Cystic Fibrosis investing in research to change lives

Appendix: Analysis of the last five years strategy (2013–2018)

Cystic Fibrosis Trust
Research Strategy 2013–2018
Appendix: Analysis of the last five years

Contents

Executive summary

The Cystic Fibrosis Trust's first research strategy published in April 2013 came to an end in April 2018. We have analysed our performance in delivering the research investments programme set out in the Research Strategy 2013–2018 to help shape the strategy for the next five years (2018-2023). Presented here is the outcome of this analysis. Overall, the research strategy 2013-18 has delivered against the majority of its objectives.

		What we said we'd do in 2013	What we did by April 2018
Funding mechanisms	1	**Fund Strategic Research Centres (SRCs)** – these were designed to be international, interdisciplinary research groups tackling problems important to people with cystc fibrosis (CF). To ensure the growth of the pool of CF researchers, an important aim was to create a cadre of at least 30 young scientists through the SRC structure.	Funded 14 SRCs,three of which are in the final stages of completion and two were newly awarded in March 2018. These SRCs comprise 96 investigators, spread over 35 institutions and 14 countries. In addition, 41 young scientists have been or still are employed through the SRC structure so far. Although not described in the research strategy, the SRCs have brought in immense added value to CF research, leveraging access to infrastructure and additional funding.
	2	**Fund Venture and Innovation Awards (VIAs)** – these were designed to leverage external financial support into CF research.	Funded 56 VIAs. Leverage with academic institutions, other medical research charities, government funding bodies, Biotech and Pharma. For every £1 we've spent, we've leveraged almost £4 of external funding, bringing in over £12 million of external money into CF research.
	3	**Run Research Sandpits** – these were designed to stimulate innovative thinking and bring new disciplines into CF research to address issues that are of importance to people with CF but not adequately covered by current research.	Held research sandpits – the GI sandpit held in 2016 generated two SRCs tackling GI problems in 2017.
	4	**Increase the capacity for clinical trial research in the UK.**	Initially funded research co-ordinators which lead to the Clinical Trials Accelerator Programme, now a freestanding flagship programme.
Underlying priorities	5	**Establish governance structures to ensure fair and transparent governance of research.**	Established the Strategic Implementation Board (SIB) to ensure governance of research awards and the award process. Established the Strategic Advisory Board (SAB) to advise on strategic direction of research investments.
	6	**Establish new ways to engage and involve people with CF and their families in research.**	CF's Got Talent: This event promotes the communication of research in a lay-friendly manner to the CF community. Funded the James Lind Alliance Priority setting partnership: to identify priorities for research identified by people with cystic fibrosis. SIB: Increased representation of people with CF and their carers on the board of SIB since its inception in 2013. Research Impact Advisor: dedicated to communicating our research stories.

Research Strategy 2013–18 overview

The 2013–18 research strategy outlined a number of overarching principles that defined the investment opportunities for research by the Trust.

- **S = Strategic**
- **C = Collaborative**
- **O = Outcome based**
- **R = Risk based**
- **E = Excellence**

In addition, the Trust created a new governance framework consistent with the sector guidelines on research management. In particular, two new structures were established with clear terms of reference.

1. **Strategy Implementation Board:** to provide the academic oversight and review of applications for grants
2. **Strategy Advisory Board:** to provide oversight of the research strategy as a whole and to provide a forum for horizon scanning to make recommendations on future directions

A key element of the research strategy was to devise funding routes that (i) maximised impact for people with CF and (ii) provided mechanisms to use Trust funds to leverage additional support for CF research from external agencies.

The strategy articulated two general areas for research; research for today, research for tomorrow. These two themes were described to ensure funding of a balanced portfolio of research with elements that everyone with CF can identify with. Crossing both themes, three enablers were described:

Two research themes	Three enabling priorities		
1. Investing in tomorrow by backing transformational science to correct the basic defect.	**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**
2. Investing in today to help allieviate and manage the symptoms of cystic fibrosis			

To achieve these aims, the research strategy established four new mechanisms to invest in research.

