# ADPKD: KDIGO 2025 Clinical Practice Guidelines

# For the Evaluation, Management and Treatment

2025 Continuing Medical Education Course
60th ANZSN Congress

Gopi Rangan
*Senior Staff Nephrologist, Westmead Hospital, Western Sydney Local Health District*
*Professor in Genetic Kidney Disease, Westmead Institute for Medical Research, The University of Sydney*

*Disclosures*

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# KDIGO 2025 Clinical Practice Guideline for the Evaluation, Management, and Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD)

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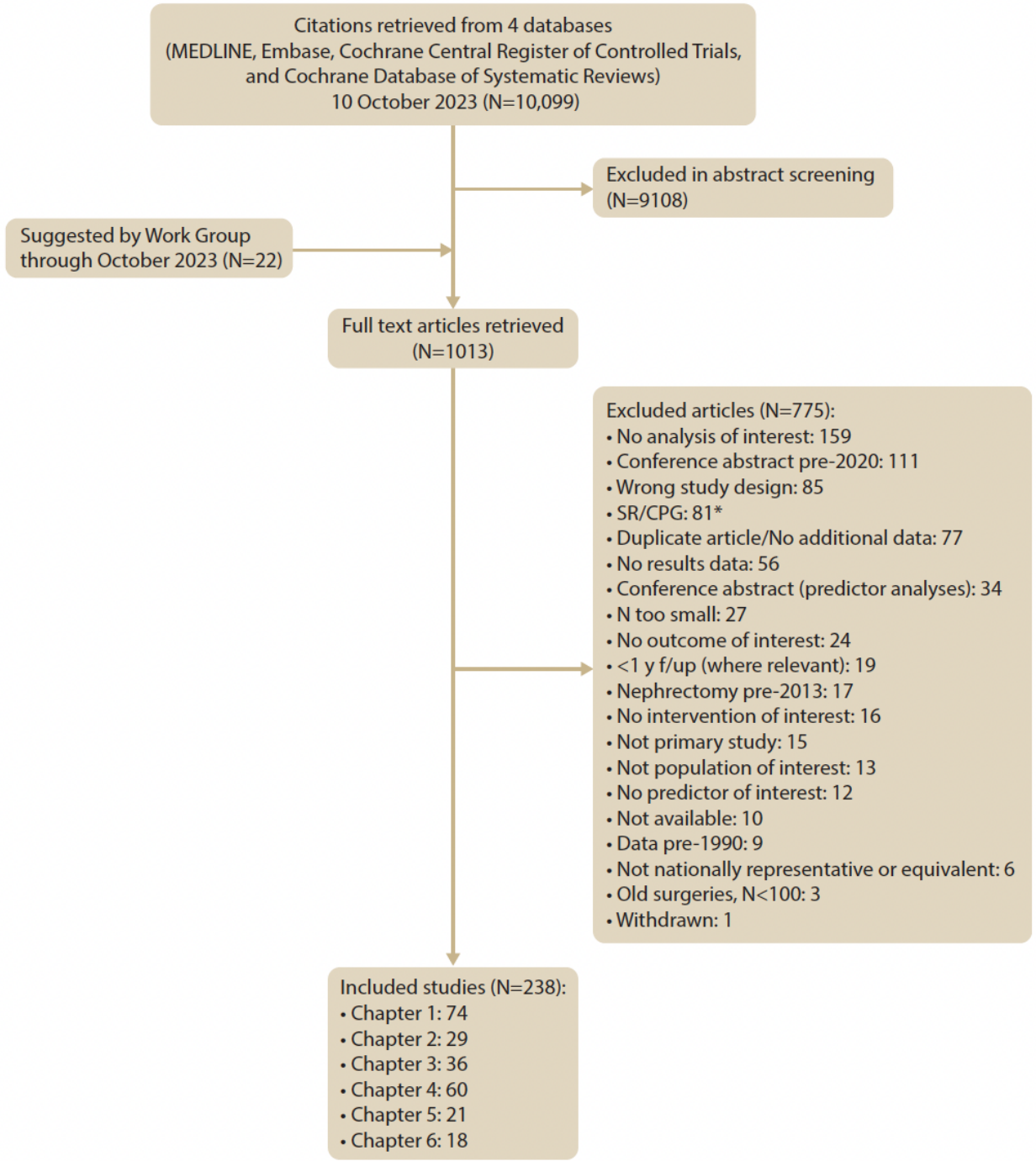



# Recommendations:

**Table 24 | KDIGO nomenclature and description for grading recommendations**

| Grade | Implications | | |
|---|---|---|---|
| | Patients | Clinicians | Policy |
| **Level 1,** "We recommend" | Most people in your situation would want the recommended course of action, and only a small proportion would not. | Most patients should receive the recommended course of action. | The recommendation can be evaluated as a candidate for developing a policy or a performance measure. |
| **Level 2,** "We suggest" | The majority of people in your situation would want the recommended course of action, but many would not. | Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences. | The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined. |

KDIGO, Kidney Disease: Improving Global Outcomes.

**Table 25 | Determinants of the strength of recommendation**

| Factors | Comment |
|---|---|
| Balance of benefits and harms | The larger the difference between the desirable and undesirable effects, the more likely a strong recommendation is provided. The narrower the gradient, the more likely a weak recommendation is provided. |
| Certainty of evidence | The higher the certainty of the evidence, the more likely a strong recommendation is warranted. However, there are exceptions for which low or very low certainty of the evidence will warrant a strong recommendation. |
| Values and preferences | The more variability in values and preferences, or the more uncertainty in values and preferences, the more likely a weak recommendation is warranted. Values and preferences were obtained from the literature, when possible, or were assessed by the judgment of the Work Group when robust evidence was not identified. |
| Resource use and costs | The higher the cost of an intervention—that is, the more resources consumed—the less likely a strong recommendation is warranted. |

**Table 26 | Classification for the grade of the certainty of evidence**

| Grade | Certainty of evidence | Meaning |
|---|---|---|
| **A** | High | We are confident that the true effect is close to the estimate of the effect. |
| **B** | Moderate | The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. |
| **C** | Low | The true effect may be substantially different from the estimate of the effect. |
| **D** | Very low | The estimate of effect is very uncertain, and often it will be far from the true effect. |

**Practice Points:** Consensus-based statements based on expert judgement of the Work Group. No systematic Review was possible

| | RECOMMENDATIONS | PRACTICE POINTS |
|---|---|---|
| **1: Nomenclature, diagnosis, prognosis, prevalence** | 1+1 =**2** | 7+19+9 = **35** |
| **2: Kidney Manifestations:** HT, pain, stones, gout, hematuria, UTI, cancer | 6+3+6+4/1 = **20 [7 ADPKD]** | 4+10+3+2+5+2 = **26** |
| **3: CKD management, transplantation and KRT** | 4+1 = **5** | 6+10+3 = **19** |
| **4: Therapies to delay kidney disease progression:** tolvaptan, water intake, mTOR, statin, metformin, SSAs, | 1+1+1+1+1+1 = **6** | 21+4+4 =**29** |
| **5: PLD:** Diagnosis/Staging, risk factors, nutrition, Mx, liver cyst infection | **1** | 4+1+3+3+7+8 = **26** |
| **6: ICAs and extrarenal manifestations** (vascular, cardiac, hernia, other) | **2** | 12+3+1+3 = **19** |
| **7: Lifestyle and psychosocial aspects:** nutrition, physical activity, lifestyle, cannabis, nephrotoxins, psychosocial care | **0** | 7+3+2+1+1+4 = **18** |
| **8: Pregnancy and reproductive issues:** overall Mx, preconception counselling, pregnancy, HT/preeclampsia in pregnancy, fetal evaluation, postpartum care | **0** | 4+5+5+4+3+2 = **23** |
| **9: Pediatric issues**: Diagnosis, BP control, follow-up, diet/lifestyle, optimal care | **2** | 10+7+10+3+3 = **33** |
| **10: Approaches to the management of people with ADPKD** | **0** | 8 |
| **TOTAL UNIQUE FOR ADPKD** | **28** | **236** |

Orange = extracted from other other guidelines

# Case #1

27F referred to clinic - has chronic back pain, recurrent UTIs (related to coitus and managed with hiprex/D-mannose) and noted to have asymptomatic kidney stones during investigation of back pain (plan X-ray).

