

Declaration for Jamie Duckers

I have the following financial interest or relationship/s to disclose:

- Consulting fees: Chiesi, Insmmed, Vertex
- Research contracts: Vertex, Boehringer, Enterprise, CF Trust, Insmmed
- Clinical trial steering committee: NOMABS DSMB
- Other [Board member]: Ambrose

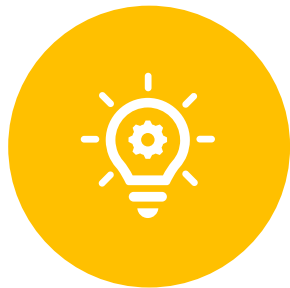
Introduction



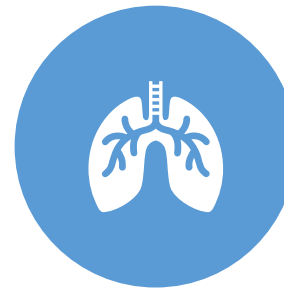
Challenge current perceptions of CF



The rise of personalized medicines in CF



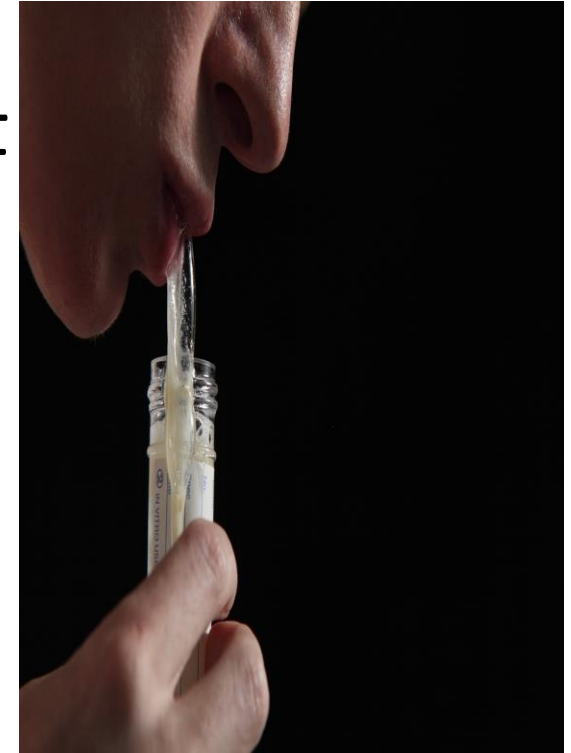
Current and future challenges/opportunities to deliver personalised care



Why should this matter to non-chest physicians?

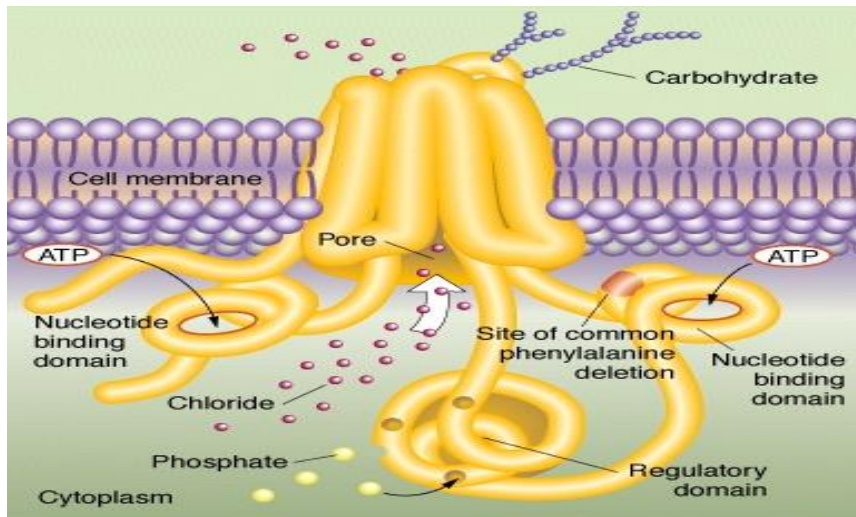


Current perceptions of CF

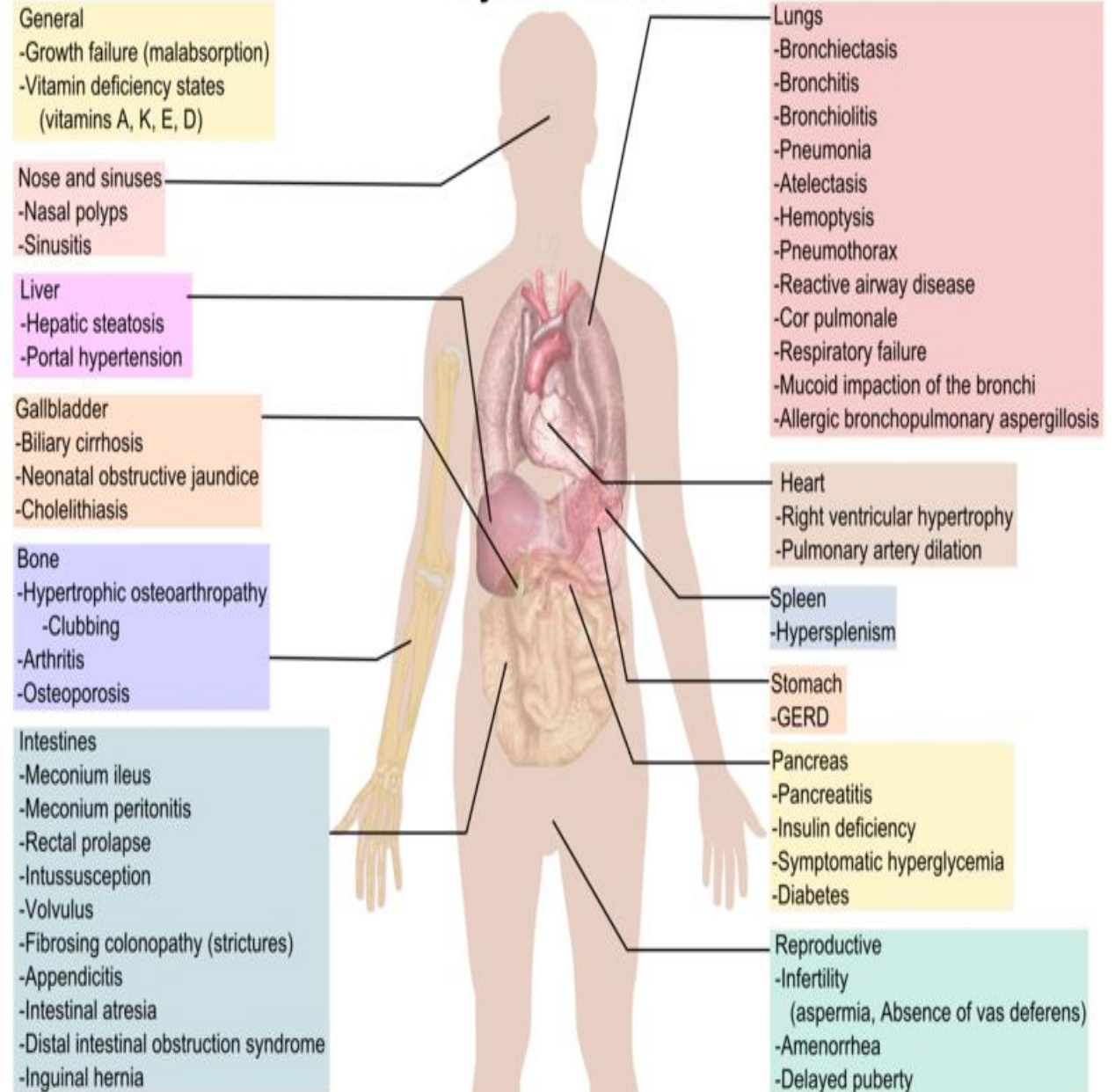


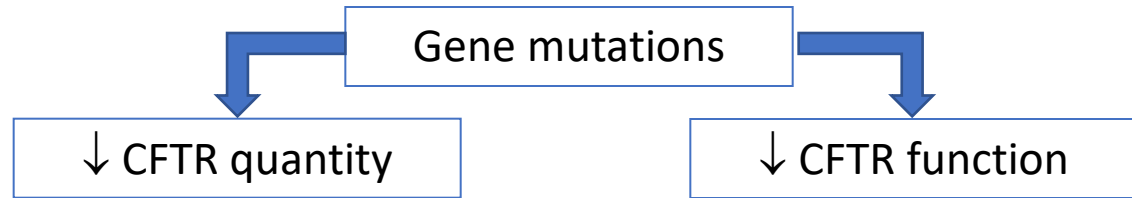
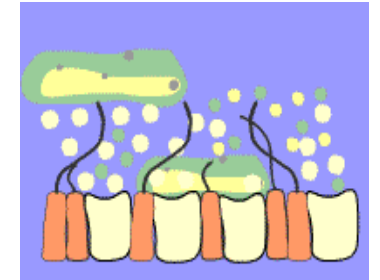
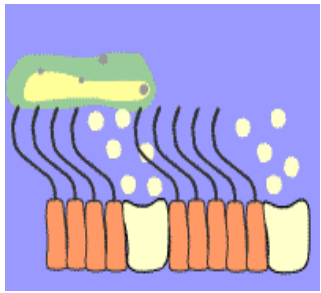
Cystic Fibrosis

- UK's most common life-threatening inherited disease
- Affects over 11,000 people in the UK
- Over two million people in the UK carry the faulty gene that causes CF
- Each week five babies are born with CF
- Median age of death in UK 33 years



Manifestations of Cystic Fibrosis





Reduced ASL

Mannitol

Impaired MCC

Bronchodilators

Obstruction

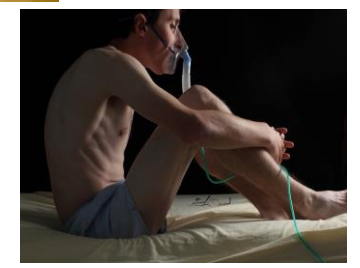
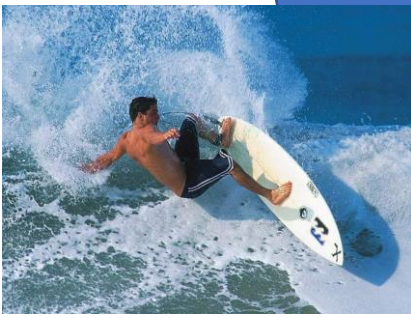
Infection