1 Strategic Research Centres (SRCs)

2 Venture and Innovation Awards (VIAs)

3 Research sandpits

4 Clinical Trials (initially research coordinators and later the Trials Accelerator)

1. Strategic Research Centres (SRCs)

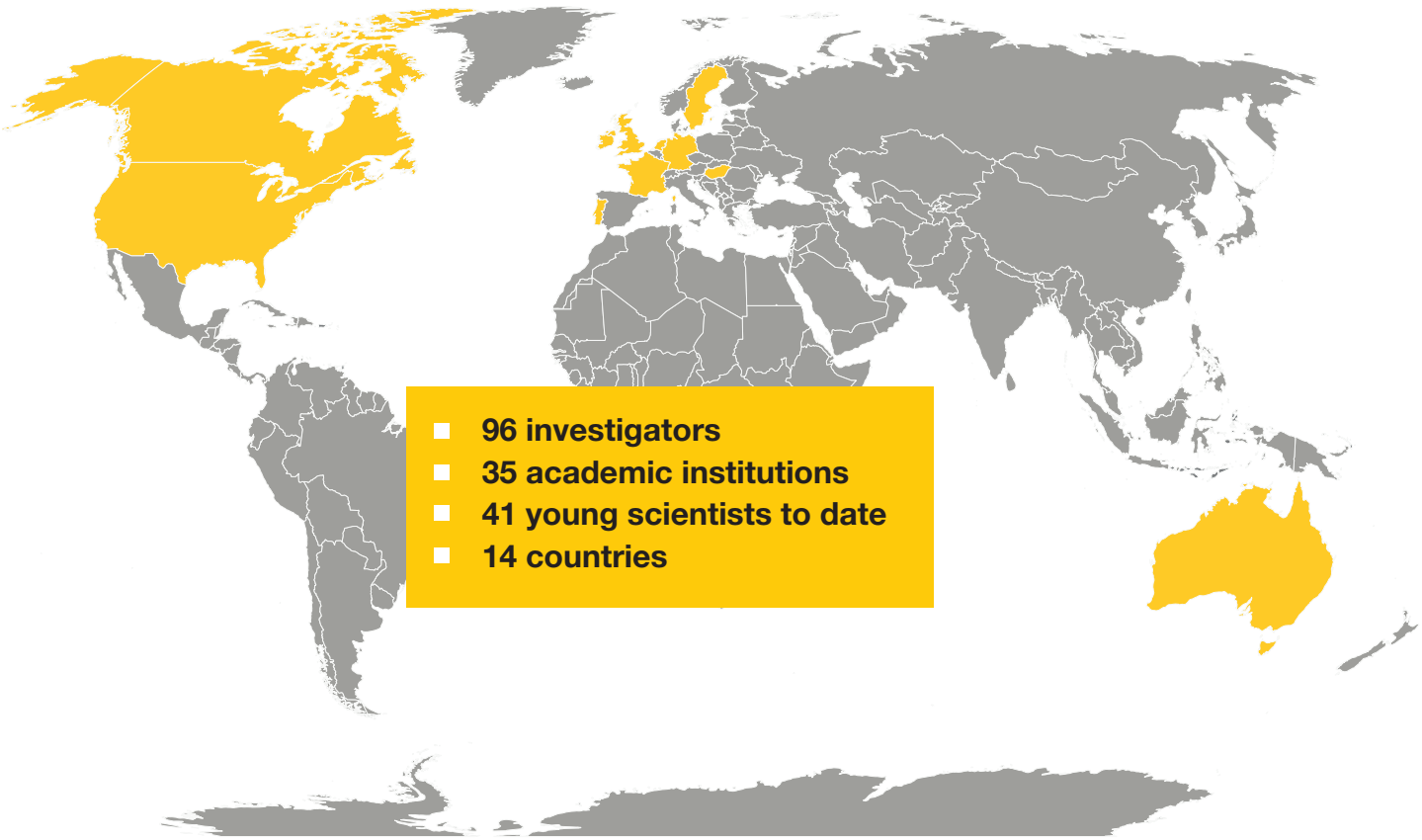
The vast bulk of the research budget was allocated to establishing Strategic Research Centres (SRCs). The aim of the SRC structure was to move away from multiple, small individual research grants that funded a lone early stage researcher to one that encouraged the development of multidisciplinary, international collaborative teams to use research to find solutions for issues that mattered to people with CF and create a framework for excellence in training for early stage researchers.

Over the last five years, the Trust has funded, on average, three SRCs per year. Details of the funded SRCs can be found on the Trust's website[1]. Each SRC was capped at £750k funding from the Trust.

A key question asked by people with CF in advance of the strategy published in 2013 related to why the Trust only funded researchers based in the UK. There was a sense that the CF community wanted to ensure that the Trust invested in the best scientists worldwide. The SRC mechanism therefore has encouraged the formation of international teams to bring together the best talent.

By necessity, each SRC has to be led from the UK. However, SRCs have given the Trust the ability to ensure talented researchers outside the UK can be funded to contribute to the scientific effort.

How have we funded?



