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Research priorities for autosomal dominant polycystic kidney disease: a UK priority setting partnership

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ABSTRACT

Objectives Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney condition, accounting for 7%–10% of patients with kidney failure. Fundamental basic science and clinical research on ADPKD is underway worldwide but no one has yet considered which areas should be prioritised to maximise returns from limited future funding. The Polycystic Kidney Disease Charity began a priority setting partnership with the James Lind Alliance (JLA) in the UK in 2019–2020 to identify areas of uncertainty in the ADPKD care pathway and allow patients, carers and healthcare professionals to rank the 10 most important questions for research.

Design The scope covered ADPKD diagnosis and management, identifying new treatments to prevent/slow disease progression and practical, integrated patient support (https://pkdcharity.org.uk/research/for-researchers/adpkd-research-priorities). We used adapted JLA methodology. Initially, an independent information specialist collated uncertainties in ADPKD care from recent consensus conference proceedings and additional literature. These were refined into indicative questions with Steering Group oversight. Finally, the 10 most important questions were established via a survey and online consensus workshop.

Setting UK.

Participants 747 survey respondents (76% patients, 13% carers, 11% healthcare professionals); 23 workshop attendees.

Results 117 uncertainties in ADPKD care were identified and refined into 35 indicative questions. A shortlist of 17 questions was established through the survey. Workshop participants reached agreement on the top 10 ranking. The top three questions prioritised by patients, carers and healthcare professionals centred around slowing disease progression, identifying persons for early treatment and organising care to improve outcomes.

Conclusions Our shortlist reflects the varied physical, psychological and practical challenges of living with and treating ADPKD, and perceived gaps in knowledge that impair optimal care. We propose that future ADPKD research funding takes these priorities into account to focus on the most important areas and to maximise improvements in ADPKD outcomes.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We used the established methodology of the James Lind Alliance (JLA) (https://www.jla.nihr.ac.uk/jla-guidebook) for this priority setting partnership (PSP)—methodology that has been used by government and charities in the UK and internationally in over 100 therapeutic areas to prioritise research.

⇒ The project was overseen by an expert Steering Group which included people affected by autosomal dominant polycystic kidney disease (ADPKD) (patients and their representatives and a carer), a range of clinical experts in ADPKD and a JLA Adviser on priority setting.

⇒ We used the proceedings of a recent international consensus conference on ADPKD management as the foundation for gathering uncertainties in the ADPKD care pathway, supplemented by additional high-quality publications.

⇒ The use of both a paper and online survey to refine the questions for research gave us broad reach, despite ADPKD being a relatively uncommon condition. However, men and persons of non-white ethnicity were under-represented in the demographics, so the PSP output might be less representative of these groups.

⇒ The health risk posed by the COVID-19 pandemic necessitated an online rather than face-to-face workshop, which may have influenced the output. The materials and format of the workshop were otherwise per JLA methodology. With attentive pre-workshop briefings and live facilitation, participant engagement was strong and consensus on the research priorities was reached.

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney disease.[1 2] ADPKD is the fourth most common reason that patients require kidney replacement therapy, and accounts for 7%–10% of patients with kidney failure.[3] It is a progressive disease associated with the unrelenting formation and expansion

of numerous cysts in the kidneys, resulting in kidney failure at an average age of the late-50s in the UK.[4 5] It is commonly associated with cyst formation in additional organs, including the liver (known as polycystic liver disease).[5]

ADPKD can greatly impact on patients' quality of life.[6 7] Patients may experience debilitating symptoms, including pain associated with enlarged organs and cyst infections.[5] Moreover, patients are at risk of potentially life-threatening complications such as stroke from ruptured intracranial aneurysms.[8]

Research in the last two decades has immeasurably improved our understanding of the disease, in turn improving management options, outcomes and information for ADPKD patients. However, many areas of uncertainty remain in the ADPKD care pathway. To maximise returns from limited future funding, the prioritisation of topics and harmonisation of efforts is essential. This is even more relevant in the shadow of the ongoing coronavirus pandemic, as funds and expertise continue to be diverted towards researching and managing COVID-19.

