CHAPTER 11

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

The incidence of treated 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.

For the past 6 years those under 10 years of age were likely to have initially commenced peritoneal dialysis as their initial ESKD treatment modality, whereas older children were more likely to have commenced haemodialysis. Over this time frame pre-emptive transplant was achieved for 20% of older patients, and 15% of younger patients. Overall prevalence of a functioning transplant for ESKD was 80% at the time of the 2017 survey in Australia and New Zealand.

In 2017, 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 2017 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

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Incidence and Prevalence

The definition of paediatric used throughout this chapter is any patient below 18 years of age (at time of commencing renal replacement therapy (RRT) for incident data, or at time of survey (31 December 2017) 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.

Figure 11.1 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 11.1.1 - Incidence of RRT - Age 0-17 Years – Australia

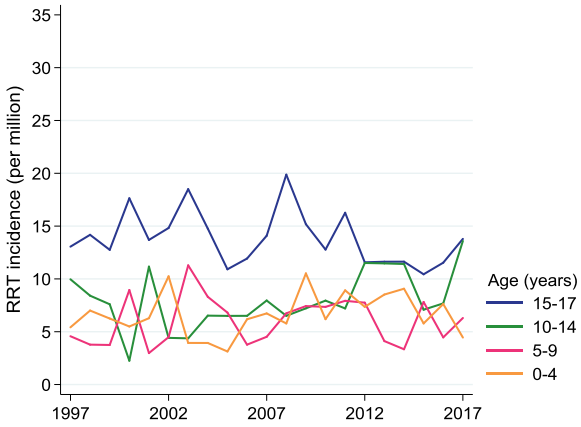
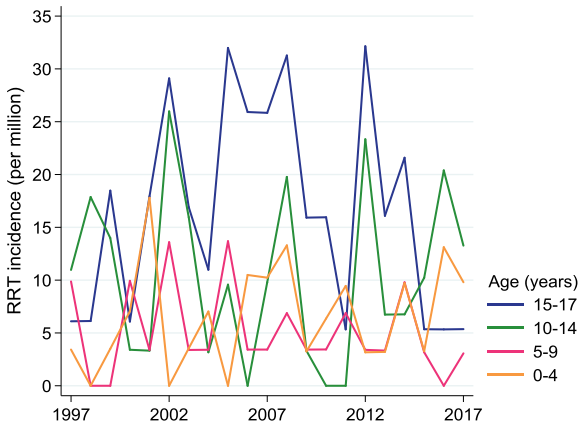


Figure 11.1.2 - Incidence of RRT - Age 0-17 Years - New Zealand



In Australia the prevalent numbers of treated ESKD have gradually increased across all age groups (figure 11.2); the trends are less clear in New Zealand.

Figure 11.2.1 - Prevalence of RRT - Age 0-17 Years - Australia

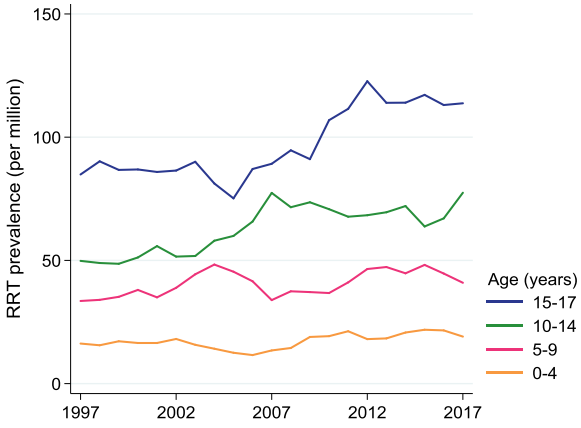
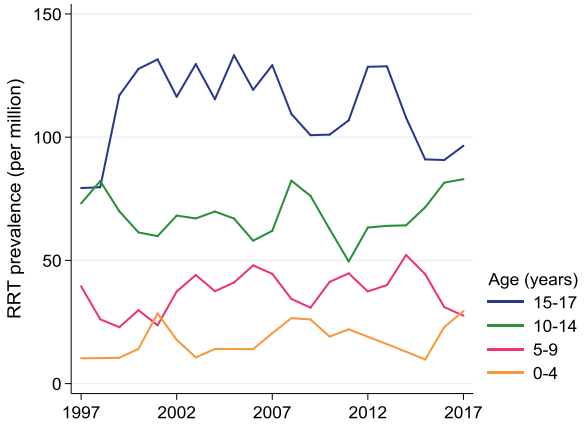


Figure 11.2.2 - Prevalence of RRT - Age 0-17 Years - New Zealand



Primary Renal Disease

Collectively, congenital abnormalities of the kidney and urinary tract (CAKUT) are the predominant cause of ESKD in younger children, with glomerulonephritis being the most common cause in adolescents.

