Cystic Fibrosis investing in research to change lives

Research Strategy 2018–2023

Putting the person into personalised medicine

Cystic Fibrosis Trust
Research Strategy 2018–2023
June 2018

Contents

Putting the person into personalised medicine

Summary

The research strategy[1] published in 2013 has successfully met all its goals, thereby laying the foundations for the next five years (see appendix 1).

In addition, over the period 2013–2018, the strategy has evolved to develop four flagship research programmes:

1. **Research aspects of the UK CF Registry**
2. **Clinical Trials Accelerator Programme (CTAP)**
3. **SmartCare/Digital Health**
4. **Innovation Hubs**

Looking towards 2023, the coming five years will provide new challenges and opportunities for people with cystic fibrosis (CF). The next iteration of the research strategy needs to anticipate these challenges and put in place mechanisms to fund the best research to provide the evidence for solutions.

Research investments are a balance between response mode and strategic. Over the last five years, the major role for research was to increase the capacity of the basic and clinical science base, principally through support of response mode research. New strategic investments using funds restricted for use include the Clinical Trials Accelerator programme, SmartCareCF and the Innovation Hub based in Cambridge.

The research strategy of the Trust will deliver a buoyant, dynamic and internationally-respected research portfolio.

Over the coming five years, the Trust will continue this balanced approach but we are now well-positioned to grow our strategic investments through the development of strong partnerships with other external funders and the industrial sectors (including biopharmaceutical, biotechnology and HealthTech). This will allow novel ways for research to promote the four key priorities that will confront people with CF within the next five years:

- Securing and promoting **access to medicines**
- Ensuring the **quality of clinical care**
- Providing and promoting effective **day to day support**
- Ensuring we are **reaching all people with cystic fibrosis**

An important role for the Trust is to push the boundaries, demonstrating leadership and innovation to ensure research is excellent, timely and relevant. The development of the four flagship programmes has created a unique platform, placing the Trust in ‘pole position’ for research to address some of the key challenges that will confront healthcare over the next decade.

Thus, over the next five years, the Trust will ensure all available assets are best used to deliver an integrated solution to the challenges facing people with cystic fibrosis.

[1]www.cysticfibrosis.org.uk/the-work-we-do/research/our-research-strategy

The landscape 2018 and a glimpse into the future 2023

Where we are now and where do we need to be in 2023?

Background

The 21st century has been described as the golden age for biomedical sciences due to the culmination and coincidence of great advances in many diverse technologies. This is creating a paradigm shift in thinking for healthcare and the development of new therapeutic agents. Previous discovery programmes for both therapeutics and care worked at population levels and treatments were aimed to benefit the population average. In this century, Personalised Medicine is the goal for everyone, meaning that treatment and care are tailored to each individual person.

Building on the research investments over the past five years, the Cystic Fibrosis Trust is in a prime position to harness this extraordinary period of opportunity and can lead the step-change in thinking and execution that will benefit the lives of each and every person with CF to reach our goal of a 'Life Unlimited'[2].

Building on a strong base. "You spoke, we listened and we implemented". Delivery of the research strategy 2013–18

Launched in 2013, our research strategy created new mechanisms to maximise the value of research. Its overall aims were guided by people with CF and their carers. Their comments helped design the way the Trust invested in research through the development of four novel funding streams:

- **Strategic Research Centres:** To create interdisciplinary, international virtual centres of excellence for research experts to collaborate world-wide to solve issues important to people with cystic fibrosis.
- **Venture and Innovation Awards:** To leverage external funds into CF research, either from other funding agencies or working in partnership with the biopharmaceutical and healthtech industries.
- **Research Sandpits:** To bring new disciplines and activities from outside CF and integrate them into the CF space to address areas of importance to people with CF but not well-covered.
- **Clinical Trials:** To increase participation in clinical trials across the country.

These approaches have delivered extraordinary results and full details can be found in the appendix. The last five years have created a clear shift in culture for CF research in the UK, providing an excellent platform for the future.

Comments from the CF community in 2013:

- **"Don't put all your eggs in one basket = balanced portfolio"**
- **"Why fund only UK science? We want the best teams regardless of location"**
- **"Collaboration"**
- **"Make our funds go further"**
- **"Let us know what you are doing"**
- **"Maximise impact"**
- **"Ensure aspects of the research portfolio are relevant to all people with cystic fibrosis"**

[2]www.cysticfibrosis.org.uk/lifeunlimited

2018 What's New?

1. Tackling the root cause of CF. Disease modifying treatments

Over the last five years, our understanding of CF has come of age, facilitated by the appearance of genotype-specific **precision medicines**. Unlike all previous advances in treatment for CF, these new drugs are disease-modifying. Of these, only Ivacaftor (Kalydeco[3]) is available for routine use in the UK. Yet, this therapeutic alone has changed our understanding of how mutations effect cystic fibrosis. This drug was once restricted for use to people carrying the specific gating mutation G551D (approx. 5% of people with CF). Since then efficacy of Ivacaftor has been shown and licensed for use in people carrying other gating mutations.