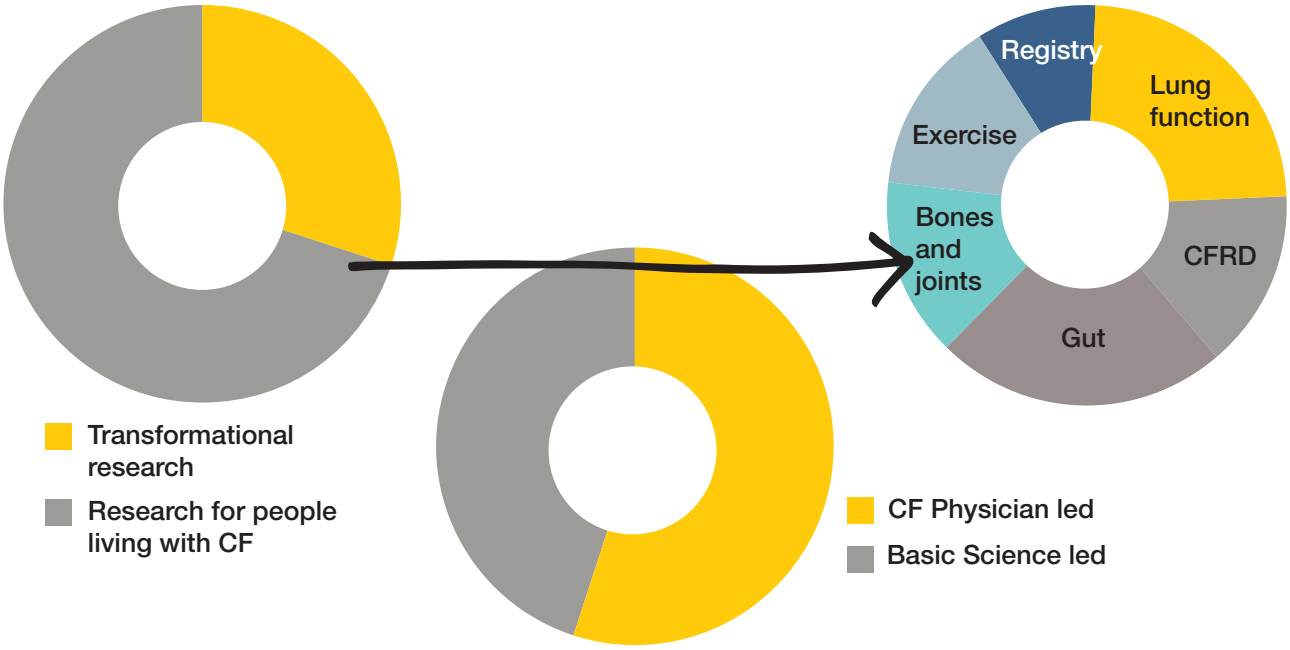
[1]www.cysticfibrosis.org.uk/src

What have we funded?

Of the funded SRCs, three are in the area of transformational therapies (research theme 1) with the majority focussing on research to address the consequences of living with CF (research theme 2). In keeping with the aim of a balanced portfolio of research, these address a variety of problems identified as important by people with cystic fibrosis.

The research strategy does not distinguish between basic science or clinical science but has attempted to ensure integration.

Strategic Research Centres: A Balanced Portfolio



The impact of our funding so far

The first tranche of three SRCs began officially operating at the end of 2014/beginning of 2015. These are drawing to a close and, although it is still too early to determine impact (this takes on average 10–15 years), the SRCs have already been very successful. Apart from publishing their research in academic journals, each SRC has shown the beginnings of impact in distinct ways.

The formation of **SRC001** has led to a number of collaborations with biopharmaceutical industries exploring the development of novel methods for treating P. aeruginosa. The expertise and tools developed as part of the SRC has ensured that this work focuses on the P. aeruginosa isolated from people with CF and any drugs are rigorously tested in conditions that mimic those found in the CF lung, thereby ensuring drug development is appropriate.

The collaborative structure of **SRC002** led to the development of North American/European consensus recommendations for the diagnosis and treatment guidelines for people with CF infected with non-tuberculous mycobacteria (NTM) (www.ncbi.nlm.nih.gov/pubmed/26666259). In addition, this group have used genomic sequencing and bioinformatics to identify transmission of NTM and the development of virulence.

Consortium work on **SRC003** has led to collaborations with several industrial partners to look into the potential of using novel chemicals to change the function of non-CFTR 'rescue' channels that may work alone, or complement the effects of CFTR modulators, to improve anion and fluid transport in CF cells.

