British Heart Foundation

British Heart Foundation

60 years of pioneering research and innovation

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Message from our Chief Executive

The last 60 years have been transformational for the nation's heart and circulatory health. Since the British Heart Foundation (BHF) was founded in 1961, it has funded pioneering research that has helped to halve the number of people dying from these diseases across the UK.

Within this research compendium we celebrate progress across the field of cardiovascular research over six decades and reflect on the profound impact this has had on the lives of people affected by heart and circulatory diseases.

I could not be prouder of the difference the BHF has made thanks to the generosity of our incredible supporters and volunteers. Powered by their support, brilliant scientists have transformed diagnosis, treatment and care for countless people affected by heart and circulatory diseases.

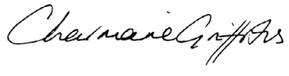
But there is still so much to do.

Today, tragically, heart and circulatory diseases are still responsible for over a quarter of UK deaths. We are still navigating from the impact of the COVID pandemic on people's health and research progress. There remains no cure for heart failure that affects nearly a million people across the UK.

Despite recent breakthroughs, we have much to learn about how specific genes trigger sudden cardiac death in the young, taking 12 people's lives before their 35th birthday every single week. And as the burden of dementia grows, we are only beginning to understand the critical role blood vessels damage plays in progression of this devastating disease.

The work of the BHF has simply never been more needed.

These pages share the story of unimaginable progress, only made real with the support of so many people across our BHF family. With thanks to all, today we look to the future with confidence and as inspired by research now as we were in 1961. For 60 years we've known that it's only by nurturing in the most talented scientists and ideas that, together, we can drive the progress patients urgently need. Together, we will power science to save lives.



Dr Charmaine Griffiths,
Chief Executive, British Heart Foundation

Message from our Medical Director

In 1961, the causes of heart and circulatory diseases were poorly understood. The concept of prevention was almost non-existent. Treatments were often palliative rather than curative.

Against this backdrop, a small group of leading cardiologists in the UK recognised the enormous need for research to improve the outlook for patients. They had the vision and tenacity to set up the BHF and raise funds to carry out new research. Ever since then, the BHF has been a powerful force in shaping the landscape for cardiovascular research across the UK.

Today, we play a critical role in the fight against heart and circulatory diseases. The BHF funds over half of non-commercial cardiovascular research in the UK. We directly fund over 1,300 research staff and support many more, from PhD students full of promise and ideas, to the world-leading Professors at the height of their careers.

To ensure our research has the best promise of impact, all applications go through stringent assessment by independent experts. Around three in four applications are unsuccessful. This high quality, and quantity, of our research enables us to fund work across the breadth of the many and inter-connected conditions that affect the heart and circulatory system. Our research gives people hope for the future.

With continued investment and support, we can achieve the changes that we want to see in the world. We can find cures for inherited heart conditions that can lead to sudden death. We can develop effective treatments for heart rhythm disorders that increase the risk of stroke and discover new therapies to slow the progression of dementia. We can harness the power of population data to predict individual risk of heart and circulatory diseases and so be able to offer better ways to prevent them.

The following pages illustrate the lasting impact of our research funding and some of the key players who made the breakthroughs leading to better treatment and care of patients. I hope they inspire you as much as they inspire me.

Professor Sir Nilesh Samani,
Medical Director, British Heart Foundation

Transforming heart attack treatment

Transforming heart attack treament

Heart attack symptoms vary from person to person. They can include sudden, persistent chest pain and pain that spreads to the left or right arm, or to the neck, jaw, back or stomach. Sometimes, a heart attack can even lead to a life-threatening abnormal heart rhythm and cardiac arrest.

Since the BHF was founded, we have supported life-saving research into the treatment, detection, and prevention of heart attacks. And supported innovative solutions to increase the number of people surviving a cardiac arrest. Our research has helped to save thousands of lives.

The BHF has been critical in transforming what is known about heart attacks and how best to treat them. Thanks to BHF-funded research, we now understand most heart attacks are caused by blood clots in the coronary arteries. Researchers have developed better combinations of medicines to administer after a heart attack. And people who suffer a heart attack now receive treatment in specialised coronary care units.

Today, seven in ten people survive a heart attack in the UK and can go home to their families and loved ones.

In the 1960s more than 7 out of 10 heart attacks in the UK were fatal.
Today at least 7 out of 10 people survive.

Pioneering care for heart attack patients

Professor Desmond Julian

Professor Desmond Julian, who later became BHF Professor of Cardiology in Newcastle and then the BHF's Medical Director, radically changed the way heart attack patients received care in hospitals. Supported by BHF funding, he recognised these patients had specific treatment requirements, different to general patients.

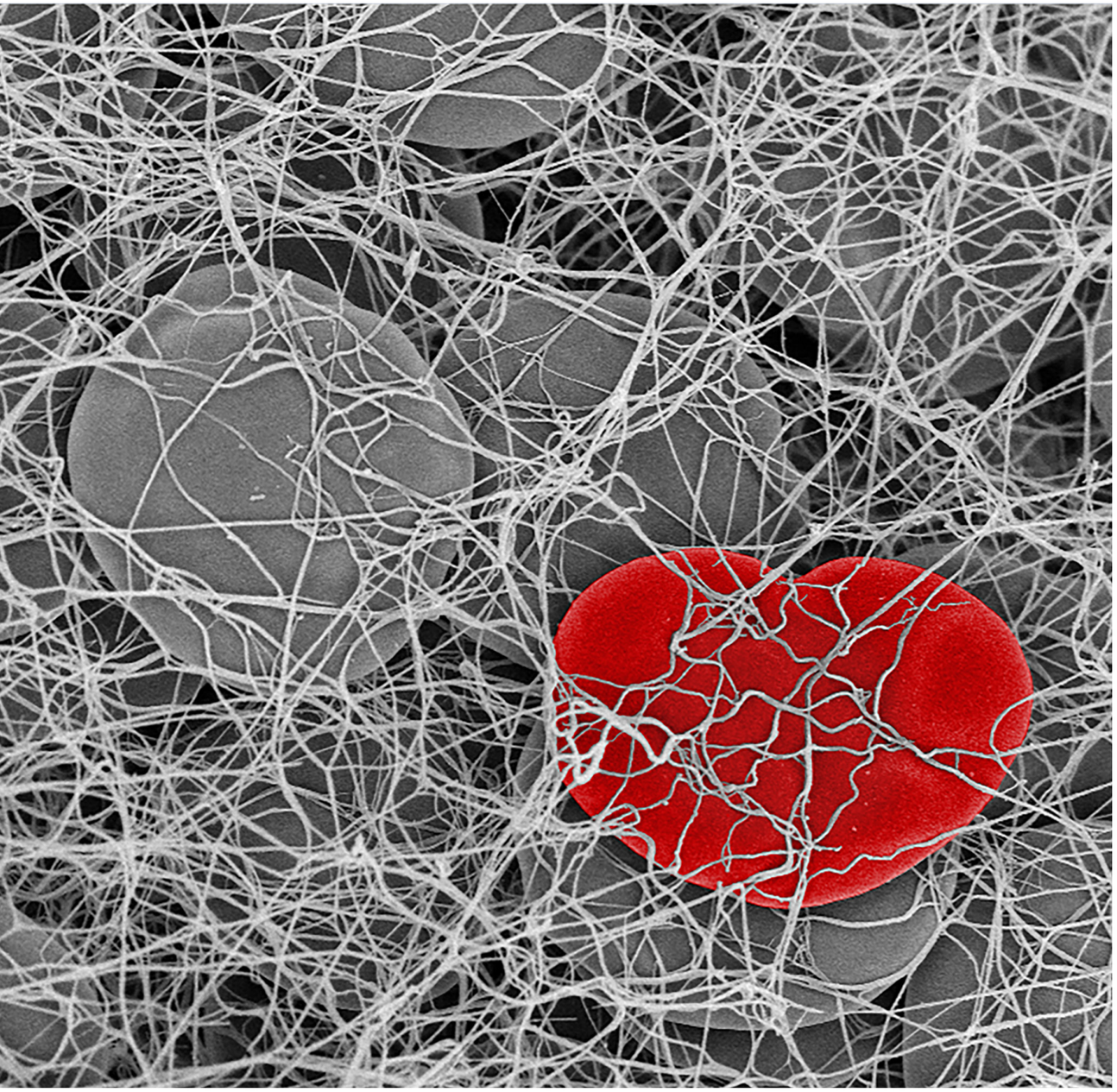
In the 1960s, the lack of treatments meant that after a heart attack many recovering patients developed a life-threatening abnormal heart rhythm. This could lead to cardiac arrest where the heart stops pumping blood around the body. Few heart attack patients survived a cardiac arrest, even those in hospital. One reason for this was that they were on general medical wards, scattered throughout the hospital. These wards lacked the skills and equipment needed to respond to a life-threatening cardiac emergency.

In 1964, the BHF funded equipment for Dr Julian to set up a coronary care unit at the Royal Infirmary of Edinburgh, working with Dr (later BHF Professor) Michael Oliver. He placed all heart patients on one ward, monitored them continuously, and had specialist equipment with trained staff on hand.

Despite initial opposition to this approach, including concerns that rushing patients to hospital by ambulance and surrounding them with monitoring equipment would "frighten people to death", the Edinburgh coronary care unit immediately proved successful. In its first year, the unit reduced deaths by more than 30%.

Professor Julian's vision of a specialised hospital ward for intensive cardiac care sparked a global transformation in the care of heart patients, dramatically improving survival rates.

Every five minutes someone is admitted to a UK hospital due to a heart attack



'Getting to the heart of the matter' by Dr Fraser MacRae. The image takes us inside a deadly blood clot - the leading cause of heart attack and stroke. In the image red blood cells are trapped in the 3D mesh of fibrin fibres, which hold the clot together. One red blood cell had been compressed into a heart shape by the contracting fibres surrounding it

Finding the cause of heart attacks

Professor Michael Davies

To be able to treat heart attacks, doctors first needed to understand what caused them. This was the discovery of BHF Professor Michael Davies in 1976, the first scientist to show clearly that almost all heart attacks are caused by blood clots in one of the coronary arteries that supply blood to the heart.

Professor Davies also found that these clots form where the arteries are narrowed by atherosclerosis, the build-up of fatty substances inside blood vessels. His work was crucial in linking coronary heart disease to heart attacks. We know now that coronary heart disease is the most commonly diagnosed type of heart disease and causes around 175 deaths every day in the UK.

Professor Davies's work overturned the widely held view that the clots were a result rather than a cause of heart attacks. Although Professor Davies carried out the work in the 1970s, his findings were so far ahead of their time that they only gained widespread international support in the 1980s. They are now in every textbook on heart disease.

Crucially, his BHF-funded breakthrough raised the possibility that drugs that reduce clotting could help to save lives after a heart attack.

Proving the benefits of anti-clotting drugs

Professor Peter Sleight

In the 1980s, BHF Professor Peter Sleight and Dr Rory Collins (now BHF Professor Sir Rory Collins) led a team of researchers in Oxford who set up the first large scale trial of anti-clotting drugs in thousands of heart attack patients.

They found in the immediate aftermath of a heart attack giving a "clot-busting" drug called streptokinase together with aspirin (which prevents more clots from forming) saved lives. Giving streptokinase and aspirin together decreased deaths after a heart attack by around 40%. This trial, which BHF part-funded, also found that the earlier this combination of medicines was given after a heart attack, the better the outcome for the patient.

Following the trial, in the 1990s clot-busters became a life-saving revolution adopted across the world. With further advances in heart attack care, we now have even better treatments. Angioplasty reopens a blocked artery with a balloon and stents are inserted into the artery to keep it open. But for some people, clot-busting treatments are still life-saving, for example, in parts of the world where angioplasty is less available or if they are too far away from a hospital. Clot-busting drugs also remain a mainstay for treatment of strokes.

Changing how NSTEMI heart attacks are treated

Professor Keith Fox

Some heart attacks, called NSTEMI heart attacks, can be caused by partial blockage of the heart's coronary arteries. In the past they were considered minor and did not always get the treatment they needed.

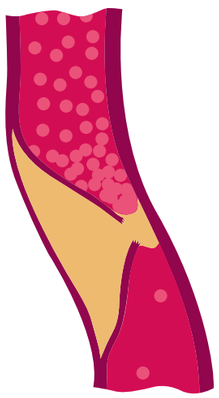
BHF Professor Keith Fox and colleagues at the University of Edinburgh decided to tackle this problem by tracking NSTEMI patients over several years. They set up the largest international database of patients admitted with chest pain, called the Global Registry of Acute Coronary Events (GRACE). From 1999 to 2009, it was used to track what happened to 100,000 patients with heart-related chest pain from nearly 250 hospitals across 30 countries. The registry revealed that many people who had an NSTEMI heart attack were at high risk of having another, potentially more serious, heart attack later in life.

To stop high-risk patients from slipping through the net, Professor Fox and his team created a scoring system – the GRACE risk score - to help doctors find which patients with NSTEMI would benefit from more intensive treatments. The GRACE risk score has been updated and is still in use today. Doctors can access it via a smartphone app, helping them make swift and accurate decisions about treatment for people with chest pain.

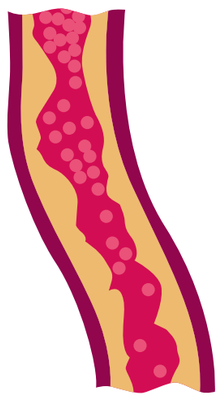
NSTEMI heart attacks represent an estimated 60% of all heart attacks in the UK

In the late 1990s, Professor Fox also led a clinical trial to find out how urgently clinicians should treat people admitted with NSTEMI. At the time, doctors were unsure whether these patients needed an urgent angiogram (a type of X-ray of their heart arteries), or they should wait to see if medication could work first. The BHF-funded trial showed conclusively that people with NSTEMI should have an early coronary angiogram, which then gives the possibility of unblocking the artery at the same time. The results changed treatment guidelines in the UK, Europe and USA. This research has made a huge difference to the care of millions of people with coronary heart disease (CHD).

Types of heart attack



STEMI
- Full blockage
- Causes extensive heart damage



NSTEMI
- Partial blockage
- Causes less extensive heart damage

How genes affect heart attack risk

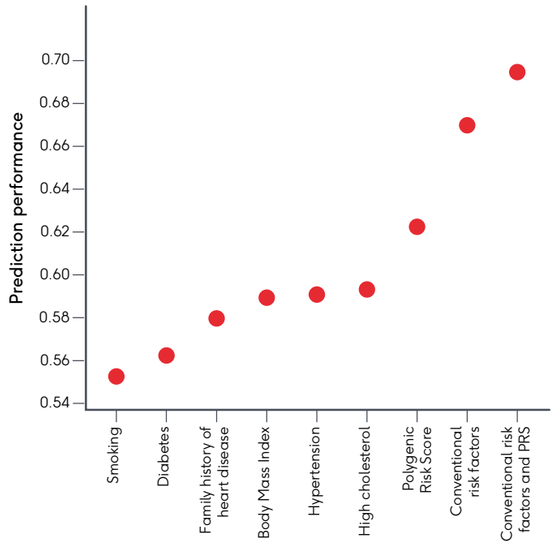
Professor Sir Nilesh Samani

Understanding how genes can affect the risk of heart disease is vital in knowing what causes heart disease. It can unlock new treatments.

The human genome carries over 3 billion 'letters' that make up our DNA. Being able to study the whole genome in large groups of people is a powerful tool for understanding the possible causes of disease. Genomic studies have shown that it is not only faults in single genes that can lead to disease but also many common variations in single letters of the DNA along our chromosomes.

The BHF Family Heart Study was set up in the early 2000s to explore the role of genetics in heart disease. The study was led by BHF Professor Stephen Ball from the University of Leeds and, now BHF Professor, Sir Nilesh Samani from the University of Leicester. The team collected blood samples for DNA testing from members of almost 2,000 families with a history of early heart attacks. Early analysis of the results suggested that small DNA changes in several areas of the genome affected the risk of having coronary heart disease. The study was extended to include more than 190,000 people to gather more information on where these changes were located, and what genes they affected. In 2013 this study identified several new DNA changes that increase the risk of developing coronary heart disease. Most of them have very little effect on their own but families that carry lots of these DNA variations are more likely to have heart attacks.

Polygenic risk score (PRS) is a better predictor of future coronary heart disease than other risk factors, including smoking or having high cholesterol.



In 2018, using data from over 480,000 UK Biobank participants, Professor Samani and colleagues were able to calculate an individual's polygenic risk score based on variations at over a million points along their DNA. The score predicts the risk of coronary heart disease as accurately as conventional risk factors such as cholesterol and blood pressure. More importantly, in people whose conventional risk score showed a moderately increased risk of early heart disease, their polygenic risk score could more accurately predict whether they would develop coronary heart disease in the next 10 years.

In future, doctors could use this score to prevent more heart attacks by better identifying people who are at risk, and therefore who could most benefit from lifestyle changes and preventive medication.

Artificial intelligence to predict heart attacks

When someone has chest pain that may be due to coronary heart disease, they usually have a CT (computerised tomography) scan of their coronary arteries to check for any narrowed or blocked areas. About three quarters of the time, the scan finds no significant narrowing of the arteries. But some of these people do have coronary heart disease, which could lead to a heart attack in the future. There are currently no tools used routinely by doctors that can identify which patients will go on to have a heart attack and who could benefit from life-saving preventive treatments.

BHF Senior Fellow Professor Charalambos Antoniades and his team at the University of Oxford have recently developed a new technology using machine learning (a type of artificial intelligence) and applying it to routine CT scans. They have found a specific combination of changes that can be seen on the CT scan, which reveal areas of inflammation and scarring in the fatty tissue around the coronary arteries. They have shown that detecting inflammation and scarring significantly increases our ability to predict a future heart attack up to five years before it strikes.

This new technology has huge potential to detect the early warning signs of future heart attack from a routine CT scan, so that people can receive the right preventive treatment, saving lives. The technology is already available in 15 NHS trusts, including hospitals in Oxford, Leicester and London.

> **By harnessing the power of AI, we've developed a fingerprint to find 'bad' characteristics around people's arteries. It can detect the early signs of disease, ultimately saving lives.**
>
> **BHF Professor Charalambos Antoniades**

Charalambos Antoniades, BHF Professor of Cardiovascular Medicine, University of Oxford

Timeline of achievements

1961
The BHF is founded

1964
Dr Desmond Julian in Edinburgh sets up the **first coronary care unit** in the UK

1964

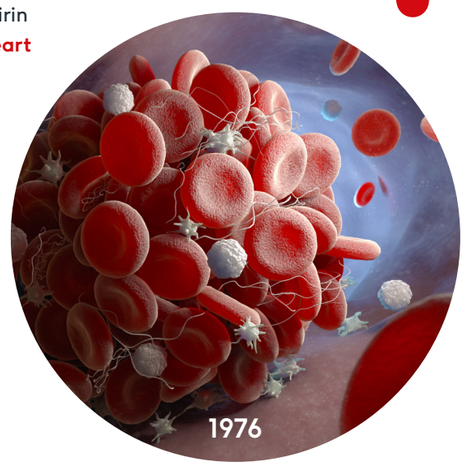
1965
Dr Frank Pantridge in Belfast develops the **first portable defibrillator** and tests for the first time having a defibrillator in an ambulance to get emergency heart attack care to where it was needed


1965

1976
BHF Professor Michael Davies finds that **blood clots cause most heart attacks**

1988
BHF Professor Peter Sleight shows that combining the clot-busting drug streptokinase with aspirin **decreased deaths after a heart attack by around 40%**

2002
BHF Professor Keith Fox reveals that what was thought of as 'minor' heart attacks can be life-threatening and **describe how they should be treated**


1976

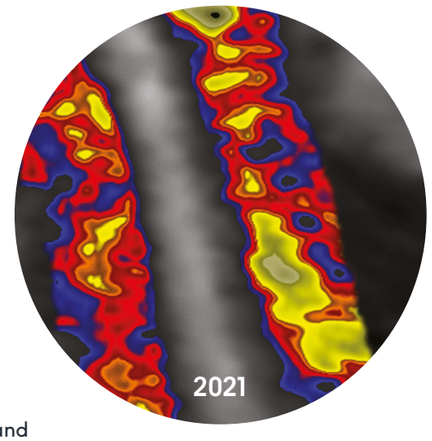
2004
Family heart study is launched, collecting DNA samples from almost 2000 families with a family history of early heart attack around the UK


2018

2018
BHF Professor Nilesh Samani and colleagues calculate an individual's "polygenic risk score" based on genetic variations along their DNA that can **predict whether they will develop coronary heart disease in the next 10 years**

2019
Professor Charalambos Antoniades develops a **new artificial intelligence tool that can predict the risk of heart attack** years before it strikes

2021
Professor Charalambos Antoniades' AI tool to **predict the risk of heart attacks** is now available in NHS trusts in England


2021

Treating heart rhythm problems

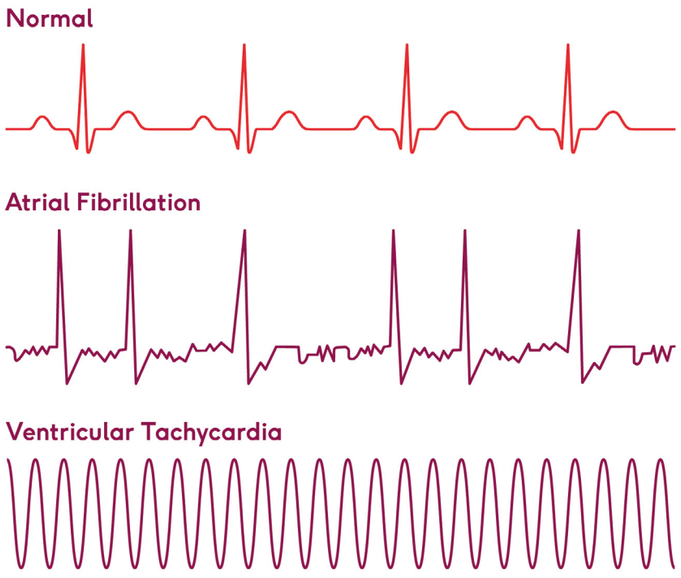
Treating heart rhythm problems

The pumping action of the heart is controlled by a conduction system which sends out electrical impulses. These impulses make the heart contract, allowing it to push blood out to the lungs, brain, and the rest of the body. These synchronized contractions create heartbeat. In a normal heart rhythm, a heart contracts regularly.

Arrhythmia is caused by a problem in this conduction system, which can make the heart beat too slowly (bradycardia), too quickly (tachycardia), or in an abnormal way (e.g. atrial fibrillation). Symptoms of arrhythmias include palpitations (a thumping or fluttering sensation in the chest), dizziness, breathlessness and sometimes chest pain.

Arrhythmia can be a complication of a heart attack, heart failure, congenital heart dsease, valve disease or cardiomyopathy (disease of the heart muscle). Some forms of arrhythmia can be life-threatening. For example ventricular tachycardia can trigger a cardiac arrest, which is when a person's heart stops pumping blood around the body. Without immediate treatment, they will die.

Since the 1960s, the BHF has been helping find innovative solutions for potentially dangerous arrhythmia by funding lifesaving research. In the pages that follow, we outline some of the breakthroughs we have made possible, thanks to our supporters.



Types of arrhythmias

Pioneering pacemakers

Professor Aubrey Leatham

Around **50,000** people are fitted with a pacemaker in the UK each year

In the 1950s, cardiologist Dr Aubrey Leatham and his technician Geoffrey Davies worked to develop a prototype pacemaker, a device to help maintain a normal heartbeat. In 1960, they implanted the UK's first internal pacemaker in a 65-year-old patient who had suffered repeated life-threatening heart rhythm disturbances.

This was a step forward, but many challenges were associated with early pacemakers. These included the need for intolerably high voltages to regulate patients' hearts, traumatic operations to their chests and the implantation of cumbersome devices.

When the BHF was formed, our founders saw the potential of Dr Leatham's research and funded his work into the development of pacemaker technology. Within five years, Dr Leatham's team had successfully treated several hundreds of patients.

Their original pacemaker had to be charged externally through an induction coil strapped around the body, which required a weekly overnight stay in hospital. This early work led to the miniature, sophisticated pacemaker devices that we see today transforming the quality of life of people with heart rhythm problems.

Modern pacemakers have a built-in battery that lasts for years and can also collect and store information about how a patient's heart is beating. Fitted under the skin, they have leads implanted into the heart. Some modern pacemakers are so tiny they can fit inside the heart itself, with no leads required.

Contemporary pacemakers can also improve the synchronisation of the pumping chambers of the heart, which can help people with heart failure, whose hearts can struggle to pump blood around their bodies. Some are now combined with a life-saving ICD (implantable cardioverter defibrillator) that can deliver electric shocks to kick-start the heart if needed.

All this progress has led to countless lives improved, prolonged, and saved, and is built on Dr Leatham's pioneering work. He himself also experienced the lifesaving power of the device first-hand. Born in 1920, Dr Leatham had a pacemaker fitted in 2009, which extended and improved the quality of his life, before he passed away in 2012.

The first defibrillator in an ambulance

Professor Frank Pantridge

Every year in the UK, there are more than **30,000** out-of-hospital cardiac arrests but less than 1 in 10 people survive

Sometimes, a heart attack can lead to a life-threatening abnormal heart rhythm and cardiac arrest. Throughout our 60-year history, the BHF has been working to increase the number of people surviving a cardiac arrest.

A cardiac arrest can happen anywhere, anytime. The heart stops pumping blood around the body, leaving someone unconscious, unresponsive, and unable to breathe. Without immediate treatment, the person will die. Every year in the UK there are more than 30,000 out-of-hospital cardiac arrests (OHCA), but less than one in ten people survive.

Early cardiopulmonary resuscitation (CPR) and a defibrillator shock can mean the difference between life and death. It is vital that anyone suffering a cardiac arrest receives treatment immediately.

BHF funding helped to set up the UK's first 'mobile coronary care unit' in 1965 to bring emergency care to those who experience a cardiac arrest outside of hospital. The unit, led by Dr Frank Pantridge, consisted of specialist staff and equipment. Located in Belfast, the unit included the world's first portable defibrillator, a machine to shock the heart back into beating again. Dr Pantridge designed and built the defibrillator, which although portable compared with earlier models, was still huge by modern standards. It was about the size of a fridge and weighed over 70kg. In later years, Dr Pantridge designed much smaller defibrillators which were genuinely portable by hand.

After the first year, Dr Pantridge reported that in Belfast, a medium-sized city, the team could reach 85% of patients within 15 minutes and 50% within 10 minutes. The Belfast experiment was a huge step forward for out-of-hospital cardiac care.

In the 1970s, Professor Douglas Chamberlain, supported by the BHF, built on Dr Pantridge's work, replicating it in Brighton by training ambulance crews to use defibrillators. This was expanded in the 1980s into a national training scheme.

In the same decade, under guidance of BHF Professor Stuart Cobbe, the BHF funded defibrillators for all Scottish ambulances and training for their staff. The life-saving results of Cobbe's project prompted the Government in 1990 to announce funding for defibrillators in every ambulance in the UK.

Tracking down public access defibrillators

Nearly **35,000** defibrillators were registered on The Circuit in September 2021

In the 1980s, Professor Chamberlain and the BHF also started campaigning to make defibrillators available in public places around the UK. The BHF has helped fund over 16,000 defibrillators across the UK.

However, in 2020 it was estimated that up to 70% of all the defibrillators in the UK could be unknown to ambulances services. OHCAs could have occurred with a potentially life-saving device nearby but no one knew where they were or how to access them.

The BHF joined forces with the NHS, St John Ambulance, and the Resuscitation Council UK to change this. Together, we launched The Circuit: The National Defibrillator Network. The Circuit synchronises every 60 seconds with the live dispatch systems within each of the UK's 14 ambulance services. This provides the emergency dispatcher with vital data on the location of the nearest defibrillator so they can direct bystanders and tell them how to use it.

The BHF plans to complete the roll-out of The Circuit to all UK ambulance services by early 2022. Over time this world-leading initiative should help to significantly increase in survival rates from OHCA through bystander defibrillation.

