PKD Australia

AN ACTION PLAN FOR CRITICAL CHANGE IN POLYCYSTIC KIDNEY DISEASE OUTCOMES IN AUSTRALIA

Action Plan for Positive Change

This action plan has been developed by PKD Australia (PKDA) in collaboration with patients and clinical and research healthcare professionals to provide policy makers with pathways to address the burden of Polycystic Kidney Disease on the individual, family and the healthcare system.

"Looking back at my father's suffering I fear what is ahead for me, looking forward at my children and grandchildren, I have guilt at what I have passed on to them"
- ADPKD patient, 52, Australia

This action plan presents a framework of evidence-based and cost-effective interventions spanning Prevention, Management, Support and Cure. Key aims of the framework are to improve the health and prognosis of PKD patients, whilst relieving pressure from the heavily burdened health system, namely by reducing the need for dialysis in the PKD population through accessible genomics and family planning, access to relevant, accurate and balanced PKD information, sustainable and varied funding into PKD research to find treatments and a cure.

Key Actions

- ✓ Accessible genetic testing for all PKD families for identification, treatment personalisation and/or family planning.
- ✓ Establishment of a clinical registry to enable optimisation of treatments targeted to individual needs to improve morbidity and mortality.
- ✓ Increased availability and access to health, wellbeing and psychosocial support for people with PKD, their care givers and families.
- ✓ Government investment to expand promising high-quality, competitive and impactful PKD research to ensure continued improvements and treatments and support PKD Australia's vision for a cure.

About Polycystic Kidney Disease

PKD is the most common life-threatening genetic disorder of the kidneys. Based on worldwide figures it is estimated that up to 60,000 Australians are likely to be affected by PKD in their life. Polycystic Kidney Disease (PKD) is a genetic disease, usually passed from parent to child. In some cases, PKD occurs when there is no family history and can arise from a new genetic mutation.

There are two types of PKD

Autosomal Dominant PKD (ADPKD).

The most common form of PKD, ADPKD affects around 1:1000 people worldwide and occurs in males and females equally. If you have ADPKD there is a one in two chance of passing the faulty gene onto each child. People with ADPKD will develop multiple fluid filled cysts in their kidneys, and can develop cysts in the liver, pancreas and other organs. As fluid-filled cysts grow and enlarge both kidneys, kidney function declines. About half of people with ADPKD will have kidney failure by 60 years of age. Hypertension is common in ADPKD with an average onset of 30 years. Other symptoms include urinary tract infections, aneurysms and heart disease. **Early detection and treatment can reduce or prevent some complications of PKD.** However, many will experience regular pain, incapacity and anxiety throughout life.

Autosomal Recessive PKD (ARPKD)

ARPKD is a much less common form of PKD affecting around 1:20,000 births. Both parents must have the faulty gene, and then they have a one in four chance of passing both faulty genes onto each of their children. Around 1:70 people are a carrier for the gene and most are unaware they are carriers. ARPKD is typically a childhood disease which develops before a baby is born and is diagnosed either before or after birth or later in young children. The most severely affected babies may not survive the first few months. If the child survives the newborn period, the chances of survival are good. For these children ARPKD can lead to renal failure or liver problems later in life and approximately half will need dialysis or a kidney transplant by the age of 10. It is difficult to predict the outcome for those diagnosed with ARPKD.

"When I was pregnant with my son he was diagnosed with ARPKD, we were told he may not survive full term, or only a short while after birth. We tried to make our 3-year-old daughter understand that the baby was not coming home but was going to heaven. When he was delivered by Caesarean I had an epidural as I wanted to be awake to hold him if he only survived a short time. The cut was made and out came a baby boy yelling the theatre down. It looked as though we would get to spend some time with him. Every time we went in to his room we wondered if he would be alive and everyday our daughter asking, 'when was he going to heaven'. Now more than 20 years on I will be donating a kidney to my son. The uncertainty of not knowing what was coming was very difficult" - Mother of ARPKD patient, 63, Australia

The needs of the PKD community

PKDA began with the vision of three families all connected by their dedication to support research to find a cure for Polycystic Kidney Disease (PKD). Since launching in 2014, PKD Australia has connected with patients, clinicians, researchers, Kidney Health Australia and rare disease groups. PKD Australia is bringing the community of PKD families together across the country for support and education and to advocate for the many families that are affected by this genetic disease.

