Cystic Fibrosis why we're here

Research in focus

Cystic fibrosis–related diabetes

Fighting for a Life Unlimited

Foreword from Dr Keith Brownlee

Cystic fibrosis (CF) is a complex condition that can affect many different parts of the body, not only the lungs. Everyone with CF will have a different experience of the condition, however almost all need to spend several hours a day, every day, completing a rigorous regime of treatments to stay healthy.

According to the latest UK CF Registry report[1], one in three adults with CF in the UK are currently living with CF-related diabetes (CFRD), a distinct form of diabetes unique to people with cystic fibrosis. Having CFRD can lead to people having a poorer lung function than other people with CF and, ultimately, shorter lives. Early detection can enable effective treatment, but this currently means insulin injection therapy. On a day-to-day level, CFRD requires careful dietary monitoring, regular monitoring of blood sugar levels, and insulin injections multiple times a day.

Cystic Fibrosis Trust-funded researchers have already come a long way in increasing our understanding of the underlying cause of CFRD and their results will change the way that future researchers investigate the condition. Later this year, a second programme of Trust-funded research will begin, which looks to apply this knowledge to explore new treatment approaches to treat CFRD in the future, that would avoid the need for insulin injections.

Preventing CFRD is a top priority for people with CF[2] and so we've made it one of our priorities too, through continued investment in leading CFRD research.

What is cystic fibrosis?

Cystic fibrosis (CF) is a devastating condition that affects over 10,500 people in the UK. It is caused by a defective gene, called the CFTR gene. As a result, the internal organs, especially the lungs and digestive system, become clogged with thick, sticky mucus resulting in chronic infections and inflammation in the lungs and difficulty digesting food.

Some adults with cystic fibrosis may also get cystic fibrosis-related diabetes (CFRD), arthritis, osteoporosis and liver problems.

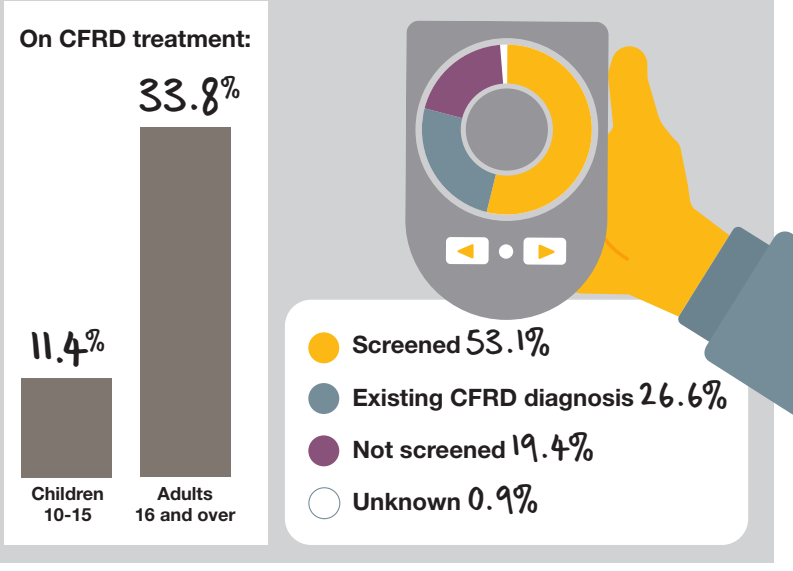
What is CF-related diabetes?

Insulin is an important hormone that helps to regulate the amount of sugar in the blood. In CFRD, the body can't release enough insulin from where it is made in the pancreas, and the body also responds differently to the insulin that is released, which means that the sugar levels in the blood aren't regulated properly. The signs and symptoms of CFRD share similarities to both Type 1 and Type 2 diabetes, but CFRD is a distinct condition, with a different underlying cause.

People with CFRD have worse lung function than people with CF who don't have CFRD, and they're likely to have shorter lives. An early diagnosis of CFRD and insulin injection treatment can have a positive benefit for health, and may protect against later diabetes-related complications, such as nerve damage.

Developing CFRD is one of the most common complications of cystic fibrosis. According to the latest UK CF Registry report, of the 7,400 people with CF who were within the age range for CFRD screening, 2,200 (of these approximately 34% were adults aged 16 and over) reported that they were receiving treatment for CFRD.

Cystic fibrosis-related diabetes (CFRD)



Impact of CFRD

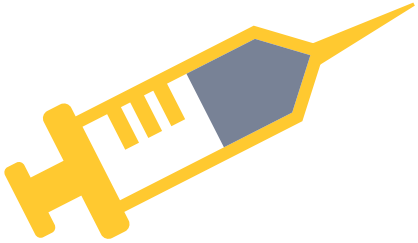
Although CFRD can't be cured, it can be treated and managed very successfully. People with CFRD are generally treated with injections of insulin, between one and four times a day. When to take insulin is determined by the levels of sugar in the blood, measured using a continuous blood monitor in the arm connected to an app, or by manual testing from a finger prick of blood. Some people use an insulin pump, which provides the body with insulin throughout the day.