The views of those living with ADPKD and their healthcare teams regarding priorities for ADPKD research have not been reported previously.

In 1995, Iain Chalmers, a founder of the Cochrane Collaboration, wisely said 'greater lay involvement in setting the research agenda would almost certainly lead to greater open-mindedness about which questions are worth addressing, which forms of healthcare merit assessment, and which treatment outcomes matter'.[9] He went on with others in 2004 to establish the James Lind Alliance (JLA) funded by the National Institute for Health Research. The JLA supports priority setting partnerships (PSPs), which aim to involve patients, carers and healthcare professionals in the setting of priorities for research.[10] PSPs are increasingly recognised as a proven means to identify priorities that are of direct relevance and potential benefit to those affected by a condition and their healthcare providers. The JLA's established PSP methodology has been used to identify priorities for research in over 100 therapeutic areas over the last 13 years.

The PKD Charity was established in December 2000 in the UK to promote health and to relieve those persons suffering from or affected by PKD through funding research, promoting awareness, and providing information, education and support. In 2019-20, the PKD Charity—in association with the JLA—conducted a PSP to identify the areas of uncertainty in the ADPKD care pathway and to allow patients, carers and healthcare professionals to identify and rank the 10 most important questions for research to address. Our goal is for researchers and funding bodies to use the top 10 list (and more extensive shortlist) to inform future research activity and grant awards. Our vision is to accelerate progress towards understanding the causes of PKD, identifying potential new therapies and improving patients' health and lives.

METHODS

This PSP was conducted by the PKD Charity in 2019–2020 in association with the JLA. The PKD Charity and JLA met to define the scope and terms of reference for the PSP in March 2019, and the priority setting was completed in December 2020. A plain language summary of the project can be found at https://pkdcharity.org.uk/research/for-researchers/adpkd-research-priorities.

Data protection

Survey responses were anonymised, and no personal data were requested. Workshop participants gave consent to take part and were not named in reports. The workshop was not recorded. In line with the PKD Charity's Data Retention Policy (www.pkdcharity.org.uk/privacy-notice), any personal data collected will be retained for 3 years and then destroyed.

Scope

The scope of the PSP was defined on 17 October 2019 by the Steering Group as 'research and healthcare priorities related to: diagnosis and management of complications in the kidneys (renal) and other areas of the body; identification of new treatments to prevent and slow PKD progression; and practical, integrated patient support'.[11] The scope and protocol are available on the PKD Charity's website at https://pkdcharity.org.uk/research/for-researchers/adpkd-research-priorities. We excluded from the scope questions about autosomal recessive PKD. Children under the age of 16 affected by ADPKD were considered in the PSP but not actively consulted. The PSP was focused on the UK experience, the survey was conducted in the English language, and the workshop was held with UK participants. It was recognised that people residing in other countries might take part in the survey and their priorities would be separated and shared with overseas PKD groups. The priorities reported in this article represent UK opinions only.

Protocol

The JLA has an established, continuously evolving method for PSPs that involves the equal participation of patients and clinicians to set priorities for research.[10] The method was first used in 2007. Our PSP used the recommended JLA method[10] with one adaptation: owing to the health risks posed by the COVID-19 pandemic, our workshop at the end of the process was held online, rather than in person. Holding the workshop online allowed us to complete the PSP during the ongoing travel and meeting restrictions and uncertainties caused by the pandemic, and also allowed us to protect participants from undue risk.

