CHAPTER 12

Paediatric Patients with End Stage Kidney Disease Requiring Renal Replacement Therapy

As well as a summary of current trends in the frequency and causes of ESKD in paediatrics, this report focuses specifically on current trends in the epidemiology and outcomes of paediatric transplantation

Contents

Executive Summary 3
Suggested Citation 3
Incidence and Prevalence 4
Primary Renal Disease 5
Modality of Treatment 5
Paediatric Assessment 6
Transplantation 8
Donor and Transplant Characteristics 8
Immunosuppression 11
Transplant Outcomes 14
Rejection 15
References 15

Executive Summary

The incidence of treated end stage kidney disease (ESKD) in patients under 18 years in both Australia and New Zealand fluctuates considerably from year to year, but the overall trend over the past 20 years is stable. The prevalent population of treated EKSD in Australia has increased over this time frame, which is a trend seen across all paediatric and adolescent age groups. No clear trend for prevalence is evident for New Zealand.

Over the past 6 years, peritoneal dialysis was the most common initial renal replacement therapy for both children under 10 years of age (57% of incident patients) and children aged 10-17 years (44%). A higher percentage of older children commenced haemodialysis as their initial renal replacement therapy compared to younger children (36% vs 24%). Over this time frame pre-emptive transplant was achieved for 20% of older patients, and 19% of younger patients. Overall prevalence of a functioning transplant at the treatment for ESKD in children was 84% at the time of the 2019 survey in Australia and New Zealand.

In 2019, those on peritoneal dialysis or with a functioning transplant were more likely to attend unmodified schooling compared with those on haemodialysis. Body mass index was evaluated for the 2019 survey using age-adjusted z-scores, which demonstrates a higher prevalence of obesity in the young Australian transplant population versus the dialysis treated group.

This year, as well as providing a summary of current trends in the frequency and causes of ESKD, the paediatric report will focus on current trends in the epidemiology and outcomes of paediatric transplantation.

Suggested Citation

ANZDATA Registry. 43rd Report, Chapter 12: Paediatric Patients with End Stage Kidney Disease Requiring Renal Replacement Therapy. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2020. Available at: http://www.anzdata.org.au

Incidence and Prevalence

The definition of *paediatric* used throughout this chapter is any patient below 18 years of age (at the time of commencing renal replacement therapy (RRT) for incident data, or at the time of the annual survey (31 December 2019) for prevalent data). It is acknowledged that some of these patients may have been receiving their care in adult renal units, and some patients treated in paediatric units who are aged 18 years or older will not be included.

Population estimates for Australia and New Zealand used throughout this chapter for the calculation of incidence per million population were sourced from the Australian Bureau of Statistics (2019)[1] and Stats NZ (2019)[2], respectively.

Figure 12.1 shows the annual incidence of RRT for end stage kidney disease (ESKD) per million age matched population. There is no clear long-term trend in the incidence of RRT in children and adolescents in either Australia or New Zealand. The small absolute numbers of incident patients produce large year to year fluctuations.

Figure 12.1.1 - Incidence of RRT - Age 0-17 Years – Australia

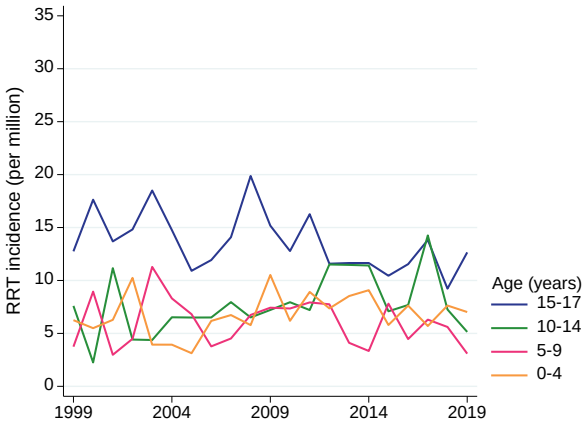
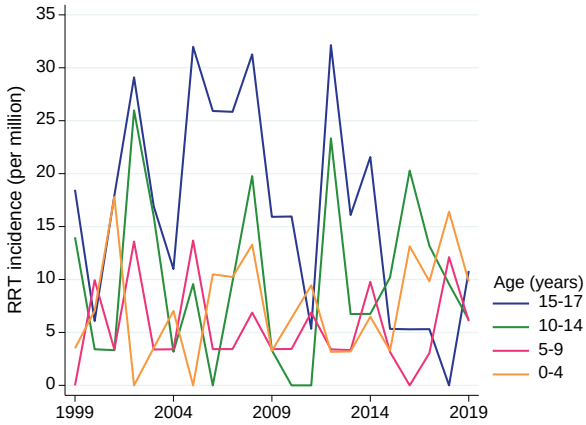


Figure 12.1.2 - Incidence of RRT - Age 0-17 Years - New Zealand



In Australia the prevalent numbers of treated ESKD have gradually increased for older paediatric age groups (figure 12.2); the trends are less clear in New Zealand.

