Australia & New Zealand Dialysis & Transplant Registry

Chapter 11

Paediatrics

ANZDATA gratefully acknowledges the contributions of the Paediatric Working Group convened by Dr Sean Kennedy

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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

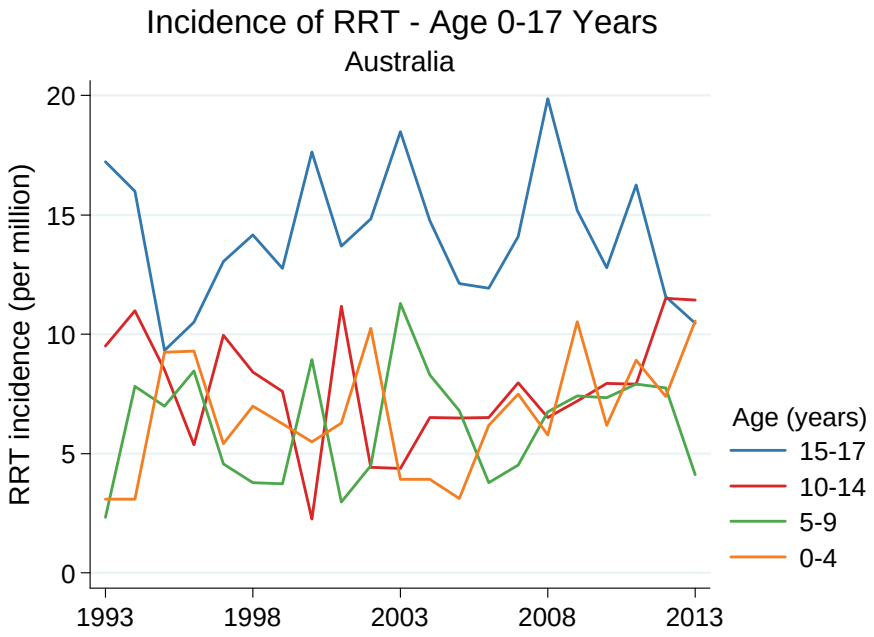
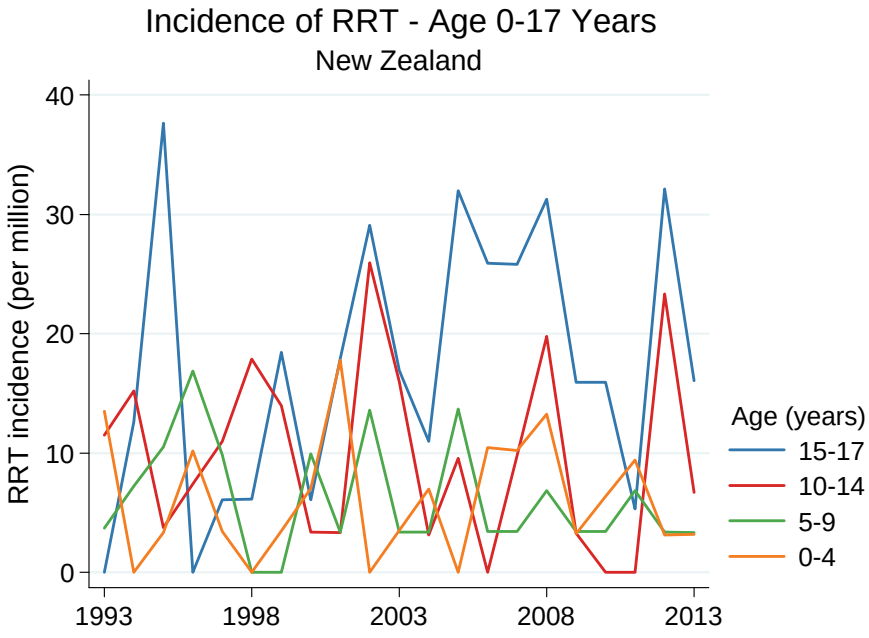


