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CYSTIC FIBROSIS CARE
A UK PERSPECTIVE

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BLACK COUNTRY ADULT CF SERVICE

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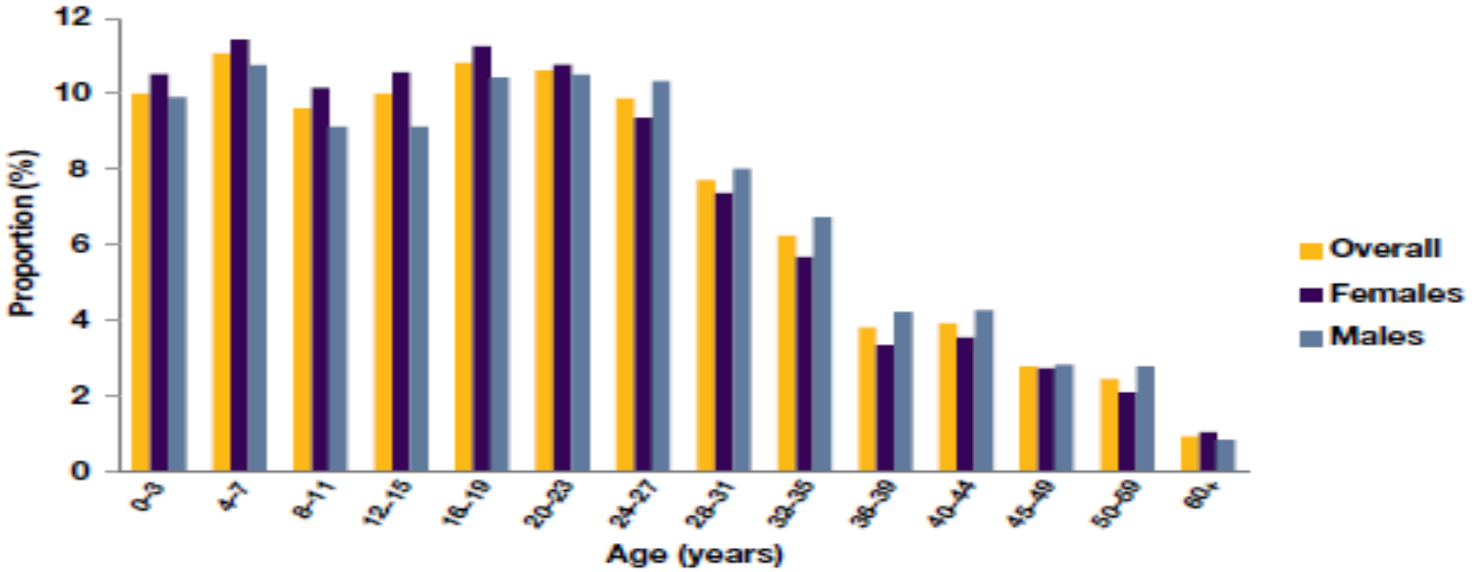
	2010	2011	2012	2013	2014
CF patients registered[1] Excluding diagnoses that year	9385	9749	10078 9804	10338 10076	10583 10356
CF patients with "complete" data [2]; n(%)	7937 (85%)	8679 (89%)	8794 (87%)	9052 (88%)	9432 (89%)
Age in years; median[3]	17	18	18	18	19
All newly diagnosed patients[4] (newborn screening and other)	301	261	285	301	227
Number of patients born each year identified by newborn screening[4]	241	203	213	177	130
Age at diagnosis in months; median[3]	3	3	3	3	2
Adults aged 16 yrs and over; %[3]	55.5	56.8	57.6	57.6	59.3
Males; %[3]	53.1	53.2	52.9	52.9	53
Genotyped; %[3]	95.2	95.6	96.2	97.2	97.7
Median predicted survival in years (95% Confidence interval)[5]	41.4 (36.8, 46.7)	41.5 (35.7, 46.0)	43.5 (37.8, 49.9)	36.6 (34.4, 41.6)	40.1 (34.6, 46.7)
Total deaths reported (%)[5]	103 (1.1%)	118 (1.2%)	106 (1.1%)	146 (1.4%)	137 (1.5%)
Age at death in years; median (95% CI)[3]	29	26	28 (25, 29)	29 (27, 31)	28 (25.5, 32)

THE UK CF POPULATION

1.2 Age distribution by gender

n=9432

The following chart shows the mix of ages and genders in the cystic fibrosis population in the UK.