Figure 12.2.1 - Prevalence of RRT - Age 0-17 Years – Australia

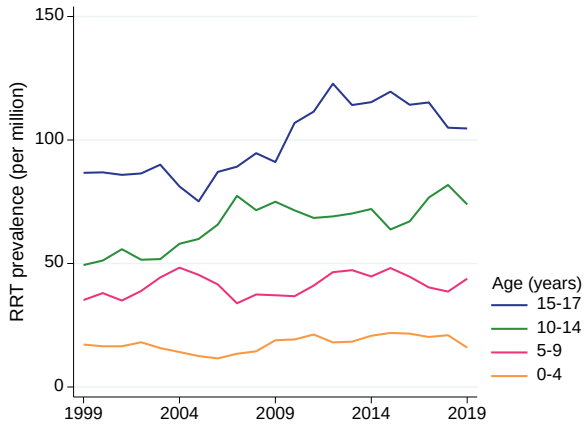
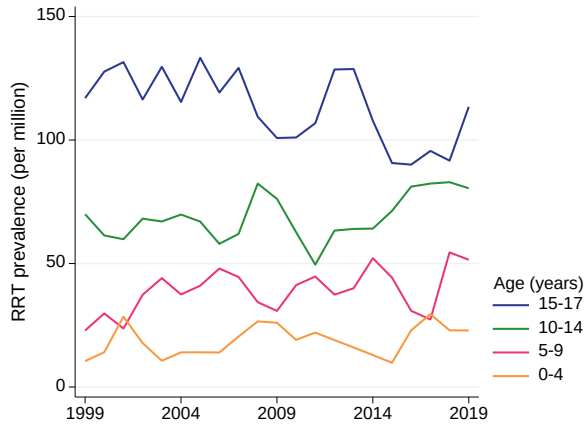


Figure 12.2.2 - Prevalence of RRT - Age 0-17 Years - New Zealand



Primary Renal Disease

Collectively, congenital abnormalities of the kidney and urinary tract (CAKUT) are a predominant cause of ESKD in younger children, with a large percentage of children also having miscellaneous or 'other' conditions documented as their primary renal disease. Glomerulonephritis is the most common single cause of ESKD in adolescents.

Please note that primary renal disease coding in ANZDATA is currently based on a legacy classification system derived from historical European Renal Association/European Dialysis and Transplantation Association classifications. The Registry recognises that in some cases, these diagnoses have failed to keep up to date with an evolving understanding of renal pathology, particularly in the categorisation of glomerulonephritis and inherited conditions. Work is currently underway to review and revise this classification system.

Table 12.1 Primary Renal Disease, Incident Patients Australia and New Zealand 2014-2019

Primary renal disease	0-4	5-10	10-14	15-17	Total
GN	4 (5%)	14 (20%)	22 (21%)	22 (29%)	**62 (18%)**
- FSGS	2 (2%)	11 (16%)	10 (9%)	8 (10%)	**31 (9%)**
Familial GN	-	-	2 (2%)	-	**2 (1%)**
Reflux Nephropathy	-	3 (4%)	7 (7%)	2 (3%)	**12 (4%)**
Polycystic Kidney Disease	6 (7%)	3 (4%)	3 (3%)	2 (3%)	**14 (4%)**
Medullary Cystic Disease	1 (1%)	8 (11%)	7 (7%)	3 (4%)	**19 (6%)**
Posterior Urethral Valve	11 (13%)	6 (9%)	6 (6%)	4 (5%)	**27 (8%)**
Haemolytic Uraemic Syndrome	-	-	4 (4%)	-	**4 (1%)**
Hypoplasia/Dysplasia	20 (23%)	8 (11%)	19 (18%)	7 (9%)	**54 (16%)**
Diabetes	-	-	-	1 (1%)	**1 (0%)**
Cortical Necrosis	-	1 (1%)	3 (3%)	-	**4 (1%)**
Interstitial Nephritis	-	-	-	1 (1%)	**1 (0%)**
Cystinosis	-	1 (1%)	1 (1%)	2 (3%)	**4 (1%)**
Uncertain	3 (3%)	-	3 (3%)	6 (8%)	**12 (4%)**
Misc/Other	40 (46%)	14 (20%)	19 (18%)	17 (22%)	**90 (26%)**
Not reported	-	1 (1%)	1 (1%)	2 (3%)	**4 (1%)**
Total	**87**	**70**	**107**	**77**	**310**

Modality of Treatment

The modality of the first renal replacement treatment for incident patients is shown in table 12.2. Although numbers are small and therefore fluctuate from year to year, around 15-20% of children and adolescents receive pre-emptive kidney transplants. Of the remainder, peritoneal dialysis (PD) is the more common initial dialysis modality. A higher percentage of older children commence on haemodialysis compared to younger children.

Table 12.2 Modality of Initial Renal Replacement Therapy by Year of First Treatment, Australia and New Zealand

Age group	2014	2015	2016	2017	2018	2019	Total
0-9 Years	**24**	**23**	**23**	**23**	**30**	**21**	**144**
HD	6 (25%)	5 (22%)	5 (22%)	9 (39%)	7 (23%)	3 (14%)	**35 (24%)**
PD	17 (71%)	11 (48%)	15 (65%)	11 (48%)	14 (47%)	14 (67%)	**82 (57%)**
Transplant	1 (4%)	7 (30%)	3 (13%)	3 (13%)	9 (30%)	4 (19%)	**27 (19%)**
10-17 Years	**32**	**23**	**28**	**38**	**22**	**23**	**166**
HD	10 (31%)	6 (26%)	14 (50%)	15 (39%)	6 (27%)	8 (35%)	**59 (36%)**
PD	14 (44%)	11 (48%)	11 (39%)	16 (42%)	10 (45%)	11 (48%)	**73 (44%)**
Transplant	8 (25%)	6 (26%)	3 (11%)	7 (18%)	6 (27%)	4 (17%)	**34 (20%)**
Total	**56**	**46**	**51**	**61**	**52**	**44**	**310**

For prevalent patients (table 12.3), a very different pattern is seen, with the great majority of children and adolescents receiving renal replacement therapy for ESKD having a functioning transplant (84% in 2019). This reflects the relatively high rate of transplantation among children.

