ADDENDUM: Rapid review of non-randomised comparative evidence for Immunosuppressive therapy for kidney transplantation in children and adolescents (review of technology appraisal 99)

In response to NICE request to identify further evidence for the committee, this addendum expands the consideration of non-randomised evidence in the section 4 "ASSESSMENT OF CLINICAL EFFECTIVENESS" (pages 80 – 147) of the report dated April 29th 2015 (Immunosuppressive therapy for kidney transplantation in children and adolescents [review of technology appraisal 99]).

The lack of non-RCTs identified in the search of systematic reviews in the report dated April 29th 2015, initiated a rapid review of non-randomised comparative evidence for immunosuppressive therapy for kidney transplantation in children and adolescents. Because of the limited time available, a basic search strategy of primary nonrandomised comparative studies was conducted. We also data extracted a limited number of outcomes (eGFR, patient survival, graft survival, BPAR and growth) at one year follow-up.

In summary, we identified ten non-RCTS in children and adolescents of which six were newly identified in the rapid review compared with the report dated April 29th 2015. All non-RCTs were small in size including between 14 and 233 children and adolescents.

Despite some new non-RCT evidence, the overall conclusion of the section "4 ASSESSMENT OF CLINICAL EFFECTIVENESS" remained the same as the conclusions of the report dated April 29th 2015.

Table of Contents

ADDENDUM: RAPID REVIEW OF NON-RANDOMISED COMPARATIVE EVIDENCE FOR IMMUNOSUPPRESSIVE THERAPY FOR KIDNEY TRANSPLANTATION IN CHILDREN AND ADOLESCENTS (REVIEW OF TECHNOLOGY APPRAISAL 99) 1

TABLE OF CONTENTS 2

1 RAPID REVIEW OF NON-RANDOMISED COMPARATIVE STUDIES 3

1.1 Methods for reviewing effectiveness 3
1.1.1 Identification of studies 3
1.1.2 Inclusion and exclusion criteria 3
1.1.3 Screening 6
1.1.4 Data extraction 6
1.1.5 Critical appraisal strategy 6
1.1.6 Methods of data synthesis 7

1.2 Results of the rapid review 7
1.2.1 Quantity and quality of research available 7
1.2.2 Quality of included studies 12
1.2.3 Baseline characteristics 17

1.3 Results of the included studies 20
1.3.1 Induction therapy 20
1.3.2 Maintenance therapy 21
1.3.3 Combination of induction and maintenance therapy; Basiliximab and tacrolimus and mycophenolate mofetil versus ciclosporin and azathioprine 27

1.4 Summary 28

2 REFERENCES 31

3 APPENDICES 36

Appendix 1 Literature searching strategies 36
Appendix 2 Data extraction forms 37
Appendix 3 Excluded studies 38

1 RAPID REVIEW OF NON-RANDOMISED COMPARATIVE STUDIES

1.1 Methods for reviewing effectiveness

1.1.1 Identification of studies

Searches were undertaken for this rapid review in the following bibliographic databases: MEDLINE, MEDLINE In-Process and EMBASE. The search syntax used takes a similar form to the primary systematic review, using the same clinical indication and intervention terms, and we have included a set of search terms for the specific child and young adult population. A study design filter was used to identify reports of non-randomised or observational studies. The searches were date limited 2002-current and to English language. These searches build on the systematic review of reviews undertaken in our primary review, and the primary clinical effectiveness reviews, to identify further evidence for the committee. Further detail, including the search syntax used, can be found in Appendix 1.

1.1.2 Inclusion and exclusion criteria

Studies retrieved from the literature searches were selected for inclusion according to the inclusion/exclusion criteria specified in Table 1. Studies only available as abstracts were included provided sufficient methodological details were reported to allow critical appraisal of study quality. Where relevant, we also contacted authors for additional data.

