pkd charity
Polycystic Kidney Disease

In association with

James Lind Alliance
Priority Setting Partnerships

TOP 10 PRIORITIES FOR ADPKD RESEARCH

For researchers and research funders developed in partnership with people affected by ADPKD and healthcare professionals.

Research is the key to better care

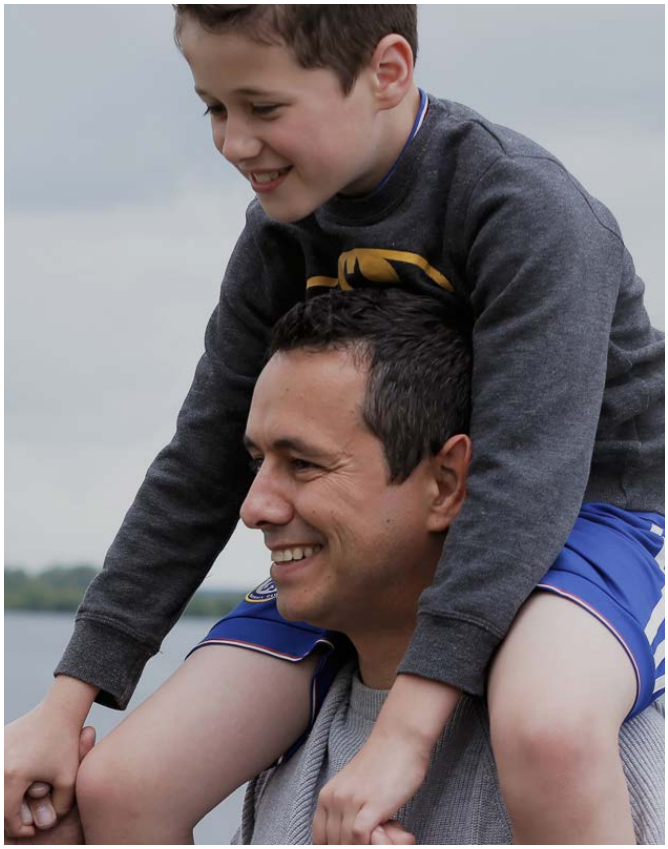
It is thanks to research that we have the life-saving healthcare and technologies that we receive today. From new prescription medicines to genetic tests and more precise surgery, research discoveries are keeping us alive for longer and improving our lives. Yet there is still so much to do!

For some areas of autosomal dominant polycystic kidney disease (ADPKD) care, we still don't know for certain what is the best approach.

The PKD Charity wants people with ADPKD to live their lives free from the fear of kidney failure, free from pain and other symptoms, and free from the risk of life-threatening complications. For that to happen, we need more research!

For an uncommon disease like ADPKD, deciding which topics researchers should work on first is especially important. Funding for PKD research is limited. Every penny donated and spent on research must count. Research could come in all shapes and sizes: from lab research, to designing and testing new drugs, to surveys to collect people's experiences, or trying out new ways for the NHS to provide care.

The views of people affected by ADPKD are vital when deciding what to research. After all, the next wave of research will shape their lives and that of future generations. We asked the James Lind



Alliance (who specialise in prioritising research) to help us prioritise the views of people affected by ADPKD and healthcare professionals. This report is the result of our work together. The quotes in the report are from people who took part in the project.

What happens next?

If you're researching ADPKD or funding ADPKD research, we ask you to focus your efforts on our top 10 priorities (or additional 7 priority areas).

By doing so, you're helping to ensure that, in the future, people with ADPKD can receive the care that they would like. What could be more important?

Our top 10 research priorities...

1 What treatments can be developed that slow or prevent progression of ADPKD and improve patients' quality of life?

Why this matters

ADPKD gets worse over time, causing damage to the kidneys. This is called progression.

Most treatments that people with ADPKD receive can reduce symptoms but don't prevent the disease progressing.

For many people, damage to the kidneys eventually means they will need dialysis or a kidney transplant.

ADPKD can also cause other health problems as it progresses. Tolvaptan (Jinarc®) is the only treatment available that can help to slow ADPKD progression in some patients.

This research question aims to find new treatments that can slow or prevent ADPKD progression and so improve patients' lives.

"There are pathways in ADPKD that can be treated with drugs, but we have not found a way to 'switch off' the disease and stop it in its tracks. ADPKD is a genetic disease, so there is potential for gene therapies."

— **John Sayer, Professor of Renal Medicine, Newcastle University**

Our top 10 research priorities...

