

## 18<sup>th</sup> Congress of the International Pediatric Nephrology Association, Venice Italy October 17-21 2019

### Oral Presentation

Clinical utility of whole exome sequencing in children with clinically suspected genetic kidney disease

**Catherine Quinlan**

*Full list of authors*

Chaliner H<sup>1</sup>, Creighton B<sup>2</sup>, Gaff C<sup>3</sup>, Hunter M<sup>2</sup>, Jarmolowicz A<sup>4</sup>, Jayasinghe K<sup>2,5</sup>, Johnstone L<sup>2</sup>, Krzesinski E<sup>6</sup>, Lunke S<sup>7</sup>, Lynch E<sup>3</sup>, Mallett A<sup>8,9,10</sup>, Martyn M<sup>3</sup>, Nicholls K<sup>4</sup>, Prawer Y<sup>2</sup>, Quinlan C<sup>3,8,10,11</sup>, Ryan J<sup>2</sup>, Stark Z<sup>7,10</sup>, Talbot A<sup>4</sup>, Trainer A<sup>4</sup>, Uebergang E<sup>1</sup>, Valente G<sup>1</sup>, Wallis M<sup>1</sup>, Wardrop L<sup>8,10</sup>, White SM<sup>7</sup>, Whitlam J<sup>1</sup>, Wilkins E<sup>7</sup>

1. Austin Hospital, VIC
2. Monash Medical Centre, VIC
3. Melbourne Genomics Health Alliance
4. Royal Melbourne Hospital, VIC
5. Monash University, VIC
6. Monash Genetics, VIC
7. Victorian Clinical Genetics Service, VIC
8. Murdoch Children's Research Institute,
9. Royal Brisbane and Women's Hospital, QLD
10. Australian Genomics Health Alliance
11. Royal Children's Hospital, VIC

### Introduction

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 children with clinically suspected genetic kidney disease who were reviewed in multidisciplinary renal genetics clinic (RGC).

### Methods

Patients were prospectively recruited through two tertiary paediatric 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 at [KidGen.org.au](http://KidGen.org.au)

### Results

We performed WES in 82 children with kidney disease. The median age at time of recruitment was 7.5 years (1 month-18 years). Preliminary results demonstrate a genetic diagnosis in 37 patients (51%). This includes (34) pathogenic variants and (11) likely pathogenic variants. When comparing the *a priori* clinical diagnosis at referral in patients with WES diagnoses, 22 (59%) had their suspected clinical diagnosis confirmed and 15 patients (41%) had a subsequent change in diagnosis. 21 patients (57%) 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 decisions. In addition, at least 26 patients (32%) had a clinically relevant negative result with management implications.

### **Conclusions**

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 cohort with kidney disease, WES is valuable for establishing a specific molecular diagnosis and demonstrates substantial quantifiable clinical utility.