Table 12.3 Modality of Prevalent Patients by Year of Treatment, Australia and New Zealand

Current treatment	2014	2015	2016	2017	2018	2019
HD	21 (6%)	19 (5%)	27 (8%)	23 (6%)	22 (6%)	15 (4%)
PD	48 (13%)	42 (12%)	53 (15%)	54 (15%)	46 (12%)	45 (12%)
Transplant	289 (81%)	295 (83%)	277 (78%)	293 (79%)	310 (82%)	313 (84%)
Total	**358**	**356**	**357**	**370**	**378**	**373**

Paediatric Assessment

The paediatric survey is collected on all children commencing renal replacement therapy before the age of 15 and collection continues until they reach 18 years of age (children aged 15 years and older at time of starting RRT are excluded from the data presented below). This survey records data on height, weight and an assessment of educational participation.

Overall, more children on PD and with functioning transplants attended unmodified school compared with children on haemodialysis (figure 12.3). Note that multiple categories of paediatric assessment have been collapsed into single groups for reporting purposes. 'School – Modified' and 'Left School' include multiple categories (see the survey form for details: (https://www.anzdata.org.au/wp-content/uploads/2020/11/PaediatricForm.pdf)

Figure 12.3.1 - Paediatric Assessment by Age Group and Treatment Modality - Australia 2019

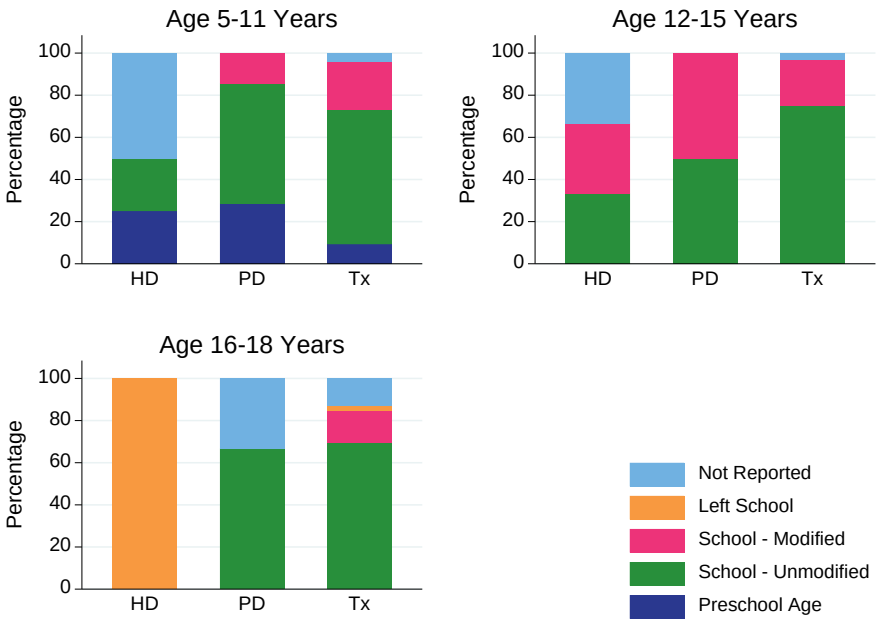
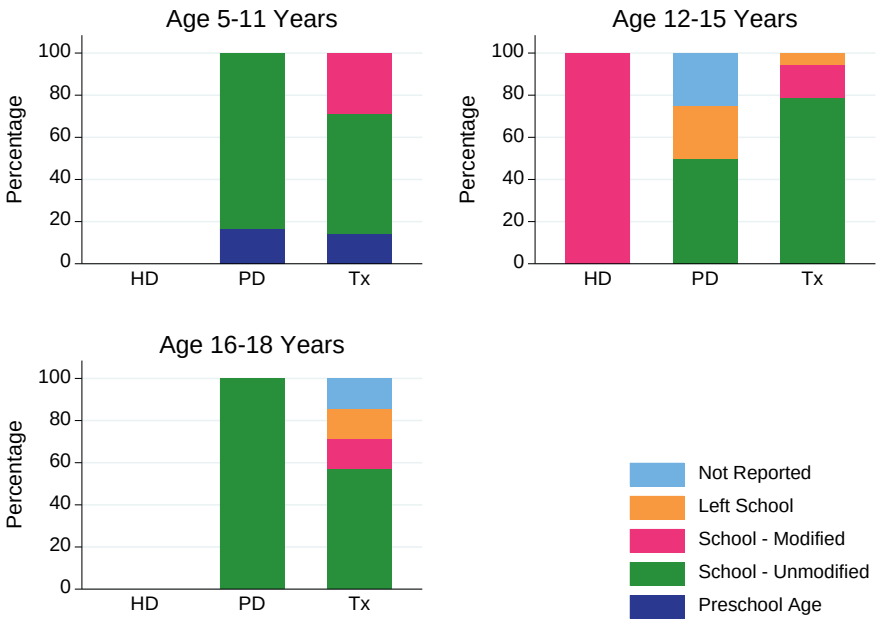


Figure 12.3.2 - Paediatric Assessment by Age Group and Treatment Modality - New Zealand 2019



Paediatric BMI categories are determined using age adjusted z-scores. In Australia, a higher proportion of transplant recipients and haemodialysis patients were overweight or obese, compared with children and adolescents treated with dialysis (figure 12.4). New Zealand data should be interpreted with caution due to low numbers of patients.

