Cystic Fibrosis

investing in research to change lives

Cystic Fibrosis Trust
Research Strategy
2013–2018

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April 2013

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We live at a time of extraordinary advances and opportunities relating to the treatment of cystic fibrosis.

I know from my own family experience that living with and caring for those with cystic fibrosis is a tough way of life. But it is also true that those with the condition are living longer and better lives as a result of more effective methods of managing and treating its symptoms. It has turned what only a few decades ago was an exclusively paediatric condition to one that today affects more adults than children.

And now, for the first time, there is a "game-changing" treatment in UK clinics that is tackling the basic genetic defect of cystic fibrosis, and transforming the lives of those with the minority G551D mutation. This is without doubt a breakthrough moment, and a pipeline of potentially transformational therapies for other mutations is now in clinical trials in the US, here in the UK and elsewhere.

Whether it is small molecule work, gene therapy or other forms of innovative research, there exists extraordinary opportunities over the next ten years to make a real difference to the lives of people with cystic fibrosis.

Research has always been at the heart of why the Cystic Fibrosis Trust exists, and this strategy seeks to ensure we are best placed to assist, enable and accelerate potential research opportunities in the interests of all with the condition.

The next few years will see exciting developments in science, biomedical and health research environments that have the potential to make a substantial difference to the lives of people with cystic fibrosis. It is timely, therefore, for us to review our approach to research and establish a robust and resilient strategy to create a balanced portfolio that builds on the successes of the past to further the quality and length of life of all people with cystic fibrosis.

In drawing up this strategy, we consulted a wide range of stakeholders within the UK and overseas. This has involved extensive dialogue with cystic fibrosis experts, the biopharmaceutical industry, academic scientists, overseas cystic fibrosis organisations and the NHS, as well as people with cystic fibrosis and their families.

This strategy sets out how we will invest our resources and utilise our key relationships with the research, clinical and patient communities both here and abroad. It explains how we intend to develop innovative partnerships that deliver results in transformational research and those projects focused on the clinical challenges of today.

In doing so, we will increase the capacity and quality of clinical trials in the UK, recruit the brightest and best to cystic fibrosis research and enhance the involvement of people with cystic fibrosis in shaping research.

This is a bold and ambitious strategy, and we make no apologies for that. Too many young people are dying early due to cystic fibrosis, and we will not rest until we have beaten it.

George Jenkins OBE
Chair, Cystic Fibrosis Trust

The Cystic Fibrosis Trust's five-year research strategy will be founded on five SCORE principles. It will be:

- **Strategic**
  by leading on the basis of clear priorities, actions and goals.
- **Collaborative**
  by working with others to maximise funding opportunities.
- **Outcome-focused**
  by being mission-driven, strategic in allocation of resources, and results-oriented.
- **Risk-based**
  by pursuing a balanced and diverse portfolio of research that benefits all people with cystic fibrosis.
- **Excellence-driven**
  by being driven by quality and harnessing expertise wherever we can find it.

The Trust's focus will be to ensure the maximum impact on people with cystic fibrosis. It will:

1. Invest in tomorrow – backing transformational science to correct the basic defect by:

- forging partnerships to develop what are costly, high-risk but high-reward projects;
- supporting basic science to understand CFTR and enhance the knowledge base, thus accelerating the process of developing the next generation of drugs; and
- considering the funding of research opportunities in small molecule interventions, gene therapy and other emerging technologies.

2. Invest in today – working to help alleviate and manage the symptoms of cystic fibrosis by:

- encouraging researchers to form multidisciplinary consortia to provide research-driven solutions to address key priority areas; and
- considering funding in key areas, including lung immunology and infections, transition and adherence, smart technologies to monitor treatments at home, nutrition and cystic fibrosis-related diabetes, transplantation, and exercise and physiotherapy.

3. Increase the capacity and quality of clinical trials in the UK by:

- developing partnerships with other funding agencies, government and the biopharmaceutical industry;
- increasing capacity for clinical research through appointing research coordinators in cystic fibrosis clinics;
- building in-house capability to support and coordinate clinical trials across the UK; and
- maximising the value of the UK CF Registry to facilitate clinical trials and use it to map the impact of transformational therapies on disease progression.

4. Recruit the brightest and best to cystic fibrosis research by:

- attracting top-class experts from disciplines outside the traditional biomedical sciences and identify ways that this science can be applied to cystic fibrosis; and
- identifying areas of synergy with other funding agencies and inviting key researchers to "research sandpits" with the intent of developing a joint research call.

5. Enhance the involvement of people with cystic fibrosis in shaping research by:

- increasing the involvement of the cystic fibrosis community in the design, commissioning and management of clinical research;
- promoting research activity more energetically and informing people with cystic fibrosis and their carers of the value of clinical trials, which trials in the UK are recruiting and where, and the outcomes of particular clinical trials in the UK and elsewhere; and
- encouraging greater discussion and debate within the cystic fibrosis community about where the Trust's research priorities should be over the longer term.

The Trust will improve the way it manages its research portfolio and form partnerships with those groups and individuals that have made the UK a world-class centre for biomedical research.

Strategic research centres will bring together the best team of key scientific experts, wherever they are based, and thereby form a cohesive group intent on using research to solve problems in cystic fibrosis.

Venture and innovation awards will leverage financial support from other agencies, including industry, research councils, the National Institute for Health Research, biomedical research charities and others to support transformational and innovative research projects.

Research sandpits will stimulate new thinking and innovation on a topic where the expertise within the cystic fibrosis research community is thin – such as "smart electronics".

Capacity for clinical trials research in the UK will be increased by a competitive research call in the UK for the part-funding of five research coordinators based in cystic fibrosis specialist clinics.

New governance of research will replace the existing Research Advisory Committee with a new Strategy Advisory Board, responsible for ongoing oversight of the strategy, and a new Strategy Implementation Board to judge funding applications against agreed criteria.

To deliver the strategy in 2013–14 we plan to:

- announce the funding of two strategic research centres at a cost of £750,000 over three to four years to solve key problems in cystic fibrosis research;
- establish venture and innovation awards (£1m), at least 50% of which will be used to promote transformational research projects;
- identify and run two research sandpits;
- part-fund five research coordinators in cystic fibrosis clinics;
- undertake an external review of the UK CF Registry;
- establish a Strategy Advisory Board and Strategy Implementation Board; and
- establish new ways of engaging people with cystic fibrosis and their families with research.

To deliver the strategy over the next five years, we plan to:

- create a cadre of at least 30 young scientists through the formation of six strategic research centres;
- raise the gearing of the venture and innovation awards so for every £1 we invest, an additional £5 will be secured from outside sources to support cystic fibrosis research;
- develop a collaborative project with a major investor, such as a biopharmaceutical company or major non-profit funder to develop new therapies; and
- increase the number of clinical trials threefold through investments in clinical trials.

Why?

Our research strategy has been developed in the light of the extraordinary changes taking place in the treatment of cystic fibrosis and in the wider research environment. It aims to build on previous achievements and provide leadership to harness these changes and thereby ensure research investments benefit all people with cystic fibrosis.

Improvements in treatment

Cystic fibrosis is a life-shortening genetic condition that slowly destroys the lungs and digestive system. The faulty cystic fibrosis gene disrupts the activity of a protein called the cystic fibrosis transmembrane conductance regulator (CFTR) – (see box, page 8).

Cystic fibrosis affects multiple organs. In the lung, mucociliary clearance is defective and this results in lung infections and inflammation, and progressive loss of lung function. In the digestive system, people with cystic fibrosis are unable to digest and absorb food so they have a low body mass index (BMI). Patients have both exogenous and endocrine pancreatic insufficiency with the consequent malabsorption and risk of cystic fibrosis-related diabetes.

Research – some of it supported by the Cystic Fibrosis Trust – and improvements in clinical care have had a significant impact on the quality and length of life of patients with the condition. What was once considered entirely a paediatric genetic disease with a typical life expectancy of fewer than four years, is now seen as one that extends well into adulthood. The improvement in both the quality and length of life has, in general, resulted from research focused on improving our understanding and treatment protocols for the complications of living with long-term CFTR dysfunction and so, to slow the progression of the disease. This has largely provided evidence-based improvement in clinical care, better control of life-threatening infections and improved nutritional status. In the UK, people with cystic fibrosis have also benefitted from the establishment of specialist cystic fibrosis clinics.

