



## RACP Foundation Research Awards

### FINAL REPORT

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|--|--|-----------------|
| <b>Project Title</b>                   | Improving the long term outcomes of children with chronic kidney disease |                 |
| <b>Name</b>                            | Dr Anna Francis  |                 |
| <b>Award Received</b>                  | 2017 Jacquot Research Entry Scholarships in Nephrology                   |                 |
| <b>Report Date</b>                     | 9 February 2018  |                 |
| <b>Chief Investigator / Supervisor</b> | Associate Professor Germaine Wong  |                 |
| <b>Administering Institution</b>       | The University of Sydney   |                 |
| <b>Funding Period</b>                  | Start Date:  | 1 February 2017 |
|  | Finish Date:   | 1 February 2018 |

#### PROJECT SUMMARY

Chronic kidney disease (CKD) or end stage kidney disease (ESKD) in children is a health issue for their entire life span. ESKD is a devastating illness associated with increased mortality, and substantial health and psychosocial impact in children. The overall annual mortality rate for children with ESKD is around 30 times higher than the age matched general population. Long term medical and psychosocial morbidity is also well recognised. Large knowledge gaps impair our ability to stratify risk factors for long-term health outcomes and target interventions to modify these outcomes.

The proposed programme of work will identify risk factors and will inform treatment decisions in order to deliver personalised care to improve morbidity and mortality for this vulnerable group of children

#### PROJECT AIMS / OBJECTIVES

Project 1. Medical complications of kidney transplantation during childhood

Cancer is a well-recognised complication of kidney transplantation. In addition, some causes of end stage kidney disease can recur in the transplanted kidney, for example focal segmental glomerulosclerosis (FSGS).

Paper 1: Incidence and predictors of cancer following kidney transplantation in childhood (published)

Aim: To determine the overall and cause-specific incidence of cancer, standardised incidence ratios and time to first cancer and in children with kidney transplants.

Paper 2: The incidence and predictors of post-transplant lymphoproliferative disease after kidney transplantation (published)

Aim: To describe the differences between long-term incidence and risk factors for PTLD between adult and paediatric renal transplant recipients

Paper 3: The incidence and predictors of death after post transplant lymphoproliferative disease (to be completed 2018)

Aim: To describe the incidence and risk factors for mortality after PTLD

Paper 4: Long-Term Outcome of Kidney Transplantation in Recipients with Focal Segmental Glomerulosclerosis (published)

Aim: To describe the incidence of recurrent FSGS and the risk of graft loss after recurrence

Publications:

- Francis A, Johnson DW, Craig JC, Wong G Incidence and predictors of cancer following kidney transplantation in childhood, American Journal of Transplantation, 2017 Oct;17(10):2650-2658. doi:10.1111/ajt.14289
- Francis A, Johnson DW, Teixeira-Pinto A, Craig JC, Wong G The incidence and predictors of post-transplant lymphoproliferative disease after kidney transplantation during adulthood and childhood: a registry study, Nephrol Dial Transplant. 2018 Jan 12. doi: 10.1093/ndt/gfx356
- Francis A, Trnka P, McTaggart S Long-Term Outcome of Kidney Transplantation in Recipients with Focal Segmental Glomerulosclerosis. Clinical Journal of the American Society of Nephrology. 2016 Nov 7;11(11):2041-2046.

Project 2. Health-related quality of life in children with chronic kidney disease

Paper 5: The impact of chronic kidney disease (CKD) health-related quality of life of children and adolescents (In progress)

Aim: To compare overall health-related quality of life (HR-QoL) and severity of disability in children and adolescents with different stages of CKD and investigate risk factors for lower QoL scores

Plan: to be completed in 2018

Project 3. Transition to adult care

Paper 6: Transition to adult care for young people with chronic kidney disease (published)

Aim: To determine the effectiveness of transition programmes in young people

Publication:

Francis A, Johnson DW, Craig JC, Wong G Moving on: transitioning young people with chronic kidney disease to adult care, accepted June 13 2017 Pediatric Nephrology

## **SIGNIFICANCE AND OUTCOMES**

These proposals will generate information on long-term medical and psychosocial outcomes for children with chronic kidney disease and the risk factors for these outcomes. Better understanding of predictors and risk profiles for long-term adverse health and psychosocial outcomes will allow us to apply personalised patient-centred management to ameliorate these adverse consequences. This will allow us to achieve better health and life outcomes for children with chronic kidney disease. The anticipated outcomes of the research are discussed below for the three project areas.

1. Medical complications of transplantations, with particular focus on cancer and disease recurrence.

Defining the long-term risk of cancer in paediatric kidney transplant recipients informs the consent process. In Incidence and predictors of cancer following kidney transplantation in childhood I have provided the best current estimate of the long-term incidence and site-specific incidence of cancer after kidney transplantation. In subsequent papers, focusing on mortality and graft loss after PTLD, we aim to identify risk factors for mortality, which will allow individualized education and care. In addition, we aim to investigate whether developing PTLD is associated with a long term increased risk of mortality and graft loss, when compared to transplant recipients who do not develop PTLD.

In Long term outcome of kidney transplantation in recipients with focal segmental glomerulosclerosis, we show that children with a live donor have improved graft outcomes. This work aims to change current practice in the allocation of living donor kidney transplants for patients with FSGS.

Currently, many paediatric centres avoid living donor transplant for FSGS, but in this large registry analysis, we show that long-term graft survival is improved with the use of living donor kidneys. We also provided the best current estimate of the risk of recurrent FSGS for children with kidney transplants.

2. CKD and quality of life

Addressing the social determinants of health is a primary approach to achieving health equity. This paper will examine the health-related quality of life in children with CKD and examine the interplay with socio-economic factors. This will allow us to identify high-risk groups.

Understanding and expanding the knowledge base of how social and economic factors may affect health outcomes in children with CKD is critical to influence program and policy activities, build partnership between government and healthcare workers, and to develop tailored interventions that target resource distribution to eliminate health disparities.

3. Transition to adult care for children with CKD

Advances in the care of children mean that adolescents with chronic kidney disease (CKD) are surviving to adulthood and requiring transition to adult care. Moving on: transitioning young people with chronic kidney disease to adult care highlights the need for further quality research into transition to adult care.

## **PUBLICATIONS / PRESENTATIONS**

Francis A, Johnson DW, Teixeira-Pinto A, Craig JC, Wong G, Incidence and predictors of post-transplant lymphoproliferative disease after kidney transplantation during childhood and adulthood: a registry study, *Nephrology Dialysis Transplantation*, Accepted Dec 2017, DOI: 10.1093/ndt/gfx356

Francis A, Johnson DW, Craig JC, Wong G, Moving on: transitioning young people with chronic kidney disease to adult care, *Pediatric Nephrology*. Accepted June 2017, DOI: 10.1007/s00467-017-3728-y

Francis A, Johnson DW, Craig JC, Wong G Incidence and predictors of cancer following kidney transplantation in childhood, *American Journal of Transplantation*, 2017 Oct;17(10):2650-2658. doi: 10.1111/ajt.14289.

Francis A, Trnka P, McTaggart S Long-Term Outcome of Kidney Transplantation in Recipients with Focal Segmental Glomerulosclerosis. *Clinical Journal of the American Society of Nephrology*. 2016 Nov 7;11(11):2041-2046.