Table 1 Non-randomised studies inclusion and exclusion criteria

	Include	Exclude
Population	Children and adolescents **≤18 years** of age undergoing kidney transplantation. The kidney donor may be living-related, living-unrelated or deceased	Studies including patients receiving multi-organ transplants
Intervention	Single treatment or combination of the following treatments: **Induction therapy:** • Basiliximab (Simulect® [Novartis]) • Rabbit anti-human thymocyte immunoglobulin (Thymoglobuline® [Sanofi]) **Maintenance therapy:** • Tacrolimus prolonged-release formulation (Advagraf® [Astellas Pharma] • Tacrolimus immediate-release formulations (Adoport® [Sandoz]; Capexion® [Mylan]; Modigraf® [Astellas Pharma]; Perixis® [Accord Healthcare]; Prograf® [Astellas Pharma]; Tacni® [Teva]; Vivadex® [Dexcel Pharma]) • Belatacept (Nulojix® [Bristol-Myers Squibb]) • Mycophenolate mofetil (Arzip® [Zentiva], CellCept® [Roche], Myfenax® [Teva]; generic mycophenolate mofetil manufactured by Accord Healthcare, Actavis, Arrow Pharmaceuticals, Dr Reddy's Laboratories, Mylan, Sandoz and Wockhardt)	Studies where the intervention is identical in both study arms (but dose reduction or withdrawal of corticosteroids or CNIs occurs in one arm).

	• Mycophenolate sodium (Myfortic® [Novartis]) • Sirolimus (Rapamune® [Pfizer]) • Everolimus (Certican® [Novartis]).	
Comparator	**Induction therapy:** • Regimens without monoclonal or polyclonal antibodies; for example, regimens that include methylprednisolone or placebo • Interventions should also be compared with each other **Maintenance therapy:** • A calcineurin inhibitor (CNI) with or without an antiproliferative agent and/or corticosteroids (CCS) • Interventions should also be compared with each other	
Outcomes	▪ Patient survival ▪ Graft survival ▪ Graft function ▪ BPAR ▪ Growth	
Study design	Non-randomised **controlled** studies (comparative quasi-experimental and observational studies). E.g.: • Non-randomised controlled trials • Retrospective/historically controlled studies • Prospective time-series with stopping and changing treatments	Single-arm studies (i.e. not controlled)

1.1.3 Screening

Titles and abstracts returned by the search strategy were independently screened for inclusion by two reviewers. (MHa, JVC). Disagreements were resolved by discussion, with involvement of a third reviewer if necessary. Full texts of identified studies were obtained and screened in the same way by a team of three reviewers (JVC, MHa, HC). Studies reported only as abstracts were included provided sufficient methodological details were reported to allow critical appraisal of study quality. In addition, studies included in the review conducted by Yao et al. 2006[1] were screened for inclusion.

1.1.4 Data extraction

Information from all studies (including those in TA99) was extracted and tabulated by one reviewer (JVC) and checked by a second reviewer (MHa, HC); information included details of the study's design and methodology, baseline characteristics of participants, and results at one year follow-up (Appendix 2). Where no one year follow-up data were available, a time point closest to one year follow-up was extracted instead (e.g. six months or two years follow-up). If we identified several publications for one study, we evaluated the effectiveness data from the most recent publication and amended this with information from other publications. For quality appraisal purposes, all publications relating to a study were assessed together.

1.1.5 Critical appraisal strategy

All included studies (including those in TA99) were quality appraised by two reviewers (HC and MHa). Since there is no agreed recommended appraisal tool for the assessment of non-randomised studies,[1] the CRD handbook suggests considering the study design, risk of bias, other issues related to study quality, choice of outcome measure, statistical issues, quality of reporting, quality of the intervention and generalisability.[2] Therefore the internal and external validity of non-RCTs was assessed according to criteria based on CRD guidance[2] (Table 2).

Table 2. Critical appraisal checklist for non-randomised control studies

Treatment allocation	1. Was the method of allocation reported? 2. Is the allocation to groups or to the study a source of selection bias?
Similarity of groups	3. Were the groups similar at baseline in terms of prognostic factors?
Implementation of masking	4. Were the care providers blinded to the treatment allocation? 5. Were the outcome assessors blinded to the treatment allocation? 6. Were the participants blinded to the treatment allocation?
Outcomes	7. Was follow-up long enough for outcomes to occur? 8. Were complete data reported, e.g. was attrition and exclusion (including reasons) reported for all outcomes? 9. Were statistical analyses adjusted to remove to account for any between group differences?
Generalisability	10. Was the group(s) representative of NHS renal transplant patients?