Dealing with a condition that has seen a substantial increase in life expectancy brings new challenges

No one single advance can account for the improvement in life expectancy. Rather, it has been achieved through a number of different factors – from better treatment of infections and changes in dietary management, to improved physiotherapy and more effective clinical management. In other words, what Sir David Brailsford, Director of Britain's all-conquering Olympic cycling team, refers to as "the aggregation of marginal gains" – or a process in which small improvements in a number of different aspects of what we do can have a huge impact on the overall picture.

As a consequence, the majority of the patients (57%) in the UK CF Registry are over the age of 16 years and the median predicted life expectancy has risen to 41.7 years.[1]

1: CF Registry 2011

Distribution of people with cystic fibrosis by age

- 0–11 years (paediatrics)
- 12–19 years (transition)
- 20+ years (adult)

20%

chance in 1964 that a child with cystic fibrosis would reach school age

57%

of people with cystic fibrosis in the UK CF Registry in 2011 were over 16

41.7

was the median predicted life expectancy of a person with cystic fibrosis in 2011

Dealing with a condition that has seen a substantial increase in life expectancy brings new challenges, too. For individual patients, new drugs and therapies can add to an already onerous treatment burden. There are wider implications for the NHS in respect of providing ongoing care for an increasing number of adults with cystic fibrosis, and for the wider research community in confronting new clinical challenges that emerge.

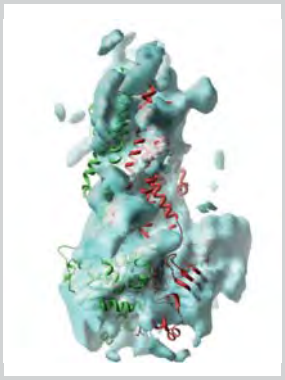
However, the ultimate goal for research in cystic fibrosis is to understand the basic fundamental defect of CFTR with a view to finding a "cure" or at least to where the condition no longer limits life and life chances. Investments in this transformational research are long term and high risk: results do not appear overnight.

For instance, the Trust has invested for over 10 years in the Gene Therapy Consortium and the Wave 1 product is now in Phase 2b clinical trials. In addition, the Trust has invested in fundamental research that provides a better molecular understanding of the basic defect and how mutations of the gene affect the functioning of the protein, CFTR. This work underpins drug discovery programmes currently funded by other agencies and the biopharmaceutical industries.

The worldwide investments in transformational research have begun to yield results and this year (2013) there has been a paradigm shift in the management of cystic fibrosis. For the first time, a small molecule drug has been developed to treat the genetic disorder. Ivacaftor (also known by its brand name, Kalydeco) tackles the root cause of the disease and has been licensed for use in the UK. It represents a step-change in managing cystic fibrosis by directly treating the dysfunctional protein. This year, patients with the G551D mutation (4%) are eligible for this new drug and this opens a whole new era for the clinical management of cystic fibrosis.

This year (2013) there has been a paradigm shift in the management of cystic fibrosis

At this time, there are a growing number of promising late-stage, clinical trials underway for other new chemical entities and gene therapy that raise the possibilities of new transformational treatments becoming available. It seems likely that future therapies will deliver personalised medicines for the cystic fibrosis community. ▸



Human CFTR structure: courtesy Professor Robert Ford (University of Manchester)

Cystic fibrosis transmembrane conductance regulator (CFTR)

Cystic fibrosis is the most common monogenic, autosomal recessive life-threatening disease in the UK, affecting about 1 in 2000 live births.

In 1989, the causal gene underlying cystic fibrosis was identified and found to encode a protein called CFTR. This protein acts at the cell membrane to allow the passage of chloride ions and water across cell membranes. If CFTR does not function correctly on the surface of cells in the airways of the lung, gastrointestinal tract (pancreas and small intestine), sweat glands and other organs, these surfaces are no longer hydrated correctly. In the airways this leads to sticky mucus and subsequent lung infection and inflammation, and in the gastrointestinal tract, to the failure to digest and absorb food.

It has only recently been possible to consider developing treatments that directly influence CFTR, the gene or protein underlying cystic fibrosis, even though the CFTR gene was discovered about 25 years ago. This is because the CFTR is a fully formed protein (1,480 amino acids) that undergoes complex folding to create the fully functioning protein at the cell surface. More than 1,000 different mutations of the CFTR gene have been identified and there is the added complexity that different mutations have different effects on the function of the CFTR protein.

For example, the G551D mutation is folded correctly at the cell surface but unable to open. Ivacaftor appears to restore the function of the channel/transporter, causing it to open, thus permitting the passage of chloride ions and water across the cell membrane.

In the most common mutation found in people with cystic fibrosis, the genetic mutation results in the deletion of the phenylalanine amino acid at position 508 (F508del), causing the protein to be mis-folded. This mis-shapen protein is targeted for degradation in the cell. Thus, very little CFTR gets to the cell surface and that which makes it functions very poorly and appears to be unstable. There are many other mutations in CFTR and the long-term goal is to understand better the effect of these mutations on CFTR function and find novel ways to treat the effects.

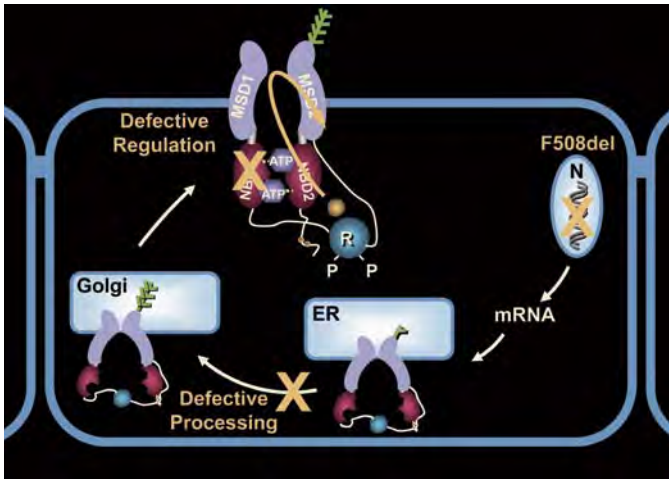
Changes in the wider research environment

Over the last year, there have also been some significant changes in the wider medical, policy and science environments that will have major influences on people with cystic fibrosis and the cystic fibrosis research community. It is important that the Trust ensures its research portfolio is ready to seize this opportunity for the benefit of all people with cystic fibrosis in the UK.

Transformational treatments
The development of ivacaftor and its adoption by healthcare systems in the US and Europe is a trailblazer for new therapies to treat the basic defect in cystic fibrosis. Significantly, it was a biomedical charity, the Cystic Fibrosis Foundation (CFF), that initiated the work by directly commissioning a biotechnology company (Aurora Biosciences) to identify the lead compound. The subsequent development of the drug through all the clinical trials and regulatory requirements was completed by a partnership between CFF and Vertex Pharmaceuticals, which acquired Aurora Biosciences. The drug was approved through the fast track procedures within the US Food and Drug Administration. In addition, healthcare systems worldwide have recognised the need for appropriate reimbursement to encourage further investment by biopharmaceutical companies in high-value specialised treatments for “niche” areas where there are only a small number of patients worldwide. The success of ivacaftor has attracted other biopharmaceutical companies to invest in drug discovery programmes specifically for cystic fibrosis.

The biopharmaceutical sector
The biopharmaceutical industry is shifting in its approach to drug development. It now places more emphasis on working with external partners, particularly in the earlier stages of drug discovery, rather than relying on its own in-house discovery programmes.

Images: courtesy Dr David Sheppard (University of Bristol)



Left: diagram of CFTR processing in the cell from gene to cell surface expression. The F508del mutation results in misfolded proteins, which cannot move to the cell surface. The G551D mutation results in CFTR at the cell surface but unable to open

Below: CFTR potentiators restore activity to F508del-CFTR. Representative recordings of individual normal "wild-type"

In addition, the industry has become less focused on developing "blockbuster drugs" that can be prescribed to millions of people worldwide and has become more interested in developing high-value medicines that have defined prescribing limits: so called personalised medicines.

