Melbourne Genomics
Health Alliance

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Clinical utility of genomics in genetic kidney disease

Background

Melbourne Genomics' Clinical Flagships have been at the forefront of determining when genomic testing makes a demonstrable difference to the safety and quality of patient care; genetic kidney disease (GKD) is one of 16 areas of health investigated.

Genetic kidney disease affects about 3% of the Australian population. One in seven adult Australians have chronic kidney disease and up to 20% of this may be genetic in origin.

Although there is no cure, early identification and proactive treatment may slow the progression of genetic kidney disease and delay the need for dialysis and kidney transplantation.

Publications

"Clinical impact of genomic testing in patients with suspected monogenic kidney disease", Kushani Jayasinghe, Zornitza Stark, Peter G. Kerr, Clara Gaff, Melissa Martyn, John Whitlam, Belinda Creighton, Elizabeth Donaldson, Matthew Hunter, Anna Jarmolowicz, Lilian Johnstone, Emma Krzensinski, Sebastian Lunke, Elly Lynch, Kathleen Nicholls, Chirag Patel, Yael Prawer, Jessica Ryan, Emily J. See, Andrew Talbot, Alison Trainer, Rigan Tytherleigh, Giulia Valente, Matthew Wallis, Louise Wardrop, Kirsty H. West, Susan M. White, Ella Wilkins, Andrew J. Mallet and Catherine Quinlan, Genetics in Medicine (2020) https://doi.org/10.1038/s41436-020-00963-4

Project description

The objective: to determine if genomic sequencing can provide a more definitive diagnosis and enable more personalised care for children and adults with GKD.

The Genetic Kidney Disease Flagship was led by A/Prof Catherine Quinlan (The Royal Children's Hospital). Key coordination was provided by Dr Andrew Talbot (The Royal Melbourne Hospital), Dr John Whitlam (Austin Health), Dr Jessica Ryan (Monash Health) and Dr Kushani Jayasinghe (Monash Health); more than 20 health professionals were directly involved[1].

Activities

Between April 2017 and October 2018, nephrologists referred patients for assessment and testing. A total of 204 patients received genomic testing through the Flagship.

Analysis was generally targeted to genes known to be involved in GKD; analysis of a wider set of disease-causing genes was offered in a limited number of cases (primarily complex patients).

Outcomes

Of the patients tested, 80 (39%) received a diagnosis, 31 of whom had their diagnosis completely reclassified.

[1] The Melbourne Genomics Genetic Kidney Disease Flagship is part of a broader Australian network of nephrologists, KidGen, which has project coordinator funding from Australian Genomics.

Genomic testing had profound implications for care, with 59% of those diagnosed experiencing a change in medical management, including other planned testing no longer being required. A planned renal biopsy was no longer required for 10 (13%) patients who received a genomic diagnosis. Other changes to patient care included alterations in medical monitoring (44%) and treatment plans (20%), as well as other specific actions such as bringing forward kidney transplantation and informing family planning (9%).

Lessons learnt

- Genomic sequencing changed or clarified diagnosis for a third of all patients tested. A definitive genomic diagnosis was made for 39% of patients, none of which would have been made using the usual testing available at the time the study began.
- Education and support from clinical geneticists enabled nephrologists to make appropriate use of genomic testing. The diagnostic utility achieved in this study is higher than in published studies that did not involve multidisciplinary assessment of referrals. Funding to support multidisciplinary assessment for kidney patients is required to ensure appropriate use of genomic testing.

Impact

Evidence generated by the Flagship enabled the national KidGen network to receive philanthropic funding to continue offering a multidisciplinary renal genetics service.

As a result of Flagship findings, pathology departments at two member hospitals are now considering requests for genomic testing from within their existing budget.

Clinical Flagship team

Name	Organisation	Role
Catherine Quinlan	RCH	Paediatric nephrologist
Andrew Talbot	RMH	Nephrologist
John Whitlam	Austin Health	Nephrologist
Jessica Ryan	Monash Health	Nephrologist
Kushani Jayasinghe	Monash Health	Nephrologist
Alison Trainer	RMH	Clinical geneticist
Anna Jarmolowicz	RMH	Genetic counsellor
Belinda Creighton	Monash Health	Genetic counsellor
Ella Wilkins	VCGS	Genetic counsellor
Emma Krzesinski	Monash Health	Clinical geneticist
Giulia Valente	Austin Health	Genetic counsellor
Heather Chalinor	Austin Health	Genetic counsellor
Ingrid Winship	RMH	Clinical geneticist
Kathy Nicholls	RMH	Nephrologist
Kirsty West	RMH	Genetic counsellor
Lilian Johnstone	Monash Health	Paediatric nephrologist
Louise Wardrop	Australian Genomics	Program manager
Mathew Wallis	Austin Health	Clinical geneticist
Matthew Hunter	Monash Health	Clinical geneticist
Sue White	VCGS	Clinical geneticist
Yael Prawer	Monash Health	Genetic counsellor
Zornitza Stark	VCGS	Clinical geneticist

The health economic evaluation for this Flagship was led by Ilias Goranitis from the University of Melbourne.