Mutations				
Nucleotide	**Protein**	**Legacy name**	**N**	**(%)**
c.1521_1523delCTT	p.Phe508del	^F508	8,327	90.38
other	other	Other	1528	16.59
not identified	not identified	Not Identified	555	6.02
c.1652G>A	p.Gly551Asp	G551D	525	5.70
c.350G>A	p.Arg117His	R117H	411	4.46
c.1624G>T	p.Gly542X	G542X	325	3.55
c.489+1G>T	no protein name	621+1G->T	207	2.25
c.3909C>G	p.Asn1303Lys	N1303K	125	1.36
c.1585-1G>A	no protein name	1717-1G->A	118	1.28
c.1766+1G>A	no protein name	1898+1G->A	110	1.19
c.1519_1521delATC	p.Ile507del	^I507	91	0.93
c.3528delC	p.Lys1177SerfsX15	3659delC	87	0.94
c.1679G>C	p.Arg560Thr	R560T	83	0.90
c.1657C>T	p.Arg553X	R553X	74	0.80
c.3717+12191C>T	no protein name	3849+10kbC->T	74	0.80
c.254G>A	p.Gly85Glu	G85E	70	0.76
c.1477C>T	p.Gln493X	Q493X	70	0.76
c.3454G>C	p.Asp1152His	D1152H	67	0.73
c.178G>T	p.Glu60X	E60X	61	0.66
c.3846G>A	p.Trp1282X	W1282X	50	0.54
c.2052delA	p.Lys684AsnfsX38	2184delA	34	0.37
c.2657+5G>A	no protein name	2789+5G->A	33	0.36
c.1040G>C	p.Arg347Pro	R347P	30	0.33
c.1646G>A	p.Ser549Asn	S549N	29	0.31
c.1558G>T	p.Val520Phe	V520F	28	0.30
c.3484C>T	p.Arg1162X	R1162X	26	0.28
c.1364C>A	p.Ala455Glu	A455E	25	0.27
c.1000C>T	p.Arg334Trp	R334W	16	0.17
c.1040G>A	p.Arg347His	R347H	16	0.17

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Paediatric CF Centres

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ADULT CF CENTRES

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NEW DEVELOPMENTS

- Research and innovation
- UK CF Society
- NICE guideline development
- National lung allocation campaign

RESEARCH & INNOVATION

UK CYSTIC FIBROSIS GENE THERAPY CONSORTIUM

- 136 Patients (aged 12 and above) assigned to either 5ml of nebulised pGM169/GL67A (gene therapy) or saline (placebo) at monthly intervals over 1 year.
- Patients who received therapy had a significant, if modest benefit in lung function compared with those receiving a placebo. After a year of treatment, in the 62 patients who received the gene therapy, FEV1 was 3.7% greater compared to placebo.
- The trial is the first ever to show that repeated doses of a gene therapy can have a meaningful effect on the disease and change the lung function of patients.

- **Pseudomonal infection in CF: better detection, better understanding, better treatment.**
  (Imperial College London, University of Amsterdam and Catholic University of the Sacred Heart, Rome)

- **INOVCF: Innovative non-CFTR Approaches for Cystic Fibrosis Therapy.**
  (Newcastle University, University of Lisbon, University of Regensburg, University of North Carolina and University of Heidelberg)

- **Tackling *Mycobacterium abscessus* infection in Cystic Fibrosis**
  (University of Cambridge, Sanger Institute and Colorado State University)

- **Personalised engineered cell therapies for cystic fibrosis.**
  (University College London, St George's University of London, University College London, University College Cork)

Harnessing data to improve lives (Imperial College London, University of Liverpool, University of Nottingham, London School of Hygiene and Tropical Medicine, The Hospital for Sick Children, Toronto and Norwich Medical School)

Investigating the F508del-CFTR protein (University of Bristol, Université de Poitiers, Utrecht University, The University of Manchester and University College London)

Physical activity, exercise, sport and recreation promotion for adolescents with cystic fibrosis (University of Exeter, University College London, Institute of Child Health, La Trobe University, The Hospital for Sick Children (Toronto, Canada)Swansea University)

BRITISH CF SOCIETY

- Still in its infancy
- Created to represent the clinical community involved in CF Care (Rudge Report)
- Overwhelmingly positive response from clinicians
- Aims to provide a unified clinical voice in the UK

NICE National Institute for Health and Care Excellence

- In 2015 the DOH requested that NICE "prepare a clinical guideline on the diagnosis and management of cystic fibrosis"
- Committee composed of clinicians from across the UK as well as patient and carer representatives.
- Aims to provide evidence-based guidelines
- Due to go out to public consultation at the end of 2016, and for publication in 2017.