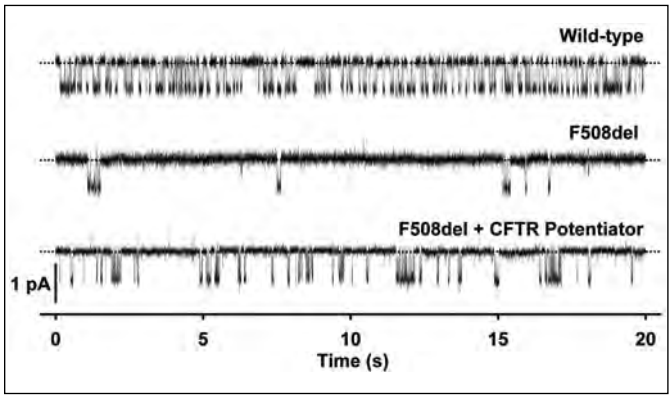
Personalised medicines

The cystic fibrosis community may be on the cusp of a significant change towards personalised medicines to treat cystic fibrosis. As different mutations of the CFTR gene result in different effects on the function of the channel/transporter, different molecular interventions will be required to restore function and so treat cystic fibrosis. Development of these new therapies that act to restore CFTR function in different genotype-dependent ways will lead to personalised medicines. In the future, it is likely that the treatment of any one patient with cystic fibrosis will be tailored to that individual and could comprise a cocktail/combination of different therapies (small molecules and gene therapy) to restore CFTR function.

The cystic fibrosis community may be on the cusp of a significant change towards personalised medicines to treat cystic fibrosis

Role of biomedical research charities

The approach adopted by the CFF to work with the biopharmaceutical sector to identify new chemical entities exemplifies changes in the way that a number of biomedical research charities operate. Drug discovery is a costly and risky business but the potential impact is very large. The risk averse nature of the biopharmaceutical sector is leading to a growing gap between high-quality basic biomedical science and the appearance of new chemical entities licensed for use in the clinic: a gap which has been referred to as the "valley of death".[2] Biomedical charities increasingly want to see that gap spanned and to assist where they can.[3]



Research focus within the new NHS

As part of its plans for restructuring the UK health service[4], the government has placed a priority on health research to benefit patient welfare and care. Under the new statute (April 2013), the NHS has a duty of research and at all levels (from the Secretary of State downwards), the new Act mandates research. New structures have been created to ensure the delivery of the research agenda. The National Institute for Health Research (NIHR) has established Academic Health Sciences Networks and Clinical Research Networks to drive the adoption of research across the NHS and help strip back some of the complexities encountered by clinical scientists, particularly in running clinical trials nationally across a number of different foundation trusts. ▶

2: http://www.publications.parliament.uk/pa/cm201213/cmselect/cmsctech/348/348.pdf; http://www.nature.com/news/2008/080611/full/453840a.html

3: www.fastercures.org

4: Health and Social Care Act 2012 http://www.legislation.gov.uk/ukpga/2012/7/contents/enacted

"Research is important to me because it has allowed me to extend and enjoy my life beyond all expectations."

Sean Bell

From Manchester

In addition, the Health Research Authority has been tasked with undertaking pilot feasibility studies. All these changes are likely to have a significant impact on biomedical research charities and it is critical that the Trust is well positioned to work with and within these new structures and take advantage of this new environment for health research.[5]

Health informatics

The development and better use of health informatics is a major component of the NHS research strategy. It is "one of the fastest growing areas within healthcare. In its simplest term, health informatics is about getting the right information to the right person at the right time. It involves capture, communication and use of patient data and clinical knowledge to support the delivery of patient care by healthcare professionals."[6] The NIHR and Medicines and Healthcare Products Regulatory Agency have jointly created the Clinical Practice Research Datalink (CPRD) which is "designed to maximise the way anonymised NHS clinical data can be linked to enable many types of observational research and deliver research outputs that are beneficial to improving and safeguarding public health".[7]

In addition, the Medical Research Council (MRC) has recently announced four e-health Research Centres of Excellence in London, Manchester, Dundee and Swansea to exploit the wealth of information available through linking various health databases or observatories.[8] Linking the UK CF Registry (see 'Who?', page 13) to these new developments in other organisations provides opportunities to expand the knowledge derived from the Registry to the benefit of people with cystic fibrosis and so strengthen its value for research with little additional investment.

New initiatives for translational research in the UK and across Europe

The gap between the strong UK biosciences and their translation to the development of new therapies is widely recognised within government agencies worldwide.[9] Within the UK, the government recently announced the Biomedical Catalyst Fund,[10] which is jointly funded by the MRC and the Technology Strategy Board to support specifically translational research.

The EU developed the Innovative Medicines Initiative (IMI) some years ago. To assist the identification of new drugs, the EU recently announced the formation of the IMI's European Lead Factory (ELF). This initiative aims to promote the identification of new and promising lead compounds and is formed through a precompetitive collaboration between biopharmaceutical companies to release 300,000 pharmaceutical industry-derived drug-like compounds to EU-funded high-throughput screening laboratories. These can be accessed both by the companies and by non-commercial groups. The ELF sites are in the process of being established, and the compound collection will be enhanced by an additional 200,000 compounds over the next five years. ■

5: The Cystic Fibrosis Trust is a member organisation of the Association of Medical Research Charities which is currently developing a position paper on the changes in the NHS called "A vision for research in the NHS", www.amrc.org.uk

6: http://www.nhscareers.nhs.uk/explore-by-career/health-informatics

7: http://www.cprd.com/intro.asp

8: 'Strategic Framework for Health Informatics in Support of Research', http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC006669

9: http://www.publications.parliament.uk/pa/cm201213/cmselect/cmsctech/348/348.pdf; http://thehill.com/resources/white-papers/science/151015-valley-of-death-translational-research

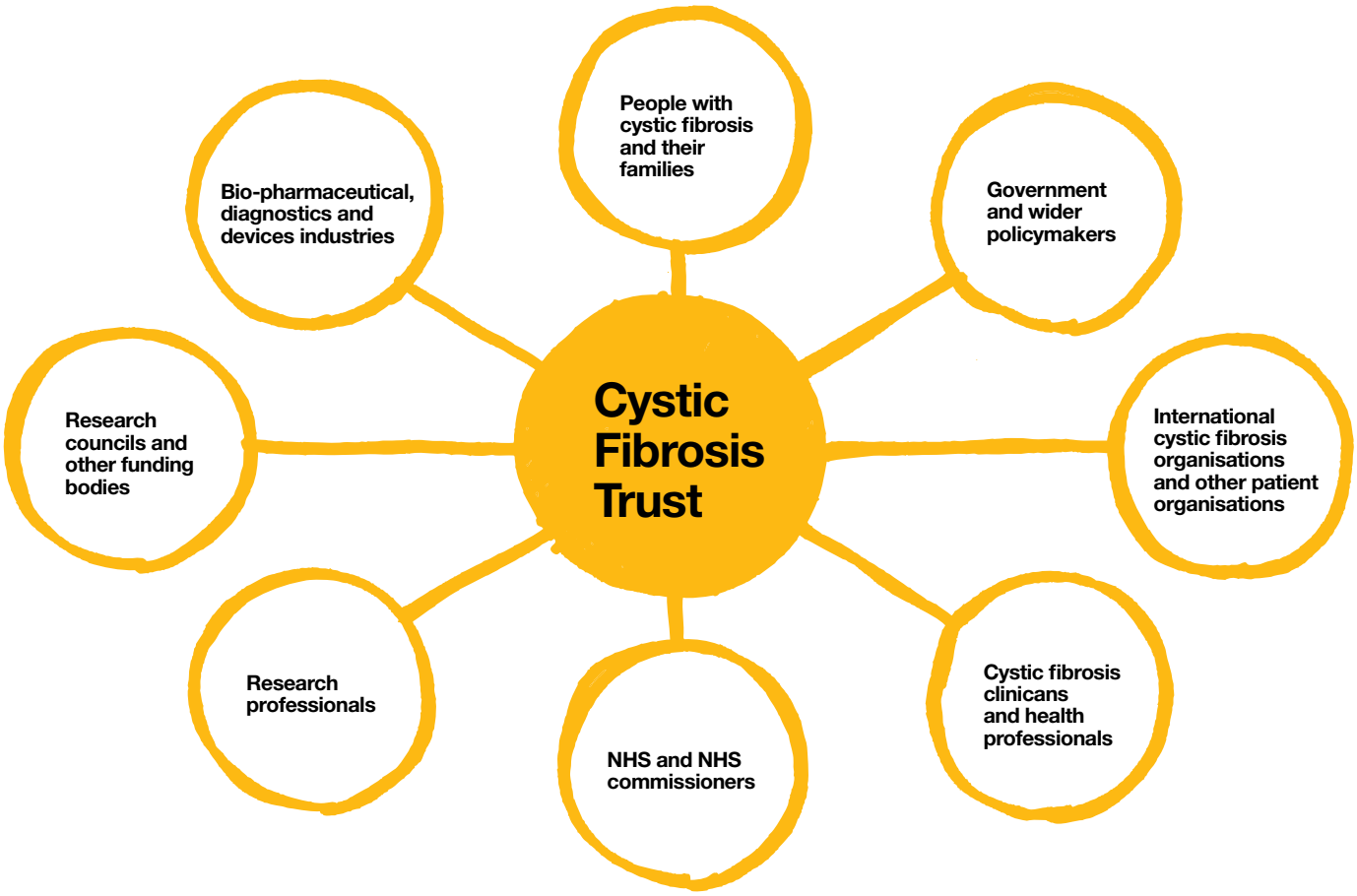
10: http://www.mrc.ac.uk/Newspublications/News/MRC008394; https://www.gov.uk/government/organisations/office-for-life-sciences

Who?