We believe involvement and empowerment of the patient voice in policymaking and regulatory decision-making is critical in making sure PKD patients and their carers are getting what they really need to make a positive impact in their lives. **PKD Australia have the vision that patients should receive effective and personalised care for their PKD that lets them live a healthy, productive and long life with the assurance that PKD patients receive adequate, appropriate, affordable and sustained access to health care. Better care will lead to better outcomes with their disease.**

PKD Australia is influenced by a comprehensive understanding of the impacts of PKD and the issues patients face today. This is informed by:

1. Our lived experiences as individuals with PKD, family and friends of people with PKD
2. Our research talking to people with PKD and their family members and the insights we gain through our work in family support, at events and with professionals
3. Academic research into the impacts of PKD

Diagnosis

Being diagnosed with PKD can be an incredibly difficult and scary time. It is important that Diagnosis is accurate and timely and that patients are offered the appropriate support at this time.

"Like many people with Polycystic Kidney Disease, I was not aware of having this affliction until my thirties and were it not for martial arts, I may not have found out until my kidney function seriously started to decline. This is a common story as PKD often shows no outward symptoms until mid-life and our bodies can seem quite well right up until near failure…The Nephrologist confirmed my diagnosis… My immediate family members were all screened and cleared as negative for PKD, which was a huge relief despite that it makes my progression somewhat more unpredictable." ADPKD patient, 37, Australia

Living with PKD

People living with PKD suffer a range of side effects including pain and hypertension. It is important that patients with PKD have their symptoms properly managed and their blood pressure controlled to prevent further injury to the kidney.

"For years I had put up with the side effects of pain, hypertension and vitamin D associated with PKD without realising that it was not normal…However, being diagnosed with PKD opened my eyes to the fact that all these seemingly separate problems were all part of a bigger problem that had been overlooked, and that needed

attention and medication in order to be correctly managed for me to be able to function better." ADPKD patient, 28, Australia

"I was officially diagnosed almost 20 years ago after I had my three children. I knew there was no cure and very little I could do about it. I was working full time and bringing up my kids. It was a busy time. And I told nobody because there was little point and I had few symptoms at that stage. As I aged I did begin to have serious blood pressure issues. I was increasingly tired…often finding it difficult to walk up hills. I did develop a small aneurysm, which we are currently monitoring and attempting to control blood pressure. I realised the PKD was affecting me." ADPKD patient, 61, Australia

Until recently the only treatment available for PKD was Renal Replacement Therapy (RRT). New treatments that avoid the need for RRT are critical for PKD.

"Knowing that you are likely to end up with kidney failure…is like having a ticking time bomb." ADPKD patient, 43, Australia

Another ADPKD patient, 47 "I try not to worry, and I regard dialysis and transplantation as inevitable."

Having a family

Patients face issues of insensitivity often by poorly informed doctors, there are cases where patients are told "not to have children" or that they "can always terminate the pregnancy". Many patients face difficulty in discussing their genetic disease with their partner. Speaking with a genetic counsellor may be of benefit to many PKD patients.

"When you are young it is quite embarrassing to have to admit there is something wrong with you". ADPKD patient 50, Australia

Patients may face difficult decisions about starting a family, whether to have children, the chance that your child may receive PKD or whether to undergo IVF. For many the decision is down to their lived experience of having the disease and the options available to them. PKD Australia support the right for people to make their own choice when it comes to starting a family and how they choose to do this. However, many of the community do not have the choice, they may not be well informed, or they may not be able to afford IVF.

