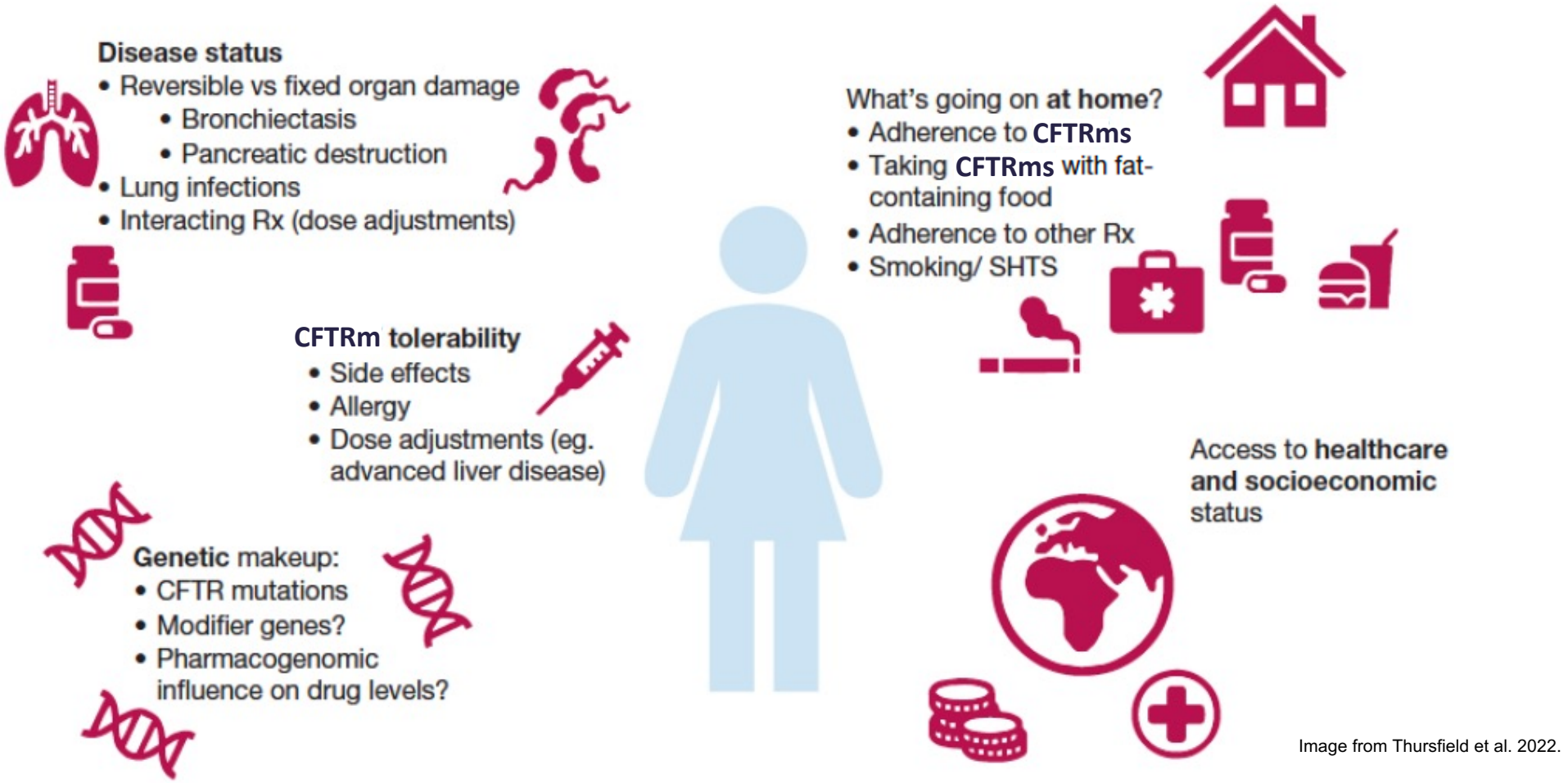

Image from Thursfield et al. 2022.