However, in a highly significant decision[4], the US Food and Drug Administration (FDA) agreed to the use of Ivacaftor for people carrying an additional 25 mutations based solely on ex-vivo data (no clinical trial required). This is a landmark decision by the FDA following extensive interactions with the CF Foundation and demonstrates how strong thought-leadership can influence decision-makers.

The disease-modifying therapeutic pipeline is very rich and occupied by a number of companies including, not exhaustively, Vertex Pharmaceuticals, Galapagos, Flatley Discovery Labs, Novartis and Proteostasis. Dual combination therapies of Lumacaftor/Ivacaftor (Orkambi) or Tezacaftor/Ivacaftor (Symdeko) benefit people carrying two copies of F508Del. Triple combination therapies currently in the development pipeline show very promising results and will likely become licensed within the next two years. These triple combinations have demonstrated efficacy even in people carrying only one copy of F508del. If these data are confirmed in Phase 3 studies, disease-modifying drugs with relevance to over 95% of the population of people with CF in the UK will likely be licensed by the FDA in 2020/21.

Beyond disease-modifying drugs, the pipeline for CF is very rich. A key concern moving into the next decade will be to ensure that the industry retains the level of investment in cystic fibrosis. Barriers to continued biopharmaceutical interest will be: (i) delays and difficulties in drug development through clinical trials and (ii) failure of reimbursement.

2. Anticipated consequences of introduction of disease-modifying drugs.

The development of these new therapeutic approaches is likely to have a dramatic effect on the expectations of everyone involved with CF but principally on people living with CF and their carers.

The advent of disease-modifying drugs offers a true paradigm shift for people with CF and in the way CF will be managed. Longer-term follow-up of the effect of disease modifying drugs on CF progression in the USA (GOAL[5] and PROSPECT[6] studies) and in the UK (Registry)[7] have shown:

- Improved life expectancy (longevity).
- Significant reduction in pulmonary exacerbations.
- Changes in requirements for long term prophylaxis dependent on their condition at the time disease-modifying drugs are introduced.
- Improved nutrition.
- Improved well-being.

However, these disease-modifying therapies also create new challenges:

- The high cost of new medicines and therefore access by people with CF in the UK in a financially constrained health service.
- Provision of clinical care to a rapidly growing adult population of people with cystic fibrosis.
- Understanding that the long term clinical management needs of people with CF will vary according to the time in their lives that disease-modifying drugs are introduced – the 'one size fits all' model of care will no longer apply.

[3]www.cysticfibrosis.org.uk/the-work-we-do/campaigning-hard/stopping-the-clock/kalydeco
[4] www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm559212.htm
[5]www.cff.org/Trials/Finder/details/430/GOAL-e2-Lung-Clearance-Index-study-in-children-who-have-a-CFTR-gating-mutation
[6]www.cff.org/Trials/Finder/details/375/PROSPECT
[7]www.cysticfibrosisjournal.com/article/S1569-1993(17)30976-1/pdf

- Significant rise in co-morbidities associated with longevity:
  - Cancer.
  - Diabetes and associated metabolic and cardiovascular complications.
  - Psychosocial and ethnographic consequences.

As research takes years to deliver, the strategy for the coming five years needs to consider where research investments can be best used to provide the evidence to help solve these new challenges.

3. Significant changes in the wider external environment

There is a vibrant research environment outside CF and the Trust will continue to tap into this to ensure that new approaches benefit people with cystic fibrosis.

There is a global shift towards interdisciplinarity in the life sciences with incorporation of mathematics, data science (machine learning and artificial intelligence), economics, biomedical engineering, nanosciences, physics etc. The Trust has responded to this shift and has already identified key areas and initiated joint research programmes.

Of critical importance, the UK government has also identified the life sciences as a key sector for further investment and growth. The **Life Sciences Industrial Strategy**[8] provides a blueprint to ensure that the UK PLC innovation engine gains traction for translation to benefit the UK.

Examples where the Trust has already invested outside traditional life sciences:

- **Chemistry:** novel, state of the art approaches to antimicrobial design
- **Bioinformatics:** global analysis of non-tuberculous mycobacteria (NTM)
- **Alan Turing Institute:** predictive modelling based on registry data
- **Microsoft Research:** Machine learning

Additional recent reports highlight areas identified by the UK government as key areas for attention:

- The appearance of **antimicrobial resistance (AMR)** is of major concern world-wide and critical to the provision of healthcare in the UK. The report[9] written by Lord O'Neill addressed the question, "Why is it so difficult to find new antibiotics?" from an economic perspective.

> **"Antimicrobial resistance poses a catastrophic threat. If we don't act now, any one of us could go into hospital in 20 years for minor surgery and die because of an ordinary infection that can't be treated by antibiotics. And routine operations like hip replacements or organ transplants could be deadly because of the risk of infection."** Dame Sally Davies[10].

