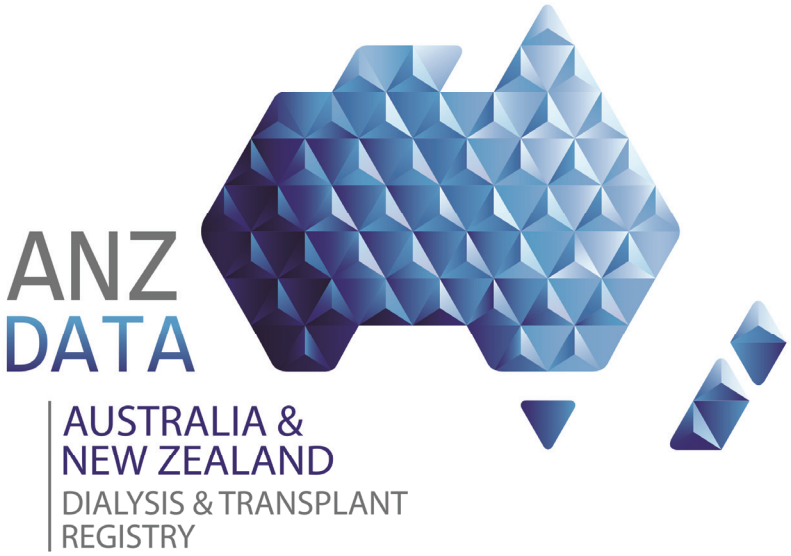
Chapter 11

Paediatrics



2016

ANZDATA Registry

39th Annual Report

Data to 31-Dec-2015

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.

Incidence and prevalence

General Overview

As shown in figure 11.1, there is no clear long term trend in the incidence of children and adolescents developing ESKD and being treated with renal replacement therapy, although there are fluctuations from year to year.

Figure 11.1.1

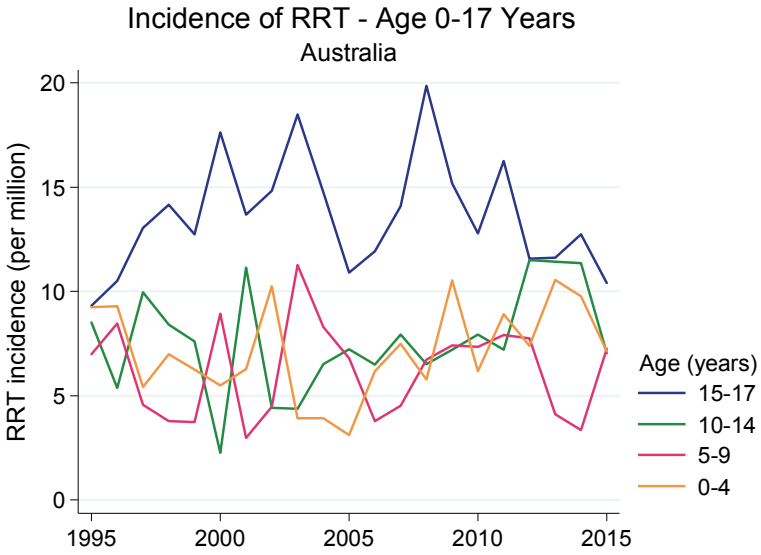
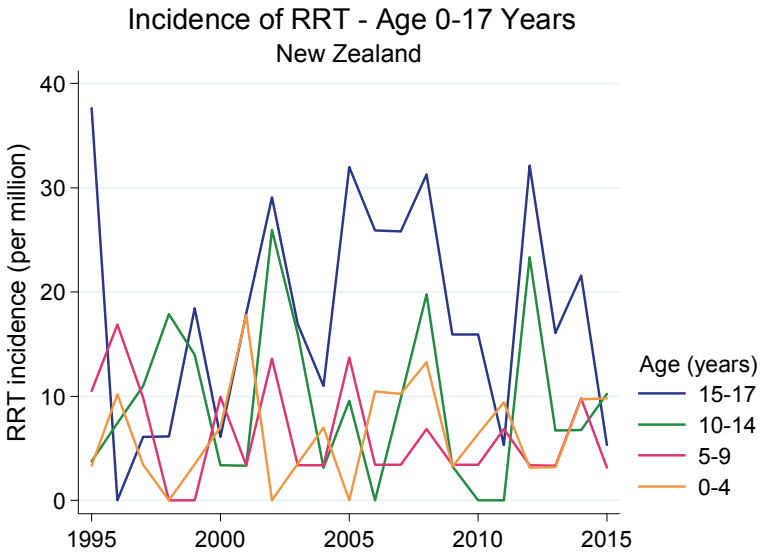