Creating a Nation of Lifesavers

Since 2014, over **7 million** people have accessed CPR training using BHF training kits

Having defibrillators in ambulances was a major advance. But even today, an ambulance might not reach a person in time to save them. The BHF has helped to revolutionise the response of the public to a cardiac arrest, so as many people as possible know how to save a life in this life-threatening medical emergency.

When the BHF was founded, CPR, which involves chest compressions to mimic the heart pumping blood, and rescue breath to help the person's breathing, was only just starting to be used as a critical resuscitation method. Professor Chamberlain, with the help of the BHF, began training members of the public in 1978 to perform CPR, dramatically increasing awareness of how to respond to a cardiac arrest.

Since then, we have been committed to creating a Nation of Lifesavers, supporting programmes to teach emergency life-saving skills to the public in the UK. Millions of people have accessed CPR training using BHF training kits at community groups and schools. And thanks to years of tireless campaigning by the BHF and other organisations, all 32 local authorities in Scotland committed to training all pupils in CPR before they left secondary school in 2019. First aid and CPR training were added to the secondary school curriculum in England in 2020. CPR training is also due to become a statutory element in secondary schools in Northern Ireland from 2022, and Wales from 2023.

Clare's story

In August 2017, Clare Doyle from Lisburn had a cardiac arrest. As her husband frantically called 999 and the operator tried to talk him through CPR, her 14-year-old daughter Melissa stepped in. She had recently been taught CPR by her school nurse using a BHF kit and knew exactly what to do. After performing CPR for nearly five minutes, the emergency services arrived with a defibrillator and Clare was taken to hospital. Thankfully, she survived. Now, Clare credits Melissa with saving her life.

Effective treatments for atrial fibrillation

Professor John Camm

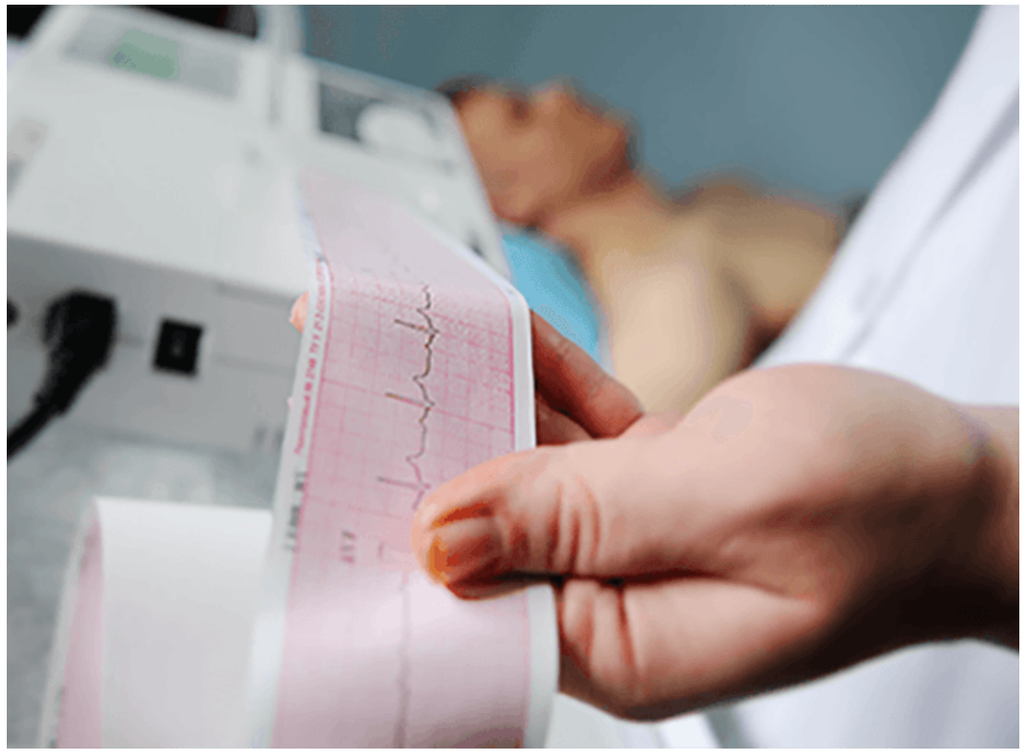
Atrial fibrillation is the most common abnormal heart rhythm. Atrial fibrillation happens when electrical impulses fire off in the upper chambers of the heart (the atria) in a disorganised way. These chaotic impulses cause the atria to quiver or twitch, which is known as fibrillation. People with atrial fibrillation have an irregular, and sometimes fast, heartbeat or pulse.

Revealing the danger of atrial fibrillation

Until the 1980s, atrial fibrillation was often regarded as harmless, because many people with the condition did not have noticeable symptoms. Only those who suffered with palpitations, sweating and difficulty breathing would be treated.

Back then, what doctors did not know was that atrial fibrillation is a major cause of strokes. Even without obvious symptoms, atrial fibrillation is associated with a fivefold increase in stroke risk. This is because a blood clot can form inside the quivering atria, and if the clot travels to the brain, it can cause a stroke. Early work by BHF Professor John Camm at St George's University of London in the 1990s unveiled the importance of heart rate and rhythm control in different patient populations, especially in people with atrial fibrillation.

Professor Camm also helped develop ablation, a procedure that uses either heat or freezing to carefully destroy the diseased area of the heart to stop abnormal electrical circuits. Ablation has become a treatment option for some patients with atrial fibrillation and the BHF is funding more research to improve this procedure.



Professor Paulus Kirchhof

1.5 million

Around **1.5 million** people have been diagnosed with atrial fibrillation in the UK

Restoring a normal heart rhythm in atrial fibrillation

Today, when people are diagnosed with atrial fibrillation, they are usually started on anti-clotting drugs to decrease the risk of stroke. They may also be prescribed drugs to lower their heart rate but not always to restore their normal heart rhythm. Despite these effective treatments, people with this condition remain at an increased risk of heart and circulatory problems.

BHF-funded Professor Paulus Kirchhof led a clinical trial to test whether bringing the heart rhythm back to normal soon after diagnosis in atrial fibrillation patients can further reduce the residual risk of heart and circulatory problems. The results of this clinical trial were published in 2020. It showed that treatment to restore normal heart rhythm, if started early after diagnosis of atrial fibrillation and with continued anti-clotting therapy, reduces complications, including strokes.

Currently, it is estimated that in Europe, only one in seven patients with atrial fibrillation are treated with rhythm control therapy. These results therefore have the potential to revolutionise how thousands of people with recently diagnosed atrial fibrillation are treated.

Looking for new treatments for atrial fibrillation

Many of the treatments available for atrial fibrillation focus on restoring a normal atrial rhythm, controlling the rate at which the heart beats or thinning the blood to reduce the risk of stroke - but they do not tackle the atrial scarring seen in people with severe atrial fibrillation.

Atrial scarring is when scar tissue forms in the heart. It is the body's way of repairing damaged cardiac tissue, with the scars themselves preventing the failure of the heart to pump blood around the body, keeping a person alive. However, this scarring can inhibit the electrical signals that control the coordination of this same pumping action by the heart.

In 2020, the BHF funded Dr Svetlana Reilly and team at the University of Oxford to decipher the mechanisms responsible for the electrical and structural changes seen in hearts affected by atrial fibrillation. Their work focussed on the hormone calcitonin, which until recently was only thought to be produced by the thyroid gland, with no known effects on the heart.

The team have revealed that cells in the upper chambers of the heart produce approximately 16 times more calcitonin than the thyroid. They also discovered that the hormone plays a role in reducing heart scarring and is decreased in people with atrial fibrillation. This discovery could lead to new treatments to prevent or repair heart scarring and could provide a lifeline to many people at risk of or living with atrial fibrillation.

> **"For a long time we've known the heart only produces a small number of hormones, and we can now add a new one to the list. Discovering that calcitonin is released by the heart should open new doors for developing heart treatments. We now need to explore how we can best restore the actions of this hormone to treat people with atrial fibrillation, and to understand when the best time to treat someone would be.**
>
> **Dr Svetlana Reilly**

BHF Fellow Dr Svetlana Reilly, University of Oxford

Finding children at risk of sudden cardiac death

Hypertrophic cardiomyopathy (HCM) is an inherited heart condition that causes the heart muscle to become thicker, making it more difficult for the heart to pump blood around the body. HCM can lead to life-threatening abnormal heart rhythms and sudden cardiac arrest.

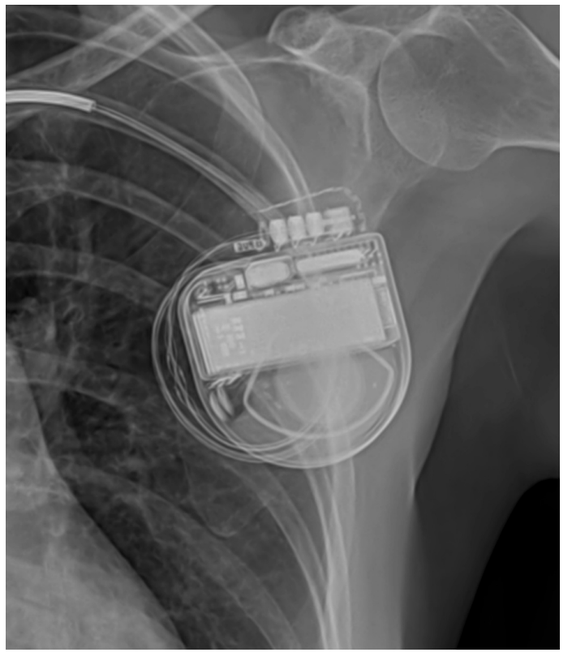
These cardiac arrests can be prevented with an ICD – a device fitted in the chest which sends electrical pulses to help regulate abnormal, dangerous heart rhythms. Therefore, it is important to identify which people with HCM are at high risk of a cardiac arrest, so they can have a potentially life-saving ICD implanted in their hearts.

In 2014, a scoring system was developed to predict which people with HCM are at high risk of a cardiac arrest. But this scoring system was not designed for people younger than 16. In 2019, BHF Fellows Dr Gabrielle Norrish and Dr Juan Pablo Kaski at University College London and Great Ormond Street Hospital led a study aiming to improve risk prediction for children with HCM.

Using anonymised medical records of over 1,000 children with HCM around the world, they identified characteristics which were associated with a higher risk of sudden death in children compared to adults. For example, they found that experiencing unexplained fainting is linked to an increased risk of sudden cardiac death in children, just as it is in adults. However, changes in some heart measurements visible on an echocardiogram and having a family history of sudden cardiac death can help predict risk in adults but not in children. This showed that the 'adult' tool can miss some children at high risk.

In 2019, Drs Norrish and Kaski used these findings to develop a tool to help doctors to better identify children with HCM who may need an ICD. The tool provides an individual risk for each patient so for patients at high risk, it gives families the option to be fitted with a device which could save their child's life. Additionally, by working out who is at low risk and therefore not in need of an ICD, the tool is a great reassurance to children affected by HCM and their families.

It is estimated that up to **1 in 500** people have hypertrophic cardiomyopathy in the UK



L-R: Research nurse Ella Field, senior researcher Dr Juan Kaski, study participant Kulthumi, lead researcher Dr Gabrielle Norrish

Kulthumi was diagnosed with cardiomyopathy when she was a baby. Heart problems are very common in Kulthumi's family with several family members sadly passing away from similar conditions all in a very short space of time.

Kulthumi is one of over 1,000 patients who participated in the research. Data from her medical records and tests to check her heart's rhythm and electrical activity were analysed together with records from other patients, and used to develop the prediction tool.

Several years ago, Kulthumi had an ICD fitted under her skin. The device constantly monitors her heart and helps correct any abnormal heart rhythms.

Using your smartphone to diagnose heart rhythm problems

Dr Matthew Reed

Each year in the UK there are hundreds of thousands of visits to accident and emergency (A&E) departments by people who are having palpitations, the sensation of feeling your own heart beating, or who are feeling faint.

These episodes are usually harmless and can be caused by stress, strenuous exercise, caffeine, or certain medications. However, in some cases they can be caused by serious heart rhythm problems.

Diagnosing the exact underlying cause of palpitations or feeling faint in A&E is often difficult. These symptoms are temporary, so often by the time the patient has arrived and been seen by doctors, they have recovered, and their electrocardiogram or ECG (a test to check their heart's rhythm and electrical activity) is normal.

To ensure those with heart rhythm problems do not slip through the net, the BHF funded a team of researchers in 2019 led by Dr Matthew Reed at the University of Edinburgh and NHS Lothian.

They tested the AliveCor® KardiaMobile, a smartphone-based ECG recorder, in 15 A&E departments across the UK. People experiencing palpitations or feeling faint were given the device to take home, with instructions to activate it when they feel palpitations or start feeling faint. The device then records the ECG which can be used to help diagnose the problem.

The researchers compared the results from 124 patients who received the ECG recorder with 116 who did not. The device enabled doctors to diagnose the cause of the palpitations in over five times as many patients than standard tests alone. Diagnoses were made more quickly, and it cut the cost of diagnosis from £1,395 to £474 per person.

These results showed that this device could improve diagnosis, spare people with harmless palpitations from further anxiety, save the NHS money and, most importantly, save lives.

Using stem cells to identify new treatments for arrhythmia

Professor Chris Denning

It is estimated that for up to one in 2,000 people in the UK, quality of life is hindered by a frightening and potentially life-threatening inherited heart disorder called long QT syndrome (LQTS). The condition can cause blackouts, stop the heart and even lead to sudden cardiac death.

The main treatment for this disorder – medicines called beta-blockers – are not always effective. Patients may need an operation to implant an ICD to restart the heart if it stops.

The BHF funded Professor Chris Denning and his team at the University of Nottingham to develop an innovative approach to gather new insights about the underlying biology of LQTS to find new, more effective treatments.

The team took skin cells from patient volunteers with LQTS and turned them into stem cells in the lab. Stem cells can grow into any type of cell but Professor Denning turned them into heart cells. In 2011, they found that the lab generated LQTS heart cells replicated the condition in a dish and that they responded appropriately to drugs used in patients, like beta-blockers. This means that these cells can now be used to test new drugs.

In 2017, after testing different types of drugs, the team identified a family of molecules that may form a new class of therapeutics for this condition. In the future, a similar approach could be used for conditions like short QT syndrome, Brugada syndrome or arrhythmogenic right ventricular cardiomyopathy. This could support the development of better treatments for patients with other inherited forms of arrhythmias.

Timeline of achievements

1961
The BHF is founded

1963
The BHF funds Dr Aubrey Leatham's pioneering work to refine **pacemaker technology**


1963

1965
Dr Frank Pantridge in Belfast develops the **first portable defibrillator** and tests for the first time having a defibrillator in an ambulance to get emergency heart attack care to where it is needed


1965

1971
Professor Douglas Chamberlain in Brighton tests **training ambulance staff** to using defibrillators and performing CPR

1978
Professor Douglas Chamberlain and the BHF **start training the public in CPR** and help fund public access defibrillators

1988
BHF Professor Stuart Cobbe leads a pilot study to **test defibrillators as standard equipment in ambulances in Scotland**

1990
The UK Government agrees to **fund defibrillators for all ambulances**

2011
Professor Chris Denning is using **stem cells to replicate inherited forms of arrhythmia** in the lab and find new treatments

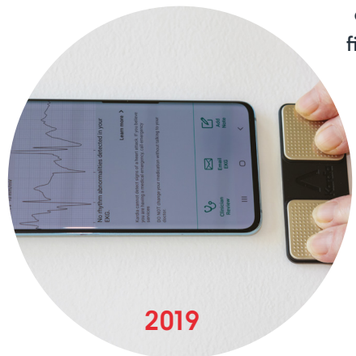
2012


2014

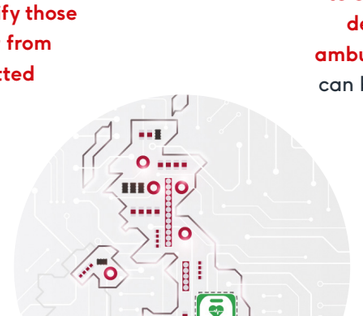
2012
Vinnie Jones urges people to "Call 999" and perform CPR by pushing "hard and fast to Stayin' Alive" if they see someone suffer a cardiac arrest in the **'Hands-Only CPR'** campaign

2014
Nation of Lifesavers is launched, aiming to teach **live-saving CPR skills to all young people and adults** throughout the UK

2019
BHF-funded researchers develop a new tool to predict risk of sudden cardiac death in children and **identify those who would benefit from having an ICD fitted**


2019

2019
BHF researchers show that diagnosis of heart rhythm problems can be **efficiently done with a smartphone**


2021

2020
BHF fellow Professor Paulus Kirchhoff demonstrates that **treatment to restore normal heart rhythm**, if started early after diagnosis of atrial fibrillation, can reduce the risk of strokes

2021
The BHF launches **The Circuit: the National Defibrillator Network, to connect public access defibrillators to NHS ambulance services** so they can be accessed quickly to help save lives

3D printed model of a patient's heart. These can be a valuable tool to help surgeons and cardiologists prepare for surgery and other procedures in children and adults born with congenital heart disease.

Keeping the heart in shape

Keeping the heart in shape

BHF-funded research over the last 60 years has helped to improve the diagnosis and treatment of people with structural heart disease. These conditions are caused by anomalies in the structure and shape of the heart that disrupt its normal function.

Some structural heart diseases develop in the womb. Each day in the UK around 13 babies are diagnosed with a congenital heart condition. BHF-funded research has developed better ways to diagnose and treat these conditions.

Other heart diseases are inherited, such as hypertrophic cardiomyopathy. Researchers supported by the BHF pinpointed some genes that cause this disease of the heart muscle. Since then, we have raised awareness and have helped make genetic testing services more widely available to help identify those families at risk.

Public support has also powered research that has helped improve outcomes for people with heart valve disease, which is when one or more of the heart's valves do not open and close properly. Heart valve disease can be congenital, develop later in life, or because of another type of structural heart condition.

Thanks to advances in research, people born with structural heart disease, or those who develop it later on, now live longer lives. The following pages explore the key breakthroughs supported by BHF funding.

Before the BHF, the majority of babies diagnosed with severe congenital heart disease died before their first birthday

Today in the UK, thanks to research, more than four out of five survive to adulthood

Improving surgery for patients with congenital heart disease

In 1977, Professor Anderson (left) and Dr Elliot Shinebourne organised for the first time an international conference in London, sponsored by the BHF, which brought together experts to discuss advances in paediatric cardiology and paediatric cardiac surgery

Congenital heart disease is a term that describes a range of conditions present at birth that affect the normal development and function of the heart. They are the most common congenital conditions in babies born in the UK.

Mapping the heart

Developing surgical techniques that can repair the hearts of babies born with congenital heart disease has greatly improved survival rates. Throughout the 1970s and 1980s, BHF Professor Bob Anderson, at the Royal Brompton Hospital, mapped the anatomy of different heart defects, showing their effect on the heart's electrical system that coordinates the heartbeat. This has enabled surgeons to avoid causing damage to the electrical circuit in the heart, making reparative surgeries safer.

New techniques and lower risks

Twenty years ago, replacement of faulty heart valves in children and adults, including children and adults with congenital heart disease, required open heart surgery. However, in 2004, we funded research at Great Ormond Street Hospital to refine a quicker and less invasive technique to replace heart valves. This technique involves using a tube inserted into a blood vessel in the top of the leg to reach the heart (also known as transcatheter valve implantation). Thousands of patients around the world have now benefited from this procedure and avoided invasive heart surgery.

> **"The support of the BHF enabled myself and other clinicians to quickly develop the paediatric cardiology unit at the Royal Brompton Hospital in London. Our work there placed the United Kingdom at the forefront of international developments in the field of congenital heart disease.**
>
> **Professor Robert Anderson, former BHF Professor of Paediatric Cardiac Morphology**

Congenital heart disease, from birth to adulthood

BHF Professor
Bernard Keavney

Dr Sonya Babu-Narayan

Screening DNA to find answers

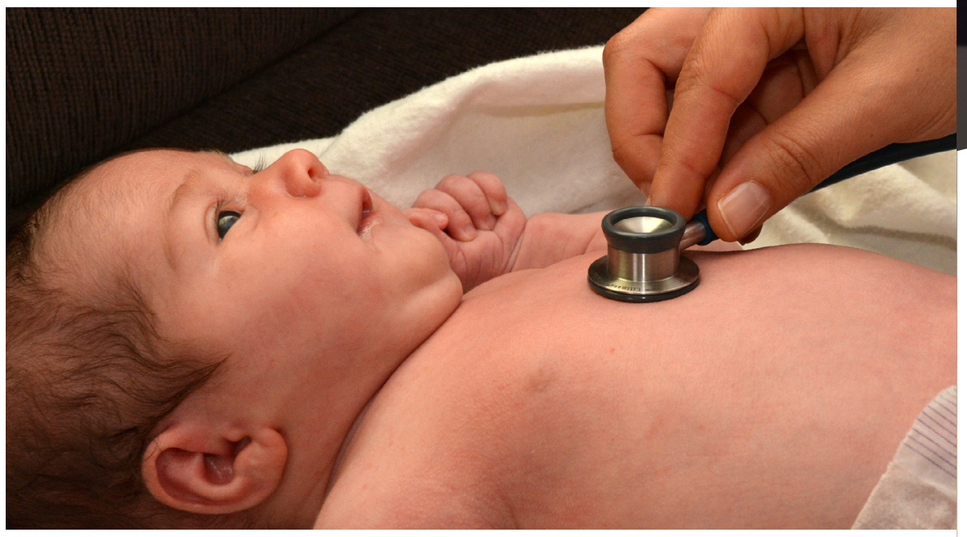
BHF-funded researchers are working to understand what stops a baby's heart developing normally. We funded BHF Professor Bernard Keavney at the University of Manchester to screen the entire DNA of people with congenital heart disease, and their parents. In 2012, the team showed the importance of tiny genetic changes in causing congenital heart disease, and showed these may explain up to 10% of cases. Screening for these genetic 'mistakes' is now part of the assessment and diagnosis of some babies and children with congenital heart disease.

Reducing the risk of sudden death

Even when the defect has been repaired with surgery in childhood, many adult patients still face an increased risk of heart failure or heart rhythm disturbances that can lead to sudden death.

In 2011, we funded Dr Sonya Babu-Narayan's work to refine ways to better identify which adults born with congenital heart disease are at increased risk of sudden death. Using cardiac MRI, Dr Babu-Narayan and her colleagues were able to work out how heart scarring seen on imaging scans can help predict which adults are at a higher risk of life-threatening heart rhythms and should be receiving treatments, such as implantable defibrillators.

Sarah (right), was born with a congenital heart disease called tetralogy of Fallot and took part in Dr Babu-Narayan's research.



Sarah's story

"To look at me, you wouldn't know anything was wrong. But repeated heart surgery can scar a heart. It could put me at risk of cardiac arrest. That's why Sonya's research really matters. Sonya's discoveries mean that if I'm at risk of a cardiac arrest, I will know. One day it could save my life. Without this research, I definitely wouldn't have the quality of life I do. I don't think I'd even be here."

Sarah

The quest for perfect replacement heart valves

Heart valve disease can be caused by congenital heart disease or cardiomyopathy, or can be the result of getting older. Thousands of people in the UK have heart valve replacement each year, and many benefit from the research and advances that the BHF has made possible.

Mr Donald Ross

The earliest breakthrough

At the start of the 1960s, scientists did not know how to treat heart valve disease. But after receiving one of our first research grants, heart surgeon Mr Donald Ross went on to pioneer and perform a world-first operation to treat people with faulty aortic valves. This technique is now known as 'The Ross Procedure'.

This ground-breaking surgery involves replacing the faulty aortic valve with the patient's own healthy pulmonary valve and replacing the pulmonary valve with a valve from a donor. The procedure cut postoperative death rates from 71% to 15% and revolutionised heart valve surgery across the globe. It is still used today to treat many patients with aortic valve disease like Robin (right).

BHF Professor Massimo Caputo

Using stem cells to grow living valve tissue

Babies born with a congenital heart disease often need valve replacement surgery using replacement grafts. Despite being lifesaving, these replacement grafts are not live tissues. This means they do not grow with the child and degenerate and fail in a few months or years. For these reasons, many children come back for more open-heart surgical operations with all the risks associated.

We are funding BHF Professor Massimo Caputo and colleagues' work at the University of Bristol. They are aiming to grow living valve tissue, composed of grafts containing stem cells isolated from the baby's umbilical cord, which has the potential to adapt to and grow with the child's heart. Once a clinical grade version of the new graft is created, the team will be ready to test it in patients.

If successful, this study will reduce the need for additional and high-risk surgical re-intervention. This would remarkably improve the quality of life of many children undergoing cardiac surgery for correction of congenital heart disease.

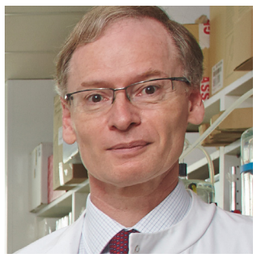
Robin was 17 when, after a routine check-up with his GP, he discovered he had a problem with his aortic valve. He later found out that he was born with a congenital heart disease. His consultant cardiologist recommended to fix the problem with his aortic valve with the Ross procedure.

This type of surgery is usually done in children, but he thought Robin was still young enough to be able to have his own pulmonary valve moved across to replace the diseased aortic valve. And it would mean Robin would avoid the complications that could come with a mechanical valve, like the need for lifelong blood thinning drugs. In his week-long recovery on the hospital ward, Robin, who was an engineer at the time, met a junior doctor who made him rethink his future career plans. Robin joined medical school and later trained in cardiology.

Today, 20 years after his Ross procedure, Robin is a cardiologist and uses his own experience as a patient to try and reassure heart patients when they are getting anxious about their own upcoming heart operation.

Discovering the causes of hypertrophic cardiomyopathy

HCM is an inherited disease that causes the muscle wall of the heart to get thicker, affecting how well the heart can pump blood around the body. In some cases, it can cause sudden death due to a fatal abnormal heart rhythm.



BHF Professor Hugh Watkins

Looking for the culprit

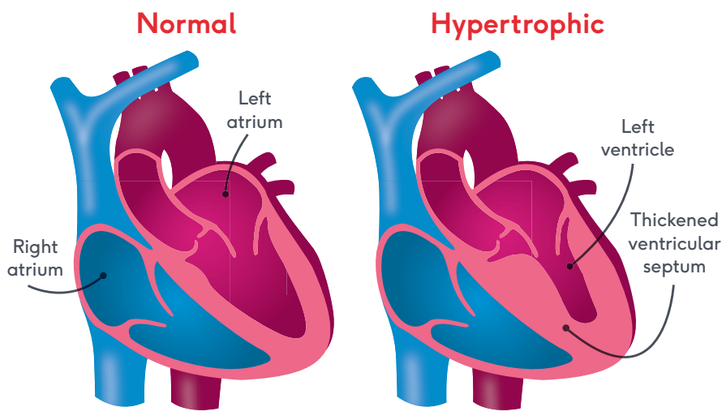
BHF-funded researchers Professor Bill McKenna and Professor Hugh Watkins started looking into possible genetic causes of HCM in the 1980s. They were among the first to find that HCM is linked to faults in genes which encode molecules needed for heart muscle cells to contract.

Professor Watkins and his team used these findings to set up the UK's first genetic testing service for HCM. The service, based in Oxford, helps relatives of someone known to have a faulty gene causing HCM, to find out if they also have the gene fault. This not only identifies people who need to get treatment to prevent a sudden death but provides reassurance to those who do not.

Making genetic testing widely available

Thanks to the generosity of our supporters, we have been able to support 13 inherited cardiac condition services across all four nations of the UK. The funding has enabled us to support existing services and help develop new services that can identify more people with HCM and importantly, test relatives of people with the condition.

More than 500 people affected by HCM have been identified so far, and supported by specialist cardiac genetic nurses and genetic counsellors. These genetic testing services are now delivered by the NHS.