Figure 11.1.2



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

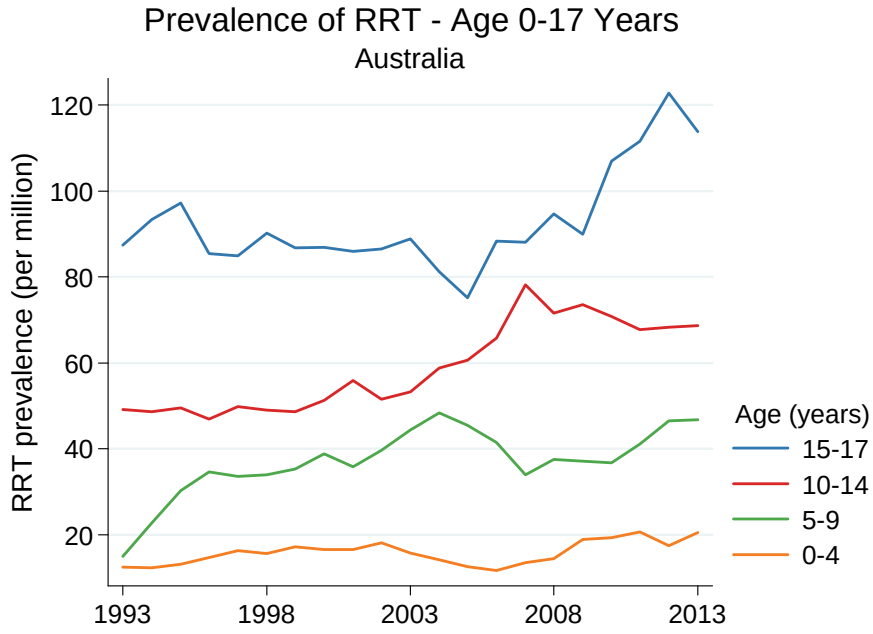
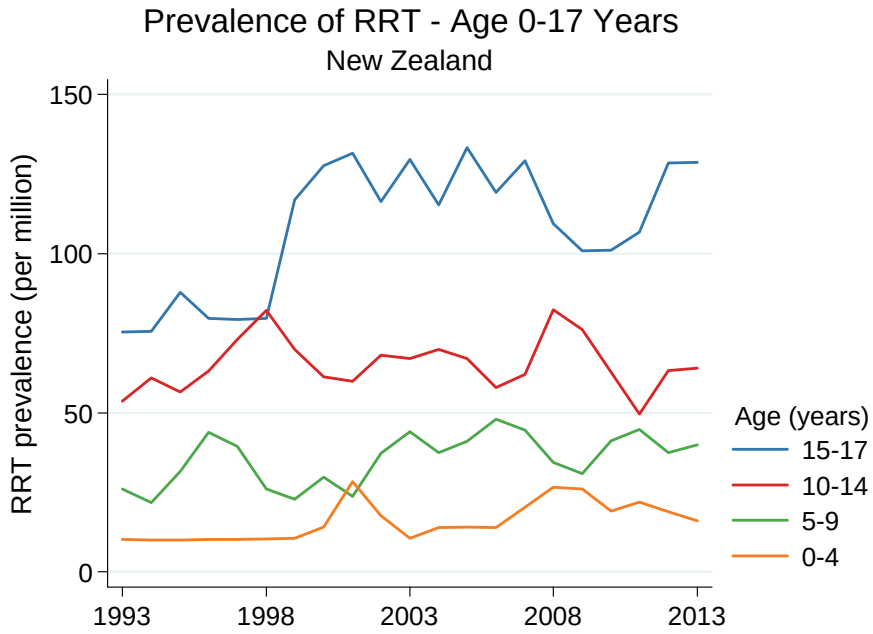


Figure 11.2.2



Primary Renal Disease

Overall, glomerulonephritis remains the most common cause of ESKD in children and adolescents (27%), 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 2008-2013