Although **SRC004** is still underway, a recent paper has produced flexible survival estimates for people with CF that can be used to inform needs in healthcare.

What do researchers in the SRCs think about the SRC structure?

We recently canvassed for opinions on the structure of the SRCs from the research teams to understand whether this structure hindered or helped drive impactful research.

Prof Jane Davies, Royal Brompton, London, PI SRC001: "The impact conferred by the term 'Centre' can't be under-estimated. It has benefits for the reputation of the host institution, and this has been recognised in our case with the senior academic appointment. But also, the external recognition of such a collaboration is high. From the second year on, we began proactively to focus on synergy between projects, which has led to substantial cross-fertilisation and a genuine feeling of collaboration, rather than a number of individual siloed projects."

Dr Patrick Harrison, Cork, Ireland, co-PI SRC006: "Being part of a bigger grouping is starting to raise the profile of the research and when you introduce your people as being part of the SRC, they seem more willing to be involved in a collaboration. Research needs critical mass to succeed and the SRC helps provide that. The fact that several SRCs have US-based PIs is really important for the global impact. The US CF foundation are now well aware of the Trust's SRC model and other US researchers are gaining a growing awareness of the scheme and interest in interacting with a broader range of collaborators. This is great not only for research but for encouraging and facilitating future training opportunities (ie post-doc positions) for PhDs currently working in SRCs. Being part of the SRC gives me an extra layer of credibility in the process of applying for such larger grants from non- CF sources".

Dr Catriona Kelly, co-PI SRC007, Ulster: "The SRC provides access to additional sites, resources and expertise that I wouldn't have been able to access on my own. If I would like to address a question and don't have the equipment or resources to do so, an SRC partner will, and all members have been very generous in helping each other out."

It can be really difficult to run the SRCs especially when scientists are not in the same country. We asked our overseas participants for their thoughts on the SRC structure.

Some comments from overseas participants

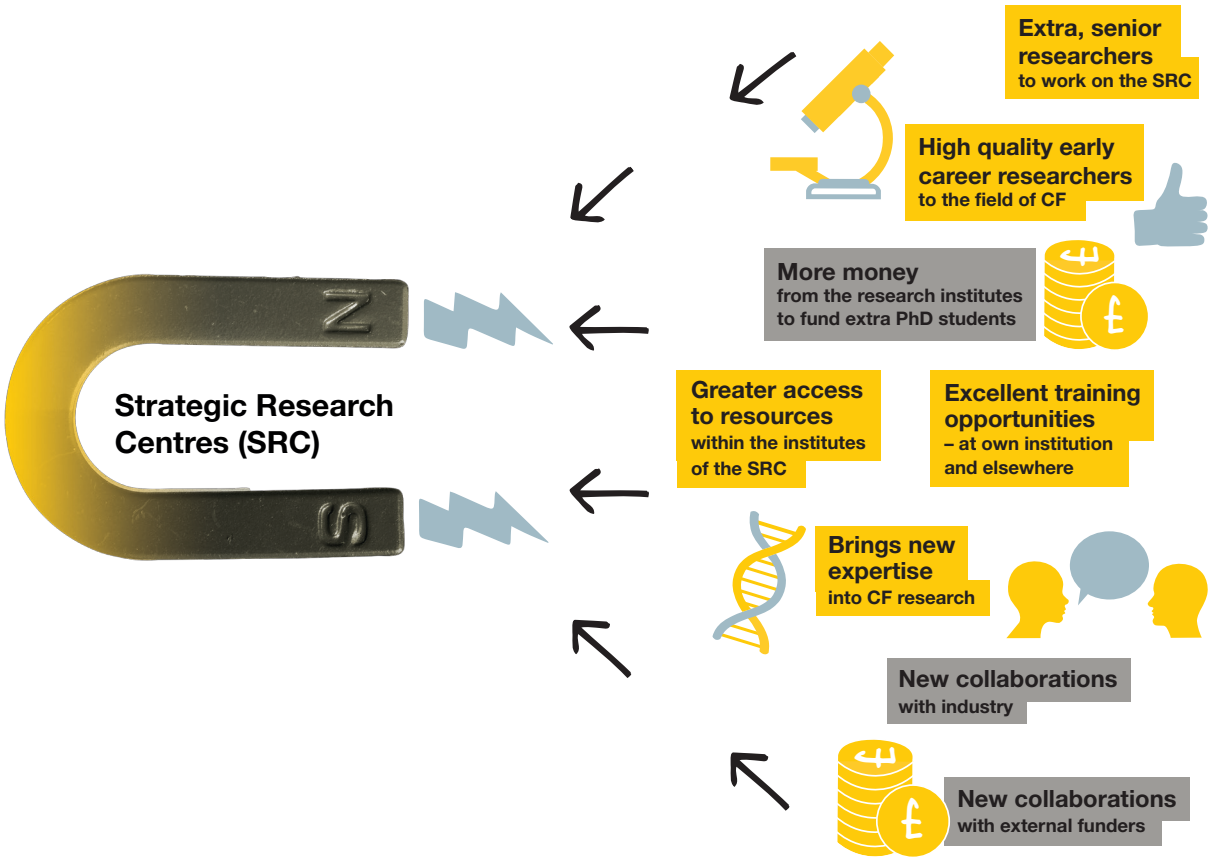
Prof Mary Jackson, co-PI SRC020 and 010, Colorado State University, USA: "The SRC structure has allowed me to initiate new collaborations with some of the best experts in the world to address the specific issue of nontuberculous mycobacterial (NTM) infections in CF patients. It allowed me to engage in CF research for the first time. I learn much about CF and I feel like the SRC program allowed me to refocus my NTM research on the most medically relevant issues."