Figure 11.1.2



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

Figure 11.2.1

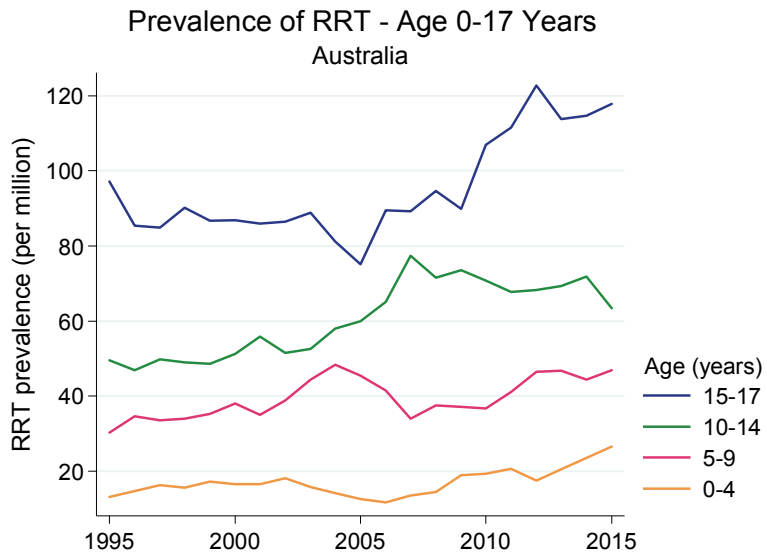
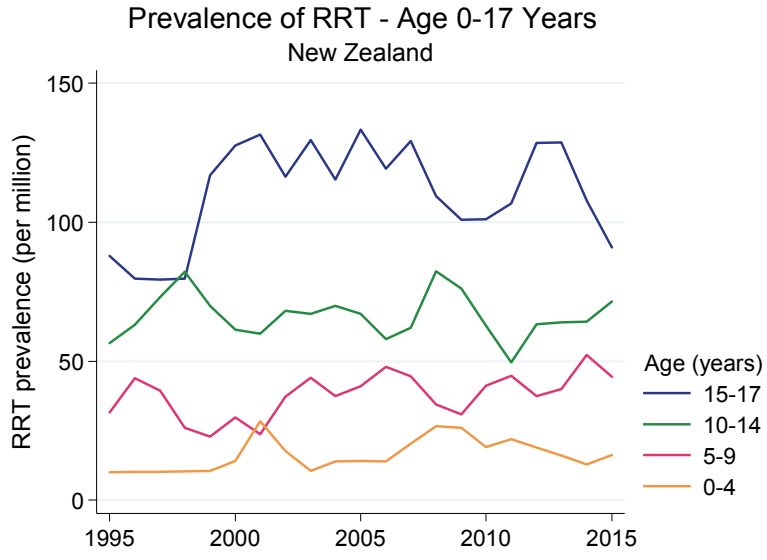


Figure 11.2.2



Primary Renal Disease

Overall, glomerulonephritis remains the most common cause of ESKD in children and adolescents (22%), but causes vary significantly with age (table 11.1). In young children renal hypoplasia/dysplasia is the most common cause while reflux nephropathy is a common cause of ESKD in adolescents.