Primary Renal Disease	0-4	5-10	10-14	15-17	Total
GN	8 (9%)	20 (27%)	25 (26%)	37 (36%)	90 (25%)
- FSGS	1 (1%)	8 (11%)	7 (7%)	6 (6%)	22 (6%)
Familial GN	3 (4%)	-	2 (2%)	3 (3%)	8 (2%)
Reflux Nephropathy	4 (5%)	3 (4%)	7 (7%)	9 (9%)	23 (6%)
Polycystic Kidney Disease	5 (6%)	4 (5%)	2 (2%)	4 (4%)	15 (4%)
Medullary Cystic Disease	-	2 (3%)	5 (5%)	2 (2%)	9 (3%)
Posterior Urethral Valve	10 (12%)	1 (1%)	13 (14%)	2 (2%)	26 (7%)
Haemolytic Uraemic Syndrome	6 (7%)	1 (1%)	1 (1%)	2 (2%)	10 (3%)
Hypoplasia/Dysplasia	26 (31%)	16 (22%)	12 (13%)	10 (10%)	64 (18%)
Diabetes	-	-	1 (1%)	1 (1%)	2 (1%)
Cortical Necrosis	2 (2%)	3 (4%)	2 (2%)	3 (3%)	10 (3%)
Interstitial Nephritis	-	1 (1%)	1 (1%)	-	2 (1%)
Cystinosis	-	1 (1%)	1 (1%)	-	2 (1%)
Uncertain	-	2 (3%)	-	4 (4%)	6 (2%)
Misc/Other	20 (24%)	11 (15%)	17 (18%)	19 (19%)	67 (19%)
Total	85	73	96	102	334

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, HD is more common in older patients (10-17 years) and PD more common in younger patients (<10 years).

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	2008	2009	2010	2011	2012	2013	Total
0-9 Years	23	27	22	29	24	24	149
- HD	6 (26%)	4 (15%)	5 (23%)	10 (34%)	8 (33%)	6 (25%)	39 (26%)
- PD	15 (65%)	17 (63%)	14 (64%)	14 (48%)	12 (50%)	16 (67%)	88 (59%)
- Transplant	2 (9%)	6 (22%)	3 (14%)	5 (17%)	4 (17%)	2 (8%)	22 (15%)
10-17 Years	38	27	25	26	39	30	185
- HD	22 (58%)	12 (44%)	13 (52%)	8 (31%)	16 (41%)	12 (40%)	83 (45%)
- PD	8 (21%)	12 (44%)	5 (20%)	12 (46%)	15 (38%)	12 (40%)	64 (35%)
- Transplant	8 (21%)	3 (11%)	7 (28%)	6 (23%)	8 (21%)	6 (20%)	38 (21%)
Total	61	54	47	55	63	54	334

Table 11.3

Modality of Prevalent Patients By Year of Treatment, Australia and New Zealand

Current Treatment	2008	2009	2010	2011	2012	2013	Total
HD	35 (11%)	29 (9%)	30 (9%)	29 (9%)	30 (8%)	30 (8%)	183 (9%)
PD	54 (17%)	57 (18%)	50 (15%)	53 (16%)	49 (14%)	46 (13%)	309 (16%)
Transplant	225 (72%)	229 (73%)	244 (75%)	250 (75%)	274 (78%)	277 (78%)	1499 (75%)
Total	314	315	324	332	353	353	1991

Transplantation

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 2002-2013.

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 remains uncommon (~2%).