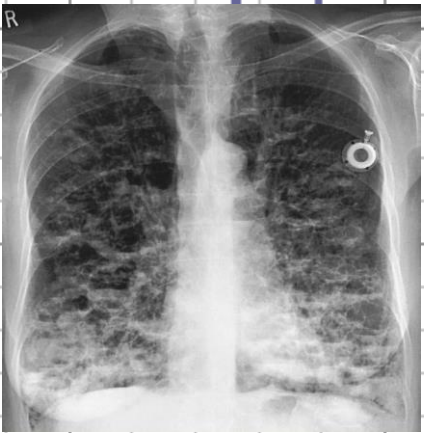
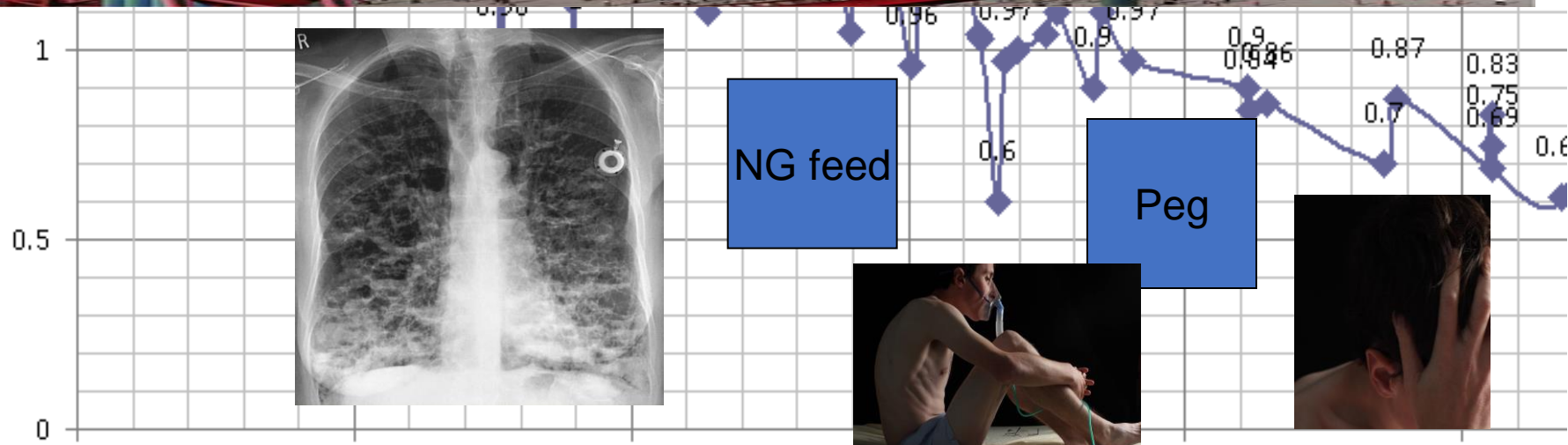
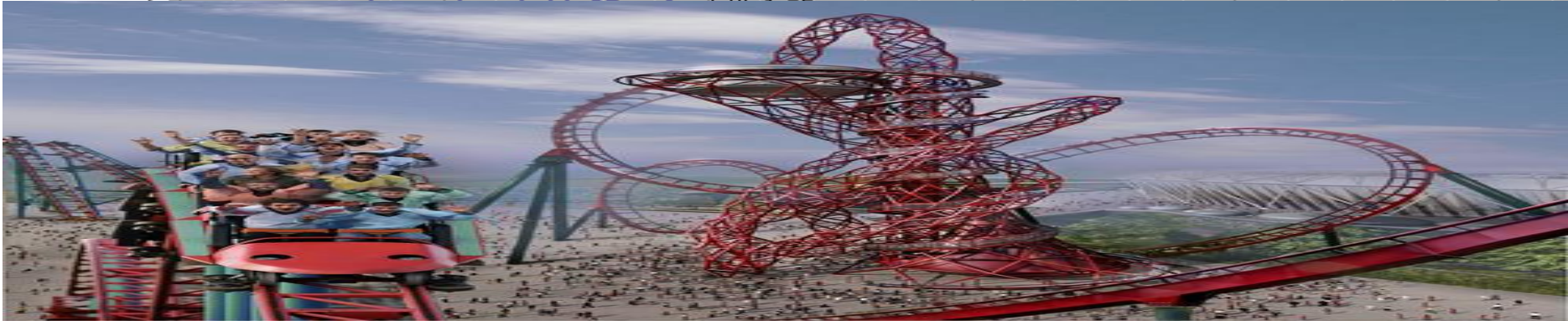
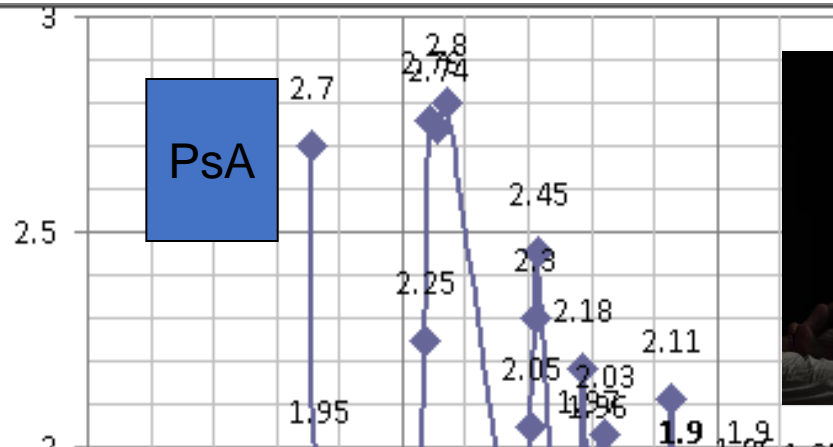
Inflammation

Progressive, irreversible lung damage

Respiratory failure

LUNG TRANSPLANT





NG feed

Peg





Gene mutations

CFTR Correctors

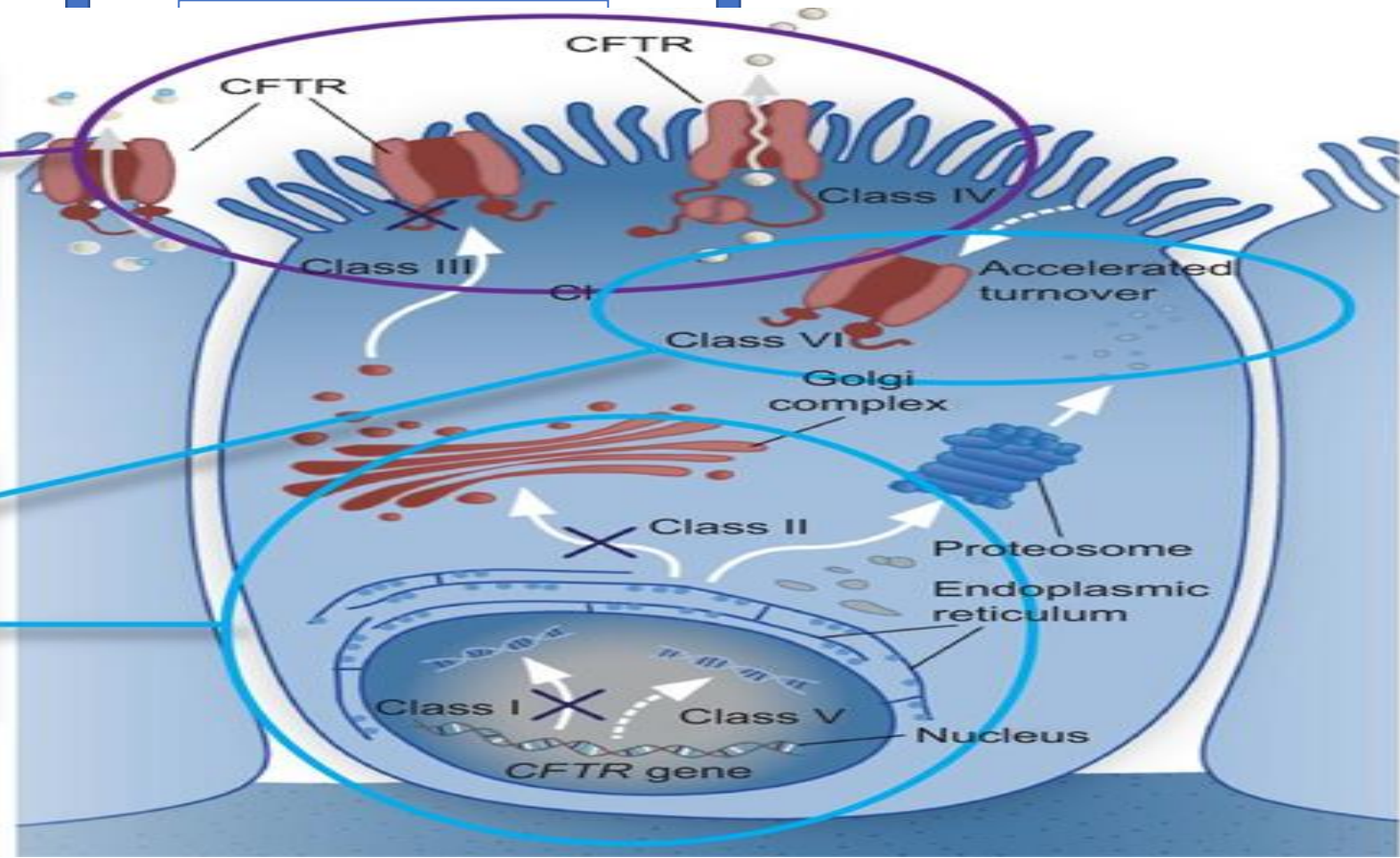
↓ CFTR quantity

↓ CFTR function

CFTR Potentiators

Mutations that reduce the **FUNCTION** of CFTR proteins at the cell surface (including gating and conductance)