"The disease (ADPKD) didn't come into any decision-making process about having children. I knew PKD was inherited, but I didn't think it would be a major issue, because I still hadn't seen any consequences for the people around me." ADPKD patient, 47, Australia

"We did talk about it a lot. IVF, apart from anything else, is a tough process for women, it is very 'medical', and it's expensive. But we decided that, for us, it made sense." ADPKD patient, 36, Australia

"Genetic testing offers hope for future generations, not to design babies but to offer choice… to assist in eradicating this genetic disease (PKD)." ADPKD patient, 61, Australia

PKD can cause difficulty during pregnancy. PKD carries an increased risk of Preeclampsia and women with PKD are advised that having more than 3 pregnancies may be damaging to the kidneys.

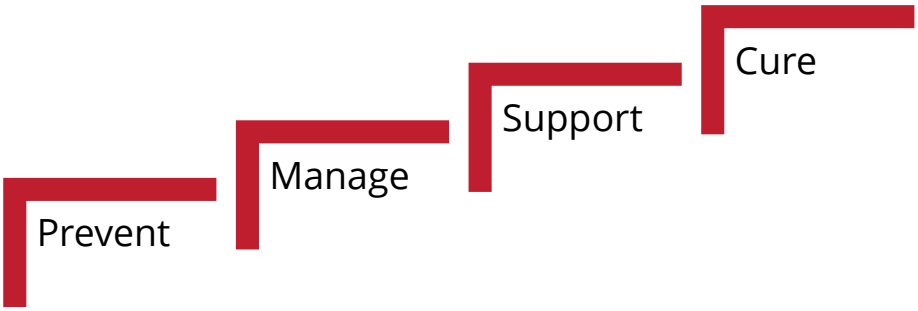
"We always dreamed to have a big family. It doesn't feel fair that having this disease should limit the size of your family or whether your body is healthy enough to even start a family, my wife really struggles with this." Partner of PKD patient, 35, Australia

Looking to the future

Investment into research for treatments and a cure for PKD would significantly change the outcomes for people with PKD. The first treatment for ADPKD was made available on the 1 January 2019 through the Australian Pharmaceutical Benefits Scheme (PBS). Tolvaptan, for those who can tolerate it, has been shown to reduce the rate of kidney function decline and may delay the onset of dialysis by a number of years.

"As a parent of a child with PKD I vividly remember seeing the ultrasound that confirmed tiny cysts growing on my son's kidneys. People with this disease live with uncertain futures as their kidney function deteriorates. Research and clinical trials that deliver new treatments are important and provide hope for the future." ADPKD patient, 30, Australia

The Framework



These initiatives can be categorised into a Key Framework: Prevention, Management, Support and Cure. Key aims of the framework are to improve the health and prognosis of PKD patients, whilst relieving pressure from the heavily burdened health system, namely by reducing the need for dialysis in the PKD population through accessible genomics and family planning, access to relevant, accurate and balanced PKD information, sustainable and varied funding into PKD research to find treatments and a cure. The Prevent, Manage, Support, Cure Framework for positive change in the treatment and management of PKD was set out by the Minister for Health, Mr Hunt when PKDA met with him in August 2018. Building upon this framework we hope to work further with policy makers and government bodies to achieve the key initiatives of this Framework and make a positive change in the lives of those suffering with PKD.

Prevention

- Genomics
- Preimplantation Genetic Diagnosis (PGD), within Assisted Reproductive Technologies e.g. IVF

Management

- Tolvaptan (Jinarc®)
- New medicines (research and clinical trials)
- Clinical Registry

Support

- Education
- Genetic Counselling
- Optimal Care Pathways
- Psychosocial Care
- Dietary Support

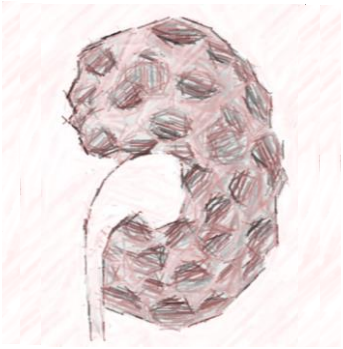
Cure

- Stem cell therapy
- Investment into research

Why is this important

Common: PKD is the most common genetic disease, affecting the kidneys of approximately 1 in 1000 Australians [1].