Mother 58 years old worried that daughter has ADPKD - Stage 3B CKD and WES showed pathogenic truncating variant in *PKD1* attended with daughter ( daughter reluctance to attend for many years)

<u>Counselling</u>

**What psychosocial factors might be involved here?**

**What are the benefits and risks of screening?**

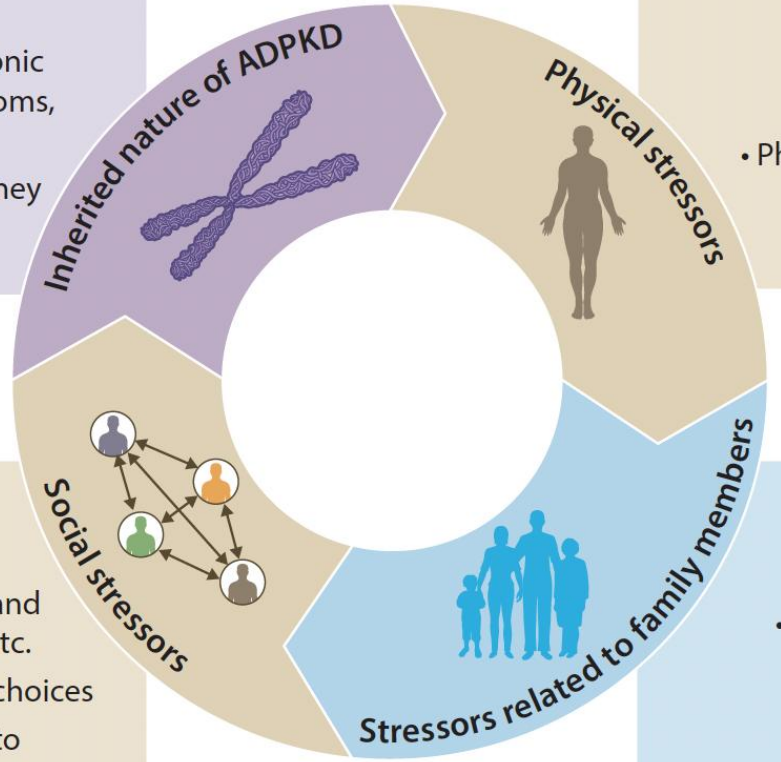
**What approach would you use to screen for ADPKD?**

**What is the role of genetic testing?**

# Psychosocial Stessors in ADPKD (Fig. 42).. subtle but they are present

Mum's Guilt

- Genetic guilt: self-blame, constant burden of guilt
- Decision on genetic testing and disclosure
- Pregnancy and family planning
- Disempowerment in self-management
- Sense of helplessness
- Health anxiety from living with a chronic incurable condition, its various symptoms, and treatment modalities
- Fear of the future: progression to kidney failure and low life expectancy




- Chronic pain
- Functional limitations of participation in recreational, sport and social activities
- Body image/dysmorphia
- Sexual dysfunction
- Dietary constraints
- Sleep disturbances
- Physical conditions related to chronic kidney disease progression

- Inability to plan ahead
- Social isolation from missing school and social activities, dietary limitations, etc.
- Employment barriers and limited career choices
- Financial burden: concerns related to insurance, healthcare costs
- Other emotional responses to social challenges

- Fear of inheritance
- Caregiver burden
- "Chosen" to be the kidney donor
- Loss of family member
- Distress in family relationship: blaming parents or partners
- Disturbed family communications on issues related to having a child, marriage, etc.
- Financial burden

Reluctance Fear

# What are benefits and risks of screening?

**Table 3 | Factors to consider when testing (by imaging and/or genetics) people at risk for ADPKD**

| Possible value of early screening | Possible complications of early screening |
|---|---|
| • **Resolve diagnosis odyssey.** The individual person and family may obtain a definite diagnosis. | • **Psychological burden of having a life-altering diagnosis.** Obtaining a diagnosis of ADPKD may lead to a range of emotions (e.g., anxiety about the future, anger, guilt about transmission to offspring). It is especially disconcerting if there is no family history of ADPKD. |
| • **Ability to manage and treat ADPKD.** Appropriate management and treatment of the affected person can be initiated. | • **Possible difficulties with employment and insurability** Despite legislation in many countries, the diagnosis of a genetic disease can have certain insurance (e.g., life, health, disability) and workplace implications. However, it is important to consider that being at risk of ADPKD, without a firm diagnosis, may also have insurability implications. |
| • **Initiate screening for extrarenal manifestations.** | • **High cost.** Some testing, including genetic testing and certain types of imaging, may not be fully covered by insurance or government-funded health plans. |
| • **Enable enrollment in clinical trials.** | • **Imaging and/or genetic testing results may be inconclusive.** In >25% of cases, genetic testing does not result in a certain diagnosis, and imaging can provide equivocal results. Both may lead to false reassurance and erroneous decision-making. |
| • **Reassurance of unaffected people.** Negative imaging and/or genetic testing results in at-risk family members will likely provide relief to the person and may influence family-planning decisions. | • **Specialist knowledge to interpret test results may not always be available.** The supply of professionals with genetics expertise for kidney diseases is limited. |
| • **Appropriate family planning.** Knowledge about the genetic nature of ADPKD might aid decision-making concerning care of the person and family planning. | |
| • **Facilitate testing of family members.** A positive genetic test allows inexpensive screening of other interested at-risk family members, allowing appropriate management of those affected. | |
| • **Implement lifestyle modifications.** Details in Chapter 7. | |

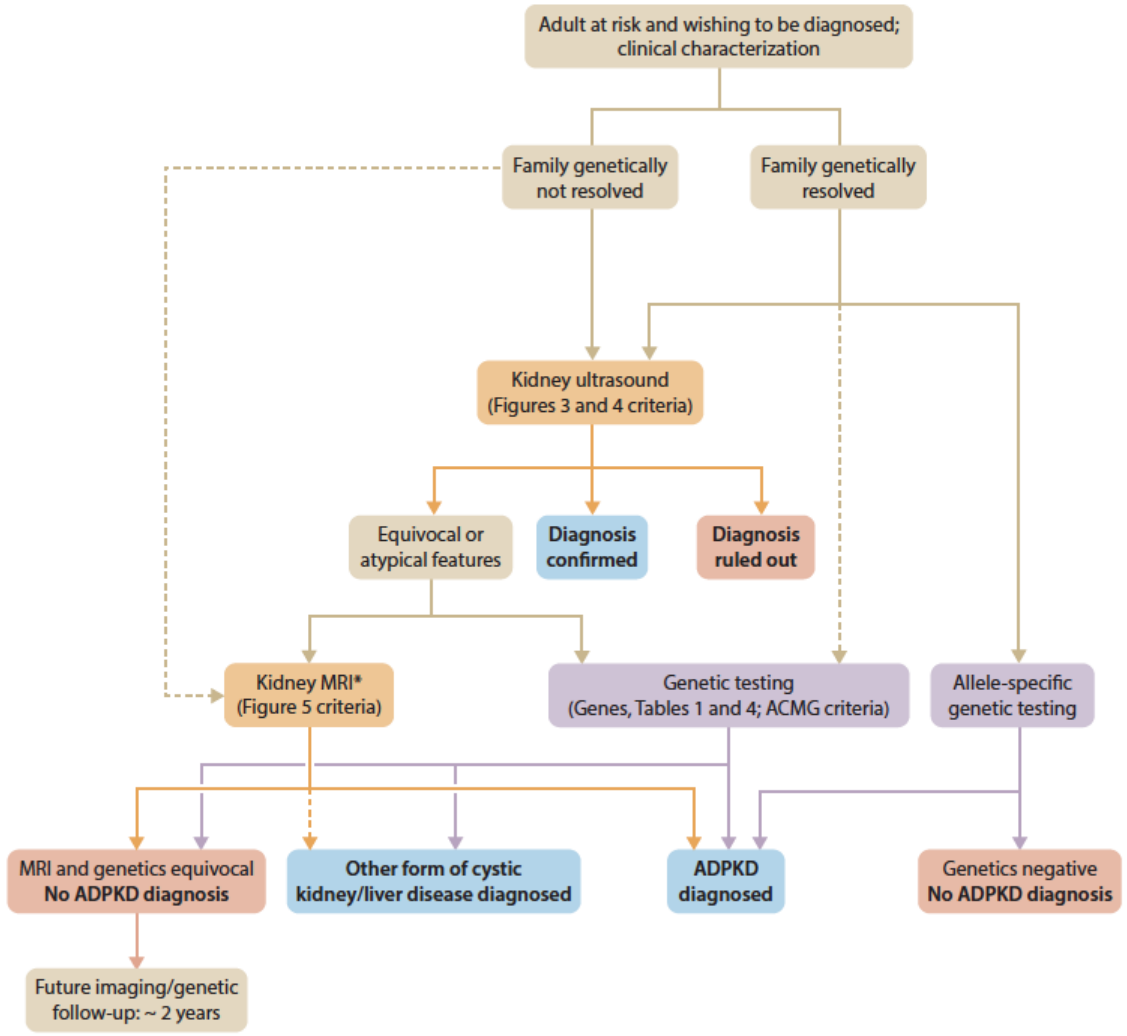
ADPKD, autosomal dominant polycystic kidney disease.