Mutations that reduce the **QUANTITY** of functional CFTR proteins that reach the cell surface



Highly effective CFTR modulating therapy

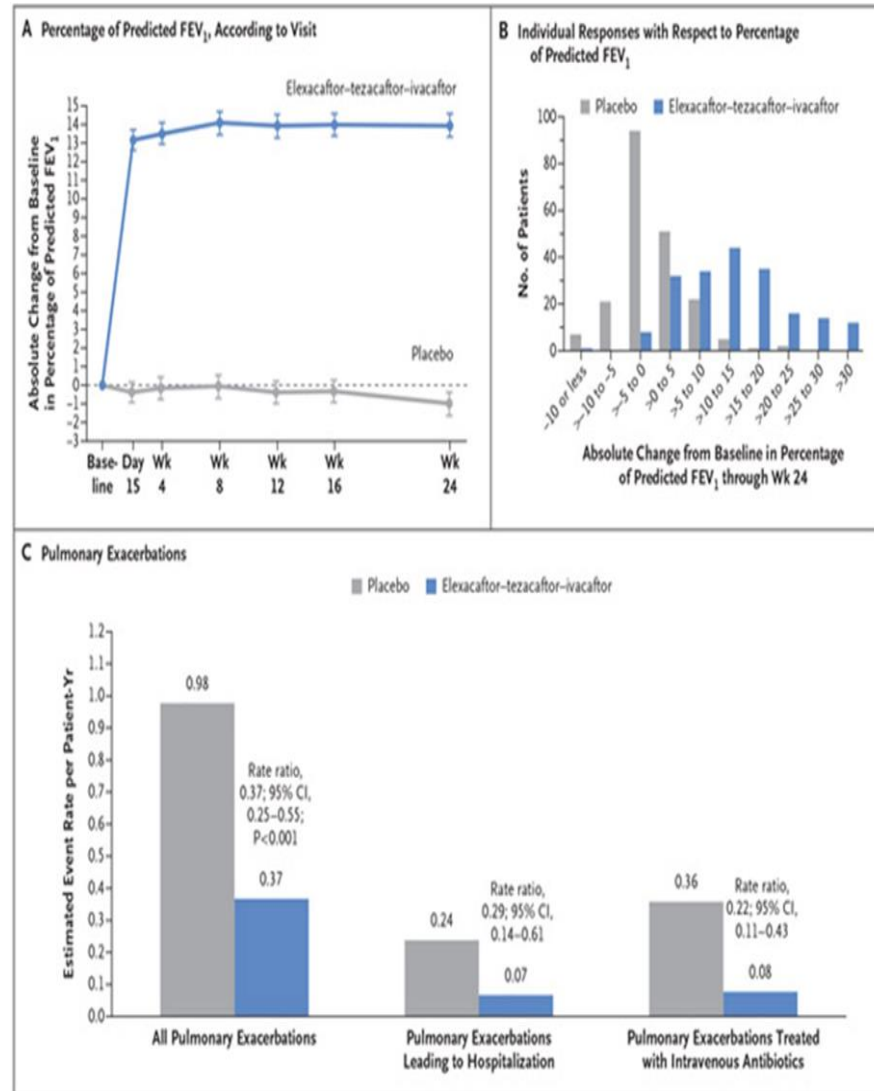


Table 1 | Effects of elexacaftor-tezacaftor-ivacaftor treatment in people with cystic fibrosis with established disease

Disease characteristic or symptom	Effect of treatment	Refs.
Pulmonary disease		
Cough and sputum	Marked decrease	12,276
Lung function	Improvement in ppFEV ₁	12,259,276
	Decrease in lung function decline	266,331
Pulmonary exacerbation	Decreased rates	12,259,276
Structural disease/bronchiectasis	Improvement in mucus plugging	267,277, 320,332
	Persistence of bronchiectasis	267,277, 320,332
Chronic bacterial infection	Persistence	108,156
Airway inflammation	Decreased but persistence	108,132
Haemoptysis	Likely decreased	NA
Pneumothorax	Likely decreased	NA
Lung transplantation	Marked decrease	262,264,265
Extrapulmonary disease		
Exocrine pancreatic insufficiency	Persistence	333
Diabetes	Persistence	334
Severe cystic fibrosis liver disease/cirrhosis	Persistence	335
Male infertility	Persistence	NA
Female infertility	Marked reduction	315,336
Metabolism	Increased body weight	12,259,276
	Risk of overweight/obesity	274,337
	Metabolic syndrome	274
Neuropsychiatric disorders	Improvement, persistence or aggravation	269,270
Risk of cancer	Effects unknown	210

NA, not available; ppFEV₁, percent predicted forced expiratory volume in 1s.

"I don't know how ill I felt
u

" My cough has
gone"

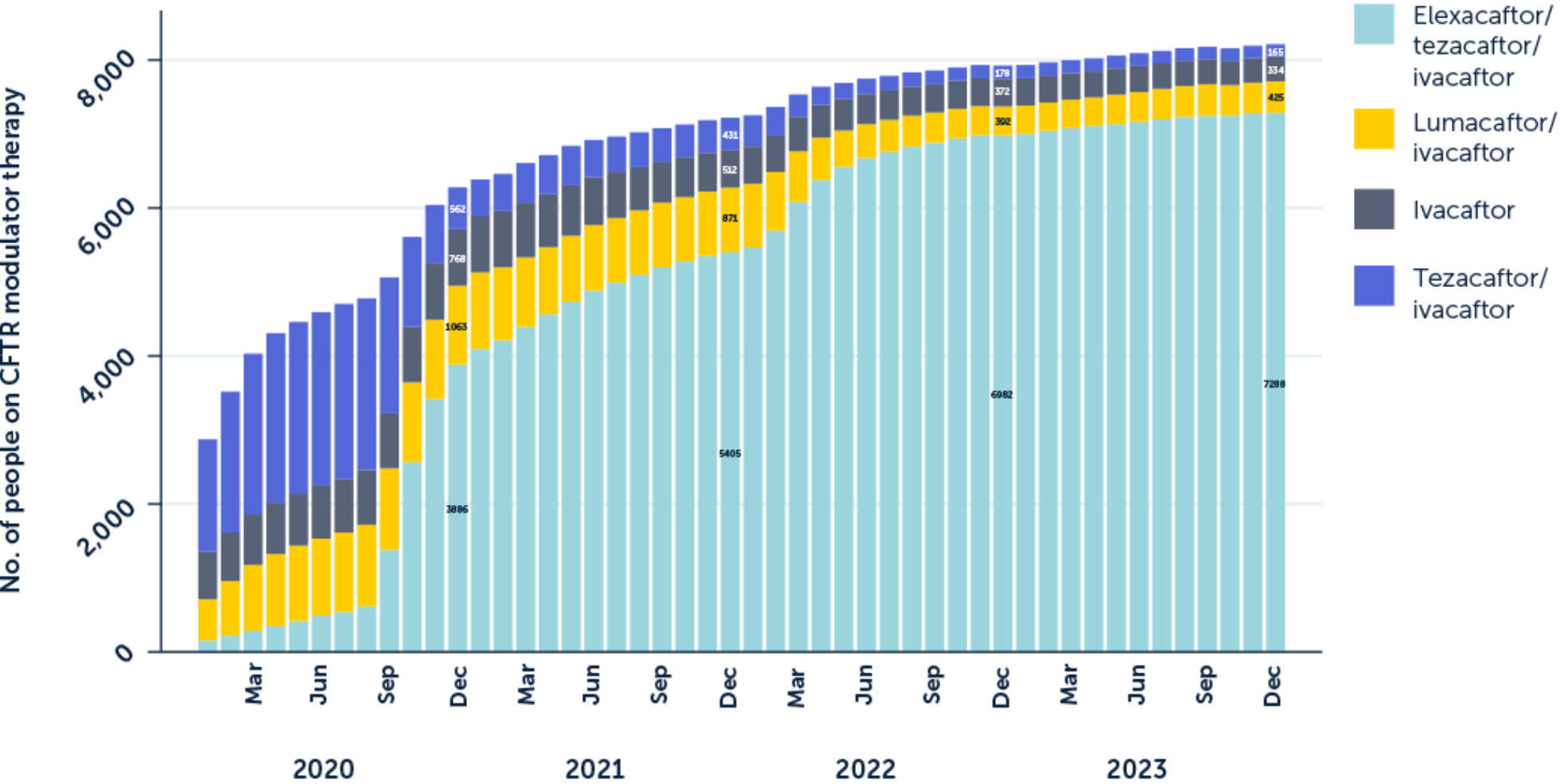
...young woman

**Miracle cystic fibrosis drug which has
been dubbed the 'holy grail' by
patients and doctors could be free on
the NHS next month**



| Luis Walker is hoping his mother will be able to buy a drug from Argentina, to help treat his cystic fibrosis

1.34 CFTR modulator use 2020–2023



Cystic Fibrosis

- one disease
- –two lives



Nucleic acid based therapies

Gene mutations

CFTR Correctors)

↓ CFTR quantity

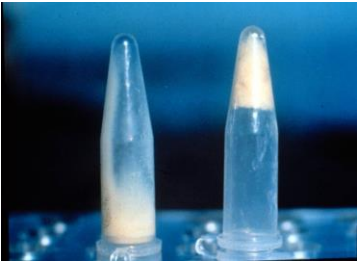
CFTR Potentiators

↓ CFTR function

Reduced ASL

Mannitol

Impaired MCC



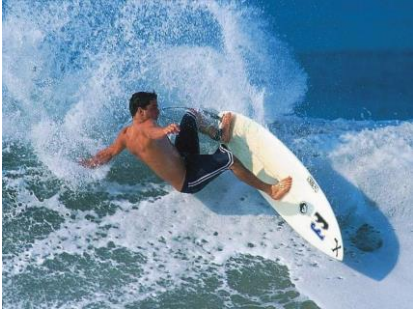
Bronchodilators

Obstruction

Infection



Inflammation



Progressive, irreversible lung damage

Respiratory failure

LUNG TRANSPLANT



CF: The journey to Improved Survival

Cystic Fibrosis Trust



64



Age (years)