Hypertrophic cardiomyopathy happens when the heart muscle becomes abnormally thick (hypertrophied)

> **It's now time we think differently about the way this hidden heart condition is detected and treated. We now have a new genetic tool that we believe will better predict which members of affected families will have a bad form of the disease, identifying those who need early intervention.**
>
> **BHF Professor Hugh Watkins, University of Oxford**

A genetic breakthrough

Until recently researchers and cardiologists were unable to explain why HCM is so varied amongst family members who have the same rare mutation and why some people without these mutations still go on to develop HCM.

In 2021, Professor Watkins and his team discovered that the inheritance of a different type of genetic fault – called 'common variants' – not involved in the contraction of the heart explains these varied outcomes. The number of these common variants, in combination with the rare mutations, determine whether a person is protected or more susceptible to the disease. This discovery provided a long-awaited missing piece to this puzzle which could help transform the diagnosis and treatment of the disease in the future.

Dilated cardiomyopathy: improving care and seeking a cure

Dilated cardiomyopathy (DCM) is a disease where the heart muscle becomes thinner causing the heart to weaken, which can lead to heart failure. It is estimated to affect up to 1 in 250 people in the UK. The condition is a leading cause for heart transplants.

Dr Brian Halliday

Understanding recovery, relapse and the role of medication

Although there is no cure for DCM, heart medicines can help heart function to recover. Some people, especially younger people with DCM, even find that their symptoms disappear completely with treatment. These people often ask whether they can stop taking their medicines.

Until recently, it was unclear whether stopping heart failure treatment in this situation was safe. A clinical trial led by BHF-funded Dr Brian Halliday and Professor Sanjay Prasad at the Royal Brompton Hospital and Imperial College London addressed this issue. In 2019, their results showed for the first time that stopping treatment would put the patient at risk of relapsing. This study provided invaluable evidence to back-up long term prescription of medication in people with DCM, even if their heart failure seems to have recovered.

Professor Stuart Cook

Hope for new treatments

DCM can be treated using common heart medications like ACE inhibitors but there are currently no treatments available developed specifically for the condition. BHF-funded research is trying to change that. We are funding the largest ever study of DCM, which will recruit 2,000 people with the condition to investigate how genes and lifestyle factors are linked to its development. The study is being led by Professor Stuart Cook at Imperial College London. As we get a better understanding of the genes and factors which cause the condition, we can hope to develop new treatments.

> **If I hadn't taken part in the trial I would have probably just tried stopping the tablets myself, and that obviously would have been dangerous. Since taking part, I am on a reduced dose – and the care I received during the trial made me feel supported at what was a difficult time.**
>
> **Clinical trial participant**

Stopping life-threatening problems in people with Marfan syndrome

Marfan syndrome is an inherited condition that affects connective tissue, which provides the structural framework to hold the body's cells in place. Some people with Marfan syndrome have a weak, expanding aorta susceptible to bursting. A ruptured aorta, called an aortic aneurysm, can be fatal.

Dr Michael Mullen

Trialling a new treatment

The aorta is the main artery that carries blood away from the heart to the rest of the body. When this major blood vessel is weakened and at risk of bursting, the only effective treatment to prevent its rupture is open heart surgery, to replace the damaged section. The BHF supported Dr Michael Mullen at Imperial College London to test whether common drugs normally used to treat high blood pressure might be able to slow the expansion of the aorta.

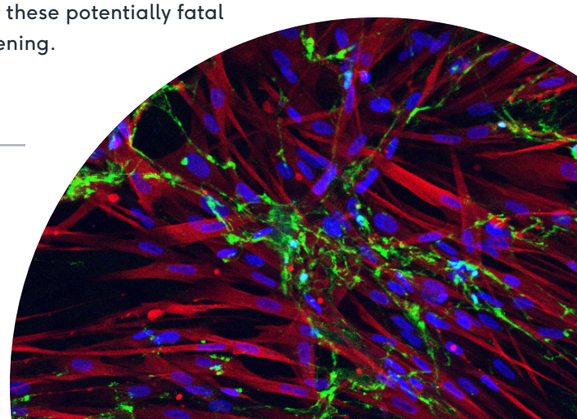
The trial tested whether an angiotensin receptor blocker, called irbesartan, could be used to treat people with Marfan Syndrome. In 2018, the trial showed the rate of expansion of the aortic root was reduced by 30% in the irbesartan group compared with the placebo group and seemed safe, even for children. These findings provided much needed evidence for using the drug as a new treatment for people with Marfan syndrome.

Professor Sanjay Sinha

Recreating Marfan blood vessel cells in a dish to find new treatments

Although irbesartan provides a new option for people with Marfan syndrome, it cannot cure or prevent an aortic aneurysm. We funded Professor Sanjay Sinha and his team at the University of Cambridge to use an innovative approach to gather new insights into Marfan syndrome.

The team took skin cells from volunteers with Marfan syndrome and turned them into stem cells in the lab. Stem cells can grow into any type of cell but Professor Sinha turned them into cells that make up the blood vessel wall. It allowed the team to find new mechanisms that are key for the development of aortic aneurysm. The team now hopes to use the lab-generated Marfan blood vessel cells to test a new drug that may prevent these potentially fatal aneurysms from happening.



Marfan blood vessel cells grown in a dish are in red (with a blue nucleus) with the connective tissue shown green

Timeline of achievements

1961
The BHF is founded

1967
With BHF funds, Mr Donald Ross performs a world-first operation to treat people with faulty aortic valves – a technique now known as **'The Ross Procedure'**

1972
BHF Professor Robert Anderson starts **mapping the anatomy of different heart defects** and their effect on the heart's electrical system, which proved crucial to make reparative heart surgeries safer

1976
Mr Magdi Yacoub, who later became BHF Professor of Cardiothoracic Surgery, develops **the arterial switch** to repair a congenital heart defect called transposition of the great arteries

1992
BHF Professor Bill McKenna and Dr Hugh Watkins are among the first worldwide to find that **HCM is linked to faults in genes** which encode molecules needed for heart muscle cells to contract

2004
A team of BHF-funded researchers refine a **quicker and less invasive technique to replace pulmonary valves**

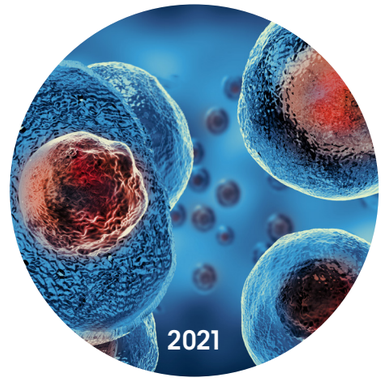
2011
The BHF funds Dr Sonya Babu-Narayan's work to **use cardiac MRI to predict which adults born with tetralogy of Fallot might be at increased risk of sudden death** so that they can be fitted with a lifesaving implantable cardiac defibrillator

2012
BHF Professor Bernard Keavney shows **the importance of tiny genetic changes in causing congenital heart disease** and that they may explain up to 10 per cent of cases

2017
The BHF supports existing genetic services and helps develop new services that can identify people with HCM and importantly, **test relatives of people with the condition**

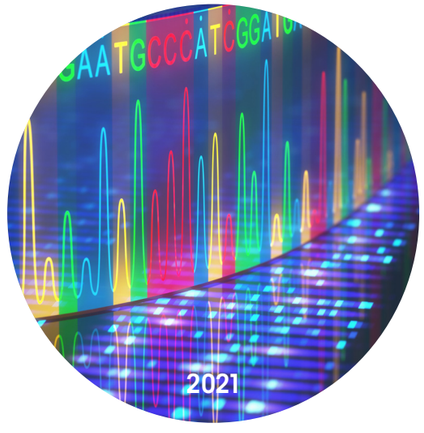
2018
The BHF funds a landmark study led by Professor Stuart Cook to investigate **how genes and lifestyle factors are linked to the development of dilated cardiomyopathy**

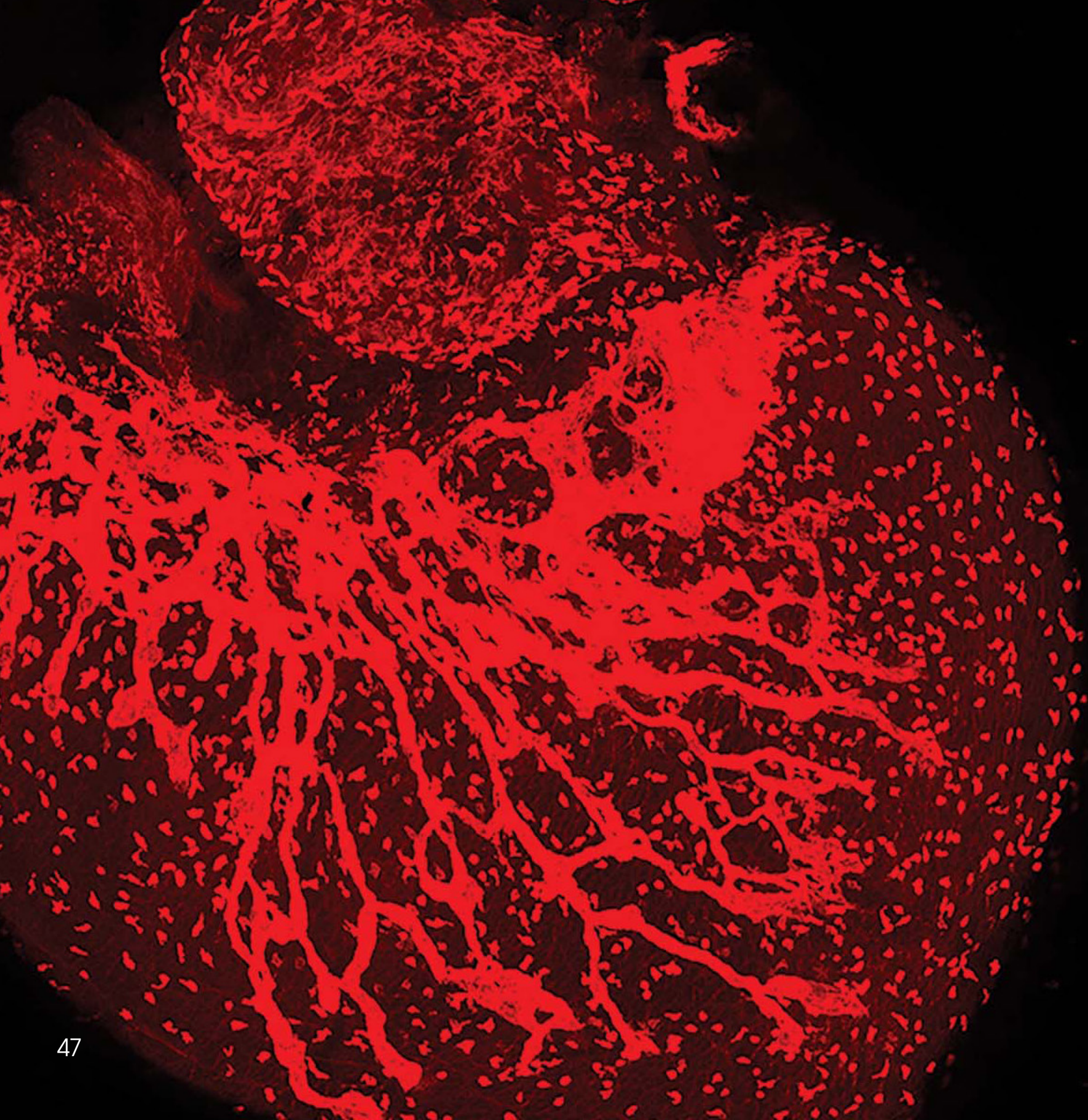
2019
BHF-funded Dr Brian Halliday and Professor Sanjay Prasad **provide invaluable evidence to back-up long term prescription of medication in people with DCM**, even if their heart failure seems to have recovered



2021
The BHF funds BHF Professor Massimo Caputo's team to create **a living valve tissue** using stem cells isolated from the baby's umbilical cord

2021
BHF Professor Hugh Watkins and his team find new genetic faults in people with HCM that could **transform the diagnosis and treatment of the disease**





This picture, by BHF professor Paul Riley's team, shows the developing cardiac lymphatics and tissue-resident macrophages- both of which play important roles in heart regeneration.

Healing failing hearts

Healing failing hearts

Thanks to our supporters, BHF-funded research has helped to significantly improve the prognosis and quality of life for people with heart failure.

Around 920,000 people in the UK are living with this potentially life-limiting condition, which means their hearts are not pumping blood around the body effectively. It develops when the heart is damaged, for example, after a heart attack or by cardiomyopathy, congenital heart disease, high blood pressure, or some types of chemotherapy.

As heart failure advances, a person's wellbeing is gradually stolen until their life is cut short. Fluid builds up in their lungs, fatigue sets in and as their heart struggles to pump, it is forced to work harder and harder.

No cure exists for heart failure, apart from a heart transplant in a small number of cases. Treatments attempt only to control the symptoms.

We have been taking significant steps forward in improving quality of life for people with heart failure. In the following pages, we will track these across six decades.

Every year, there are around

200,000

new diagnoses of heart failure in the UK

Three game-changing drugs for heart failure treatment

Professor Stephen Ball

Professor Allan Struthers

Professor Sian Harding

Heart failure gradually gets worse without treatment. Fortunately, BHF research has shown that treatments given immediately after a heart attack can help limit this long-term damage.

Unlocking the benefits of a common heart medicine

In 1993, BHF Professor Stephen Ball and colleagues at the University of Leeds showed that common medicines called ACE inhibitors (angiotensin-converting enzyme inhibitors), given to patients with signs of heart failure in the days after a heart attack, could save lives.

In a ground-breaking trial, the team prevented one death for every 18 patients treated. The trial provided evidence that ACE inhibitors gave heart attack patients a better chance of recovery, with significantly higher survival rates and improved quality of life.

Boosting the effectiveness of ACE inhibitors

In 1995, Professor Allan Struthers led a team funded by the BHF at the University of Dundee. For the first time, they showed that adding a diuretic (water tablet) to ACE inhibitors increased their beneficial effect. These results were later confirmed in a larger international clinical trial that evidenced this combination reduced death rates in people with heart failure by 30%.

Reviving the use of beta blockers to treat heart failure

Until the late 1990s, beta-blockers were ruled out for use with people living with heart failure. Research led by Professor Sian Harding and colleagues at Imperial College London changed this perception. The team uncovered the benefits of long-term use of beta-blockers in failing human heart cells. After several international clinical trials in the early 2000s, these findings were applied to patient care. Beta blockers are now recommended in all international guidelines for the treatment of chronic heart failure.

Thanks, in part, to BHF-funded research, these drugs form a vital part of care and treatment we see, in the UK and worldwide, for heart failure today.

A blood test to help diagnose heart failure

Professor Phillip Poole-Wilson

Heart failure can be hard to diagnose because its symptoms, including breathlessness and fatigue, are common in other conditions.

In 1997, BHF-funded Professor Allan Struthers and BHF Professor Phillip Poole-Wilson were part of a team that discovered a simple blood test could transform early diagnosis of heart failure. The test measured levels of a molecule called B-type natriuretic peptide (BNP) in the blood. This can be used to help identify patients who need an echocardiogram to find out if their breathlessness might be due to heart failure.

This test has meant that doctors can make faster referrals for further diagnostic tests to confirm or rule out the diagnosis of heart failure. In 2010, national guidelines for clinicians included the BNP test as part of the gold standard for heart failure diagnosis and by 2016, MPs were urging all GP surgeries across the UK to adopt it.

Stopping deaths from an inherited blood disorder causing heart failure

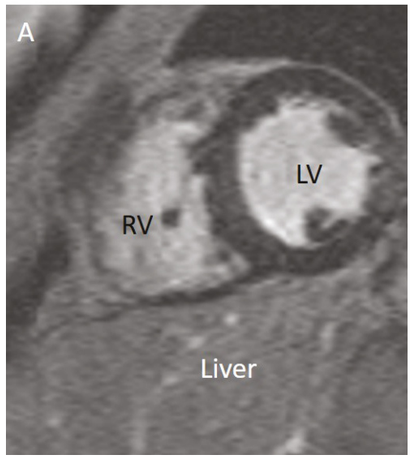
Professor Dudley Pennell

Thalassaemia is an inherited blood disorder that means the body produces too little haemoglobin, the molecule carrying oxygen in the blood. To survive, most people with severe thalassemia need blood transfusions from a very young age and throughout their lives. However, the iron from transfused blood that accumulates in the body, including in the heart, can lead to heart failure.

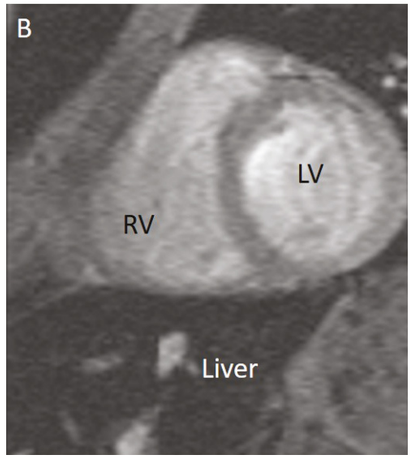
The development of drugs to remove iron from the body helped with this problem. But for a long time, there was no safe way to measure the iron overload in the heart, and it was hard to know whether the drugs to remove iron were needed or had been successful.

That changed in the late 1990s when Professor Dudley Pennell and BHF-funded fellow Dr Lisa Anderson at Royal Brompton Hospital in London developed a new MRI technique called T2* MRI. This technique can measure how much iron is in the heart muscle and monitor how successful the treatment to remove it is.

Heart failure used to be the most common cause of death for people with severe thalassemia. But since the introduction of iron removal therapy and T2* MRI monitoring, the number of people dying from severe thalassemia in the UK and around the world has dramatically reduced.



A) Liver signal normal (grey) indicating no iron loading, but the left ventricle of the heart (LV) is dark showing heavy iron loading. This patient is at risk of heart failure



B) Liver signal iron dark indicating heavy iron loading, but the heart signal is normal (grey). This patient is unlikely to have heart complications at this time.

Advances in heart transplants

Mr Donald Ross

Since our inception, the BHF has funded research into heart transplantation - pre-dating even the world's first heart transplant in 1967.

Transplant pioneers

In 1968, heart surgeon Mr Donald Ross performed the UK's first, and world's 10th, heart transplant on heart patient Fred West (right), following five years of BHF-funded research into heart transplant surgery techniques in preclinical models.

In the 1970s, BHF-funded Professor David Hearse made a major breakthrough, developing a fluid to preserve donor hearts for longer. This fluid has been used in hospitals all over the world and helped make many more heart transplants possible.

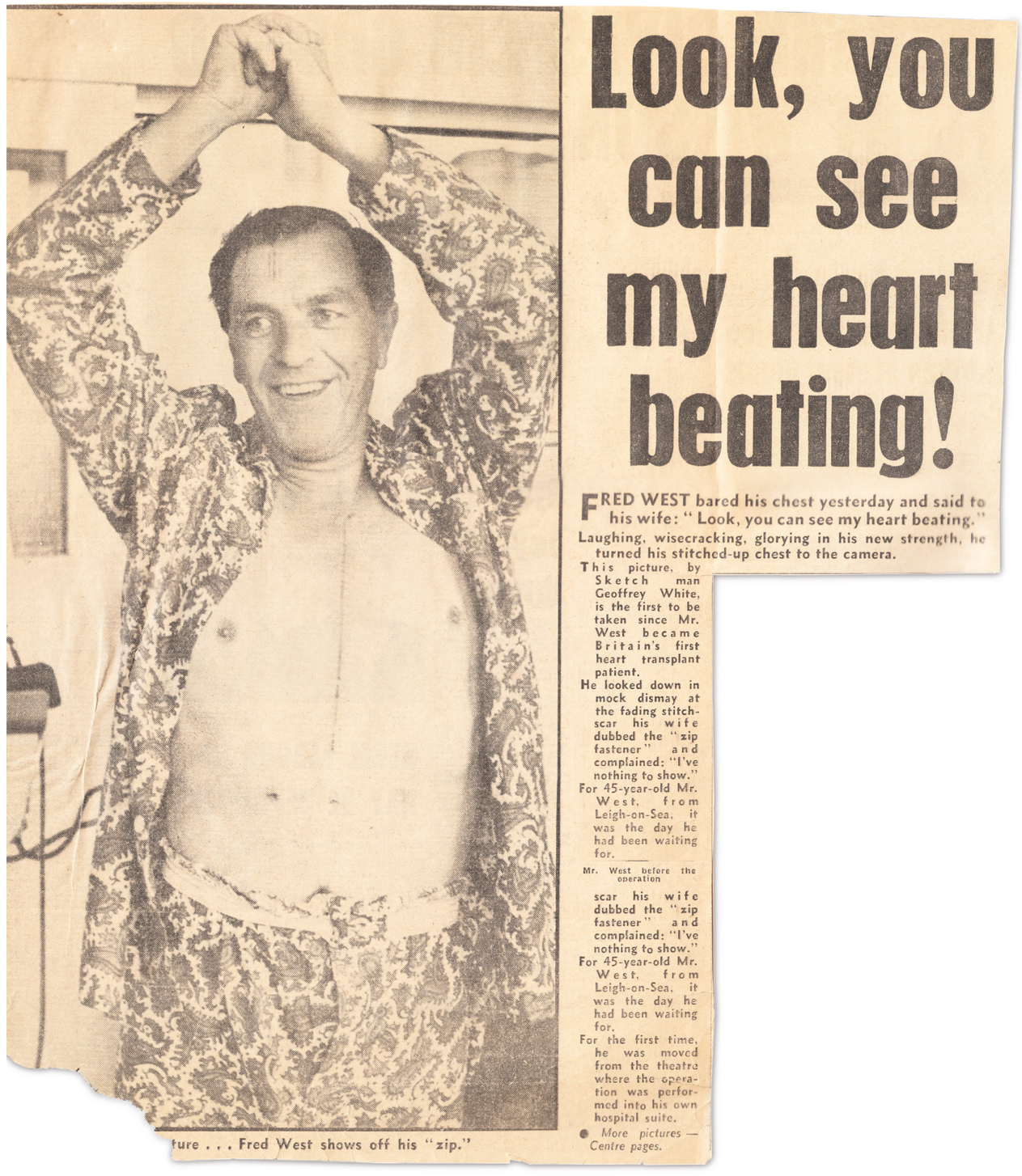
BHF Professor
Federica Marelli-Berg

Overcoming organ rejection

Despite the initial excitement, it became clear that rejection of the donor heart was a major challenge. This happens when the body's immune system recognises the new heart as a foreign object and attacks it, just as it would attack an infection. To prevent their new heart from being rejected, transplant recipients must take drugs to suppress their immune system for the rest of their lives.

Since the 1980s, we have been funding research to fight organ rejection. BHF Professor Federica Marelli-Berg and colleagues at Queen Mary University London, are using an innovative approach to tackle heart transplant rejection. Her team is trying to 'hijack' the immune system and stop it attacking the transplanted heart. When immune cells are alerted to the donor heart, they travel through the body to reach it. The team discovered that to find their target, immune cells are armed with surface proteins that act like a GPS system, using the 'area code' for the heart to reach their destination. Blocking this 'navigation system' could lead to new treatments to reduce organ rejection.

> **We are talking about transferring this into humans, but we need to do more work. First, we need to confirm that the same type of immune cells are present in humans.**
>
> **BHF Professor Federica Marelli-Berg**



Look, you can see my heart beating!

FRED WEST bared his chest yesterday and said to his wife: "Look, you can see my heart beating."
Laughing, wisecracking, gloryingin his new strength, he turned his stitched-up chest to the camera.
This picture, by Sketch man Geoffrey White, is the first to be taken since Mr. West became Britain's first heart transplant patient.
He looked down in mock dismay at the fading stitch-scar his wife dubbed the "zip fastener" and complained: "I've nothing to show."
For 45-year-old Mr. West, from Leigh-on-Sea, it was the day he had been waiting for.

Mr. West before the operation

scar his wife dubbed the "zip fastener" and complained: "I've nothing to show."
For 45-year-old Mr. West, from Leigh-on-Sea, it was the day he had been waiting for.
For the first time, he was moved from the theatre where the operation was performed into his own hospital suite.
● *More pictures — Centre pages.*

ture . . . Fred West shows off his "zip."

Heart patient Fred West

Breakthrough in child heart transplantation

Dr Richard Issitt

Right now, around 50 children are waiting for a heart transplant in the UK. But small hearts are hard to find as the donated heart needs to come from a child roughly the same size.

Over the last 20 years, doctors have increased the number of organs available to children needing a transplant by using donor hearts with different blood types from theirs. However, to ensure the 'mismatched' heart isn't rejected, the child's blood is slowly replaced with a blood type that matches the donated heart. This means the procedure is limited to smaller children who require less donor blood, typically 4 years old or younger, and older children must wait for a heart that matches their blood type.

We funded Dr Richard Issitt and colleagues at Great Ormond Street Hospital to develop a new technique that uses a blood filtering device that removes the mismatched antibodies in the blood that can lead to transplant rejection. The filter is added into the heart and lung machine used to support the child during surgery. This machine keeps their blood flowing, delivering vital oxygen and nutrients throughout their body until the new heart is in place.

By filtering out the specific antibodies, the child's blood doesn't need to be completely removed and replaced. This consequently halves the amount of donated blood required during the transplant itself and in the intensive care unit afterwards, allowing larger, older children to have an 'incompatible' transplant – making them more likely to be matched with a suitable heart.

The team have now performed mismatched heart transplant with the new antibody filtering device on 10 children, including Lucy (right), and compared their outcomes to 27 children who had the standard mismatched heart transplant technique, where all blood was removed and replaced. All of the children who had a transplant using the new device survived, there was no need for re-transplantation and there was no difference in the length of hospital stay. This new technique has the potential to double the number of children able to receive a heart transplant.

Lucy's story

Lucy is one of the children who benefited from Dr Issitt's research. In 2020, age 8, she became the oldest person known world-wide to receive a mismatched heart transplant, more than double the age that was previously possible. Her mum Jenny says that after waiting three and a half years on the list, Lucy was only able to get the heart because of this new research. Lucy was never able to do much activity-wise, but since the operation she is so eager to try everything. She got to enjoy paddleboarding, trampoline parks and high wire obstacles course, activities she could never have done before.

Making more donor hearts available

Fearghal McKinney, head of BHF Northern Ireland, campaigning with heart patients for the introduction of opt-out organ donation system.