Case #1: Discussion beneficial - revealed patient had not contemplated the consequences – agreed to screen

# What approach would you use to screen people at-risk for ADPKD?

**Recommendation 1.3.1: For screening adults at risk of ADPKD, we recommend first using abdominal imaging by ultrasound, in the context of the family history, kidney function, and comorbidities (*1B*).**

Case #1: Form given to do abdominal US



# Case #1

27F referred to clinic - has chronic back pain, recurrent UTIs and noted to have asymptomatic kidney stones during investigation of back pain (plan X-ray). Mother 58 years old, stage 3B CKD and WES showed pathogenic truncating variant in *PKD1* attended with daughter ( daughter reluctance)

**Agreed to ultrasound but also asked - if positive - what can I do about it?**

<u>Counselling</u>

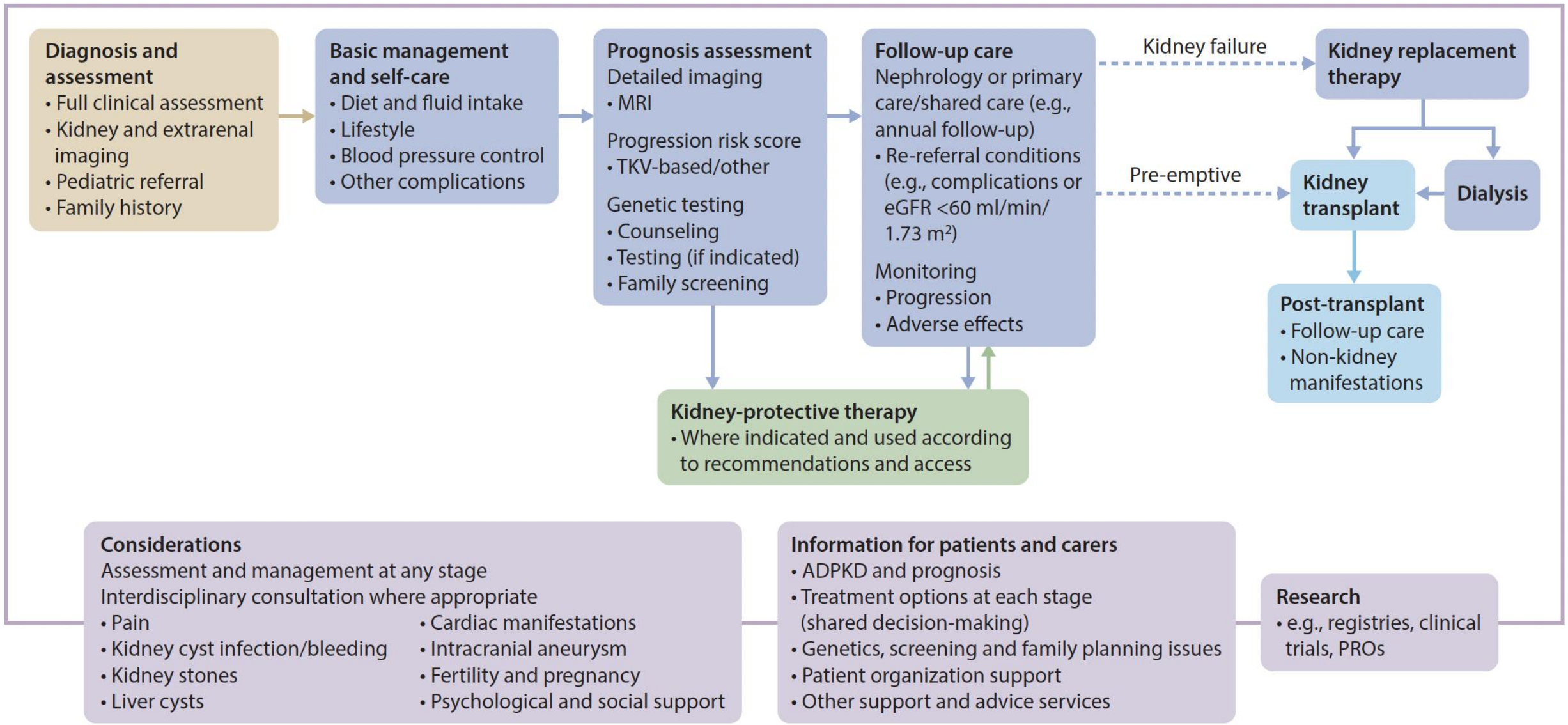
**How do you see overall care pathway if the diagnosis is positive?**

**What are first-line treatments?**

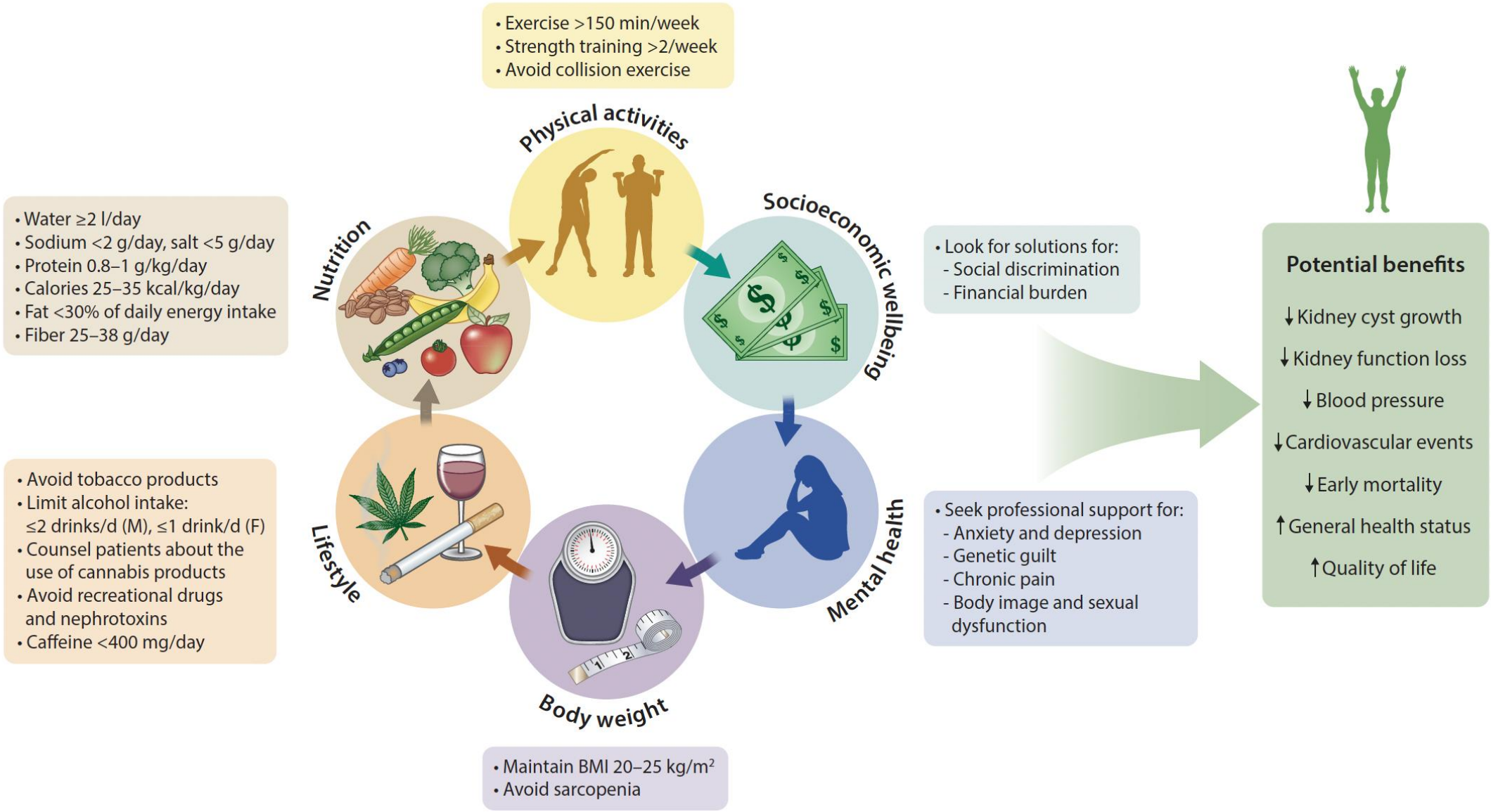
**Would you offer tolvaptan if US met ADPKD criteria in Stage 1 CKD?**

**How to determine prognosis?**

# Proposed ADPKD Care Pathway (Fig. 56)



# First line Rx: Lifestyle & Psychosocial Care to Improve ADPKD



# 1st line Rx: KDIGO Guidelines for Hypertension Management in ADPKD

**Recommendation 2.1.3: For people with ADPKD aged 18–49 years with chronic kidney disease (CKD) G1-G2 and high BP (>130/85 mm Hg), we recommend a target BP of ≤110/75 mm Hg as measured by HBPM, if tolerated (*1D*).**