Figure 12.4.1 - Body Mass Index of Prevalent Paediatric Patients by Treatment Modality - Australia 2019

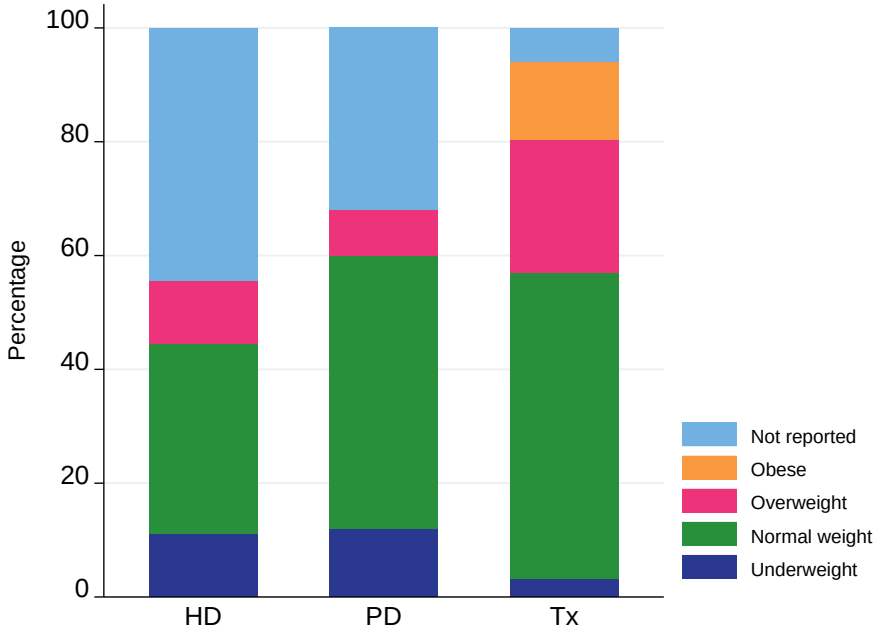
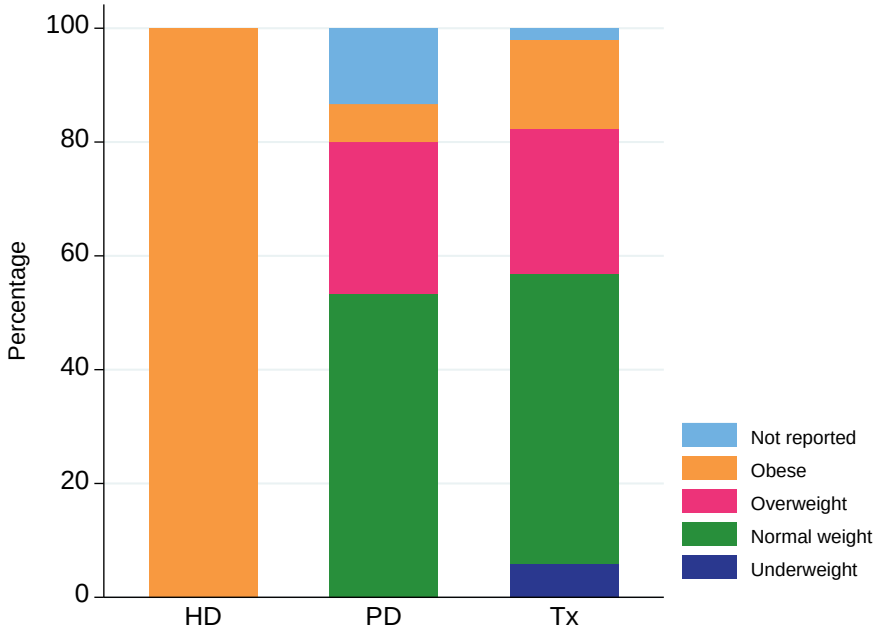


Figure 12.4.2 - Body Mass Index of Prevalent Paediatric Patients by Treatment Modality - New Zealand 2019



Transplantation

Donor and Transplant Characteristics

Figures 12.5-12.8 and tables 12.4-12.5 show the trends in paediatric kidney transplantation over the 12-year period from 2008-2019 including donor source, donor and recipient age by donor type, overall HLA matching, time to transplantation and graft numbers.

Table 12.5 Donor Source by Year, Paediatric Kidney Transplants 2010-2019, Number (% of Transplants)

Donor type	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
LD pre-emptive	10 (23%)	10 (22%)	12 (21%)	8 (17%)	9 (18%)	13 (27%)	6 (17%)	9 (15%)	15 (29%)	7 (16%)
LD not pre-emptive	19 (44%)	10 (22%)	26 (46%)	20 (42%)	18 (36%)	22 (45%)	10 (28%)	20 (34%)	12 (23%)	13 (29%)
DBD	11 (26%)	20 (44%)	17 (30%)	18 (38%)	19 (38%)	12 (24%)	18 (50%)	27 (46%)	17 (33%)	19 (42%)
DCD	3 (7%)	5 (11%)	1 (2%)	2 (4%)	4 (8%)	2 (4%)	2 (6%)	3 (5%)	8 (15%)	6 (13%)
Total	**43**	**45**	**56**	**48**	**50**	**49**	**36**	**59**	**52**	**45**

Table 12.4 Graft Numbers, Paediatric Kidney Transplants 2010-2019 Australia and New Zealand

Graft number	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
1	40	43	55	43	46	48	33	51	49	43
2	3	2	1	5	3	1	3	8	3	2
3	0	0	0	0	1	0	0	0	0	0