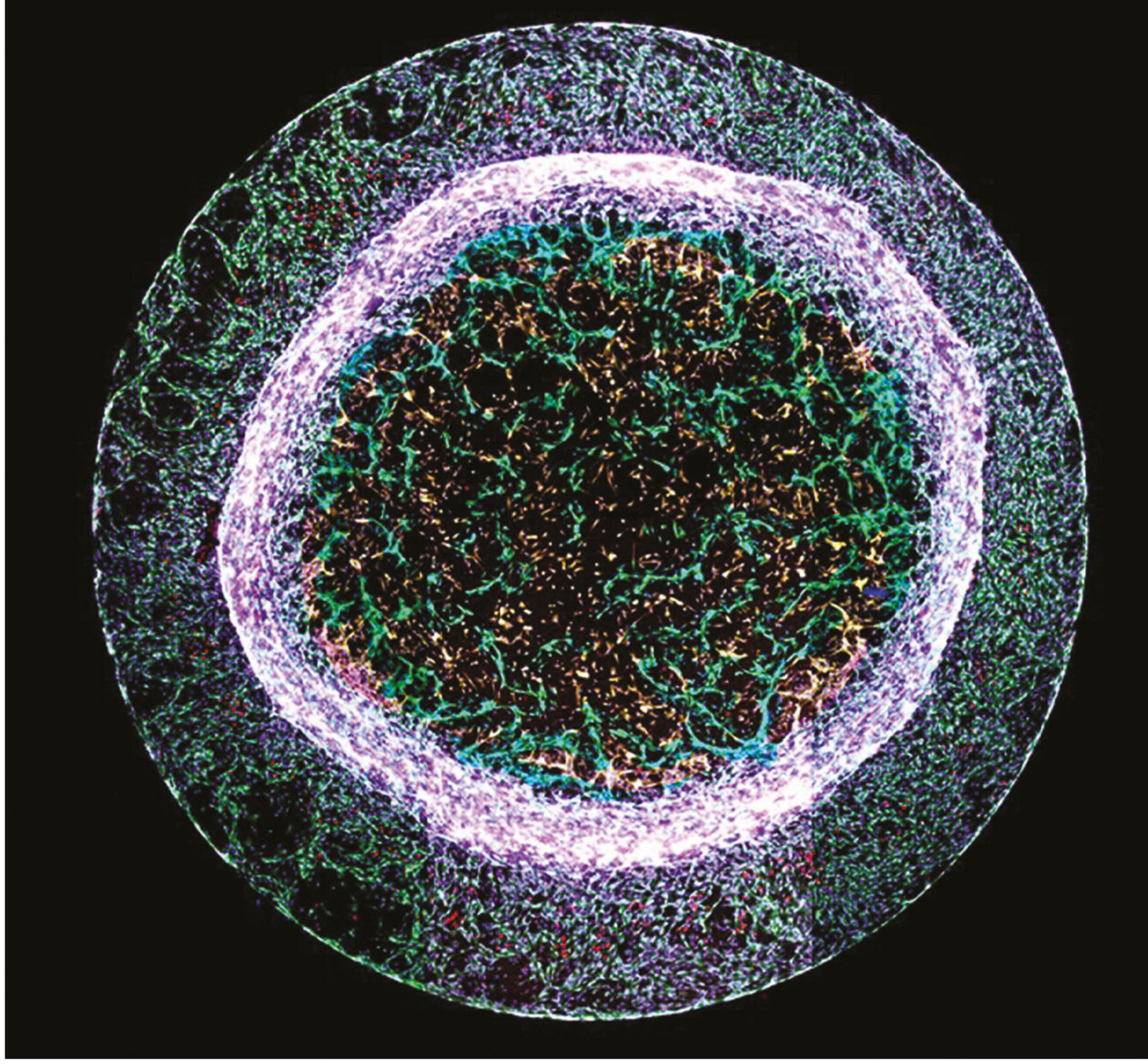
Each year in the UK, around **100** people die in need of a new heart

Though the BHF has driven forward progress in heart transplantation, shortage of donor organs remains a significant issue.

That's why we spent many years campaigning for an opt-out organ donation system. It means that everyone is presumed to consent to donating their organs unless they register their decision to opt-out on the NHS organ donation register.

We were pleased to witness Wales adopt the system in 2015, England in 2020 and Scotland in 2021. In 2021, a draft bill was signed off by the Northern Ireland Executive and passed final stage at Assembly in February 2022.

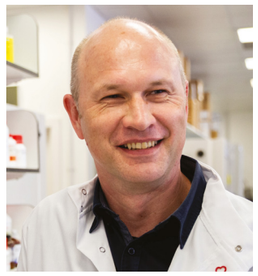
These changes are increasing the consent rate for organ donation and will not only give more people severe heart failure hope for the future, but also those with other organ failure.



'Recreating heart blood vessels' by Dr Elisa Avolio, University of Bristol. Although at first glance it appears to resemble a luminous jelly fish, this image shows new blood vessel-like structures (pictured in green) sprouting from a 3D gel. Encouraging new blood vessels to form after a heart attack to replace those that have died could help to re-establish blood supply to damaged areas of the heart and aid recovery.

Regenerating the heart

Currently there is no cure for heart failure. Treatments available attempt only to control the symptoms and improve quality of life. If heart failure is severe and other treatments cannot help, a person may be considered for heart transplant surgery. But while this can be transformative, it is an option only in a small fraction of cases, mostly due to the shortage of donor hearts.



BHF Professor Paul Riley

Dr Richard Jabbour

The promise of regenerative medicine

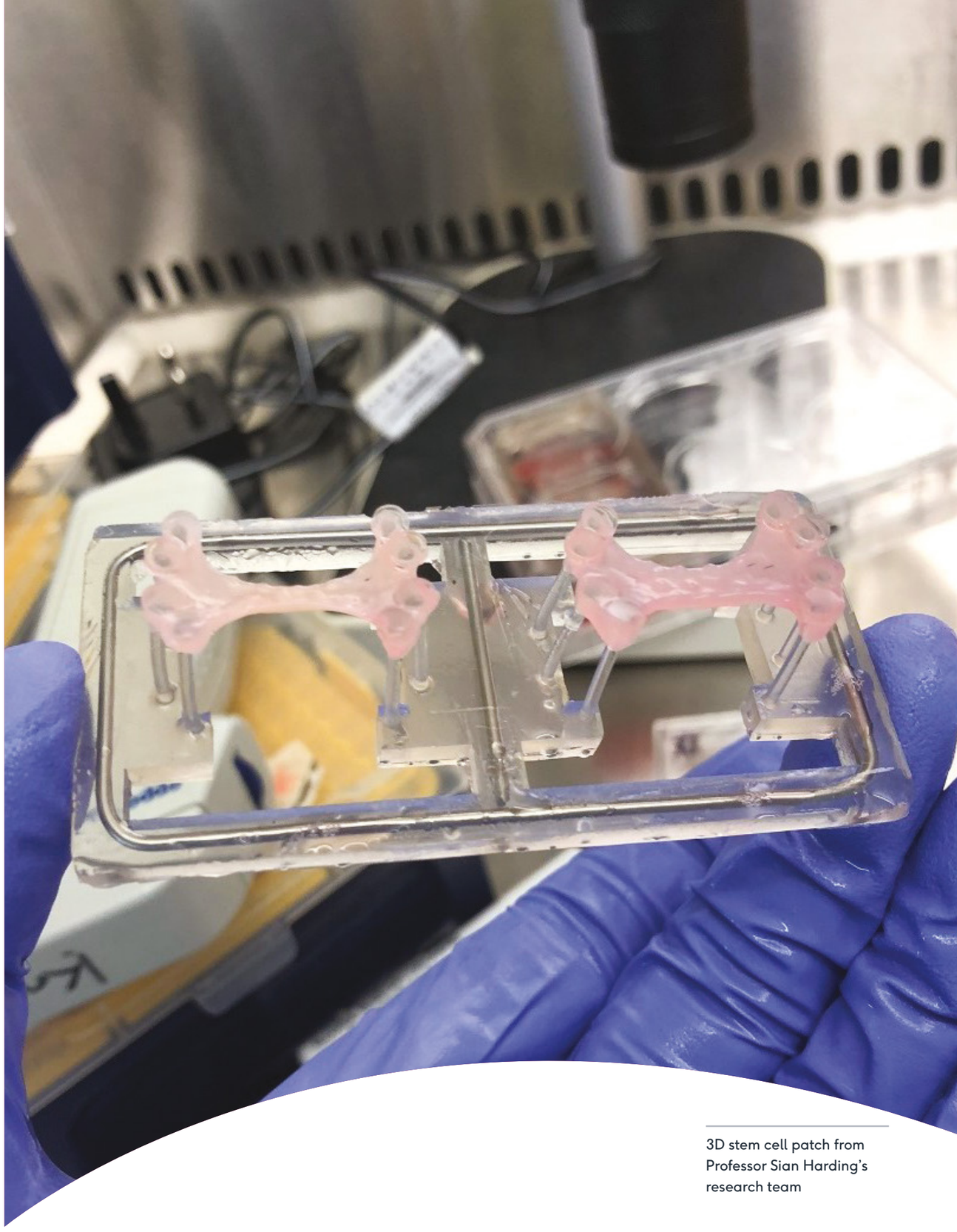
In 2002, scientists amazed the world by showing that a zebrafish heart, unlike a human heart, can completely heal itself after injury, demonstrating the incredible potential of regenerative medicine. The BHF has been supporting this exciting field of research that holds the promise to regrow, repair or replace damaged heart tissue and blood vessels.

In 2007, BHF-funded research led by Dr Paul Riley, who later became our first BHF Professor of Regenerative Medicine, showed how mouse heart cells can be activated to repair damage caused by a heart attack.

BHF Centres of Regenerative Medicine

In 2011, we launched the Mending Broken Hearts Appeal, which has since funded around £39 million of research into regenerative medicine across the UK. This includes three pioneering Centres of Regenerative Medicine, unique collaborations between leading researchers from different institutions, fields, and parts of the world, united in finding a solution for heart failure.

Coordinated from Imperial College London and the Universities of Edinburgh and Oxford, each centre has a different scientific focus. For example, researchers at Imperial College London, led by Professor Sian Harding, are attempting to generate new cardiac muscle, or heart tissue from stem cells, to repair damaged hearts. Dr Richard Jabbour and colleagues developed a 3D stem cell patch that can 'beat'. These patches adhere to a damaged heart, physically supporting the muscle and helping it pump more efficiently, whilst releasing natural chemicals that stimulate heart cell repair and regeneration. Early studies have shown the patches are safe in animals and the team are now planning safety trials in humans.



3D stem cell patch from Professor Sian Harding's research team

Demonstrating the value of specialist heart failure nurses

With access to the right services and support, people with heart failure can go on to have a good quality of life for many years. Since the 2000s, the BHF has been developing and testing new ways of delivering care for heart failure patients, including at home.

Between 2004 and 2007, the BHF tested a home-based heart failure programme led by heart failure specialist nurses. We funded 76 nurses in 26 NHS primary care organisations in England who saw approximately 15,000 patients. This programme led to a 35% reduction in hospital admissions, and significant cost savings. Thanks to our supporters, heart failure specialist nurse services are now well-established and working with patients in communities across the UK.

In 2020, as part of our continued efforts to improve care for people with heart failure, we worked with healthcare professionals to produce the report Heart Failure: A blueprint for change. This led to a campaign to highlight the main barriers to improving heart failure diagnosis and care in the UK.

The BHF called for an improved awareness of heart failure as a long-term condition and suggested key areas for change to deliver high-quality and consistent heart failure care, including equal access to BNP testing and home or community-based care.

> **“The fact that someone really appreciates the difference I've made in their life is the most rewarding part of my job.**
>
> Community Heart Failure Nurse Specialist

Supporting heart failure patients online

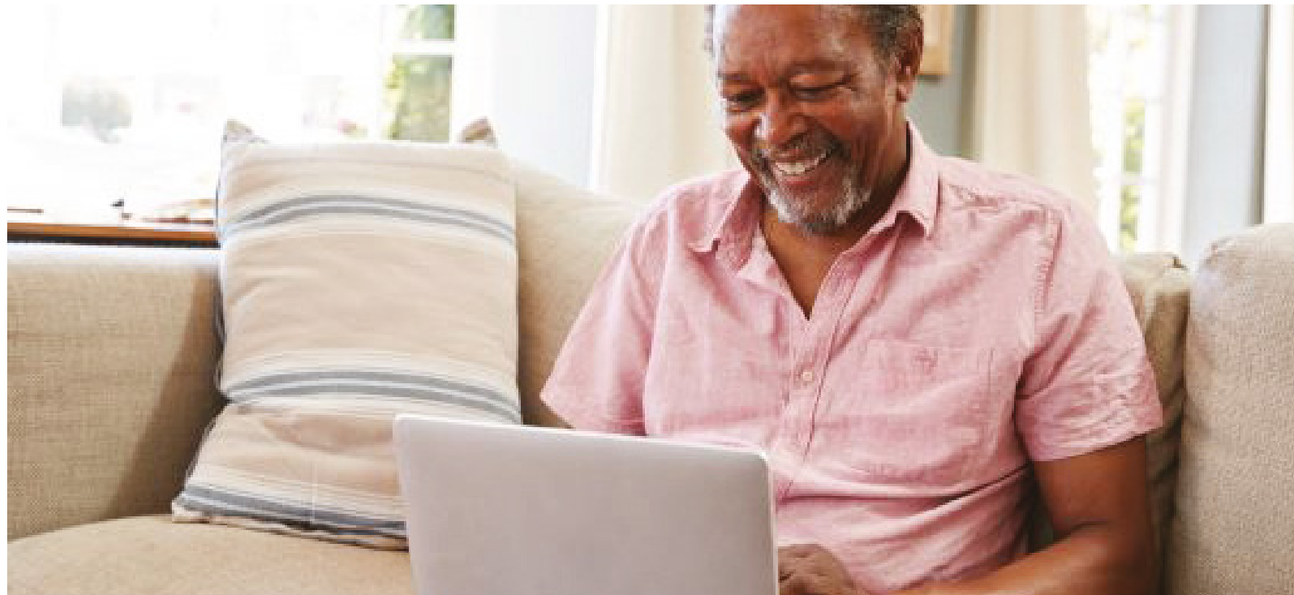
> **“I was really struggling before, and they have made me feel supported. They have really helped and I feel so much more positive and confident now. Thank you, you were my lifeline.**
>
> Cardiac rehab patient about the Cardiac rehab at home product.

Research funded by the BHF and others has shown that cardiac rehabilitation is vital in improving the day-to-day life of, and outlook for, people with or at risk of heart failure.

Normally a clinically supervised programme of exercise and education, cardiac rehabilitation has been proven to reduce the risk of having another cardiac event and being readmitted to hospital whilst positively impacting on wellbeing and quality of life. It is usually offered to people after a cardiac event such as a heart attack, heart surgery or stent procedure.

Around one in eight people diagnosed with heart failure in England and Wales get referred for cardiac rehabilitation when they leave hospital. But during the COVID-19 pandemic, many of these potentially life-saving services reduced or closed due to social distancing measures, and cardiac rehab healthcare professionals being redeployed.

Responding to this need, in 2020, the BHF developed a Cardiac Rehabilitation at Home product which simulates a cardiac rehabilitation experience digitally. ‘The online programme supports patients to exercise safely in their own homes, provides information on healthy eating and helps them understand how to best manage their condition. A year and a half after its launch, the hub and its resources had been viewed more than half a million times.



Timeline of achievements

1961
The BHF is founded

1968
Mr Donald Ross performs the **first heart transplant** in the UK, following five years of BHF-funded research into heart transplant surgery techniques in preclinical models

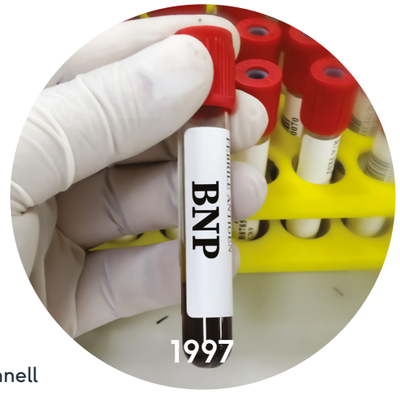

1968

1976
First clinical use of a **new fluid that can preserve donor heart for longer**, developed by BHF-funded David Hearse and colleagues

1979
The **UK's first transplant with long-term success** is performed by Mr Terence English who later received BHF funding for research on transplant rejection

1993
BHF Professor Stephen Ball and colleagues report for the first time that **ACE inhibitors given to patients** with signs of heart failure in the days after a heart attack **improve their long-term survival** and quality of life

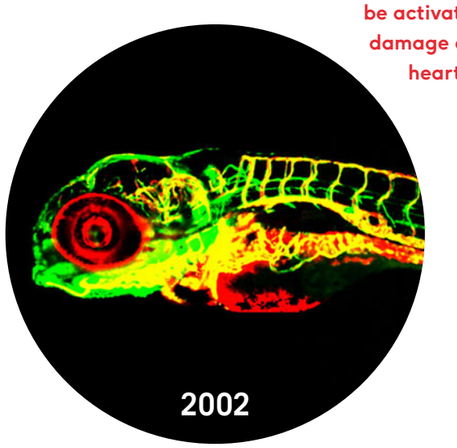
1997
BHF-funded Professor Allan Struthers and BHF Professor Phillip Poole-Wilson discover that a simple test **measuring the level of a molecule called BNP in the blood could transform early diagnosis of heart failure**



1997

1998
BHF-funded Dr Dudley Pennell and colleagues develop a **novel MRI technique** to measure iron levels in the heart that **helped prevent people with thalassaemia dying from heart failure induced by iron overload**

2002
Scientists amazed the world by showing that a **zebrafish heart, unlike a human heart, can completely heal itself after injury**, demonstrating the incredible potential of regenerative medicine


2002

2004
The BHF funds heart failure specialist nurses to test new ways of delivering care for heart failure patients, including at home

2007
With BHF funding Dr Paul Riley shows how **mouse heart cells can be activated to repair damage caused by a heart attack**

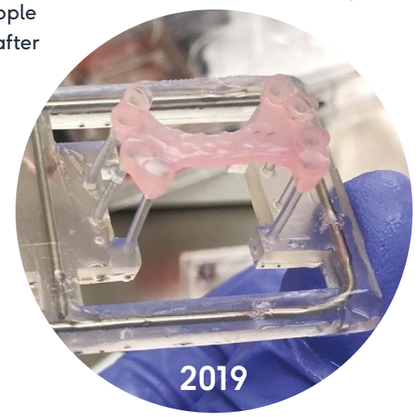
2011
Mending Broken Hearts fundraising appeal is launched to enable us to **fund research into cardiovascular regenerative medicine**

2011

2013
The BHF **launches three new BHF Centres of Regenerative Medicine,** to support collaborations between leading researchers from different institutions, fields, and parts of the world, united in finding a solution for heart failure

2015
After years of campaigning by the BHF and others, **Wales becomes the first of the four UK nations to adopt the opt-out organ donation system.**

2019
BHF-funded research led by Professor Sian Harding show that **heart 'patches' grown in the lab** are safe to move on to trials in people with hearts damaged after a heart attack

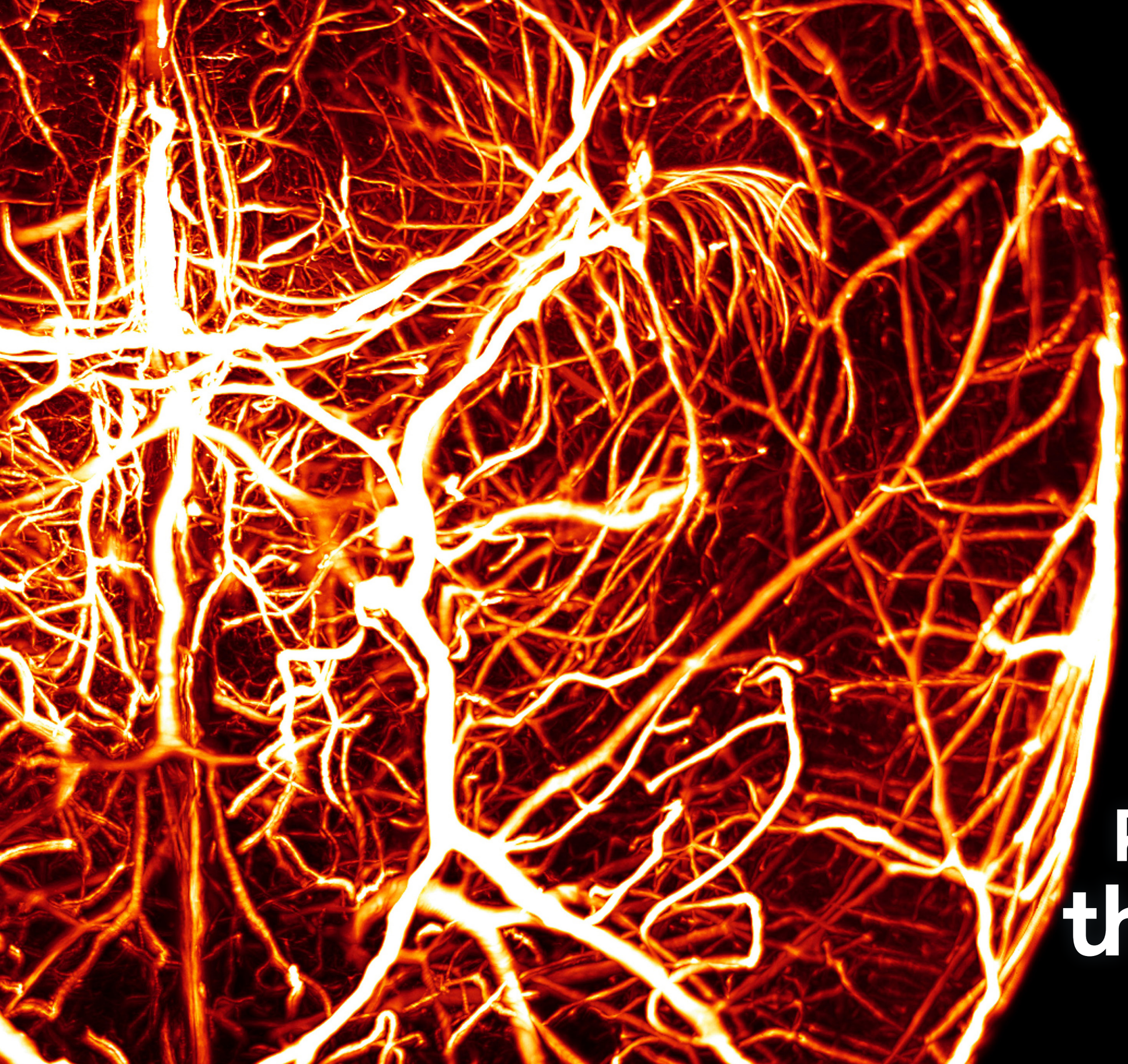

2019

2020
England adopts the opt-out organ donation system, also known as Max and Keira's law

2021
Dr Richard Issitt and colleagues show that a **new technique** they have developed makes **a heart transplant possible for more children in need**


2021

2021
Scotland adopts the opt-out organ donation system and the bill is making it's way through the Northern Ireland Assembly



‘A rush of blood to the head’ by Dr Michael Drozd and Dr Nicole Watt. This picture shows the complex network of blood vessels in the brain of a mouse.

Protecting the brain

Protecting the brain

When the BHF was founded in 1961, the very first research project funded was to support Dr Enid Acheson to identify the causes of strokes. Little was understood about the condition at this time. Since then, we have grown to become one of the largest independent funders of stroke research in the UK.

Strokes cause around 34,000 deaths a year in the UK alone, and are the single biggest cause of severe disability. A stroke happens when the blood supply to part of the brain is disrupted. This usually occurs as a result of a blockage in one of the brain's blood vessels, called an ischaemic stroke; or when a blood vessel bursts, causing a bleed in the brain called a haemorrhagic stroke. After a stroke, brain cells can become damaged or die, affecting how the mind and body function.

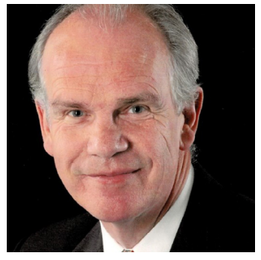
If a person survives a stroke, recovery can take months or even many years. A stroke affects people in different ways, depending on which area of the brain has been affected. Common effects of a stroke that significantly affect a person's quality of life include paralysis, communication difficulties, memory problems and extreme fatigue.

People are at increased risk of developing dementia within the first year of surviving a stroke. Vascular dementia is a type of dementia caused by reduced blood flow to the brain and affects at least 150,000 people in the UK. It is a progressive and incurable disease, devastating for both the person diagnosed and those closest to them.

The BHF is committed to finding better ways to prevent and treat strokes as they happen, and rapidly after, to reduce the devastation and long-term damage they can cause. The following pages summarise our work in this area.

By 2050 it's predicted that the number of people in the UK living with vascular dementia could double

Taking statins to reduce the risk of ischaemic stroke



Professor Stuart Cobbe

BHF-funded research has helped to test whether medicines to help control people's cholesterol levels can reduce their risk of having a stroke.

In the 1970s, it became clear that a high level of cholesterol was associated with an increased risk of having a stroke. Cholesterol is a fatty substance found in blood and if there is too much of it, it can build up inside the walls of blood vessels. This clogs them up causing narrowing of the arteries and increasing the risk of having a stroke or heart attack.

Statins, efficient cholesterol-lowering drugs, became available in the 1980s. Soon after, BHF Professor Stuart Cobbe and colleagues in Glasgow launched a clinical trial looking at the effect of statins on over 6,000 men who had high cholesterol, which put them at high risk of a heart attack or stroke. The team showed that people with high cholesterol taking cholesterol-lowering statins had a lower risk of having a stroke. The team followed up the same group of people after 10 and 15 years. They showed in 2007 that the benefit of taking statins appeared to extend to at least 10 years after the original trial.

In the 2000s, BHF Professor Rory Collins and colleagues in Oxford tested if statins could also help people with 'normal' cholesterol levels or with diabetes. The results published in 2004 showed that statins reduced the risk of having an ischaemic stroke by a third in both groups of people.

A clot-busting drug to improve the outlook for stroke patients

The BHF is funding several clinical trials looking at how a "clot-busting" drug, tenecteplase, could be used to improve the outlook for stroke patients.

Professor Keith Muir

Acting fast to treat ischaemic stroke

Giving a clot-busting drug to break down the clot and restore blood flow through the brain in the first few hours after an ischaemic stroke can greatly improve the chances of recovery. Currently, doctors use a drug called alteplase. But tenecteplase, a newer clot-busting drug used in other fields of medicine, is less expensive, easier and quicker to administer.

In 2016, the BHF and the Stroke Association joined forces to support Professor Keith Muir at the University of Glasgow, to compare tenecteplase with alteplase in thousands of people with an ischaemic stroke, to see which is best at helping patients recover.

> "Every minute is crucial in treating stroke and we need better treatment options. Any treatment that is easier to deliver and potentially safer could mean the difference between a good recovery and someone suffering seriously debilitating long term effects.
>
> **Professor Keith Muir, University of Glasgow**

Every 5 minutes

someone is admitted to a UK hospital due to a stroke

Improving outcomes after a mini-stroke

Around half of all strokes cause minor symptoms. However, despite seeming mild, these strokes known as transient ischaemic attacks or mini-strokes can lead to long-lasting disability.

Professor Muir is also investigating whether tenecteplase could help doctors stop mild strokes from causing disability. People who have had a mini-stroke are not usually offered clot-busting drugs like tenecteplase because their symptoms do not seem serious enough, or the patient appears to be recovering rapidly. Clot-busting drugs can also cause bleeding in the brain, so doctors are careful to give them only when it's clear that they could help.

Professor Muir and his team have received BHF funding to take part in an international clinical trial. The trial is testing whether tenecteplase improves recovery in people with who have suffered a mini-stroke, compared with usual treatments, such as aspirin. The study could lead to a new way to treat this kind of stroke, helping prevent lifelong disability.

Professor Thompson Robinson

Wake-up stroke

To be effective, clot-busting drugs have to be given within hours of the stroke happening. But about one in five strokes occur when someone is asleep and then wakes up with symptoms. People who have a 'wake-up stroke' are not offered clot-busting treatment. This is because it is not known what time the stroke happened and whether the treatment would work.

In 2017, the BHF and the Stroke Association funded Professor Thompson Robinson at the University of Leicester to participate in an international clinical trial involving people who present with a wake-up stroke. Professor Robinson is comparing tenecteplase with usual treatment to see if the drug helps improves recovery in this patient group.

Should antiplatelet drugs be restarted after a haemorrhagic stroke?

The BHF funded Professor Rustam Salman and his team at the University of Edinburgh to explore a controversial issue: whether doctors should avoid antiplatelet drugs (drugs like aspirin and clopidogrel, that reduce the chances of a heart attack) after a brain bleed.

Many people who have a brain bleed are already prescribed aspirin, often because they have coronary heart disease. Aspirin is a blood thinner, which reduces the chance of clots forming that could cause a heart attack or ischaemic stroke. But if someone has just had a bleed in the brain, it is important for their blood to be able to clot so that the bleeding stops. Guidance advises to stop taking aspirin immediately so that a haemorrhagic stroke does not worsen. But it is unclear whether these patients should then restart their aspirin.

Professor Salman led a clinical trial to find out. In 2019, his team published their findings showing that it is safe for people who have had a stroke caused by bleeding in the brain to restart blood-thinning drugs.

The results suggested this would not raise the risk of another brain bleed and could potentially even reduce the risk of further bleeding in the brain. The BHF is currently funding further research to confirm whether this is indeed the case. The findings could have major implications for the treatment and management of people who have suffered a haemorrhagic stroke.