**Recommendation 2.1.4: For people with ADPKD aged ≥50 years with any stage of CKD (CKD G1-G5), we suggest a target mean systolic blood pressure (SBP) of <120 mm Hg, if tolerated, as assessed using standardized office BP measurement (*2C*).**

**Recommendation 2.1.5: For people with ADPKD and high BP, we recommend using renin-angiotensin system inhibitors (RASi) (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin II receptor blocker [ARB]) as first-line treatment to achieve the recommended target BP (*1C*).**

**Recommendation 2.1.6: We recommend avoiding any combination of ACEi, ARB, and direct renin inhibitor (DRI) therapy in patients with ADPKD, with or without diabetes (*1B*).**

| Hypertension in ADPKD | | |
|---|---|---|
| **Monitoring** | **Non-pharmacologic interventions** | **Medical management** |
| • Standardized office BP measurement in preference to routine office BP measurement<br>• HBPM is preferred to office only measurements<br>• Consider ABPM in children and adults with difficult BP control, LVH, proteinuria, or declining kidney function but normal office BP readings<br>• Consider work up for secondary high BP when >3 BP medications are needed in the setting of medication and dietary compliance | • Reduce dietary sodium including minimizing processed foods<br>• Optimize body weight with a healthy diet and regular exercise<br>• Optimize pain management | • Inhibition of RAS provides the cornerstone of BP management and includes the use of an ACEi or ARB<br>• Optimize BP with a 2nd-line agent, if needed<br>• Individualized therapy is indicated |

# 2nd line Rx: KDIGO Guidelines for Tolvaptan

**Recommendation 4.1.1.1: We recommend initiating tolvaptan treatment in adults with ADPKD with an estimated glomerular filtration rate (eGFR) ≥25 ml/min per 1.73 $m^2$ who are at risk for rapidly progressive disease (Figure 25) (*1B*).**

**Initiation of tolvaptan should be offered to adults with ADPKD and:**
eGFR ≥25 ml/min per 1.73 $m^2$

**AND**

**Risk of rapid disease progression* as indicated by either:**
Mayo class 1C† to 1E
**OR**
Historical rate of eGFR decline‡ (≥3 ml/min per 1.73 $m^2$ per year)

| TEMPO 3:4 | CKD G1–G3a |
|---|---|

**Study population**
n=1445
18 to 50 years old
TKV >750 ml in CKD

**Dose of tolvaptan***
120 mg/d (55%), 90 mg/d (21%), 60 mg/d (24%)

**Main results**
- Primary endpoint: reduced rate of increase in TKV: 2.8%/year in tolvaptan group vs. 5.5%/year in placebo
- Secondary endpoints: slower decline in kidney function (reciprocal of the serum creatinine level, –2.61 $[mg/ml]^{-1}$/year vs. –3.81 $[mg/ml]^{-1}$/year, $P$ <0.001); lower rates of worsening kidney function (2 vs. 5 events per 100 person-years, $P$ <0. 001) and kidney pain (5 vs. 7 events per 100 person-years of follow-up; $P$=0.007).

**Adverse effects**
Tolvaptan associated with aquaresis and abnormal liver function tests and higher discontinuation rate (23% vs. 14% in the placebo group).

| REPRISE | CKD G3–G4 |
|---|---|

**Study population**
n=1390
18–55 years old + (eGFR 25–65 ml/min per 1.73 $m^2$)
56–65 years old + (eGFR 25–44 ml/min per 1.73 $m^2$)

Ability to tolerate tolvaptan after an 8-week run-in

**Dose of tolvaptan***
120 mg/d (61%), 90 mg/d (30%), 60 mg/d (10%)

**Main results**
- Primary endpoint: Reduced rate of decline in eGFR by –2.34 ml/min per 1.73 $m^2$ in the tolvaptan vs. –3.61 ml/min per 1.73 $m^2$ in the placebo; $P$ <0.001).

**Adverse effects**
Reversible increases in the ALT to >3 times the normal range (5.6% in the tolvaptan group vs. 1.2% in the placebo group)

# 2nd line Rx: KDIGO Guidelines for Tolvaptan

**Benefits**
- Reduces eGFR decline (–1.3 ml/min per 1.73 $m^2$/year)
- Reduces increase in total kidney volume (greatest in first year of treatment)
- Reduces acute pain events (stone and urinary tract infection)

**Harms**
- Aquaretic side effects (polyuria, polydipsia, thirst)
- Risk of drug-induced hepatoxicity
- Requirement for lifelong blood tests to monitor liver function tests (monthly for first 18 months and then 3 monthly)
- Drug interactions
- Cost

**Uncertainties**
1. Can tolvaptan delay onset of kidney failure?
2. What is the long-term tolerability of tolvaptan?
3. What are the long-term effects of increase in endogenous AVP levels?

**Table 9| Checklist of contraindications to initiating and/or maintaining tolvaptan use**

| |
|---|
| **Absolute** |
| - Planning pregnancy, pregnancy, or breastfeeding |
| - Medical conditions associated with or at high risk of volume depletion |
| - Inability to respond to or perceive thirst |
| - Uncorrected baseline hypernatremia |
| - Urinary tract obstruction |
| - Strong CYP3A inhibitors[a] |
| - Significant liver disease unless due to PLD |
| **Relative** |
| - eGFR at initiation <25 ml/min per 1.73 $m^2$ |
| - History of gout or hyperuricemia |
| - Moderate CYP3A inhibitors[b], P-gp inhibitors[c], grapefruit and Seville orange consumption |
| - Urinary incontinence |

# Australian Context: Indications for initiating Tolvaptan: PBS requirements

| Criteria | Specified requirements as per the PBS |
|---|---|
| Practitioner | Must be treated by a nephrologist |
| Kidney function | Must have an eGFR 30–89 mL/min/1.73 $m^2$ at the time of starting drug treatment |
| Historical evidence of rapidly progressing kidney disease | Must have an eGFR decline of either >5 mL/min/1.73 $m^2$ in 1 year<br>OR<br>>2.5 mL/min/1.73 $m^2$/year over 5 years |

Thievendran et al. Aust Presc 45: 167, 2022

Clinical Practice Tips:

- Decline in eGFR can be complex: linear (60%), non-linear (20%) stable (20%) (Brosnahan et al. 71: 666, 2018)
- Consider all clinical explanations for eGFR change
- Is baseline medical management maximal?
- Difference in Australian Practice: Not approved for CKD Stage 1 ADPKD

# KDIGO Recommendations on Other Interventions

SGLT2 inhibitors: Not recommended outside of a clinical trial

Hypoxia-inducible factor prolyl hydroxylase inhibitors: No

Glucagon like peptide-1 receptor agonists: No comment

Ketogenic Diet/Supplements: Not recommended outside of trial

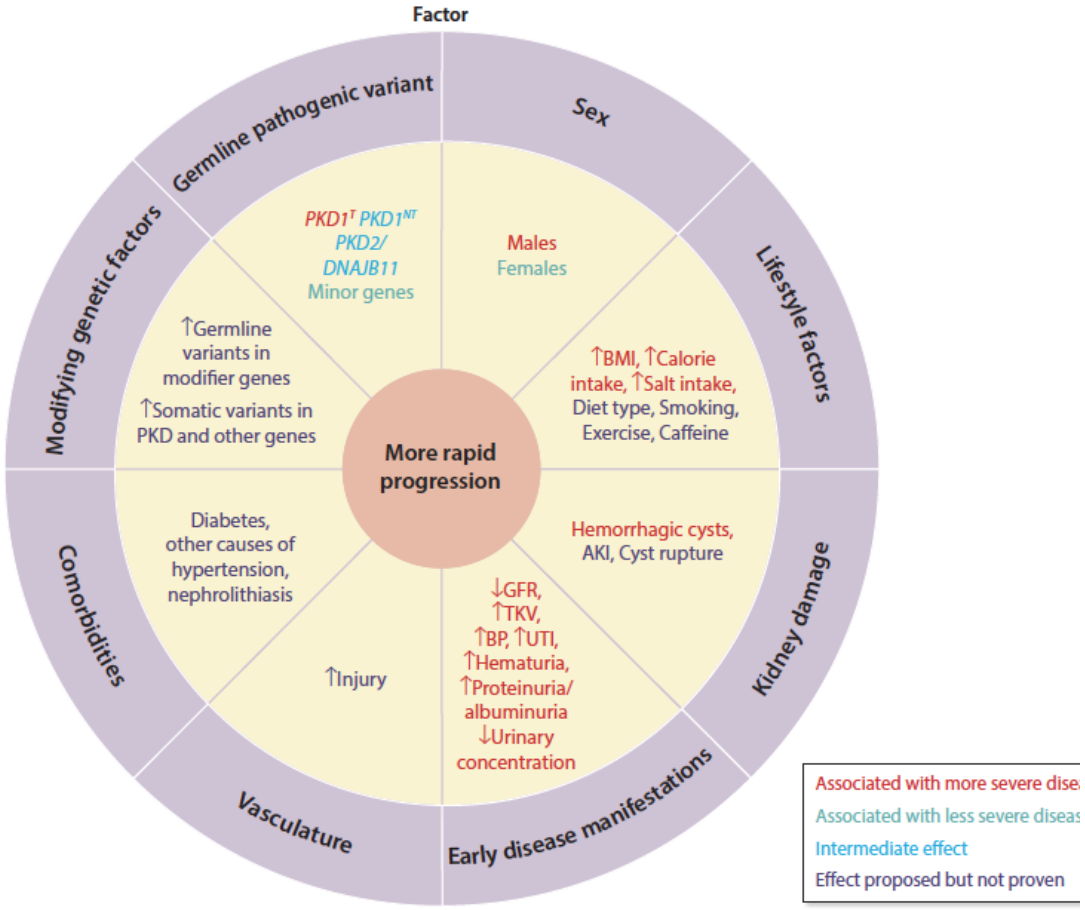
Statins: Use for other reasons but not to slow kidney disease progression

