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# RACP Foundation Research Awards

# FINAL REPORT

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| **Project / Program Title** | | The impact of social disparity on access to care and overall health outcomes of children with chronic kidney disease |
| **Name** | | Dr Rowena Lalji |
| **Award Received** | | 2020 Jacquot Research Entry Scholarships |
| **Report Date** | | 10/03/2021 |
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## PROJECT SUMMARY

Chronic kidney disease (CKD) is a significant and debilitating health condition of global concern across the lifespan. Unlike adults who have completed their formative growth and development before diagnosis, CKD in childhood is a devastating illness affecting multiple organ systems. Kidney failure is associated in children with an increased mortality, reduced quality of life, impaired growth, neurocognitive impairment and psychosocial maladjustment. Children and adolescents with kidney failure are at risk of dying prematurely largely due to cardiovascular disease, with a mortality rate 30-fold higher than age-matched peers. Even after transplantation, children have a life expectancy 20 years shorter than the general population.

The primary aim of this research project is to identify barriers and facilitators in accessing quality care on local, national and international levels amongst children with chronic kidney disease (CKD) and to define risk factors for patient relevant outcomes. The outcomes of my proposal will address some of the critical gaps in current paediatric nephrology research. This includes (but is not limited to) risk factors for increased morbidity and mortality related to both paediatric dialysis and transplantation, vascular access trends for haemodialysis in children in Australia and New Zealand (and how this compares on an international level), risk factors for infection (both peritonitis and line related) and quality of life measures for children diagnosed with nephrotic syndrome. My research will cover the broad spectrum of CKD across the paediatric lifespan from birth to transition to adult services.

## PROJECT AIMS / OBJECTIVES

**Hypothesis:**
The over-arching objective of my research is to define the risk factors, barriers and equity of access to kidney care that affect health outcomes in children with chronic kidney disease (CKD) worldwide.
**Aims:**
1. To elucidate the predictors of adverse health outcomes in children with ESKD receiving kidney replacement therapy.
2. To define the impact of childhood nephrotic disease on overall QOL and identify potential modifiable factors that are amenable to intervention.
3. To identify national and global disparities in access to, and utilization of kidney replacement

therapies.
4. To systematically review the effectiveness and efficacy of patient navigator programs in children with chronic illness.

**Study 1 – Assessment of risk factors** for peritoneal dialysis-related peritonitis rates and outcomes in Australasian children using data from the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) (addresses aim 1) We will determine the relationship between sex and peritonitis rates (2003-2018), adjusting for age and ethnicity. Outcomes include peritonitis rates (primary outcome), time to first peritonitis, organism-specific peritonitis (Gram-positive, Gram-negative, fungal, polymicrobial, culture-negative) and peritonitis outcomes (cure, catheter removal, HD transfer, hospitalisation, relapse, death). Covariates include age, sex, primary kidney disease, ethnicity, remoteness index (ARIA) and socioeconomic indices for areas (SEIFA). Statistical analysis will use Poisson regression and multivariable Cox proportional hazards regression accounting for competing risks.

**Study 2 – Determining the incidence**, predictors and outcomes of vascular access in Australasian children on haemodialysis (HD) using the ANZDATA registry (addresses aim 1) Using ANZDATA registry data, we will determine the association between sex, ethnicity and time on dialysis for all patients aged 0-19 years commencing HD from 2004 to 2017. This will be done using mixed effects, negative binomial regression and multivariable Cox proportional hazards models accounting for competing events. Covariates include age, primary kidney disease, ethnicity and comorbidity. Specified outcomes include incident vascular access type (fistula vs catheter), haemodialysis catheter prevalence and access
type at last HD.

**Study 3 – Assessment of health-related quality of life** (HR-QOL) in children with nephrotic syndrome (addresses aim 2) The Kids with CKD (KCAD) is a cohort of 377 children aged 6-18 years with CKD recruited from 6 Australasian paediatric nephrology units (2012-2016). This unique cohort is a longitudinal mixed methods design with a record linkage dataset which examines temporal and other relationships between exposure variables. Outcome measures include psychological, neurocognitive, educational and kidney-related issues across the CKD spectrum. We will specifically analyse health-related quality of life scores (health utilities index), National Assessment Program – Literacy and Numeracy (NAPLAN) results and fullscale intelligence quotients for children with nephrotic syndrome using multivariable linear regression and ordinal logistic regression.

**Study 4a & 4b – Investigation of health disparities** in children's access to KRT worldwide (addresses aim 3) – COMPLETED and PUBLISHED
A topical policy forum (4a) will act as a 'call to action' for clinicians and policy maker alike to improve kidney health outcomes for children residing in lower income countries. A multifaceted approach is suggested including; improved prevention and community awareness programs, health data collection, workforce training and seeking cost effective
and sustainable dialysis options through advocacy and policy changes at all levels.

The Global Kidney Health Atlas survey (2018) is a collaborative evaluation of the global scope of kidney disease and patterns of health care utilisation between ISN and WHO. It spans 160 countries and approximately 98% of the world's population. For this research proposal component (4b), current global capacity to deliver KRT to children and adolescents will be examined by quantitative analysis and qualitative thematic analysis. There will be a specific focus on care disparities between children and adults based on geographical, economic and country-specific factors.