Figure 12.5 - Donor Age by Donor Source, Paediatric Kidney Transplants 2008-2019

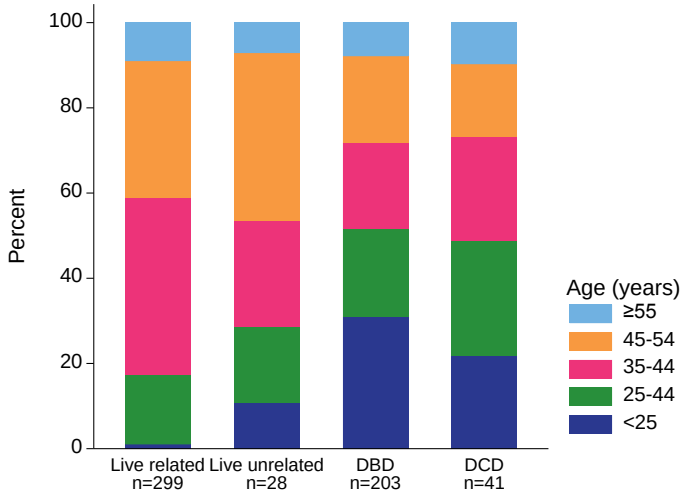


Figure 12.6 - Recipient Age by Donor Source, Paediatric Kidney Transplants 2008-2019

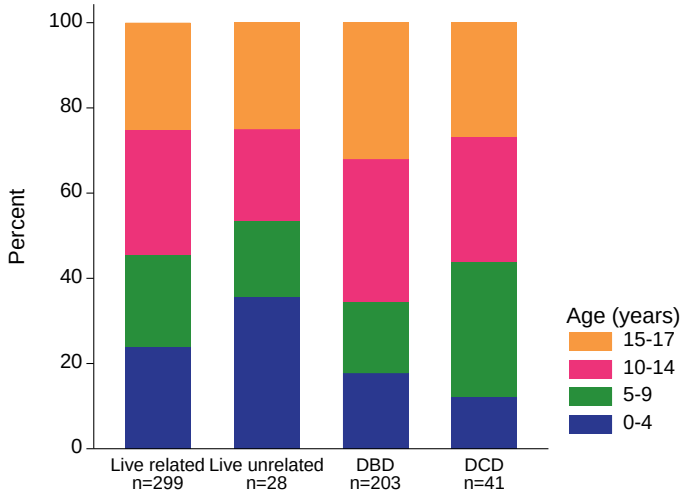


Figure 12.7 - Time to First Kidney Transplant, Paediatric Kidney Transplants 2008-2019

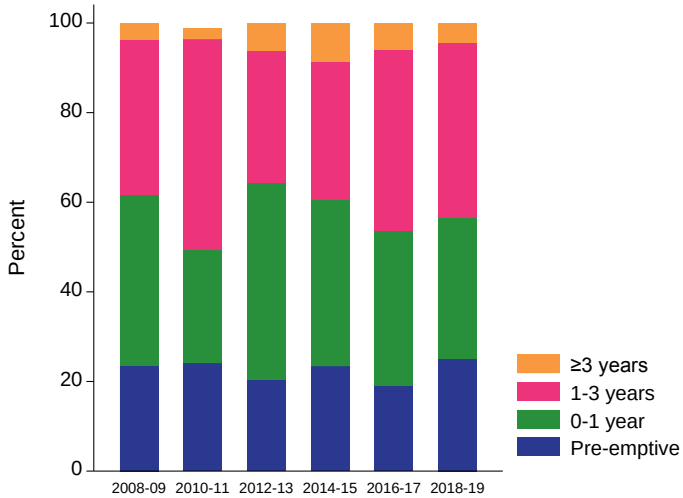
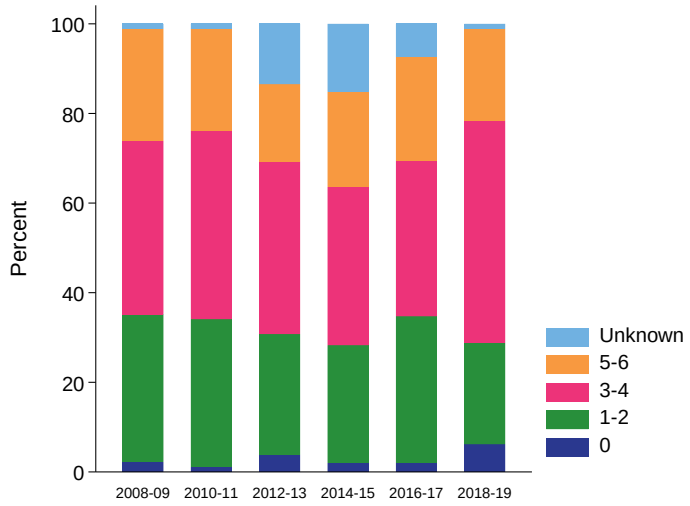


Figure 12.8 - Number of HLA Mismatches, Paediatric Kidney Transplants 2008-2019



Immunosuppression

The majority of patients in both countries receive induction antibody therapy with anti-CD25 agents (table 12.6).

Table 12.6 Antibody Use for Induction Immunosuppression in Paediatric Kidney Transplants, Number Receiving (%)

Country	Type of agent	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Australia	Intravenous immunoglobulin	0 (0.0%)	2 (4.9%)	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)
	Anti-CD25	35 (92.1%)	37 (90.2%)	42 (91.3%)	40 (93.0%)	44 (95.7%)	33 (80.5%)	25 (83.3%)	52 (96.3%)	44 (97.8%)	28 (84.8%)
	Rituximab	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)
	T cell depleting polyclonal Ab	2 (5.3%)	2 (4.9%)	1 (2.2%)	1 (2.3%)	1 (2.2%)	3 (7.3%)	1 (3.3%)	1 (1.9%)	0 (0.0%)	1 (3.0%)
	Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)
	Not reported	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	3 (10.0%)	1 (1.9%)	0 (0.0%)	3 (9.1%)
	Total new transplants	**38**	**41**	**46**	**43**	**46**	**41**	**30**	**54**	**45**	**33**
New Zealand	Intravenous immunoglobulin	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Anti-CD25	1 (20.0%)	4 (100.0%)	10 (100.0%)	5 (100.0%)	4 (100.0%)	8 (100.0%)	6 (100.0%)	5 (100.0%)	7 (100.0%)	8 (66.7%)
	Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	T cell depleting polyclonal Ab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Not reported	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (33.3%)
	Total new transplants	**5**	**4**	**10**	**5**	**4**	**8**	**6**	**5**	**7**	**12**

Tacrolimus is the most commonly used calcineurin inhibitor (CNI) at induction and at 1, 5- and 10-years post-transplant and mTOR inhibitor use is uncommon in paediatric transplant recipients (figures 12.9-12.12).