40
35
30
25
20
15
10
5
0

1930

1940

1950

1960

1970

1980

1990

2000

2010

1st pathologic description

Discovery of high salt in sweat

Sweat chloride test developed

Centre care

National Registry
CF gene identified

Neonatal screening

RCTs

Pancreatic Enzymes

antipseudomonal antibiotics

antistaphylococcal antibiotics

Airway clearance

Inhaled colistin

antipseudomonal antibiotics

Azithromycin

Inhaled Tobramycin

rhDNase

HTS

TIP

AZLI

Stratified/Precision Medicine for CF

Colobreathe

Bronchitol

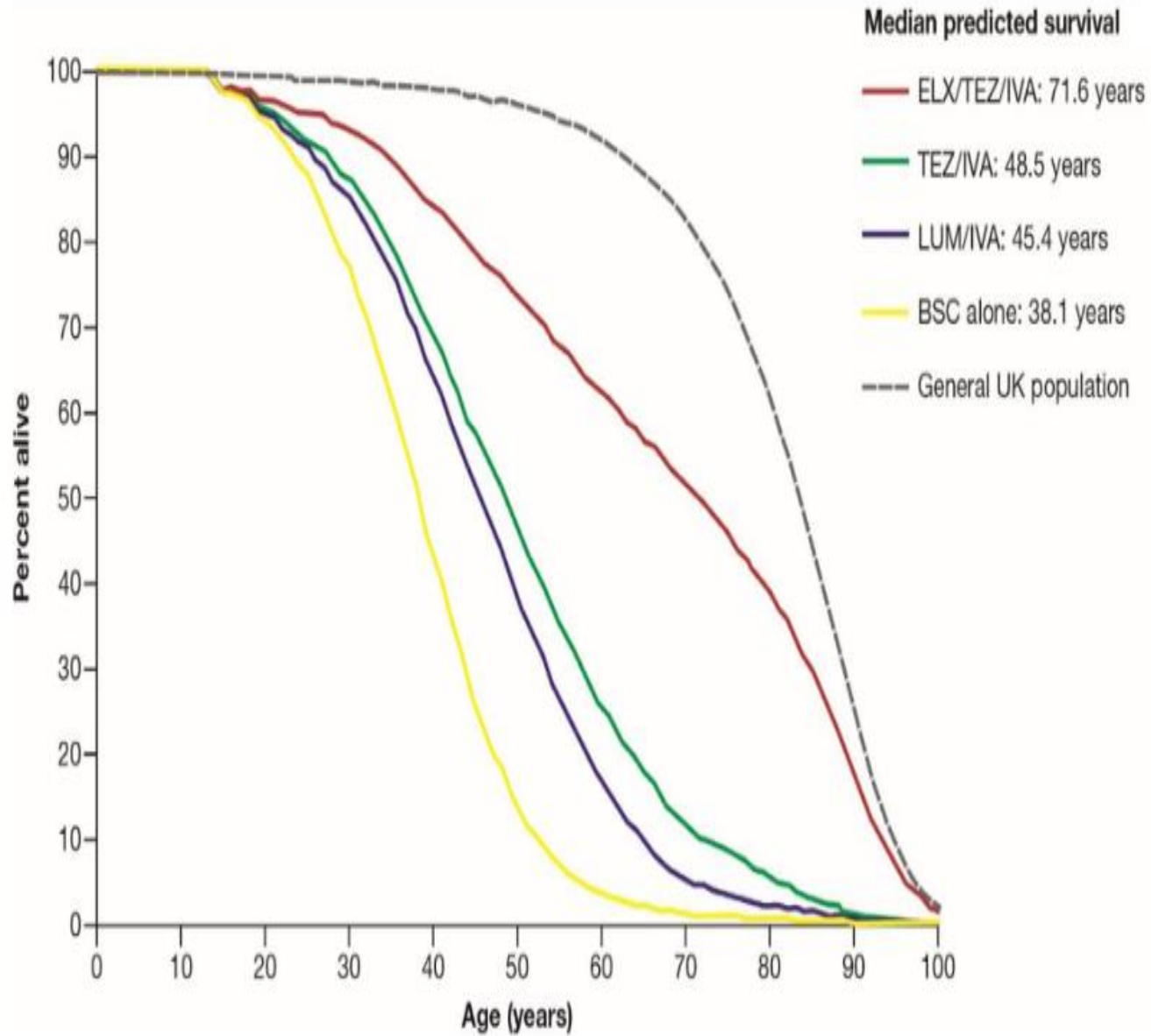
Ivacaftor

Lum/Iva

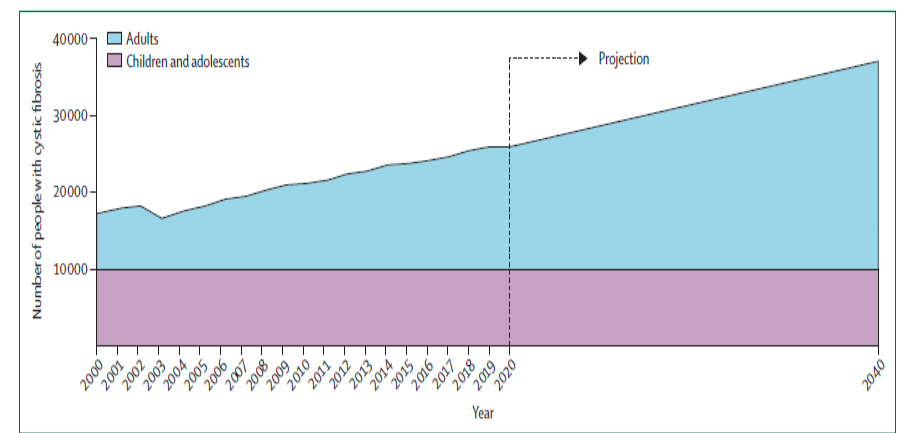
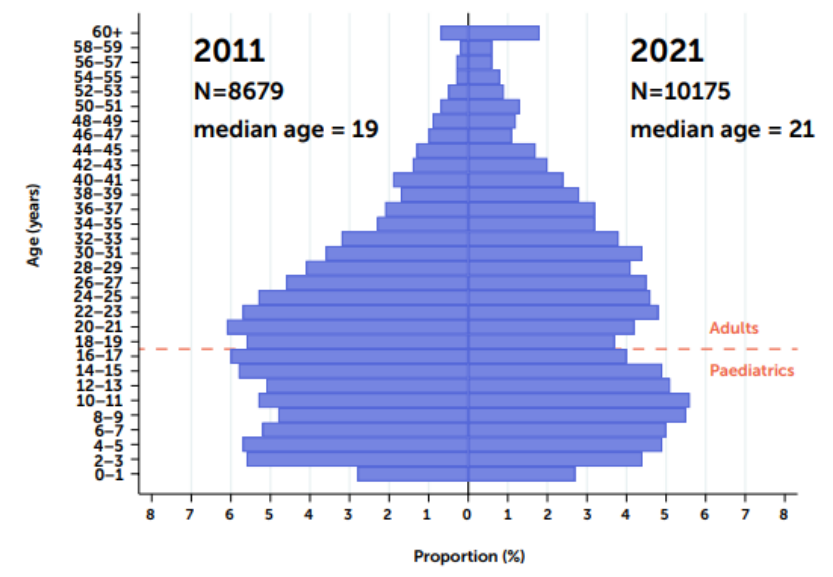
Tez/Iva

ETI

2024



1.3 Age distribution of the UK CF population in 2011 vs 2021



Bathe Me

I want you to bathe me,
cleanse me of this putridity within.
As my body soaks in that which
is meant to remove the foul poison,
I am drowning.
The weight of the tubes,
the pills, the needles, the aerosols pulls me
down like an anchor in a deep sea,
it controls who I am, my time, my life.
I should be floating in a bubble bath
of elegance, luxury, perfection.
Instead, there are no bubbles, they all burst.
It's just me and this bath of disease.

I. Stenzel

<http://www.thebreathingroom.org>



“I spent my entire
life wanting to grow
older. And now I’m
over 50 and my
body is showing
normal but
challenging signs
of ageing with CF.
Menopause, aches
and pains, bone
loss, poor
eyesight....I try to
remember these
are all the benefits
of staying alive”

David 59:



* **MEDICAL CONDITIONS.** *

ASTHMA - HYPERTENSION - SINUSITIS.
BRONCHIECTASIS - ASPERGILLOSIS (ALLERGIC).
OSTEOPOROSIS - ARTHRITIS - CHRONIC PAIN
SHALLOW BREATHING - HYPOVENTILATION.
BROKEN RIBS - CRACKED RIBS.
ACUTE PANCREASITIS - SLEEPING APNOEA.
CYSTIC FIBROSIS. FIBROMYALGIA
BLOOD GLUCOSE = INTOLERANT.
HAD SINUS REPAIRED IN MY ELBOW.
HAD STEROID INJECTIONS.
HAD POLYPUUS REMOVED. - HAD SHINGLES
HAD TONSILS " AROUND 3-4 TIMES
HAD HERNIA REPAIR.
HAD PAIN BLOCKS.
HAD NOSE OPERATION TWICE.
HAD ENDOSCOPE.
HAVE HAD M.R.S.A. SIX TIMES.
HAD ENDECSOPE AND BEOFSY.
HAD SETIMPLANT INPLANTABLE PORT SYSTEM

* **HAVE** *
C PAP MACHINE.