Table 11.1 Primary renal disease, incident patients Australia and New Zealand 2010-2015

Primary Renal Disease	0-4	5-10	10-14	15-17	Total
GN	6 (7%)	16 (23%)	25 (25%)	30 (33%)	77 (22%)
- FSGS	2 (2%)	8 (11%)	7 (7%)	7 (8%)	24 (7%)
Familial GN	3 (3%)	-	1 (1%)	3 (3%)	7 (2%)
Reflux Nephropathy	2 (2%)	4 (6%)	5 (5%)	5 (6%)	16 (5%)
Polycystic Kidney Disease	7 (8%)	4 (6%)	1 (1%)	5 (6%)	17 (5%)
Medullary Cystic Disease	-	4 (6%)	11 (11%)	2 (2%)	17 (5%)
Posterior Urethral Valve	9 (10%)	2 (3%)	11 (11%)	4 (4%)	26 (7%)
Haemolytic Uraemic Syndrome	1 (1%)	-	3 (3%)	1 (1%)	5 (1%)
Hypoplasia/Dysplasia	24 (27%)	14 (20%)	18 (18%)	7 (8%)	63 (18%)
Diabetes	1 (1%)	-	-	2 (2%)	3 (1%)
Cortical Necrosis	2 (2%)	2 (3%)	2 (2%)	2 (2%)	8 (2%)
Cystinosis	-	1 (1%)	1 (1%)	-	2 (1%)
Uncertain	2 (2%)	2 (3%)	-	4 (4%)	8 (2%)
Misc/Other	30 (33%)	13 (18%)	14 (14%)	17 (19%)	74 (21%)
Not reported	1 (1%)	1 (1%)	1 (1%)	1 (1%)	4 (1%)
Total	90	71	100	90	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 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.

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

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

Age Group	2010	2011	2012	2013	2014	2015	Total
0-9 Years	22	29	24	24	26	26	151
HD	5 (23%)	10 (34%)	8 (33%)	6 (25%)	8 (31%)	6 (23%)	43 (28%)
PD	14 (64%)	14 (48%)	12 (50%)	16 (67%)	17 (65%)	13 (50%)	86 (57%)
Transplant	3 (14%)	5 (17%)	4 (17%)	2 (8%)	1 (4%)	7 (27%)	22 (15%)
10-17 Years	25	25	39	31	33	23	176
HD	13 (52%)	8 (32%)	16 (41%)	13 (42%)	10 (30%)	5 (22%)	65 (37%)
PD	5 (20%)	12 (48%)	15 (38%)	12 (39%)	14 (42%)	11 (48%)	69 (39%)
Transplant	7 (28%)	5 (20%)	8 (21%)	6 (19%)	9 (27%)	7 (30%)	42 (24%)
Total	47	54	63	55	59	49	327

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

Current Treatment	2010	2011	2012	2013	2014	2015	Total
HD	30 (9%)	29 (9%)	30 (8%)	31 (9%)	24 (7%)	23 (6%)	167 (8%)
PD	50 (15%)	53 (16%)	49 (14%)	46 (13%)	48 (13%)	43 (12%)	289 (14%)
Transplant	244 (75%)	250 (75%)	274 (78%)	277 (78%)	289 (80%)	295 (82%)	1629 (78%)
Total	324	332	353	354	361	361	2085

Transplant Demographics

Figures 11.3-11.6 and tables 11.4-11.5 show the trends in paediatric transplantation over the 12 year period from 2004-2015.

Approximately 60% of kidneys come from living related donors; this percentage has remained stable over time. Living donor kidneys (living related and unrelated) mostly come from donors in the 35-44 year age group. In contrast, the proportion of deceased donors aged <25 is higher than in 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 11.5) has remained largely unchanged over this period. Second transplants during childhood are a rare occurrence.