> **“I think we have confirmed the safety of antiplatelet therapy for survivors of brain haemorrhage with these findings. But more work is now needed to see if aspirin might actually lower the risk of brain bleeds as well as clots.**
>
> **Professor Rustam Salman, BHF funded researcher**

Professor Rustam Salman

Professor Joanna Wardlaw

Studying the link between stroke and vascular dementia

around
150,000
people in the UK have vascular dementia

Professor Joanna Wardlaw at the University of Edinburgh focuses her research on understanding the causes and risks factors of stroke and cerebral small vessel disease. Through her work, Professor Wardlaw aims for the improved prevention, diagnosis and treatment of people who have a suffered a stroke and the reduction of long-term complications, like vascular dementia.

Finding out how to treat lacunar stroke to prevent vascular dementia

People who have had a stroke, even a minor one, are at increased risk of developing vascular dementia. This is particularly true for a lacunar stroke, which is caused by damage to one of the small blood vessels deep within the brain.

There is currently no treatment for lacunar stroke. To help change this, the BHF is funding a clinical trial led by Professor Wardlaw to test whether two drugs, cilostazol and isosorbide mononitrate, could help reduce the damage to the small blood vessels in the brain after a lacunar stroke.

If successful, this research could lead to a larger trial of the two drugs, which are already used to treat other heart and circulatory diseases, to treat lacunar strokes. The hope is that one day the drugs could be proved effective enough to reduce cases of dementia.

Understanding more about the causes of vascular dementia

Together with Stroke Association and Alzheimer's Society, we funded a collaboration between experts in stroke and vascular dementia. Led by Professor Wardlaw, the goal was to answer fundamental questions about the two conditions: who will develop memory and thinking problems after stroke, why does this happen, and how can we treat it?

The study is following 2,000 people who have had a stroke using memory tests and thinking tests to measure who develops problems in the two years following the stroke. The researchers are looking at lifestyle factors and genes to try to find out what factors may cause vascular dementia and how we can predict and prevent it. They will also use blood tests and brain scans to find out how to spot vascular dementia early and make it easier to diagnose.

The detailed knowledge gathered from this research should make it possible for researchers to design clinical trials that target specific groups of patients. This could speed up the development of diagnostic tests and treatments for vascular dementia.

Investigating the causes of vascular dementia

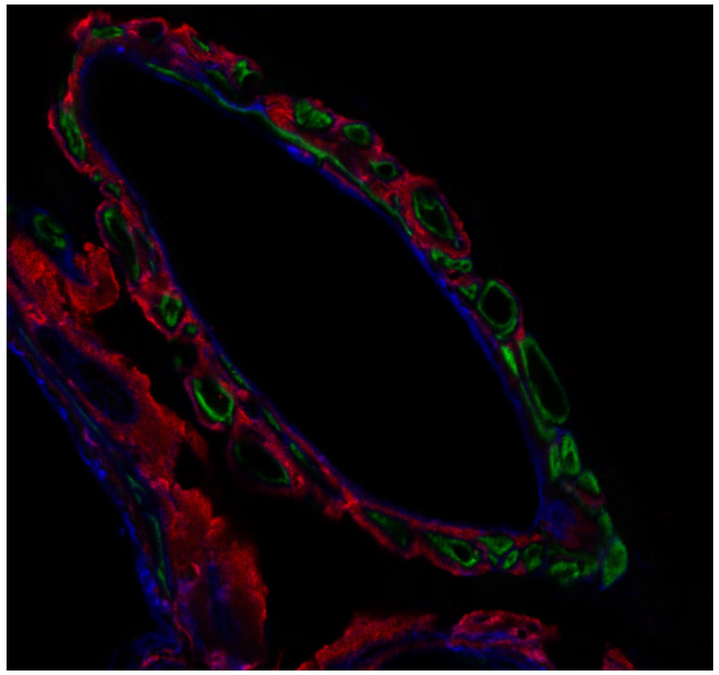
Professor Roxana Carare

Vascular dementia is the second most common type of dementia, seen in around **1 in 4** cases.

Every cell in the body produces toxic waste products, including brain cells. The brain removes waste products by draining it out using extremely thin pathways embedded in the walls of blood vessels. Professor Roxana Carare and colleagues, from the University of Southampton, believe vascular dementia develops because the brain can't get rid of waste and fluid properly.

The Southampton team believes these pathways are damaged in vascular dementia, which would mean that waste cannot be eliminated properly from the brain. In 2017, the BHF joined forces with the Stroke Association and Alzheimer's Society to fund their research.

By investigating the mechanisms involved, the team hopes to find new treatments for vascular dementia, perhaps even leading to drugs that drain waste fluid from the brain, to stop or slow down vascular dementia.



The image shows the cross section of an artery in the brain of a vascular dementia patient.

"I can tell it's slowly getting worse. I'm expecting anything at any time. I try to do memory puzzles and games, just to keep my mind active, but I've noticed it's getting worse. On a bad day I can't even put a sentence together. I try not to think about the future, but I can't help it. I am thankful to the British Heart Foundation, and other institutions, for investing in and raising awareness of vascular dementia. I really appreciate that.

Lesley Jackson, diagnosed with vascular dementia at the age of 50 after her second mini-stroke

Do short episodes of atrial fibrillation lead to stroke and dementia?

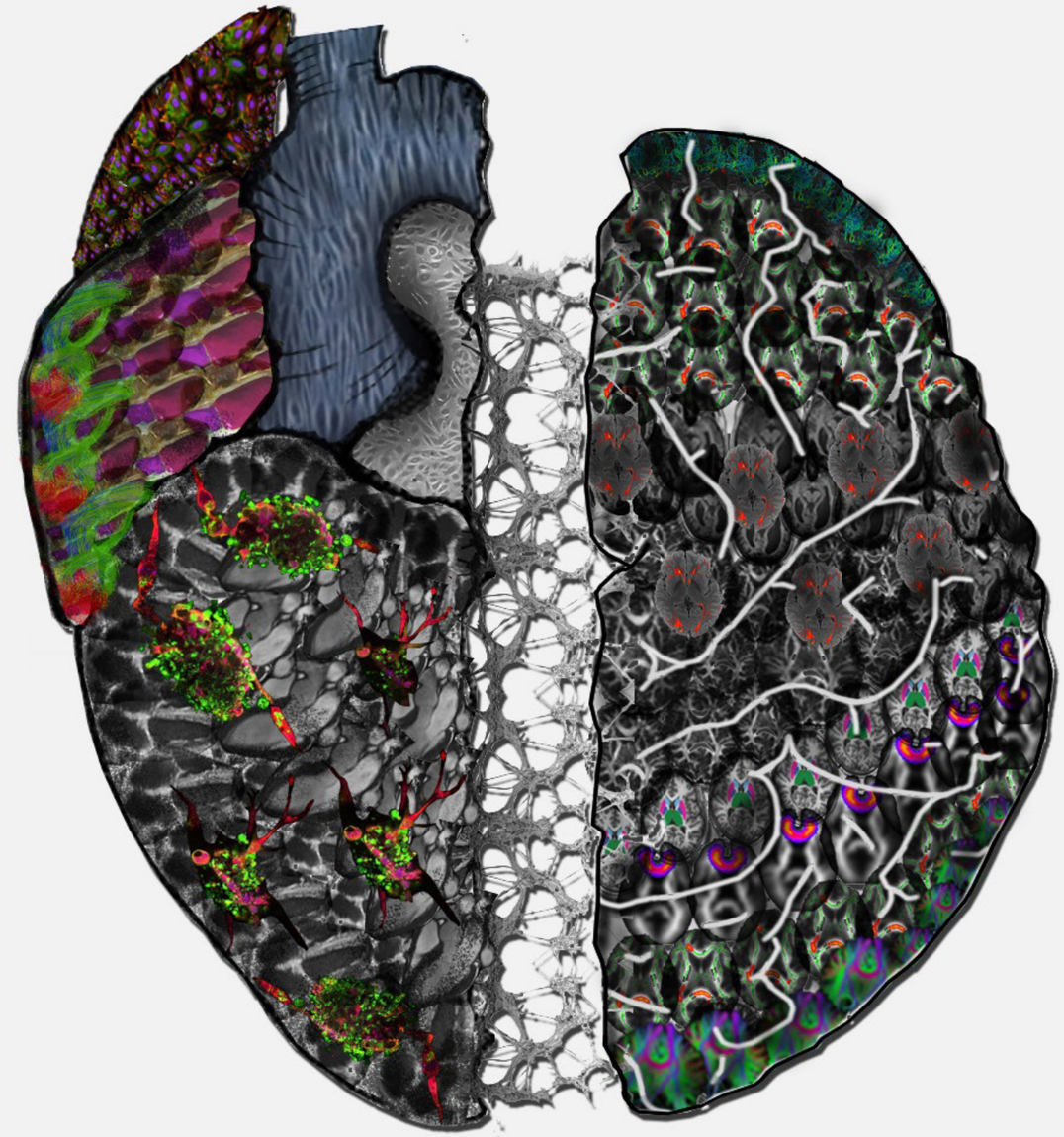
BHF Professor
Barbara Casdei

Atrial fibrillation is the most common abnormal heart rhythm and is a major cause of strokes. Around 1.5 million people have been diagnosed with atrial fibrillation in the UK. Atrial fibrillation can present in short episodes, particularly in older people, and can go unnoticed. Many people are living with the condition undiagnosed. But we do not know if these "silent" episodes can cause damage to the brain, leading to a subsequent decline in brain function.

To find out, we are currently funding BHF Professor Barbara Casadei and colleagues at the University of Oxford to follow 20,000 people registered in UK Biobank. They will monitor the heart rhythm of participants using a skin patch recorder and and screen for any damage to blood vessels in the brain using MRI scans, in addition to conducting tests that measure people's brain function.

If this research shows that silent atrial fibrillation increases the risk of stroke and dementia, then close monitoring and treatment of atrial fibrillation may avoid many occurrences of stroke and slow down or prevent the development of dementia. This would be a major step forward.

> **"Abnormal heart rhythms – where the heartbeat is too fast, too slow or irregular – can raise the risk of a stroke, which in turn raises the risk of vascular dementia. Lots of people have abnormal heart rhythms that are undiagnosed, and our research is looking at whether this might be causing 'mini strokes', which leads to cognitive decline. These three conditions are connected, and our research needs to be too.**
>
> **BHF Professor Barbara Casadei, University of Oxford**



The Heart and Brain Axis, by Cheryl Tan, Maryam Alsharqi, Dr Winok Lapidaire, Dr Mariane Bertagnolli and Dr Adam Lewandowski. The image reflects the interaction between the heart (left) and the brain (right). The colours show the different imaging techniques, including: magnetic resonance imaging of the heart and brain, ultrasound imaging of the heart, and fluorescent imaging of the heart and blood vessels.

Timeline of achievements

1961
The BHF is founded

1963
The **BHF awards its very first grant** to Dr Enid Acheson to **identify the causes of strokes**

1987
Statins are commercialised

1995
BHF Professor Stuart Cobbe and colleagues show that **people with high cholesterol taking cholesterol-lowering statins have a lower risk of having a stroke**

2004
BHF Professor Rory Collins and colleagues show that **statins reduce the risk of stroke** by a third in people with 'normal' cholesterol levels or with diabetes

2010
The **BHF joins forces with the Stroke Association** to jointly fund high value clinical studies in stroke

2015
The BHF funds Professor Keith Muir and colleagues to test if a new clot-busting drug, called **tenectaplase could be a cheaper and more straightforward way to improve the outlook for stroke patients**

2015
The BHF funds a clinical trial led by Professor Joanna Wardlaw to **test whether two drugs could be repurposed to prevent vascular dementia after a lacunar stroke**

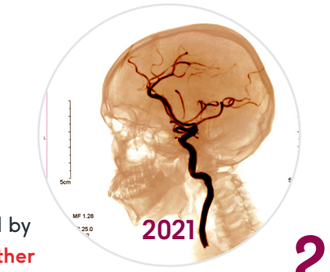
Alzheimer's Society
United Against Dementia

2016

2016
The BHF joins forces with Alzheimer's Society and the Stroke Association to jointly fund research into vascular dementia

2017
The BHF funds Professor Thompson Robinson and colleagues to find out if people who have a **stroke while asleep and wake up with symptoms should be treated with clot-busting drugs**

2017
The BHF funds a clinical trial led by Professor Joanna Wardlaw to **gather new knowledge about the causes of vascular dementia**



2018
BHF Professor Barbara Casadei and colleagues **investigate whether short episodes of atrial fibrillation can lead to stroke and dementia**

2018
The BHF funds Professor Keith Muir and colleagues to test whether the clot-busting drug **tenecteplase could help doctors stop mini-strokes from causing disability**

2019
BHF-funded research by Professor Rustam Salman and colleagues show that it is safe for people who have had a stroke caused by bleeding in the brain to **restart blood-thinning drugs without raising their risk of another brain bleed**

2021
Research part-funded by the BHF and led by Dr Adam Greenstein shows that a drug **already used to treat high blood pressure could be repurposed as the first treatment to tackle a type of vascular dementia** caused by damaged and 'leaky' small blood vessels in the brain

Stroke association

2010

‘Lighting and Thunder’, by Dr Tamara Girbl. This image represents a network of blood vessels (blue and green) transporting blood and nutrients throughout a muscle.

Controlling blood pressure

Controlling blood pressure

The heart pumps blood around the body to deliver oxygen and nutrients to the organs. Blood pressure is the force the heart uses to pump blood around the body through the arteries.

High blood pressure, or hypertension, has long been recognised as a leading risk factor for heart and circulatory disease. Around half of heart attacks and strokes in the UK are associated with the condition, where blood pressure is consistently too high, putting extra strain on blood vessels, the heart and other organs. It can also cause diseases such as heart failure and vascular dementia.

Although the benefits of lowering blood pressure were well recognised in the 1960s, the condition was often poorly managed.

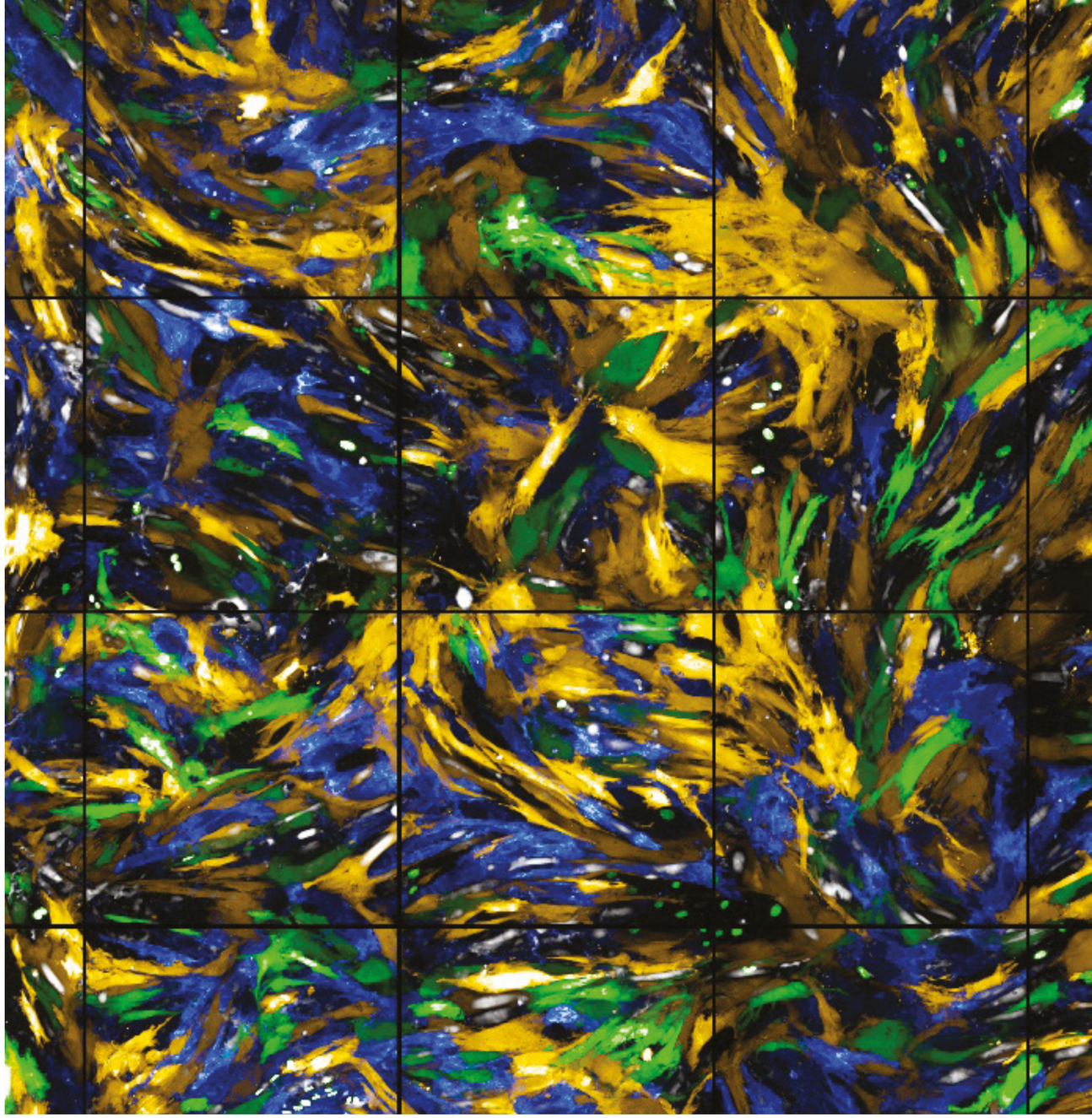
Powered by our supporters, BHF-funded research has helped doctors around the world understand more about what the best drugs are to treat high blood pressure and which patients can benefit from them.

Our research has also helped to further understanding of other, sometimes even fatal, conditions that are related to changes in blood pressure such as pulmonary hypertension, pre-eclampsia and septic shock.

An estimated 28% of adults in the UK have high blood pressure – that's around

15 million

adults – at least half of them are not receiving effective treatment.



'A Sea of Cells' by Iona Cuthbertson, PhD student at the University of Cambridge. This image could be mistaken for the thick brushstrokes of a Vincent van Gogh painting bringing to life an ocean bloom, it is in fact a close-up of smooth muscle cells that surround the blood vessels in mice. The smooth muscle cells, which are partly responsible for the control of blood flow by narrowing or widening blood vessels, are marked with differently coloured fluorescent proteins.

Finding the best ways to treat hypertension

Professor Christopher Bulpitt

Blood pressure naturally goes up and down, and it is normal for it to go up while moving about. However, having blood pressure that is always high, even at rest, is a serious condition that affects one in four adults in the UK.

Treating high blood pressure in the over 80s

While the benefits of blood pressure lowering drugs have been understood for decades, until 15 years ago it was unclear whether it was safe to treat high blood pressure in people aged over 80. Most previous studies of blood pressure lowering drugs had not included the over 80s so there was a lack of evidence.

To answer this question, the BHF part-funded a clinical trial, led by Professor Christopher Bulpitt at Imperial College London. In 2007, the trial found that people receiving blood pressure medication had significantly lower death rates, and a reduction in the rate of stroke and development of heart failure. Importantly, the over-80 age group tolerated blood pressure drugs well.

This study has helped to shape clinical guidelines for doctors in the UK and worldwide, and provided a safe, effective treatment option for patients who are over 80.

Professor Bryan Williams

Developing a treatment plan for high blood pressure

There are many different types of drugs available to treat high blood pressure. However, sometimes it is not clear which drugs or combination of drugs would best suit each patient. To find the right drugs for the right patients, the BHF has funded a series of clinical trials that supported the development of a personalised medicine approach for treating high blood pressure.

Professor Morris Brown then at the University of Cambridge, with Professor Bryan Williams of University College London and Professor Tom MacDonald of the University of Dundee, led a programme of clinical trials called PATHWAY, funded by the BHF.

Between 2009 and 2014, a number of different issues were addressed in the studies. For example, is it better to start newly diagnosed patients on a combination of blood pressure-lowering drugs rather than starting with one drug and adding more as required? And what is the best "add-on" treatment for people with uncontrolled high blood pressure who are already on high doses of all three of the recommended types of blood pressure medication?

The drugs tested in these trials were old enough to be off patent, meaning there was little hope of the pharmaceutical industry funding these studies. BHF funding was crucial in ensuring these trials could be carried out.

This research has been instrumental in providing evidence to develop guidelines for clinicians to help them decide which drugs should be chosen to control a patient's high blood pressure.

Around 50% of heart attacks and strokes are associated with high blood pressure in the UK

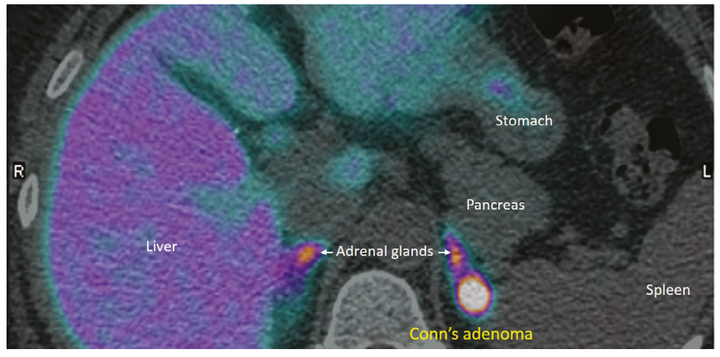
Beating drug-resistant hypertension

Professor Moris Brown

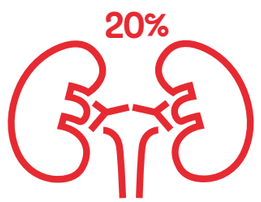
While there are many effective drugs to treat high blood pressure, they don't work for everyone. Drug-resistant high blood pressure can be caused by Conn's syndrome, a small non-cancerous tumour on one or both adrenal glands that pumps out too much of a hormone called aldosterone, raising blood pressure. It's increasingly recognised that Conn's syndrome is a far more common cause of high blood pressure than previously thought, being present in at least 10% of all people with high blood pressure, and up to 20% of people with drug-resistant hypertension.

Developing a non-invasive diagnosis test

Very few people get tested for Conn's syndrome. This is because making the diagnosis requires an invasive procedure, where blood samples are taken from both adrenal glands. But in 2007 the BHF funded Professor Brown to develop a new imaging technique to simplify the diagnosis of Conn's syndrome. Building on work originally done by Swedish researchers, Professor Brown and his team developed a non-invasive PET-CT scan using a radiotracer that lights up the tiny tumours which are responsible. This PET-CT scan has the potential to transform the diagnosis of Conn's syndrome.



Conn's adenoma visualised using a new PET-CT scan technique developed by Professor Morris Brown's team.



Conn's syndrome is responsible for up to **20%** of drug-resistant high blood pressure

A less invasive technique to remove Conn's adenoma

Currently the usual treatment for an adrenal gland tumour is the removal of the whole adrenal gland by keyhole surgery. But doctors are often reluctant to remove the whole gland to get rid of what they regard as a tiny, non-cancerous tumour. A potential exciting solution is to use an electric current to remove the nodule without affecting the rest of the adrenal gland, avoiding the need for surgery. The BHF is currently funding a clinical trial led by Professor Brown designed to compare the effectiveness of this approach with keyhole surgery. The results of this study could transform the treatment of people with Conn's syndrome and reduce their risk of complications from high blood pressure, such as heart attacks and strokes.

> **"No-one with hypertension is untreatable. There is a significant group of high blood pressure patients whose condition is seemingly resistant to treatment. From our studies, we now believe these people, with so-called 'resistant hypertension', are absolutely treatable.**
>
> **Professor Morris Brown**

Understanding pulmonary hypertension better to improve treatment

Blood pressure can also rise in the blood vessels supplying the lungs, and the smaller blood vessels within the lungs. This is called pulmonary hypertension, a serious condition which leads to damage to the right side of the heart. If left untreated, the condition can lead to death from heart failure within a few years.

Professor Martin Wilkins

Finding new treatments for pulmonary hypertension

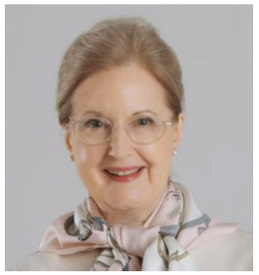
In the 1980s, researchers around the world were trying to identify how the body controls blood pressure – specifically, the way blood vessels expand and contract. A crucial molecule was identified, called nitric oxide (NO), which is produced by cells in the blood vessel wall and causes blood vessels to dilate. We funded Professor Tim Higenbottam at the University of Cambridge who showed in the late 1980s that having low levels of NO in the blood vessels of the lungs is a key factor in pulmonary hypertension. For the first time, they gave NO to people with severe pulmonary hypertension and showed that it reduced the blood pressure in their lungs.

This pioneering work paved the way for the development of further treatments that target the way blood vessels release NO. As a result, new drugs called phosphodiesterase inhibitors were developed, one of the best known is sildenafil. In 2005, BHF-funded work by Professors Martin Wilkins and Lan Zhao at Imperial College London first demonstrated the benefits of using sildenafil to treat pulmonary hypertension. Today, sildenafil and related drugs are the most prescribed medicines in the UK and worldwide for the treatment of pulmonary hypertension, helping to relieve breathlessness and improving lives.

Protecting children with pulmonary hypertension

Pulmonary hypertension can be a complication of congenital heart disease and can also affect children. By 2002, the great strides in new treatments for pulmonary hypertension in adults offered a potential solution. Although, careful adaptation is needed when using drugs developed for adults in children.

In 2002, BHF Professor Glennis Haworth founded the UK Pulmonary Hypertension Service for Children, which she led for many years. This clinical network, then the first of its kind in the world, helped to identify the best treatments for children with pulmonary hypertension, and still cares for children throughout the UK with the condition. Professor Haworth's work has been instrumental in improving the survival rates of these children.



Professor Glennis Haworth

Finding the genes causing pulmonary hypertension

BHF Professor Nick Morrell

In the 1950s, many scientists started to describe how a form of pulmonary hypertension, called pulmonary arterial hypertension (PAH), ran in families and realised that the condition can be inherited. But until 2000, no one knew which gene or genes were involved.

In 2000, BHF-funded research led by Professor Richard Trembath at the University of Leicester showed that mutations in the gene BMPR2 caused inherited PAH. Today, we know that mutations in this gene are responsible for around 70% of inherited cases of PAH. Their findings means that it is possible to introduce a screening programme that can identify those at risk and provide better information to patients and their families.

In 2001, Professor Trembath and Dr Nick Morrell (now BHF Professor of Cardiopulmonary Medicine at the University of Cambridge) built on this work, showing how changes in BMPR2 affect the blood vessels in the lungs and lead to PAH. Since then, we have supported research that has shed more light on the role of BMPR2 in the development of PAH, as well as looking at how we can block these effects in order to stop or reverse the development of PAH.

In 2015, Professor Morrell and his team identified a molecule that can stop the harmful effects of this change in the BMPR2 gene. They showed that in mice, this treatment can reverse PAH. These results demonstrated the potential of targeting the effects of the BMPR2 gene mutation, in order to offer a new treatment for PAH. This work led to the creation of the spin-out company Morphogen-IX to develop new PAH treatments. The company aims to begin studies of these treatments in humans in 2022.

Kat has idiopathic pulmonary hypertension, which means that what causes her condition is not known. Kat was tested for the two most common genes identified with inherited PAH. When the results came through, she felt a sense of a huge relief to be told that no genetic faults were found, making it very unlikely that it would be passed on to her two daughters.