Prof Hugo de Jonge, co-PI SRC011, Erasmus University, Netherlands: "A great aspect of the SRC initiative is its crossing of boundaries between nations, which is very unusual for a national CF foundation but allows the recruitment of specialists within a certain research area regardless of their location in the world. Compared to most other CF-focussed grants, the funding is very generous and sufficient to allow both basic and translational research (except expensive clinical trials) at a fairly high level. The SRC funding may also promote continuous collaboration between the various labs even after the funding period is expired".

Dr Sanja Stanojevic, co-PI SRC004, Hospital for Sick Children, Canada: "I really think the overall program is fantastic. It provided me an ideal opportunity to build on existing collaborations and meet new people outside of my immediate network of collaborators. The funding provided for PhD students is an excellent way to introduce new investigators into CF research. The collaborative network has been critical to providing additional support/ideas to students/projects, which has resulted (in my opinion) in better projects that are more thoroughly conducted and results are better interpreted".

Prof John Engelhardt, co-PI SRC 007, University of Iowa, USA: "The interactions with European SRC members would not have occurred at the level it is happening without this grant. In some cases this has avoided duplications and in other cases allowed for greater focus on what are the likely mechanisms at play (ie avoided going down dead ends in research directions that will likely no pan out)".

Unexpected added value of the SRC structure



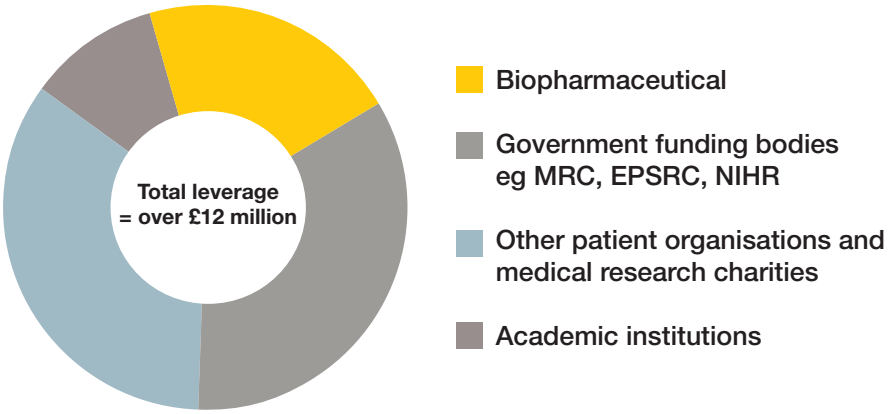
The SRC structure has additionally demonstrated a number of unexpected valuable outcomes.

- The network of influence and cooperation is much wider than just the named participants within the SRC. In a number of cases, the SRC has acted as a nucleus to attract additional talented senior researchers to join the SRC despite the fact that these principal investigators receive no funding from the Trust. This equates to just over 20% of the co-investigators.
- The creation of the SRC global structure is an attractive drawcard for early stage researchers in selecting CF for their postgraduate and postdoctoral studies. The quality of these early stage researchers has been excellent and the posts have not been difficult to fill.
- The SRC structure has brought in access to infrastructure located in the institution of the investigators and made that accessible to all members of the SRC.
- The SRC has acted as a nucleus to attract core institutional funding such as PhD studentships from the block grant awarded to institutions. Approximately £3.2m non-Cystic Fibrosis Trust funding has been secured by our SRCs so far, supporting funding for additional early stage researchers.
- The multidisciplinary and international features of the SRC has provided the early stage researchers with excellent training opportunities and possibilities to train in other sites.
- Through the SRC structure, the biopharmaceutical and biotechnology industries have developed additional strong collaborations.
- The SRCs appear to have developed new collaborations that will seek funding from external agencies.
- SRCs have created a mechanism to draw senior academic researchers from outside the CF research world to address their talent and expertise to help address issues encountered by people with cystic fibrosis. More than half of the co-investigators associated with our SRCs are not historically associated with CF research but have been drawn in through the SRC structure.