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

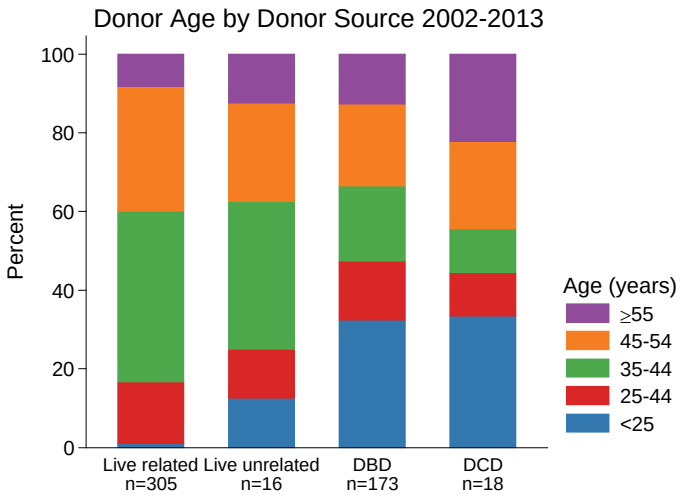


Figure 11.4

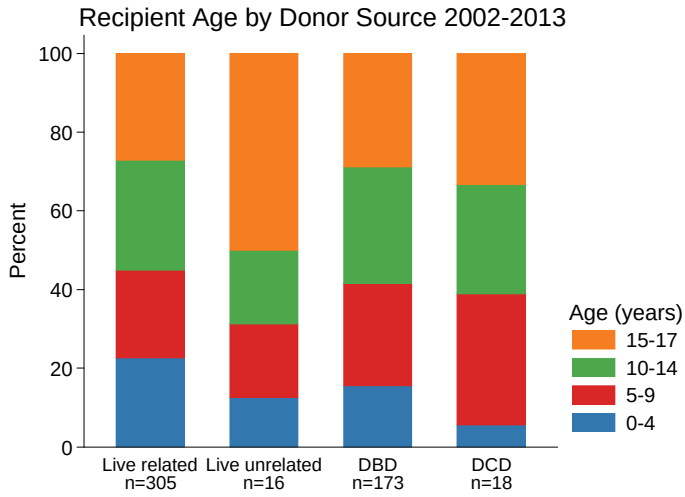


Figure 11.5

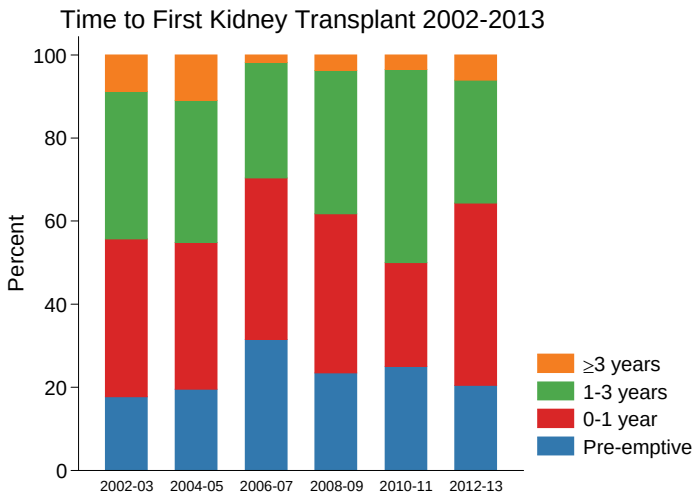


Figure 11.6

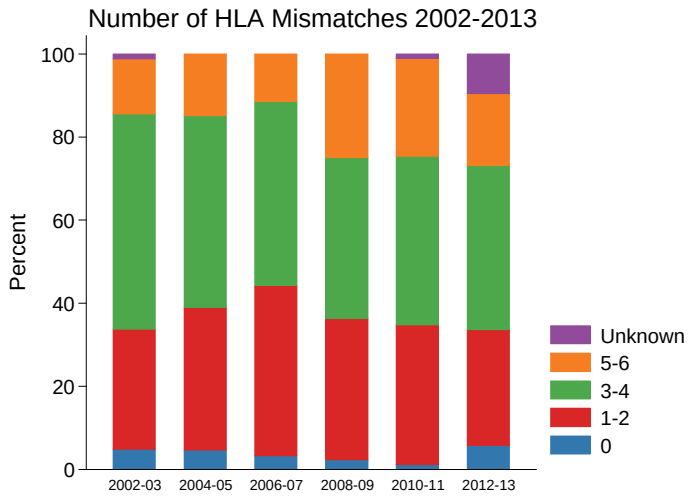


Table 11.4

Graft Numbers 2004 - 2013 Australia and New Zealand

Graft Number	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
1	35	47	26	28	45	36	40	44	55	43
2	4	1	4	3	4	3	3	2	1	5

Table 11.5

Donor Source by Year 2004 - 2015, Number (% of Transplants)

Donor Type	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
LD pre-emptive	5 (13%)	10 (21%)	7 (23%)	8 (26%)	9 (18%)	9 (23%)	10 (23%)	10 (22%)	12 (21%)	8 (17%)
LD not pre-emptive	19 (49%)	20 (42%)	15 (50%)	13 (42%)	24 (49%)	16 (41%)	19 (44%)	10 (22%)	26 (46%)	20 (42%)
DBD	15 (38%)	17 (35%)	8 (27%)	9 (29%)	13 (27%)	12 (31%)	11 (26%)	21 (46%)	17 (30%)	18 (38%)
DCD	0 (0%)	1 (2%)	0 (0%)	1 (3%)	3 (6%)	2 (5%)	3 (7%)	5 (11%)	1 (2%)	2 (4%)
Total	39	48	30	31	49	39	43	46	56	48

Immunosuppression

The majority of patients in both countries receive induction antibody therapy with andi-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 11.7-11.10).

