Who should have a genomic test in the Kidney Clinic?

‘Traffic light’ tool for paediatric patients

GREEN:
Initiate test in nephrology clinic

- Chronic kidney disease with raised creatinine
- Cystic kidney disease
- Glomerular disease other than SSNS
- Kidney disease with positive family history
- Tubulopathy

AMBER:
Pause and discuss with KG-MDM

- Presence of extra renal features
- Unclear diagnosis
- Haemolytic uraemic syndrome
- Unexplained nephrocalcinosis
- Need for rapid diagnosis
- Cascade testing
- Previous negative or inconclusive genomic sequencing

RED:
Do not test. Consider referral to renal genetics clinic or discuss in KG-MDM

- Isolated CAKUT with normal kidney function
- Previous genetic diagnosis
- Steroid sensitive nephrotic syndrome
- Complex family situation
- Testing of unaffected individual with positive family history

Melbourne Genomics Health Alliance

This resource was produced as part of the Scaling Up Genomics in Nephrology Project, June 2023.

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

Explanatory notes

This framework is intended to be utilised by pediatric nephrologists and was developed in consultation with a multidisciplinary stakeholder cohort from May to June 2021 including all pediatric nephrologists in Victoria, the RCH renal genetics MDT and other clinical geneticists and genetic counselors who provided written feedback and verbal correspondence. Finally, to ensure the framework would be relevant to patients and families, a consumer voice was incorporated. This consumer provided written feedback about the framework. The framework was modified until consensus from key stakeholders was reached.

GREEN: 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.

AMBER: these patients need further clarification before testing can be initiated and will benefit from discussion with the KG-MDT prior to initiating testing

RED: 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 preferable in the Renal Genetics clinic or general genetics clinic.

KG-MDM is the regular Kidney Genetics multi-disciplinary meeting. Patients for discussion can be proposed via email or flagged with Brendan Cusack.

Chronic Kidney disease:

- Defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. CKD is classified based on Cause, GFR category (G1–G5), and Albuminuria category (A1-A3).
- CKD associated with raised creatinine in childhood is associated with a high diagnostic yield.
- Patients with an immunological basis to their CKD eg lupus should not be considered for testing in the nephrology clinic though they could be discussed at the KG-MDM.

Cystic kidney disease:

- One or more renal cysts AND a positive family history of ADPKD (Gimpel et al 2019)
- Bilateral renal cysts (more than 1) (Gimpel et al 2019)
- Large kidneys OR
- Bright kidneys not related to AKI

Glomerular disease:

- Steroid resistant nephrotic syndrome
- Persistent haematuria with negative immune workup
- Testing for steroid sensitive nephrotic syndrome has low clinical utility and should be discussed at the KG-MDM meeting

Unclear diagnosis or presence of extra-renal features:

- Patients with an unclear diagnosis and those whose kidney disease is part of an overall syndromic presentation may benefit from the enhanced phenotyping of the renal genetic clinic or the general genetics clinic

Haemolytic uraemic syndrome:

- At present genomic sequencing for HUS is sent to the Westmead and the KG-MDT can assist with the logistics of ordering this test.
- Patients with classical STEC+ HUS are unlikely to benefit from genomic sequencing

Rapid diagnosis:

- Rapid testing has a turnaround time of 3-weeks; ultra-rapid testing has a turnaround time of 5 days.
- A rapid diagnosis may avoid a biopsy for children with glomerular disease or facilitate complex care planning in neonates with kidney failure.
- Rapid testing is NOT funded by MBS and needs to be approved by the KG-MDT

Cascade testing:

- If a family member has a confirmed genetic diagnosis, then discuss with the KG-MDT prior to ordering. The patient will only require testing for the family variant rather than full analysis and the KG-MDT can provide support tracking down information.

Previous negative or inconclusive genomic sequencing:

- Reanalysis should be considered after 3-years or if new gene/phenotype associations have been defined

Congenital anomalies of the kidney and urinary tract (CAKUT):

- This is a heterogenous group of structural anomalies of the kidney and urinary tract including dysplasia, single kidneys, posterior urethral valves, hydronephrosis, duplex kidneys. They are estimated to occur in 0.5% of pregnancies.
- The causes of CAKUT are complex and it is likely that a combination of genetic and environmental factors contributes to their occurrence.
- Counselling around recurrence in future pregnancies is complicated by incomplete penetrance.

Complex family situations:

- Some medically or socially complex families may benefit from the diagnostic focus and longer appointment times available in the renal genetics clinic.
- Depending on the clinical judgement of the treating nephrologist these patients should be referred to the renal genetics clinic.

Steroid sensitive nephrotic syndrome:

- Unlikely to benefit from genomic sequencing

Predictive testing for unaffected individuals with a positive family history:

- Predictive testing for adult-onset conditions is generally best left until the child is able to give informed consent. If the family is keen for sequencing, then discuss with the MDT and consider referring to the renal genetics clinic.