2 Which people with ADPKD would benefit from early treatment and how can doctors identify them?

Why this matters

For some people, early treatment may slow the progression of ADPKD and reduce the problems it causes.

For other people, some treatments may not work as well or might cause too many side effects.

This research will help doctors identify the people who will benefit from each treatment.

This means patients can start to benefit from the right treatment sooner.

"A significant proportion of children and young people with ADPKD develop hypertension and have evidence of the effect of hypertension on their heart and blood vessels. A few pounds spent now on screening and early intervention are likely to save many thousands of pounds later by delaying hypertensive complications and kidney disease."

— **Dr Manish Sinha, Paediatric Nephrologist, Evelina London Children's Hospital**

Our top 10 research priorities...

3 What are the best ways to organise the care of people with ADPKD to improve their outcomes?

Why this matters

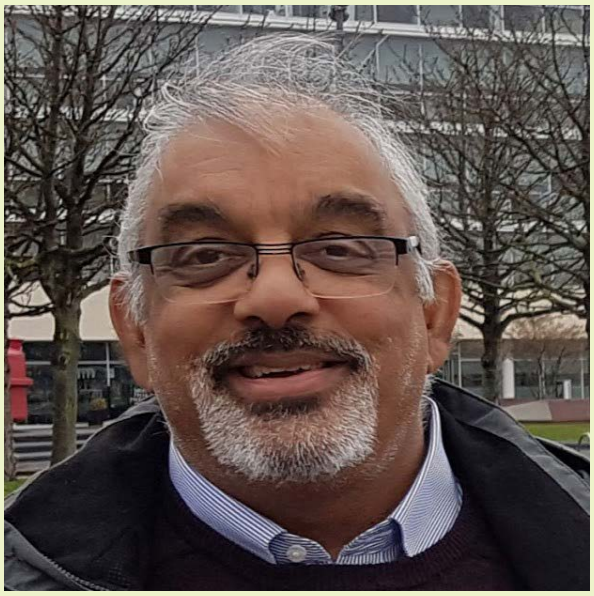
ADPKD doesn't only affect the kidneys — it can affect other parts of the body too, such as the liver.

This means people with the disease usually need to see a range of doctors specialising in different parts of the body during their lives.

Some people with ADPKD tell us that they experience inconsistencies or gaps in their care.

This can leave people frustrated and unsure whether they are getting the best care.

This research question aims to work out the best ways that different specialists providing care to people with ADPKD can work together consistently to support their patients' health.



"As a GP of 35 years' standing, I have had to care for people at various stages of ADPKD throughout their lives. Our list of ten research objectives attempts to cover the entire lifespan of the disease from birth and early diagnosis through to prevention, monitoring and the treatment of complications."

— **Dr Bert Jindal, GP**

"As patients, we can sometimes feel we have a duty to remind different specialists that they are treating one body."

— **Stefania, person with ADPKD**

Our top 10 research priorities...

4 What effect does pregnancy have on women with ADPKD including their pregnancy health, kidney function, and liver cysts?

Why this matters

We do not know much about how pregnancy affects the bodies of women with ADPKD.

For example, does carrying a baby cause extra damage to the kidneys of women with ADPKD?

Can it make their liver cysts grow faster?

Based on this research, doctors will be able to give women with ADPKD a clearer picture of any risks of pregnancy to them and their babies.

This research may also help to work out which treatments could reduce the chance of these problems occurring.

"1 in 2 of the population is female and pregnancy has an enormous impact on the body. For ADPKD (like all long-term conditions), it is so important to understand the effect of pregnancy on the disease. This research may also help us to understand the role of female hormones in ADPKD."

— **Gina, person with ADPKD and Head of Research and Development in an NHS Trust**

Our top 10 research priorities...

5 What are the benefits and harms of drugs that can be used for the management of ADPKD including polycystic liver disease (PLD)?

Why this matters

There are a number of treatments to help manage ADPKD. For patients to be able to choose between the different treatments they are offered, they need to know the possible benefits and side effects of each.

Yet there is not much research on risks and benefits, making it hard for healthcare professionals to give detailed advice on this.

This research will give patients and healthcare professionals a clearer picture of the benefits and risks of each treatment so they can be confident in selecting the right one together.

"It is so important for the choice of the best treatment plan to be a collaborative process between the patient, their specialist and health care professionals. Discussion of the known benefits and disadvantages of available therapies and collection of more evidence as new therapies are developed will help to achieve a personalised approach tailored to the needs of each individual patient."