Table 11.1 Primary Renal Disease, Incident Patients Australia and New Zealand 2012-2017

Primary renal disease	0-4	5-10	10-14	15-17	Total
GN	4 (5%)	13 (20%)	25 (20%)	29 (34%)	**71 (20%)**
- FSGS	2 (2%)	8 (12%)	9 (7%)	8 (9%)	**27 (8%)**
Familial GN	3 (4%)	-	2 (2%)	1 (1%)	**6 (2%)**
Reflux Nephropathy	-	3 (5%)	9 (7%)	2 (2%)	**14 (4%)**
Polycystic Kidney Disease	5 (6%)	3 (5%)	3 (2%)	4 (5%)	**15 (4%)**
Medullary Cystic Disease	1 (1%)	6 (9%)	12 (10%)	2 (2%)	**21 (6%)**
Posterior Urethral Valve	12 (15%)	4 (6%)	7 (6%)	4 (5%)	**27 (8%)**
Haemolytic Uraemic Syndrome	-	-	4 (3%)	1 (1%)	**5 (1%)**
Hypoplasia/Dysplasia	22 (27%)	10 (15%)	27 (22%)	5 (6%)	**64 (18%)**
Diabetes	-	-	-	1 (1%)	**1 (0%)**
Cortical Necrosis	-	1 (2%)	2 (2%)	1 (1%)	**4 (1%)**
Cystinosis	-	1 (2%)	-	-	**1 (0%)**
Uncertain	2 (2%)	2 (3%)	1 (1%)	5 (6%)	**10 (3%)**
Misc/Other	30 (37%)	13 (20%)	20 (16%)	20 (24%)	**83 (23%)**
Not reported	-	2 (3%)	1 (1%)	2 (2%)	**5 (1%)**
Total	**81**	**66**	**122**	**85**	**327**

Modality of Treatment

The modality of the first renal replacement treatment is shown in table 11.2. 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, PD is more common in younger patients (<10 years), and for older patients similar numbers start on HD and PD.

Table 11.2 Modality of Initial Renal Replacement Therapy by Year of First Treatment, Australia and New Zealand

Age group	2012	2013	2014	2015	2016	2017	Total
0-9 Years	**24**	**21**	**25**	**23**	**23**	**21**	**137**
HD	7 (29%)	5 (24%)	7 (28%)	5 (22%)	5 (22%)	9 (43%)	**38 (28%)**
PD	13 (54%)	14 (67%)	17 (68%)	11 (48%)	15 (65%)	9 (43%)	**79 (58%)**
Transplant	4 (17%)	2 (10%)	1 (4%)	7 (30%)	3 (13%)	3 (14%)	**20 (15%)**
10-17 Years	**39**	**31**	**32**	**23**	**28**	**37**	**190**
HD	16 (41%)	13 (42%)	10 (31%)	6 (26%)	14 (50%)	14 (38%)	**73 (38%)**
PD	15 (38%)	12 (39%)	14 (44%)	11 (48%)	11 (39%)	16 (43%)	**79 (42%)**
Transplant	8 (21%)	6 (19%)	8 (25%)	6 (26%)	3 (11%)	7 (19%)	**38 (20%)**
Total	**63**	**52**	**57**	**46**	**51**	**58**	**327**

For prevalent patients (table 11.3), a very different pattern is seen, with the great majority (80% in 2017) of children and adolescents with a functioning transplant. This reflects the relatively high rate of transplantation among children.

Table 11.3 Modality of Prevalent Patients by Year of Treatment, Australia and New Zealand

Current treatment	2012	2013	2014	2015	2016	2017
HD	29 (8%)	27 (8%)	21 (6%)	19 (5%)	27 (8%)	**23 (6%)**
PD	50 (14%)	47 (13%)	48 (13%)	42 (12%)	53 (15%)	**51 (14%)**
Transplant	275 (78%)	278 (79%)	288 (81%)	293 (83%)	276 (78%)	**295 (80%)**
Total	**354**	**352**	**357**	**354**	**356**	**369**

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 11.3). Note that multiple categories of paediatric assessment have been collapsed into a single group of 'School - Modified' for reporting purposes; see the survey form for details: https://www.anzdata.org.au/wp-content/uploads/2016/10/8PaediatricForm2017.pdf

Paediatric BMI categories are determined using age adjusted z-scores. In Australia, a larger proportion of transplant recipients were overweight or obese, compared with children and adolescents treated with dialysis (figure 11.4). New Zealand data should be interpreted with caution due to low numbers of patients.