- Individuals may respond differently to CFTRms, based on a huge number of factors which may be interrelated, such as the situation at home, socioeconomic and disease status
- When weighed against these cumulative impacts, any distinction between children and adults is arbitrary

CFTR, cystic fibrosis transmembrane regulator protein; CFTRm, CFTR modulator; Rx, therapy; SHTS, second-hand tobacco smoke.
Thursfield RM, et al. Chest. 2022;161:21–4.

Emerging issues

Drug-related[1–3]

- Renal disease: 42.5% adults (n=34/80), creatinine clearance <80 ml/min/1.73 m^2
- Ototoxicity (n=153): 50.8% adults had mild/moderate-to-severe severity
- Polypharmacy

Age-related[4–6]

- Obesity: 11% adults (n=21/187) BMI ≥25 kg/m^2
- Hypercholesterolemia (n=334): 24% PI and 43% PS adults
- Ischaemic heart disease – case reports

Drug-/CF-/age-related[7–11]

- Cancer: ↑GI malignancy (SIR: 3.5; 95% CI: 2.6–4.7)
- Colonoscopic screening programme: ≥40 years and FEV_1 ≥40%
- Cardiovascular disease
- Treatment adherence
- Pregnancy

25% advanced adenomas and 3% carcinoma[8]

All images from Unsplash.com.[11]

BMI, body mass index; CI, confidence interval; CF, cystic fibrosis; FEV_1, forced expiratory volume in one second; GI, gastrointestinal; PI, pancreatic insufficient; PS, pancreatic sufficient; SIR, standardised incidence ratio.

1. Al-Aloul M, et al. Pediatr Pulmonol. 2005;39:15–20; 2. Conrad DJ, et al. Pharmacogenet Genomics. 2008;18:1095–102; 3. Sareen A, et al. Breathe (Sheff). 2021;17:210005; 4. Coderre L, et al. J Cyst Fibros. 2012;11:393–7; 5. Rhodes B, et al. J Cyst Fibros. 2010;9:24–8; 6. Professional opinion of the speaker; 7. Maisonneurve P, et al. J Natl Cancer Inst. 2013;105:122–9; 8. Niccum DE, et al. J Cyst Fibros. 2016;15:548–53; 9. Saunders T, et al. Nature Cardiovascular Research. 2022;1:187–88; 10. Eakin MN and Riekert KA. Curr Opin Pulm Med. 2013;19:687–91; 11. Gur M, et al. J Clin Med. 2023;12:1468; 11. Unsplash. Available from https://unsplash.com/. Accessed September 2023.

Where should specialist adult CF centres be situated?

Most of the mortality and morbidity in CF relates to the lung disease caused by infection and the consequent inflammatory processes which cause mucus plugging, bronchiectasis and air trapping and the associated reduction in measures of lung function such as FEV1 [52]. The medical care of adults with CF should therefore be delivered by pulmonologists who have had specific training in CF, understand the pathogenesis of CF and are aware of all of the potential interventions that will reduce the impact of infection and inflammation. The need for management of pulmonary complications, such as exacerbations, major haemoptysis, pneumothorax and respiratory failure, as well as for a clear understanding of how to prevent and manage these complications, suggests adult CF care is best based in adult pulmonology services. Other core physician team members could include infectious disease physicians, internists and gastroenterologists.

Figure from Elborn et al. 2016.

CF, cystic fibrosis; FEV_1, forced expiratory volume in one second.
Elborn JS, et al. Eur Respir J. 2016;47:420–8.

Is there an ideal size for a CF centre?

The optimal size of an adult CF centre has not been addressed in the scientific literature; however, according to the ECFS standards of care for CF centres, consensus is that a designated specialist adult centre should usually be a minimum of 100 patients (but not below 50 patients) and, where care is provided in smaller centres, there should be specific links with a larger centre to ensure access to appropriate multidisciplinary expertise. There is no research to indicate if there is an optimal maximum size for a CF centre. The size of adult centres will usually depend on physical and staffing constraints; however, there are currently only a few centres providing CF specialist care for more than 500 patients.

Figure from Elborn et al. 2016.