**Study 4c – National and state disparities in healthcare access** and outcomes for children treated with KRT (addresses aim 3) - IN WRITE UP
Using ANZDATA registry data, national and state variations in healthcare access and health outcomes among children on KRT will be evaluated according to ARIA and SEIFA scores. Key outcomes measures include graft loss (primary outcome), patient survival, acute rejection, time to transplant, sex differences in kidney donors and recipients. For children on dialysis, patient survival time to transplantation, PD-specific outcomes, haemodialysi s-specific outcomes and all-cause mortality are outcomes of interest. Covariates include age, primary kidney disease, race, comorbidity, height, weight, late nephrology referral, first KRT modality, state. Statistical analysis will

use multivariable Poisson regression with robust variance estimates for dichotomous outcomes. Potential interactions between age or ethnicity and the relationship between sex and patient survival and/or graft loss will be assessed.

**Study 5 – Systematic review and meta-analysis** of health benefits and costs of patient navigator programs for children with chronic disease (addresses aim 4) – PROTOCOL IN PRINT (accepted March 2021)
This systematic review will identify randomised trials examining the benefits, efficacy and costs of patient navigator programs versus standard patient care for children aged 0-19 years diagnosed with chronic disease. Pertinent studies will be identified using MEDLINE, Embase, CENTRAL and CINAHL. The Cochrane risk of bias tool will be used. Certainty of the evidence will be assessed using GRADE recommendations. Heterogeneity will be explored through meta-regression and subgroup analyses. Key outcomes include death (primary outcome), QOL, hospitalisation and patient satisfaction.

## SIGNIFICANCE AND OUTCOMES

This program of work will provide high quality evidence regarding risk factors, barriers and equity of healthcare access issues that affect health outcomes in children with CKD in Australia and globally. As a paediatric nephrologist with extensive ties to national and international collaborators, I am well placed to ensure my research findings are incorporated at both health service delivery and patient care levels.

The impacts of sex, ethnicity, remoteness and socio-economic disparities on healthcare access and outcomes for children and adolescents undergoing KRT in Australia will be defined using robust statistical modelling and geospatial evaluation. This will identify areas amenable to interventions to improve health outcomes for paediatric patients nationally and may be will also be applicable to children worldwide. Indeed, the exploration of disparities in, and barriers to kidney care through detailed responses in the GKHA survey has been instrumental to inform global policy currently being developed by the ISN in partnership with the World Health Organisation.

Additionally, analysis of the current state of vascular access in Australian children on haemodialysis will provide essential insight into patient- and centre-related factors underpinning variations between current practice and recommended best practice. This will facilitate the implementation of targeted interventions, better informed health policies and reduced healthcare costs.

This research will evaluate potential risk factors for PD peritonitis in children, including distance from treating centre, which is often considerable for Australian children living in regional and remote areas away from the single specialist paediatric nephrology care. This allows for better risk stratification and facilitates more personalised interventions, aiming to decrease morbidity, mortality and health-related costs associated with peritonitis. The research will inform health policies for resource distribution, aiming to minimise health disparities.

The quality of life for children with nephrotic syndrome will be assessed using a large longitudinal cohort study (KCAD) involving children with all stages of CKD (n=377), across 5 different sites in Australia and New Zealand. This novel study will facilitate the better understanding of illness burden for Australasian children with nephrotic syndrome and provide a window of opportunity to ascertain potential targets for health intervention.

Patient navigator programs have the potential to transform and improve clinical and patient-reported outcomes of children with complex chronic disease by simplifying access and engagement with health care by providing a single contact point. My systematic review will determine the evidence underpinning patient navigator programs in children with chronic disease, and define potential barriers and facilitators for implementation.

The outcomes of my proposal will address some of the critical gaps in current paediatric nephrology research and cover the broad spectrum of chronic kidney disease including dialysis and kidney transplantation. This research is paramount in the design, development and implementation of an

integrated, multifaceted, multi-layered and comprehensive approach to reduce healthcare disparities and preventable causes of poor outcomes in children with CKD in Australia and beyond.

## PUBLICATIONS / PRESENTATIONS

• As a result of my publications into the disparities in kidney care for children globally, I have been invited to write a commentary by Kidney International Reports on the "Kidney outcomes for First Nations children in Australia". This will be submitted by the end of March 2021 for review by the KI Reports editorial team.
• In late 2020, I became an associate investigator and site coordinator at QCH for the NAVKIDS2 trial – a multicentre randomised controlled trial of patient navigator interventions\ in children with chronic kidney disease. More recently, the COVID pandemic has given rise to a sub-study (NAV-COVID) which will specifically examine and assess the impact of the COVID virus and social distancing restrictions on children's access to kidney care.
• As a consequence of the COVID pandemic and the resultant financial constraints on the public health system in Australia, I have developed an interest in health economics. I am in the process of implementing a new test for the diagnosis of iron deficiency anaemia in children which is more efficient, more sensitive and specific than current iron studies (particularly for children with chronic kidney disease) and is substantially cheaper. This will be written up for publication mid-late 2021.

## ACKNOWLEDGEMENTS

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2 Lalji R, Francis A, Johnson D, Wong G. Video Presentation at ANZSN 2020 – 'Factors associated with allograft loss in Australian and New Zealand Paediatric Kidney Transplant Patients.'

3. Lalji R, Francis A, Wong G et al, Video Presentation at ASN Kidney Week 2020 'Disparities in end-stage kidney disease care for children: a global survey.'

4. Lalji R, Francis A, Wong G, et al. Disparities in end-stage kidney disease care for children: a global survey. Kidney Int. 98(3):527-32, 2020

5. Lalji R, Francis A, Johnson DW, McCulloch M. Health disparities in access to kidney replacement therapy amongst children and adolescents with end-stage kidney disease in low- and lower-middle-income countries. Kidney Int. 2020;97(3):463-465.