Stella- 89

FEV1 90%, BMI 22

ETI therapy (sweat cl 76-21)

PsA colonised

AF

Hip OA

+ve FIT test, doesn't want Ix

Memory issues

Hearing aids

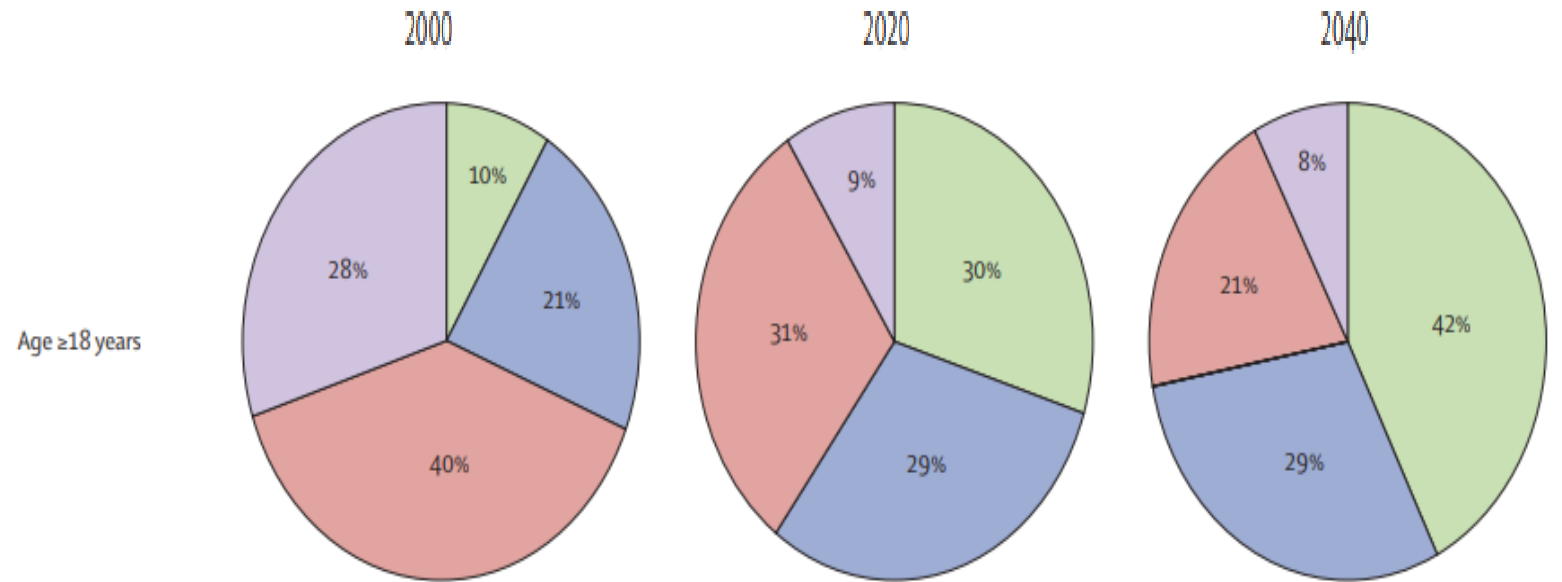
Glaucoma and macular degen

Lives alone (second floor flat)

Recurrent falls

Lung function

- FEV₁ normal (>90% predicted)
- FEV₁ mild (>70–90% predicted)
- FEV₁ moderate (>40–70% predicted)
- FEV₁ severe (<40% predicted)



Hisert et al Lancet 2023



Linda - 56

Lung transplant 2013

CFRD

PI +Recurrent DIOS

R hemicolectomy 2013 adenoca

CFLD

PSA colonisation - multiresistant

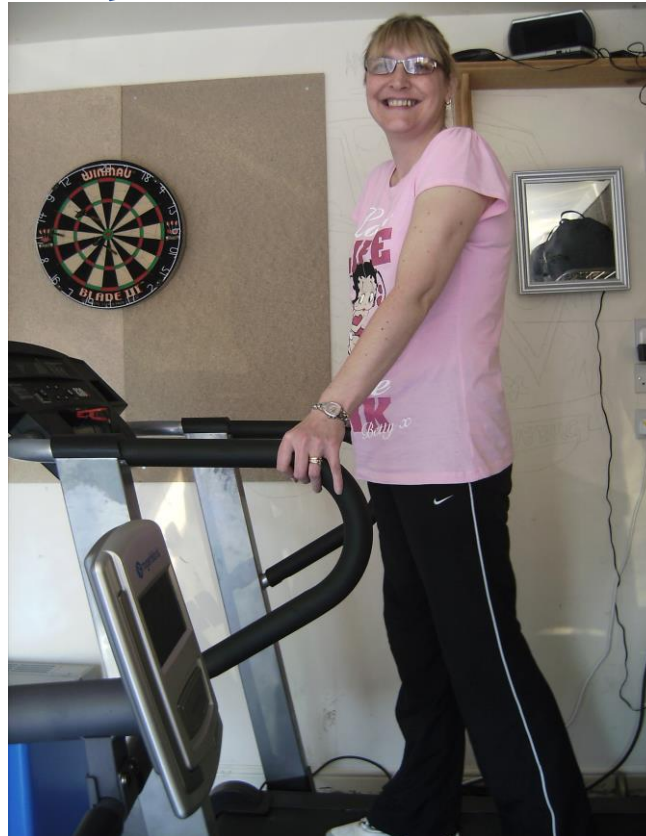
Progressive CKD –HD via fistula-
awaiting renal transplant assessment

4 children (one with disability)

1 grandchild

elderly parent

“work of being a patient includes much more than drug management and self monitoring. It also includes organising doctors’ visits and laboratory tests and explaining CF”



Compared to the general population, people with CF develop CVD, CKD, kidney stones, and cancer

MORE FREQUENTLY

at a median age of at least

20 YEARS EARLIER

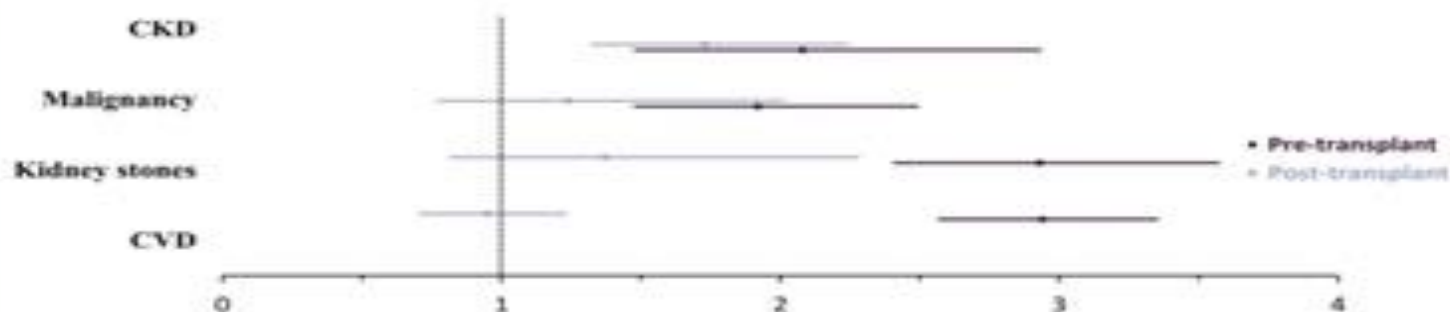
Table 1: Estimated rates per 1000 person years (95% CI) of complications in CF and non-CF patients by transplant status, adjusted for sex and age at cohort entry

	Pre-transplant (n=16,437,035)		Post-transplant (n=1,473)	
	CF (n=1,435)	Non-CF (n=16,435,600)	CF (n=208)	Non-CF (n=1,265)
CVD	24.51 (21.45-28.01)	8.35 (8.34-8.37)	115.27 (88.62-149.93)	121.92 (112.09-132.62)
Malignancy	5.82 (4.49-7.55)	3.03 (3.02-3.04)	34.98 (22.67-53.99)	28.12 (24.13-32.76)
Kidney stones	7.37 (6.05-8.98)	2.51 (2.51-2.52)	14.16 (8.60-23.34)	10.36 (8.09-13.27)
CKD	3.73 (2.65-5.24)	1.79 (1.78-1.79)	631.39 (501.39-795.48)	365.85 (338.75-395.12)

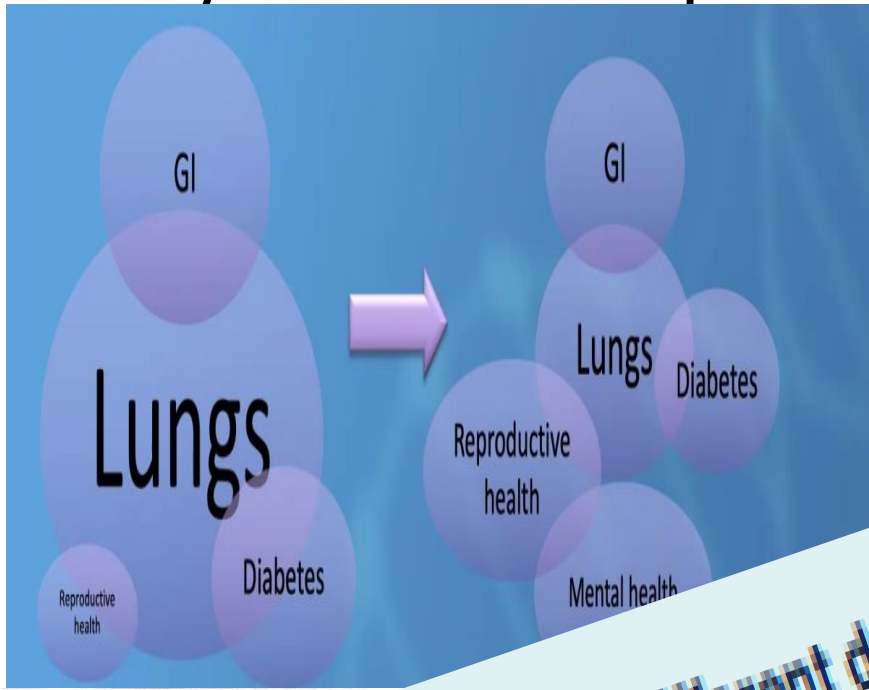
Table 2: Median age in years (95% CI) at the time of non-pulmonary complications in CF and non-CF patients by transplant status

	CVD		Malignancy		Kidney Stones		CKD	
	CF	Non-CF	CF	Non-CF	CF	Non-CF	CF	Non-CF
Pre-transplant	33 (24-47)	67 (53-77)	47 (30-56)	67 (57-76)	31 (25-39)	51 (39-62)	37 (29-52)	76 (68-83)
Post-transplant	35 (28-45)	63 (56-68)	37 (31-48)	67 (60-71)	32 (27-39)	63 (56-70)	32 (27-41)	63 (57-68)

Figure 1: Forest plot of rate ratios (95% CI) of complications in pwCF compared to non-CF patients by transplant status, adjusted for sex and age at cohort entry



Why is this important to you?