Figure 12.9 - Calcineurin and mTOR Inhibitors at Induction – Paediatric Kidney Transplant Cohorts 2008-2019

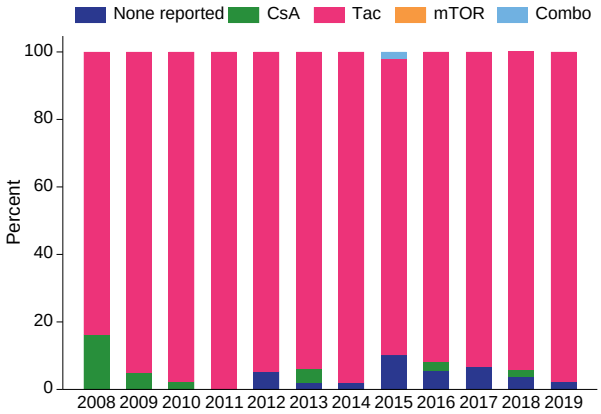


Figure 12.10 - Calcineurin and mTOR Inhibitors at One Year - Paediatric Kidney Transplant Cohorts 2008-2018

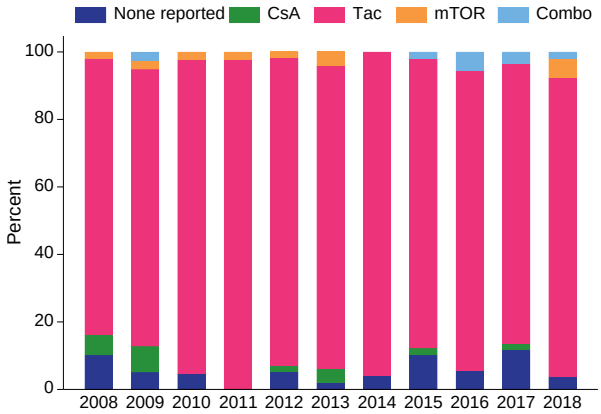


Figure 12.11 - Calcineurin and mTOR Inhibitors at Five Years – Paediatric Kidney Transplant Cohorts 2008-2014

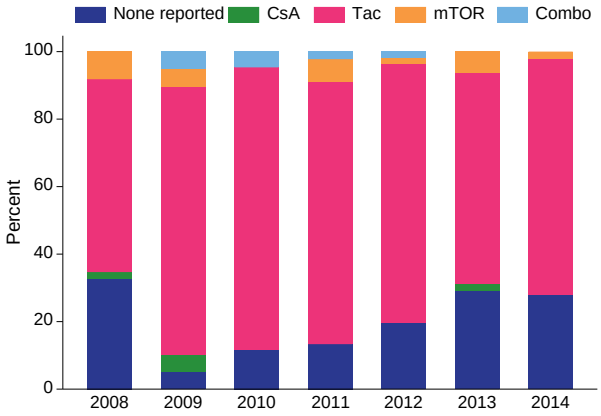
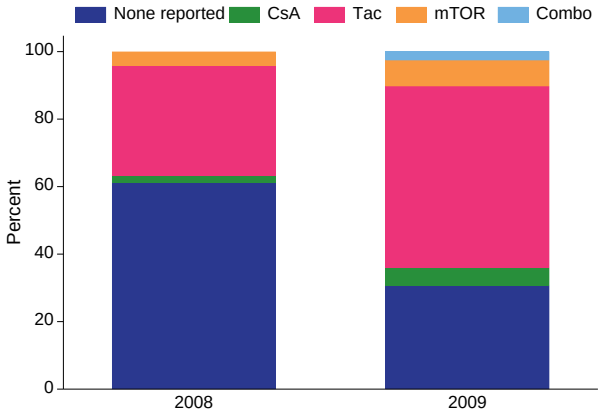


Figure 12.12 - Calcineurin and mTOR Inhibitors at Ten Years – Paediatric Kidney Transplant Cohorts 2008-2009



Mycophenolate is the most commonly used antimetabolite at induction and long-term use has increased over time, with only a small proportion of patients treated with azathioprine (figures 12.13-12.16).