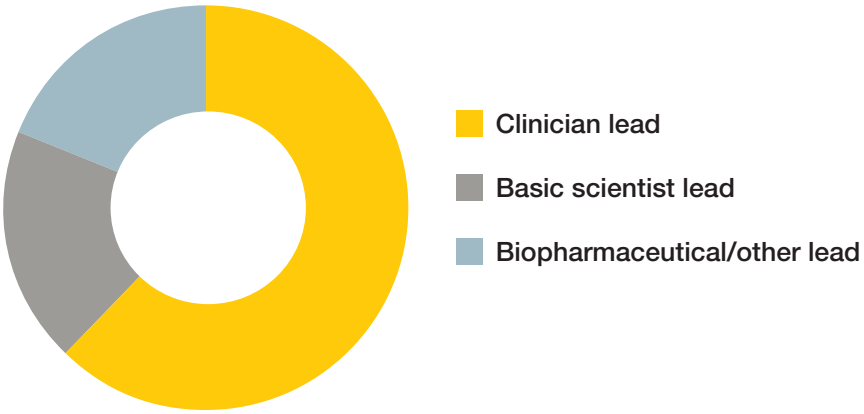
2. Venture and Innovation Awards

This funding stream was established to encourage more funding for CF from sources outside the Trust and to facilitate investment in translational research.

For academic researchers, the intent was to identify ways to support applications to other funding agencies such as the research councils, National Institute for Health Research (NIHR), the Wellcome Trust and other biomedical charities such as Action Medical Research. The VIA scheme has also provided a mechanism to manage ongoing support for the Wave 2 (viral delivery) programme by the Gene Therapy Consortium.



For translational research, the VIA offered a way for the Trust to co-fund small biopharmaceutical companies working in areas of strategic importance to cystic fibrosis. Over the five years, for every £1 invested by the Trust almost £4 from other sources has been invested in CF research, bringing into CF research more than an additional £12 million.



3. Research sandpits

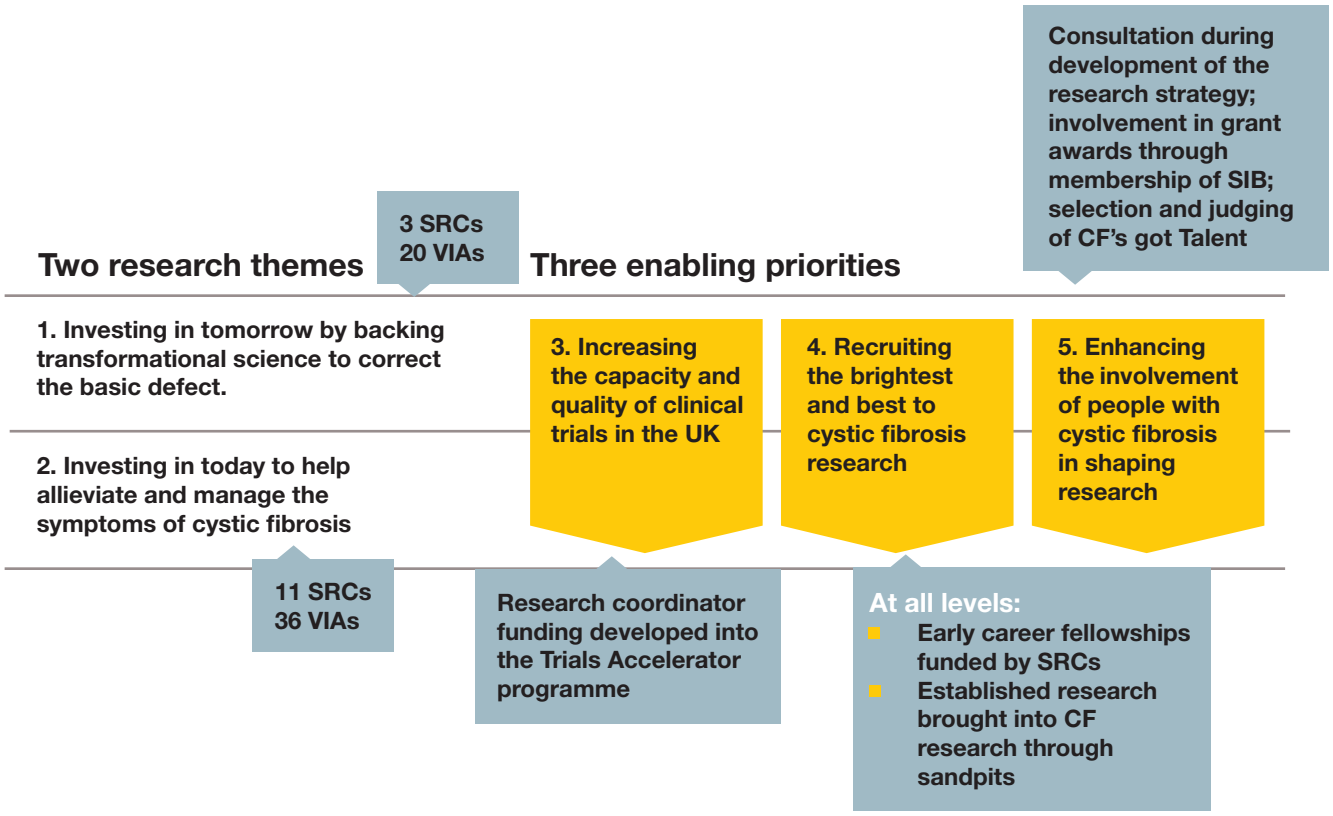
Research sandpits are interactive workshops that aim to drive a step change in research by fostering inter-disciplinary, lateral thinking research groups. Sandpits usually target under-researched areas that are considered of high importance.