Figure 11.3

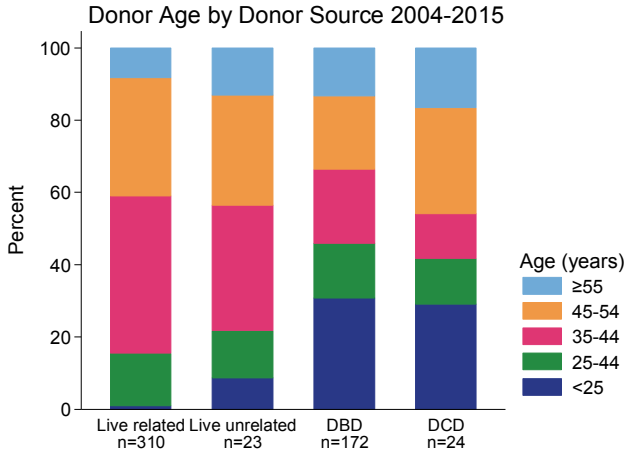


Figure 11.4

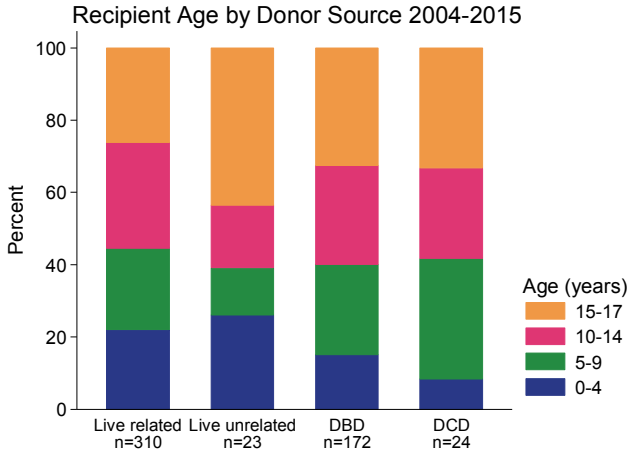


Figure 11.5

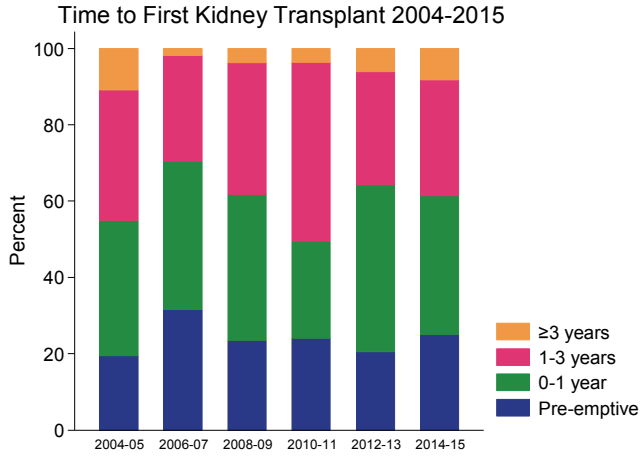


Figure 11.6

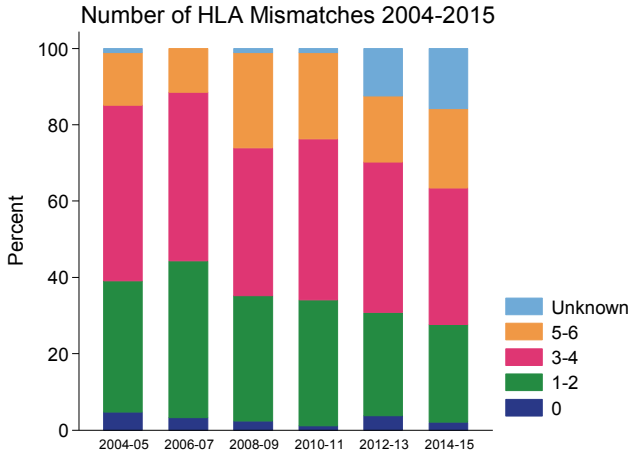


Table 11.4 Graft Numbers 2006 - 2015 Australia and New Zealand										
Graft Number	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**
1	26	28	45	36	40	43	55	43	48	48
2	4	3	4	3	3	2	1	5	3	1
3	0	0	0	0	0	0	0	0	1	0