Diabetes

Immunology

Gastro/Hepatology

Microbiology

Cardiology

Older People's/ Geriatric Elderly

"Ricocheting between different departments wastes everyone's time and meant my symptoms weren't sorted sooner. It's also not a cost-efficient way of working."

Cardiology

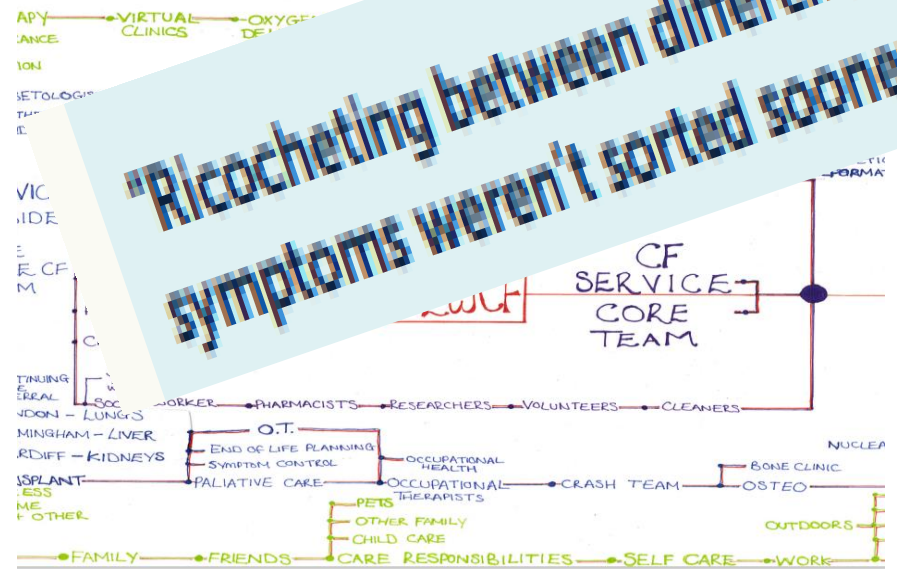
Genetics

Fertility, Obs & Gynae

Palliative care

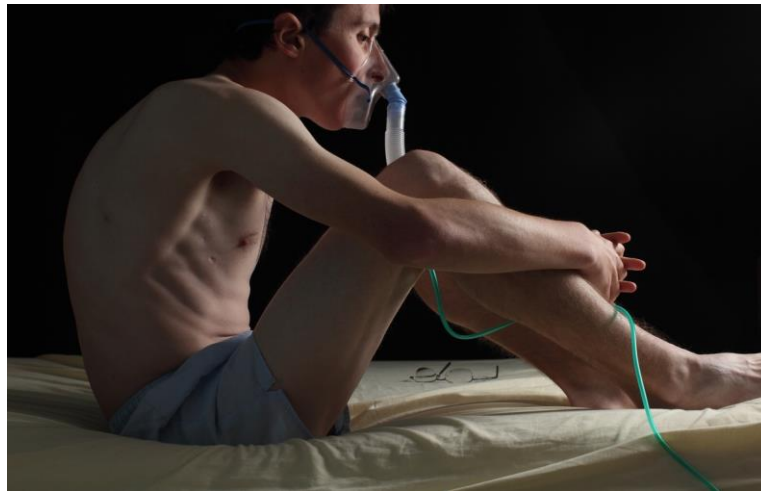
Renal

Rheumatology



#Notjustlungs

One size does not fit all

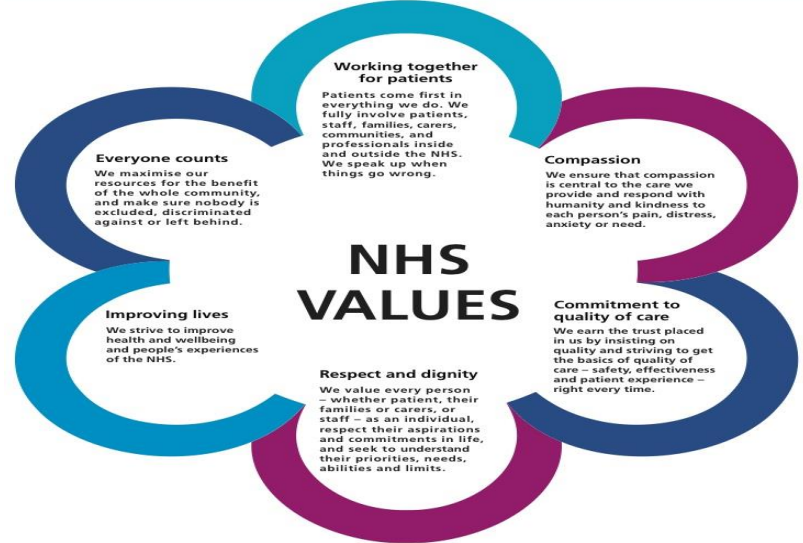


People with long term conditions spend <1% of their time in contact with HCP.

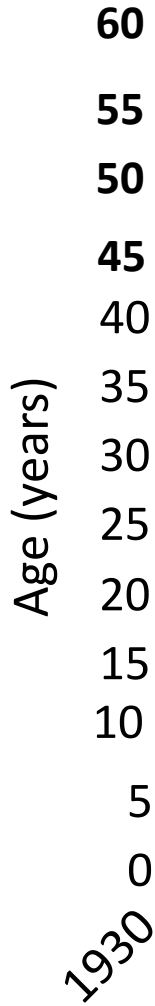


Majority of their care such as monitoring symptoms, administering medications and therapies they or their carers manage on a daily basis

“put patients at the heart of everything it does”



The doctor will see you now...



‘what matters to someone’ is not just ‘what’s the matter with someone’.



‘shared responsibility for health’



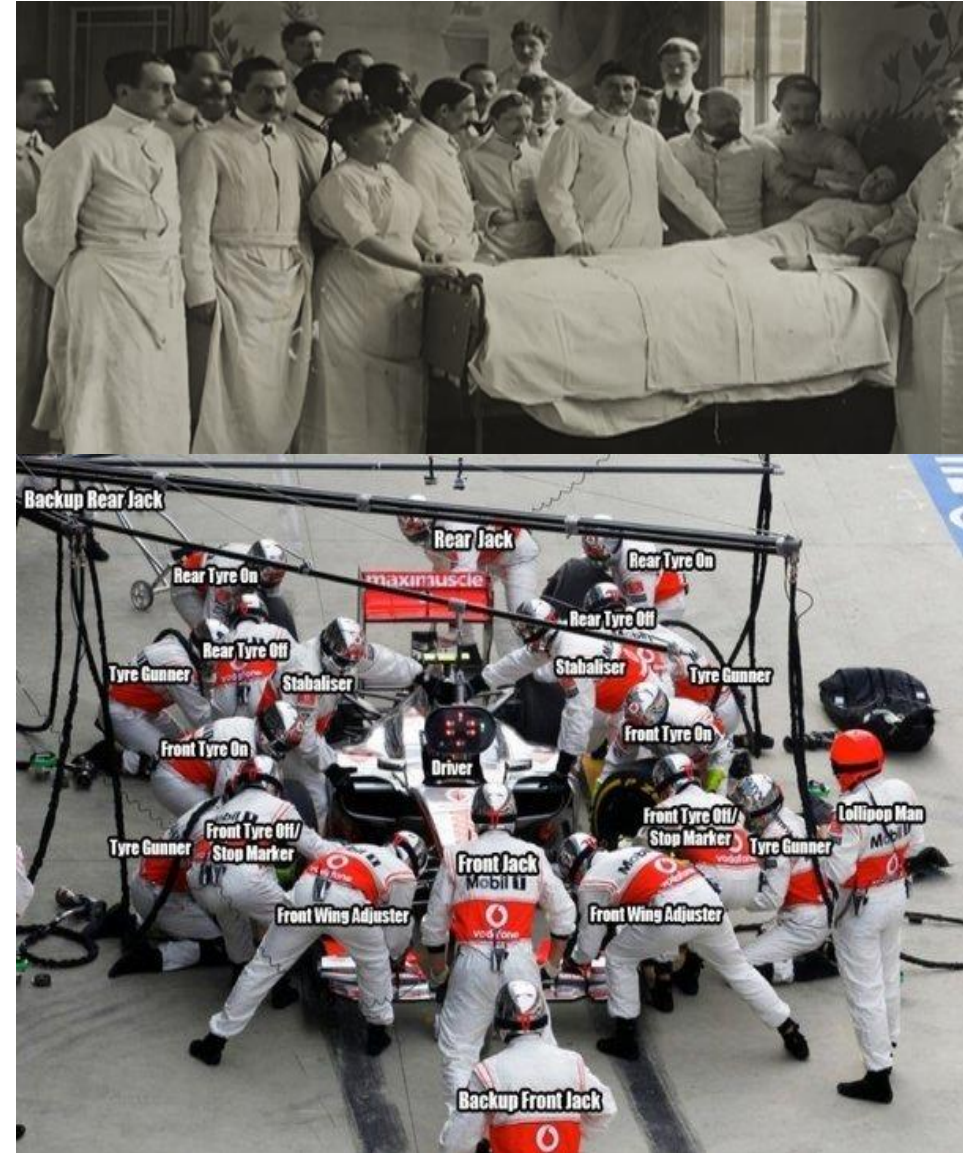
The NHS Long Term Plan



Person centred care: a philosophy

People are equal partners in planning, developing and assessing care to make sure it is responsive to peoples individual abilities, preferences, lifestyles and goals.

“No health care to or for people, but with...”