Four sandpits have been run over the last five years. The first two sandpits were aimed at creating partnerships between industry, academic researchers and people with cystic fibrosis. The first was run in February 2014 to explore the use of remote monitoring to deliver healthcare. The second was focused on clinical trials and brought together other organisations who had developed clinical trial networks, people with CF and their carers, industry, regulators and key academic researchers.

The second two sandpits were focused on specific areas of research: the area of adolescence and understanding more about gastrointestinal tract-related symptoms of cystic fibrosis. These two sandpits preceded a strategic SRC call (alongside the response mode ‘open’ call). No awards were made following the call focused on adolescence as the proposals were not considered to meet the required excellence. By contrast, the call focused on the GastroIntestinal Tract in CF generated two successful applications. The difference may well relate to the timing of the research sandpits relative to the call for SRCs. This will be considered for future sandpits.

4. Clinical trials

A limited number of CF centres have been engaged in clinical trials at a national/international level. Provision of research coordinators alone failed to impact on the number of centres engaged in delivery of trials. The Trust therefore developed a business plan to boost participation in clinical trials; known as the Clinical Trials Accelerator Platform (CTAP). Funding ($3m) was realised in May 2016.



What else have we done in the last five years?

1. Involvement and engagement of people with CF

The research strategy has attempted to include people with CF and their carers at every stage of the process. At the outset the CF community had enormous influence in guiding the principles of the strategy that was published in 2013. The funding mechanisms were designed to respond to many of their comments; in particular the need to recruit the brightest and best talent and to bring in international scientists and expertise.

During the course of the strategy / in addition, various initiatives have been designed to improve involvement:

1. **UK CF Conference (UKCFC).** Over the last four years, the UK CF conference has been live-streamed and made available as archived files for later viewing. The conference has developed as a themed event that makes cutting-edge science accessible to people interested in hearing more detail. We have brought in international speakers to ensure the programme is less parochial.

2. **'CF's got Talent'.** In the margins of UKCFC, we have developed events to highlight the work of the early stage researchers employed through the SRCs. This is called 'CF's got Talent'. It has been run for the last two years and was established specifically for people with CF and their carers. It is managed via Facebook Live and provides a mechanism to link the CF community with early stage researchers funded by the Trust, working on the SRCs.

   The purpose is to help these young scientists to better communicate their work and its relevance to people who have the most understanding and knowledge of CF but may not have the scientific knowledge and

jargon. The emphasis is on communication. People with CF or their carers are the sole reviewers of the abstracts to select the best five or six to be presented and only the Facebook Live audience votes for the best presentation.

3. **The Trust co-funded the Priority Setting Partnership led by the James Lind Alliance.** This organisation provides a proven framework to work through the differing priorities for clinical research as perceived by the CF community. The outputs from this can be found on the web site2. Further work is now taking place to delineate these more finely.

