Pioneering renal research in Scotland
Kidney Research UK has a long history of supporting research and collaboration in Scotland. Of the £65.6 million that the charity has invested in research over the last thirty years, £9.5 million has been spent in Scotland – more per head of population than the charity spends in any other UK nation. The proportionately high amount of funding is down to the very high quality of research taking place and reflects the charity’s support for fast developing research areas. In addition, the role of Scottish academics and clinicians in two major UK-wide clinical initiatives is essential to their success.

Scotland’s innovative renal research promises revolutionary changes to kidney patients’ experiences, as the examples in this publication will demonstrate.

Kidney disease is common in Scotland; around 3.2% of the population have been diagnosed with chronic kidney disease and countless others are currently undiagnosed. In fact, we know that there are three million people across the UK with moderate to severe chronic kidney disease, and one million of these are undiagnosed and thereby at higher risk. Meanwhile the number of people being treated for kidney failure (and requiring transplant or dialysis) is on the increase.

Since 1985, Kidney Research UK has invested £9.5 million in renal research in Scotland – that’s 57p for every Scottish citizen.

The number of people being treated for complete kidney failure is increasing with around 5,000 people in Scotland on renal replacement therapy (dialysis or transplant).

Pictured on front cover:
Dr Paddy Mark Reader and Honorary Consultant Nephrologist at the Institute of Cardiovascular and Medical Sciences, University of Glasgow
Harnessing white blood cells
Kidney Research UK has invested £1 million over a ten-year period to enable Dr David Kluth and team at the University of Edinburgh to investigate the role that macrophages (a type of large white blood cell) could play in treating chronic kidney disease.

The researchers have developed macrophage cell therapy in kidney disease. They can derive macrophages from bone marrow and get them to produce an anti-inflammatory protein HO-1. When injected into mice after the onset of damage to the kidney, caused by insufficient blood supply, these cells were able to reduce the severity of renal failure. The team are now looking at whether they promote the recovery of kidney function and whether they can produce these cells from stem cells. They have also used a drug called heme arginate to increase the amount of HO-1 produced by macrophages in patients receiving renal transplants to protect the kidney from injury. The group now aims to perform a UK wide study to see if heme arginate can improve renal transplant outcomes.

Further work has studied the role of endothelin, or ET-1, which is a compound that is over-produced in chronic kidney disease (CKD), constricting blood vessels and raising blood pressure (hypertension). The team’s work has established that macrophages reduce the hypertensive effects of ET-1. They have gone on to show that inhibiting ET-1 reduces CKD after an abrupt decline in the function of the kidney in mice. This is a common clinical problem and a clinical trial is now planned to translate this into human treatment.

Explaining how diabetes causes salt retention and high blood pressure
The kidneys have a vital role in excreting the salt we eat from the body, controlling blood volume and blood pressure. This function is compromised in diabetes. Since salt intake in Scotland is about 30% higher than the recommended 6g per day, diabetes can lead to salt retention in the body, high blood pressure and kidney disease. In fact, diabetes is the most common cause of kidney failure; about 20% of people starting dialysis having diabetes. Dr Matthew Bailey at the University of Edinburgh is researching why diabetes leads to salt retention and how blood pressure is affected. His work explores the possibility that the root of the issue lies in problems with hormones that control salt appetite and influence blood flow to the kidney. Using Doppler ultrasound, a technique that uses sound waves to ‘see’ how blood flows through vessels, he addresses important mechanisms that initiate the commonest cause of CKD.

Research in practice

Funding from £127,372

Approximately 2,000 people in Scotland are dependent on dialysis to stay alive

www.kidneyresearchuk.org
Jim Hayton is from Paisley. He has recently retired from a successful career in local government, latterly as Director of Housing at one of Scotland’s largest local authorities. Diagnosed with early stage kidney disease at the age of 34, he was on dialysis eight years later and had a kidney transplant a year after that. Jim feels hugely gratified that his transplanted kidney continues to function well and that he is able to lead a full life. This feeling is particularly acute due to the impact that kidney disease has had on his wider family.

Jim’s father was diagnosed with kidney disease in 1977 and sadly died at the age of 44, only months after diagnosis. All three of Jim’s uncles have also been diagnosed with kidney failure and gone on to receive successful kidney transplants. Children of three of the four brothers developed kidney disease. Interestingly, none of Jim’s aunties appear to have contracted the disease or passed it onto their children.

In total, nine close family members have required transplants since 1984, although sadly three, including Jim’s younger brother Alan, have since passed away. None of the family has ever been told the name of the inherited condition, other than that it appears not to be Alport’s (a rare form of kidney disease) or polycystic in nature. On attending Kidney Research UK’s Fellows Day this year (the charity’s annual conference), Jim and his brother Ronnie shared their family story and were able to make contact with experts who have offered to help try to identify the condition.