CF, cystic fibrosis; ECFS, European Cystic Fibrosis Society.
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Report of the ERS/ECFS task force on adult CF care

The multidisciplinary team	100 patients	150 patients	⩾250 patients
Consultant 1	0.5	1	1
Consultant 2	0.3	0.5	1
Consultant 3			0.5
Staff grade/fellow	0.5	1	1
Specialist registrar	0.4	0.8	1
Specialist nurse	2	3	5
Physiotherapist	2	4	6
Dietician	0.5	1	2
Clinical psychologist	0.5	1	2
Social worker	0.5	1	2
Pharmacist	0.5	1	1
Secretary	0.5	1	2
Database coordinator	0.4	0.8	1

Table from Elborn et al. 2016.

CF, cystic fibrosis; ECFS, European Cystic Fibrosis Society; ERS, European Respiratory Society.
Elborn JS, et al. Eur Respir J. 2016;47:420–8.

Barriers and challenges associated with CF transition

Patient-related Barriers	Health care Utilization	• Lower rates of health care system utilization • Difficulties navigating the health care system • Increased gaps in CF care during transition
	Medical Complexity	• Increased burden for pwCF and caregivers due to complex treatment regimens • Increased technology assistance • Increasing disease complexity with age (eg, CFRD, ACFLD)
	Adolescence and Emerging Adulthood	• Increased risk-taking behavior • Poor medication adherence • Difficulty with executive function, eg, time management, memory, planning • Inconsistency with meeting caloric needs • Family planning and the challenges of pregnancy for PwCF • Worsening depression and anxiety
	Transition Readiness	• Lack of CF-related knowledge • Lack of self-management skills • Neurocognitive deficits and developmental limitations
	Family and Caregivers	• Fears associated with leaving pediatric care • Reluctance to provide independence/autonomy with CF care
Provider-related Barriers	Patient-Centered Care Education	• Lack of time alone with pwCF during visits • Inadequate education and counseling regarding CF care
	Structured Transition	• Delayed initiation of transition services • Inconsistent methods of transition across providers • Inconsistent skill-building to support transition • Inappropriate timing of transfer
System-related Barriers	Access to Care	• Lack of primary care providers comfortable with the complexity of CF care • Gaps in insurance coverage during transition
	Guidelines	• Lack of updated CF care guidelines related to transition
	Research Limitations	• Paucity of standardized assessment tools to gauge the efficacy of transfer • Lack of prospective studies evaluating the long-term impact of transition strategies

Table from DeFilippo et al. 2022.

ACFLD, advanced cystic fibrosis lung disease; CF, cystic fibrosis; CFRD, cystic fibrosis-related diabetes; pwCF, people with cystic fibrosis.

DeFilippo EMM, et al. Clin Chest Med. 2022;43:757–71.

Barriers and challenges associated with CF transition: Patient-related barriers

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Barriers and challenges associated with CF transition: Provider- and system-related barriers

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Best practices for optimising CF transition

Patient-Focused	Health care Utilization and Self-Management	• Develop skills in health care navigation: Making appointments, communicating with providers, maintaining insurance • Develop skills in self-management: Treatment adherence, equipment use, adequate caloric intake, exercise
	Medical Complexity	• Simplify medication regimens • Ensure early referral to transplant for ACFLD and optimize palliative care • Defer transition if disease is unstable
	Adolescence and Emerging Adulthood	• Assess neurodevelopmental ability • Counsel PwCF regarding time management and keeping a schedule • Provide anticipatory guidance regarding smoking, substance use, peer pressure influence, and reproductive health • Provide mental health screening and support services
Provider-Focused	Patient-Centered Care	• Improve communication skills (listening, empathy, honesty); Increase telehealth utilization • Devote a portion of scheduled visits to time alone with pwCF • Provide targeted family and caregiver support and education, eg, support groups
	Structured Transition	• Initiate transition services when developmentally ready; use shared decision-making regarding the timing of transfer • Provide developmentally appropriate education about CF and rationale for treatments • Measure transition readiness using validated tools, eg, TRAQ survey • Create a medical summary, treatment plan, and emergency care plan for pwCF • Assess social complexity and provide social work support • Schedule the first adult visit; consider a joint visit between pediatric and adult care teams • Monitor for the successful transition, including changes in lung function
	Access to Care	• Establish relationships with local primary care providers who are willing to care for pwCF • Ensure maintenance of insurance coverage prior to transition
System-Focused	Guidelines	• Update CF care guidelines to include optimal transition strategies
	Next Steps in Research	• Define outcomes of successful transition and standardize assessment tools in CF transition • Utilize registry data (including patient-reported quality-of-life outcomes) in CF transition research • Integrate registry date with patient-reported quality-of-life outcomes • Increase QI initiatives between pediatric and adult CF care teams

Table from DeFilippo et al. 2022.