- The **Accelerated Access Review (AAR)**[11] asks why it takes 10–15 years to develop new drugs. The expense of the traditional drug development pipeline deters innovation, results in risk avoidance and contributes, in part, to the high cost of new drugs. This report makes strong recommendations and places the individual at the heart of the process.

- The **Five Year Forward View**[12] and **Personalised Health and Care 2020**[13] documents begin to address at a strategic level, the issues of sustaining provision of healthcare.

All these reports give insight into government thinking and development of policy. Frequently, as a consequence, the Government invests in infrastructure and directs support to deliver its goals. For instance, the Government will invest £2.4b to deliver the Life Sciences Industrial Strategy. Their target is not CF but rather conditions that affect millions of people in the UK such as oncology, cardiovascular and dementia. Yet all these reports have relevance to cystic fibrosis. As such, the Trust needs to remain alert and plugged into these initiatives and will need to engage proactively with these initiatives, otherwise people with CF will not benefit. This will be a key focus of the Trust's work to influence government policy over the life of this strategy.

[8]www.gov.uk/government/publications/life-sciences-industrial-strategy
[9]https://amr-review.org/
[10] http://bsac.org.uk/antimicrobial-resistance-poses-catastrophic-threat-says-chief-medical-officer/
[11]www.gov.uk/government/publications/accelerated-access-review-final-report
[12]www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf
[13]www.gov.uk/government/publications/personalised-health-and-care-2020

So, what does the Trust do now?

The core fundamental principles for the delivery of the research portfolio for CF were established in 2013 (see Appendix 1). These core principles are still as relevant today as they were in 2013. Importantly, funding routes were established that have successfully driven capacity building of world-class researchers, a wider diversity of academic disciplines applied to CF and a change in behaviour of the research community to align to the goals of the Trust and people with cystic fibrosis.

General principles to take us successfully to 2023

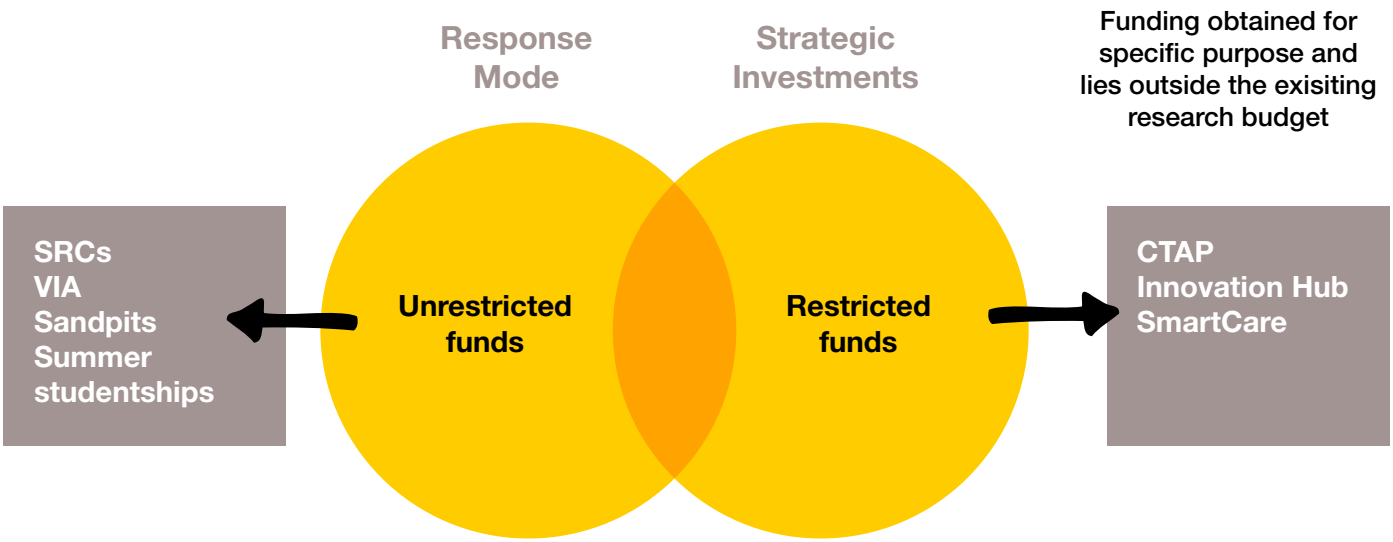
Balance between response-mode and strategic investments

The building blocks have been established and it is now a matter of using these to deliver further impact and change. Maintaining a balanced portfolio is key to success but, over the coming five years, the Trust will play a more directive role to ensure strategic alignment between the world-class research community and the new challenges posed by the advent of disease-modifying drugs.

While response-mode funding will continue, the balance between this and strategic investments needs to shift in favour of targeted strategic investments, but this must not be at the expense of excellence.