Table 11.5 Donor Source by Year 2006 - 2015, Number (% of Transplants)										
Donor Type	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
LD pre-emptive	7 (23%)	8 (26%)	9 (18%)	9 (23%)	10 (23%)	10 (22%)	12 (21%)	8 (17%)	9 (17%)	14 (29%)
LD not pre-emptive	15 (50%)	13 (42%)	24 (49%)	16 (41%)	19 (44%)	10 (22%)	26 (46%)	20 (42%)	19 (37%)	21 (43%)
DBD	8 (27%)	9 (29%)	13 (27%)	12 (31%)	11 (26%)	20 (44%)	17 (30%)	18 (38%)	20 (38%)	12 (24%)
DCD	0 (0%)	1 (3%)	3 (6%)	2 (5%)	3 (7%)	5 (11%)	1 (2%)	2 (4%)	4 (8%)	2 (4%)
Total	30	31	49	39	43	45	56	48	52	49

Immunosuppression

The majority of patients in both countries receive induction antibody therapy with andi-CD25 agents (table 11.6). The numbers reported In 2015 may reflect under reporting and caution is advised when interpreting them.

Tacrolimus is the most commonly used calcineurin inhibitor (CNI) at induction and at 1, 5 and 10 years post-transplant (figures 11.7-11.10).

Table 11.6 Antibody Use for Induction Immunosuppression, Number receiving (%)											
Country	**Type of agent**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**
Australia	**Intravenous immunoglobulin**	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	2 (4.9%)	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)
	Anti-CD25	20 (76.9%)	19 (73.1%)	37 (94.9%)	33 (97.1%)	35 (92.1%)	36 (87.8%)	42 (91.3%)	40 (93.0%)	46 (95.8%)	30 (73.2%)
	Rituximab	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	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%)	1 (2.9%)	2 (5.3%)	2 (4.9%)	1 (2.2%)	1 (2.3%)	1 (2.1%)	3 (7.3%)
	Total new transplants	26	26	39	34	38	41	46	43	48	41
New Zealand	**Intravenous immunoglobulin**	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Anti-CD25	0 (0.0%)	0 (0.0%)	6 (60.0%)	0 (0.0%)	1 (20.0%)	4 (100.0%)	10 (100.0%)	5 (100.0%)	4 (100.0%)	7 (87.5%)
	Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	1 (12.5%)
	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%)
	Total new transplants	4	5	10	5	5	4	10	5	4	8