Table 11.6

Antibody Use for Induction Immunosuppression, Number receiving (%)

Country	Type of Agent	2009	2010	2011	2012	2013
Australia	Intravenous immunoglobulin	1 (2.9%)	0 (0.0%)	2 (4.8%)	0 (0.0%)	2 (4.7%)
	Anti-CD25	33 (97.1%)	35 (92.1%)	37 (88.1%)	41 (89.1%)	36 (83.7%)
	Rituximab	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	T cell depleting polyclonal Ab	1 (2.9%)	2 (5.3%)	2 (4.8%)	1 (2.2%)	1 (2.3%)
	Total new transplants	34	38	42	46	43
New Zealand	Intravenous immunoglobulin	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)
	Anti-CD25	0 (0.0%)	1 (20.0%)	4 (100.0%)	10 (100.0%)	4 (80.0%)
	Rituximab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	T cell depleting polyclonal Ab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Total new transplants	5	5	4	10	5

Figure 11.7

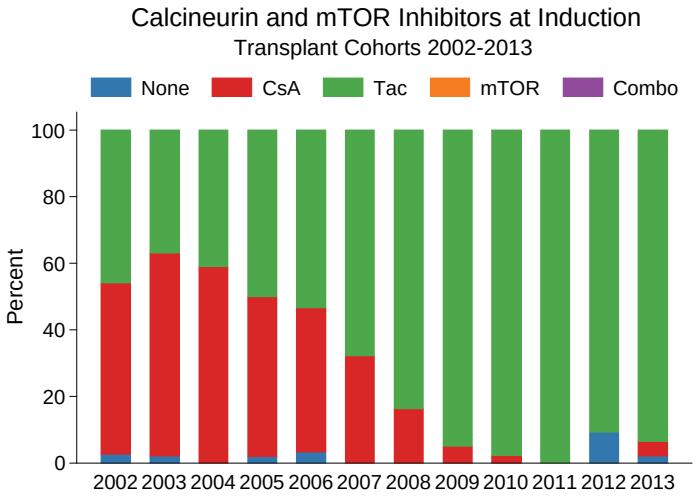


Figure 11.8

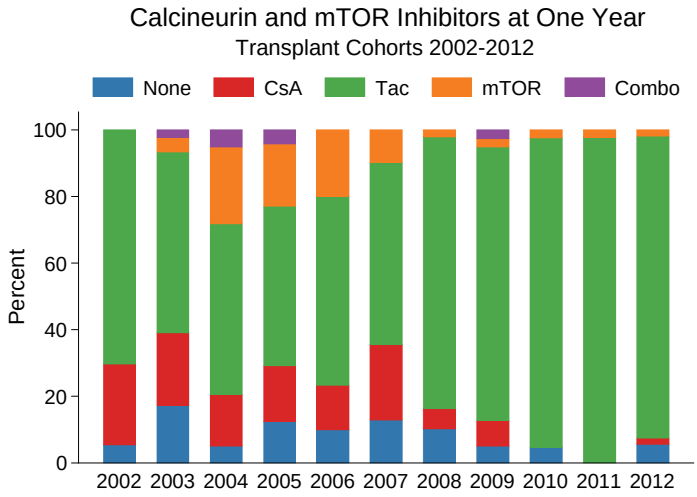


Figure 11.9

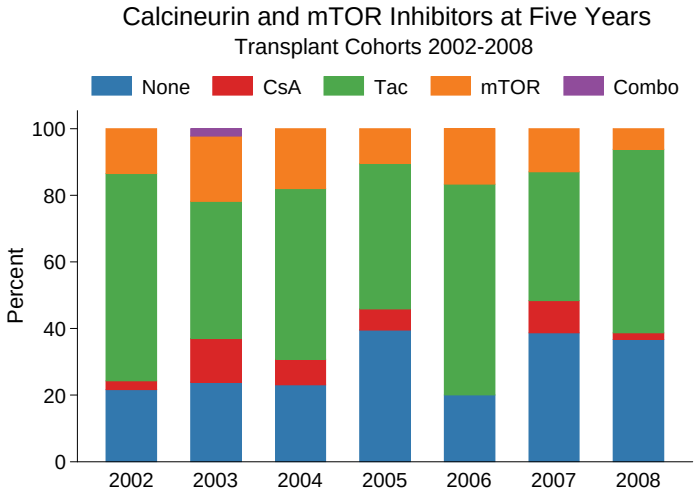
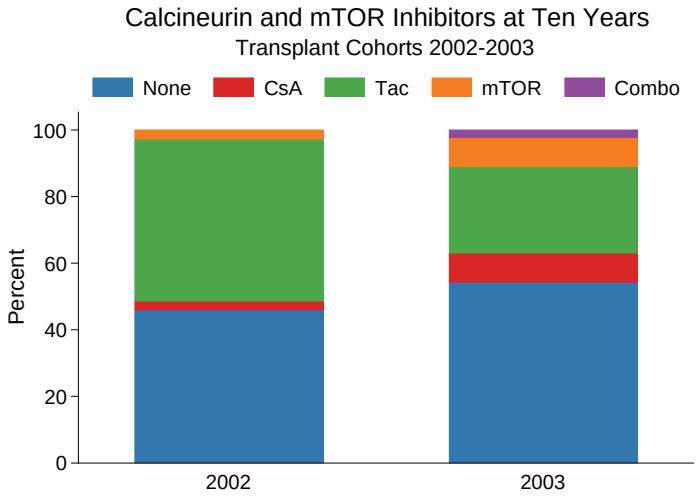


Figure 11.10



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 aside from the five and ten year cohorts (figures 11.11-11.14).

The proportion of prednisolone-free patients at induction is virtually zero, reflecting a trend since 2005 for near universal use of prednisolone at induction. Similarly, there are appears to be a trend since 2005 for a decreasing proportion of steroid-free use in longer term transplants.