— **Professor Pat Wilson, UCL Centre for Nephrology, Royal Free London**

Our top 10 research priorities...

6 For people with ADPKD experiencing pain, what treatments work best to reduce this pain?

Why this matters

Kidney pain caused by ADPKD can be disabling and have a big impact on people's lives. ADPKD pain can be hard to treat.

Sometimes the source of the pain (such as a cyst infection) is difficult to find or treat.

If researchers can discover which treatments are most effective for ADPKD pain, they can make a massive difference to some people's lives.

"I've had three cyst infections linked to my ADPKD and all were painful. Each time I had to be hospitalised. Medics need better standard processes to help treat infections quickly."

— **Natasha, person with ADPKD**

"Driven by my experience living with ADPKD and that of others I have spoken to, I would like to see more research on pain management. It has impacted my quality of life greatly."

— **David, person with ADPKD**

Our top 10 research priorities...

7 What changes to lifestyle, exercise and/or diet (including amount of water drunk) benefit people with ADPKD and polycystic liver disease (PLD)?

Why this matters

Many people with ADPKD want to know what steps they can take to stop their disease worsening. We know that a healthy lifestyle and certain changes to diet (for example, not eating too much salt) can help.

We don't have all the answers yet though, such as whether drinking a lot of water helps to keep the kidneys healthy.

This research can provide those answers, and so help people with PKD to take more active steps to protect their health and be in control of their disease.

"I see lots of people on our Facebook group with questions on exercise, diet and lifestyle. 'What can I do to manage my PKD?' We all want the answer to this."

— **Maggie, person with ADPKD**

Our top 10 research priorities...

8 When people are newly diagnosed with ADPKD, how does this affect them psychologically and what impact does it have on their life? What information and support would help people at this time?

Why this matters

A diagnosis of ADPKD can turn your life upside down and trigger a wide range of emotions.

Getting the right information and support can make an enormous difference. It can help you to cope, feel in control, and plan positively for the future.

People with ADPKD tell us that we still have more to do in this area.

This research will give people with ADPKD the chance to be heard. The results will mean better information and support for all patients, whether newly diagnosed or living with ADPKD for some time.

"I was diagnosed at age 25, when my career and life were taking off. I hid it from my employer. I got no emotional support — there wasn't any available. Things have improved a lot since then in terms of support available, but I feel it remains an important area to research."

— **David, person with ADPKD**

Our top 10 research priorities...

9 What are the benefits and harms of screening for and diagnosing ADPKD in children and young people (up to 18 years) at risk of having inherited this condition?

Why this matters

Tests are available to check for ADPKD in people who might have inherited the condition. This is called screening.

Screening for ADPKD in children who might have inherited the condition has some clear benefits. For example, children found to have ADPKD can begin to receive any treatments that might help. However, screening can also cause harm, such as making children and their parents anxious about their health and future.

This research will explore the benefits and harms of screening children. It will help us to understand which benefits and harms are most important to children, young people, and their families. The results will help similar people in the future choose whether or not they want to have screening tests.

"As a parent of two young children, with their best interests at heart, I am keen to know how beneficial it would be to have them screened at an early age for ADPKD."

— **Suzanne, parent of children with ADPKD**

"In the past, most people would have thought the harms of screening children would outweigh the benefits, but there are more options for managing the disease now, so the benefits of screening should be reconsidered."

— **Gillian, person with ADPKD**

Our top 10 research priorities...

10 What causes enlarged blood vessels (aneurysms) in some people with ADPKD and what is the most effective way to screen for and treat aneurysms?

Why this matters

ADPKD can increase the risk of getting a swollen blood vessel (an aneurysm), particularly in the brain.

Brain aneurysms often don't cause a problem, but in some people they burst and bleed, which can cause a stroke or death. This makes aneurysms a source of great fear for some people with ADPKD, especially if other family members have had one. Some procedures can treat aneurysms before they burst.

This research will help us to understand more about aneurysms: why they occur in people with ADPKD, how they can be spotted early (through screening), and how they can be treated.

This research could save lives, reduce disability and reduce the anxiety that aneurysms cause.

"Over the years, I have known quite a few patients have an aneurysm. One young patient in particular was extremely reluctant to have a screening test as three of her relatives had died of aneurysms in the past."

— **Jacqueline, Registered Nurse**

How we made the top 10 list

The process we used to find the top 10 areas for ADPKD research is called a 'Priority Setting Partnership' (PSP). We asked the James Lind Alliance (JLA) to guide us through the process, as they are very experienced in helping people to work together in this way. Here are the steps we used. For more detail, see our web page www.pkdcharity.org.uk/research/proritising-adpkd-research.