Figure 11.7

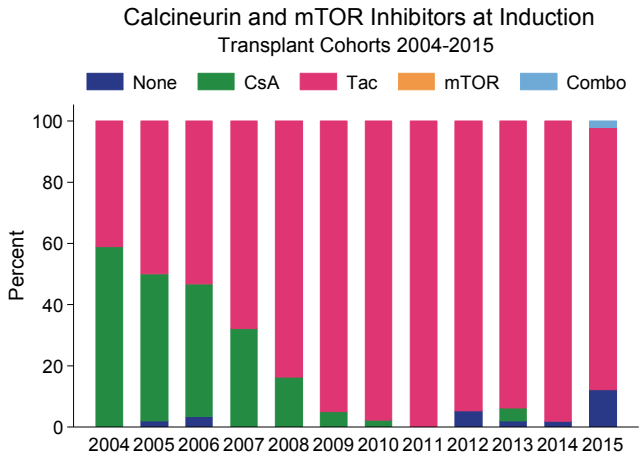


Figure 11.8

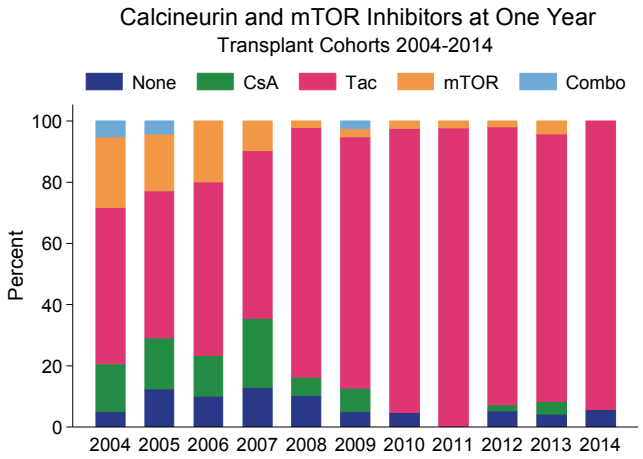


Figure 11.9

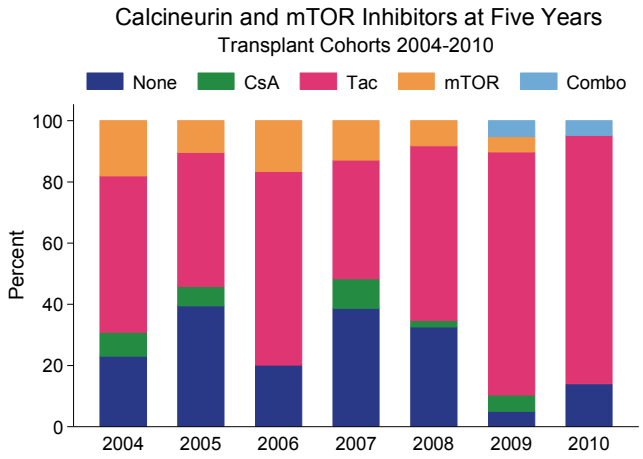
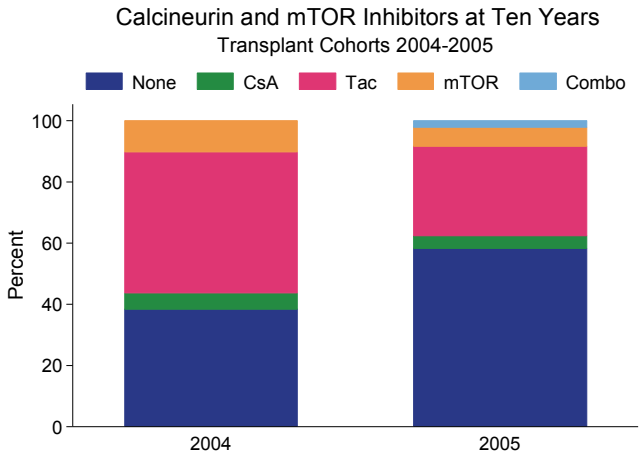


Figure 11.10



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 11.11-11.14).

The proportion of prednisolone-free patients at induction had been virtually zero from 2004-2013. More recently, in the last two years, a slight increased trend of steroid-free induction is apparent. The steroid-free percentage however, over a longer term post transplant, has a decreasing trend.