The PSP process used is summarised in figure 1. In brief, the PSP process comprised: (1) identifying the uncertainties in ADPKD research through a review of key literature; (2) verifying that uncertainties were unanswered; (3) summarising the uncertainties into a longlist of indicative questions verified by the Steering Group; (4) ranking

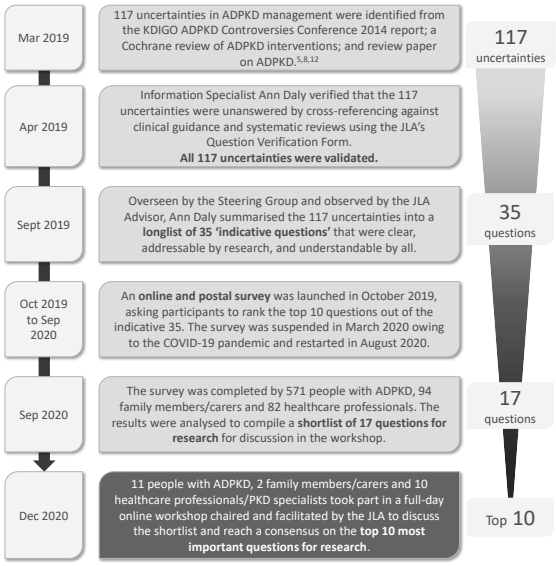

Figure 1 Overview of the process used for the priority setting partnership. The stage of the process that differed to the JLA's standard methodology is shown in dark grey, as described in the Methods section. ADPKD, autosomal dominant polycystic kidney disease; JLA, James Lind Alliance; KDIGO, Kidney Disease: Improving Global Outcomes.

these via an online and paper survey to produce a shortlist of questions for final prioritisation in the workshop and (5) discussing and ranking the 10 most important questions for future research in an online consensus workshop held with persons with ADPKD, carers, family members and healthcare professionals facilitated by JLA Advisers.

Indicative questions were not worded as research questions. Rather, they were framed to capture themes and topics arising from the consensus conference and additional literature.

Oversight

The PSP was overseen by a Steering Group comprising four persons affected by ADPKD and their representatives (2 persons with ADPKD, 1 carer and 1 representative from Kidney Research UK), 12 healthcare professionals of ranging specialisms and with expertise in ADPKD (8 nephrologists/nephrology specialists, 1 paediatric nephrology specialist, 1 nurse specialist, 1 general practitioner [GP] and 1 clinical geneticist), and four project coordinators (Tess Harris, PKD Charity Chief Executive Officer, PSP Lead and ADPKD patient; Jane Pugh, PKD Charity Engagement Manager, ADPKD patient and PSP Manager; Maryrose Tarpey, JLA Adviser and Chair of the Steering Group; and Ann Daly, Information Specialist). The Steering Group met four times and corresponded by email between meetings. In addition to guiding the process, the Steering Group also oversaw the development of the list of 35 indicative questions to ensure that the original 117 uncertainties were interpreted appropriately and question wording aided understanding by all audiences. The JLA Adviser observed the development of the list of 35 indicative questions to ensure accountability and transparency.

Identifying and validating uncertainties

Per JLA recommendations, uncertainties are gathered by a survey and a literature review. We focused on the latter approach, as uncertainties were well documented in the field owing to recent collaborative efforts. A recent international consensus conference on controversies in ADPKD management that involved multidisciplinary clinical experts and patients provided a strong foundation for our literature review. Independent information specialist AD identified uncertainties in the ADPKD care pathway from the Kidney Disease: Improving Global Outcomes conference proceedings and additional high-quality literature. To ensure no topics were missed, survey respondents were invited to submit suggestions for additional questions for research after considering the longlist (see later).

AD verified that the identified uncertainties were unanswered by cross-referencing clinical guidance and systematic reviews identified through searches of the Cochrane database of systematic reviews and PubMed, using established JLA methodology.

Questionnaire methodology

The ranking of the 35 questions was achieved through an online consultative questionnaire hosted on QuestionPro (Texas, USA) and mailed paper copies. The wording of the questions was refined by HRB and the PKD Charity lay reviewers. A balance was sought in making the wording accessible while succinctly and accurately reflecting the identified uncertainties.