Key: NHS, National Health Service.
Notes: Criteria were based on CRD guidance.[2]

1.1.6 Methods of data synthesis

Data were tabulated and discussed in a narrative review. For binary data, odds ratio (OR) was calculated as a measure of treatment effect. If the number of events was zero in one of the studies arms, a value of 0.5 was added to all study arms to allow for statistical analyses. For continuous data (i.e. graft function), means and standard deviations (SD) were compared using t-tests in Stata 13.[3]

1.2 Results of the rapid review

1.2.1 Quantity and quality of research available

The rapid review summarises non-randomised controlled evidence. The assessment of effectiveness is reported separately for induction and maintenance regimens. Our searches returned 1738 unique titles and abstracts, with 308 papers retrieved for detailed consideration.

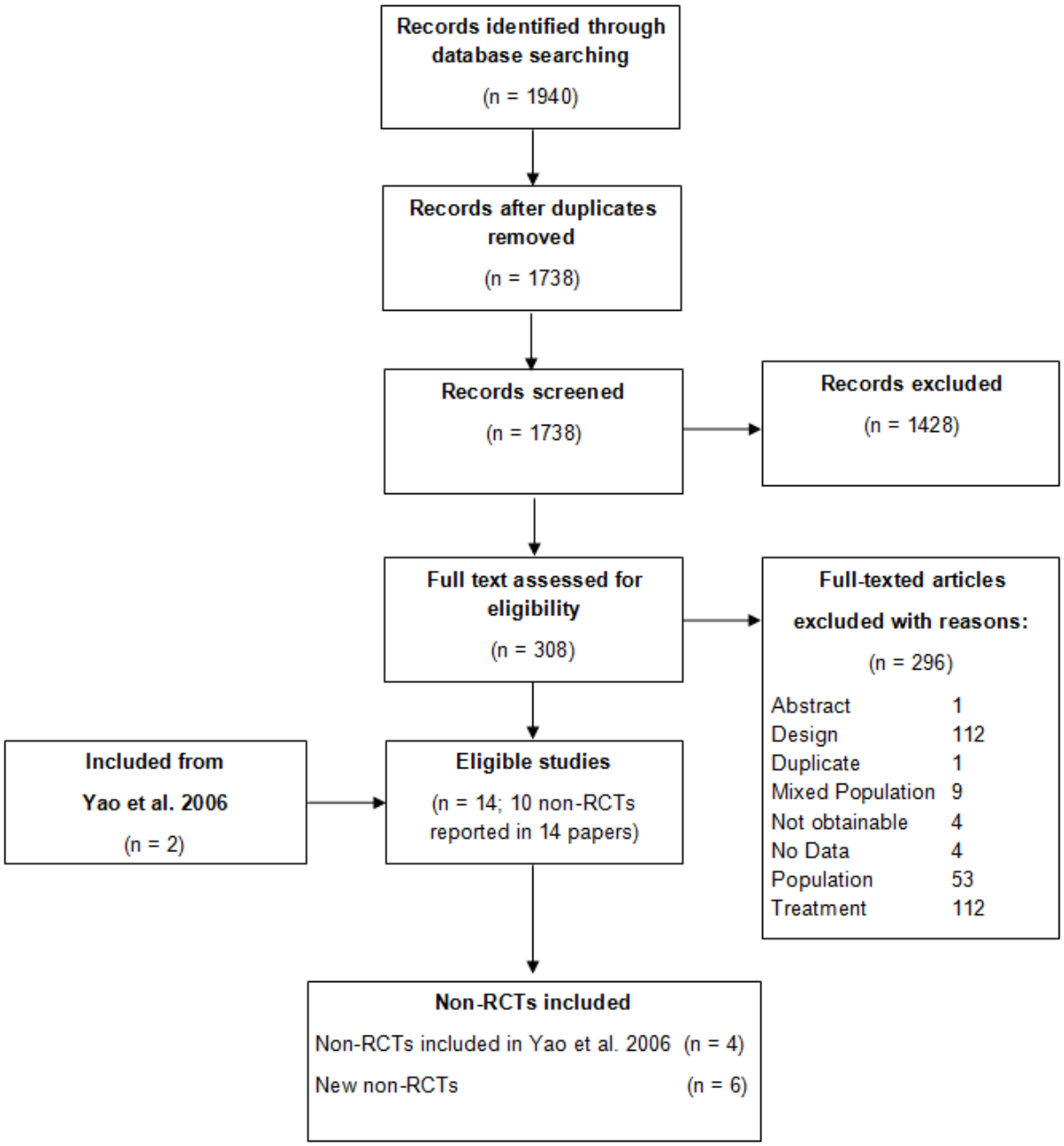
Of the 308 full text papers retrieved, 296 were excluded, (a list of these records with reasons for their exclusion can be found in Appendix 3, Table 14). In addition, non-randomised comparative trials in children that were older than 18 years (e.g. children defined as ≥21 years), trials not reporting the age of included children, and trials including both adult and children/adolescent population were excluded (coded as mixed population in Table 14). To