Bearing in mind the comments of the community "not to put our eggs in one basket", the balance between physician-led and basic science-led research must be maintained.

Across the entire research portfolio, the standard of excellence must remain our benchmark for the Trust-funded research to remain respected and to facilitate partnerships and leveraged income.



Excellence must underpin all decision-making

In terms of general principles, SCORE (Strategic, Collaborative, Outcome-focused, Risk-based, Excellence-driven) remains highly relevant. However, moving forwards to 2023, it will be essential for the Trust:

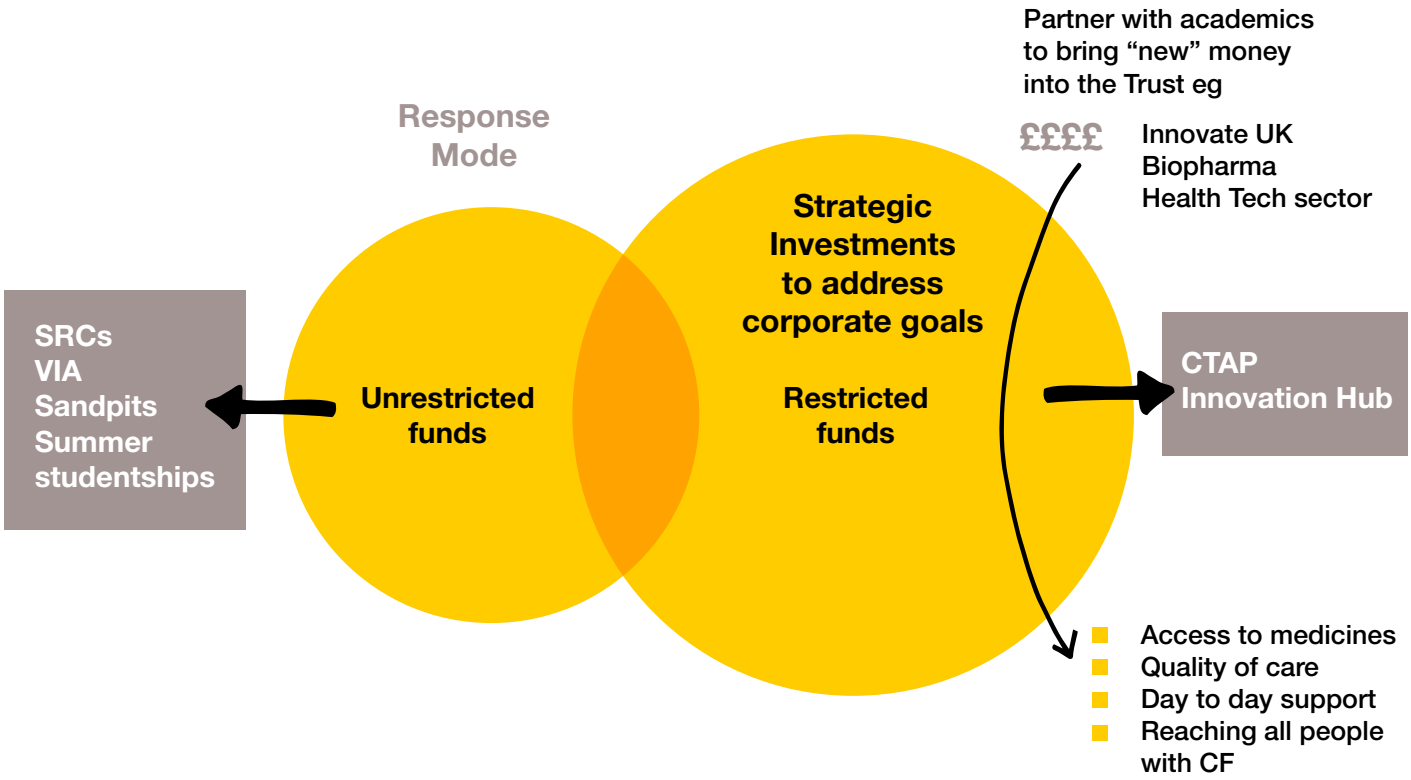
(i) **To maximise the impact** of its investments for the benefit of people with cystic fibrosis. This is particularly relevant for the flagship programmes which were developed to enable the Trust to meet some of the future challenges.

(ii) **To develop strong partnerships** to exploit the recognised world-leading expertise in the UK for life sciences and the life sciences industrial environment, both financially and intellectually. There are enormous opportunities for the Trust to develop thought-leadership and use research to promote the activity of the Trust. Although CF affects only a small percentage of the population, it is a particularly well-defined and information-rich population. This poises CF as the exemplar condition to address aspects raised by these government reports.

(iii) **To work with the biopharmaceutical industry** to maintain their level of research investment in CF and identify areas where research can make an impact on people with CF but lies outside the scope/interest of the industries.