ACFLD, advanced cystic fibrosis lung disease; CF, cystic fibrosis; pwCF, people with cystic fibrosis; QI, quality improvement; TRAQ, Transition Readiness Assessment Questionnaire.
DeFilippo EMM, et al. Clin Chest Med. 2022;43:757–71.

Table from DeFilippo et al. 2022.

Best practices for optimising CF transition: Patient-focused

Patient-Focused	Health care Utilization and Self-Management	• Develop skills in health care navigation: Making appointments, communicating with providers, maintaining insurance • Develop skills in self-management: Treatment adherence, equipment use, adequate caloric intake, exercise
	Medical Complexity	• Simplify medication regimens • Ensure early referral to transplant for ACFLD and optimize palliative care • Defer transition if disease is unstable
	Adolescence and Emerging Adulthood	• Assess neurodevelopmental ability • Counsel PwCF regarding time management and keeping a schedule • Provide anticipatory guidance regarding smoking, substance use, peer pressure influence, and reproductive health • Provide mental health screening and support services

Table from DeFilippo et al. 2022.

ACFLD, advanced cystic fibrosis lung disease; CF, cystic fibrosis; pwCF, people with cystic fibrosis.
DeFilippo EMM, et al. Clin Chest Med. 2022;43:757–71.

Best practices for optimising CF transition: Provider-focused

Provider-Focused	Patient-Centered Care	• Improve communication skills (listening, empathy, honesty); Increase telehealth utilization • Devote a portion of scheduled visits to time alone with pwCF • Provide targeted family and caregiver support and education, eg, support groups
	Structured Transition	• Initiate transition services when developmentally ready; use shared decision-making regarding the timing of transfer • Provide developmentally appropriate education about CF and rationale for treatments • Measure transition readiness using validated tools, eg, TRAQ survey • Create a medical summary, treatment plan, and emergency care plan for pwCF • Assess social complexity and provide social work support • Schedule the first adult visit; consider a joint visit between pediatric and adult care teams • Monitor for the successful transition, including changes in lung function
	Access to Care	• Establish relationships with local primary care providers who are willing to care for pwCF • Ensure maintenance of insurance coverage prior to transition

Table from DeFilippo et al. 2022.

CF, cystic fibrosis; pwCF, people with cystic fibrosis; TRAQ, Transition Readiness Assessment Questionnaire.
DeFilippo EMM, et al. Clin Chest Med. 2022;43:757–71.