The changing landscape faced by cystic fibrosis research requires an integrated approach involving a wide range of organisations and individuals. As it approaches its 50th anniversary, the Cystic Fibrosis Trust is uniquely positioned to transfer and exchange knowledge and experience throughout this community.

At the heart of the cystic fibrosis community

The Cystic Fibrosis Trust is the only UK-wide charity making a daily difference to the lives of people with cystic fibrosis and those who care for them. It lies at the centre of the cystic fibrosis community, with connections to the specialist NHS cystic fibrosis clinics and centres, clinicians, academic research groups, and, of course, the almost 10,000 people in the UK with the condition. In addition, it provides a contact point



Cystic Fibrosis why we're here

The Cystic Fibrosis Trust

- invests in cutting edge research
- drives up standards of care
- offers support and advice to people with cystic fibrosis and their families
- campaigns hard on behalf of the almost 10,000 people with cystic fibrosis in the UK
- shouts loud to raise awareness, increase understanding of cystic fibrosis and raise vital funds

for government and NHS managers and is developing stronger links with international sister organisations like the US Cystic Fibrosis Foundation and the European Cystic Fibrosis Society.

It provides a conduit for the exchange of information on cystic fibrosis research and management between the whole of this network of groups and people. It also works directly with providers of clinical care to improve standards and funds a variety of fundamental and clinical cystic fibrosis research.

Clinical care

The Trust works closely with the specialist cystic fibrosis centres and clinics across the UK, professional bodies and commissioners to improve quality of care through national standards and a process of peer reviews of those centres and clinics.

Research has also been instrumental in driving up standards of care, most notably through the screening of newborns for cystic fibrosis, a development that innovative research at the UCL Institute of Child Health enabled (see box, below) and for which the Trust campaigned vigorously.

The UK CF Registry forms an invaluable resource, unmatched for any inherited genetic disease in the UK

The Trust also hosts the UK CF Registry, which contains audited data on genotype and phenotype on 90% of the people with cystic fibrosis in the UK. This forms an invaluable resource, unmatched for any inherited genetic disease. Through the longitudinal data made available by annual assessments of clinical parameters, the impact of therapeutic interventions on disease progression can be established and issues for research identified. The Registry is already used as a valuable tool to monitor the long-term safety of therapeutics in Phase 4 post-licensing studies. ▸

Researchers at the UCL Institute for Child Health, led by Professor Janet Stocks, have developed expertise in measuring lung function in infants and young children. Recent introduction of newborn screening on routine blood samples through the standard heel-prick test allows the diagnosis of cystic fibrosis shortly after birth, with opportunities for novel early therapeutic interventions. Professor Stocks has also led the multi-institutional, Trust-funded London Cystic Fibrosis Collaboration (LCFC), which combines expertise from Great Ormond Street Hospital (GOSH), King's College London, the Royal Brompton Hospital, Barts and the London Hospital, University Hospital Lewisham and Queen Mary's Hospital for Children, Epsom & St Helier. This has been studying the evolution of lung function in children with cystic fibrosis and its relationship to clinical status for the past 15 years. Current Trust-funded work by the LCFC has focused on assessing lung function and structure in infants with cystic fibrosis diagnosed by newborn screening from birth to two years of age in order to clarify the best time to start such treatments.

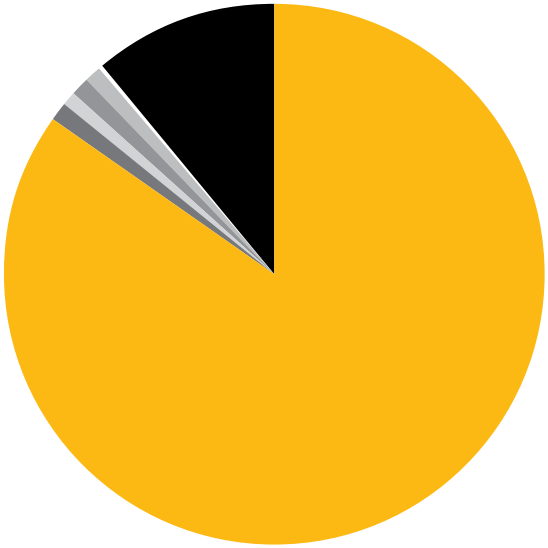
"Research is important to me because it helps my Mummy and Daddy to understand cystic fibrosis and helps me to understand what's happening to my body."

Eva, aged 5

From Manchester

Total Cystic Fibrosis Trust research funding since 2001

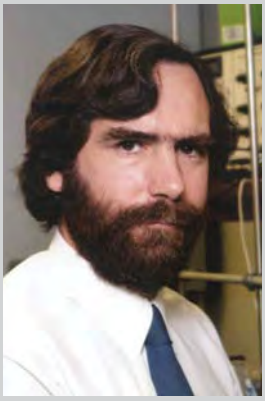
- Gene Therapy Consortium
- UK Microbiology Consortium
- UK CF database development (Dundee)
- Lung transplantation research, in collaboration with National Institute for Health Research (DEVELOP–UK)
- Edinburgh CF microlab and repository database
- Editorial support for Cochrane
- Grants to 44 individual scientists



The Trust recently commissioned a review of the Registry and as part of this review it will establish how better to access the data to inform research questions, assist clinical trials and forecast trends – under the appropriate safeguards and guidelines issued by the Department of Health and in compliance with data protection regulation.

Research supported by the Cystic Fibrosis Trust

Over the last decade, the majority of Trust research funding has supported the Gene Therapy Consortium (GTC) in a strategic move by the Trust to develop a novel treatment based on delivering CFTR to the airways of patients with cystic fibrosis. In addition, the Trust has invested a number of other research programmes.



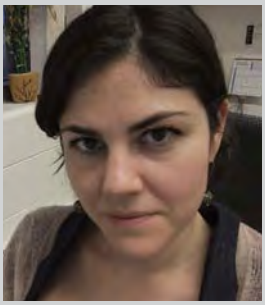
Eric Alton is Professor of Gene Therapy and Respiratory Medicine, National Heart & Lung Institute, Imperial College London (ICL) and Honorary Consultant Physician, Royal Brompton Hospital. Professor Alton coordinates the UK CF Gene Therapy Consortium, which brings together 80 scientists and clinicians at ICL, the University of Edinburgh and the University of Oxford.

Gene therapy
The work of the GTC, established in 2001 (see box, below left), aims to deliver the normal CFTR gene to the airways by nebulising the gene either in liposomes (Wave 1) or in a viral vector (Wave 2).

This pioneering work has advanced to the stage where the Wave 1 product is currently in a Phase 2b clinical trial. This is the largest gene therapy trial worldwide. The GTC was successful in securing additional funds from the government-funded Efficacy and Mechanism Evaluation to complement funding provided by the Trust. The results of this trial will be available in 2014.

The Wave 2 project uses a viral vector to deliver the CFTR gene to the airway epithelia. This programme of work is considered by the GTC to have the potential to offer better efficacy but is still at preclinical stage, being several years behind the Wave 1 product. The consortium was successful in securing funding for this programme through a grant from the MRC's Developmental Pathway Funding Scheme. In February 2013, the Trust awarded a grant to the GTC which will assist the project until February 2014.