mTOR inhibitors: Not recommended due to risk of harm and lack of efficacy

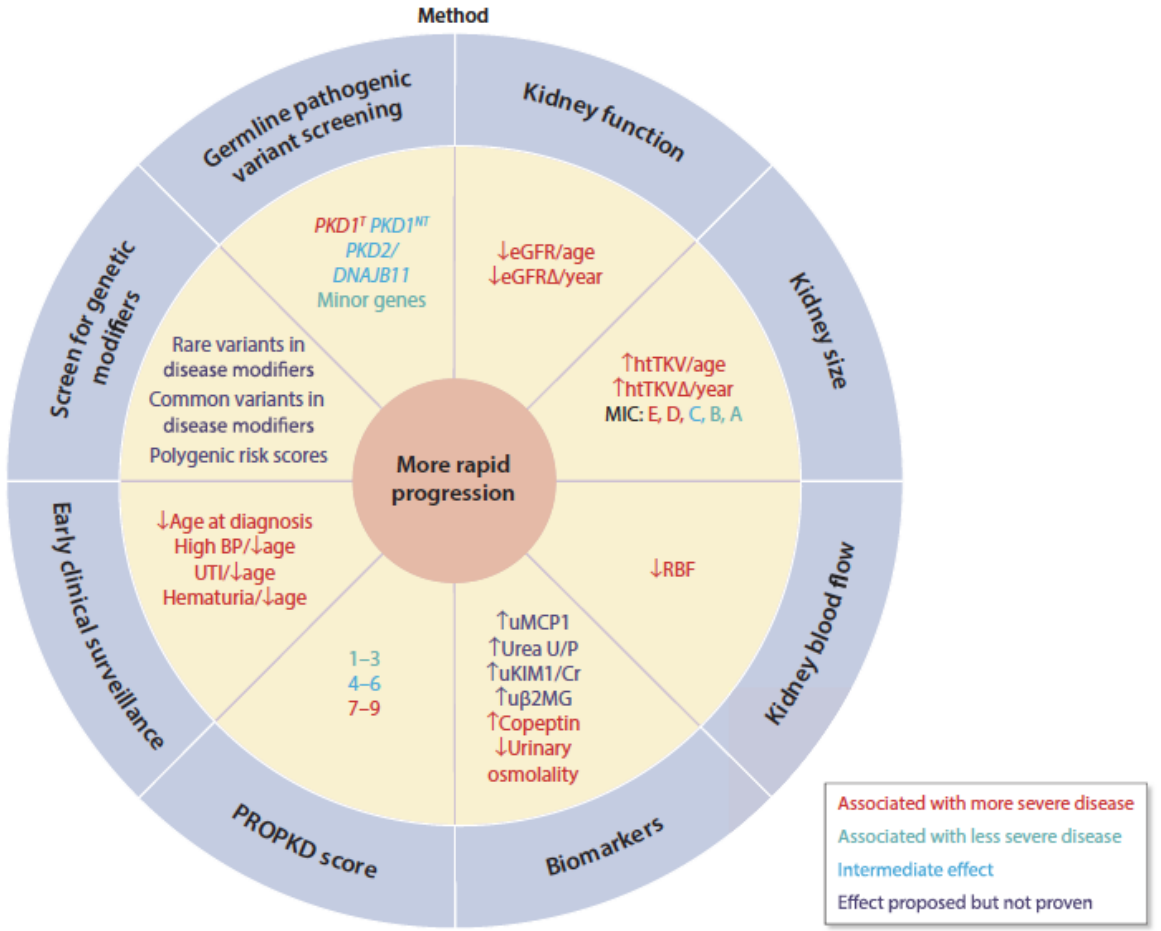
Somatostatin analogues: consider if severe symptoms due to PLD or massively enlarged kidneys when no better options exist – not slowing eGFR decline - four clinical trials; ALADIN-1, ALADIN-2, DIPAK, LIPS

# KDIGO Recommendations on Risk Factors and Tools to Predict Prognosis

## Clinical Risk Factors




## Tools



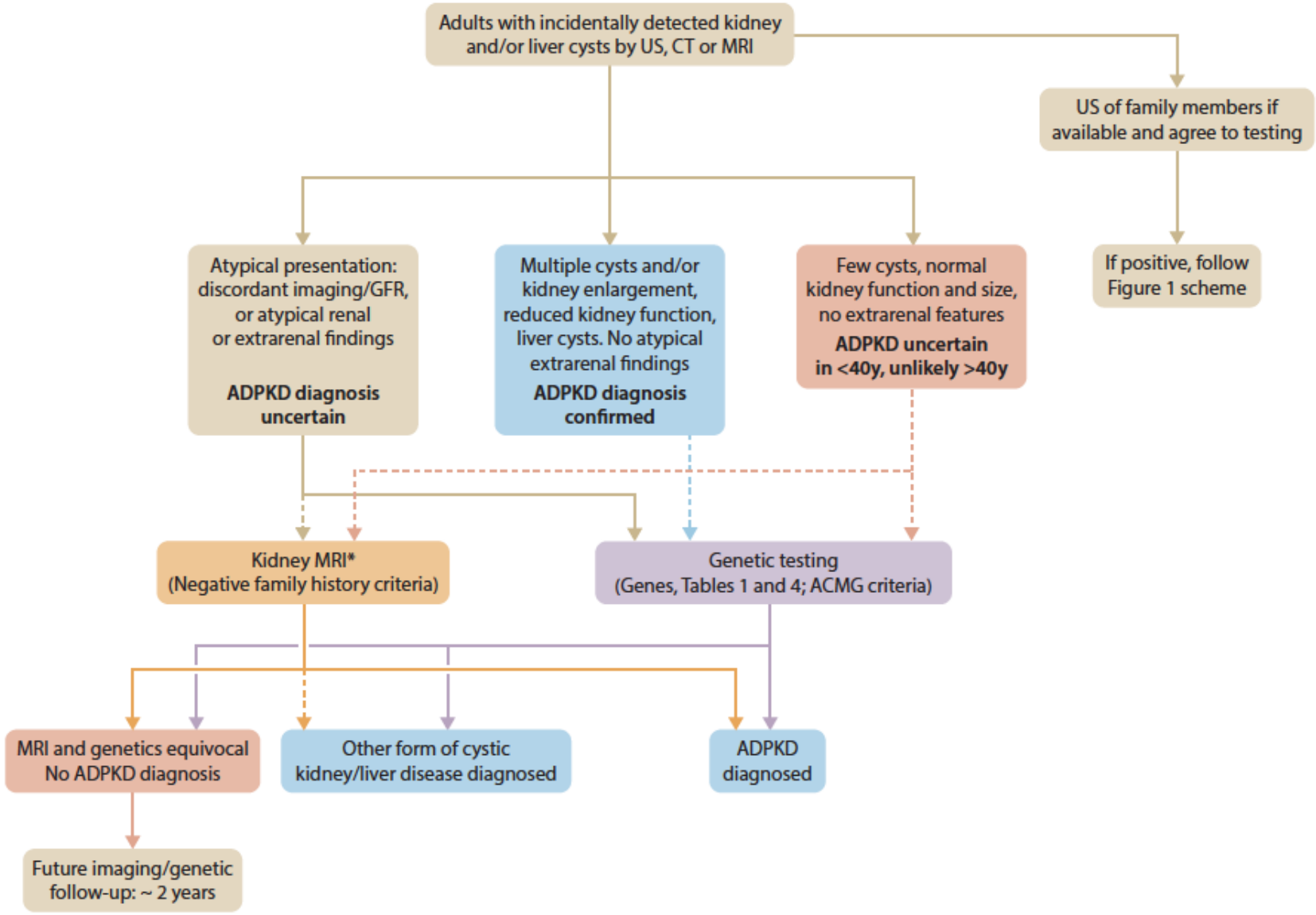

My Comment: Predicting Prognosis is an area for future development and will evolve as future therapies become molecular-based. In Australian context, kidney length on ultrasound (>16.5 cm and family history of kidney failure can provide quick pragmatic information to guide follow-up.