Stopping the fatal drop in blood pressure in sepsis

Professor David Lambert

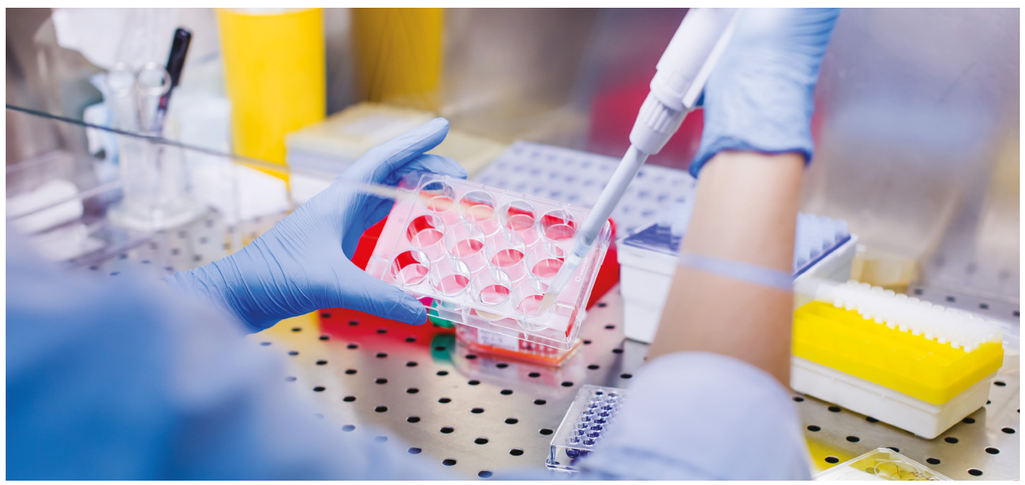
Every hour 5 people die with sepsis in the UK

Sepsis, also called blood poisoning or septicaemia, is a very serious reaction to an infection. At least 250,000 people get sepsis every year in the UK. More than one in five of those will die. While antibiotics can treat the infection, the body's response to the infection can cause dangerously low blood pressure leading to multiple organ failure and death, a condition called septic shock. Currently, there's no treatment that directly tackles the life-threatening drop in blood pressure. And people who survive sepsis may experience significant, life changing impacts on their health.

Looking for a novel therapeutic target

Researchers in Leicester led by Professor David Lambert have previously found that people treated for sepsis in intensive care carry higher levels of a molecule called nociceptin, which is produced by immune cells. They believe this chemical can cause blood vessels to relax and is partly responsible for the dangerous drop in blood pressure, which can lead to organ failure.

In 2019, the BHF funded the team to study in details the role of nociceptin in sepsis. If we are able to more clearly define its role, this could pave the way for the development of new drugs to target this molecule, which could reverse its actions.



Professor James Leiper

Could we be close to a new drug for sepsis?

Over the last 20 years, the BHF and other funders have supported the work of Professor James Leiper, now Associate Medical Director at the BHF, to understand the mechanisms that regulate the production of NO. This molecule plays a crucial role in the regulation of blood pressure but also in the control of the immune system and could be targeted to treat sepsis.

Professor Leiper and his team identified a suitable target to block NO production selectively in blood vessel cells. They went on to develop drugs to block it and patented their most promising candidate in 2007. They tested their new drug in an animal model of sepsis and showed that it blocked the fatal blood pressure drop and improved survival.

But taking a drug out of the lab and into clinic is a long journey. In 2015, Professor Leiper received a BHF translational award to transform their potential drug into a treatment that could help people affected by sepsis. The translational award helped Professor Leiper engage with the US Food and Drug Administration (FDA) to find the best way to design a clinical trial to test if the drug works in people.

This work led to the creation of Critical Pressure, a drug development spin-out company which attracted private investment to test the safety and efficacy of this new drug. If the trials prove successful, the drug could provide a more effective and safe treatment for septic shock patients around the world.

> **"I joined the BHF in 2020 and now oversee the work of the Translational awards committee that funds researchers to progress the development of novel, innovative technologies towards patient benefit. It's a very exciting committee that encompasses discovery research, commercial investment, intellectual property and the whole drug development pipeline.**
>
> **That's one of the reasons why I was really interested in this job. To be able to share my experiences with other people, and in some ways stop them making the mistakes I made.**
>
> **Professor James Leiper, Associate Medical Director, British Heart Foundation**

Preventing long-term effects of pre-eclampsia

Dr Suchita Nadkarni

Pre-eclampsia is a very serious condition in pregnant women, where a severe rise in blood pressure is accompanied by the presence of proteins in the urine. Pre-eclampsia affects up to one in 25 pregnancies in the UK and research suggests that the condition doubles the risk of coronary heart disease, stroke and heart attacks and quadruples the risk of high blood pressure later in life.

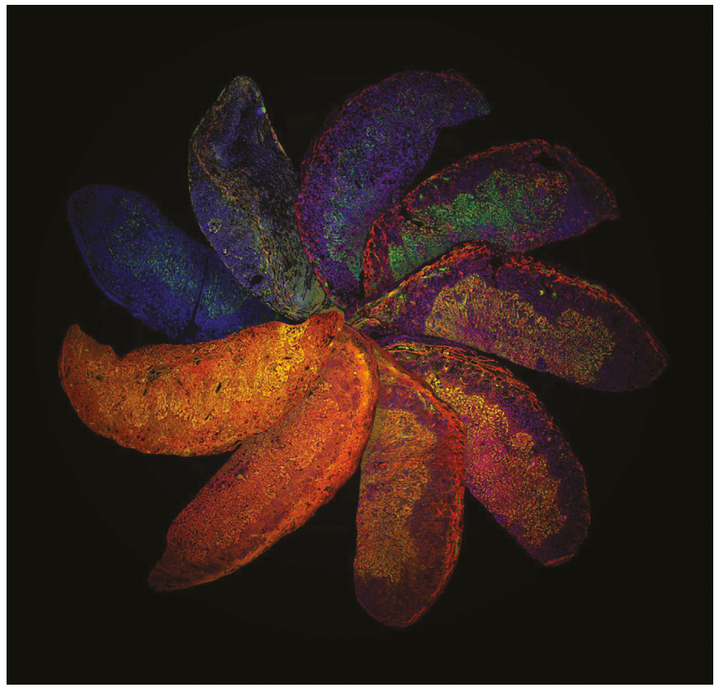
Studying the immune system in pre-eclampsia

Pre-eclampsia is caused by the placenta not developing properly. The immune system is thought to play a key role in this.

Dr Suchita Nadkarni at Queen Mary University London has evidence to suggest that the immune system might also play a key role in the changes in the heart structure and function observed in pre-eclampsia.

In 2019, we funded Dr Nadkarni's research to find out more about the link between the maternal immune system and heart function during pre-eclampsia. This research could help to identify new targets for medication and therapies to improve the heart health of women with pre-eclampsia during and after pregnancy.

'Placenta Rainbow' by Dr Nadkarni. The placentas are from mice whose immune cells called neutrophils have been removed during pregnancy, which leads to abnormal placental development. Blue represents the nucleus, where DNA is stored; blood vessels are stained in red; and trophoblasts, the first cells to form in the developing embryo, are stained in green.



Professor Paul Leeson

Pre-eclampsia affects up to one in 25 pregnancies in the UK

How an app is helping mothers manage their blood pressure

High blood pressure caused by pre-eclampsia can affect blood vessels in the mother's body and damage organs like the heart, brain or kidneys. After women with pre-eclampsia give birth, their blood pressure can remain high for weeks or months, and the damage in their body can be long-term. These women are at higher risk of cardiovascular diseases in later life.

Supported by BHF funding, Professor Paul Leeson and his team at the University of Oxford gave new mothers who have had pre-eclampsia a blood pressure monitor. This allowed them to take their own blood pressure readings for the first couple of months after they had given birth. Professor Leeson found that when a smartphone app advising the mothers on what medication to take in response to their readings was used, it resulted in lower blood pressure six months after the birth of their children.

The team will use sophisticated scans to understand whether the improved control of blood pressure is accompanied by improved blood vessel function in the heart and brain. This could reduce the risk of heart disease and stroke.

If successful, this could revolutionise how doctors care for new mothers who have had pre-eclampsia in the period after birth and help improve their long-term health.

Timeline of achievements

1961
The BHF is founded

1966
The BHF **appoints its very first BHF chair, Professor Peter Harris** who worked closely with Professor Donald Heath to **understand the causes of pulmonary hypertension**

1969
American scientist Jerome Conn describes an **aldosterone-producing tumour on the kidney's adrenal gland causing high blood pressure,** known as **Conn's adenoma**

2000

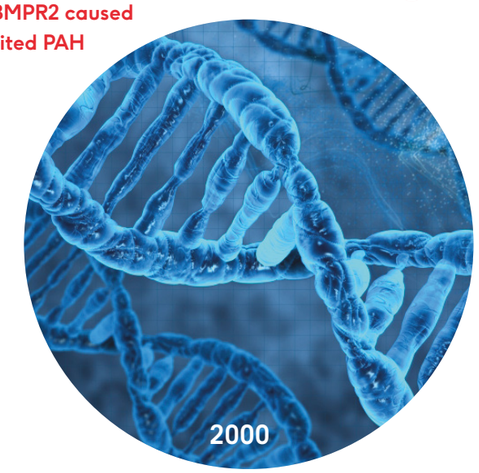
1977
ACE inhibitors and calcium channels blockers, drugs commonly used to treat high blood pressure, become available

1979
BHF Professor Andrew Henderson works on a **molecule produced by blood vessel cells, which causes blood vessels to dilate,** later found to be the gas nitric oxide (NO) by international researchers

1996
Professor Tim Higenbottam and colleagues give **NO to people with severe pulmonary hypertension** for the first time and show that it **reduces the blood pressure in their lungs**

2000
Blood pressure UK launches **'Know Your Numbers!'** annual campaign to raise awareness of high blood pressure, **encouraging all UK adults to get a blood pressure check**

2000
BHF-funded research led by Professor Richard Trembath shows that **mutations in the gene BMPR2 caused inherited PAH**


2000


2002

2002
BHF Professor Glennis Haworth founds the UK Pulmonary Hypertension Service for Children, first of its kind in the world

2005
BHF-funded work by Professors Martin Wilkins and Lan Zhao shows for the first time the **benefits of sildenafil in pulmonary hypertension.**

2007
A clinical trial part-funded by the BHF and led by Professor Christopher Bulpitt shows that it is **safe for people over 80 to take blood pressure medication**

2009
BHF funds landmark **clinical trials** to find out **which blood pressure drugs, the timing, doses and add-on treatments** should be **chosen to control a patient's high blood pressure**


2009

2015
BHF Professor Nick Morrell and his team **identify a molecule that can stop the harmful effects of the change in the BMPR2 gene** seen in patient with PAH and launch a spin-out company to develop new drugs against the disease

2017
Professor James Leiper and colleagues launch Critical Pressure, a spin-out company based aiming at **developing a new drug for sepsis,** after more than 20 years of research, some funded by the BHF

2020
The BHF funds Professor Morris Brown to **test whether ablation could be used to remove Conn's adenomas causing drug-resistant high blood pressure**

Keeping
cholesterol under control

Keeping cholesterol under control

High LDL (“bad”) cholesterol is associated with 1 in 4 heart and circulatory disease deaths in the UK

Cholesterol is a fatty substance found in the blood, produced naturally in the liver. It is an essential component of every cell in the body. Cholesterol is carried in the blood by proteins. When cholesterol and proteins combine, they are called lipoproteins.

There are two main types of lipoproteins. High-density lipoproteins (HDL) and non-high-density lipoproteins or non-HDL, which include low density lipoproteins (LDL).

Non-HDL can be harmful if their levels in the blood are too high. They can build up in the walls of blood vessels, which react and thicken in a process called atherosclerosis. This results in “plaques” that can restrict blood flow. This makes high cholesterol a significant risk factor for developing heart and circulatory diseases. Over time, high cholesterol can lead to:

- Angina – usually a pain or discomfort in your chest. This happens when the blood supply to the heart muscle is restricted.
- Heart attack – if a plaque breaks in a coronary artery, a blood clot forms inside that artery that can cut off the supply of blood to part of the heart, causing a heart attack.
- Stroke - if a plaque in an artery leading to the brain breaks and a clot forms, part of the brain’s blood supply is cut off, which can lead to a stroke.
- Peripheral arterial disease (PAD) – it develops when plaque builds up inside the arteries of the legs and not enough blood can get to the muscles. This can cause pain in the calves, hips, buttocks and thighs, usually when walking or exercising.

It is estimated that almost half of adults in the UK are living with total cholesterol levels above national guidelines. If a person’s cholesterol is very high and lifestyle changes are unable to control it, their doctor may suggest cholesterol-lowering medication like statins. These are the main type of medicine used to reduce cholesterol.

With the help of our supporters, the BHF has been funding pioneering research to understand how elevated cholesterol is harmful and prove that lowering it can save lives. In the following pages, we chart our advances in this area since the 1970s.

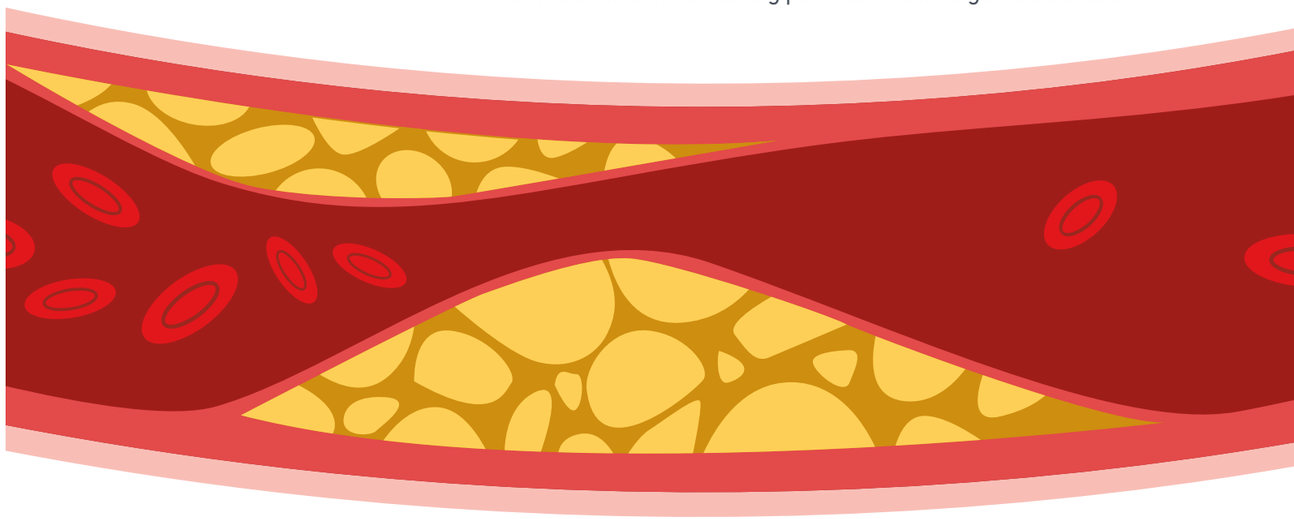
Revealing the danger of cholesterol

Professor Michael Oliver

Cholesterol was already suspected to cause blocked arteries when the BHF was founded in 1961. But although there was a large amount of evidence linking high cholesterol with a higher risk of having a heart attack, scientists did not have the evidence they needed to show that high cholesterol was a direct cause of coronary heart disease and heart attacks.

To prove this, BHF Professor Michael Oliver at the University of Edinburgh led the first international studies to find out whether lowering cholesterol using a medicine called clofibrate could reduce deaths from heart disease and stroke.

In 1978, Professor Oliver led a large clinical trial sponsored by the World Health Organization. He found conclusive evidence showing that cholesterol causes coronary artery diseases. Though clofibrate is no longer used in patients because of its unfavourable side effects, Professor Oliver’s work confirmed the life-saving potential of lowering blood cholesterol.



Atherosclerosis is the build-up of fatty material (atheroma) inside the arteries. It is what causes most heart attacks and strokes.

Proving that statins save lives

BHF Professor Sir Rory Collins

Cholesterol-lowering statins became available in the late 1980s. Soon after, BHF Professor Stuart Cobbe and colleagues in Glasgow launched a clinical trial looking at the effect treatment with a statin had on over 6,000 men with high cholesterol.

The study showed that over five years, the statin cut the risk of heart attacks and death from heart diseases by a quarter. The men who took part in the trial were followed, and even after 20 years, those who took a statin were still 25% less likely to have had a heart attack or to die from heart disease.

Subsequently, BHF Professor Rory Collins led a clinical trial of over 20,000 people to test if a statin reduced the risk of heart attack in people with existing coronary heart disease or diabetes. It ran for five years and the results, published in 2002, showed that those taking a statin were about 25% less likely to have a heart attack or stroke, or to die from heart disease, regardless of their cholesterol levels at the start of the trial.

Thanks to this world-leading BHF-funded research, statins are now often prescribed to patients who have had a heart attack, have diabetes or are at high risk of coronary heart disease. These medicines save thousands of lives each year across the UK, and many more around the world.

Statins: side effects or not?

Professor Darrel Francis

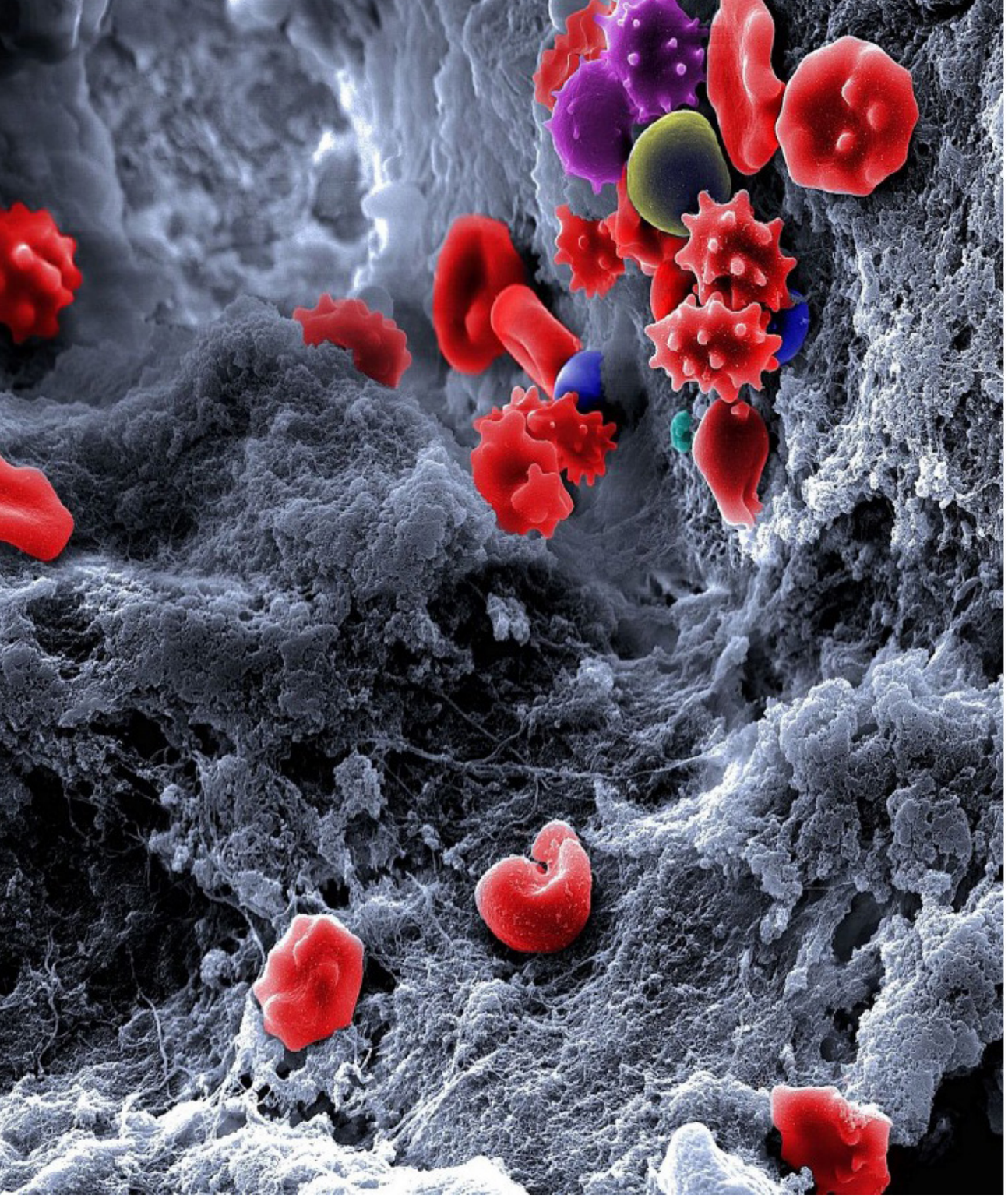
Side effects, most notably muscle weakness or pain, are reported by up to a third of people when they start taking statins. This has caused worry and reluctance by others to take statins. And a significant proportion of people have even gone as far as to stop taking their medication altogether, losing the vital protection that statins provide.

The BHF funded a clinical trial which took a personalised approach to understanding more about the side effects people experience while taking statins. Led by Professor Darrel Francis at Imperial College London, the study recruited 60 people who had recently stopped taking their statins due to side effects. The study ran for a year, and each month participants were randomly assigned to take a statin, or an identical placebo tablet, or no tablet. Each day, they recorded whether they had taken their pill and how they felt on a scale of 0 (no symptoms) to 100 (worst imaginable) using a smartphone app. If the symptoms became too severe, they were able to stop taking the tablets for that month.

The research showed that 90% of the symptoms that people reported while taking a statin were also experienced while they were taking a placebo. People experienced more symptoms when they were taking a tablet (either statin or the placebo) than when they were not taking a pill and were just as likely to temporarily stop taking their placebo tablets due to side effects as they were with statins. The results, which were reported in 2020, suggest that these symptoms are nearly all linked to the "nocebo" effect – where people experience side effects from a treatment because of a negative association with it, rather than an actual biological effect of the drug.

After participants received an explanation of their results at the end of the study, half of them successfully restarted their statin. The trial showed that this type of personalised approach can help to empower people to get back onto a lifesaving therapy. The study also meant that other options can be explored for the very small number of people who do experience side effects that are directly linked to statins.

> **"I was so surprised that my aches and pains were not due to the statins themselves – you can convince yourself of anything! I'm now very happy to be taking my statins again. Looking back, I walk a lot in the valley where I live and have plenty of stairs in my home that I go up and down multiple times a day. No wonder my body was feeling these pains!**
>
> **Janice, trial participant**



‘The Clot Thickens’ by Dr Fraser MacRae. This image shows a blood clot in close detail. The thick grey mesh is the clot, capturing a mixture of different cells – seen in different colours.

Identifying new risk factors

BHF Professor Hugh Watkins

Thanks to research by the BHF and others, we now know much more about treating some of the important factors that can lead to heart attacks and strokes - such as high cholesterol.

The blood contains thousands of different molecules (sometimes called biomarkers) and these can be measured. Cholesterol is an example of a biomarker that directly causes heart and circulatory diseases. We know that lowering cholesterol, for example with statins, reduces the risk of heart attacks and strokes.

There are other biomarkers known to be raised in people with heart and circulatory diseases, but it is not always clear whether they increase the risk of disease. If this is the case, they could be targeted in the future by new medicines.

One way to find out is to use genomics – the study of the over 3 billion ‘letters’ that form our DNA and genes. Variations in single letters in the genes can lead to a difference in the level of a biomarker. If the risk of disease, for example a heart attack, is higher in people with a particular gene variant, it is very likely that the gene is directly involved in causing disease. That means that the biomarker that the gene is linked to is also likely to be a cause of disease.

In 2009, we funded BHF Professor Hugh Watkins and colleagues at the University of Oxford. They used the power of genomics to show that gene variants that lead to increased levels of another type of lipoprotein, called lipoprotein (a) or LP(a), are strongly linked with coronary heart disease. This suggested that lowering levels of LP(a) could be useful in reducing the risk of heart disease.

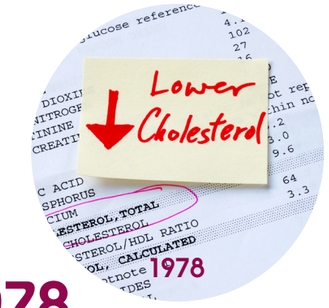
This led directly to drug companies around the world designing drugs to lower LP (a) and the first of these are now being tested in clinical trials.

> **“Discovering new genes that cause heart diseases could be the first step in finding new treatments that could improve and save many more lives.**
>
> **BHF Professor Hugh Watkins, University of Oxford**

Timeline of achievements

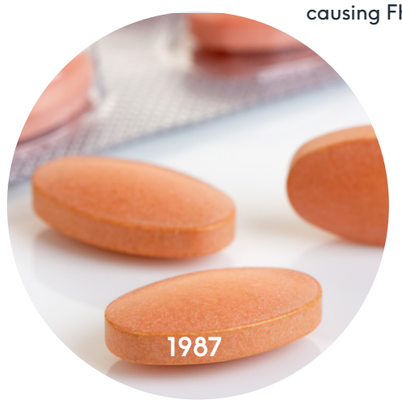
1961
The BHF is founded

1975
American researchers identify for the first time **genes associated with FH**



1978
BHF Professor Michael Oliver and colleagues show that **lowering cholesterol can reduce deaths from heart disease and stroke**

1987
Statins are commercialised



1995
BHF Professor Stuart Cobbe and colleagues show that people with high cholesterol taking statins **cuts their risk of heart and circulatory disease by 25%**

1996
Researchers around the world, including BHF Professor Steve Humphries and BHF-funded Professors Paul Nicholls and Ian Young find **more genetic faults** causing FH

1997
BHF Professor Steve Humphries sets up the **first genetic testing service** for FH in London

2004
BHF Professor Rory Collins and colleagues show that **statins reduce the risk of stroke by a third** in people with 'normal' cholesterol levels or with diabetes

2007
BHF Professor Stuart Cobbe and his team show that **the benefits of taking statins on the risk of heart disease and stroke extends to at least 10 years** after the original trial

2009
BHF Professor Hugh Watkins and colleagues identify a molecule in the blood, called lipoprotein(a), that is **strongly linked with the risk of developing heart disease**

2010
BHF Professor Steve Humphries and colleagues develop a **quicker and cheaper diagnostic test for FH**, which looks for 20 of the most common genetic faults causing the disease in the UK

2020
A BHF-funded trial led by Professor Darrel Francis reports that **people experience the same side effects when taking statins or a dummy pill**, reassuring people to get back onto a lifesaving therapy

2021
Pharmaceutical companies around the world are **testing new ways to decrease lipoprotein(a)** which could form the next generation of cholesterol-lowering treatments

Creating healthier environments

Creating healthier environments

Over the last 60 years, BHF has helped raise awareness of certain conditions, habits and unhealthy environments which increase the likelihood of developing heart and circulatory diseases.

BHF-funded research has shown that smoking, air pollution and obesity can all increase the risk of cardiovascular diseases.

The BHF has also been taking the latest research findings to the Government to influence public health policy. By creating healthier environments, fewer people will be affected by heart and circulatory diseases.

The following pages detail how we have been tackling some of the country's biggest health challenges, and what our aspirations are for the future.

In the UK, it is estimated that **air pollution reduces the average life expectancy by 6 months**, and is associated with up to **11,000 cardiovascular deaths** every year

In the UK, **64% of adults** and around **30% of children** have a body-mass index (BMI) defined as **overweight or obese**

Physical inactivity is associated with **thousands of deaths** from heart and circulatory diseases each year in the UK

In the UK, at least **15,000 deaths** each year from cardiovascular disease are attributed to **smoking tobacco**

Reducing sugar intake to address obesity

Professor
Peter Scarborough

Excess weight or obesity can increase your risk of cardiovascular diseases, including heart attack, stroke, type 2 diabetes and vascular dementia. The BHF has been working for decades to reduce levels of obesity and improve public health. Our focus has been towards changing public health policy, rather than individual behaviours.

In 2016, BHF-funded Associate Professor Peter Scarborough and colleagues at the University of Oxford calculated what effect reducing sugar intake could have on obesity levels in adults and children, and their risk of developing heart and circulatory diseases. This work was included in the Public Health England review of options for reducing childhood sugar intake, and Professor Scarborough provided evidence at the parliamentary Health Select Committee inquiry into childhood obesity. This evidence contributed to the decision to announce the Soft Drinks Industry Levy, or 'sugar tax', in 2016. The levy came into effect in 2018 and added a tax to soft drinks that are high in sugar.