Lung immunology and microbiology
The Trust awarded funding to four principal investigators who came together in 2005 to create the UK Microbiology Consortium (see box, page 23). This funded five young scientists in the early part of their careers and brought together expertise from four different institutions. The consortium met annually to allow the cross-fertilisation of ideas. This meeting has continued following the end of the grant award and ▸



Dr Jo Fothergill was one of four PhD students funded through the UK Microbiology Consortium and studied under the supervision of Professor Craig Winstanley at the University of Liverpool. Her research investigated the variation in virulence of different *Pseudomonas aeruginosa* populations, which is important in cystic fibrosis. "Although our PhD projects were only loosely linked, we have met regularly as individuals and in larger groups with more established researchers in the field," Jo explains. "And we continue to do so with more people joining us since the funding ended." Her interest in cystic fibrosis was sparked by her PhD studies, which launched her career in this area of research. She was recently awarded a prestigious Leverhulme Trust Fellowship.

last year, nearly 80 scientists attended the conference to discuss research in the area of lung infections. Three of the five young scientists – including Dr Jo Fothergill (see box, left) – are still working in this area, ensuring valuable expertise in cystic fibrosis research is retained.

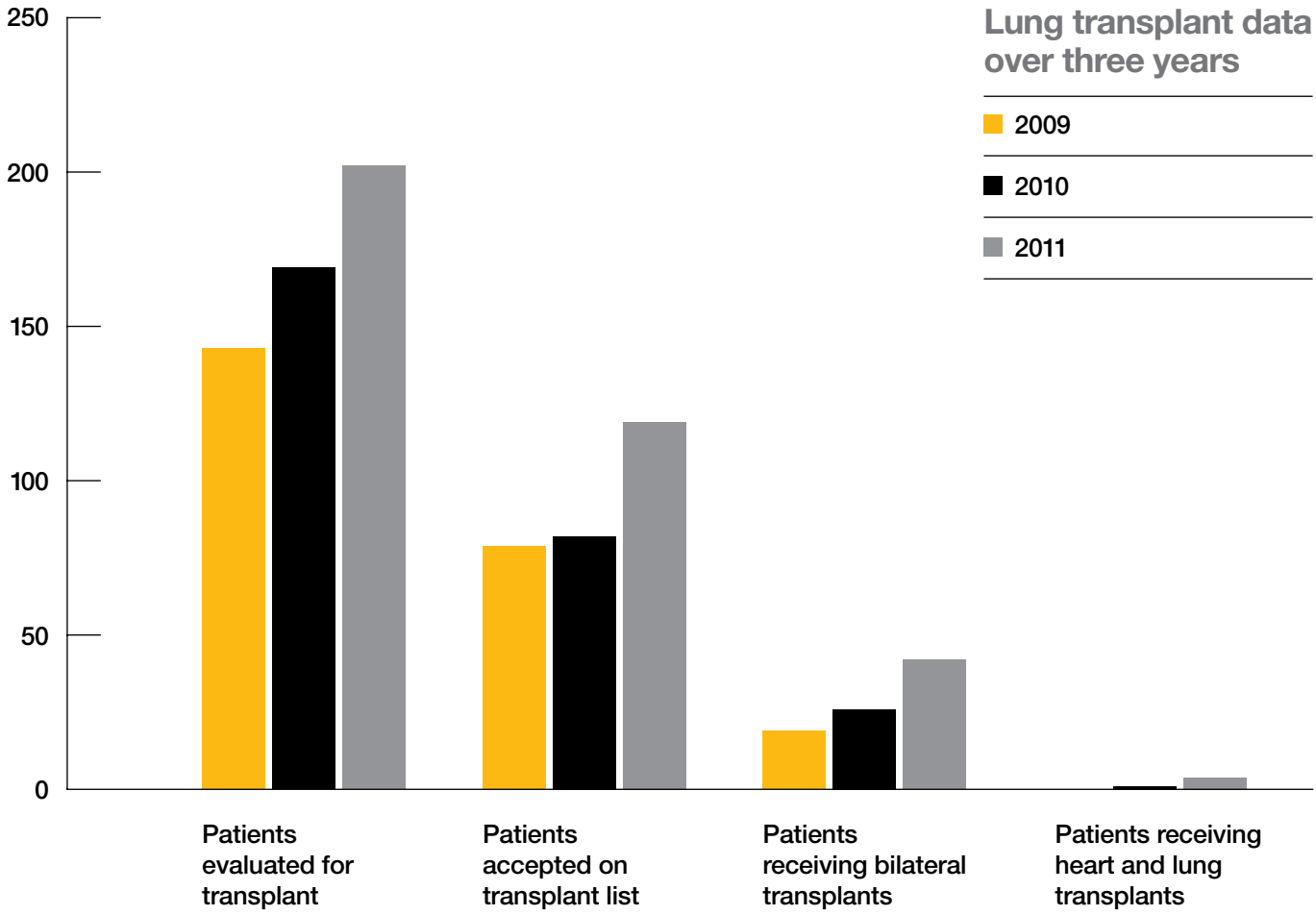
Lung transplantation

Research at the University of Newcastle funded by the Trust, with support from the Robert Luff Foundation since 2007, has demonstrated that improving the quality of donor lungs prior to transplantation through a procedure known as ex-vivo lung perfusion increases the number of lungs suitable for transplantation. This is important as the number of donor organs is small and only a fraction of those people with cystic fibrosis needing transplants are able to benefit.

Clinical trials

The Cystic Fibrosis Trust has supported a number of clinical trials that have had an impact on clinical care. For example, the TOPIC trial was fully funded by the

Above: Professor Andrew Fisher, Head of the Fibrosis and Repair Group in the Institute of Cellular Medicine at the University of Newcastle, is improving the quality of donor lungs using ex-vivo lung perfusion



Cystic Fibrosis Trust.[11] Results from this trial provided the evidence to support a change in the way that an antibiotic, tobramycin, was prescribed. The study showed that once daily treatment was equally effective and less toxic to the kidneys than the conventional three-time daily therapy. Over the last decade, clinical practice has changed in line with these findings and guidelines have been amended in the UK, US and Australia.

Dr David Sheppard at the University of Bristol has been studying the CFTR at a basic molecular level for a number of years. This fundamental research relating CFTR structure and function, part funded by the Cystic Fibrosis Trust through project grants, has led to a better understanding of how mutations in the gene influence the activity of CFTR within the cell. In addition, Dr Sheppard has a major interest in understanding how small molecules interact with CFTR and affect its function. He says: "The Trust has been very supportive of our work to understand how new drugs work."

Structure function of CFTR

Trust-funded research projects, such as the one led by Dr David Sheppard at the University of Bristol (see box, left), have increased the fundamental understanding of the structure and function of the CFTR at a detailed molecular level. This basic science is critically important in understanding how individual mutations change the way the CFTR functions. With the development of small molecule interventions for cystic fibrosis, this knowledge is crucial to underpin new drug discovery programmes and so allow the possibility of correcting the defective CFTR to restore normal function. Part of this work provides detailed understanding at a molecular level of how the CFTR functions to transport ions and water. Additional studies contribute to our understanding of the molecular structure of CFTR. ■

11: Smyth A et al TOPIC study group, Lancet (2005), 365, 573-8

What?

This research strategy aims to build on past achievements and enable the Trust to take full advantage of the new and exciting opportunities being developed within cystic fibrosis research and in the wider research environment. The Trust will play a leading role in responding to these changes for the benefit of people with cystic fibrosis in the UK.

Five principles guide the Trust's approach to its research strategy. These are: Strategic, Collaborative, Outcome-focused, Risk-based and Excellence-driven (SCORE) and recommendations for funding will be judged on how well they achieve these SCORE objectives.

Strategic: The Trust will lead on the basis of clear priorities, actions and goals. The research strategy will have a singular focus on – and a significant stake in – getting promising therapies and technologies from the lab to the clinic as rapidly as possible. To ensure this happens, the Trust will use its position at the heart of the cystic fibrosis community to provide leadership, become more proactive and focus solely on the potential for impact on the lives of people with cystic fibrosis.