Several pilots were conducted to ensure the questionnaire process for ranking questions worked. Dissemination of the questionnaire aimed to reach a wide audience of people affected by ADPKD and healthcare professionals through the PKD Charity's social media channels (Facebook and Twitter) and reposting by other kidney charities, the JLA and individual healthcare professionals. Printed versions in large, easy-to-read font were mailed to 3000 households of persons affected by ADPKD in the PKD Charity's database to help ensure those who were uncontactable by email were reached. The Steering Group members were encouraged to promote the survey to their networks. Completion of the survey on behalf of someone else was not actively encouraged.

Respondents were asked to choose their top 10 priorities for research from the randomised longlist of 35 indicative questions. The questionnaire had four components: (1) first, respondents were presented with the 35

questions in a random order and asked to choose the ones they found most important, which could be more than 10; (2) next, each respondent's chosen questions were re-randomised and they were asked to choose up to 10 that they viewed as most important; (3) respondents were invited to submit additional questions for research; (4) finally, respondents were asked to complete a series of demographic questions. The responses were analysed by the JLA Adviser and PSP Lead who ranked the 35 questions separately by importance attributed by patients/carers and by healthcare professionals.

The Steering Group met to review the results and determine the number of questions to be discussed at the workshop. Guided by the JLA's experience they agreed on the shortlist.

Selection of workshop participants and workshop format

All persons who responded to the survey were invited to register for the workshop. The workshop participants were selected by the JLA Adviser and project coordinators to best reflect the demographic of ADPKD patients and their carers in the UK and the variety of healthcare professional specialisms relevant to their care.

A full-day online workshop was held on 15 December 2020 using the videoconference platform ZOOM (California, USA) with 23 active participants plus JLA facilitators, technical support and observers. The facilitators were involved in precall briefing materials and live facilitation to support all attendees in actively engaging with and participating in the workshop. Participants were offered technical support and training in the videoconference platform beforehand. In small breakout sessions (four groups of six participants), each participant was invited to share and justify their top three priorities chosen from the shortlist of 17 questions, as well as their bottom three. A summary of each group's results was then used to aid small group discussion to rank the 17 questions in order. In the afternoon, the ranking (1 to 17) produced by each of the four groups was presented to all participants by the JLA Adviser. Participants were divided into new breakout groups in which they debated the rankings from the morning sessions and ranked the top 10 priorities, with an aim to reach consensus.

The results from the four groups were combined using an aggregated score for each question; the near-final order was then presented to all participants in a plenary session, with opportunities for reflection and provision of post-meeting comments.

The top 10 list was approved by the Steering Group, who agreed minor changes to the wording of some indicative questions to accurately reflect the scope of each question that was discussed in the workshop.

Patient and public involvement

Patient and public involvement sits at the heart of this project. The PKD Charity initiated the PSP. Patients, carers and their representatives contributed to the scoping, design and execution of the PSP through Steering Group involvement. The Steering Group included two persons with ADPKD, one carer and one representative of persons affected by ADPKD. The PSP Lead (TH) is a person with ADPKD and expert patient representative. Moreover, patients and carers worked together with healthcare professionals through our survey and workshop to contribute equally to the prioritisation of research questions. In addition to this manuscript, we have developed a Plain English summary of the findings (available at: https://pkdcharity.org.uk/research/for-researchers/adpkd-research-priorities), which was reviewed by the Steering Group's patient members. That summary uses accessible wording and explains for each question 'why this matters', that is, the potential positive impact of research on each topic. It was shared through the PKD Charity's e-newsletter and social media channels.