(iv) To use research to maximise relationships with the emerging and fast-moving **Digital and Healthtech** industries

Anticipated growth in strategic investments over the period of the research strategy (2018–2023)



Excellence must underpin all decision-making

Expanding on the foundations created by the first strategy

The existing funding mechanisms will be continued but with modifications to improve their strategic fit to the Trust's corporate plan.

Whether or not the next generation of disease-modifying drugs become available for use over the next five years, the following key issues, among others, have been identified as requiring research investments:

- Progressive lung damage (Pulmonary infection and inflammation)
- CF-related diabetes and associated metabolic and cardiovascular complications
- Co-morbidities associated with longevity (Cancer; Mental and emotional health)
- Burden and complexity of care
- Role of regenerative medicine +/- gene therapies

However, the next generation of disease-modifying drugs provide hope for the vast majority of people with CF and their families.

Key issues that these new drugs will pose for people with CF are:

- High cost of new medicines limiting their access to all eligible people with cystic fibrosis;
- Provision of healthcare under the existing model for a rapidly expanding number of adults with cystic fibrosis;
- Evaluating the consequences early on and necessity for existing medications/treatments/ polypharmacy for individuals depending on the age new therapies are introduced. The burden and complexity of care was identified as the key priority through the Priority Setting Partnership managed by the James Lind Alliance[14].

There are additional issues equally important but with less obvious immediate impact on people with cystic fibrosis:

- How to ensure the continued investment of the pharmaceutical industry in developing new therapies to tackle cystic fibrosis. The first drug or drug combination is not always the best possible treatment option for a condition. It will be important for the Trust to create the environment within the UK to encourage companies to remain innovating in cystic fibrosis. The creation of CTAP provides a mechanism to engage with companies and ensure that these new medicines are available to people with cystic fibrosis.
- Understanding better the biology of CFTR (in tissues and organs not normally associated with the CF phenotype).

The existing funding mechanisms that have been so effective since 2013 can be used to address many of these issues but new ways of thinking and delivering are required to tackle some of these bigger ones.

Delivery of research using existing tools.

Although partnerships are an excellent way of delivering strategic imperatives, it is equally important to manage a balanced portfolio for research. We will therefore continue the existing programmes that have delivered so well against the previous objectives for the charity research strategy. The Trust needs to remain open to new approaches and ideas.

Strategic Research Centres (SRCs): The Trust will build on the success of the existing SRC programme modifying the call to take us forward from 2018. Key characteristics that will be retained and enforced are:

- Multidisciplinarity
- Internationalisation
- Strategic relevance to people with cystic fibrosis – impact plan
- Training, reporting and governance

In addition, every year the call for applications will combine the 'open' call (response mode) and a 'strategic' call. The focus of the latter will be proposed annually by the Research Scientific Advisory Board through horizon scanning in consultation with the Trust. To draw in the necessary expertise, **research sandpits** will be reconfigured to provide small pump-priming grants to better position the sandpit outputs to gain funding either directly from the Trust SRC programme

[14]www.cysticfibrosis.org.uk/news/your-research-priorities-revealed

through our competitive peer review process or from other funding agencies such as MRC, Wellcome Trust, NIHR, EU. This mechanism has the added-value of raising the profile of CF research within these agencies.

Creating a cohort of the "brightest and best" early stage researchers was a key objective (now met) of the initial strategy. In the coming five years, the Trust needs to ensure this cohort are offered the career opportunities to become the next generation of academic CF researchers. This is best achieved through staged autonomy via **career development fellowships**. In the first instance, we will explore working in partnership with other funding agencies such as the MRC and NIHR.

Venture and Innovation Awards (VIAs): This scheme was designed to attract more funding from other agencies to CF research and so use the funds of the Trust as leverage. This scheme has proved successful and will continue. The scheme has also allowed the Trust to work directly with industry. These projects are generally very early stage.

Over the next five years, we will expand our engagement with the industry sector, using VIAs as a springboard to move the Trust towards later stage projects. We have developed a collaboration with the **Medicines Discovery Catapult** to create the first charity syndicate (CF syndicate) and plan to work with them in key areas where their business expertise and convening power help us deliver impact for people with cystic fibrosis. Catapults have been created and are funded by the UK government (eg MDC budget is £100m) to help bridge the gap between the early and late stages of research. We are working to develop links with other catapults such as that in Gene and Cell Therapy and Digital.

Integration across the four flagship programmes provides an opportunity for the Trust to demonstrate thought-leadership and deliver solutions relevant not only to people with CF but also many other conditions which are facing similar problems (eg cancer). To be effective, the Trust must (i) partner with other organisations and the industries and (ii) ensure that new government initiatives are exploited for use by CF researchers. The excellence of the science base built up over the last five years is crucial to permit the Trust to deliver these key strategic priorities. It is essential that research excellence remains the sole driver for research investments.