Collaborative: The Trust will work with others to maximise funding opportunities. The Trust cannot achieve all its ambitious research objectives on its own. It will need to leverage income and attract other funding agencies to work in partnership to harness the excellent UK science base for the benefit of the cystic fibrosis community. The Trust will work to explore synergies and areas where joint funding of research can maximise the opportunities for cutting-edge research to be channelled to solve problems. Addressing the important questions set out in this strategy will require multi-funder efforts and frequently multidisciplinary approaches. In addition, the Trust needs to be alert to opportunities of working with the biopharmaceutical, devices and diagnostic industries.

Outcome-focused: The Trust will be mission-driven, strategic in allocation of resources, and results-oriented. Its new approach needs to be based on adopting some of the tools and techniques of venture capital finance, and the strategies and tactics of high-technology business management. This transition will promote the realignment of incentives around one goal, and one goal alone: accelerating the development of treatments, therapies and technologies for cystic fibrosis.

Risk-based: The Trust will pursue a balanced and diverse portfolio of research that benefits all people with cystic fibrosis. It will invest in a mixture of projects intended to bring both rapid and longer-term results. Many of the areas that potentially offer the biggest gains will also present the greatest difficulties and so the strategy will aim to balance the risks involved.

Excellence-driven: The Trust will be driven by quality and harness expertise wherever it can get it. High-quality research and talented people are the bedrock of science that delivers benefits to people with cystic fibrosis and attracts co-investment from other funding agencies and the private sector. The UK is fortunate in having some of the best biomedical scientists and research facilities in the world[12] and it is vital that the Trust makes every effort to work in partnership to ensure these skills are harnessed to address issues for cystic fibrosis.

To ensure the maximum impact on people with cystic fibrosis the Trust has identified two research themes that are underpinned by three enabling priorities.

Two research themes

1. Investing in tomorrow by backing transformational science to correct the basic defect
2. Investing in today by working to help alleviate and manage the symptoms of cystic fibrosis

Three enabling priorities

3. Increasing the capacity and quality of clinical trials in the UK
4. Recruiting the brightest and best to cystic fibrosis research
5. Enhancing the involvement of people with cystic fibrosis in shaping research

1. Research theme: Investing in tomorrow by backing transformational science to correct the basic defect

Transformational treatments include small molecule and gene therapy interventions. Over the next five years, research to develop such treatments will have an increasing impact on the cystic fibrosis community. The Trust also needs to remain alert to new and emerging opportunities that are currently at a much earlier stage but could become important, such as induced pluripotent stem cells and possibly genomic editing.

The Trust is keen to work collaboratively with other agencies and commercial partners to assist in the development of new therapies

Creating new, effective and safe therapies that tackle the basic defect are multi-million pound development projects that take many years to progress from basic ideas to clinically useful treatments. Such projects are high risk and beyond the resources of the Trust if acting as the sole funder. However, the Trust can play a crucial role in this research by forging partnerships able to take on such costly, high risk, but potentially very rewarding work. The Trust is keen to work collaboratively with other agencies and commercial partners to assist in the development of new therapies. In addition, the Trust can invest in the basic science to understand CFTR and thereby enhance the required knowledge base that underpins drug discovery and development and so accelerate the process of developing the next generation of drugs in the same class and the new therapies.

12: Thomson Reuters' National Science Indicators database, http://thomsonreuters.com/products_services/science/science_products/a-z/national_science_indicators

Research opportunities

Small molecule interventions
Ivacaftor is the first drug that directly affects CFTR function in patients with the G551D mutation (4% of mutations). Vertex has recently announced Phase 3 trials for combination treatment involving ivacaftor and lumacaftor (also known as VX809) in patients homozygous for the more common mutation, F508del.

Understanding the structure of CFTR and the effect of mutations on its function is a crucial part in the development of new drugs that tackle the basic defect. The UK has particular expertise in this area of science and the Trust will continue to support this research to accelerate the development of new molecular entities, both for novel mutations and also for making the next generation of drugs within any one class.

It is also clear that other biopharmaceutical companies are developing a variety of novel chemical entities that will potentially affect CFTR function in cystic fibrosis. It is important for the Trust to be alert to activity in industry and develop partnerships where appropriate. Investments in the research capacity of the cystic fibrosis clinics and use of the UK CF Registry to inform clinical trials both provide opportunities that will encourage potential industry partners to bring trials to the UK and so encourage early adoption of new transformational therapies.

The Trust also will seek opportunities to develop novel approaches to identify new chemical entities by accessing opportunities as they arise. Examples include accessing the European Lead Factory (see 'Why?', page 11). It will also consider seed funding other opportunities that arise, but always with the intention of developing partnerships and collaborations. ▸

"Research is important to me because it means I can live a normal life and stay well!"

Zanib Nassim

From Manchester

Gene therapy
The Trust has been the major funder of the GTC over the past decade (see 'Who?', page 15), and its work has been pioneering. This work has now progressed to stages where the financial costs to continue the research cannot be met by the Trust alone. Funding for the current Phase 2b trial is secure and, if successful, a commercial partner will be required to take the product through a Phase 3 trial and other future regulatory obligations. The GTC has successfully secured additional funding from the MRC to fund the longer-term Wave 2 project and the Trust awarded a further grant for this work in February 2013.

Gene therapy is an important future therapeutic opportunity for many people with cystic fibrosis and the Trust will continue to consider funding applications in this area, based firmly on the principle of sharing costs with external funding agencies.

Other emerging technologies
Over the five-year strategy, the Trust will also seek to explore the value of new and emerging technologies and their application to cystic fibrosis, including induced pluripotent stem cell therapy, genomic editing and synthetic biology. When appropriate, it will look to form alliances with other organisations to explore the value of these new technologies to cystic fibrosis.

2. Research theme: Investing in today by working to help alleviate and manage the symptoms of cystic fibrosis

Research funded through the Trust has made a major contribution to improvements in clinical care, which have had such a marked effect on morbidity and mortality for people with cystic fibrosis. Under the new strategy, the Trust aims to continue supporting projects in areas that have an impact on quality and length of life.

The Trust's own experience and that of other funders is that research into complex problems (as seen in cystic fibrosis) frequently requires the formation of multidisciplinary teams to bring together the relevant expertise to address the question. Building on this experience, the Trust will encourage researchers to form multidisciplinary consortia to tackle major problems for cystic fibrosis. These consortia or strategic research centres will address a key priority area by creating a multidisciplinary team of the best researchers with the expertise (wherever based) to provide research-driven solutions.

It may also be appropriate to create bespoke research calls along the lines of project grants as a joint venture with the other funders.

Research opportunities

Lung immunology and infections
Research has already had a significant impact on the management of lung infections. However, as with all scientific research, further work offers opportunities to improve clinical treatment. Examples include: more effective treatments for bacterial lung infections; emerging infections, including aspergillus and non-tuberculous mycobacteria; control of biofilm formation; novel antibiotics and vaccines; and novel delivery systems for inhalers and nebulisers.

Transition and adherence
Current treatment regimes are time-consuming and relentless and so people with cystic fibrosis may have difficulty maintaining regular adherence to treatment protocols, particularly during adolescence and their transfer from paediatric to adult care centres. A holistic approach to this will require psychosocial approaches, training, different physiotherapy regimes and novel interventions.

This area may well lend itself to smart technologies using novel diagnostics and devices to measure key clinical parameters in the home setting and thereby empower teenagers to manage their cystic fibrosis and permit earlier therapeutic interventions.

Development of smart technologies to monitor treatments at home
The development of home monitoring using smartphone apps empowers and motivates individuals to understand and self-manage their condition, particularly adolescents and adults with cystic fibrosis. Use of smartphone technologies can provide instant feedback to patients while simultaneously feeding information through to the specialist clinics. Adults with cystic fibrosis are encouraged to lead normal lives and yet conventional treatment requires regular clinic visits, often when they are healthy. Development of devices that can accurately assess patient well-being and provide suitable advance warning for treatment can be used to monitor patients at home. They would then have to visit clinics only when necessary or for an annual check.

Nutrition and cystic fibrosis-related diabetes
Good nutrition is key to both the physical and mental well-being for any patient, so studies to improve gastrointestinal function remain an important priority. Additionally, due to the increased numbers of adults with cystic fibrosis, the incidence of cystic fibrosis-related diabetes is a growing concern.

Exercise and physiotherapy
Improved physiotherapy and exercise techniques have played an important role in enhancing longevity and quality of life in people with cystic ▸

fibrosis, so this will continue to provide a focus of future research.