Costly: Dialysis represents 13% of hospitalisations in Australia [2]. PKD represents about 8-10% of the dialysis burden[3].



Severe: About half of people with ADPKD will have end stage kidney disease (ESKD) or kidney failure by 60 years of age, requiring dialysis or kidney transplant [4].

PKD is the most common genetic cause of ESKD, accounting for 6% of new patients requiring renal replacement therapies, representing a significant burden to the community [3]. Recent economic analysis shows that the ongoing cost for dialysis is $100,056 per patient per year [5]. The cost of a kidney transplant procedure is $119,521, which does not take into consideration ongoing costs associated with kidney transplant

maintenance and medication [6]. Early detection and treatment can reduce or prevent some complications of PKD [7].

Making the Change

Prevent

The genetics of PKD have been unravelled in Australia. PKDA have invested into genetic research that has contributed to the first clinically appraised Whole Genome Sequencing test for PKD in Australia. In about 10% of cases the genetic cause of PKD is unknown. PKD Australia in collaboration with PKD Foundation US is funding Australian research to identify new genetic causes of ADPKD. For ADPKD, in 90% of cases there is a known family history of the disease and those diagnosed with PKD have a 50% chance to pass the condition onto their children. Genetic testing will accelerate our understanding of the underlying cause of PKD. However currently genetic testing is not accessible for most patients with PKD.

Genetic testing can allow patients to:

- be diagnosed sooner
- better understand the condition in their own family
- personalise treatment
- provide interventions earlier for better outcomes
- better inform their family planning decisions
- enable identification of appropriate living kidney donors for transplantation

PKDA is supportive of the $20 million pilot trial "Mackenzie's Mission" that is the cornerstone of the $500 million Australian Genomics Health Futures Mission. The Federal Health Minister has stated that the gene/s causing ARPKD will be included in the "Mackenzie's Mission" Carrier Screening Program. About 1 in 70 people is a carrier for the gene causing ARPKD, but most are unaware they are carriers.
Pre-implantation Genetic Diagnosis (PGD) for both ARPKD and ADPKD can be used in an IVF setting to select PKD free embryos, making it an option for parents that choose and can afford to undergo this treatment to reduce the risk of passing the mutation on to their children.

What needs to be done to prevent PKD

- There should be accessible genetic testing for all PKD families for identification and/or family planning purposes. Currently access for PKD patients to receive genetic testing is not equitable. Genetic testing is currently paid for by state health systems, but which tests are paid for is totally dependent on the individual hospital. Some hospitals will pay for any genetic testing, some hospitals pay for genetic testing only if it is very likely to change the patient's management, and other hospitals don't pay for any testing. This variability is the reason we are strongly advocating for Medicare-rebatable genetic testing - so all PKD patients in Australia can have the same access to genetic testing. The Medical Services Advisory Committee (MSAC) recently supported the application (1449) for MBS funding of genetic testing for the diagnosis of Alport's Syndrome in clinically affected individuals and cascade testing for selected family members of these individuals who are genetically confirmed to have Alport syndrome.

- Evidence supports a multitude of patient benefits through access to a multidisciplinary team approach to care, with all relevant specialities in one centre or clinic for ADPKD patients [8]. PKDA supports the KidGen team-based multidisciplinary renal care model (where families are seen by teams including nephrologists, clinical geneticists and genetic counsellors) that is being progressively introduced Australia wide. Their vision to develop a comprehensive translational pipeline from patient to lab to treatment with the mission to equitably deliver genomics, where appropriate, to seek a genetic diagnosis for Australians with genetic forms of kidney disease and further research into inherited kidney disease to improve patient treatments and outcomes.
- There should be easy, affordable and timely access for PKD patients that choose to undergo PGD IVF treatments for genetic selection of PKD-free embryos. After considering the evidence presented in relation to safety, clinical effectiveness and cost effectiveness, MSAC supported public funding of pre-implantation genetic diagnosis, but considered that it was not appropriate for usual listing on the MBS. This issue now lies with the Department of Health to investigate the implementation issues.