For people with CFRD their diet must control blood sugar levels **and** incorporate the high calorie diet that nearly all people with CF need. A high calorie diet is needed, as the body uses up more energy if you have CF, and to compensate for the difficulties in absorbing food from the stomach.

Treatment for CFRD comes in addition to the usual rigorous daily regime of treatments that people with CF often undergo to stay healthy. This can include taking inhaled and injected drugs to clear mucus and fight infections, taking enzyme pills to digest food and having physiotherapy morning and night.

When I was first diagnosed with CFRD it was a huge extra treatment burden and I really struggled to adjust. It's extra equipment to carry around and just the thought of another condition to manage was quite overwhelming and stressful. It can affect my mood and gets worse when I am unwell or on certain treatments.

– Lynsey, who has CFRD



Life-saving drugs and CFRD

Treatment for CF has undergone a transformation in the last five years, due to access to life-saving CFTR modulator drugs, such as Kalydeco, Orkambi and Symkevi, which improve lung function for people with cystic fibrosis. It is widely hoped that the impact of many complications of CF, including CFRD, will be reduced by these drugs too, but much more research is needed.

Finding out more about the effects of CFTR modulators on CFRD will require more studies from lab- and clinic-based researchers around the world. We can also learn about possible beneficial effects by following the health of people with CF over time, through databases such as our UK CF Registry. A UK CF Registry-based study on Kalydeco[3], the first precision medicine made available on the NHS, has shown there were fewer cases of CFRD among those who had been taking Kalydeco for three to four years, compared to those who weren't taking the drug.

Following a NICE decision in 2019, eligible people with CF in the UK will have access to the CFTR modulators Orkambi and Symkevi. The UK CF Registry will monitor the effectiveness of the drugs once people start taking them, including monitoring their effect on CFRD.

What our funding has achieved so far

Although it's a well-known condition to CF doctors, exactly how CFRD develops on a cellular level isn't yet fully understood. By understanding what's happening in CFRD through research, we hope that much more can be done to reduce the impact of this condition and develop better ways to treat it for the benefit of people with cystic fibrosis.

In 2017 we awarded Professor James Shaw and colleagues a Cystic Fibrosis Trust Strategic Research Centre grant of £750,000 over three years to investigate the causes of CFRD. The money funded eight investigators in four countries with a range of different expertise, all working together to find answers to this important complication of cystic fibrosis.

The researchers have been pursuing three 'lines of enquiry' to find what might be causing CFRD:

1. Is there any CF protein in the parts of the pancreas where insulin is made, that may be malfunctioning?

2. Is it the direct action of the CFTR in other parts of the pancreas that is preventing the production and release of insulin?

3. Is there something happening as a consequence of the damage caused to the parts of the pancreas releasing digestive enzymes?

Recently, in answer to the first question above, Professor Shaw and his team have found that there is no CF protein in the parts of the pancreas involved in insulin release[4]. This is a really important finding as it has allowed them and other researchers in this field to eliminate the first line of enquiry from their investigations. This is also a call to action to researchers to look at the consequences of what's happening in the rest of the pancreas to truly understand what's causing CFRD.


Dr Lucy Allen

Biomedical research can help us answer really tricky questions, many of which are so complex that they may only be answered collaboratively, through the work of multidisciplinary teams often based at multiple institutions. Our Strategic Research Centre programme is designed to tackle these questions for CF, by attracting high quality investigators from across a range of disciplines, some of whom may not have previously worked in cystic fibrosis. The recent finding from Professor Shaw's team demonstrates the value of this approach.

– Dr Lucy Allen, Director of Research, Cystic Fibrosis Trust

Looking to the future

Following on from this success, Professor James Shaw will lead a second Strategic Research Centre, to investigate how signals from the rest of the pancreas affect how and whether CFRD develops. The researchers will look at the way signals move from the digestive-juice-producing parts of the pancreas to the insulin-producing cells. They will also investigate which signals cause the most damage and whether these signals can be measured in the blood of people with cystic fibrosis.


Professor James Shaw

We believe that CFRD is caused by signals from damage to the digestive-juice-producing part of the pancreas, which stop insulin-producing cells from working properly. Understanding more about these signals could lead to entirely new approaches to treating diabetes, avoiding the need for insulin injections.

– Professor James Shaw, Professor of Regenerative Medicine for Diabetes at Newcastle University

CFRD is the most common complication that people with CF develop, and therefore much more research is needed to better understand the condition and improve detection and treatment. This would mean the condition would have less of an impact on the lives of people with CFRD, and that far fewer people would develop CFRD in the first place.

References

1. UK Cystic Fibrosis Registry, Annual Data Report 2018, Published August 2019. www.cysticfibrosis.org.uk/registry
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3. Volkova N et al, J Cyst Fibros 2020, 19(1), 68-79 (doi: 10.1016/j.jcf.2019.05.015)
4. MG White et al, J Clin Endocrinol Metab 2020, 105(5) (doi: 10.1210/clinem/dgz209)

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