Do I need to order a genomic test for my patient?

‘Traffic light’ tool for nephrologists

Genetic counsellors are available to support you. Visit **kidneygenomics.org.au** to find your closest genetics expert. Use this to tool to help identify patients that may be suitable for genomic testing and prioritise which patients to test in the nephrology clinic (mainstream testing).

GREEN: Initiate genomic testing in nephrology clinic

These patients have a high likelihood of monogenic disease and high clinical utility from genomic sequencing. Initiation of test in the nephrology clinic is appropriate. Refer to clinical pathway. Support is available via genetic counsellor support line. Note: Testing of suspected Alport and cystic kidney disease should be prioritised in the mainstream setting.

- ESKD<=50 with unclear cause[1]
- Multiple renal cysts[2]
- Suspected Alport syndrome or thin basement membrane nephropathy[3]
- >6 months haematuria with no obvious cause[4]
- A specific gene associated with kidney disease is suspected[5]

AMBER: Discuss with kidney genetics multidisciplinary team

These patients need further clarification before testing can be initiated and will benefit from genetics support via discussion with the Kidney Genomics MDT or the genetic counselling support line prior to initiating testing. Some patients may be more suitable for testing in the Multidisciplinary Renal Genetics Clinic.

- Presence of extra renal features
- Haemolytic uraemic syndrome[6]
- Unexplained chronic kidney disease
- Prior genetic testing
- Need for rapid diagnosis[7]
- Cascade testing[8]
- Other suspected genetic kidney disease[9] based on family history/other features[10]

RED: Do not proceed with genomic testing. Consider referral to multidisciplinary renal genetics clinic or discuss in multidisciplinary meeting

These patients are either 1) unlikely to have monogenic kidney disease, or 2) testing may not be indicated at this stage or 3) testing may be more appropriate in the MD-RGC

- CAKUT[11] with normal kidney function
- Previous genetic diagnosis
- Steroid sensitive nephrotic syndrome
- Immunological cause of kidney failure
- Limited capacity for consent
- Testing of an asymptomatic individual with positive family history

Melbourne Genomics Health Alliance

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Monash Health · The Royal Melbourne Hospital · The Royal Children's Hospital Melbourne · Austin Health

About the Traffic Light Tool

This tool was based on current available evidence and guidelines and after discussion between an expert working group comprising of nephrologists, geneticists, and genetic counsellors. A small number of patients may fall into more than one category; contact your local genetic counsellor if you need further clarification or if you have any feedback regarding this tool.

Visit **kidneygenomics.org.au** for more information and contacts for the Kidney Genomics Multidisciplinary Team (KG/MDT) and the Genetic Counsellor support line.

Footnotes

1. Based on the HIDDEN study (manuscript under review) the diagnostic yield was 10% in those without family history and 24% in those with a family history of kidney disease. Manuscript under review (Soraru et al., 2022).
2. Individuals with multiple kidney cysts (excluding those patients with suspected acquired cystic kidney disease) (Park et al., 2021).
   - Individuals who meet ultrasound criteria for ADPKD but have no family history of cystic kidney disease.
   - Individuals who have a clinical diagnosis of ADPKD where a genomic diagnosis will potentially benefit the individual being tested or their family member.

   Examples include reproductive planning, identification of at-risk relatives for prognosis/donor selection/ screening, where there are atypical features (e.g. size of kidneys or kidney function decline).

   Acquired cystic kidney disease should be suspected if there are ≥ 3 cysts in each kidney in a patient with CKD and small or normal sized kidneys. If unclear, screening family members with ultrasound may help to differentiate (Chapman et al., 2021).
3. This may be based on persistent haematuria of unknown cause and positive family history, or more specific features of Alport syndrome or thin basement membrane nephropathy (TBMN) such as eye and ear findings, biopsy findings that suggest Alport nephropathy.
4. If a genomic diagnosis would negate the need for a renal biopsy, consider genomic testing prior to biopsy in diagnostic workup (Jayasinghe et al., 2021).
5. When there is a specific gene that you suspect, for example, FSGS due to INF2 variant, Gitelman syndrome due to biallelic SLC12A3 variants.
6. Consider testing when there is a family history of kidney disease OR if responsive to C5 inhibitor therapy and considering discontinuation OR prior to transplantation.
7. Standard turnaround time for genomic testing is 3 months. Testing may be able to be expedited by (TAT around 1 week if required) please contact your local genetic counsellor hotline for advice. Indications for urgency include high-cost drug, invasive investigation (or biopsy) that may be avoided with a timely result, imminent reproductive decision-making implications.
8. The process of offering genetic testing to at-risk blood relatives of individuals who have been diagnosed with a monogenic condition.
9. There are many other groups of genetic kidney disease apart from Alport syndrome/cystic kidney disease that may benefit from genomic testing.
10. GKD risk factors (one of more of the following): Young age (<35) of presentation, family history of kidney disease, parental consanguinity
11. CAKUT = Congenital abnormalities of kidney and urinary tract.

References

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