Benefits of Person Centred care

- ✓ Improve clinical outcomes¹
- ✓ Less use of emergency services²
- ✓ More likely to stick to treatment plan³ and take therapy correctly⁴
- ✓ More satisfied with care⁵
- ✓ More likely to choose treatments based on their values than those of their clinicians⁶
- ✓ Tend to choose less invasive and costly treatments⁷
- ✓ More likely to engage in positive health behaviours⁸
- ✓ Patient engagement increases health care staff performance and morale⁹



1. De Silva D. *Helping people help themselves*. London: The Health Foundation, May 2011, p6. www.health.org.uk/publications/evidence-helping-people-help-themselves

2. De Silva D. *Helping people help themselves*. London: The Health Foundation, May 2011. www.health.org.uk/publications/evidence-helping-people-help-themselves

3. De Silva D. *Helping people share decision making*. London: The Health Foundation, July 2012. www.health.org.uk/publications/helping-people-share-decision-making

4. National Institute of Health and Care Excellence (NICE). *Medicines adherence*:

5. De Silva D. *Helping people share decision making*. London: The Health Foundation, July 2012

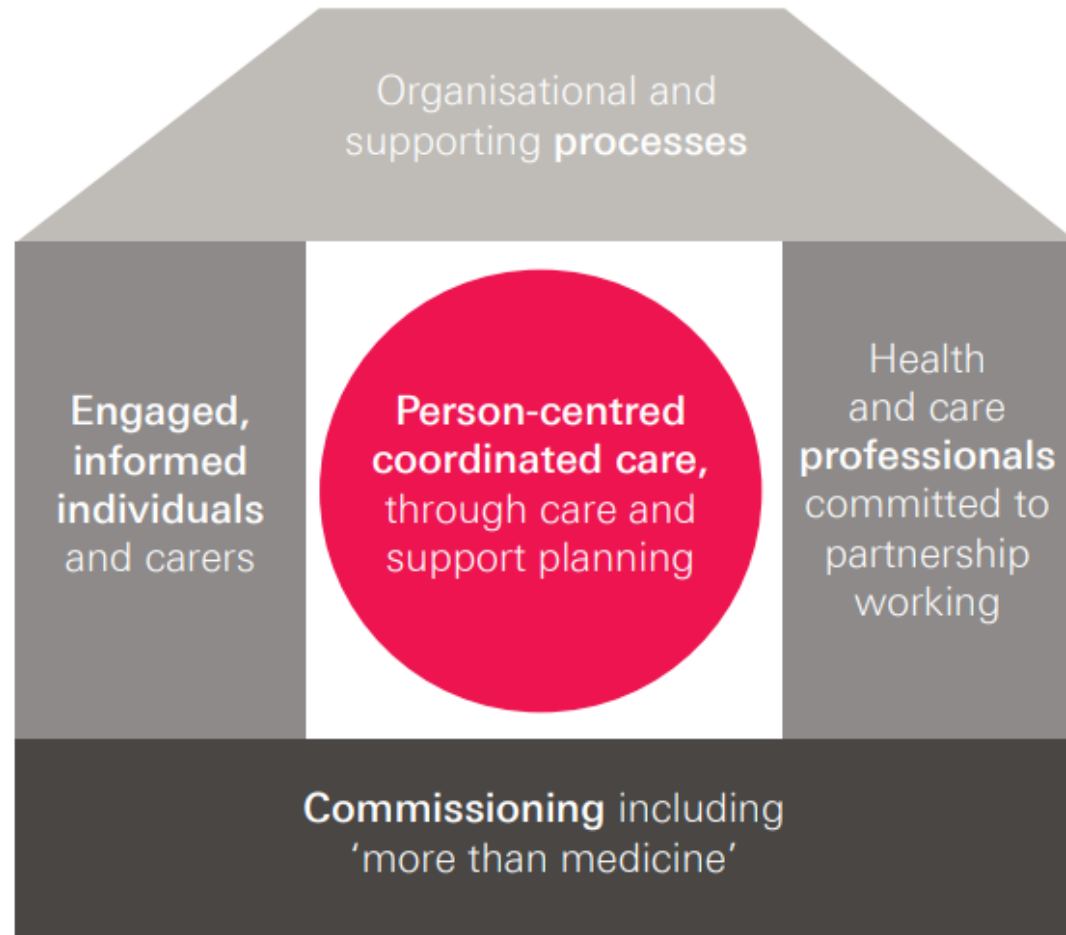
6. O'Connor AM, et al. *Modifying unwarranted variations in health care: shared decision making using patient decision aids*. Health Affairs, web exclusive, 7 October 2004.

7. De Silva D. *Helping people share decision making*, The Health Foundation, June 2012, p.12

8. Hibbard J, Gilbert H. *Supporting people to manage their health: An introduction to patient activation*. The King's Fund, 2014.

9. The King's Fund. *Leadership and engagement for improvement in the NHS: Together we can*. London: The King's Fund, 2012.

Figure 2: The House of Care, Coalition for Collaborative Care (C4CC)⁸⁾

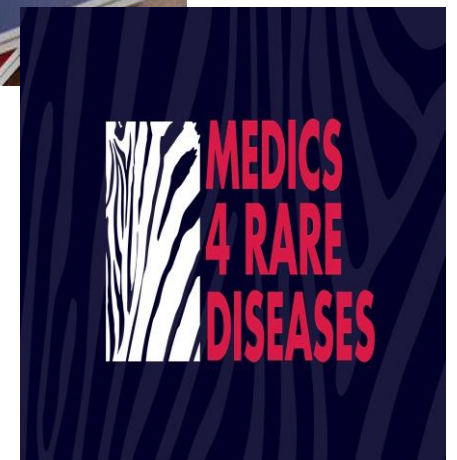


‘Shift from “what is the matter with you?’ to ‘what matters to you?’ shared responsibility across a health care system

Education Programmes for Patients



Helping you to manage a long-term health condition



Shared Decision making

“...an approach where clinicians and patients **share the best available evidence** when faced with the task of making decisions, and where **patients are supported to consider options**, to achieve **informed preferences**.”

Pwcf:

- Become more active and empowered in their own healthcare
- Have better relationships with their health care professionals
- Feel more satisfied with their choices



ALL WALES ADULT CF CENTRE

380 adult patients

16 bed inpatient unit

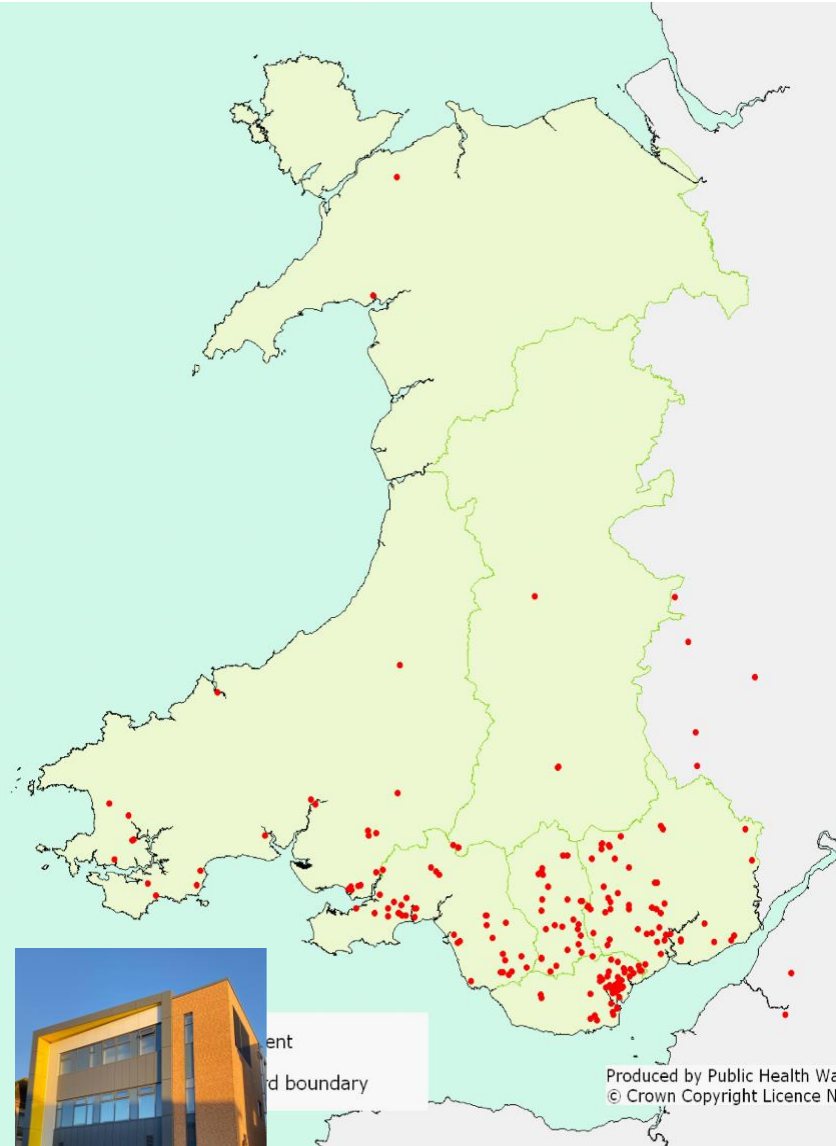
Clinics everyday

Virtual clinics

Satellite clinics

Joint speciality
+ Transition clinics

ON CALL SERVICE
CONSULTANT CONNECT



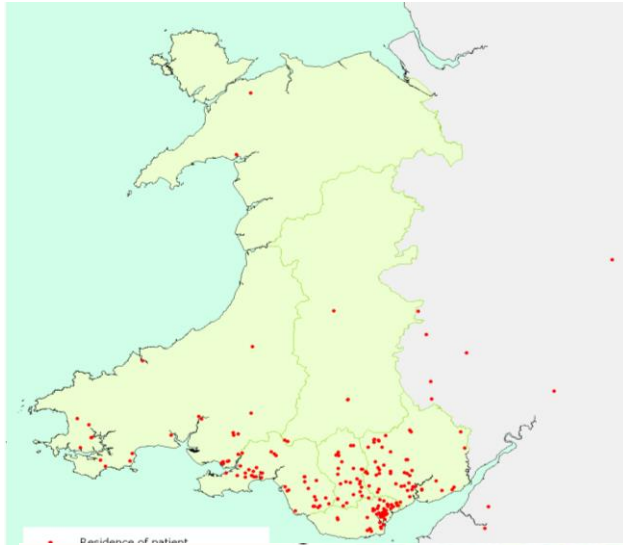
- 3.7 WTE Consultants
- 1.8 WTE Speciality doctors
- 6.0 WTE CNS
- 5.5 WTE Physiotherapists
- 2.5 WTE dietitians
- 2.5 WTE psychologist
- 1.0 WTE youth worker
- 0.8 WTE social worker
- 2.0 WTE pharmacist
- 2.7WTE Research nurse
- 1.0 WTE Research fellow
- 1.0 WTE service manager