March 2019

The PKD Charity met with Maryrose Tarpey from the JLA to discuss the process. We made a change to the usual JLA process: we started with a long list of 117 uncertainties in ADPKD care identified from recent published reports, rather than using online survey. This was appropriate because the uncertain areas in ADPKD care are well reported.

April 2019

Ann Daly, an information specialist, checked guidance for doctors (clinical guidance) and detailed reports on research (systematic reviews) to see if any of the 117 uncertainties were already answered.

September 2019

We organised the first Steering Group meeting of patients, carers, their representatives and healthcare professionals. This group guided the PSP. The Steering Group worked with Ann to group the long list of 117 uncertainties into 35 'summary' questions.

October 2019

We made a survey with the 35 summary questions and shared it with patients, family members, carers and healthcare professionals (for example, doctors, nurses, dietitians). The survey was available online and was posted to 3,000 households of people living with ADPKD in our database. We asked everyone to rank the top 10 questions that were most important to them.

March 2020

We had to pause the survey owing to COVID-19.

August 2020

The Steering Group agreed to re-start the survey. We also agreed to hold the upcoming workshop online rather than face to face. We did this due to travel and meeting restrictions associated with the COVID-19 pandemic and to protect participants who were more vulnerable to the virus.

September 2020

571 people with ADPKD, 94 family members/carers and 82 healthcare professionals from the UK took part in the survey. The results were analysed to make a 'shortlist' of 17 questions for discussion at the online workshop.

December 2020

10 people with ADPKD, 2 family members and 10 healthcare professionals and PKD specialists took part in a full-day online workshop. They discussed the shortlist and agreed on the top 10 most important research questions. The workshop was chaired and facilitated by the JLA.

Priorities 11 to 17...

Here are the 7 additional research questions from the shortlist that did not make the top 10 priority list. These are also important to research.

11 What symptoms are associated with cyst infection in people with ADPKD, and how are cyst infections best managed (investigated and treated)?

Why this matters

The symptoms of cyst infections might be confused with other conditions, which can delay treatment. This research will help patients and doctors know what signs to look out for. It will also help doctors know which tests and treatments to use. This means cyst infections might be caught earlier and patients might recover faster.

12 What causes severe (acute) and long-term (chronic) kidney pain in people with ADPKD?

Why this matters

Kidney pain caused by ADPKD can be disabling and have a big impact on people's lives. It is sometimes hard to know what is causing the pain. This research will help us understand the causes of severe and long-term kidney pain. This links to priority 6, on pain treatment.

13 What are the most effective treatments for high blood pressure (hypertension) for people (children and adults) with ADPKD?

Why this matters

ADPKD can cause high blood pressure. This can increase your future risk of cardiovascular problems (for example, a stroke) and can damage your kidneys. So, it is important to treat high blood pressure properly. This research will discover which treatments for high blood pressure work the best.

Priorities 14 to 16

14 In which circumstances should removal of a kidney (known as nephrectomy) be considered in people with ADPKD, and are there alternative treatments?

Why this matters

If a person with ADPKD has a diseased kidney that is causing ongoing problems (for example, pain or repeated infections), a treatment option may be to remove the kidney. This surgery can work well but has some risks. This research will help doctors and patients to know when such surgery might help and what are the other options.

15 Does early treatment of high blood pressure improve the long-term health of people with ADPKD and/or reduce the risk of thickened heart walls (left ventricular hypertrophy)?

Why this matters

ADPKD can cause high blood pressure. This can increase your future risk of cardiovascular problems (for example, a stroke) and can damage your kidneys. High blood pressure forces the heart to work harder, which can thicken the heart walls over time (known as left ventricular hypertrophy). This research will see whether starting treatment promptly helps people to avoid these problems.

16 When a person is found to have kidney cysts but they do not have a family history of ADPKD, what tests should be performed to confirm their diagnosis and check for ADPKD?

Why this matters

Uncommonly, ADPKD can occur in people who do not have relatives with the disease. This research will look at which tests (such as a scan or genetic test) can be used to confirm whether the person has ADPKD so he or she can get the right healthcare.

Priority 17

17 Why do the symptoms and severity of PLD vary between people?

Why this matters

The symptoms of PLD can vary between people, but we are not sure why. This research will help us to find which factors are linked to worse PLD. This knowledge might help doctors to better plan the care of people with PLD in the future.