Figure 11.11

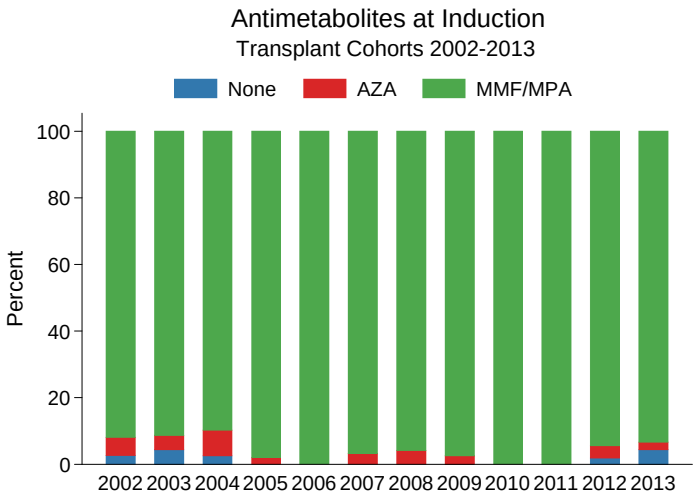


Figure 11.12

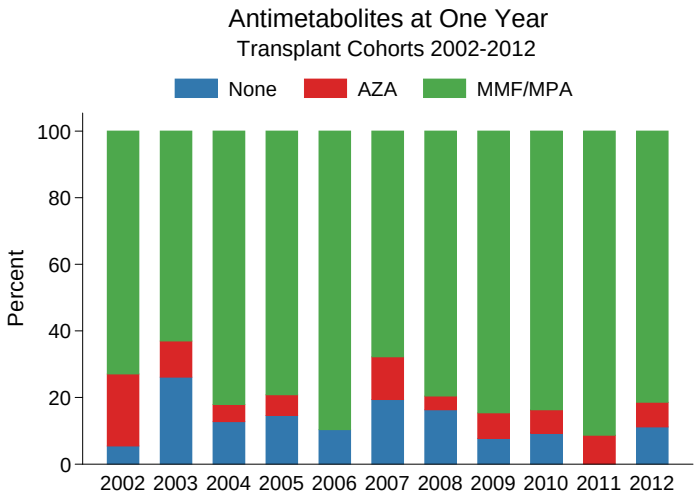


Figure 11.13

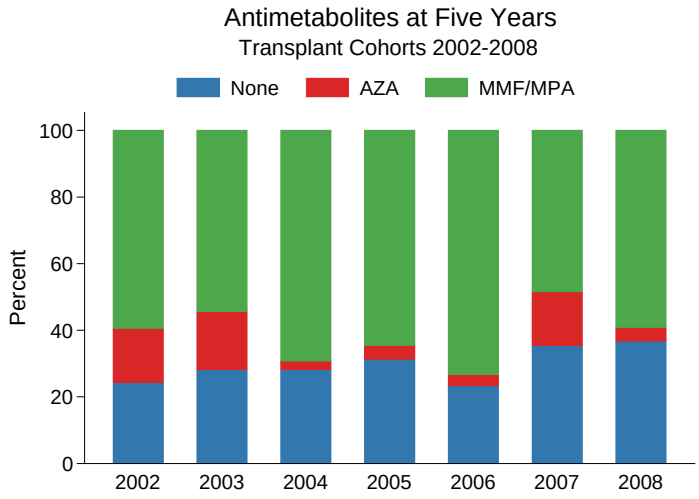


Figure 11.14

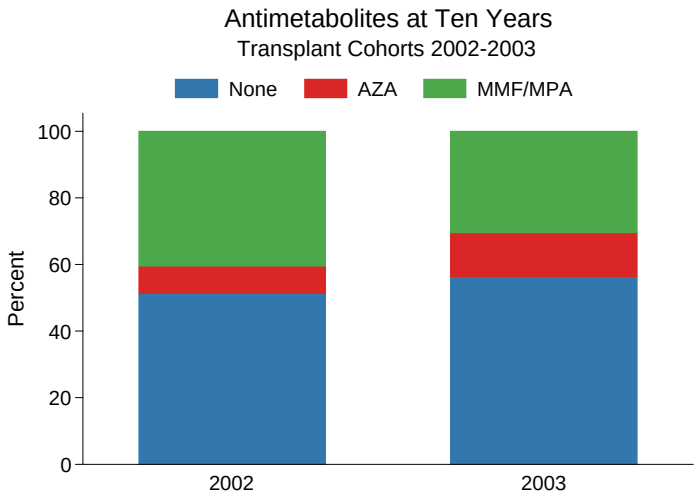
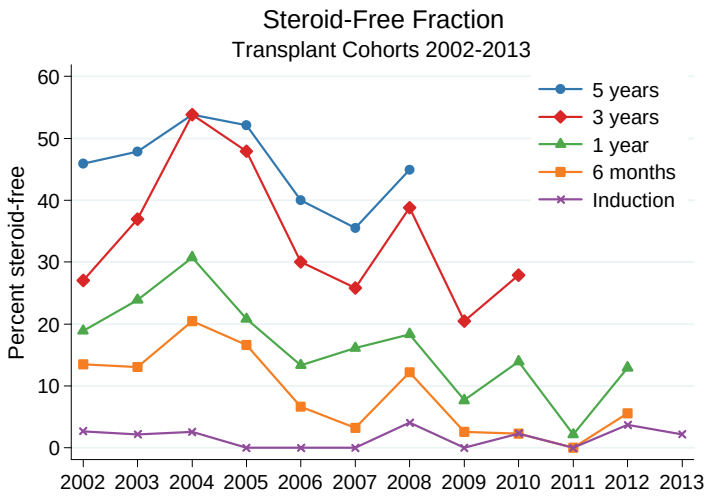


Figure 11.15



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, is shown in table 11.7 . Unadjusted one, three and five year survival have remained relatively stable over the past ten years, although graft survival in the 2010-11 and 2012-13 cohorts are excellent to date.

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

Table 11.7

Patient and Graft Survival, Paediatric Transplant Recipients 2004 - 2013 (95% CI)

Outcome	Transplant year (N)	6 months	1 year	3 years	5 years
Patient	2004-05 (n=87)	100	99 (92-100)	98 (91-99)	96 (89-99)
	2006-07 (n=61)	100	100	98 (89-100)	98 (89-100)
	2008-09 (n=88)	100	100	100	100
	2010-11 (n=89)	100	99 (92-100)	99 (92-100)	-
	2012-13 (n=104)	99 (91-100)	99 (91-100)	-	-
Graft	2004-05 (n=87)	97 (90-99)	95 (88-98)	88 (79-94)	76 (66-84)
	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)	84 (74-90)
	2010-11 (n=89)	100	98 (91-99)	96 (88-98)	-
	2012-13 (n=104)	99 (91-100)	97 (90-99)	-	-