RESULTS

Identifying and validating uncertainties

Three recent key publications informed the uncertainties list: proceedings of a recent international consensus conference on controversies in improving outcomes in ADPKD,[8] a Cochrane review of interventions in ADPKD (including implications for future research),[12] and an expert review of how recent research insights have advanced the ADPKD field.[5] In total, 117 uncertainties were identified regarding ADPKD diagnosis and the management of complications in the kidney (renal) and other areas of the body; identification of new treatments to prevent and slow PKD progression; and practical integrated patient support. Following the validation exercise by the information specialist, all 117 uncertainties were confirmed as not having been answered by prior research and so were kept in scope. A list of the 117 uncertainties can be downloaded at https://www.jla.nihr.ac.uk/priority-setting-partnerships/autosomal-dominant-polycystic-kidney-disease/.

Refinement of indicative questions

The 117 uncertainties were refined into the 35 indicative questions presented in table 1. In total, 571 people with ADPKD (76%), 94 family members/carers (13%) and 82 healthcare professionals (11%) took part in the survey to rank the list of indicative questions. Approximately 80% of persons responded online, while 20% responded by post. Of the 571 people with ADPKD, 71% were female, 80% had chronic kidney disease (CKD) stages 1–4, and 93% were white. A wide range of ages participated, with just over half of patients (54%) falling in the 45–64 year-old age bracket. Of the 94 carers, 78% were female, 48% were aged 45–64, and 81% were white. Of the 82 healthcare professionals, 38% were adult nephrologists, 21% were renal nurses, and 10% were GPs. Following analysis of the responses and review by the Steering Group, the uncertainties were reduced to a shortlist of 17 questions (table 1).

Table 1 The longlist of 35 indicative questions* that appeared in the survey, grouped by theme and with shortlisted questions shown first

Theme	Question	Shortlisted
Diagnosis	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?	✓
	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?	✓
Symptoms, disease course and pathogenesis	What effect does pregnancy have on women with ADPKD including their pregnancy health, kidney function, and liver cysts?	✓
	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 do the symptoms and severity of polycystic liver disease (PLD) vary between people?	✓
	How does ADPKD affect children and young people (up to 18 years), including those who might not have symptoms (eg, those diagnosed based on an ultrasound of their kidneys or genetic test).	
	In people with ADPKD, do kidney stones increase the risk of kidney function decline?	
	If a woman with ADPKD is pregnant, what effect does her condition have on her child before birth?	
	For women with PLD, does using oral contraceptives to prevent pregnancy or hormone replacement therapy to treat the menopause affect their PLD?	
Management of ADPKD	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)?	✓
	What are the most effective treatments for high blood pressure (hypertension) for people (children and adults) with ADPKD?	✓
	What symptoms are associated with cyst infections in people with ADPKD, and how are cyst infections best managed (investigated and treated)?	✓
	What causes severe (acute) and long-term (chronic) kidney pain in people with ADPKD?	✓
	For people with ADPKD experiencing pain, what treatments work best to reduce this pain? For example, treatments might include removing nerves in the kidney or draining the liquid out of kidney cysts.	✓
	What treatments can be developed that slow or prevent progression of ADPKD and so improve patients' quality of life?	✓
	In which circumstances should removal of a kidney (known as nephrectomy) be considered in people with ADPKD, and are there alternative treatments?	✓
	Which people with ADPKD would benefit from early treatment and how can doctors identify them?	✓
	What are the benefits and harms of drugs that can be used for the management of ADPKD including PLD?	✓
	What are the benefits and harms of treating high cholesterol and/or high uric acid (known as hyperuricaemia) in people with ADPKD?	
	How common is it for people with ADPKD to have blood in their urine and how should this be assessed and treated according to severity and complications?	
	For people receiving medicines to reduce the risk of a blood clot during dialysis or transplantation, what is the risk of having blood in the urine and what problems can this cause?	
	How can other measures of kidney structure and function be used alongside commonly used measures such as kidney length or total kidney volume to monitor disease progression in people without symptoms or with early stage ADPKD?	
Kidney failure	Are people with ADPKD and kidney failure who are receiving peritoneal dialysis more likely to suffer complications or failure of this treatment than people without ADPKD?	
	What are the risks of complications of kidney transplantation in people with ADPKD (during transplantation and in the long term) compared with patients without ADPKD?	
	What proportion of people with ADPKD and kidney failure develop kidney cancer, and what tests and care should patients with signs of kidney cancer receive?	