Additional research questions

You can find the 35 summary questions and the long list of 117 uncertainties on the website of James Lind Alliance: www.jla.nihr.ac.uk/priority-setting-partnerships/autosomal-dominant-polycystic-kidney-disease/.

With thanks

We would like to thank every person with ADPKD, family member, carer, and healthcare professional who took part in this PSP and the JLA facilitators. Without their time and opinions, this PSP would not have been possible. We thank Kidney Research UK for their support.

Thanks also to Maryrose Tarpey of the JLA for her guidance and Ann Daly for her work checking the long list of questions.

A special thank you to the Steering Group members and volunteers, Kam and Martin, and writer Hannah Bridges.

— **Tess Harris, PKD Charity, PSP Lead**

Steering Group

People affected by ADPKD and their representatives

Mr Patrick Barton	Carer
Mrs Natasha O'Brien	Person with ADPKD
Mrs Gillian Mundy	Person with ADPKD
Mr Peter Storey	Formerly Kidney Research UK

Healthcare professionals

Wendy Brown	Nurse Specialist, Imperial College Healthcare Trust
Dr Ragada El-Damanawi	Adult Nephrologist, Sheffield Kidney Institute
Dr Bert Jindal	GP, Huddersfield Primary Care Group
Dr Maryam Khosravi	Adult Nephrologist, Royal Free Hospital
Professor Albert Ong	Adult Nephrology, University of Sheffield
Dr Albert Power	Adult Nephrology, Southmead Hospital Bristol
Dr Richard Sandford	Genetics, Addenbrooke's Hospital
Professor John Sayer	Adult Nephrology/Genetics, Institute of Genetic Medicine, Newcastle
Dr Roz Simms	Adult Nephrologist, Sheffield Teaching Hospitals
Professor Pat Wilson	PKD Charity Research Advisory Board & UCL Centre for Nephrology
Professor Paul Winyard	Paediatric Nephrology, UCL Great Ormond Street Institute of Child Health
Dr Grahame Wood	Adult Nephrology, Salford Royal Hospital

Project coordination roles (also Steering Group members)

Ms Tess Harris	PKD Charity CEO, person with ADPKD Priority Setting Partnership Lead
Mrs Jane Pugh	PKD Charity Engagement Manager, person with ADPKD Priority Setting Partnership Project Manager
Maryrose Tarpey	James Lind Alliance Adviser Chair of the Steering Group
Ann Daly	Information Specialist

About the PKD Charity

The PKD Charity was founded in 2000 by an ADPKD patient and a genetics doctor. It is patient/family led and its mission is to transform the quality of life of all those affected by PKD through providing support, raising awareness and funding research.

Over the past 20 years, the Charity has supported thousands of patients and their families coping with the often devastating impact of a ADPKD diagnosis and its progression. The Charity provides information written by medical experts, organises educational events (in-person and online) around the UK, moderates large online communities, and gives personalised peer support via trained volunteers and staff. The Charity also seeks to raise awareness amongst the Government, NHS and the public about the clinical, economic and psychological disease burden. It has created strong relationships with stakeholders in the kidney, liver, genetics and rare disease communities in the UK and internationally.

The Charity funds capacity-building research in the UK and funds a vital bio-resource bank of human PKD and age-matched normal control tissues, cell lines and animal models that faithfully recapitulate the genotypic and phenotypic characteristics of PKD. The Charity regularly contributes to national and international research projects and studies. For more information, please visit the PKD Charity website, follow us on Twitter, Facebook and LinkedIn.

About the James Lind Alliance

The James Lind Alliance (JLA) www.jla.nihr.ac.uk/about-the-james-lind-alliance is a non-profit making initiative established in 2004 and now hosted by the National Institute for Health Research. It brings patients, carers and clinicians together in Priority Setting Partnerships (PSPs) www.jla.nihr.ac.uk/priority-setting-partnerships to identify and prioritise the Top 10 unanswered questions www.jla.nihr.ac.uk/top-10-priorities or evidence uncertainties that they agree are the most important.

The aim of this is to make sure that health researchers and funders are aware of the issues that matter most to the people who need to use the research answers in their everyday lives.

The JLA priority setting method supports people who don't usually get a chance to shape the research agenda to have their say. The method has been developed and refined since the completion of the first PSP in 2007 and, since that first PSP, over 100 more have been completed in the UK and internationally.

The best long-term result for any JLA PSP is that at least some of the uncertainties identified are turned into research studies, and that these go on to have a life-changing impact on the treatments or services available to patients and the way in which these are delivered.

Notes

pkdcharity.org.uk

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