Manage

The mechanisms of cyst growth are well understood, and scientists are currently working on how to stop or slow cyst growth.

"We are on the cusp of a breakthrough in PKD treatment – we know why the cysts form and have an idea of why they grow. Now we need to stop them growing. The Uber moment for PKD is within our grasp." - Professor Jeremy Chapman A.C.

Hypertension is common in ADPKD with an average onset of 30 years. Other early symptoms include pain, urinary tract infections, aneurysms and heart disease. Those living with ADPKD must control blood pressure, reduce cardiovascular risk factors and manage their symptoms with medications to try to slow disease progression and reduce the risk of complications. There is no cure yet for PKD, however there is a new treatment available in Australia for adults with ADPKD that can help slow disease progression and prevent cysts from enlarging.

Treatments for PKD that slow disease progression and push out the need for dialysis or kidney transplant require investment into research and clinical trials. Such research has the potential to make a huge difference in the lives of those affected by PKD and the possibility to prevent and or reduce ESRD.

The current national ANZDATA registry collects data on ESRD and as such does not capture patients at earlier stages of renal disease. The inheritance pattern of ADPKD means that patients are often aware of their condition before the symptoms start to arise enabling early diagnosis. The effectiveness of early intervention can be easily modelled in PKD with a clinical registry which would provide an ideal means to study and mitigate the progression of PKD and to inform clinical trials.

A clinical registry for PKD can define the characteristics and health service utilisation of patients with ARPKD and ADPKD. Global data suggest the level of utilisation of health services for PKD patients in both outpatient[9] and inpatient settings[10] is increased, even at early disease stages[11]. In Australia, patients with ADPKD were identified from the CKD.QLD Registry as having higher associated healthcare costs, higher incidence of dialysis and more hospital admissions (excluding dialysis) compared with all CKD causes in QLD[12].

Registry data such as this is critical to guide health service planning and prioritisation in Australia. As PKD is one of the most common inheritable disorders there is significant potential to improve experiences and reduce morbidity and mortality for affected patients through improved understanding of population-level characteristics and health service utilisation.

Registries can longitudinally characterise a cohort of patients with ADPKD or ARPKD to model the impact of treatment as well as customise treatment which can be matched to certain variables such as stage of CKD and create evidence for best practice in clinical care and future clinical trials as well as hasten trial recruitment.

The PKD cohort offers a group of people with largely predictable future progression of kidney function decline offering ideal candidature for long-term longitudinal studies. Patient data collected through the international ARegPKD registry effort [13] has been used to evaluate important outcomes in patients with Autosomal Recessive PKD (ARPKD), highlighting the importance of registries to determine best practice for patients and to inform research [14]. Conducting studies in rare diseases such as ARPKD and paediatric ADPKD are by nature difficult for many reasons. Registries can help determine optimal management plans and are an important aspect in the path forward for PKD. In the research of rare disease, patient registries have been described as the best tool to close the gap between research and therapeutics [15].

Registries will provide benefits to the government in terms of better health care planning, evidence for cost effectiveness of treatments, efficacy of research and treatment, and will provide numerous benefits to patient, including improved care with treatments targeted to individual needs that will lead to improvements in morbidity and mortality.

What needs to be done to improve the management of PKD

- Investment into research and clinical trials for PKD

Since the establishment of PKD Australia in 2014, 11 research projects selected by our Scientific Advisory Board have been supported, representing a > $325,000 investment. PKD Australia invests in Australian research that aims to provide a deeper understanding of PKD and/ or improves the outlook and quality of life for PKD patients.

Grants are available for:

1. Basic scientific research
2. Clinical research
3. Translational research
4. Psychosocial and Public Health Research
5. Other: research may be targeted at specific issues relevant to the disease manifestation of PKD

PKD research receives no ongoing government funding, therefore PKD Australia aims to provide a sustainable research program by securing diverse and sustainable fundraising and identifying research funding opportunities, including government and philanthropic funds. Government support to invest in and expand promising high-quality, competitive and impactful PKD research is necessary. Government funding into research will ensure continuous improvements in prevention and treatment and the search for a cure.