# Case #2

56F referred to renal genetics clinic with multiple bilateral ’small’ 1 cm renal cysts with kidney size 10-11 cm on ultrasound Normal eGFR, blood pressure. No extra-renal or syndromic features. No family history of ADPKD. One adult son aged 20 years old.

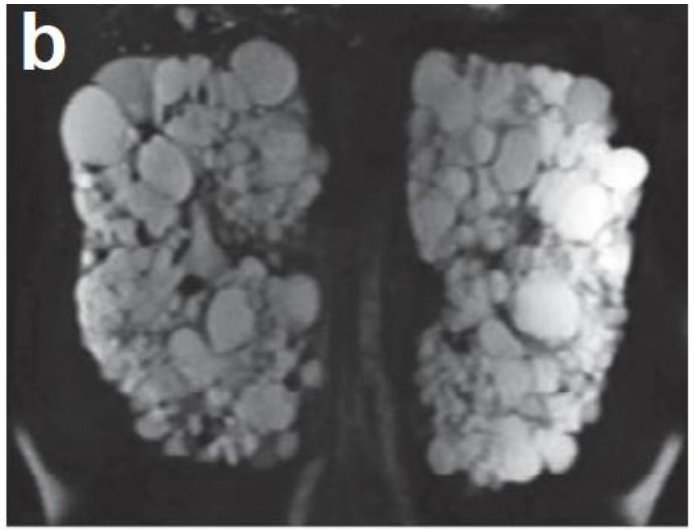
**Should genetic testing be offered?**

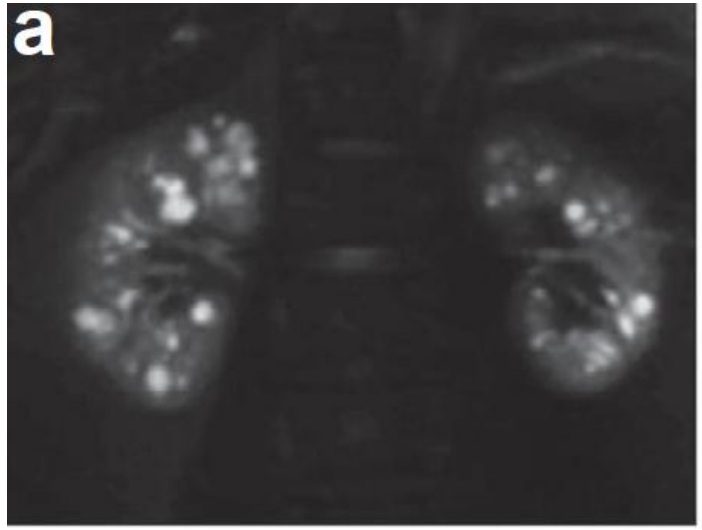
# Approach to incidentally-detected kidney cysts



# KDIGO Imaging

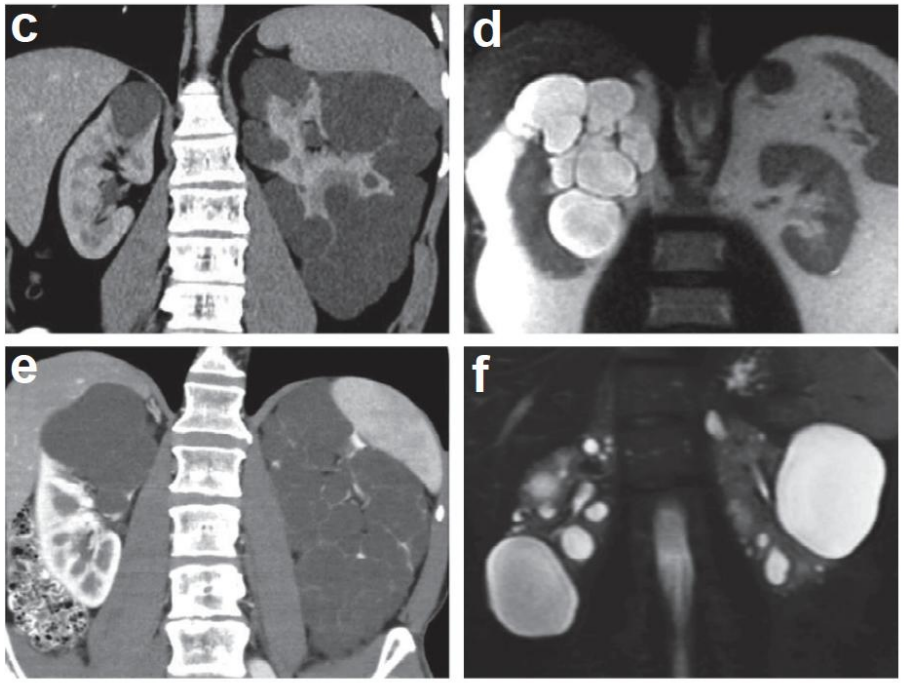
**TYPICAL ADPKD**



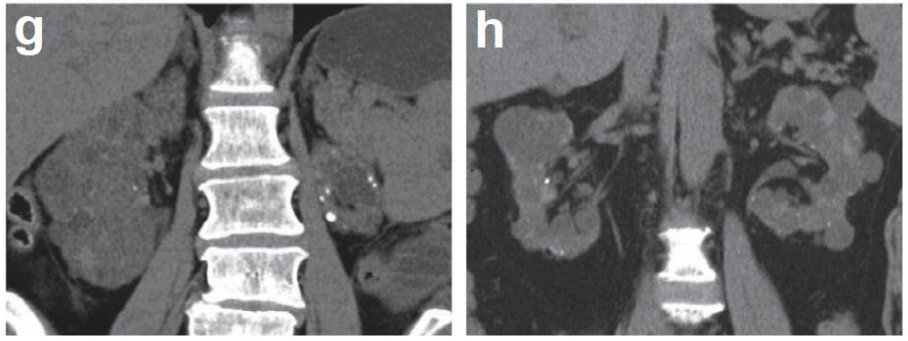




Bilateral, diffuse, mild-severe, all cysts
Contribute to kidney volume

**ATYPICAL ADPKD**




2A
Unilateral
Segmental
Assymmetric
Lopsided




2B
Unilateral or
bilateral atrophy

# KDIGO Genetics in ADPKD: More genes than before…

**Major Genes:** *PKD1, PKD2* = causative genes in **95% of typical cases**

- Look typical on imaging
- Classical phenotype that we recognise (big kidneys, liver cysts, kidney failure)
- Disease nomenclature: ADPKD-PKD1, ADPKD-PKD2

**Minor Genes:** Atypical imaging

- ALG5: mild moderate cyst development, limited kidney enlargement
- ALG9: mild moderate cyst development, CKD in older adults
- DNAJB11: Bilateral small cysts, no kidney enlargement, fibrosis, tubulonterstitial disease
- GANAB: Mild cyst development, limited CKD
- **IFT140:** Few, large bilateral cysts with preserved renal fucntion
- NEK8: Bilateral PKD, kidney enlargement, kidney failure in children

Disease nomenclature: *ADPKD-gene*

# KDIGO: Example disorders that present with kidney cysts

**GENETIC/DEVELOPMENTAL**

- Developmental disorders: *HNF1B, JAG1, NOTCH 2*
- Collagen Disorders: *COL4A1, COL4A2, COL4A3, COL4A4,*
- Urinary Stone Diseases: *CYP24A1, SLC34A3, HOGA1*
- ADTKD: *MUC1, REN, SEC61A1, UMOD*
- Recessive PKD: eg. *PKHD1*
- Tumourous disorders: eg. *TSC1/TSC2*
- Syndromic forms: e.g. *OFD1, NPHP, many others*

*Included in most cystic kidney disease panels*

**ACQUIRED**

- Simple cysts
- Acquired cystic disease: CKD
- Drugs: Lithium
- Metabolic: Chronic hypokalaemia