Figure 11.3.1 - Paediatric Assessment by Age Group and Treatment Modality - Australia 2017

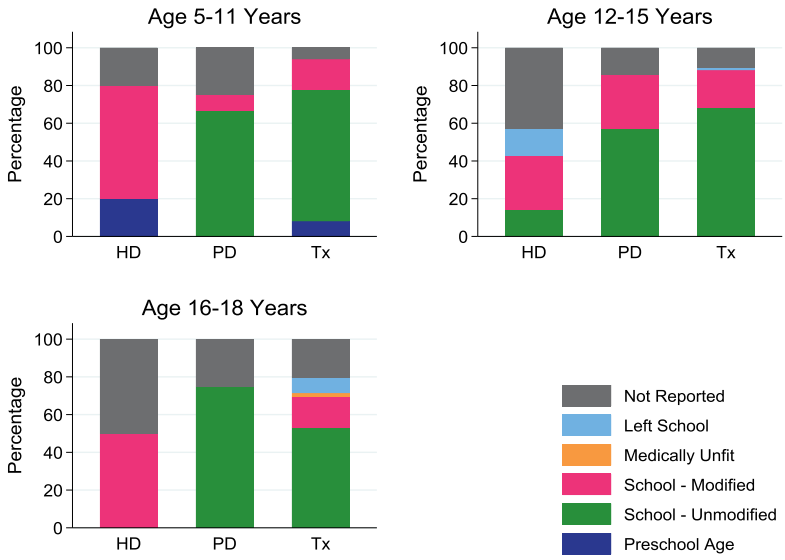


Figure 11.3.2 - Paediatric Assessment by Age Group and Treatment Modality - New Zealand 2017

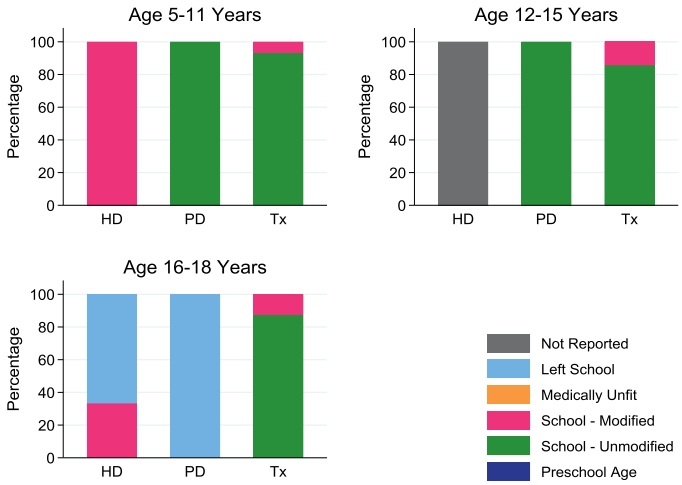


Figure 11.4.1 - Body Mass Index of Prevalent Paediatric Patients by Treatment Modality - Australia 2017

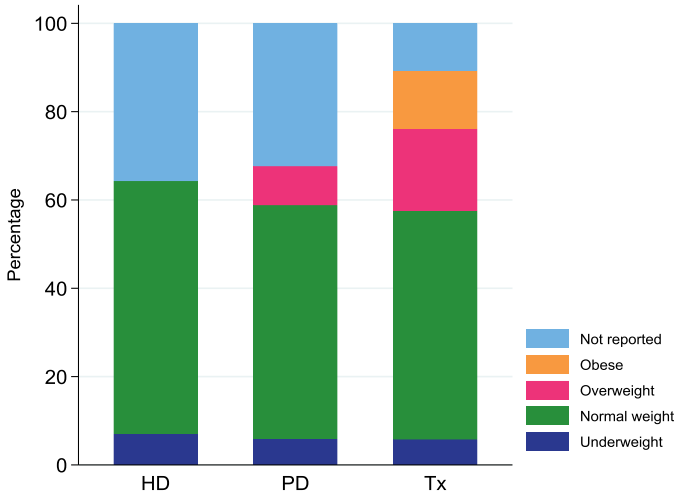
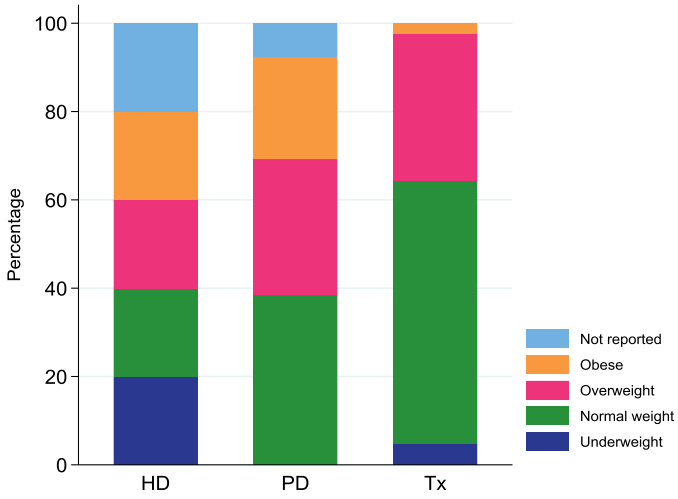


Figure 11.4.2 - Body Mass Index of Prevalent Paediatric Patients by Treatment Modality - New Zealand 2017



Transplantation

Transplant Demographics

Figures 11.5-11.8 and tables 11.4-11.5 show the trends in paediatric transplantation over the 12 year period from 2006-2017.

Approximately 55% of kidneys come from living genetically-related donors; this percentage has remained stable over time. Living donor kidneys (living genetically-related and genetically-unrelated) mostly come from donors aged 35-54 years. In contrast, the proportion of deceased donors aged <25 is higher than for living donors. There are no significant trends in the type of donor according to recipient age. The use of donor after circulatory death (DCD) kidneys in children and adolescents is less common than in adults

The time to first kidney transplant (figure 11.7) has remained largely unchanged over this period. Second transplants during childhood are a rare occurrence.