PKD Australia encourage Australian participation in international clinical trials for PKD and will assist in trial recruitment.

- Government funding to support the establishment of a national registry

The two, existing state-based kidney registries, ROKD (Registry of Kidney Disease-Victoria) and CKD.QLD (Queensland), and the nascent ARRK (The Australian Registry of Rare and Genetic Kidney Disease-National) have the capability to collaborate and "house" a PKD Registry if secure funding was available.

On March 5th, 2019 a meeting chaired by Professor Stephen McDonald was held with the Scientific Advisory Board of PKD Australia; A/Professor Gopi Rangan, Professor Carmel Hawley, Professor Randall Faull, Professor Sharon Ricardo, Professor Judith Savige, Dr. Michael Eccles and Professor Eric Haan as well as Nephrologists with expertise in PKD; Professor Andrew Mallett and Dr. Amali Mallawaarachchi to discuss planning to establish a unified PKD Registry. The group felt that a unified and national PKD registry was vital to eradicating PKD as a cause of kidney failure, as it would serve several important functions: (i) identification of epidemiological, genomic and disease characteristics for treatment; (ii) a platform to test clinical trial interventions; (iii) monitoring of outcomes. This would have capability of linkage with other international registries in PKD as well ANZDATA.

Support

PKD Australia plays a key role in the support of PKD patients and their carers. PKD affects many aspects of one's wellness including but not limited to, physical, financial and emotional impacts. Anxiety and depression are highly prevalent in chronic kidney disease patients and are reported by >60% of those with ADPKD. Health professionals must actively listen and have empathy for psychological and emotional concerns of PKD patients, including anxiety about lifestyle, body image, and sexual dysfunction. [8]

The diagnosis of PKD in a patient may bring about mental health issues associated with the prognosis. Furthermore, being aware of the presence of ADPKD within your family can cause a psychological burden within families and individuals before the onset of symptoms. Decision-making around diagnosis (via imaging or genetic) is ethically challenging with psychosocial implications, and thus requires an in-depth understanding of the patients' attitudes, priorities, and perspectives of genetic testing or screening. For example, genetic testing could empower some patients to take control of their health whilst for others, receiving a confirmed diagnosis of PKD could cause unnecessary stress and anxiety over a disease that they could not control or prevent. Until more and better treatments are available this will require increased expert counselling and support for entire families. Referral to genetic counselors may be one way the psychological and social consequences of the testing to the individual and the family can be addressed. Difficulties surrounding decision-making may be eased by arming patients with thorough information and support and by providing patients with a chance to be listened to and understood.

What needs to be done to support patients with PKD

- Create awareness of the health and wellness implications of PKD.
- Increase the availability of health, wellbeing and psychosocial support for people with PKD, carers and families
- Provide opportunities for PKD patients to connect through support groups such as the PKD Australia Wellness Groups.
- National access to multidisciplinary renal genetics clinics could be achieved through support and expansion of the KidGen team-based multidisciplinary renal care model (where families are seen by teams including nephrologists, clinical geneticists and genetic counsellors) that is being progressively introduced Australia wide
- Support the publication of accurate, balanced and up to date information about PKD to enable and

empower patients to become advocates of their own care, through our website, social media and PKD Australia patient education seminars.

- Support and maintain up-to-date diagnostic and management guidelines e.g. CARI guidelines.
- Develop Optimal Care Pathways from PKD. This could be achieved across multiple appointments that address 1) The diagnosis and clinical aspects of PKD; renal imaging; treatment of hypertension and other complications. 2) Prognosis across all aspects of the disease; patient information; connection to support networks; referral to a dietitian; genetic counselling, genetic testing if indicated; phycological support if required; detailed imaging; referral for other specialists if required and 3) Treatment; Initiation of treatments; option to enrolment in registries or trials; determination of follow up visit frequency.[16]
- Support psychosocial research to and the development of Patient reported-outcome measures (Standardised outcomes in nephrology-SONG-PKD) and will continue to publicise findings.
- Support and encourage patient involvement in consumer advisory groups (e.g. BEAT-CKD Consumer advisory Committee)

Cure

Today there are glimmers of hope for those families with PKD, from a pharmaceutical drug that will slow the decline of kidney function for some patients with ADPKD, to the possibility of eradicating PKD from your branch of the family tree using genetic testing and IVF together. Research is currently being carried out to find more mechanisms to treat the symptoms of PKD with the ultimate aim to discover a cure. PKD is an intergenerational disease that affects not just the kidney, and not just the patient with the symptoms and the cysts, but their entire family, both current and future.