Although I lead a full life at the moment thanks to my kidney transplant, myself and my family are concerned about the impact that this inherited disease could have on our children not yet diagnosed. We are extremely grateful for the work that Kidney Research UK has done and continues to do to combat kidney disease. Jim Hayton
Award winning human rights lawyer, Jelina Berlow-Rahman built her own law firm whilst also managing a grueling dialysis regime. Jelina's kidneys started failing at the age of 18. This was discovered when her aching hands and painful lesions on her lips and tongue led her to have tests which revealed she had an aggressive form of lupus. The lupus was attacking her kidneys, causing them to inflame. Steroids were prescribed to boost her kidney function and she threw herself into obtaining her law degree. Whilst completing her traineeship she met her future husband Matthew. She qualified as a solicitor, despite her kidney function rapidly deteriorating.

A bout of flu in November 2005 led to an emergency admission to hospital. Jelina had no option but to begin dialysis to stay alive as her kidney function had become so poor. She was on the waiting list for a kidney transplant, but with no telling how long the wait would be. Jelina dialysed for 4-5 hours, three times a week. She even tried peritoneal dialysis whilst working, but she had to move to haemodialysis when the peritoneal dialysis had little impact and was causing more harm than good. She managed to stay positive despite constant fatigue and the knowledge that a kidney transplant was her only hope.

Two years later she was hospitalised with agonising acute pancreatitis and contracted a superbug infection. Her doctors decided Jelina wasn't well enough for surgery and she was taken off the transplant waiting list. It was two years before she was back on the register. There was one emotional false alarm when a prospective donor kidney was damaged in transit and couldn't be used, then Jelina finally had a successful transplant in December 2009 after four punishing years on dialysis.

Today, Jelina continues her brilliant career, is a staunch supporter of Kidney Research UK and proud mum to Aliyah.

“When I lost my kidney, I lost my freedom. I was reliant on a machine to keep me alive. Having a transplant meant freedom, one most people take for granted. I will always be grateful to the donor's parents, who made that ultimate decision. The ongoing research work by Kidney Research UK is vitally important. Thanks to research I'm blessed not only with a kidney, but with a beautiful baby.”

Jelina Berlow-Rahman
People with kidney failure requiring dialysis have a very high risk of heart disease. The enlargement of the muscle of the left ventricle, the main chamber of the heart, is thought to be one contributing factor. As well as muscle enlargement, scarring of the heart muscle can put patients at risk of abnormal heart rhythms (arrhythmia), which can be life threatening.

Dr Paddy Mark, Reader and Honorary Consultant Nephrologist at the Institute of Cardiovascular and Medical Sciences, University of Glasgow, has led a study using a new method of MRI scanning to detect scar tissue within the left ventricle, which puts patients at higher risk of arrhythmia. It is hoped that this MRI method will also allow the identification of patients at higher risk, to ensure that they can be targeted with better treatment in future.

Meanwhile, Dr Mark Findlay, also from the University of Glasgow, was awarded a Training Fellowship in order to investigate connections between stroke and dialysis. Patients with kidney failure requiring dialysis have a high risk of stroke and memory problems. It appears that this risk goes up soon after patients start dialysis – suggesting unique treatment-based risks. By combining two existing national databases of kidney failure and stroke patients (the Scottish Renal Registry and Scottish Stroke Care Audit) Dr Findlay and his colleagues will determine the frequency, risk factors and outcomes of stroke patients with kidney failure in Scotland.

They are also studying patients requiring dialysis using ultrasound, MRI scanning and patient questionnaires. This will help us examine the immediate and long term effects of dialysis treatment on blood flow to the brain, brain anatomy and memory.

Research in practice
Tackling cardiovascular risks for people with kidney disease

Funding from Kidney Research UK
£39,850

Over half of people with kidney disease will die from cardiovascular diseases such as heart disease and stroke because these are side effects of kidney disease.

25 years
A person on dialysis aged 25 years has the same cardiac prognosis as the average 75-year-old.

Funding from Kidney Research UK
£144,295
The representation of Scotland’s scientists, clinicians and kidney patients has been vital to two of Kidney Research UK’s biggest ever initiatives.

The charity’s investment in research nurse posts at Glasgow, Kirkcaldy, Dundee and Edinburgh have ensured Scottish patients’ participation in the world-leading trial into iron deficiency and anaemia in kidney patients on dialysis, known as the PIVOTAL trial. The four-year trial will determine the optimum levels of iron for patients on dialysis and has the potential to impact iron management in dialysis patients around the world.

Likewise, renal units in Scotland are joining the ASSIST-CKD project which uses software to map data from routine blood tests, creating graphs of kidney function over time. When deteriorating kidney function is detected, the participating laboratories send a report to the GP with a prompt that specialist advice may be needed. As the system identifies people with CKD who are at most risk of disease progression, GPs then have the opportunity to prevent patients having an unplanned entry into renal replacement therapy, for which the outcomes are worse.

There is an ongoing lack of available kidneys: between April 2014 and March 2015, 442 people were on the active kidney transplant waiting list in Scotland.

The average waiting time for a kidney transplant is 1,000 days.