Figure 12.13 - Antimetabolites at Induction - Paediatric Kidney Transplant Cohorts 2008-2019'

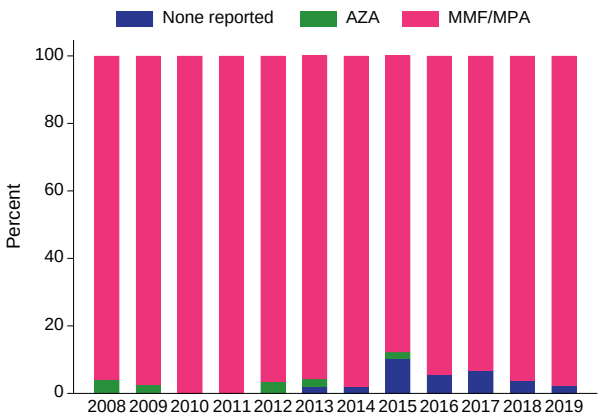


Figure 12.14 - Antimetabolites at One Year - Paediatric Kidney Transplant Cohorts 2008-2018

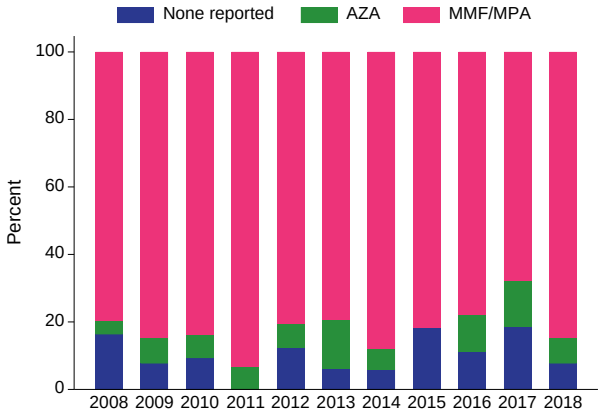


Figure 12.15 - Antimetabolites at Five Years - Paediatric Kidney Transplant Cohorts 2008-2014

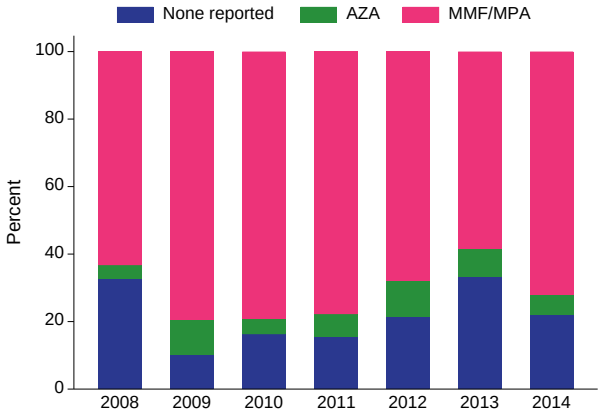


Figure 12.16 - Antimetabolites at Ten Years - Paediatric Kidney Transplant Cohorts 2008-2009

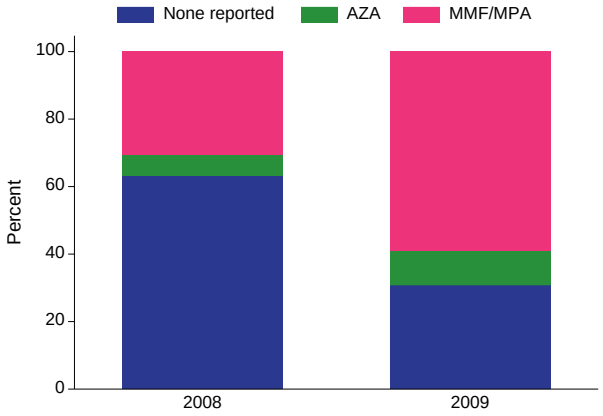
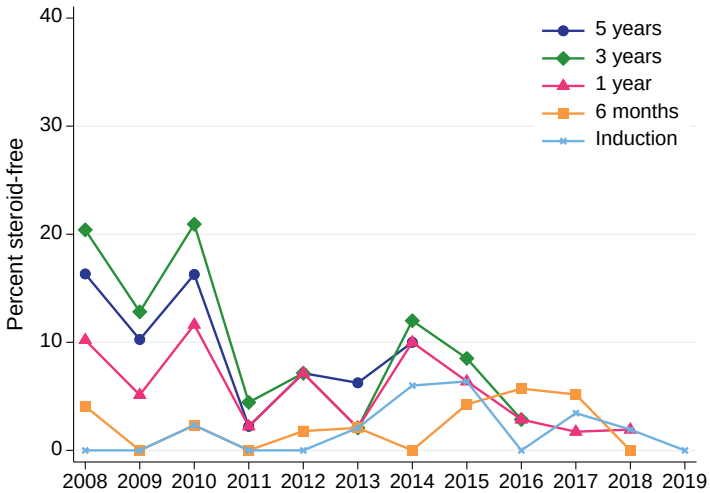


Figure 12.17 - Steroid-Free Fraction – Paediatric Kidney Transplant Cohorts 2008-2019



Transplant Outcomes

Graft and patient survival for grafts performed in Australia and New Zealand on recipients aged <18 years, calculated by the Kaplan-Meier method, are shown in table 12.7. Unadjusted one, three- and five-year patient survival have remained relatively stable over the past ten years, with graft survival improving after the 2008-09 cohort.

Table 12.7 Patient and Graft Survival (95% CI), Paediatric Kidney Transplant Recipients 2010-2019

Outcome	Transplant year (N)	6 months	1 year	3 years	5 years
Patient Survival	**2010-11 (n=88)**	100	99 (92-100)	99 (92-100)	99 (92-100)
	2012-13 (n=104)	99 (93-100)	99 (93-100)	98 (93-100)	98 (93-100)
	2014-15 (n=99)	100	100	100	100
	2016-17 (n=95)	99 (93-100)	99 (93-100)	99 (93-100)	-
	2018-19 (n=97)	100	100	-	-
Graft Survival	**2010-11 (n=88)**	100	98 (91-99)	94 (87-98)	93 (85-97)
	2012-13 (n=104)	99 (93-100)	98 (93-100)	93 (86-97)	88 (80-93)
	2014-15 (n=99)	97 (91-99)	97 (91-99)	93 (86-97)	87 (78-92)
	2016-17 (n=95)	97 (90-99)	97 (90-99)	97 (90-99)	-
	2018-19 (n=97)	99 (93-100)	99 (93-100)	-	-

The causes of graft loss by age at transplant and age at graft loss are shown in tables 12.8 and 12.9 respectively. The Registry is in the process of revising the reportable causes of graft loss and the historical term 'chronic allograft nephropathy' will be replaced with more specific terminology in future data collection.