Due to its intergenerational nature and clear inheritance pattern it is very easy to identify those family members with ADPKD, and with the advent of genetic testing it is now possible to confirm the diagnosis, in most cases, long before the advent of serious symptoms and in ample time for the person to make conscious lifestyle decisions to prolong wellbeing, commence treatment with the currently available drug that slows kidney function decline, and to take part in future clinical trials.

An Australian register of patients with PKD is critical to guide health service planning and prioritisation in Australia, and to provide an effective way to recruit for clinical trials and create a best practice for PKD, including individualised treatment within Australia. Every PKD patient who will not need a kidney transplant or to go onto dialysis will have a much better and more productive life and will save the Australian health system a significant amount of money and resources.

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References

1. Dalgaard OZ. Acta Med Scand Suppl 1957;328: 1–255
2.(Australian Institute of Health and Welfare. Admitted patient care 2014-15: Australian hospital statistics. Health services series no. 68. Cat. no. HSE 172. Canberra: AIHW.; 2016)
3. ANZDATA Registry. 40th Report, Chapter1:2018.
4. Rossetti S et al. J Am Soc Nephrol 2007;18(7):2143.
5. Costs of dialysis used in the model was drawn from a survey-based costing study by NSW Health (NSW Dialysis Costing Studies, 2009) and adjusted for inflation to 2017 values. Costs were based on a weighted average cost of in-centre, satellite, home haemodialysis and peritoneal dialysis (ANZDATA 2016). Costs included dialysis service costs, health professional costs, pharmaceuticals, diagnostic tests, out-of-pocket patient costs, and relevant admitted hospital costs. *Possibly slight underestimation due to a high haemodialysis use expected for ADPKD.*
6. Howard et al 2010 and Wong et al 2012, in 2016 values. Cost of kidney transplant procedure from Howard et al. (2010) and Australian CASEMIX data (version 8.0, Round 19; 2014-15), inflated to 2017 values. The final cost is a weighted average based of proportion of living and deceased donor procedures from the ANZDATA Registry 2016 ($60,572). Cost of induction/immunosuppression therapies in the first year after transplant were from Wong et al. (2012), inflated to 2017 values.[b] Based on Australian data from a study modelling the economic benefits of kidney transplantation and dialysis in a cohort with an average age of 45 years and significant comorbidities including history of cardiovascular disease, diabetes mellitus, cerebrovascular disease, obesity, current smoking and varying ages at listing and transplantation. Estimated costs included were induction therapies (basiliximab, anti-thymoglobulin antibodies), immunosuppression, and follow-up consultations ($58,949).
7. Rangan, G et al. Nephrology 2016;21:705–716.
8. Chapman, AB et al. Kidney Int. 2015 Jul;88(1):17-27.
9. Eriksson, D et al. BMC health services research. 2017;17(1):560.
10. Blanchette, CM et al. J Med Econ. 2015;18(4):303-11.
11. Knight, T et al Clinicoecon Outcomes Res. 2015;7:123-32.
12. Mallett, A et al. Nephrology 23, Suppl. 3 (2018) 19–70
13. https://www.aregpkd.org/index.php?id=about_arpkd
14. Burgmaier et al. The Journal of Pediatrics, Volume 199, 22 – 28.e6
15. EURODIS NORD CORD, Joint Declaration of 10 Key Principles for Rare Disease Patient Registries
16. Ong, AC et al. Lancet. 2015 May 16;385(9981):1993-2002.

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