Continued

Table 1 Continued

Theme	Question	Shortlisted
Practical integrated patient support	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?	✓
	What lifestyle, exercise and/or dietary changes (including amount of water drunk) are beneficial for people with ADPKD and PLD?	✓
	How should the care of people with ADPKD be organised to improve their outcomes (ie, reduce illness and death)? How can we ensure that this care includes appropriate access to consistent, specialist care provided by a team of experts?	✓
	What information resources are required to support family planning for people with ADPKD?	
	How does social inequality affect long-term outcomes in people with ADPKD?	
	When researching ADPKD, including new treatments, what measurements such as kidney size, kidney function, quality of life and other side effects reported by patients themselves can be used?	
	How can healthcare practitioners recognise the need for and provide a holistic approach to the care of people with ADPKD and family members?	
Monitoring kidney disease	Can assessment of the way the blood is flowing through the kidney be used to see how much a person's ADPKD has progressed (ie, how much damage it has caused to the kidney)?	
	How useful is assessment of glomerular filtration rate (as a way to measure kidney function) in the early stages of ADPKD?	
	Is measuring levels of protein in a person's urine helpful for assessing how far their ADPKD has progressed?	

*The questions are group by theme for ease of reference only. Indicative questions were presented in a random order in the survey.
ADPKD, autosomal dominant polycystic kidney disease.

When the survey responses were stratified by type of respondent (patients/carers or healthcare professionals), there was concordance between which questions were considered among the most important in many instances. Patients/carers and healthcare professionals alike prioritised questions about slowing or preventing progression, treatments for pain, the organisation of care, identifying those who would benefit from early treatment, and the causes of aneurysms. However, there were some differences. Patients/carers placed greater priority on questions about lifestyle, diet and exercise than did healthcare professionals (ranked 2 vs 12, respectively), and also more highly ranked a question on cyst infections (ranked 7 vs 26, respectively). In contrast, healthcare professionals placed greater priority on the psychological impact of diagnosis (ranked 5 vs 11, respectively), the benefits and harms of screening at-risk children and young persons (ranked 6 vs 14, respectively) and accurate diagnosis of those without a family history (ranked 9 vs 26, respectively) than did patients/carers.

Consensus on the top 10 priorities for research to address

Thirty-two people attended the online workshop: 11 people with ADPKD, 2 carers, 4 adult nephrologists, 1 paediatric nephrologist, 1 genetics consultant, 1 GP, 2 nurses, 1 scientist, 4 JLA facilitators, 1 volunteer/peer supporter, 1 technical support representative and 4 observers. In the online workshop, consensus was reached on the ranking of the top 10 research questions (table 2). In all four breakout groups, the question 'What treatments can be developed that slow or prevent progression of ADPKD and so improve patients' quality of life?' was ranked number 1. There were some differences in ranking of other questions, with the final ranking produced using an aggregated score and group discussion.

Discussion

To our knowledge, this is the first PSP on ADPKD. It has given insight into the most important areas for future research in ADPKD based on the values, views and experiences of persons with ADPKD, their family members/carers, healthcare professionals and PKD specialists. We encourage researchers and funding bodies to use the top 10 ranking to help them define the scope and aims of future research proposals. Given that the choice of cut-off of 10 most important questions is somewhat arbitrary—with 10 being chosen for familiarity and traction—we encourage researchers and funders also to consider research on the other seven questions that made our shortlist.