Professor Scarborough and colleagues went on to study the effect of the tax and the increased awareness of the sugary drinks problem. They found that before the tax came into effect in 2018, it helped reduce sugar content through incentivising reformulation of drinks by manufacturers. Between 2015 and 2018, there was a 30% decrease in the volume of sugar from soft drinks sold per person in the UK. Consumers also changed their habits with sales of the most sugary soft drinks subject to the tax falling by 50%, and sales of low- or zero-sugar soft drinks rising by 40%.

Reducing smoking to save lives

The BHF has been fighting against smoking for decades, from demonstrating that passive smoking in public places kills to influencing Government policy.

Professor Jill Pell

The danger of passive smoking

In the 1990s, we started funding the British Regional Heart Study to broaden our understanding of the factors that can cause coronary heart disease (CHD). CHD is when the coronary arteries become narrowed by a build-up of fatty material within their walls. This increases the risk of having a heart attack or stroke. In 2004, using data from this study, Professor Peter Whincup and his team at St George's, University of London showed that breathing in other people's tobacco smoke in public places can increase the risk of coronary heart disease. They found passive smoking could increase a person's risk as much as if they were smoking nine cigarettes a day. This crucial study highlighted the need for a smoking ban in public places, which was included in the 2006 Health Act.

In 2006, Scotland was the first of the UK nations to introduce a complete indoor smoking ban in public places. We partially funded Professor Jill Pell and colleagues at the University of Glasgow to evaluate whether the ban was protecting the heart health of non-smokers exposed to passive smoking. The team showed that just one year after the ban came into force, overall hospital admissions for heart attacks had decreased by 17% overall in nine hospitals around the country, with a 21% reduction among people who had never smoked. The team also reported that exposure to second-hand smoke was down by 40% among adults and children.

Professor Pell's results confirmed that the legislation was protecting the health of non-smokers. This study has been used around the world to further strengthen the public health case for smoking bans. After Scotland banned smoking in enclosed public spaces, Wales, Northern Ireland and England all followed suit in 2007.

Campaigning to bring down smoking rates

We've been campaigning for years to raise awareness on the dangers of cigarette smoking and for stricter controls on tobacco. In 2004, we ran a hard-hitting advertising campaign showing a cigarette dripping fat. It made headlines and had a real impact on smokers, with 83% of surveyed people saying it made them consider quitting. Thanks to years of campaigning from us and others, the last 20 years have seen a series of tobacco control measures, including a ban on advertising in billboards and media, plain packaging for cigarettes, and bans on cigarette vending machines, advertising in shops and smoking in cars with a child present.

Before the BHF was founded, more than half of adults in the UK were smokers. Today that has fallen to around one in seven. And the number of heart and circulatory disease deaths linked to smoking has fallen by two thirds in the last three decades.

But the job is not finished. We want everyone to live in a Smoke-free UK, defined as fewer than 1 in 20 adults smoking. That is why we are a core funder of Action on Smoking and Health, and a member of the Smoke Free Action Coalition.

Protecting our health from air pollution

We've been funding research for over a decade to understand how air pollution damages the heart and blood vessels, and we are using the evidence to influence government policy.

BHF Professor David Newby

Showing why air pollution is a problem

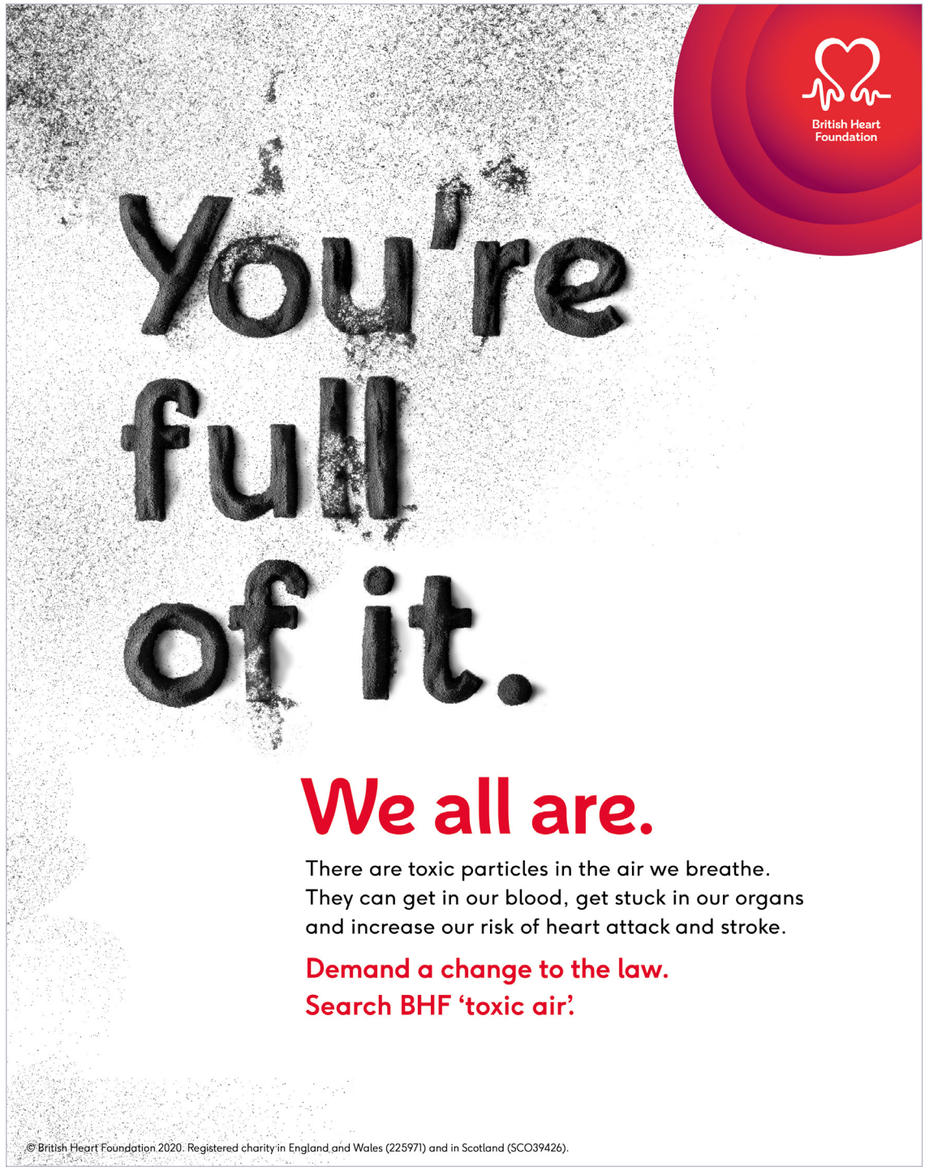
BHF-funded researchers were among the first to show how exposure to air pollution damages the heart and blood vessels. In 2005, we funded BHF Professor David Newby and his team at the University of Edinburgh who found that breathing in diesel fumes at the levels found in a polluted city stops blood vessels relaxing properly and encourages blood to clot. The team also found that exposure for as little as an hour produces these damaging effects, which remained for more than 24 hours after exposure had ended.

In the last 10 years, researchers have investigated fine particulate matter known as $PM_{2.5}$. This matter is made up of particles smaller than 2.5 micrometres in diameter and are generated by a variety of sources, including heavy industry and road traffic, especially diesel exhaust. In 2015, the Edinburgh team found that short-term exposure to high levels of $PM_{2.5}$ was linked with an increase in the risk of having a stroke in the following week.

Calling for the Government to go further and faster on air pollution

The BHF has been highlighting these research findings to the Government to ensure a better understanding of the link between exposure to $PM_{2.5}$ and heart attacks and strokes. We were pleased to see that the Clean Air Strategy, published in 2019, recognised the huge health burden of air pollution and pledged to reduce the most harmful pollutants. But we believe that there is more that can be done to tackle this urgent problem.

That's why we launched the 'We're all full of it' campaign in 2020 (right). The campaign called for the World Health Organization's (WHO) guideline limits for $PM_{2.5}$, which are much stricter than the limits we currently adhere to, to be adopted into law by 2030. The campaign launch coincided with the Government introducing the Environment Bill, which commits to the introduction of new limits on $PM_{2.5}$ but stops short of including the WHO guidelines. While the Government has not adopted these targets within the Bill, we will continue to support sector efforts to improve air quality as the Government continues to consider its new target for $PM_{2.5}$.



"In the 1950s, when there was a lot of smog, the problem used to be that particles were big and they stuck in the upper airways. But these PM2.5 go straight past, deep into the lungs, even into the bloodstream. We have a clear link between air pollution levels and heart attacks, and we believe the particles in the air are the cause of this.

BHF Professor David Newby, University of Edinburgh

Why being active is good for the heart

Dr Barbara Jefferis

It has long been known that keeping active can help to improve a person's health – from reducing the risk of heart attacks and strokes to improving mental health. But despite this, more than a third of people in the UK don't meet the physical activity recommendations. Being active can also be a challenge for some people with certain health problems. We've been funding research that showed the benefits of being physically active at all ages, and for people with heart and circulatory diseases too.

It doesn't take a marathon

In 2018, BHF-funded research led by Dr Barbara Jefferis at University College London showed that any amount of physical activity, no matter how long or short, is good for heart and circulatory health. We're all recommended to do at least 150 minutes of moderate activity a week (or 75 minutes of vigorous activity) but this can be made up of as many shorter sessions as you want. Before that, the recommendation had been to do at least 10 minutes at a time. Dr Jefferis' research provided evidence that this recommendation was no longer necessary and influenced the Chief Medical Officers' physical activity guidelines for the UK published in 2019.

Dr Jonathan Beard

Exercise for all

Exercise can be a particular challenge for some people with peripheral arterial disease (PAD), which is caused by a build-up of fatty deposits inside the walls of the arteries in the legs. This reduces blood flow to the legs and feet and can lead to leg pain when walking. BHF-funded research led by Professor Jonathan Beard at the University of Sheffield showed in 2014 that Nordic pole walking (a type of gentle exercise that exercises the full body, with the help of special walking poles), makes it easier for people with PAD to exercise. Nordic pole walking is now recommended on the NHS website to help everyone improve their fitness and to lose weight.

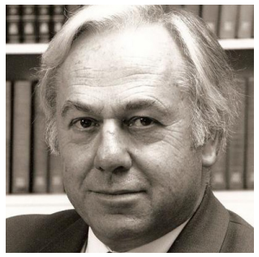
Professor Russ Jago

Getting children moving

It's also important to understand more about why children don't exercise as much as they should. The BHF is funding a study led by Professor Russ Jago and his team at the University of Bristol, looking at how parents, friends and other factors influence a child's exercise levels. Worryingly, the team have already found that UK children aged eight to nine are less active than those aged five to six. This research could reveal new ways to get children more active, helping to prevent health problems in later life.

There have been many school initiatives to encourage children to be more physically active. Back in 1987, we launched the "Jump Rope for Heart" challenge, to encourage children to get skipping to keep fit while raising vital funds for BHF research. In the last 33 years, the challenge has involved thousands of schools and youth groups throughout the UK and has helped to raise over £10 million to fund life-saving research.

Heart disease risk begins before birth



Professor David Barker

The BHF has funded several large studies to find out more about how heart and circulatory disease risk is connected to the parents' lifestyle and what happens in the womb during pregnancy.

Investigating the earliest origins of heart and circulatory conditions

In the 1990s we helped to fund groundbreaking work by Professor David Barker at the University of Southampton. His work revealed that premature babies, and those who have a low weight at birth, go on to develop some conditions more frequently in later life, including high blood pressure, coronary heart disease and type 2 diabetes. The "Barker hypothesis", also known as the "fetal origins of disease hypothesis", proposes that the development of heart and circulatory diseases, type 2 diabetes and even obesity in adulthood might be triggered by circumstances of development in the womb. Whilst this theory was controversial at the time, it has now been confirmed by other studies across the world.

BHF Professor Mark Hanson

Finding out how our lifestyle and environment can influence the heart health of our children

The BHF has been supporting the Southampton Women's Survey (SWS) since 1998. The study was the first of its kind to follow women from before they became pregnant. It is now studying the health of their children.

Using findings from the survey, BHF Professor Mark Hanson highlighted to the Government in 2017 the importance of 'preconceptual health', pointing, for example, to the advantage of folic acid supplementation and the missed opportunities to promote health in women of reproductive age. Evidence from the study has also helped to provide guidance for healthcare professionals working with women around the time of pregnancy.

The Southampton Women's Survey has also taught us more about how a mother's diet affects the health of her children. Work led by Professor Keith Godfrey in 2015 showed that higher oily fish consumption in pregnancy is associated with healthier blood vessels in their children, which may have potential long-term health benefits. Whilst the finding has not yet been added to NHS guidance for expectant mothers, it has added to what we know about the importance of eating oily fish.

Lessons in health for future generations

BHF Professor Mark Hanson is one of the founders of LifeLab – a purpose-built educational laboratory which helps teenagers understand how their current lifestyle can affect their future heart health and even that of their future children. In LifeLab more than 11,500 young people from the south of England have engaged with the science behind the health messages. In addition to promoting cardiovascular health across generations, LifeLab may inspire today's young people to become the heart researchers of the future.

One student said "LifeLab made me think about my lifestyle and the way it affects me and perhaps my children."

A teacher commented: "Meeting scientists at LifeLab was awesome - it really inspired the kids and was the first contact most of them have ever had with real science".

> **"LifeLab is so important, because today's adolescents will be the parents of tomorrow. By engaging them with modern science, we can encourage them to have a healthier lifestyle and to pass that on to future generations.**
>
> **BHF Professor Mark Hanson**

Timeline of achievements

1961
The BHF is founded

1984
Educating and informing the public about heart and circulatory diseases, **becomes a new priority**, with information leaflets distributed in GP surgeries and new health education projects and campaigns

1987
Jump Rope for Heart challenge is launched and has now **raised over £10m** to fuel our life-saving research

1998
The BHF starts supporting the Southampton Women Survey to learn more about the **diet and lifestyle factors** that influence the health of women and their children


2004

2004
Professor Peter Whincup and colleagues show that passive smoking in public places can **increase the risk of coronary heart disease**

2004
The BHF launches its 'Cigarette dripping fat' **anti-smoking advert** to show smokers the effect that smoking can have on the build-up of fatty deposits in the arteries

2005
The BHF joins forces with government departments, research councils and medical charities to **encourage research into the prevention of heart disease** and trying to understand, at the community level what factors affect people's behaviour and lifestyle choices

2006
Scotland is the **first UK nation to introduce a smoking ban** in all enclosed public spaces, followed by England, Northern Ireland and Wales a year later


2006

2007
BHF-funded research led by Professor Jill Pell shows that just one year after the indoor smoking ban came into force in Scotland, **hospital admissions for heart attacks had decreased by 17%**

2008

2008
BHF Professor Mark Hanson co-found LifeLab, **an educational laboratory where young people learn how their lifestyle may affect their future heart health** and that of any children they might have


2015

2015
BHF Professor David Newby and colleagues find that short-term exposure to high levels of particulate matter **increases the risk of having a stroke in the following week**; BHF highlights all research findings to Government

2016
BHF-funded Professor Peter Scarborough models the **impact of a sugar reduction programme** on child and adult obesity and heart and circulatory diseases which informs the introduction of a 'sugar tax' by the Government

2017
Introduction of **standardised packaging for cigarette packs** after years of campaigning by the BHF and others

2020

2020
The BHF launches its **'We're all full of it!'** campaign to urge the Government to adopt the WHO's air quality limits into law to protect the nation's health

2021
Government introduces legislation into Parliament to **bring in a 9pm watershed on television and online restrictions on advertising junk food products**


2021


Tackling
health
inequalities

Tackling health inequalities

Health inequalities are differences in health status, healthcare, and health-related risks between different population groups that are unfair and avoidable.

For decades, the BHF has been funding research to understand and address the reasons why gender, ethnicity, and social and economic status are associated with cardiovascular health inequalities.

We want to ensure that everyone, irrespective of who they are or where they are from, has access to the treatment, care and support that they need to live longer, healthier lives.

In England, there is a nine year life expectancy gap between people living in the most and least deprived areas. Cardiovascular diseases are the largest contributor to that gap and reduce the life expectancy of people living in the most deprived areas by nearly two years.

Key facts and figures

Women in the UK are **50% less likely than men** to receive **recommended heart attack treatments**

Women in the UK are **50% more likely than men** to receive the **wrong initial diagnosis** for a heart attack

Social and economic factors like living in high-density urban areas, working in transport or health and living with elderly relatives **increased the risk of being infected from COVID-19** during the pandemic

Death rates from heart and circulatory diseases are **higher for people living in the most deprived areas compared to the least deprived areas** in the UK

People with **African or African Caribbean** ethnic backgrounds living in the UK are at higher risk of developing **high blood pressure** and having a stroke than the rest of the population

People with **African, African Caribbean or South Asian** ethnic backgrounds living in the UK are more likely to develop **type 2 diabetes** than the rest of the population

Demanding better heart attack care for women

BHF Professor Nick Mills

The BHF Bias and Biology report, produced in 2019

Women are often overlooked for heart attack treatment compared to men. The BHF has been funding research to understand and address the reasons behind this disturbing fact.

A BHF-funded study led by Dr Chris Gale and team from the University of Leeds showed in 2018 that women having heart attacks were less likely to receive the correct initial diagnosis than men. It is estimated that over a decade, the lives of more than 8,200 women in England and Wales who died as a result of a heart attack could potentially have been saved if they had received the same standard of care as men. The researchers warned that getting a timely diagnosis is essential for prompt treatment. Delays risk lives.

In 2019, further BHF-funded research led by Professor Nick Mills and team at the University of Edinburgh showed that even when women are correctly diagnosed with heart attacks, they were still half as likely as men to get the recommended treatments. The team also helped debunk the myth that women usually suffer different heart attack symptoms. There is no distinct set of "men's symptoms" or "women's symptoms", and atypical symptoms can happen regardless of gender.

Raising awareness

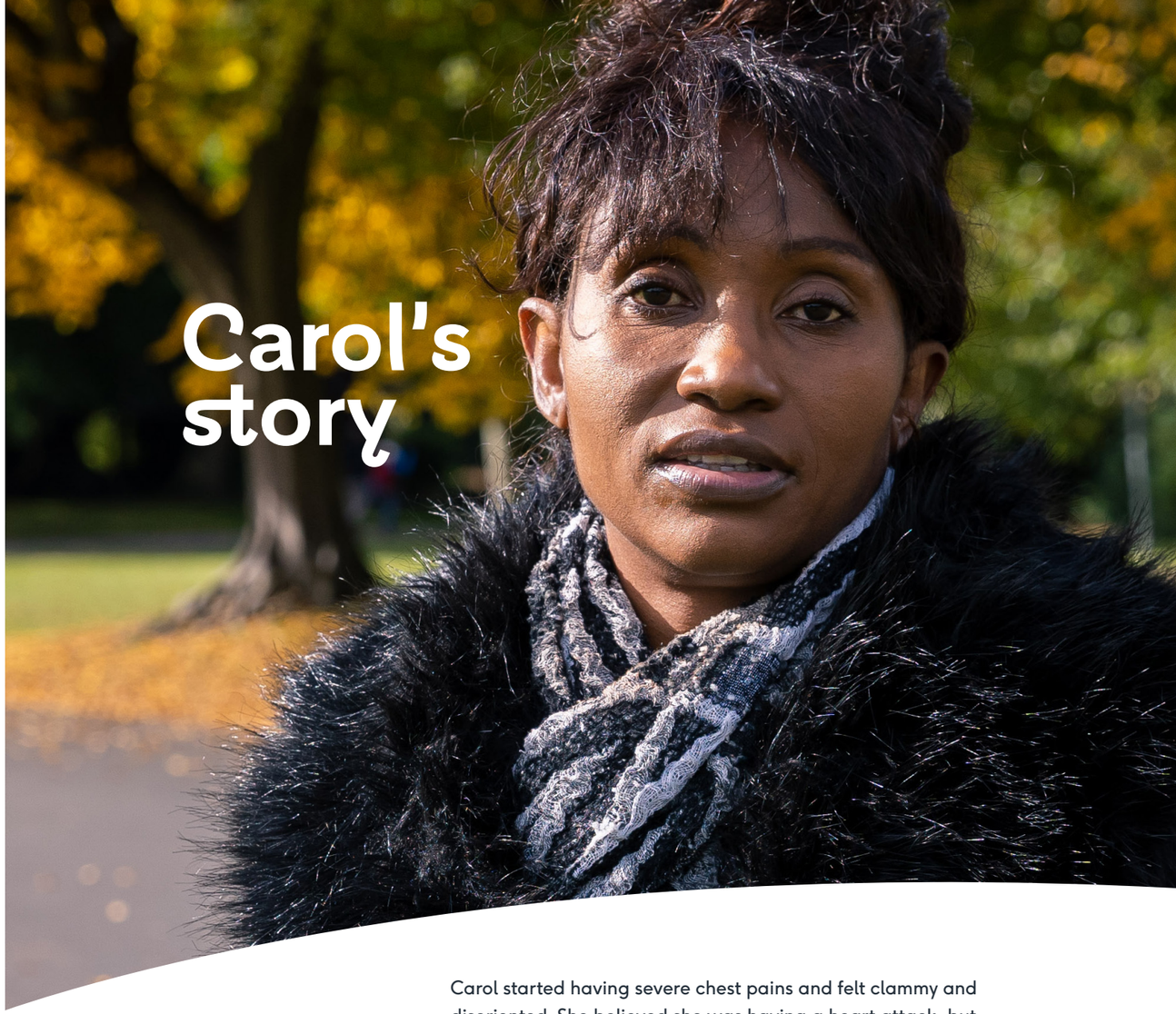
In 2019, we launched an awareness campaign – Bias and Biology – to expose the heart attack gender gap. We reached thousands of women with information about heart attack symptoms and urged women to dial 999 immediately if they ever experienced them.

We highlighted evidence that women are often not empowered with correct information on the symptoms of a heart attack. Not only do women who are having a heart attack delay getting help a lot longer than men, they are offered medical care less quickly and are given fewer treatment options than men.

Our Bias and Biology campaign also emphasised the poorly recognised issue that coronary heart disease is the single biggest killer of women worldwide. We will keep fighting for changes in public awareness and perception, as well as changes in heart attack treatment and care.

"Decades of research have transformed the likely outcome for someone suffering a heart attack. Yet if you are a woman, the odds are stacked differently. We want to change the whole public perception of women and heart attacks so that, in the future, more women's lives are saved, and women make a better recovery following a heart attack.

Dr Sonya Babu-Narayan, Associate Medical Director, British Heart Foundation



Carol's story

Carol started having severe chest pains and felt clammy and disoriented. She believed she was having a heart attack, but when the ambulance arrived the paramedic asked Carol to walk from her car to the ambulance. Initially, the doctors wrongly thought that the blood supply to Carol's heart was only partly blocked, so she wasn't treated as an emergency.

She needed to be transferred to a heart unit for treatment, but a shortage of beds there meant Carol waited 12 hours until she was finally transferred at 4am the following morning. There, she was diagnosed as having had a 'missed STEMI', meaning that her heart attack had been the most serious type, where an artery supplying the heart is completely blocked. But doctors had missed the window to protect her heart from serious damage. At 9am she had a stent fitted to restore blood flow to her heart.

Carol is now living with heart failure as a result of her heart attack.

Ethnicity and the risk of heart and circulatory diseases

The BHF has been funding research to understand better how ethnic background affects the risk of developing heart and circulatory diseases and diabetes.

The BHF has supported two major ongoing research studies – called LOLIPOP and SABRE – which aim to reveal how ethnicity can affect the risk of common diseases and conditions, including heart disease and diabetes.

The LOLIPOP study has been following 30,000 volunteers living in West London for nearly 20 years to identify the environmental and genetic factors that contribute to heart disease, stroke, and other diseases, and to develop new tools to spot people at increased risk. Among other things, the findings could help uncover why people of Indian Asian ethnic background living in the UK have a higher risk of developing heart diseases than other ethnic groups.

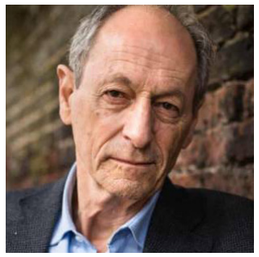
The SABRE study started over 30 years ago, to study the health of a group of nearly 5,000 people of European, South Asian, African and African Caribbean ethnic backgrounds in the London boroughs of Brent and Southall. Participants, now in their 70s, 80s and 90s, were recently followed up by the research team led by Professor Nish Chaturvedi at University College London. They found that the risk of developing type 2 diabetes before the age of 80 was roughly double for people with a South Asian or African Caribbean ethnic background, compared with White Europeans.

Inequalities between ethnic groups regarding heart and circulatory diseases are driven by a combination of different factors. It is vital that people with all ethnic backgrounds have opportunities to take part in research and have access to the best available treatments and care. Recognising health inequalities linked to ethnic background is the first step to addressing the issues in society that lead to them.

> **Our goal is to gather the information required to make sure that all population groups receive optimal support, ensuring prevention, and timely diagnosis and treatment of heart and circulatory diseases. Everyone, no matter their background or heritage, deserves the highest level of care.**
>
> **Professor Nish Chaturvedi, University College London**

Professor Nish Chaturvedi

The social determinants of health



Professor Sir
Michael Marmot

Heart diseases used to be thought of as a problem for stressed-out executives. But a world-renowned study that the BHF has helped to fund for decades has shown just how far the world view of these conditions has moved on.

The Whitehall study, set up in 1967, was a long-term research programme to track the health of around 18,000 UK male civil servants. A major finding of the study, published in 1978, was that those in the 'lowest employment grade' were twice as likely to develop heart disease and die prematurely when compared to those in the 'highest employment grade', even after risk factors like smoking and obesity were taken into account.

A follow-on study, called Whitehall II, in which a third of the participants were women, was launched to try and understand more about the parameters at play, with a particular focus on psychological, social and economic factors.

Since then, the Whitehall studies and others have brought to light the social determinants of health - the conditions in which people are born, grow, live, work and age - and how unfair and avoidable differences in these can lead to health inequalities.

The lead author of the Whitehall studies, Professor Sir Michael Marmot, expanded on these findings in a 2010 Government-commissioned report called the Marmot Review and proposed new ways of reducing health inequalities in England.

The findings of the Whitehall studies, and the subsequent Marmot Reviews of health inequalities in England, underpin the work we and others are doing to address the impact health inequalities have on heart and circulatory diseases in the UK.

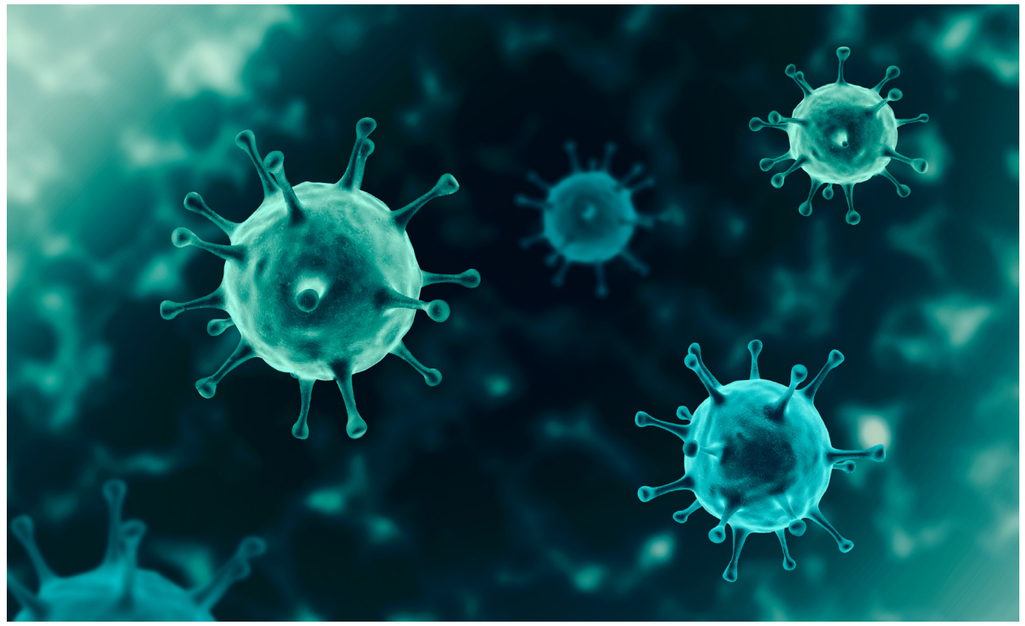
> **"Action to reduce inequalities lies at the heart of the BHF's mission and we're redoubling our efforts. We are currently developing a comprehensive programme of work that will set out how the BHF contributes to the prevention and reduction of health inequalities linked to cardiovascular disease so that everyone can live longer, healthier lives, regardless of their background.**
>
> John Maingay, Director of Policy and Influencing, British Heart Foundation

How the COVID-19 pandemic worsened health inequalities

In early 2020, Professor Marmot published a report highlighting how health inequalities have widened over the past ten years. And the coronavirus pandemic amplified pre-existing inequalities in heart and circulatory diseases, particularly in relation to socioeconomic deprivation and ethnicity.