4. **This year, the Trust has engaged an Impact Adviser whose main role is to ensure the Trust communicates our funded research.** The aim for this new post is to embed Trust representation in all Trust-funded research and to bring forward items of interest for publicity.

5. **The representation of people with CF and their carers on the Strategy Implementation Board has risen over the last few years.** This board is involved in the peer review and award of funding by the Trust to support the successful grants.

2. Flagship programmes

The Trust has been developing a number of flagship programmes that are not designed solely as research but have the potential to impact on many different aspects of the Trust's activity.

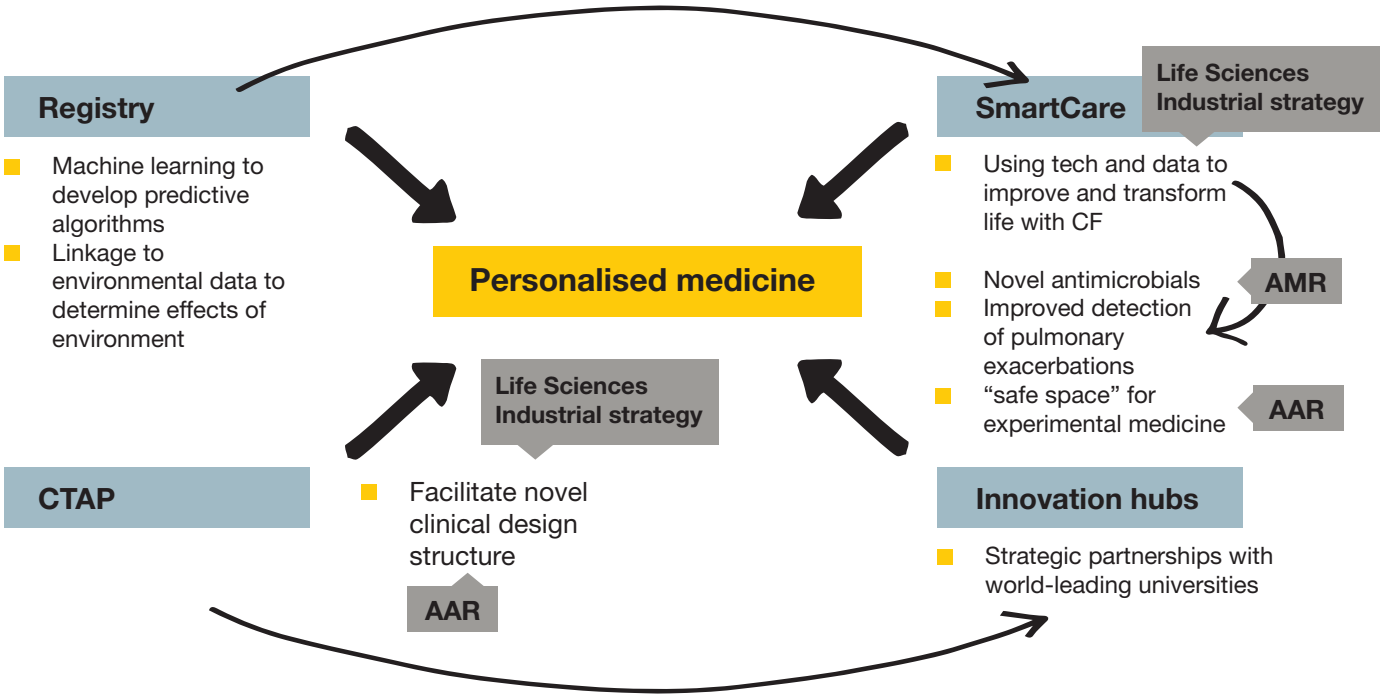
The flagship programmes are:

1. UK CF Registry	2. SmartCare CF/digital health	3. Clinical Trials Accelerator Platform	4. Innovation Hubs

Over the last year, the Trust has started to build on the success of the existing research strategy to develop the concept of Innovation Hubs. These are a mechanism for the Trust to create strategic partnerships with universities in crucial areas. The Innovation Hubs are new for the Trust but replicate similar developments for other charities such as the British Heart Foundation, the Wellcome Trust and Alzheimers Research. They are designed as true partnerships, with the Trust and the university sharing goals and objectives, funding and risks. The first hub has been established (February 2018) in partnership with the University of Cambridge to focus on lung health. Further hubs will be developed as part of the new strategy.

By integrating activity across the flagship programmes, the Trust has the opportunity over the coming five years to drive the Personalised Medicine agenda

Integration of research aspects of the flagship projects



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