improve understanding of the quality of non-randomised evidence available the study characteristics and reasons for exclusion are described in Appendix 3 (Table 15).

Ten non-randomised comparative trials in children published in 14 papers were included.

The process is illustrated in detail in **Error! Reference source not found.**

Figure 1 Rapid review flow chart



Key: non-RCT, non-randomised comparative study.

Of the ten non-randomised comparator studies, five historically controlled studies Benfield et al. 1999, Chavers et al. 2009, Delucchi et al. 2007, Staskewitz et al 2001, and Valenzuela et al. 2008,[4-7] four retrospective cohort studies Cransberg et al. 2008, Garcia et al. 2002, Hymes et al. 2011, and Mosaad et al. 2012,[8-10] one nonrandomized cotrolled trial Antoniadis et al. 1998.[11] In addition, two non-RCTs comparing TAC+MMF and AZA+CSA regimens, Delucchi et al. 2007[6] and Valenzuela et al. 2008 [7] were conducted at the same centre in Chile, share some co-authors, and reported similar study designs. Therefore it is possible that both papers are reporting the same study. The authors have been contacted to clarify this, but no reply has been received to date.

Finally, of the ten non-randomised comparator studies (Table 3), six were newly identified, four were included in the previous HTA by Yao et al. 2006;[12] one study (Staskewitz et al 2001[13]) published five years follow-up data (Jungraithmayr et al. 2007[14]) that were not included in the previous HTA.

Table 3. Summary table of included non-randomised studies

Study, year	N[a]	Treatment (n)	Outcomes	Multiple publications	Yao et al. 2006[12]
		Induction and maintenance therapy			
Cransberg et al 2008[8]	233	**BAS**+**CSA**+**MMF**+CCS *vs* CSA+ **MMF**+CCS	Mortality, graft loss, graft function, AR, AE	NA	–
		Maintenance therapy			
Antoniadis et al. 1998[11]	14	CSA+ **MMF**+CCS *vs* CSA+**AZA**+CCS [b]	Mortality, graft loss,BPAR, graft function, AE	NA	✓
Benfield et al. 1999[c 4]	67	(OKT3 or CSA)+**MMF** + CCS *vs* (OKT3 or CSA)+ **AZA**+CCS	BPAR	NA	✓
Chavers et al. 2009[5]	60	ATG+**MMF**+CSA+CCS *vs* ATG+**AZA**+CSA+CCS	Mortality, graft loss, graft function, BPAR, growth, AE	NA	–
Delucchi et al. 2007[6]	46	BAS+**TAC**+**MMF**+CCS *vs* BAS+**AZA**+**CSA**+CCS[f]	Mortality, graft loss, graft function, BPAR, growth, AE	NA	–
Garcia et al. 2002[9]	24	BAS+**TAC**+**AZA**+CCS *vs* BAS+**CSA**+**MMF**+CCS	Mortality, graft loss, graft function, BPAR, AE	NA	✓
Hymes et al. 2011[15, g]	47	BAS+**SRL**+MMF+CCS *vs* BAS+**TAC**+MMF+CCS	Graft function, growth	Hymes et al. 2008[16] and Hymes et al. 2011[17]	
Staskewitz et al. 2001[13]	139[d]	CSA+**MMF**+CCS [e] *vs* CSA+**AZA**+CCS	Mortality, graft loss, graft function, BPAR, AE	Jungraithmayr et al. 2003;[18] Jungraithmayr et al. 2007[14]	✓
Mosaad et al. 2012[10]	63	CSA+CCS *vs* **CSA**+**AZA**+CCS vs **BAS**+**TAC**+**MMF**+CCS *vs* BAS+TAC+MMF	Graft survival, growth	NA	–
Valenzuela et al. 2008[7]	23	BAS+**TAC**+**MMF**+CCS *vs* BAS+**AZA**+**CSA**+CCS	BPAR, graft function, growth	NA	–