Four flagship programmes

1. **UK CF Registry:** Over the last five years, there has been increased use of the data contained within the Registry for research. The Trust has invested in novel approaches to enhance and maximise the information that can be gleaned from the registry to benefit people with cystic fibrosis. Examples include the linking of Registry data with other data sets such as those of air and other environmental pollutions to better understand the influence on people with CF and perhaps provide explanations for the '"clustering' of NTM.

   In addition, in a small pilot project, we have invested in a collaboration with the Alan Turing Institute to use advanced mathematics to establish whether the longitudinal data contained in the registry can be used to predict CF outcomes at an individual level.

2. **SmartCareCF:** Two studies have been funded to assess the feasibility of remote monitoring in cystic fibrosis. The data from the adult study is currently being analysed using both supervised and unsupervised machine-learning. The paediatric study is on-going.

3. **Clinical Trials Accelerator Platform:** The Trials Accelerator has ring-fenced funding for four years. In keeping with other international clinical trials networks, the Trials Accelerator has been designed to pump-prime the network in its early phases to become self-sustaining financially over this period. The purpose of the Trials Accelerator is to widen access to trials for all people with CF regardless of location. An additional key role is to build relationships with the biopharmaceutical industry and facilitate the adoption of their clinical trials.

4. **Innovation Hubs:** Innovation Hubs are a different way of ensuring research remains focused on the Trust's strategic objectives. Unlike standard research grant awards, a Hub is a strategic investment with the university, with shared goals, shared investment and shared governance. The first UK CF Innovation Hub is centred on the Biomedical Campus at the University of Cambridge. These Hubs provide the 'safe space' to explore issues of experimental medicine.

Experimental Medicine: The need for strong strategic partnerships to create the step-change in research to deliver solutions to the key priorities identified by the Trust

The environment is ripe to build on the successes of the previous strategy, to use Trust investments to create partnerships that draw more funding, knowledge and expertise from non-Trust sources. Many of the issues faced by CF in the coming five years are shared across many other conditions.

- High cost drugs and their unaffordability is not unique to cystic fibrosis. The Government, industry and healthcare professions are all seeking ways to address this.
- Provision of healthcare in a system that was not designed for managing long term chronic conditions, such as CF, is an issue. The past approach for CF through the development of specialist CF centres and multidisciplinary teams together with 'one size fits all' standards of care have been very effective in improving the lives of people with CF but is both unsustainable and incompatible with the aspiration of a Life Unlimited.
- Understanding the pathophysiology of CF progressive lung damage and the need for the development of new therapies including new antibiotics to combat antimicrobial resistance and safer anti-inflammatories to reduce pulmonary scarring.

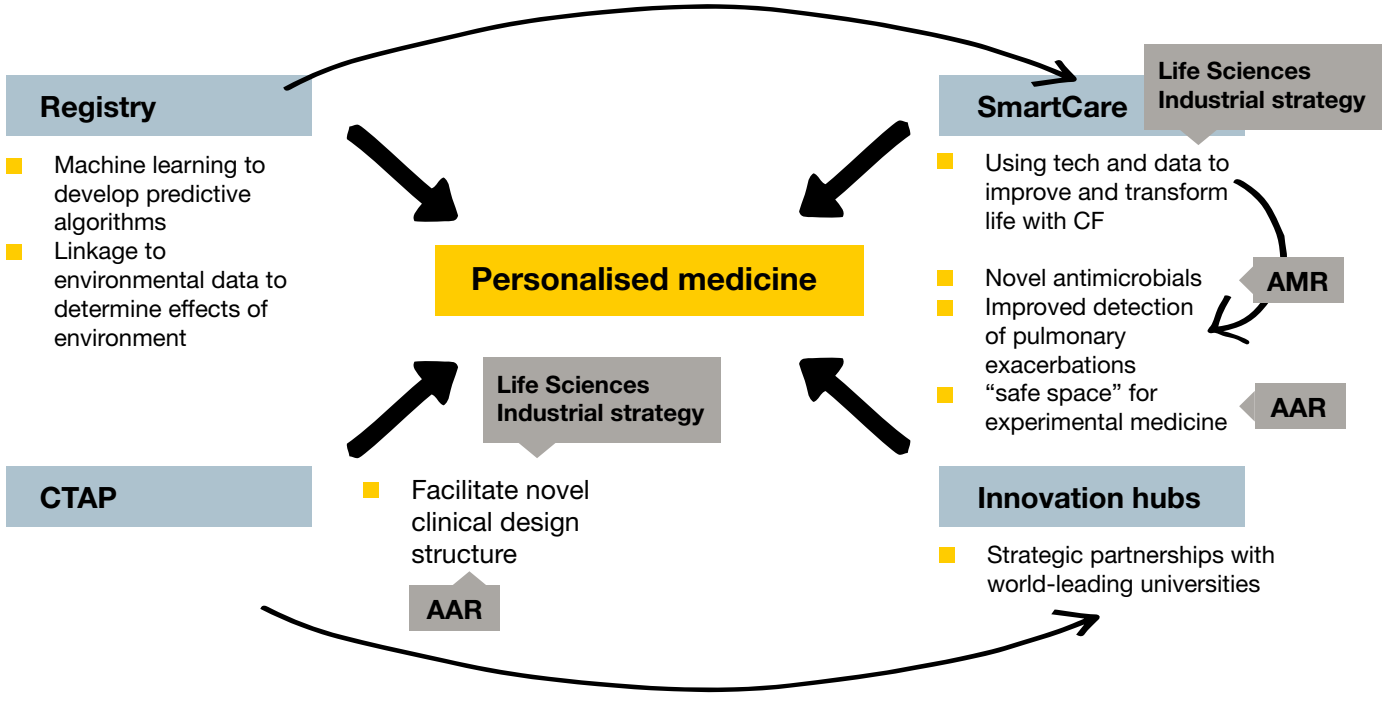
Solving these issues is well beyond the financial resources of the Trust. However, CF is well-placed for thought-leadership to use research to find solutions and thereby exploit the major government initiatives.