Patients with ADPKD face unique health challenges and experiences (such as complications in areas of the body other than the kidney) compared with patients with kidney disease in general, which could be expected to translate into distinct research priorities. However, we have uncovered similarities in priorities too. In a 2014 Canadian PSP for patients with CKD not on dialysis, the number 1 priority focused on the prevention of the

Table 2 Final ranking of the shortlisted indicative questions for research following the workshop

Rank	Indicative question
1	What treatments can be developed that slow or prevent progression of ADPKD and so improve patients' quality of life?
2	Which people with ADPKD would benefit from early treatment and how can doctors identify them?
3	What are the best ways to organise the care of people with ADPKD to improve their outcomes?
4	What effect does pregnancy have on women with ADPKD including their pregnancy health, kidney function and liver cysts?
5	What are the benefits and harms of drugs that can be used for the management of ADPKD including polycystic liver disease (PLD)?
6	For people with ADPKD experiencing pain, what treatments work best to reduce this pain?
7	What changes to lifestyle, exercise and/or diet (including amount of water drunk) benefit people with ADPKD and PLD?
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?
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?
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?
11	What symptoms are associated with cyst infection in people with ADPKD, and how are cyst infections best managed (investigated and treated)?
12	What causes severe (acute) and long-term (chronic) kidney pain in people with ADPKD?
13	What are the most effective treatments for high blood pressure (hypertension) for people (children and adults) with ADPKD?
14	In which circumstances should removal of a kidney (known as nephrectomy) be considered in people with ADPKD, and are there alternative treatments?
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)?
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?
17	Why do the symptoms and severity of PLD vary between people?

ADPKD, autosomal dominant polycystic kidney disease.

development and progression of kidney disease,[13] similarly to our number 1 priority. Lifestyle interventions and diet to slow progression and improve quality of life also featured in the CKD PSP top 10. This indicates that ADPKD and CKD patients share desires to prevent the seemingly inevitable march of progression to kidney failure and want to take back control of their lives. These desires are demonstrated in these participants' views shared in our workshop:

> We should focus on prevention so we can stop people getting the disease. (Person with ADPKD)

> 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. (Person with ADPKD)

Although the scope of our PSP was broader than those questions that could be answered only by clinical trials, it is of interest to contrast our results with recent studies aiming to crystallise the clinical trial measures that matter the most to healthcare professionals and patients. A number of the themes featuring in our top 10 list also came to the forefront of a recent consensus workshop by the Standardised Outcomes in Nephrology-PKD initiative, which aimed to identify the core outcomes that should be measured in ADPKD clinical trials.[14] In that workshop, fear of disease progression (as signalled by a decrease in kidney function), the need for more prominence of pain management (driven by under-recognition and inadequate management), and the importance of measuring cardiovascular disease risk all featured as central themes. A recent Delphi survey to determine core outcome domains in ADPKD clinical trials[15] and a nominal group technique to identify patient-important outcomes[16] also noted the high priority of endpoints measuring progression (eg, kidney function, end-stage kidney disease, kidney size/growth and survival), blood pressure, cerebral aneurysms and pain. Taken together, our PSP and these recent reports may be used together in clinical trial design to select not only what to research but how to measure it. However, the scope of our PSP was broader than clinical trials. Indeed, many of the topics featuring in our top 10 list (such as the optimal organisation of care, psychological impact of diagnosis, the benefits and risks of screening children, and causes of aneurysms) lend themselves to alternative forms of research.

One of the observations on which the JLA's PSP methodology is based is that healthcare professionals and those living first-hand with the disease can place distinct value

on different topics for research, and equal weight should be placed on each perspective.[10] The results of our survey lend further support to this theory, with some questions ranked quite differently by professionals versus patients/carers. Traditionally, it has been expected that healthcare professionals may place more value on research aiming to further therapeutic options, while patients may place more value on research addressing their experiences of living with the disease. This theory held true in our PSP to some extent, with patients/carers placing a higher value than did professionals on the actions they could take themselves (lifestyle, diet and exercise) and on tackling cyst infections. The focus on cyst infections possibly reflects the pain and detrimental impact that these episodes can have on patients, as reflected on by this workshop participant:

> 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. (Person with ADPKD)

Our survey showed some additional and surprising nuances between the priorities of healthcare professionals versus patients. Healthcare professionals more highly ranked questions about the psychological impact of the disease and patients' information and support needs as well as on the benefits and risks of screening children and adolescents for ADPKD. This perhaps reflects the challenges that professionals perceive in providing information to patients and caregivers on topics where research evidence is limited. Regardless of the reasons for these differences, our PSP highlights the need to give voice to both groups and to facilitate active discussion, in order that balance between conflicting priorities may be found.

