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### Poster Presentation

Session Title: Genetic Diseases of the Kidney - III [PO1002-3]

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Poster Board #: SA-PO405

### Diagnostic and clinical utility of whole exome sequencing in a cohort with clinically suspected genetic kidney disease

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**Background:** Genomic technologies enable rapid and cost-effective sequencing of DNA and have demonstrated a definitive diagnosis in several patient groups such as childhood syndromes and oncology. We sought to determine the diagnostic and clinical utility of WES in a cohort of adults and children with clinically suspected genetic kidney disease who were reviewed in multidisciplinary renal genetics clinic (RGC).

**Methods:** Sequential patients were prospectively recruited through five tertiary academic centres in Australia. Patients were referred by their treating nephrologist to a dedicated RGC. Following review by a multidisciplinary team consisting of a nephrologist, clinical geneticist and genetic counsellor, patients underwent genomic sequencing with analysis for a pre-determined phenotype specific list of genes of interest. We measured the diagnostic yield and the effect on short term clinical management. Full author list online at KidGen.org.au

**Results:** We performed WES in 204 patients (82 paediatric and 122 adults) with CKD. The median age at time of recruitment was 29 years (0-72). Preliminary results demonstrate a genetic diagnosis in 77 patients (38%). This includes (69) pathogenic variants and (25) likely pathogenic variants. When comparing the a priori clinical diagnosis at referral in patients with WES diagnoses, 48 (62%) had their suspected clinical diagnosis confirmed and 29 patients (38%) had a subsequent change in

diagnosis. 42 patients (54%) with positive diagnoses had recommended changes to clinical management. This included the avoidance of immunosuppression, avoidance of renal biopsy, initiation of surveillance for extra-renal disease and facilitating transplant and reproductive decisions. In addition, at least 26 patients (13%) had a clinically relevant negative result with management implications.

**Conclusion:** To our knowledge this is the first study to report diagnostic and clinical utility of genomic sequencing in a pragmatic clinical setting. Our results confirm that in a clinically selected paediatric and adult cohort with kidney disease, WES is valuable for establishing a specific molecular diagnosis and demonstrates substantial quantifiable clinical utility.