Figure 11.5 - Donor Age by Donor Source 2006-2017

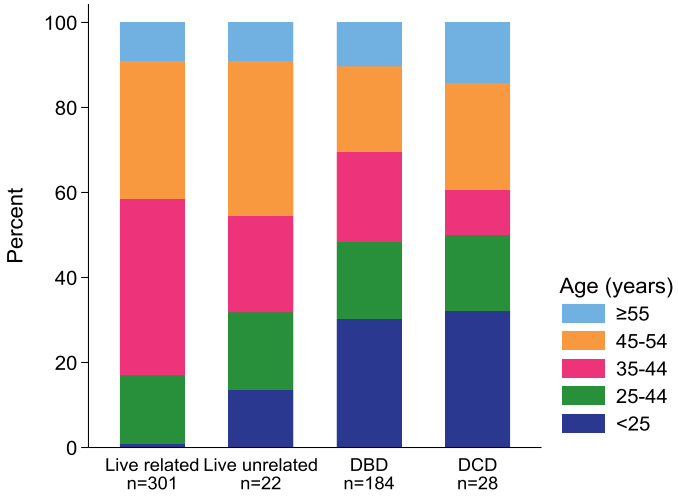


Figure 11.6 - Recipient Age by Donor Source 2006-2017

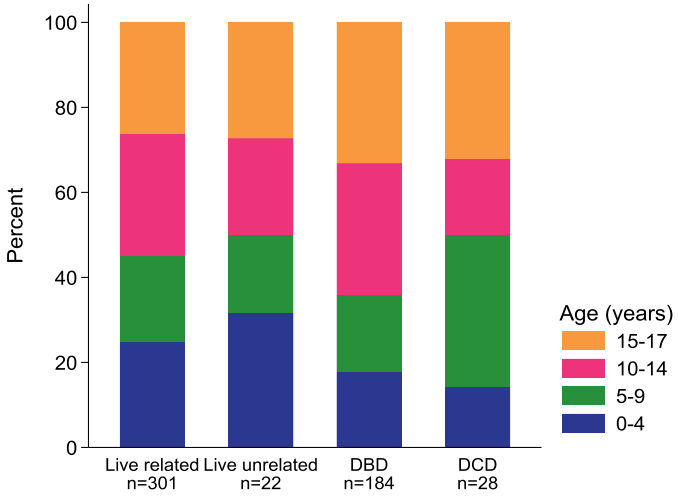


Figure 11.7 - Time to First Kidney Transplant 2006-2017

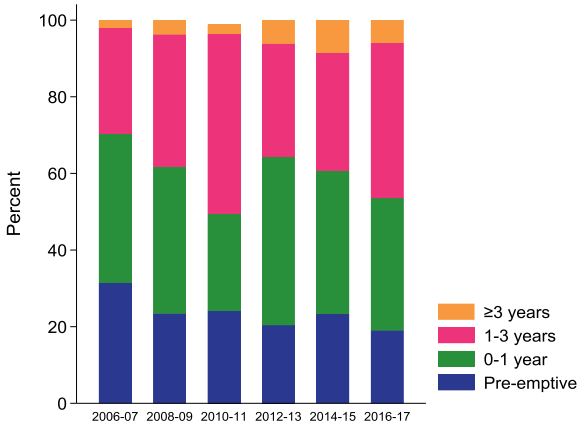


Figure 11.8 - Number of HLA Mismatches 2006-201

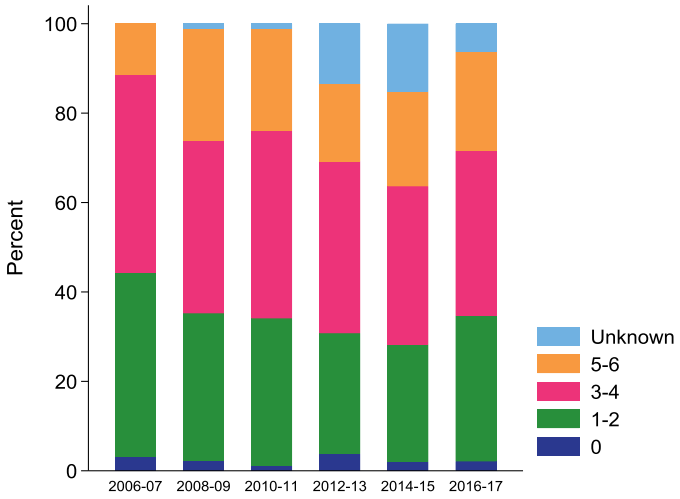


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Table 11.4 Graft Numbers 2008-2017 Australia and New Zealand

Graft number	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
1	45	36	40	43	55	43	46	48	33	51
2	4	3	3	2	1	5	3	1	3	8
3	0	0	0	0	0	0	1	0	0	0