A strength of this PSP was that we used established methodology that was developed by the JLA and has been used by government and charities to shape the future research agenda in over 100 therapeutic areas. Our Steering Group featured strong expertise and experience on both the clinical side and patient experience, allowing mindful oversight of the process from start to finish. Observation and facilitation by JLA experts ensured accountability and transparency.

Another strength was the number of survey respondents (N=747). We were delighted to have such strong engagement in a PSP focussing on a relatively uncommon condition. ADPKD has a variable disease course and age of progression. The sizeable patient (76%) and carer (13%) representation in the survey gave us confidence that the varied views of this heterogenous population were captured and reflected.

We cannot rule out the possibility that workshop participants may have based rankings not only on perceived topic importance, but also on perceived feasibility or broadness of questions (eg, more highly ranking those questions that they felt would encompass a larger amount of research). For example, in workshop breakout sessions, some groups favoured ranking only one of the two pain-related questions in the top 10 as the question was hoped to be sufficiently broad to incorporate the other pain topic.

A potential weakness of our PSP was that we collated uncertainties using a review of key literature (rather than a survey). This was for the reasons outlined in the methods section. Some uncertainties, especially those from the perspective of people living with ADPKD, could have gone undetected through this approach. Importantly, our quality assurance measures to validate the uncertainties and to prompt suggestions from survey respondents did not raise concern of significant gaps or imbalances in the uncertainties identified.

Survey invitations were sent through multiple channels including the PKD Charity's network. Healthcare professionals and lay persons interacting with the charity might have different appreciation of and perspectives on numerous issues surrounding ADPKD than other persons, which may have influenced the survey results. However, in an uncommon disease the approach was justified to support strong survey engagement.

Over 75% of patients and carers who took part in our survey were female. This reflects the profile of the ADPKD community that engages with the PKD Charity but means that the male ADPKD population was somewhat underrepresented. Non-white ethnic groups with ADPKD were also underrepresented in our survey. Having identified these imbalances in our sample, they can be addressed in future initiatives.

This PSP was conducted in the UK: a developed nation with a governmentally funded national health service. As such, the findings might be of less relevance to countries with differing economies, healthcare models and access to ADPKD treatments and support.

The COVID-19 pandemic altered the delivery of healthcare and the experiences of patients, carers and healthcare professionals in a multitude of ways that are not yet fully documented. It is possible that these impacts shaped respondents' views and interactions with our consultation. A direct impact was that we opted to convene an online workshop following substantial postponement of a planned face-to-face event for COVID-19-related reasons. The workshop otherwise followed the JLA approach. While we cannot rule out a possible influence of a virtual format on the workshop output, there is no indication that results of online JLA workshops are any less valid than those conducted face-to-face. Moreover, the impact of ongoing postponement posed greater risk to the validity of an active project and to the timely conclusion and reporting of results.

As mentioned previously, the cut-off of 10 top priorities is somewhat arbitrary, and we encourage readers to consider those questions that fell just below this threshold.

In conclusion, the top 10 priorities identified in this partnership give clear direction to researchers and funding bodies on the questions that people with ADPKD, their carers and healthcare professionals would like to see answered. The priorities reflect the varied physical,

psychological and practical challenges faced by persons living with and treating ADPKD, as well as the perceived gaps in knowledge that impair optimal disease management. We hope that researchers and funding bodies in the field of ADPKD align their future research with the themes identified as most important in our PSP, to maximise improvements in ADPKD outcomes.

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