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LUNG TRANPLANTATION

	2010	2011	2012	2013	2014
Number of patients that year with annual review data evaluated for transplants	169	204	225	220	247
Number accepted on the transplant list	82	121	120	136	146
Number receiving transplants (<16)	3	3	3	3	5
Types of transplants received:					
Bilateral lung	2	3	2	2	2
Heart and lung	0	0	0	0	0
Liver	1	0	1	1	3
Other	0	0	0	0	0
Number receiving transplants (≥16)	26	48*	52**	54*	67**
Types of transplants received:					
Bilateral lung	24	40	43	48	59
Heart and lung	1	4	1	0	0
Liver	0	2	6	3	5
Other	1	3	4	4	5

“Hope for more” Campaign

- 412 days is the average wait for adults on the lung transplant list
- 2 years is the life expectancy for an adult on the transplant list who doesn’t receive a transplant
- 1 in 3 People with cystic fibrosis on the lung transplant waiting list will die before receiving a transplant

“Hope for more” Campaign

- Introducing a national lung allocation system.
- Increasing the pool of available donor lungs by recognising extended criteria organs.
- Giving patients the information needed to make informed decisions about accepting such organs.
- Delivering a model of care that empowers the patient population.

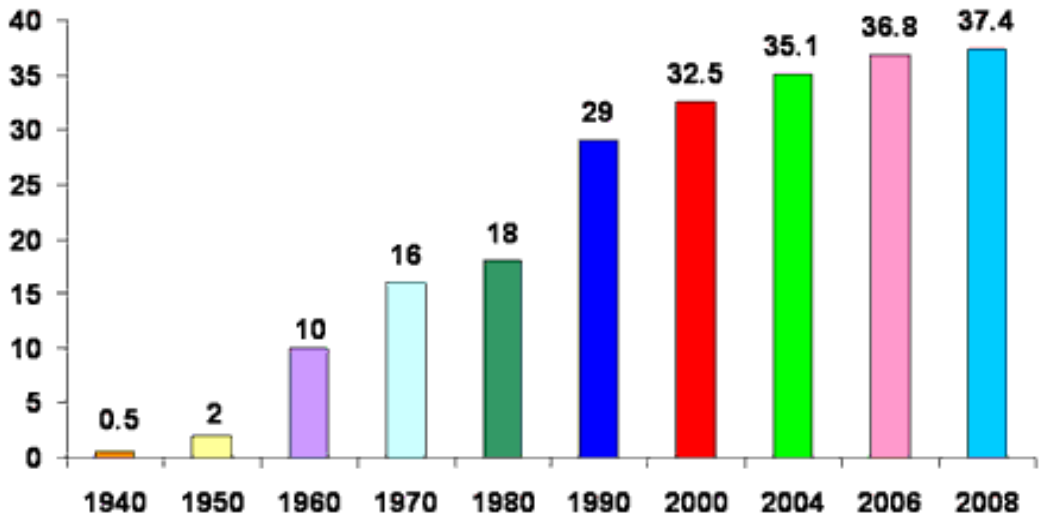
CHALLENGES

- Increasing complexity as patients live longer
- Increasing size of adult centres
- Cost of novel treatments

LIFE EXPECTANCY

Age at death	Number of cystic fibrosis patients
0-3	2
4-7	1
8-11	3
12-15	0
16-19	11
20-23	25
24-27	22
28-31	13
32-35	22
36-39	9
40-43	4
44-47	4
48-51	8
52-55	5
56+	8
Total	**137**