# KDIGO Advice on Genetic Testing in ADPKD

**Table 4 | Situations in which genetic testing can clarify the diagnosis and aid in determining a prognosis**

| Situation | Genetic findings |
|---|---|
| Limited number of cysts | Positive result can show a genetic origin (minor gene or hypomorphic allele). |
| Variable disease severity in a family | Mosaicism or biallelic/digenic disease can explain some extreme variability. |
| Atypical findings with imaging, such as asymmetric or unilateral disease | Positive result can show a genetic origin (including mosaicism or minor gene involvement). |
| Discordance between structural (MIC) and functional (GFR) ADPKD severity[a] | Genetic testing may reveal an atypical form of the disease or additional genetic or contributory factors, but nongenetic factors may also be important. |
| Negative family history | Positive result can show a genetic origin (*de novo* mutation can be proven). |
| Very-early-onset (VEO) ADPKD | Biallelic disease may be found (Chapter 9). |
| Related living transplant donor (aged <30 yr, especially if a few cysts detected) | Genetic testing can exclude the familial variant, if known, and test for other genetic causes. |
| Family planning and preimplantation genetic diagnosis (PGD) | Obtaining a genetic diagnosis can aid in family planning and enable PGD (Chapter 8). |
| All people | Genetic testing can confirm the diagnosis, identify the responsible gene and variant, and provide prognostic information. |

**Evolving practice**

- **increasing implementation of genetic testing → future expectation of precision medicine**
- **Enrollment into Clinical Trials (e.g. Regulus Therapeutics, PYC Therapeutics, Vertex Pharma**

# Diagnosis: Genetic Testing Funded by Australian Medicare Benefits Scheme on 1st July 2022

| Item Number | Indication | Cost Covered by Government |
|---|---|---|
| 73401 | Characterisation, by whole exome or genome sequencing and analysis, of germline gene variants in one or more of the genes implicated in **heritable cystic kidney disease**, if:<br><br>(a) the service is requested by a a clinical geneticist; or nephrologist; and<br><br>(b) the patient has a renal abnormality and is strongly suspected of having a monogenic condition<br><br>Applicable <u>once per lifetime</u> | $A2,100 |
| 73403 | Re-analysis of test from item 73401 | $A500 |
| 73405 | Genetic testing of a reproductive partner of an individual who is known to carry a genetic variant(s) associated with heritable kidney disease | $1,200 |

Data from https://www9.health.gov.au/mbs/search.cfm accessed 10th December 2023

# Diagnosis of ADPKD: Approach for Genetic Testing in Australia

| | |
|---|---|
| **Indications** | 1. To assist with family planning (pre-implantation genetic diagnosis)<br><br>2. atypical clinical phenotype (i.e. negative family history, equivocal renal imaging, and unusual clinical phenotype, especially in syndromic forms or early-onset disease)<br><br>3. Screening of living-related donor |
| Current Limitations | Universal genetic testing in all patients with ADPKD using **current technologies** not recommended because: the results are inconclusive or negative in 10% of patients with typical ADPKD or as high as 50% with a clinical phenotype that is atypical; genetic testing is 10 x more expensive than kidney ultrasound; and genotyping does not correlate with phenotypic severity.<br>*But, Likely to change with evolution of technology and new disease-modifying treatments becoming available* |
| Method | All patients must complete a genomic consent form<br><br>Sample collection organised by nephrologist with copy of result to renal genetics team<br>Adults: 4ml EDTA Blood; Children: 1-2ml EDTA Blood<br>Buccal/saliva collection is an option if blood collection is challenging<br><br>Panel exome test: PanelApp Australia (renal cystic disease 119 genes) https://panelapp.agha.umccr.org/ |
| Current Challenges | <u>Workforce issues:</u> Nephrology workforce education and renal genetic clinics availability in rural areas/capacity<br><br><u>Laboratory:</u> Delay (6-12 weeks) workload and interpretation of variants of unknown significance (10-50% cases) |

Data local renal genetic clinic protocols, Westmead and Royal Prince Alfred Hospital

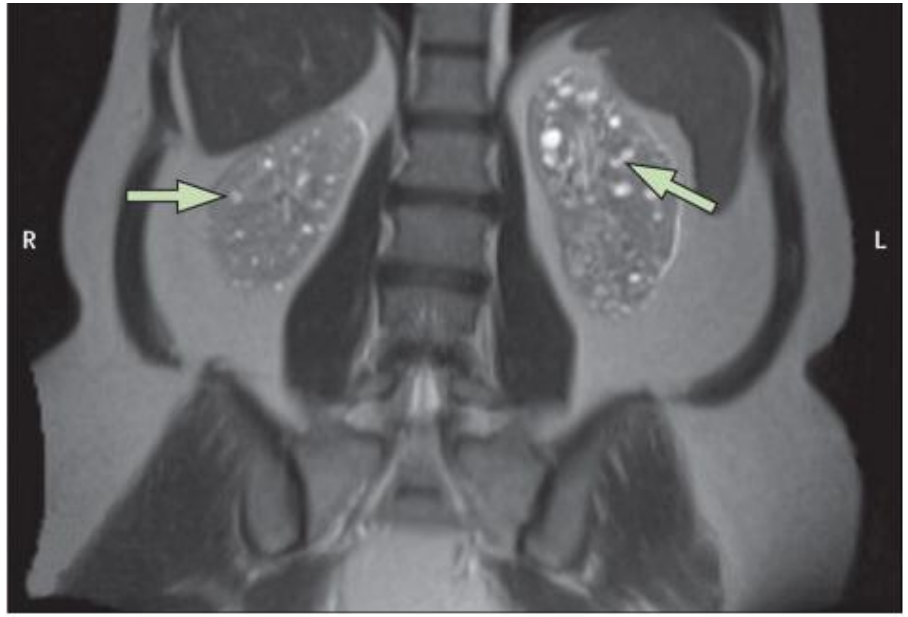
# Back to Case #2

56F referred to renal genetics clinic with multiple bilateral 'small' 1 cm renal cysts with kidney size 10-11 cm on US and MRI. Normal eGFR, blood pressure. No extra-renal or syndromic features. One adult son

Additional history: Bipolar disorder, Lithium use for 10 years (1x ICU admission with toxicity)

**Genetic testing?**

- Reviewed scans - appearances suggestive of Li-induced microcysts
- Suggest screening son
- If cysts positive, there could be implications and genetic testing to be discussed




Shah et al. Lancet 375, 1024, 2010

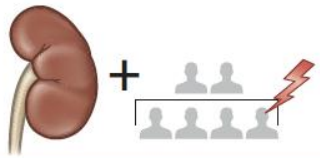
**This case illustrates the nuances of clinical decision-making (patient history, values and preferences of the patient + also highlights the value of genetic multi-disciplinary meetings to discuss cases…i.e. no right or wrong approach**

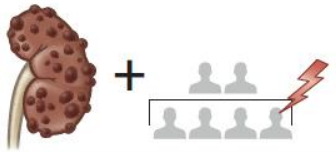
# Case #3

48M was referred to your clinic with a new diagnosis of ADPKD during presentation with back pain. Migrated from Afghanistan at age 18. His father died at 55 years with “cardiac arrest or stroke”.

**How would you discuss ICA risk and would you screen for an ICA?**

# Recommendation 6.1.1: We recommend informing adults with ADPKD about the increased risk for ICAs and SAB (1C)





| | General population | General population with family history of ICA or SAH | ADPKD population | ADPKD population with family history of ICA or SAH |
|---|---|---|---|---|
| **Prevalence of ICA** (95% CI) | 2.9% (1.9–4.5) | 3.4 (1.9–5.9) higher risk[a] | 12.9% (10.4–15.4) (Figure 36) | 17.1% (13.4–21.1)[b] |
| **Incidence rates of SAH** (per 1000 person-years, 95% CI) | 0.079 (0.069–0.09)[c] | 3–7 higher risk | 0.57 (0.19–1.14) (Figure 37) | Likely higher (based on data from general population) |

# Recommendation 6.1.2: We recommend informing adults with ADPKD about the increased risk for ICAs and SAB (1C)

## Practice Point 6.1.1: All people with ADPKD should be educated to recognise thunderclap headache

**Definition:**
- Strikes suddenly
- Intense pain: "worst headache in my life"
- Reaches maximal intensity within 60 seconds

**May be associated with or followed by:**
- Nausea or vomiting
- Seizures
- Altered mental state/loss of consciousness

**What to do:**
- Seek immediate medical attention
- Have evaluation in an emergency department equipped with CT scan
- Inform caregivers about the increased risk for subarachnoid hemorrhage associated with ADPKD

# Recommendation 6.1.2: We recommend ICA screening for ICA with ADPKD and a personal history of SAH or a + family history of ICA, SAH, or unexplained sudden death in those eligible for Rx and a reasonable life expectancy (1D).