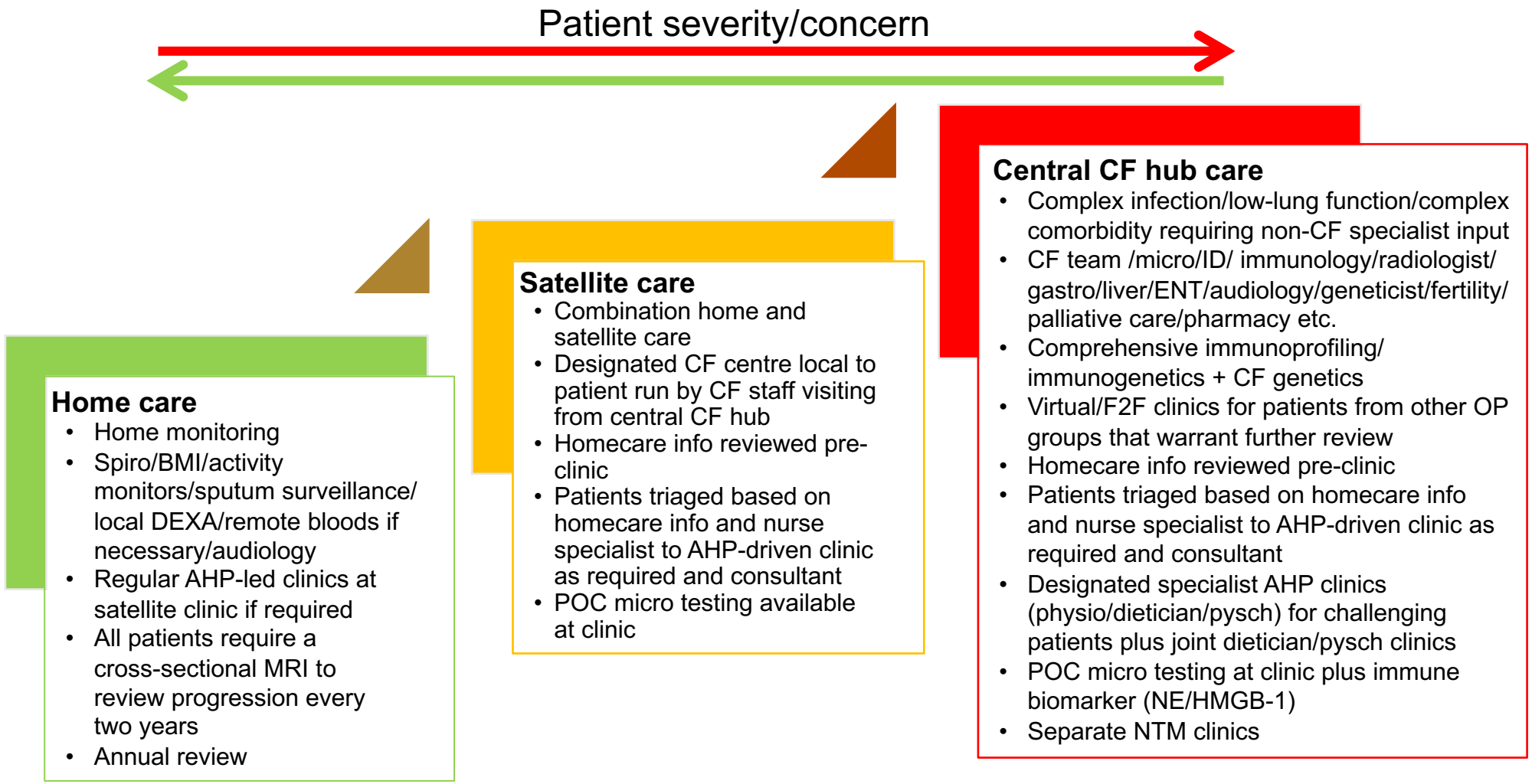
Best practices for optimising CF transition: System-focused

System-Focused	Guidelines	• Update CF care guidelines to include optimal transition strategies
	Next Steps in Research	• Define outcomes of successful transition and standardize assessment tools in CF transition • Utilize registry data (including patient-reported quality-of-life outcomes) in CF transition research • Integrate registry date with patient-reported quality-of-life outcomes • Increase QI initiatives between pediatric and adult CF care teams

Table from DeFilippo et al. 2022.

CF, cystic fibrosis; QI, quality improvement.
DeFilippo EMM, et al. Clin Chest Med. 2022;43:757–71.

Future adult CF outpatient care delivery model



AHP, allied health professional; BMI, body mass index; CF, cystic fibrosis; DEXA, dual-energy X-ray absorptiometry; ENT, ear, nose and throat; F2F, face-to-face; HMGB-1, high-mobility group box 1; ID, intradermal; MRI, magnetic resonance imaging; NE, neutrophil elastase; NTM, non-tuberculous mycobacteria; OP, outpatient; physio, physiotherapy; POC, point-of-care; psych, psychiatry.
Professional opinion of the speaker.

The future

- Large number of drugs in clinical development[1]
- Pre-clinical pipeline across the industry is strong[2]
- Challenges of how do we use them, when do we use them, what combinations will work best?[2]
- The natural history of CF will alter:[2]
  - Likely rise in comorbidities
  - Tailor drug therapies over time

This is an unprecedented time for CF research[2]

CF, cystic fibrosis.
1. Allen L, et al. Nat Commun. 2023;14:693; 2. Professional opinion of the speaker.

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