Key: ATG, anti-lymphocyte globulin; AE, adverse events; AZA, azathioprine; BAS, basiliximab; BPAR, biopsy proven acute rejection; MMF, mycophenolate mofetil; CCS, steroids; TAC, tacrolimus; CSA, ciclosporine; SRL, sirolimus; OKT3, Orthoclone OKT3.

Notes: a, Intention-to-treat population; b, Methylprednisolone induction in all participants; c, this was randomised trial of OKT3 vs CSA at the time of transplantation. First 31 participants were given AZA and subsequent 36 participants were given MMF. In addition participants were randomly assigned to receive Sandimun or Neoral CSA preparations. Only a subgroup of participants was considered in this review.; d, Staskiewitz et al. 2001 reported results for 65 MMF and 54 AZA participants, however the following two publications (Jungraithmayr et al. 2003 and Jungraithmayr et al. 2007) reports on 85 MMF and 54 AZA participants; e, participants received Prednisone/ methylprednisolone induction in this arm, no induction reported for the historical control arm (CSA+AZA+CCS); f, in TAC+MMF arm CCS were given for 7 days, in AZA=CSA arm CCS were given

daily; g, Hymes et al. 2011 [15] reports a subgroup of children aged 1-15 years of a larger study by Hymes et al. 2008[16] (with 5 years follow-up by Hymes et al. 2011[17]). The study by Hymes et al. 2008[16] include 117 children (but do not specify the age inclusion criteria, the mean (SD) ages of the two groups are 11 (3) vs 11 (2) for SRL and TAC respectively.

The previous assessment report

An overview of the nine non-randomised studies included in the Yao et al. 2006[12] assessment with reasons for inclusion/exclusion in the current review is provided in Table 4. Five studies were excluded from the rapid review (Table 4):

- Duzova et al. 2003[19] (compared BAS and no induction) administered triple therapy of (CSA or TAC) + (AZA or MMF)+CCS, however, a breakdown of the numbers (and results) in each combination was not reported, in addition, the mean recipient age was 14.9 ± 3.6 years (range 7–21 years);
- Pape et al. 2002[20] recruited a child with a combined kidney-liver transplantation;
- Swiatecka-Urban et al. 2001[21] included children, adolescents, and adults (inclusion criteria age: < 21 years);
- Neu et al. 2003[22] included children, adolescents, and adults (inclusion criteria age: >2 and < 21 years) and the use of induction therapy varied in the study;
- Steffen et al. 2003[23] was published as an abstract only, and did not include enough information to allow critical appraisal.

Table 4. Yao et al. 2006[12]; children and adolescents non- randomised studies

No	ID	Multiple ID	N[a]	Treatments	Included in rapid review (reason)
			Induction therapy		
1	Duzova et al. 2003[19]	NA	43	**BAS**+(CSA or TAC)+(AZA or MMF)+CCS *vs* (CSA or TAC)+(AZA or MMF)+CCS	No (design & population)
2	Pape et al. 2002[20]	NA	77	**BAS**+CsA+CCS *vs* CSA+CS	No (population)[b]
3	Swiatecka-Urban et al. 2001[21]	NA	32	**BAS**+TAC+CCS *vs* TAC+CCS[c]	No (population)
			Maintenance therapy		
4	Garcia et al. 2002[9]	NA	24	BAS+**TAC**+**AZA**+CCS *vs* BAS+**CSA**+**MMF**+CCS	Yes
5	Neu et al. 2003[22]	NA	986	**TAC**+MMF+CCS *vs* **CSA**+MMF+CS	No (population)
6	Antoniadis et al. 1998[11]	NA	14	CSA+**MMF**+CCS *vs* CSA+**AZA**+CS[d]	Yes
7	Steffen et al. 2003[23]	NA			No (abstract)
8	Staskewitz et al 2001[13]	Jungraithmayr et al. 2003[18]	120	CSA+**MMF**+CCS[e] *vs* CSA+**AZA**+CCS	Yes
9	Benfield et al. 1999 [f, 4]	NA	678	(OKT3 or CSA)+**MMF**+CCS *vs* (OKT3 or CSA)+**AZA**+CCS	Yes