Bwrdd Iechyd Prifysgol
Caerdydd a'r Fro
Cardiff and Vale
University Health Board



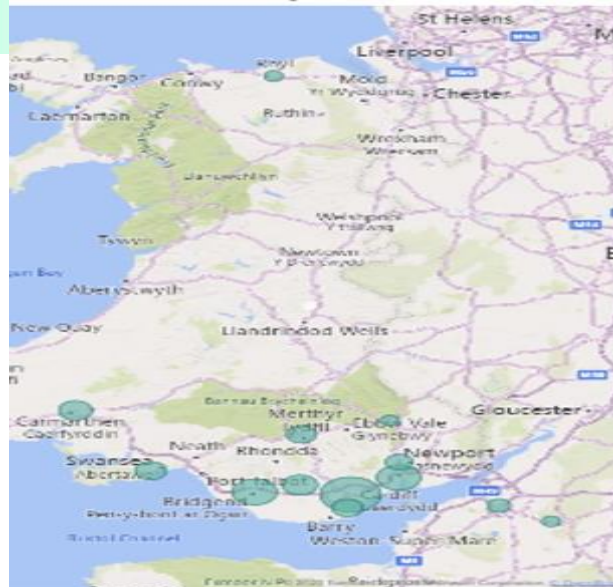
Themes : delivering care closer to home



83/380 patients live 1hr+ away (driving distance)

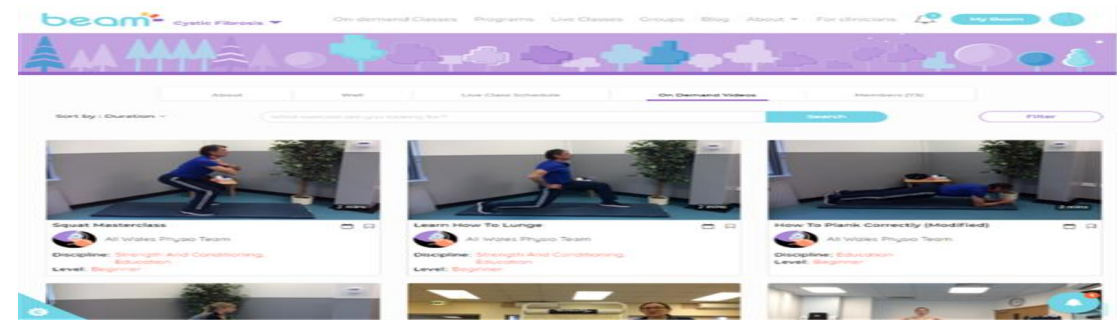
Median 21.8 miles (Range 1.2-161 miles e/w)

Actual time



Median 41 minutes each way

(Range 3-228 mins e/w)



ACE-CF: Artificial Intelligence to Control Exacerbations in adult CF

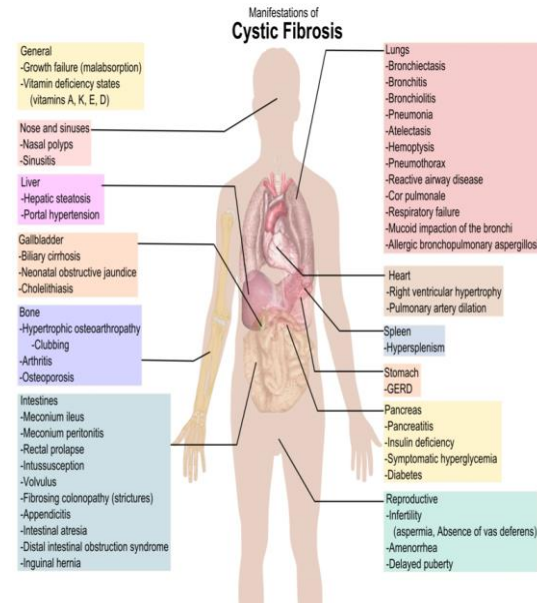
Led by: Andres Floto, Charles Haworth, and Lucy Gale, Royal Papworth Hospital, Cambridge; John Winn and Damian Sutcliffe, Microsoft Research Institute, Cambridge and Kirsty Hill, Magic Bullet (Social Enterprise company)

Additional adult CF centres: Jamie Duckers, Cardiff (All Wales), Gordon MacGregor, Glasgow (SW Scotland), Robert Gray, Edinburgh (South East Scotland), Damian Downey, Belfast (All NI) and Caroline Elston (KCL, London)



Themes: Embracing novel advances/ applying to clinical practice

- Frailty _Siobhan—ageing CF population
- Hepatology- Andrew
- Genetics- Ian --- novel therapies
- Renal and renal transplants—Sian
- Palliative care –Charlie
- Cardiology- Charlotte
- CF on the medical take—instead of Parkinsons— consultant connect— cf on call



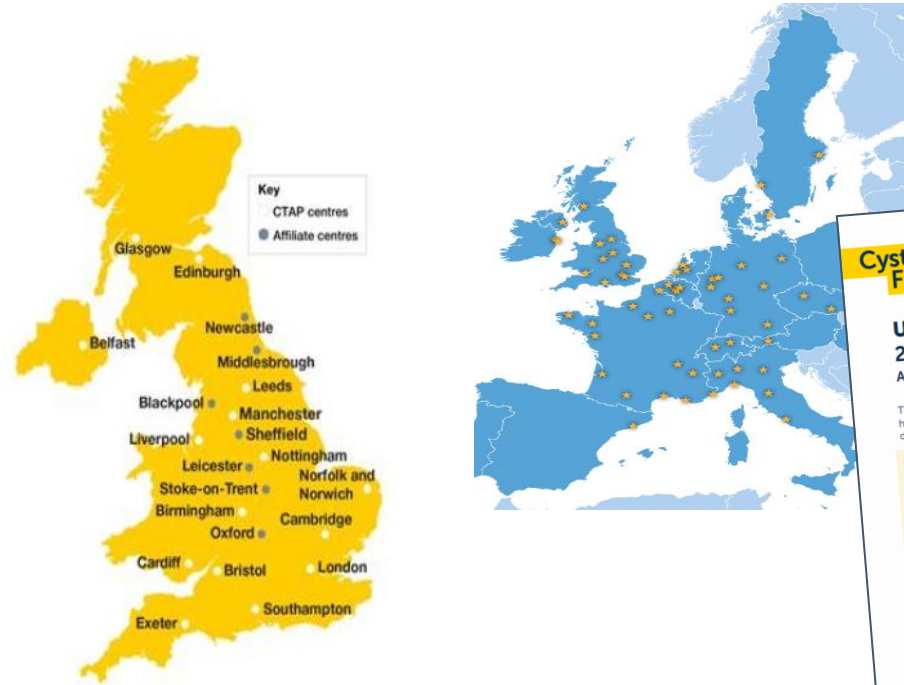
Themes: Medicine is so much bigger- Wales and beyond



Cystic Fibrosis Trust

UK CF Clinical Trials Accelerator Platform (CTAP)
Early phase trial programme

Uniting for a life unlimited



ECFS PATIENT REGISTRY

Cystic Fibrosis Trust

UK Cystic Fibrosis Registry 2021 Annual Data Report
At a glance

This 'at a glance' version of the UK Cystic Fibrosis Registry Annual Data Report 2021 highlights some of the key information about people with cystic fibrosis (CF) in the UK during 2021. For more detail, see the full report at cysticfibrosis.org.uk/registry

Number of people with CF 10,908 registered patients*

10,175 annual reviews recorded

Annual reviews in UK by devolved nation*

Northern Ireland	401
Scotland	777
England	8,587
Wales	410

* People who have had at least one annual review recorded in the past three years

* based on location of the CF centre where patient receive care

In December 2021 a total of 7,384 people with CF were taking a CFTR modulator:

ivacaftor	606
Lumacaftor/ivacaftor	942
Tezacaftor/ivacaftor	515
Elexacaftor/Tezacaftor/ivacaftor	5,321

Mean FEV₁ % predicted in 2020 and 2021

Year	Under 18 years	18 years and older
2020	88.2%	66.0%
2021	92.0%	72.4%

Intravenous antibiotics (IV) in 2020 and 2021

Year	at least one course of IV antibiotics
2020	39.2%
2021	24.3%

2020: 23.6% at hospital, 15.7% at home
2021: 18.7% at hospital, 15.6% at home

CARDIFF AND VALE UNIVERSITY HEALTH BOARD

CONFIDENTIAL
NOT TO BE REMOVED

AWACFC RESEARCH PARTICIPATION RECORD

STUDY	TAKING PART	DECLINED/NOT ELIGIBLE	NEEDS ASKING	OUTCOME
BIOBANK	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	INTERESTED DECLINED RECRUITED
PROJECT BREATHE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	INTERESTED DECLINED RECRUITED
CF STORM	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	INTERESTED DECLINED RECRUITED
MEMORY/MRI	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	INTERESTED DECLINED RECRUITED

V1 14FEB2022



Lab James Lind Alliance

Cystic Fibrosis Trust

University of Nottingham
UK | CHINA | MALAYSIA

Your top 10 refreshed CF research priorities

- 21st Century CF care is exciting and fast paced
- Therapeutic options are widening
- People with CF are coming to a clinic near you!!
- Making medicine precise is not the same as person centred care