Table 11.8

Cause of Graft Loss, Transplants Performed 2004-2013 by Age at Transplant

Cause of Graft Loss	0-4	5-9	10-14	15-17	Total
Death with function	0	2	1	2	5
Acute rejection	1	2	1	5	9
Chronic allograft nephropathy	1	3	10	9	23
Vascular	2	1	2	3	8
Technical	0	0	1	1	2
Glomerulonephritis	0	2	4	1	7
Non-compliance	0	0	0	4	4
Other	1	1	3	2	7
Total	5	11	22	27	65

Table 11.9

Cause of Graft Loss, Transplants Performed 2004-2013 by Age at Graft Loss

Cause of Graft Loss	0-4	5-9	10-14	15-17	Total
Death with function	0	1	0	4	5
Acute rejection	0	3	0	4	7
Chronic allograft nephropathy	0	0	3	14	17
Vascular	2	0	3	3	8
Technical	0	0	1	1	2
Glomerulonephritis	0	1	4	1	6
Non-compliance	0	0	0	2	2
Other	0	1	3	2	6
Total	2	6	14	31	53

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 fallen over the last four years, although the confidence intervals are wide due to low numbers (figure 11.8). The proportion experiencing rejection between 6-24 months post transplant has remained largely unchanged over the past five years (figure 11.9). The majority of rejection episodes are either cellular or not biopsied (table 11.10)

Figure 11.16

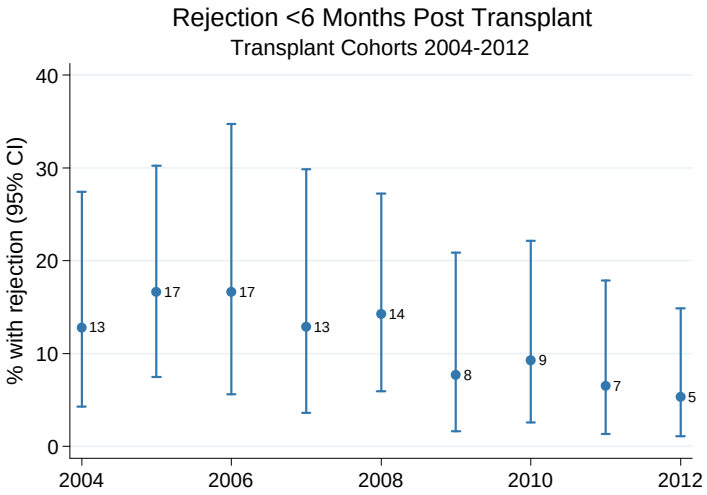


Figure 11.17

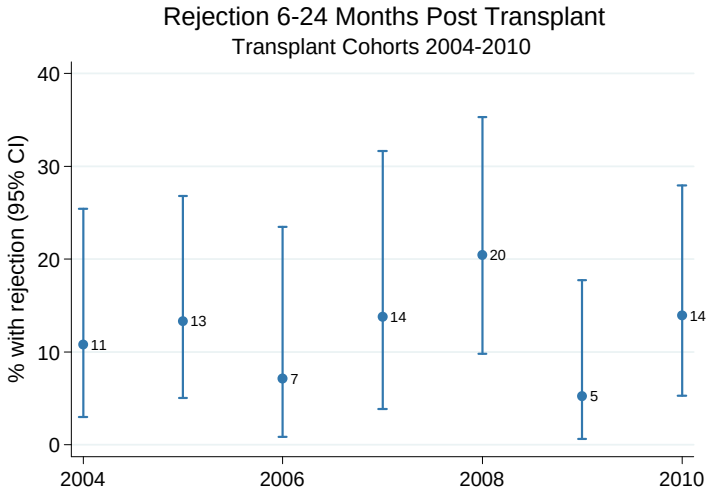


Table 11.10

Type of Rejection

Timing of Rejection	Type of Rejection	2004	2005	2006	2007	2008	2009	2010	2011	2012
<6 months	No biopsy	2	5	6	2	0	1	3	2	0
	Cellular	5	6	2	4	6	2	3	3	2
	ABMR	0	0	0	0	0	0	1	0	0
	Cellular + ABMR[1]	0	1	0	0	1	0	0	0	0
6-24 months	No biopsy	3	3	1	0	1	0	1	-	-
	Cellular	2	5	1	4	12	3	6	-	-
	ABMR	0	0	0	1	0	0	0	-	-
	Cellular + ABMR[1]	0	0	0	0	1	0	2	-	-

Footnote: [1] ABMR - antibody-mediated rejection

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