- frequency of ICA in ADPKD + positive family history of SAH or ICA undergoing screening is 17% (4 x probability of finding an ICA vs. whole ADPKD population
- Note: 50-60% diagnosed with ICA and 40% with ruptured ICA do not have a family history
- Rupture of ICA is devastating: mortality 30% and morbidity 50%

# KDIGO: Advantages and Disadvantages of ICA Screening

| Advantages | Limitations |
|---|---|
| • May allow intervention if an ICA at risk of rupture is identified, allowing prevention of death or significant comorbidity | • May lead to the identification of ICA with very low risk of rupture (≤5 mm/ anterior circulation) that do not require intervention but require long-term follow-up |
| • May allow adequate imaging follow-up if an ICA with low risk of rupture is identified | • Does not exclude the risk of *de novo* ICA development and rupture after screening |
| • May reduce anxiety and provide reassurance when no ICA is detected | • May lead to procedures with possible treatment failure or complications, including death or significant morbidity |
| | • May cause anxiety when an ICA is identified |
| | • May limit access to life insurance, loans, or driver's licenses |
| | • May limit work opportunities |

My opinion: KDIGO suggests a shared-decision to guide approach to screening and emphasises targeted screening. Relative indications are variable and influenced by local clinical protocols (e.g. pre-transplant, preconception planning) and individual patient factors influence decision and previous physician experience. Be prepared to have an approach to discuss with patient. Most scans will be negative.

# Back to Case #3

48M was referred to your clinic with a new diagnosis of ADPKD during presentation with back pain. Migrated from Afghanistan at age 18. His father died at 55 years with “cardiac arrest or stroke”.

## ICA Screening

- Proceeded to MRA brain
- 2.5 mm aneursym identified at bifurcation of the left M1 (neck <1mm)
- Referred to neurosurgeon but is yet to attend [suspect anxiety]

# Women with ADPKD of childbearing age (Fig. 45)

## Hormone therapy

- Counsel about risk/benefit of estrogen/progesterone therapy in ADPKD women with regard to PLD
- IUDs (including levonorgestrel-releasing IUD) and gestagen OCPs may be preferred for women with PLD

## Preconception counseling

- Discontinue potential teratogenic drugs before becoming pregnant (e.g., tolvaptan, RASi)
- Review the risks of preeclampsia, pregnancy induced hypertension, and premature delivery in ADPKD women
- Genetic counseling. Information on risk of inheritance of ADPKD for each pregnancy, nature of fetal/childhood outcomes in affected offspring, and the potential risk/benefit of PGT/PT/egg-sperm donation

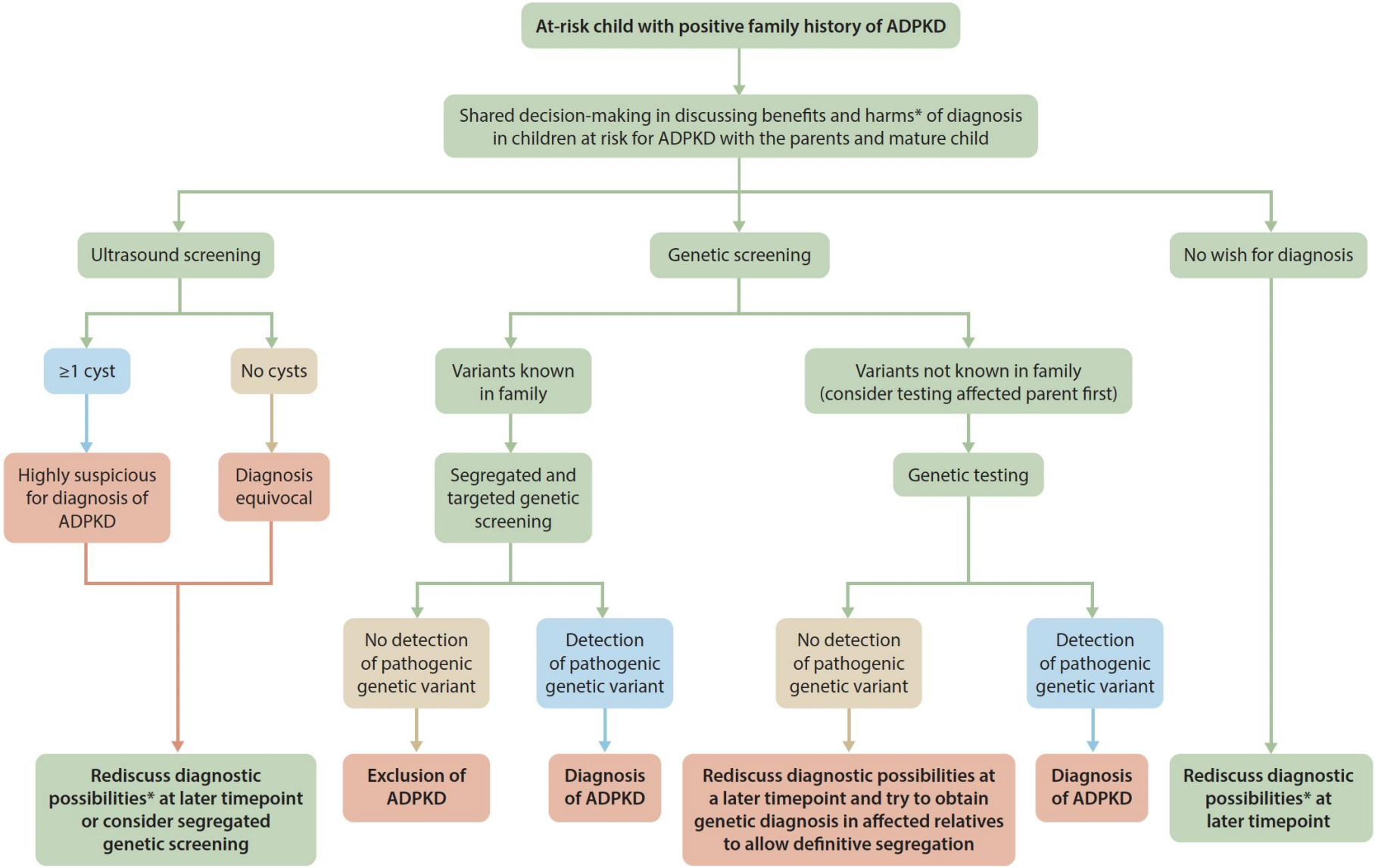
## Management during pregnancy

- Regular monthly assessment of BP, kidney function, and proteinuria by a health care provider
- Home BP monitoring is encouraged
- Suggested target BP <135/85 mm Hg
- Low dose of aspirin from week 12 to week 36 is recommended for all pregnant ADPKD women
- Monthly screening for UTI is advised. Those with positive urine cultures should be treated adequately
- Encourage increased fluid intake

## Management after pregnancy

- Tolvaptan is contraindicated during breastfeeding and should not be prescribed during this time
- Some ACEi such as enalapril or captopril have very low penetration into human milk and can be used with careful monitoring of the infant for signs of hypotension, if other agents are not adequately controlling blood pressure.
- Women with bladder instability or urinary incontinence after pregnancy should be offered pelvic floor physical therapy, especially when tolvaptan will be prescribed

# Pathway for ADPKD Diagnosis in Children (Fig. 50)



# Post-transplant Complications

| Post-transplant complication | |
|---|---|
| New-onset diabetes | Pooled RR 1.92; 95% CI: 1.36–2.70[a] |
| Erythrocytosis | Recipients with post-transplant erythrocytosis were more likely to have PKD than other kidney diseases (17% vs. 6%; P <0.001)[b] |
| Valvular heart disease | Greater risk for worsening of tricuspid, mitral and aortic valve regurgitation[c] |
| Aortic root dilatation | Greater risk for dilation of sinus of Valsalva and ascending thoracic aorta[d] |
| Subarachnoid hemorrhage | 3.8/1000 hospital admission in kidney transplant recipients with ADPKD compared to 0.9/1000 in kidney transplant recipients without ADPKD[d] |
| Thromboembolic events (DVT, PE) | 8.6% of 534 patients with ADPKD vs. 5.8% of 4779 patients without ADPKD after kidney transplantation ($P = 0.009$)[e] |
| Skin cancers: SCC, BCC, melanoma | Adjusted ORs 1.22, 1.30, 1.21, respectively[f] |
| Urinary tract infections | Weak evidence only |
| Cyst infection | Cumulative IR 3%, 6 % and 12% (63% kidney, 37% liver) at 1, 5 and 10 years after transplantation (1.6 episodes per 100 person-years). Increased risk with history of cyst infection before transplantation, HR: 3.47; 95% CI: 1.29–9.31[g] |
| Colon diverticulitis | Prevalence (2006–2013) in kidney transplant recipients with compared to without ADPKD (2.6% vs 0.8%)[h] |

# Guidelines can help provide generic information on selected topics for clinical practice and can lead to more questions!

- Should I start tolvaptan in someone with Stage 1 CKD
- Review BP targets: Can we do better?
- How much water people ADPKD should drink?
- Are OCPs OK in ADPKD
- Are there are any drugs for severe PLD
- ICA Screening in de novo ADPKD
- When to provide preconception counselling
- When should children be screened for ADPKD?

Plus many others…