Table 12.8 Cause of Graft Loss, Paediatric Kidney Transplants Performed 2010-2019 by Age at Transplant

Cause of graft loss	0-4	5-9	10-14	15-17	Total
Death with function	1	2	0	2	**5**
Acute rejection	0	2	1	5	**8**
Chronic allograft nephropathy	1	1	5	3	**10**
Vascular	0	0	2	2	**4**
Technical	0	1	0	0	**1**
Glomerulonephritis	0	1	1	5	**7**
Non-compliance	0	0	3	5	**8**
Other	2	0	2	0	**4**
Not reported	0	0	2	2	**4**
Total	**4**	**7**	**16**	**24**	**51**

Table 12.9 Cause of Graft Loss, Paediatric Kidney Transplants Performed 2010-2019 by Age at Graft Loss

Cause of graft loss	0-4	5-9	10-14	15-17	Total
Death with function	1	1	1	1	**4**
Acute rejection	0	0	2	5	**7**
Chronic allograft nephropathy	0	1	1	5	**7**
Vascular	0	0	2	2	**4**
Technical	0	0	1	0	**1**
Glomerulonephritis	0	0	1	2	**3**
Non-compliance	0	0	0	5	**5**
Other	0	0	3	0	**3**
Not reported	0	0	0	1	**1**
Total	**1**	**2**	**11**	**21**	**35**

Rejection

The proportion of patients experiencing at least one episode of acute rejection (biopsy proven or clinically diagnosed) in the first six months post-transplant has remained low (figure 12.18). The proportion experiencing rejection between 6-24 months post-transplant has remained largely unchanged for cohorts since 2010 (figure 12.19). The majority of rejection episodes reported to the registry are cellular rejection (table 12.10).

Figure 12.18 - Rejection <6 Months Post-Transplant – Paediatric Kidney Transplant Cohorts 2010-2018

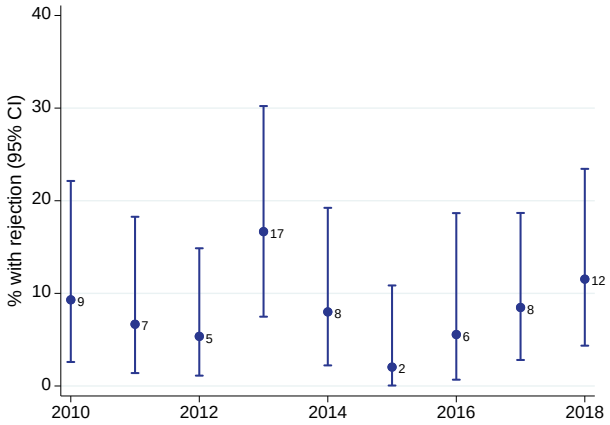


Figure 12.19 - Rejection 6-24 Months Post-Transplant – Paediatric Kidney Transplant Cohorts 2010-2016

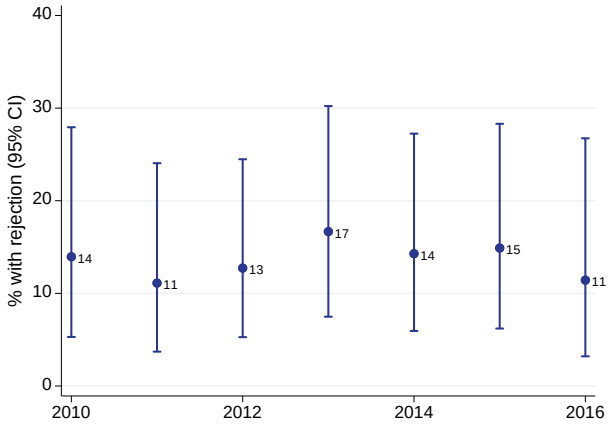


Table 12.10 Type of Rejection, Paediatric Kidney Transplants 2010-2018

Timing of rejection	Type of rejection	2010	2011	2012	2013	2014	2015	2016	2017	2018
<6 months	No biopsy	3	2	0	1	0	0	0	1	0
	Cellular	3	3	2	7	4	1	4	3	5
	ABMR	1	0	0	1	0	0	0	0	1
	Cellular + ABMR	0	0	0	0	0	0	0	3	1
6-24 months	No biopsy	1	0	0	1	0	0	0	-	-
	Cellular	6	2	9	11	8	8	5	-	-
	ABMR	0	1	0	1	0	0	0	-	-
	Cellular + ABMR	2	0	3	1	1	2	0	-	-

ABMR - antibody-mediated rejection

References

[1] *Australian Bureau of Statistics, 2019, Australian Demographic Statistics, Jun 2019, time series spreadsheets, cat. no. 3101.0, viewed 19 Dec 2019, https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3101.0Jun%202019?OpenDocument*

[2] *This work is based on/includes Stats NZ's data which are licensed by Stats NZ for re-use under the Creative Commons Attribution 4.0 International licence. Stats NZ, 2019, Estimated Resident Population by Age and Sex (1991+) (Annual-Jun), NZ Infoshare, viewed 19 Dec 2019, http://archive.stats.govt.nz/infoshare/SelectVariables.aspx?pxID=782e8afc-96ab-49e7-bb65-994c51b2e715*