Harnessing the four flagship programmes to deliver our corporate objectives

These flagship programmes provide an unprecedented opportunity for the Trust to act as a leader in this area to benefit people with CF and lead to the goal of a Life Unlimited. Ensuring the flagship programmes are not treated as silos, their research integration will safely explore key features that will eventually lead to treating people with CF as individuals and not cohorts. The Innovation Hubs are an essential feature for delivery as they provide a 'safe experimental medicine space' using high performing academic institutions with a track record of high quality clinical research necessary to push the boundaries of what is possible.

The figure below illustrates how existing and potential research aspects of the four flagship programmes can be integrated to deliver personalised medicine. It also shows where these research areas address government priorities (Life Sciences Industrial Strategy; Antimicrobial Resistance (AMR) and Accelerated Access Review (AAR)).

Integration of research aspects of the flagship projects



Access to medicines: Research to identify ways for faster adoption of new drugs at lower cost

New drug discovery is slow, expensive and very high risk with the consequent high cost of new medicines. The Accelerated Access Review (AAR) identifies many of the reasons that cause delay and result in attrition and the high expenses of clinical development.

The cost of clinical studies, particularly Phase 3, are prohibitively high. The AAR recognises the need to bring together all interested parties prior to making changes and to disrupt the current time-consuming sequential approach to drug clinical development. The review places the patient voice at the heart of these discussions and includes:

- Academic thought-leaders
- Pharmaceutical industry
- Regulators
- Payers
- HealthTech

The Trust is excellently placed to convene the necessary expertise and influencers to explore new methods of delivering clinical trials. This will need to be based in an Innovation Hub, as a strategic partnership with an academic institution.

We will seek to develop an Innovation Hub, ideally placed at Imperial College London, where the Trust can convene the academic experts in novel trial design within the safe research setting of an Innovation Hub. It seems likely following some early discussions that the biopharmaceutical industries recognise the need for a "neutral broker" to create an environment for Precompetitive Research. We have discussed with the Medicines Discovery Catapult the option of working with them to access the required business development expertise to deliver such an opportunity. It will also probably be useful to share expertise and knowledge by developing a partnership with Cancer Research UK, the only other biomedical charity to understand the urgent need to experiment in this space to deliver Precision/Personalised Medicine. The investment in the Trials Accelerator offers the ideal vehicle to rollout any advances from the Hub to the entire UK.

Antimicrobial resistance

The economics of drug discovery is a crucial factor that limits investment by the biopharmaceutical industry in the development of new antibiotics9. Finding more efficient ways to deliver clinical trials, thereby reducing the cost of clinical development, will assist the delivery of new antibiotics.

One research arm of the first UK CF Innovation Hub based at Cambridge is specifically to explore infection and inflammation for multidrug resistant bacteria in cystic fibrosis. There is additional work taking place across the UK both within the academic setting and in the biopharmaceutical industries. We have already developed several co-funding opportunities with a number of small biotechnology companies. The learning obtained from the VIA investments in these companies will be taken to a new level. We have started discussions with the Medicines Discovery Catapult to explore creating the appropriate academic/industry partnership to maximise access to their unique resources and expertise both for academic and industry partners.

Quality of clinical care. Research to explore the use of digital technologies to disrupt existing Standards of Care

The biggest future research challenge will lie in the changes created by the disease-modifying drugs. Unlike past interventions, these drugs will slow progression or arrest the pathology associated with cystic fibrosis. However, the effect on each individual will depend on the time of introduction of the disease modifying drugs. The earlier the drugs are introduced, the less irreversible damage to organs. This, together with the increase in the number of adults with CF (the result of longevity), means that existing "one size fits all' Standards of Care will be challenged. There is an urgent need for research to explore new models of care and so offer a route to personalised medicine. Research within CF can pioneer thinking and act as a test-bed to generate the evidence-base for implementation of personalised medicine more widely. This requires a radical change in thinking to break away from the 'more of the same' culture prevalent in UK CF centres.