Average Life Expectancy in Cystic Fibrosis
Better Treatment = Improved Survival



Source: Cystic Fibrosis Foundation

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	Overall (n=9432)	<16 years (n=3840)	≥16 years (n=5592)
	N (%)	N (%)	N (%)
Respiratory Related			
Nasal polyps requiring surgery; n (%)	214 (2.3)	41 (1.1)	173 (3.1)
Sinus disease; n (%)	828 (8.8)	36 (0.9)	792 (14.2)
Asthma; n (%)	1368 (14.5)	516 (13.4)	852 (15.2)
ABPA; n (%)	1017(10.8)	298 (7.8)	719 (12.9)
Haemoptysis; n (%)	775 (8.2)	41 (1.1)	734 (13.1)
Pneumothorax requiring chest tube; n (%)	67 (0.7)	3 (0.1)	64 (1.1)
Nontuberculous mycobacteria or atypical mycobacteria; n (%)	433 (4.6)	208 (5.4)	225 (4.0)
Pancreas & Hepatobiliary Disease			
Liver enzymes; n (%)	1071 (11.4)	251 (6.5)	820 (14.7)
Liver disease; n (%)	1322 (14.0)	342 (8.9)	980 (17.5)
Cirrhosis with no portal hypertension; n (%)	126 (1.43	27 (0.7)	99 (1.8)
Cirrhosis with portal hypertension; n (%)	163 (1.7)	20 (0.5)	143 (2.6)
Gall bladder disease requiring surgery; n (%)	36 (0.4)	0 (0.0)	36 (0.6)
Pancreatitis; n (%)	68 (0.7)	4 (0.1)	64 (1.1)
GI bleed req hosp variceal; n (%)	9 (0.1)	2 (0.1)	7 (0.1)
Upper Gastrointestinal			
GORD; n (%)	1494 (15.8)	348 (9.1)	1146 (20.5)
Peptic ulcer; n (%)	6 (0.1)	0 (0.0)	6 (0.1)
GI bleed req hosp non variceal; n (%)	9 (0.1)	2 (0.1)	7 (0.1)

INCREASING COMPLEXITY

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Lower Gastrointestinal			
Intestinal obstruction; n (%)	556 (5.9)	123 (3.2)	433 (7.7)
Fibrosing colonopathy/ colonic structure; n (%)	3 (0.0)	0 (0.0)	0 (0.0)
Rectal prolapse; n (%)	31 (0.3)	24 (0.6)	7 (0.1)
Renal			
Kidney stones; n (%)	85 (0.9)	5 (0.1)	80 (1.4)
Renal failure; n (%)	50 (0.5)	3 (0.1)	47 (0.8)
Muscolo-Skeletal			
Arthritis; n (%)	163 (1.7)	11 (0.3)	152 (2.7)
Arthropathy; n (%)	532 (5.6)	19 (0.5)	513 (9.2)
Bone fracture; n (%)	46 (0.5)	12 (0.3)	34 (0.6)
Osteopenia; n (%)	1225 (13.0)	30 (0.8)	1195 (21.4)
Osteoporosis; n (%)	519 (5.5)	2 (0.5)	517 (9.2)
Other			
Cancer confirmed by histology; n (%)	33 (0.3)	2 (0.1)	31 (0.6)
Port inserted or replaced; n (%)	552 (6.0)	202 (5.3)	350 (6.3)
Absence of vas deferens (males only); n (%)	666 (7.1)	1 (0.3)	665 (12.0)
Depression; n (%)	415 (4.4)	3 (0.1)	412 (7.4)
Hearing loss; n (%)	213 (2.3)	28 (0.7)	185 (3.3)
Hypertension; n (%)	236 (2.5)	2 (0.1)	234 (4.2)

ADULT CENTRE CAPACITY

- Main adult centres built at a time when size of adult population was static (ie. No. transitioning = no of deaths)
- Life-expectancy increasing all the time with increasing complexity and new treatment options
- Many adult centres in UK need to expand or new centres need to be created.
- Funding challenges – many centres have raised their own funds

COST OF NOVEL TREATMENTS

- Ivacafor (Kaleydeco)
  - Licensed for patients aged 6yrs and over since June 2012
  - At least 1 copy of the genotype G551
  - Cost of treatment per year £ 187 000

Number of patients on ivacaftor in the UK	402
	Median (IQR)
Sweat chloride before ivacaftor	104 (95-114)
Sweat chloride 6-8 weeks after ivacaftor	50 (36-64)
FEV_1% before ivacaftor	61.1 (38.5-69.8)
FEV_1% 6-8 weeks after ivacaftor	71.6 (56.6-82.6)
Number of patients stopped ivacaftor	10

COST OF NOVEL TREATMENTS

- Lumicaftor – Ivacaftor (Orkambi)
  - Licensed for patients with F508del mutation
  - In the UK, 2 750 patients have this genotype
  - Cost of treatment per year is £104 000
  - An independent committee (NICE) has not recommended the use of this drug for the treatment of CF in the UK

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QUESTIONS?

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