Transplantation
Transplantation is a critical area for patients with severe lung disease. Research can have a major impact on the outcome of transplantation. Areas that may be important are optimising recipients prior to transplantation and the preparation of donor organs, and increasing understanding of the immunology of transplantation. There are considerable synergies between the Trust's objectives in this area and those for NHS Blood and Transplant (NHSBT), which has developed extensive infrastructure to support research programmes in organ transplantation. The Trust will aim to ensure that the two organisations collaborate where synergies exist.

3. Enabling priority: Increasing the capacity and quality of clinical trials in the UK

Clinical trials are the bedrock of translational sciences as they ensure that people with cystic fibrosis benefit from the high-quality basic science in the UK. Within this broader context, engagement in clinical trials provides the evidence base to inform the best therapeutic regimes for a complex condition such as cystic fibrosis and demonstrates the benefit of early access to new potentially life-transforming drugs.

The costs of the later stage trials (particularly Phase 2b and Phase 3) are considerable and require support from those with sufficient financial resources such as private companies (biopharmaceutical industry), public agencies such as the NIHR and larger charities such as the Wellcome Trust.

The Cystic Fibrosis Trust has a pivotal role to play in encouraging efforts to set up clinical trials in the UK. As part of the new research strategy, the Trust will make strategic investments to build research capacity in cystic fibrosis clinics and aim to use the UK CF Registry better to inform clinical trials and provide long-term follow up of clinical interventions.
To achieve this goal, the Trust will invest in five research coordinators in 2013 to increase capacity for clinical trials and has commissioned a review of the Registry, in part to establish how this tool could be better used to facilitate research and speed up the adoption of clinical trials in the UK. In addition, the Trust plans to build in-house expertise in this area. Staff will work closely with the Clinical Trials Networks in the UK and overseas, as well as with the new health research structures of the NHS to ensure that cystic fibrosis research can capitalise on these changes. As many clinical trials span both paediatric and adult cystic fibrosis clinics, the in-house expertise will assist with some of the regulatory issues that currently act as a roadblock to the widespread adoption of trials nationally.

4. Enabling priority: Recruiting the brightest and best to cystic fibrosis research

There is an urgent need to recruit talented biomedical and clinical researchers to build a cystic fibrosis research community. We plan to put in place mechanisms to recruit the brightest and best young biomedical scientists and clinicians to cystic fibrosis research. This will draw on the past experience of the Trust, which has demonstrated that relatively small amounts of money invested in launching the careers of young researchers can produce significant long-lasting interest in this field of research. For example, in 2005–08, the Trust supported Alex Horsley's PhD research; Dr Horsley is now an established clinician scientist in the field of cystic fibrosis at the University of Manchester (see box, below).

Graduate research studentships and fellowship grants like those that established by the UK CF Microbiology Consortium (see box, right) can produce excellent science and establish an enduring interest among

Dr Alex Horsley is a clinician scientist at the University of Manchester and Manchester Adult Cystic Fibrosis Centre Wythenshawe Hospital. His research interest in cystic fibrosis started in 2005 with his PhD, funded by the Cystic Fibrosis Trust, at the University of Edinburgh. His clinical training was partly supported through a Trust fellowship held at Manchester. He has recently received a grant from the National Institute of Health Research (NIHR) over five years for a prestigious NIHR fellowship. This will allow him to continue his interest in clinical sciences by combining research with his clinical care of people with cystic fibrosis. "The Trust has been very much engaged in my work from the beginning. As well as giving me funding, its support was instrumental in getting the grant from NIHR."

Professor John Govan, University of Edinburgh, is a member of the UK Microbiology Consortium, which was established in 2005 to form a multi-institutional approach to tackling the issue of bacterial infection of the lung in cystic fibrosis. Microbiologists based at four institutions – the University of Liverpool, University of Edinburgh, Cardiff University and Queens University, Belfast – formed the consortium to improve the speed and accuracy in the diagnosis and treatment of infections and so improve the quality of life of young people. "If those people had been working in isolation, I don't think they would have had anything like the same impact as they have as a group," said Professor John Govan, pictured with colleague Dr Cathy Doherty.

talented young career scientists in those problems that are the focus of cystic fibrosis research. The Trust intends to create a sense of "belonging" among all young scientists supported by the Trust and will hold an annual meeting of this cadre of scientists and clinicians for them to share their research and to integrate the different aspects of research being supported by the Trust.

Research that lies at the interface between disciplines frequently yields a step-change in results, so the Trust plans to attract existing (top-class) experts from disciplines outside the traditional biomedical sciences – such as bioinformatics, biomedical engineering and electronics – and identify ways that this science can be applied to cystic fibrosis. This can be achieved through encouraging multidisciplinary approaches within strategic research centres. We will also identify areas of synergy with other funding agencies and invite key researchers to "research sandpits" with the intent of developing a joint research call.

5. Enabling priority: Enhancing the involvement of people with cystic fibrosis in shaping research

The Trust wants to increase the involvement of the cystic fibrosis community in delivering all aspects of this ambitious research agenda. The future of cystic fibrosis research relies on the active engagement and support of those affected both in terms of the funds invested from the Trust to support this work, and by directly involving people with cystic fibrosis in vital clinical trials to develop treatments and therapies.

The Trust also wants to ensure people with cystic fibrosis are more fully involved in the design, commissioning and management of clinical research, and we will be exploring ways to ensure the voice of patients and their families are better heard in this area.

The Trust plans to promote research activity more energetically within the cystic fibrosis community itself, with more proactive information on its website to inform people of the value of clinical trials, which trials in the UK are recruiting and where, and the outcomes of particular clinical trials in the UK and elsewhere. In particular, the Trust will learn from the success of the Medicines for Children Research Network and engage with the cystic fibrosis community in the design and delivery of those trials.

The Trust strongly supports initiatives like CF Unite to engage cystic fibrosis patients in research debates, and we will work with public organisations like the NIHR, as well as other patient-based groups, to enhance our work in this area.

We will also look to enhance greater discussion and debate within the cystic fibrosis community about where the Trust's research priorities should be over the longer term. People with cystic fibrosis and their families will continue to be represented on all the Trust's committees to advise on all aspects of operational and strategic research decisions. ■

How?

To deliver its new strategy, the Cystic Fibrosis Trust will refine the way it manages its research portfolio. By becoming more outward-looking and seeking to identify synergies with other funding agencies, the Trust will form partnerships with the institutions, individual scientists and funding agencies (public and private) that have made the UK a world-class centre for biomedical research.

The Trust's five-year strategy will be resilient and adaptable to ongoing changes in the wider environment. To deliver its research themes and enabling priorities, the Trust is establishing a range of activities backed by funding streams:

Strategic research centres

Biomedical research addresses complex questions that may only be answered through the work of multidisciplinary teams, often based at multiple institutions. The Trust helped to create such a team through its support for the UK CF Microbiology Consortium (see 'What?', page 23). It will build from this experience and create further consortia as strategic research centres by encouraging the formation of the multidisciplinary teams required to tackle a complex condition such as cystic fibrosis.

In the first year, the Trust will run a competitive research call to support two of these new centres. Funding will typically support five young career scientists (PhD studentships, research assistants or early postdoctoral scientists) to bring together the best team of key scientific experts, wherever they are based, and thereby form a cohesive group intent on using research to solve problems in cystic fibrosis.

Under this initiative, the Trust plans to fund each centre up to a total of £750,000 over three to four years and will have sufficient lead time to attract the brightest and best young scientists into problem-solving research for cystic fibrosis. Previous experience indicates that this approach creates a closely-knit community of scientists, many of whom go on to spend their careers working in this field. The centres will be encouraged to bring in additional graduate students through use of funding from local university awards, industry and other funding bodies.

Delivering our new strategy

- Virtual centres of excellence
- Venture and innovation fund
- Research sandpits
- Supporting clinical trials
- Governence of research investments

Venture and innovation awards

The Trust will establish venture and innovation awards that will offer an agile and timely response to new opportunities. The success of these awards will depend on their ability to draw additional funding from other agencies, including industry, research councils, the NIHR, biomedical research charities and others. These awards will only be used for leverage to direct funding from external sources into cystic fibrosis research within our strategic priorities.

At least 50% will be used to support transformational research projects in partnership with other agencies. The trust will look to support collaborative projects with senior scientists working outside the biomedical sciences who have not previously applied their knowledge to the problems of cystic fibrosis treatment and management. This is likely to take the form of collaborative joint research calls with the external agencies, or of pump-priming with the Trust providing seed funding to demonstrate the feasibility of a project, before other funding bodies assume responsibility for its subsequent development.