Key: AZA, azathioprine; BAS, basiliximab; CSA, ciclosporin; ID, identification; No, number; MMF, mycophenolate mofetil; CCS, steroids; OKT3, Orthoclone OKT3; TAC, tacrolimus.

Notes: a, an intention to treat population; b, one child had a combined kidney-liver transplantation; c, a single AZA dose perioperatively in 7/8 participants in the non BAS; d,Methylprednisolone induction in all participants; e, participants received Prednisone/ methylprednisolone induction in this arm, no induction reported for the historical control arm (CSA+AZA+CCS); f, this was randomised trial of OKT3 vs CSA at the time of transplantation. First 31 participants were given AZA and subsequent 36 participants were given MMF. In addition participants were randomly assigned to receive Sandimun or Neoral CSA preparations.

In summary, ten non-randomised comparator studies met the inclusion criteria and were considered eligible for inclusion; four were also included in the assessment report by Yao et al. 2006,[12] and six were newly identified in the rapid review.

1.2.2 Quality of included studies

Of the ten included studies, eight studies investigated maintenance treatments, one study focused on induction treatments, and one study compared a combination of induction and maintenance regimes.

Overall assessment

For all ten studies, half or fewer of the items constituting the quality appraisal assessment were adequately addressed (Table 5). However, for all studies at least four of the ten quality appraisal items were either not applicable (due to study design), not reported, or not clearly reported. It is possible that items that were not clearly reported in the papers were in fact adequately conducted in the studies.

Treatment allocation

Allocation to groups: nine of the non-randomised studies adequately described what the treatment and control groups were and the general basis for allocating participants to a particular treatment. In five studies allocation to groups was dictated by changes to the treatment protocol in the study centres (i.e. they were historically controlled studies).[4-7, 13] Four studies compared retrospective cohorts (where treatment allocation was unrelated to the study design).[8-10, 15] Despite being a prospective non-randomised, controlled trial, the remaining study did not report the basis for allocation to treatment groups.[11]

Avoidance of selection bias: As well as being clear about the basis of allocation to groups, two of the studies clearly specified that all eligible participants were enrolled.[8, 10] However, seven studies did not provide any evidence that selection bias was minimized and were rated as 'unclear'. [4, 6, 7, 9, 11, 13, 15] The remaining study was rated as 'inadequate' on this criterion because, for the treatment group, not all patients were enrolled onto the study. Instead, participants were selected by clinicans.[5]

Similarity of groups

Baseline characteristics: Six of the ten studies did not clearly report whether treatment groups were similar at baseline on a range of prognostic factors, because they omitted key statistical information,[4, 6, 8, 11] omitted to report baseline characteristics for an important prognostic factor,[6, 8, 15] or did not report baseline characteristics by group.[10] In two of the ten studies the age of participants statistically significantly differed between treatment groups.[9, 13] In another study there were statistically significant between group differences in height at baseline, number of previous transplants and sex. [5] The remaining study reported a statistically significant between-group baseline difference in sex.[7]

Implementation of masking

None of the non-randomised studies reported whether treatment allocation was masked from treatment providers, outcome assessors or participants. However, for nine of the studies this was not applicable, because blinding could not be reasonably expected given the study

design.[4-10, 13, 15] The remaining study was a prospective non-randomised controlled trial, so masking of care providers, outcome assessors (by using independent assessors) and participants could be done but was not reported.[11]

Length of follow-up

Nine of the non-randomised studies had an adequate length of follow-up, with all participants followed for at least six months.[4-8, 10, 11, 13, 15] The remaining study was rated as 'partial' because not all participants were followed for at least six months but delayed graft function was included as an outcome (this outcome would usually be assessed within the first month of transplantation).[9]