Figure 11.11

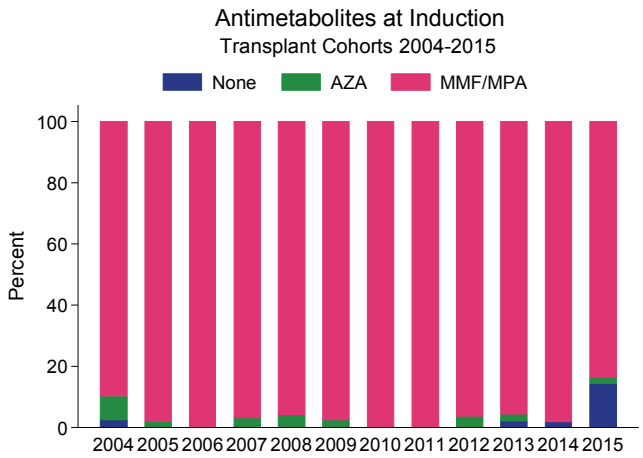


Figure 11.12

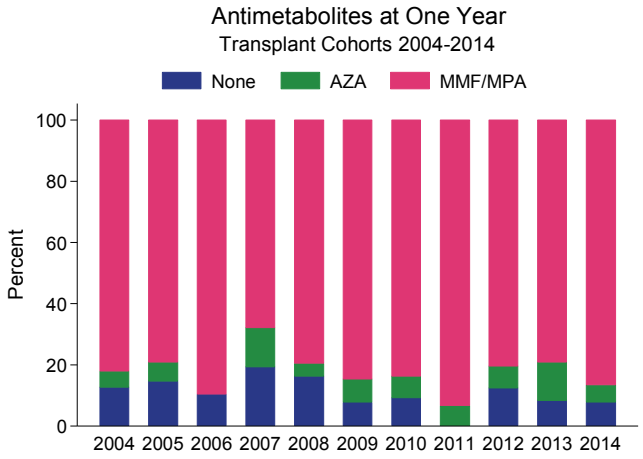


Figure 11.13

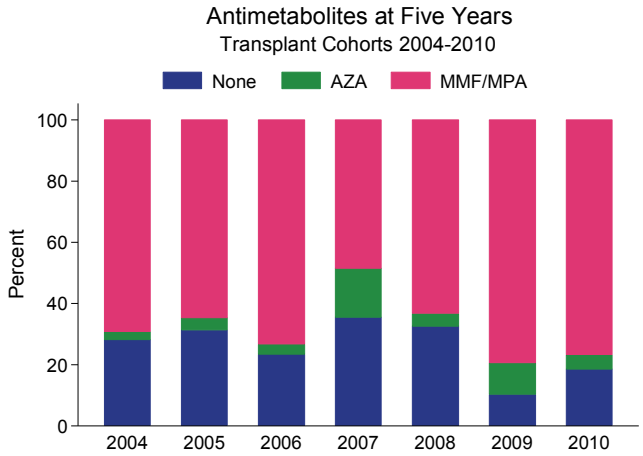
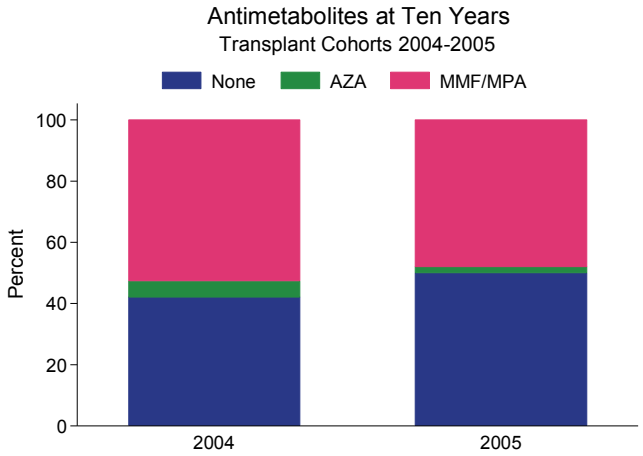


Figure 11.14



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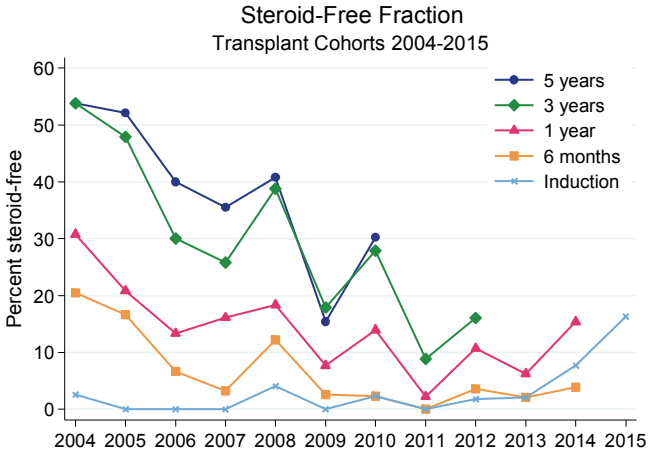

Transplant Outcomes

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 survival have remained relatively stable over the past ten years, with 3 and 5 year graft survival in the 2010-11 and 2012-13 cohorts to date.

Table 11.7 Patient and Graft Survival (95% CI), Paediatric Transplant Recipients 2006- 2015

Outcome	Transplant year (N)	6 months	1 year	3 years	5 years
Patient	2006-07 (n=61)	100	100	98 (89-100)	98 (89-100)
	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)	-
	2014-15 (n=101)	100	100	-	-
Graft	2006-07 (n=61)	93 (83-97)	90 (79-95)	82 (70-90)	79 (66-87)
	2008-09 (n=88)	94 (87-98)	94 (87-98)	87 (78-93)	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 (84-97)	-
	2014-15 (n=101)	98 (92-99)	98 (92-99)	-	-

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 2006-2015 by Age at Transplant