People who live in deprived areas had higher diagnosis and death rates than those living in less deprived areas. There were also disproportionately high cases of Covid-19 and deaths in intensive care among people with Black, Asian, Mixed and 'Other' ethnic backgrounds. The reasons for this are complex. And pre-existing disparities in the burden of existing health conditions, like heart and circulatory diseases and their risk factors, may explain the disproportionate impact of the pandemic to some extent.

Health inequalities are complex and driven by a combination of different inequalities. There are a multitude of factors at work, which often overlap and can be complex to unravel. It is vital that more research is done to understand these important issues and to find out what we can do to protect everyone.



Timeline of achievements

1985

The BHF starts funding Professor Marmot and colleagues to study the risk factors for heart disease **among Asians and White Europeans** in the UK

1961

The BHF is founded

1978

Professor Marmot and colleagues report that people in the **'lowest employment grade'** are more likely to develop heart disease and die prematurely

1988

The BHF starts supporting research into a large multi-ethnic group of people living in Southall and Brent (SABRE), London, to investigate the **causes of diabetes and heart and circulatory diseases** among Indian Asian and African Caribbean men and women

2005

The BHF joins forces with government departments, research councils and medical charities to encourage research to **understand at the community level the modifiable risks** for developing cardiovascular disease, to develop efficient prevention strategies

2009

The BHF **launches the Hearty Lives programme** aimed at reducing inequalities in heart disease by working in partnership with local authorities, the NHS and non-profit organisations to improve the health of people at greatest risk

2015

The BHF funds a follow-up study of the SABRE multi-ethnic cohort to look into **risk factors or early signs of cognitive decline and dementia**

2010

Professor Michael Marmot leads on an independent review requested by Government which stemmed from pivotal BHF-funded research and proposed **new ways of reducing health inequalities**

2018

BHF-funded research by Dr Chris Gale and colleagues reveals that **women having heart attacks** are less likely to receive the correct initial diagnosis than men

2019

BHF-funded research led by Professor Nick Mills and team shows that even when women are correctly diagnosed with heart attacks, **they are still half as likely** as men to get the recommended treatments

2019

The BHF launches an awareness campaign – **Bias and Biology** – to expose the heart attack gender gap

2021

The COVID-19 pandemic further **exposes existing health inequalities** in the UK in the UK - people with minority ethnic backgrounds are hit disproportionately hard

2020

Professor Marmot co-authored an updated version of his 2010 report, which finds that **health inequalities remain a profound issue** in UK society

Using the power of big data

Using the power of big data to tackle heart and circulatory diseases

Advances in technology have propelled us into an age of digital medicine, where there has been an increase in datasets of a quality, volume, variety, and complexity previously unseen. These valuable resources can be tapped into at every stage of the research pathway, from discovery science to clinical research, and if analysed and interpreted effectively, could lead to improvements in prevention, diagnosis, prognosis and treatments.

To find hidden patterns in the data that will maximise benefits for patients, the BHF has invested in research into advanced analytic approaches, including artificial intelligence and machine learning, as well as large-scale infrastructure to make data available and enable research. In the next pages, we highlight some of our most recent research projects and strategic initiatives which aim at harnessing the power of big data.

Some definitions

Big data

describes large, hard-to-manage volumes of complex data, so large that traditional data management tools struggle to store it or process it efficiently.

Advanced analytics

is the autonomous or semi-autonomous examination of data or content using sophisticated techniques and tools, including but not limited to machine learning, to gain deeper insights, make predictions, or generate recommendations.

Artificial intelligence

is the simulation of human intelligence processes by machines, especially computer systems.

Machine learning

is a branch of AI and computer science which focuses on the use of data and algorithms to imitate the way that humans learn by identifying patterns, making decisions and gradually improve accuracy as more data is analysed.

Algorithm

is a process or set of rules to be followed in calculations or other problem-solving operations, especially by a computer.

Biobank

is a repository that stores human biological samples (such as blood) and associated health information for use in research.

Genomics

is the study of the structure, function, and inheritance of the complete genetic information of an organism. Raw data from one genome is about 200GB which would occupy most of the average laptop's hard drive.

Epidemiology

is the study of the patterns of disease in large groups of people and the reasons underlying those patterns. It requires the collection of large volumes of data, which can include genetics, health or lifestyle data.

Using machine learning to find hidden patterns in heart scans

Professor Declan O'Regan

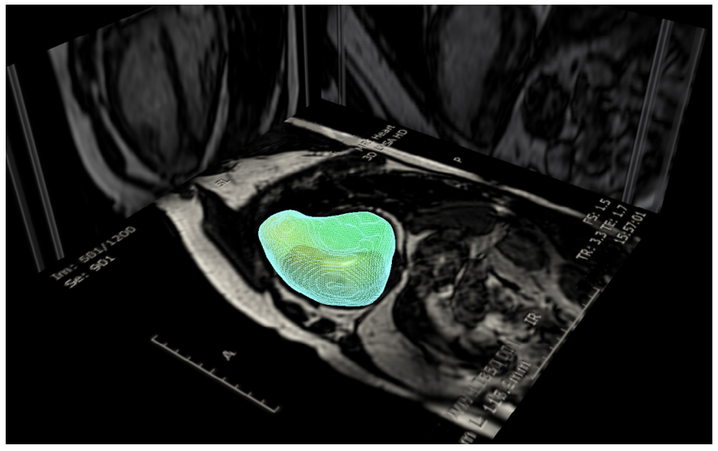
Scans of the heart and other modern tests can provide vast amounts of information. This wealth of information is a perfect opportunity for using artificial intelligence to improve diagnosis and guide decisions about treatment.

BHF-funded researchers around the UK have been exploring the potential of artificial intelligence to help diagnose and treat people with pulmonary hypertension. This is a serious and life-threatening condition caused by high blood pressure in the arteries of the lungs. The walls of the arteries become thicker and stiffer, which means they are less able to expand and contract as the heart pumps blood. This in turn puts a strain on the right side of the heart: the side that pumps blood to the lungs. The heart needs to work harder, which can lead to heart failure.

In 2017, Professor Declan O'Regan and colleagues at Imperial College London developed a computer program which analysed a patient's moving heart MRI scans, to create an individual 'virtual 3D heart' replicating the way the heart contracts during each beat. The researchers then trained the program with historic healthcare data of around 250 patients with pulmonary hypertension. By linking these data with the virtual 3D heart, the program automatically learned which MRI features were the earliest predictors of heart failure and death.

In 2019, funded in part by the BHF, the team then confirmed the accuracy of the new technology on data from 300 additional patients with pulmonary hypertension. The program outperformed humans in predicting patient outcomes from this data, and was able to correctly predict a patient's survival 75% of the time.

Heart MRI scans analysed with the computer program developed by Professor O'Regan



In the future, this new technology will help to identify which people are at risk of their condition worsening. This could make a big difference to the decisions that doctors make about how best to treat patients before their condition deteriorates.

Studying large groups of people to learn about cardiovascular risk

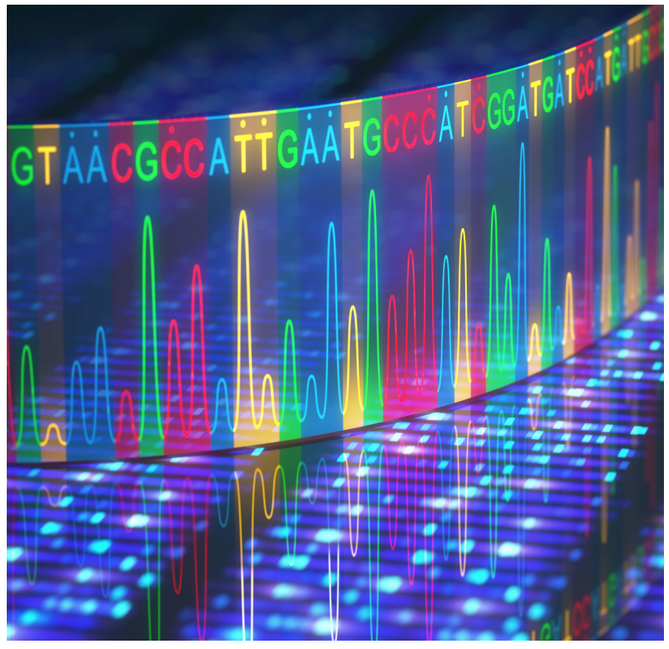
BHF Professor John Danesh

Studying data about the genetics, health or lifestyle of large numbers of people is a valuable tool to find new insights about cardiovascular health and disease. New technologies based on artificial intelligence and machine learning are helping researchers identify patterns hidden in the data.

The BHF has supported many epidemiologic studies to improve the prevention, diagnosis, and treatment of heart and circulatory diseases, with one example presented below.

Genomics – the study of the over three billion 'letters' that form our DNA and genes – can help identify factors that increase, or not, the risk of heart and circulatory diseases.

C-Reactive Protein (CRP) is a molecule that has been known for years to be raised in people at high risk of heart disease, but scientists were unsure whether it was a cause or effect of heart disease. In 2011, BHF Professor John Danesh at the University of Cambridge, in collaboration with an international consortium, was able to sequence the CRP gene in almost 200,000 people to answer this question. They showed that gene variants that caused naturally high levels of CRP in the blood were not associated with an increased risk of heart disease, proving that high CRP levels do not cause coronary heart disease.



This has meant that scientists do not need to look for CRP treatments as a way of preventing heart disease and can focus their efforts on finding other new treatments instead.

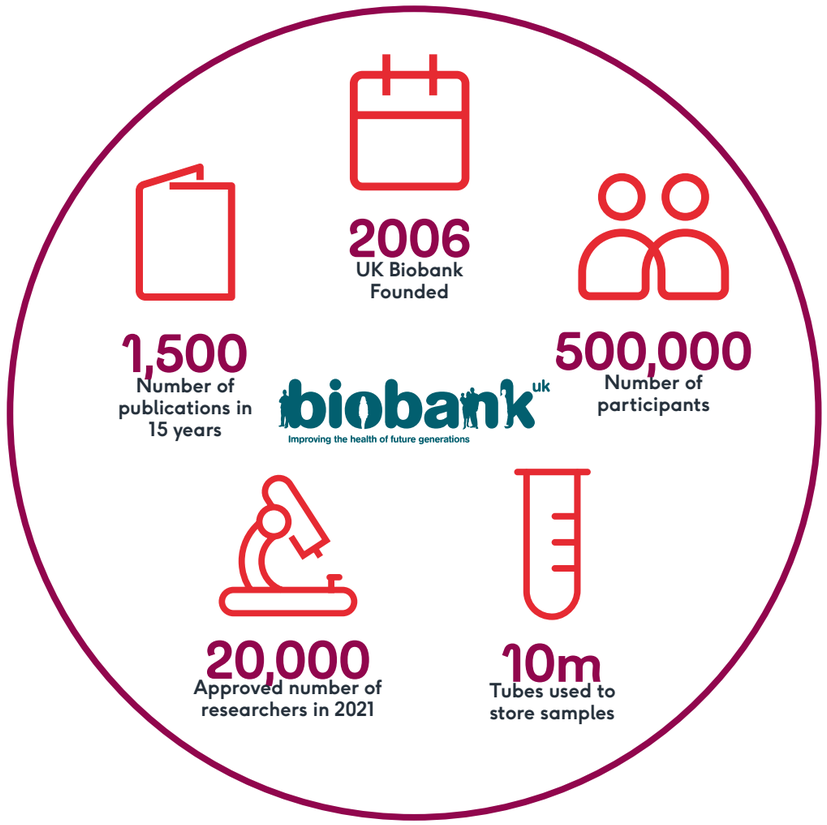
UK Biobank, a national resource for health research

BHF Professor
Sir Rory Collins

The BHF is one of a group of funders who support UK Biobank, a research resource set up in 2006. It is a large-scale biomedical database, containing biological samples and in-depth genetic and health information from half a million UK participants. The visionary project is led by Sir Rory Collins, BHF Professor at the University of Oxford.

Over the past 15 years, UK Biobank has gathered huge quantities of data on its 500,000 volunteers – including their lifestyle, weight, height, diet, physical activity and brain function, as well as genetic data from the analysis of DNA in blood samples. This data is already being linked to a wide range of health records, including GP data.

The data – the largest and richest dataset of its kind – is anonymised and safely made widely accessible by UK Biobank to researchers around the world. These researchers use the data to make new scientific discoveries about common and life-threatening diseases – such as heart disease and stroke – in order to improve public health.



Professor Steffen Petersen

Learning from heart scans of UK Biobank participants

In 2016, the BHF funded a heart imaging study in 100,000 of the Biobank participants led by Professor Steffen Petersen at Queen Mary University London. These volunteers had MRI scans to look at their heart size, heart function, heart weight and stiffness of their blood vessels. Using these data, in 2018 the researchers showed that air pollution was linked to changes in the structure of the heart, similar to those seen in the early stages of heart failure. These changes were seen even in people who lived outside major UK cities and where air pollution levels were within UK guidelines.

Higher exposures to the pollutants were linked to more significant changes in the structure of the heart, and those living close to a busy road were more likely to have changes to their hearts. These findings were highlighted to Government in the BHF's 2020 campaign called 'We're full of it'. The campaign called for the World Health Organization's guideline limits for fine particulate matter (one of the damaging components of air pollution) to be adopted into UK law and reached by 2030.

Using UK Biobank data to better understand COVID-19

We continue to benefit from UK Biobank data today as new areas of research are identified. The UK Biobank team is planning to carry out MRI imaging on at least 3,000 of its volunteers, who were also scanned before the COVID-19 pandemic. Their scans before and after the pandemic will be compared with each other and, depending on whether or not they suffered COVID-19, used to look for changes in the heart following infection. This will add to our understanding of the medium and long-term effects of the virus on the heart and circulatory health.

> **"The vast range of expertise already being applied to the UK Biobank data means that there's likely to be many ways in which these data can be used to help develop strategies to address this pandemic. These data will help researchers understand the differences between individuals. What are the differences in their genetics? Are there differences in the genes related to their immune response? Are there differences in their underlying health?**
>
> **BHF Professor Sir Rory Collins**

The BHF-Turing Cardiovascular Data Science Awards

In 2017, we joined forces with The Alan Turing Institute, named after the British mathematician and pioneer of computing science, to bring together data scientists and cardiovascular scientists. The BHF-Turing Cardiovascular Data Science Awards seek to solve cardiovascular problems with data science data science approaches based on the latest artificial intelligence methods, including machine learning.

We have funded 12 BHF-Turing projects so far. Some awards aim to help make earlier and more accurate diagnoses of heart diseases, so that patients can be treated sooner. Others aim to help doctors deliver more precise treatments, reducing pressure on the health system as a whole, while allowing patients to monitor and manage their own conditions at home. The following two projects illustrate the potential for data science to help patients.

> **“As we enter the era of digital medicine, there's a growing need to foster excellence in applying data science solutions to cardiovascular problems. At the BHF, we recognise the enormous potential of data science and want to create an environment where we can realise that potential. The BHF-Turing awards are a major step towards using data science to make transformational improvements in preventing, detecting and treating heart attacks and strokes, as well as other heart and circulatory diseases.**
>
> Professor Metin Avkiran, Associate Medical Director, BHF

BHF Professor Nick Mills

Machine learning for personalised prescribing after a heart attack

After a heart attack, people are prescribed drugs to reduce the risk of another. This includes medicines to prevent blood clots, often described as ‘thinning’ the blood. Unfortunately, this does increase a person’s risk of uncontrolled bleeding, with potentially life-threatening consequences. The balance of harms and benefits of blood thinning drugs differs between different people, but we don’t currently have a good way of measuring this to enable doctors to make personalised decisions about a person’s care after a heart attack.

Professor Nick Mills at the University of Edinburgh and Dr Ionna Manolopoulou from the Alan Turing Institute are using clinical information from over 50,000 heart attack patients in Scotland, combined with advanced computational techniques, to develop and test a personalised risk predictor.

Their aim is to create a tool to support doctors when prescribing blood thinning drugs to people following a heart attack. It may be able to identify those for whom a short course of treatment is advisable, and those for whom the benefits of prolonged treatment truly outweigh the risks of bleeding. This decision-making tool could become a key aid to help doctors prescribe drugs more safely for individuals who have had a heart attack.

BHF Professor
Gianni Angelini

Using artificial intelligence to identify good candidates for heart surgery in the UK

BHF Professor Gianni Angelini, a heart surgeon at the University of Bristol, and Professor Chris Holmes, a statistician at the University of Oxford, are leading a team of doctors and data scientists to improve risk prediction in people having heart surgery. People who require open heart surgery must be informed about the risks related to the operation. Currently, heart surgeons in the UK calculate the risk using a mathematical model called EuroSCORE. But this model is no longer considered to be accurate in the UK, due to improvements in anaesthetics, surgical and post-operative care. EuroSCORE tends to overestimate the risk of death, which means patients or surgeons may choose not to go ahead with surgery that in reality would have a good chance of success.

The team will apply machine learning to a large dataset of all patients undergoing major heart surgery in the UK to create an improved risk prediction score. This will help surgeons better identify patients who are likely to have successful heart surgery, prolonging and saving their lives.

The BHF Data Science Centre

Professor
Cathie Sudlow

In 2018, the BHF joined a consortium of funders to establish Health Data Research UK (HDR UK), to develop and apply cutting-edge approaches to clinical, biological, genomic and other multi-dimensional health data, addressing the most pressing health research. In 2019, the BHF and HDR UK, in partnership with the NHS, patients and the public, launched the BHF Data Science Centre. The centre has a particular focus on cardiovascular health data, paving the way for researchers to use data science and artificial intelligence to find solutions for the cardiovascular patient.

Under the leadership of Professor Cathie Sudlow, the Centre is rapidly establishing itself as a national resource for researchers, clinicians, and policymakers. For instance, it is already an important part of the data analysis and insight that informs the recommendations to Government of the Scientific Scientific Advisory Group for Emergencies (SAGE).

While not holding any data itself, the BHF Data Science Centre works with data controllers to provide knowledge and expertise to help researchers find, access, understand and connect the UK's unique cardiovascular big data distributed across national registries, anonymised NHS electronic records electronic records and other relevant databases. This will not only enable more ambitious discovery science and observational studies, but will also lead to improved and faster clinical trials.

Building a strong network of data for COVID-19 research

The pandemic has highlighted the importance of the BHF Data Science Centre's mission. Major issues around the relationship between COVID-19 and heart and circulatory diseases must be addressed. These can only be resolved if tools are developed that link national hospital, primary care, and mortality data with COVID-19 test data and with specialist cardiovascular healthcare datasets.

Professor Sudlow took up this challenge and established the CVD-COVID-UK consortium. This initiative involves over a dozen partners across the UK, including the custodians of all the major national generic and cardiovascular health datasets. Together, they are utilising the unique infrastructure and expertise of the Centre to coordinate, identify and connect relevant datasets across the UK's four nations. These are being analysed at the population level by researchers to provide data-led insights on big unanswered questions. For example, how genetic, demographic and lifestyle factors related to heart and circulatory health are linked to an individual's level of risk from COVID-19.

> **"The importance of data and deriving insights from it has become increasingly publicly prominent. It's been great to be involved at the time that more doors than normal have been open. There has been more progress in the last 12 months than there had been for quite a few years before that – it's really important we don't now go backwards.**
>
> **Professor Cathie Sudlow, Director of the BHF Data Science Centre**

The Cardiovascular Catalyst Awards

At the BHF, we see the significant impact that large, complex datasets could have on the NHS and other healthcare systems, helping to address the challenges of heart and circulatory diseases.

In September 2021, we launched the Cardiovascular Catalyst Awards with support from HDR UK and the Turing Institute to fund research into the use of advanced analytics to improve cardiovascular care delivery and outcomes in the NHS. We are calling for research proposals under the Cardiovascular Catalyst Awards scheme that seek to improve the delivery of care and/or outcomes of patients with heart and circulatory diseases through development and application of advanced analytic approaches on routinely collected data within the NHS.

We hope to help clinicians and healthcare professionals decipher faster and more accurately which information is important for patients' diagnosis, prognosis, or treatment options. Thus, they will be able to prioritise, coordinate, and manage care in a more personalised and effective way.

Patients and members of the public will be involved in shaping the research and in decisions on how the data will be used. At the BHF we believe it is vital to engage and involve patients in our research, promoting trust and understanding in the use of health data to improve patient care.

"For the BHF, the proximity of this kind of research to patients is the unique and most exciting feature of these awards. We have an opportunity to fast-track a real improvement in the delivery of care that will save and improve lives.

Professor Sir Nilesh Samani,
Medical Director, British Heart Foundation

Patient and public involvement at the BHF

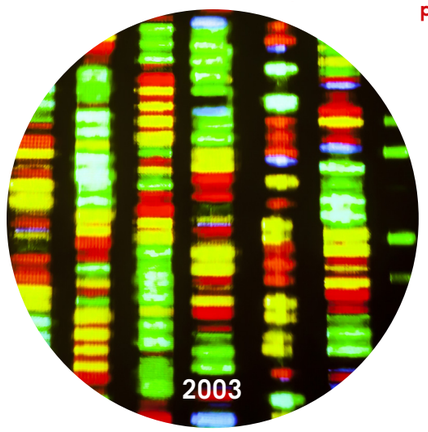
"It is six years since the BHF in cooperation with CRUK set up a Patient Data Reference Panel to help these organisations formulate their submissions to the National Data Guardians Review of health data security. This was an important subject, especially to patients like me. It sought to make our health data available for planning and research purposes as well as benefit our personal treatment via modern data management technology, but importantly without breaching our individual health privacy. I am so grateful that the BHF had the foresight to get involved as we are all aware of what an important role the use of health data has played in the fight against Covid. I am excited as it is obvious to me that the use of patient data will be crucial to many exciting new developments being led by the BHF into preventing and treating heart disease well into the future." – Kelvin Pitman, member of the Patient Data Panel

Timeline of achievements

1961
The BHF is founded

1976
BHF Professor Veitch Lawrie and Professor Peter MacFarlane develop a computer program to **automatically interpret electrocardiograms**, now used worldwide

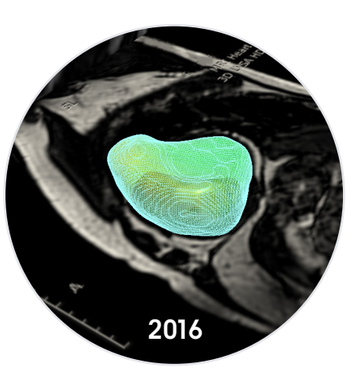
2003
Completion of the **Human Genome Project**



2006
UK Biobank starts recruiting participants to build a large-scale biomedical database and research resource, containing in-depth genetic and health information from half a million UK participants

2011
The BHF joins a consortium of funders to establish four e-health centres to support the **safe use of patient data for medical research across all diseases**, including cardiovascular disease, obesity, diabetes and cancer

2013
The BHF supports the genetic profiling of all UK Biobank participants to allow researchers to **identify gene variants that increase the risk of cardiovascular disease or affect the response of people to drugs** used to treat heart disease



2016
The BHF funds heart imaging of **100,000** UK Biobank participants

2017
The BHF and The Alan Turing Institute launch a new funding scheme to **promote and fund collaborative research between cardiovascular researchers and data scientists**

2018
The BHF joins a consortium of funders to establish HDR UK, to **develop and apply cutting-edge approaches to clinical, biological, genomic and other multi-dimensional health data**, addressing the most pressing health research

2019
The BHF and HDR UK launch the **BHF Data Science Centre** which aims to improve the public's cardiovascular health through the power of large-scale data and advanced analytics

2020
The BHF Data Science Centre acts as a cornerstone upon which **crucial COVID-19 research** in the UK is being built

2021
The UK government announces a new implementation plan to deliver **world-leading genomic healthcare** in the UK to improve diagnosis, treatment and prevention

2021
The BHF announces launches a new scheme - the Cardiovascular Catalyst Awards - to **fund research into the use of advanced analytics** to improve cardiovascular care delivery and outcomes in the NHS

Looking to the future

Looking to the future

We are proud of the BHF's track record of funding research, which has had real impact on cardiovascular health. It has only been possible due to the generosity of the public in supporting our mission. The research examples in this compendium illustrate the many ways in which the BHF has played a critical role. We have been able to improve the outlook for many people at risk of or suffering from a heart or circulatory disease, and the research we have funded has contributed to the substantial reduction in premature death from cardiovascular diseases over the last 60 years.

Nonetheless, there is still much more that needs to be done. Heart and circulatory diseases remain a major cause of disability and premature death, driving individual suffering, inequalities, and enormous economic burden. Around 19 million people die each year globally from cardiovascular disease. This is projected to rise to more than 23 million by 2030.

We are determined to continue to invest in the talented researchers, novel ideas and technology needed to make the next breakthrough discoveries. The BHF's Strategy to 2030 sets out global ambitions for improved cardiovascular health. These aims are designed to galvanise other research funders, researchers, industry, government and the public to work with us to help to achieve this. While some of the goals may appear to be science fiction today, we are confident that they can be reached and turn science fiction into facts.

BHF-funded research has helped the huge improvements in survival and recovery from heart attacks since 1961, but this has led to increased numbers of survivors at subsequent risk of progressive heart failure, where treatment options are limited and often poorly effective. We want new ways to mend broken hearts and we will continue to explore how to harness the potentially transformative powers of regenerative medicine to achieve this.

We want to be able to cure inherited heart conditions. BHF-funded researchers include world leaders investigating the genetic causes of these currently incurable diseases, and thanks to advances in technology, the possibility of correcting faulty genes to permanently treat these conditions is no longer beyond the realms of possibility.

Survival from stroke is significantly worse than survival from a heart attack. We want the number of people dying or being severely disabled by a stroke to be halved by 2030. We will continue to fund new and improved treatments to prevent or reduce the consequences of stroke to help achieve this goal. At the same time stroke survivors are at increased risk of vascular dementia, a major and increasing contributor to the burden of dementia in the population. We therefore want to find new ways to prevent and treat vascular dementia.

Current dramatic advances in computer science and technology have enabled the handling and analysis of vast sets of data and ushered in the era of digital medicine. We want better ways to identify people at risk of heart and circulatory conditions and help them avoid disease We will achieve this by continuing to invest in research to apply data science and machine learning, spearheaded by the BHF Data Science Centre.

Research saves lives. The examples above are just some of the areas where we anticipate substantial progress over the next decade. They make the need for further cardiovascular research abundantly clear. Public support is what enables us to continue funding research and help to turn science fiction into reality. We thank all of you who have made possible our successes so far and look forward to your support in future.

2022

Acknowledgements

We thank all the researchers who generously helped with their time and expertise in compiling this compendium. Within the BHF it has been a project involving many teams across the organisation, led by Dr Lucie Duluc (Senior Research Advisor, Impact Evaluation). My thanks to all of them, but especially to Lucie, whose tenacity and attention to detail were critical throughout.

Professor Jeremy Pearson

Associate Medical Director (Research Impact Evaluation)

British Heart Foundation