Table 11.5 Donor Source by Year 2008-2017, Number (% of Transplants)

Donor type	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
LD pre-emptive	9 (18%)	9 (23%)	10 (23%)	10 (22%)	12 (21%)	8 (17%)	9 (18%)	13 (27%)	6 (17%)	9 (15%)
LD not pre-emptive	24 (49%)	16 (41%)	19 (44%)	10 (22%)	26 (46%)	20 (42%)	18 (36%)	22 (45%)	10 (28%)	20 (34%)
DBD	13 (27%)	12 (31%)	11 (26%)	20 (44%)	17 (30%)	18 (38%)	19 (38%)	12 (24%)	18 (50%)	27 (46%)
DCD	3 (6%)	2 (5%)	3 (7%)	5 (11%)	1 (2%)	2 (4%)	4 (8%)	2 (4%)	2 (6%)	3 (5%)
Total	**49**	**39**	**43**	**45**	**56**	**48**	**50**	**49**	**36**	**59**

Immunosuppression

The majority of patients in both countries receive induction antibody therapy with anti-CD25 agents (table 11.6).

Tacrolimus is the most commonly used calcineurin inhibitor (CNI) at induction and at 1, 5 and 10 years post-transplant (figures 11.9-11.12).

Table 11.6 Antibody Use for Induction Immunosuppression, Number Receiving (%)

Country	Type of agent	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Australia	Intravenous immunoglobulin	0 (0.0%)	1 (2.9%)	0 (0.0%)	2 (4.9%)	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)
	Anti-CD25	37 (94.9%)	33 (97.1%)	35 (92.1%)	37 (90.2%)	42 (91.3%)	40 (93.0%)	44 (95.7%)	32 (78.0%)	25 (83.3%)	50 (92.6%)
	Rituximab	1 (2.6%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	T cell depleting polyclonal Ab	0 (0.0%)	1 (2.9%)	2 (5.3%)	2 (4.9%)	1 (2.2%)	1 (2.3%)	1 (2.2%)	3 (7.3%)	1 (3.3%)	1 (1.9%)
	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%)	1 (1.9%)
	Not reported	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	3 (10.0%)	3 (5.6%)
	Total new transplants	**39**	**34**	**38**	**41**	**46**	**43**	**46**	**41**	**30**	**54**
New Zealand	Intravenous immunoglobulin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Anti-CD25	6 (60.0%)	0 (0.0%)	1 (20.0%)	4 (100%)	10 (100%)	5 (100%)	4 (100%)	8 (100%)	6 (100%)	5 (100%)
	Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	1 (12.5%)	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%)	0 (0.0%)
	Total new transplants	**10**	**5**	**5**	**4**	**10**	**5**	**4**	**8**	**6**	**5**

Figure 11.9 - Calcineurin and mTOR Inhibitors at Induction - Transplant Cohorts 2006-2017

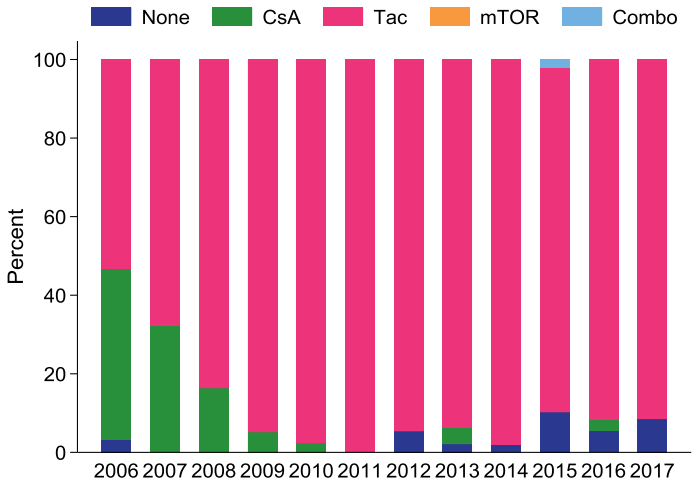


Figure 11.10 - Calcineurin and mTOR Inhibitors at One Year - Transplant Cohorts 2006-2016

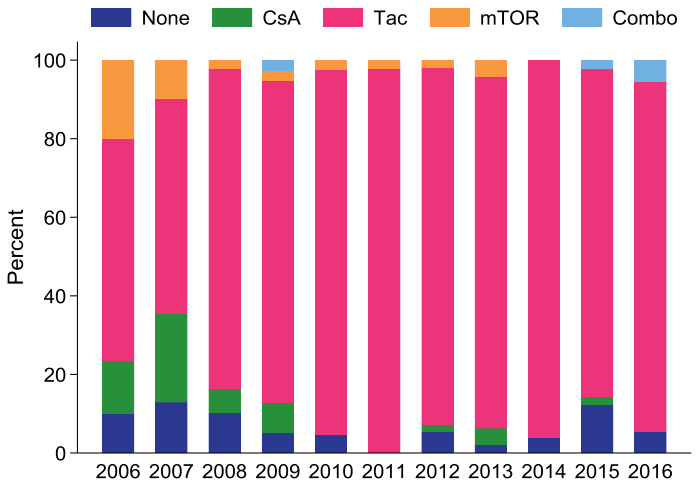


Figure 11.11 - Calcineurin and mTOR Inhibitors at Five Years - Transplant Cohorts 2006-2012