Research sandpits

An important part of the Trust's long-term strategy is to be alert to new developments and be ready to respond (horizon scanning). "Research sandpits" are a proven mechanism, used by the government-funded Research Councils and others, to stimulate new thinking and innovation. They have become particularly effective as a way to fertilise the cross-disciplinary approaches required to find solutions to complex biomedical problems.

The concept is to identify a topic where the expertise within the cystic fibrosis research community is thin – such as "smart electronics" – and create an environment for experts in the field to meet with established cystic fibrosis researchers to assess the feasibility of working together to crack a major problem. Areas amenable to such an approach could include: applications of biomedical engineering; novel smartphone apps for teenagers to manage adherence; electronics industries; better predictive diagnostics and devices for remote care at home; development of new antibiotics; new innovative approaches to biofilm formation; understanding of emerging lung infections; the use of induced pluripotent stem cells; genomic editing technologies; nanotechnology; and synthetic biology. Promising ideas may then be the subject of joint research calls in collaboration with other funding organisations.

Supporting clinical trials

Evidence-based approaches to optimising treatment are now well-established within the UK.[13] Clinical trials are the bedrock of translational research and are essential to establish the evidence to inform clinical practice and also to attract the appearance of new therapies at an early stage to the UK.

Due to the huge cost of late-stage clinical trials, these are usually supported by the larger public funding bodies such as the NIHR and MRC or through private investments by the biopharmaceutical industry. Nevertheless, the Trust still plays a significant role through its support for early-stage pilot studies and in helping to organise later studies (Phase 2b and Phase 3) by building capacity for research in clinical trials in the clinics and in-house. This year, the Trust will run a competitive research call in the UK for funding of research coordinators. ▸

13: http://www.cochrane.org/

"Research is important to me because I want to find a cure that would give us the opportunity to change ALL of our futures."

Sam Norman

From Manchester

The Trust also plans to use its website to provide clear information on clinical trials to people with cystic fibrosis and their carers. Additionally, the Trust will recruit in-house expertise to assist the uptake and delivery of clinical trials within the UK. Such expertise can be used to engage people with cystic fibrosis and their carers with trial protocol design and to help physicians navigate efficiently some of the current roadblocks to the adoption of clinical trials, such as the need for multiple regulatory approvals for multi-centre trials involving many different hospital trusts. The staff responsible will forge links with the existing Clinical Trials Networks in the UK and in Europe.

Governance of research investments

The Trust will restructure the governance of its research by establishing two committees to replace the existing Research Advisory Committee. These two committees will have broad representation from within the cystic fibrosis community but also involve outside experts. The members will have clear roles and responsibilities, and provide advice to the Trust's Executive and Board of Trustees.

The new Strategy Advisory Board will be responsible for oversight of the research strategy implementation and measuring success of the new strategy. In addition, this new Board will ensure the resilience and adaptability of the research strategy by highlighting new developments in biomedical sciences that could have an impact on cystic fibrosis.

The new Strategy Implementation Board will be appointed to manage the peer-review process to ensure fairness, transparency and ensure recommendations for funding achieve the Trust's SCORE objectives (see 'What?', page 18). It will be tasked with judging how well funding applications meet the Trust's criteria prior to making recommendations to the Executive.

The Trust supports the positions of the Association of Medical Research Charities on issues such as the use of animals in scientific research, the registration of clinical trials and publication of findings. It will award grants under the terms and conditions consistent with those of other public funders and biomedical charities such as the Wellcome Trust. ■

When?

The Trust's research strategy for 2013–2018 was published in April 2013. In addition to describing what the strategy is, and how it will be delivered, the strategy also sets out what the Trust intends to deliver over the first year (2013–2014) and over the strategy's full five-year duration.

What happens now

In the financial year 2013–14 the Trust will:

- run a competitive research call to announce the funding of two strategic research centres for multidisciplinary and, where necessary, multi-institutional teams equipped to address a significant problem for cystic fibrosis and find solutions.
- establish the venture and innovation awards scheme and use this effectively to leverage funding from other sources. At least 50% will be used to promote transformational research projects in partnership with public and private organisations.
- identify and run two research sandpits. If successful, we will use the research sandpit output to run a joint research call with at least one other agency in the following financial year (2014–15) using the venture and innovation awards.
- run a competitive research call to part-fund five research coordinators in cystic fibrosis clinics and recruit a research coordinator to build in-house capability.
- undertake an external review of the UK CF Registry, which will include assessing access to Registry data for research and how to link the Registry to the new developments and networks developed by the Department of Health and MRC. The outcomes of the review relevant to research will be implemented.
- make significant efforts to build relationships with other stakeholders in clinical and basic research, key research funding bodies in the UK and overseas, and other cystic fibrosis organisations and industry, including biopharmaceuticals, devices and diagnostics.
- raise the profile of research and clinical trials on its website.
- establish the two new research advisory boards (Strategy Advisory Board and Strategy Implementation Board).
- establish new forms of interactive communication about research and clinical trials, aimed at enhancing engagement with and providing better information to people with the condition and their families.

2013

Our research strategy

- strategy launch April 2013
- five year duration

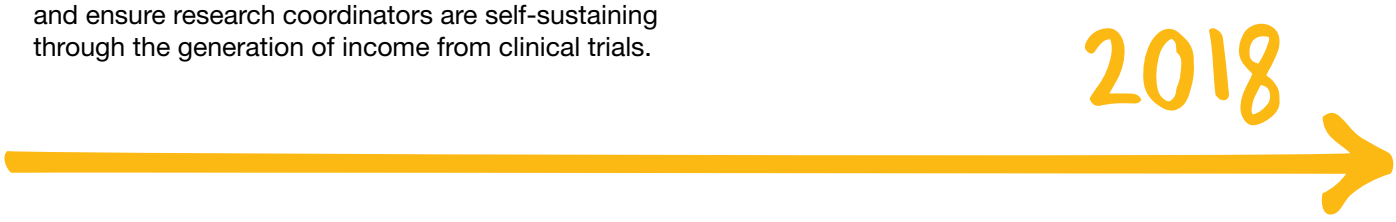
What happens next

Over the next five years, the Trust will:

- create a cadre of at least 30 young scientists through the formation of six strategic research centres. Through leverage, at least an additional six PhD studentships will have been secured through non-Trust funding. At least one of the strategic research centres will have demonstrable links with industries and at least two will have attracted talent from the non-biomedical space to address cystic fibrosis questions.
- raise the gearing of the venture and innovation awards scheme to 1:5 – so for every £1 invested by the Trust an additional £5 will have been secured from outside sources to support research in cystic fibrosis.
- develop a collaborative project with a major investor such as a biopharmaceutical company or major funder (for example, the MRC, Wellcome Trust or CFF) in transformational space to develop new therapies.
- leverage funding and bring innovative thinking to cystic fibrosis research by running successful research sandpits in collaboration with external funders (public or private) that lead to two collaborative joint research calls with the funding agencies.
- increase the number of clinical trials threefold through investments in clinical trials, whether industry sponsored or supported by public funding, and ensure research coordinators are self-sustaining through the generation of income from clinical trials.
- raise the quality of the trials by assisting with their adoption nationally through the cystic fibrosis clinics and so increase recruitment rates.
- promote the value of clinical trials among people with cystic fibrosis and their carers, and ensure its website is an authoritative and informative source about clinical trials (measured by hit rates and references).

This strategy is designed to guide the Trust's work over the next five years. It is, however, vital that the Trust remains flexible and adaptable to respond to changing circumstances and the wider landscape. The Trust will seek advice from the Strategy Advisory Board and will also adopt a consultative approach so that the views and opinions of stakeholders are heard, including people with cystic fibrosis and their families.

If you have any comments on the Trust's Research Strategy, please email research.strategy@cysticfibrosis.org.uk



"Research is important to me because it ensures there is a positive future for my little boy and the many children out there like him."

Reiss, aged 6

From Merseyside

Quote from Reiss's mother, Deborah

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Cystic Fibrosis investing in research to change lives

"Research is important to me because it means I can ride my bike for longer. Without the research into ivacaftor this wouldn't have been possible."

David Noonan

From Coventry

Ivacaftor is also known by its brand name Kalydeco