Converting data to information is an essential feature of digital health, requiring the Trust to interact with disciplines such as mathematics, data science and potentially artificial intelligence. Based on the previous strategy, the Trust has already initiated research programmes to explore the value of applying these new disciplines. To test the potential power of these new technologies to reduce the complexity and burden of care, will be a key objective of the next research strategy.

Vision for Digital Health
Our vision is that every person with CF should have the tools **THEY** need to manage **THEIR** health and treatments in a way that enables them to stay healthy while living a life as fully and independently as possible.

Investments made by the Trust in the last few years are now bearing fruit and delivering valuable insights into the power of these approaches. The Trust has been working with the Alan Turing Institute to explore the use of applied mathematics to create predictive algorithms on disease progression using the Registry data. In addition, the Trust co-invested in SmartCareCF studies at University of Cambridge and Imperial College London. The adult study (led from Cambridge) has already generated very valuable insights into the acceptability of remote monitoring in cystic fibrosis. The data is being analysed using both supervised and unsupervised machine learning within the Microsoft Research Institute based in Cambridge. The paediatric study (led from Imperial College London) is still recruiting to the study. Data derived from the paediatric study will be added to the machine learning work to enrich the analysis.

The Trust is exploring how to take this forward within an experimental medicine setting. As such, it is essential that any such research is physician-led and predominantly takes place in the safe space of 'Innovation Hubs'. Digital health is a prominent feature in the Life Sciences Industrial Strategy and high-level discussions with Innovate UK are in progress.

Day to day support

The digital revolution will assist people with CF by empowering them to manage their own condition and so relieve some of the tensions so clearly stated in the James Lind Alliance Priority Setting Partnership[14]. The number one priority for this is: "What are the effective ways of simplifying the treatment burden of people with CF?".

The Trust's Insight Survey in 2017[15] provided powerful data on the impact of living with cystic fibrosis. The digital revolution provides an opportunity to reduce this impact by adopting 21st century technologies, for example reducing travel to CF centres when well. Reduction in clinic visits when not required will reduce the burden on the individual (such as disruption to family life and work, travel expense) and on the health system.

Reaching all people with cystic fibrosis

There is an urgent need to develop novel interventions to target the adolescent community. There is some evidence to suggest that the concept of digital health in the form of m-health/telehealth provides a pathway to reach the adolescent community. This audience will be taken into account in the development of digital health technologies.

[15]www.cysticfibrosis.org.uk/life-with-cystic-fibrosis/cf-insight-survey

Putting the person into personalised medicine – how?

In the year 2018/19, we will:

Launch the new strategy

Fund 2–3 SRCs

Restructure sandpits to synchronise timing with SRC call

Develop and integrate the Trust Corporate strategy with the VIA

Continue existing ground-breaking research in the area of Digital Health

- Develop strong links with the two academic centres pioneering this work (University of Cambridge and Imperial College London)
- Build strong collaborations with the ICT sector
- Explore the novel biosensor biotechnology sector and incorporate into CF

Innovation Hubs

- Deliver the strategic partnership established with the University of Cambridge
- Negotiate and develop thinking for second Innovation Hub at Imperial College London. Work with the MDC/Imperial Innovations to engage corporate sector for funding

Improve involvement of people with CF with research

- Communications – Senior Impact Advisor (Dr Belinda Cupid)
- JLA – use priorities as a focus for research sandpits after consideration by SAB
- Evolve and enhance “CF’s Got Talent”
- Deliver cutting-edge science programme for UKCFC
- Improve the use of technology solutions to engage better with people with CF

Over the 5 years, we will:

- Maintain SRCs at steady state of 9 active at any one time
- Establish partnerships with other funding agencies to support future fellowship schemes to ensure that the best early stage researchers are retained in CF research
- Build relations with the industrial sectors using the VIA as a springboard to access joint funding with the industry accessing funds delineated by the Life Sciences Industrial Strategy
- Create at least one Precompetitive Research collaboration with the Trust acting as the neutral trusted broker between industry and the strong academic base in the UK

Governance

Two different independent committees were established in 2013 that underpin research investments by the Trust.

The strategy implementation board (SIB) that is involved in the peer review of grant investments and makes recommendations to the executive on the applications that meet the funding criteria. They are also responsible for on-going review of the award grants. The SIB is working well with clear rules on rotation as per AMRC guidelines. However, the terminology here is confusing, so SIB will be renamed Research Grant Review Committee.

The research strategy advisory board (SAB) provides the executive and Board of Trustees, high level, independent, oversight of the research portfolio. A major role for SAB is to provide the Trust with high level strategic review and horizon scanning. The SAB has clear terms of reference which remain unchanged but it is proposed that SAB is also best placed to recommend to the research team appropriate topics for the research sandpits. A further change to SAB is the instillation of regular annual meetings and the proposal that it should be chaired by a senior person independent of the Trust.

Cystic Fibrosis Trust

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