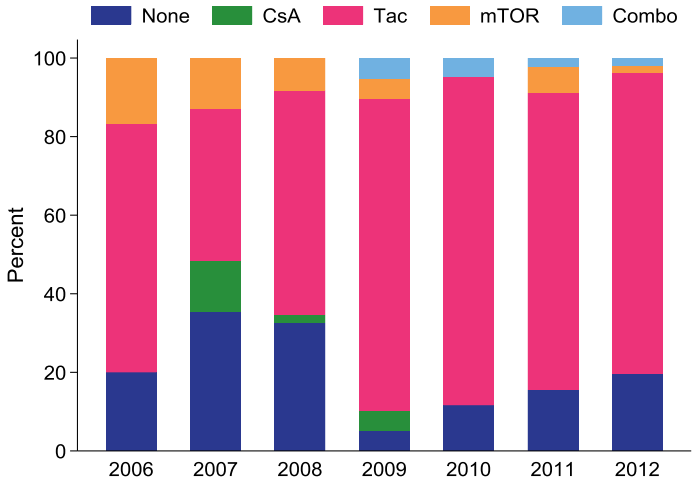
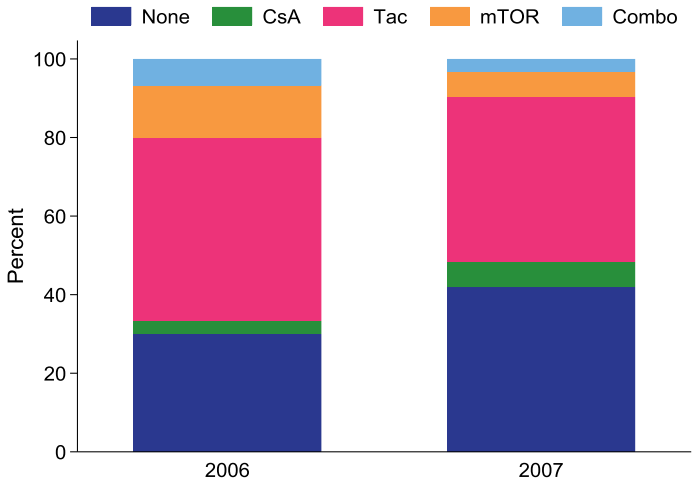


Figure 11.12 - Calcineurin and mTOR Inhibitors at Ten Years - Transplant Cohorts 2006-2007



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 11.13-11.16).

The proportion of prednisolone-free patients at induction had been virtually zero from 2006-2013. More recently, in the last four years, a slightly increased trend of steroid-free induction is apparent. The steroid-free percentage however, over a longer term post-transplant, has a decreasing trend.