Cause of Graft Loss	0-4	5-9	10-14	15-17	Total
Death with function	0	3	1	3	7
Acute rejection	1	1	1	6	9
Chronic allograft nephropathy	1	3	7	9	20
Vascular	2	0	3	3	8
Glomerulonephritis	0	1	3	0	4
Non-compliance	0	0	1	2	3
Other	0	1	3	1	5
Total	4	9	19	24	56

Table 11.9 Cause of Graft Loss, Transplants Performed 2006-2015 by Age at Graft Loss

Cause of Graft Loss	0-4	5-9	10-14	15-17	Total
Death with function	0	1	2	3	6
Acute rejection	0	2	1	3	6
Chronic allograft nephropathy	0	1	4	7	12
Vascular	2	0	3	3	8
Glomerulonephritis	0	0	4	0	4
Non-compliance	0	0	0	3	3
Other	0	0	3	2	5
Total	2	4	17	21	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 11.16). The proportion experiencing rejection between 6-24 months post transplant has remained largely unchanged over the past four years (figure 11.17). The majority of rejection episodes are either cellular or not biopsied (table 11.10)

Figure 11.16

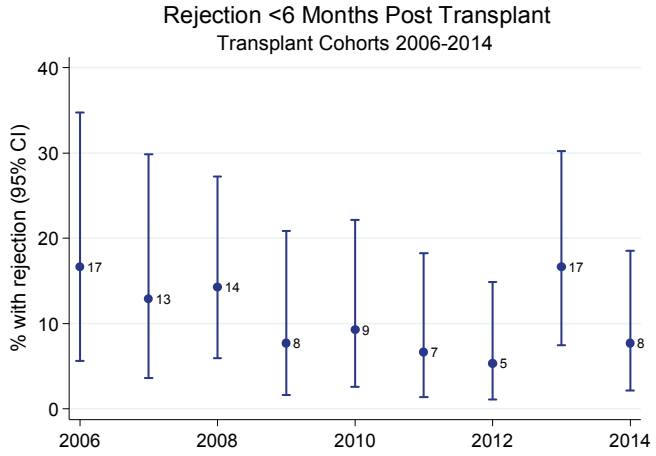

Figure 11.17

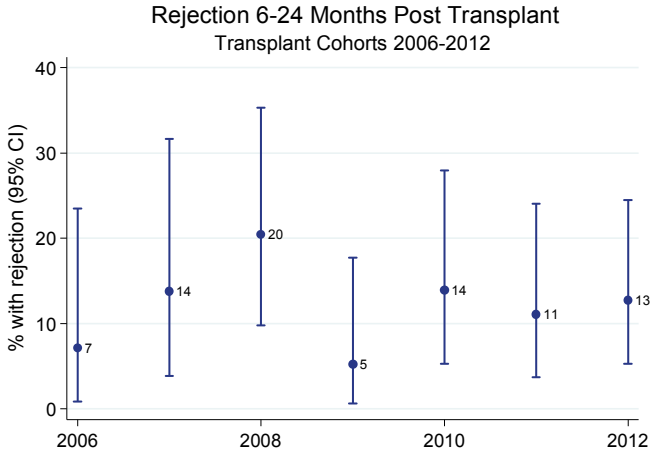

Table 11.10 Type of Rejection 2006-2014

Timing of Rejection	Type of rejection	2006	2007	2008	2009	2010	2011	2012	2013	2014
<6 months	No biopsy	6	2	0	1	3	2	0	1	0
	Cellular	2	4	6	2	3	3	2	8	4
	ABMR	0	0	0	0	1	0	0	0	0
	Cellular + ABMR	0	0	1	0	0	0	0	0	0
6-24 months	No biopsy	1	0	1	0	1	0	0	-	-
	Cellular	1	4	12	3	6	2	9	-	-
	ABMR	0	1	0	0	0	1	0	-	-
	Cellular + ABMR	0	0	1	0	2	0	3	-	-

Footnote: ABMR - antibody-mediated rejection

Suggested Citation:

ANZDATA Registry. 39th Report, Chapter 11 Paediatrics: Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2017. Available at: http://www.anzdata.org.au

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