Figure 11.13 - Antimetabolites at Induction - Transplant Cohorts 2006-2017

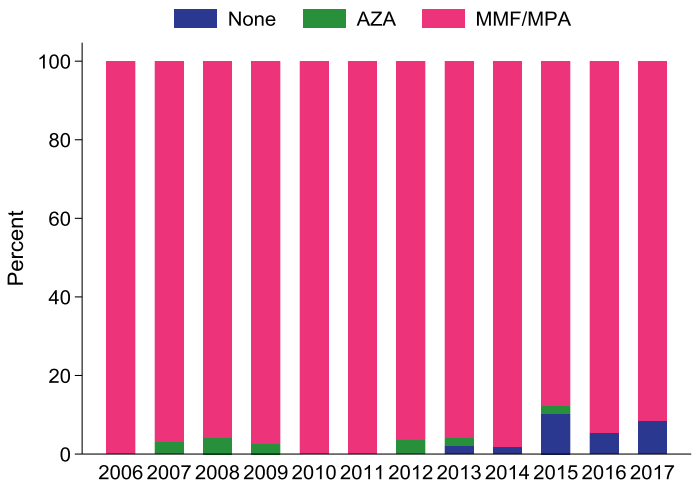


Figure 11.14 - Antimetabolites at One Year - Transplant Cohorts 2006-2016

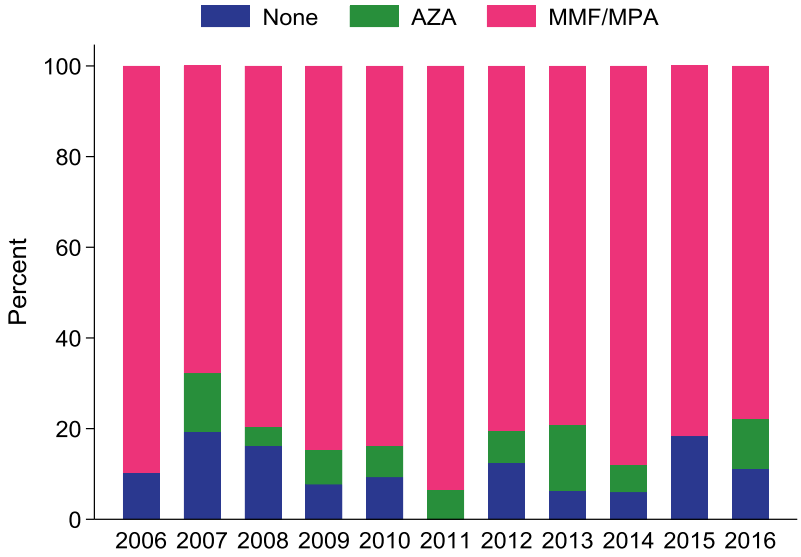


Figure 11.15 - Antimetabolites at Five Years - Transplant Cohorts 2006-2012

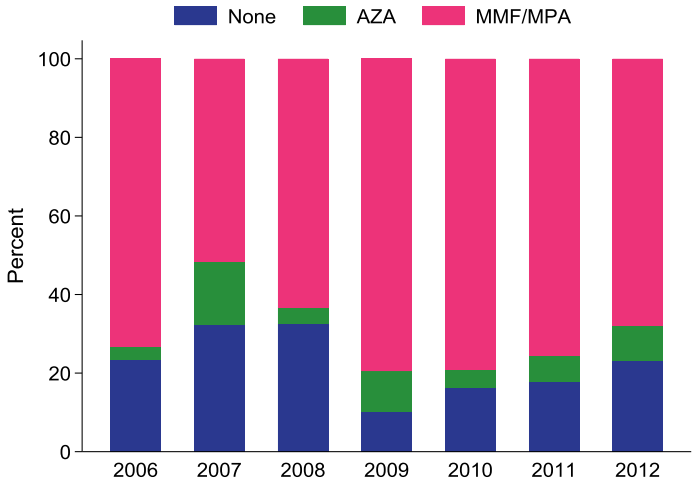


Figure 11.16 - Antimetabolites at Ten Years - Transplant Cohorts 2006-2007

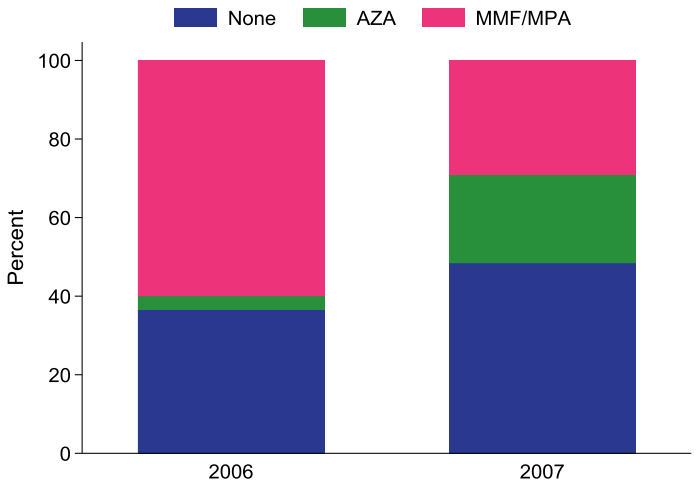
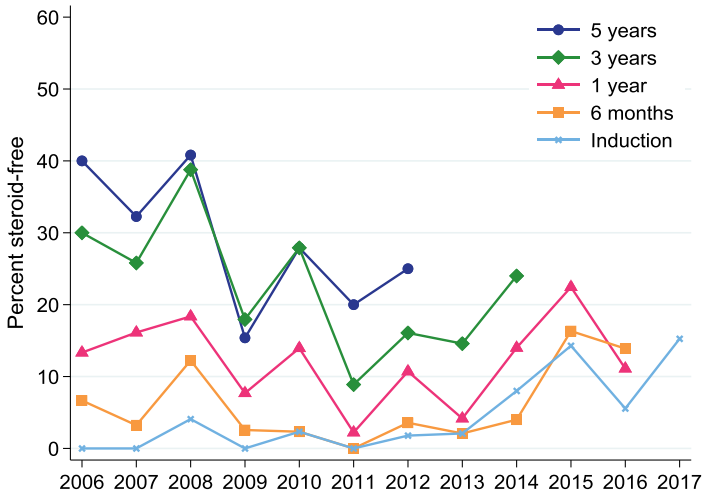


Figure 11.17 - Steroid-Free Fraction - Transplant Cohorts 2006-2017



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 11.7. 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 11.7 Patient and Graft Survival (95% CI), Paediatric Transplant Recipients 2008-2017

Outcome	Transplant year (N)	6 months	1 year	3 years	5 years
Patient	**2008-09 (n=88)**	100	100	100	100
	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	-
	2016-17 (n=95)	99 (91-100)	99 (91-100)	-	-
Graft	**2008-09 (n=88)**	94 (87-98)	94 (87-98)	88 (79-93)	83 (73-89)
	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)	91 (84-95)
	2014-15 (n=99)	97 (91-99)	97 (91-99)	93 (84-97)	-
	2016-17 (n=95)	97 (90-99)	97 (90-99)	-	-

The causes of graft loss by age at transplant and age at graft loss are shown in tables 11.8 and 11.9 respectively.

Table 11.8 Cause of Graft Loss, Transplants Performed 2008-2017 by Age at Transplant

Cause of graft loss	0-4	5-9	10-14	15-17	Total
Death with function	1	3	0	2	**6**
Acute rejection	0	1	1	6	**8**
Chronic allograft nephropathy	1	4	6	10	**21**
Vascular	1	0	4	1	**6**
Technical	0	1	0	0	**1**
Glomerulonephritis	0	1	2	3	**6**
Non-compliance	0	0	3	3	**6**
Other	2	0	4	0	**6**
Total	**5**	**10**	**20**	**25**	**60**

Table 11.9 Cause of Graft Loss, Transplants Performed 2008-2017 by Age at Graft Loss

Cause of graft loss	0-4	5-9	10-14	15-17	Total
Death with function	1	1	2	1	**5**
Acute rejection	0	1	1	4	**6**
Chronic allograft nephropathy	0	1	4	6	**11**
Vascular	1	0	4	1	**6**
Technical	0	0	1	0	**1**
Glomerulonephritis	0	0	2	2	**4**
Non-compliance	0	0	0	5	**5**
Other	0	0	5	1	**6**
Total	**2**	**3**	**19**	**20**	**44**

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 11.18). The proportion experiencing rejection between 6-24 months post-transplant has remained largely unchanged for cohorts since 2010 (figure 11.19). The majority of rejection episodes are cellular (table 11.10).

Figure 11.18 - Rejection <6 Months Post Transplant - Transplant Cohorts 2008-2016

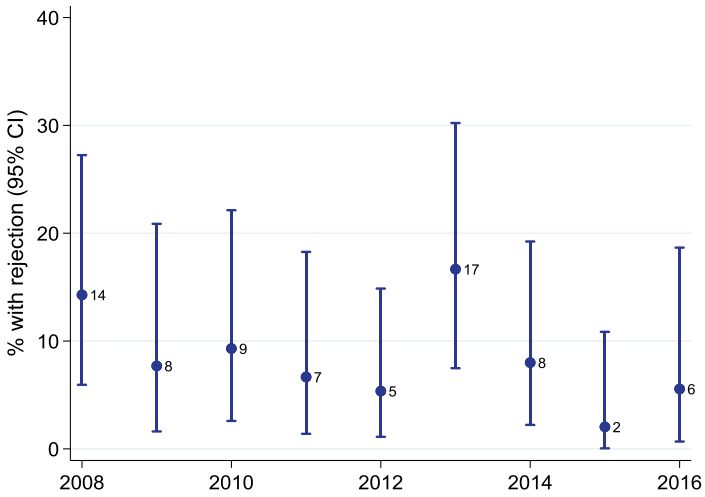


Figure 11.19 - Rejection 6-24 Months Post Transplant - Transplant Cohorts 2008-2014

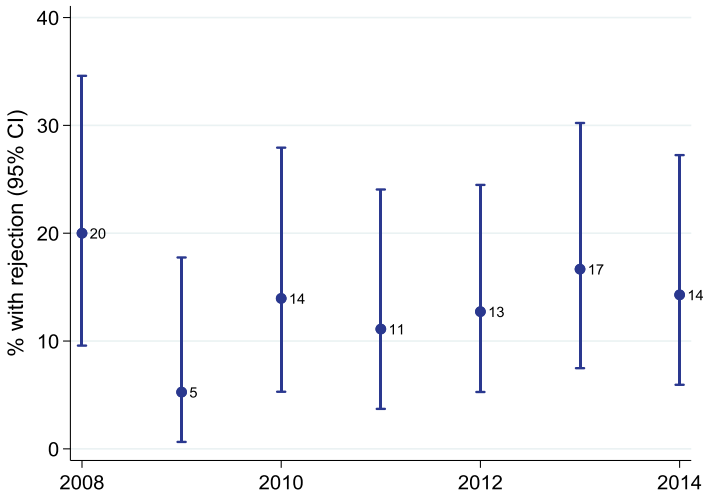


Table 11.10 Type of Rejection

Timing of rejection	Type of rejection	2008	2009	2010	2011	2012	2013	2014	2015	2016
<6 months	No biopsy	0	1	3	2	0	1	0	0	0
	Cellular	6	2	3	3	2	8	4	1	4
	ABMR	0	0	1	0	0	0	0	0	0
	Cellular + ABMR	1	0	0	0	0	0	0	0	0
6-24 months	No biopsy	1	0	1	0	0	1	0	-	-
	Cellular	12	3	6	2	9	11	8	-	-
	ABMR	0	0	0	1	0	1	0	-	-
	Cellular + ABMR	1	0	2	0	3	1	1	-	-

ABMR - antibody-mediated rejection