Completeness of trials

Eight of the non-randomised studies adequately described the completeness of the study, either by describing withdrawals or drop-outs (including reasons) or by making it clear that all enrolled participants completed the study.[4, 6-9, 11, 13, 15] The other two studies did not report sufficient information on withdrawals and dropouts.[5, 10]

Adjustment for bias in non-randomised studies

This item of the quality appraisal assessment was applicable to all ten studies. However, only one study made adequate statistical adjustments for baseline characteristics.[8] Five of the studies did not perform any adjustment for bias in their analyses.[4-6, 13, 15] For four studies, this item could not be assessed, because analyses were not fully or clearly reported.[7, 9-11]

Applicability of trials to the current NHS in England

None of the non-randomised studies was considered to be clearly applicable to the NHS in England. Three studies were rated as inadequate because the study population was not representative of the current NHS in England; in two of these studies all kidneys were from living donors[10, 11] and in one study >90% of kidneys were from cadaveric donors.[13] The other seven studies were rated as 'unclear', either because the populations were not recruited from the EU,[4-7, 9] and/or because there was no data reported on at least one key population characteristic.[6-8, 15]

Table 5. Quality assessment; non-randomised studies

Study	Design	Was the allocation to group(s) reported?	Is the allocation to groups or to the study a source of selection bias?	Were the groups similar at baseline in terms of prognostic factors?	Were the care providers blinded to the treatment allocation?	Were the outcome assessors blinded to the treatment allocation?	Were the participants blinded to the treatment allocation?	Was follow-up long enough for outcomes to occur?	Were complete data reported, e.g. was attrition and exclusion (including reasons) reported for all outcomes?	Were analyses adjusted to remove bias in non-randomised studies?	Was the group(s) representative of NHS renal transplant patients?
Antoniadis et al. 1998[11]	Non-randomized controlled trial	NR	Unclear	Unclear	NR	NR	NR	Adequate	Adequate	NR	Inadequate
Benfield et al. 1999[4]	Historically controlled study (a)	Adequate	Unclear	Unclear	NA	NA	NA	Adequate	Adequate	Inadequate	Unclear
Garcia et al. 2002[9]	Retrospective cohort study	Adequate	Unclear	Inadequate	NA	NA	NA	Partial	Adequate	NR	Unclear
Staskewitz et al 2001[13]	Historically controlled study	Adequate	Unclear	Inadequate	NA	NA	NA	Adequate	Adequate	Inadequate	Inadequate
Hymes et al 2011[15]	Retrospective cohort study	Adequate	Unclear	Unclear	NA	NA	NA	Adequate	Adequate	Inadequate	Unclear
Chavers et al 2009[5]	Historically controlled study	Adequate	Inadequate	Inadequate	NA	NA	NA	Adequate	NR	Inadequate	Unclear

Cransberg et al 2008[8]	Retrospective cohort study	Adequate	Adequate	Unclear	NA	NA	NA	Adequate	Adequate	Adequate	Unclear
Delucchi et al 2007[6]	Historically controlled study	Adequate	Unclear	Unclear	NA	NA	NA	Adequate	Adequate	Inadequate	Unclear
Mosaad et al 2012[10]	Retrospective cohort study	Adequate	Adequate	Unclear	NA	NA	NA	Adequate	NR	Unclear	Inadequate
Valenzuela et al 2008[7]	Historically controlled study	Adequate	Unclear	Partial	NA	NA	NA	Adequate	Adequate	Unclear	Unclear

Key: NA; not applicable; NR, not reported. Notes: a, this was randomised trial of OKT3 vs CSA at the time of transplantation. The first 31 participants were given AZA and the subsequent 36 participants were given MMF. In addition participants were randomly assigned to receive Sandimun or Neoral CSA preparations. Therefore we consider there to be two additional studies embedded within

1.2.3 Baseline characteristics

Baseline characteristics of the ten non-randomised studies are summarised in Table 6. The Antoniadis et al. 1998[11] study was conducted in a single Greek centre; the Benfield et al. 1999[4] study was conducted in two centres in the USA; Chavers et al. 2009[5] and Hymes et al. 2011[15] were each conducted in a single centre in the USA (Minnesota and Atlanta respectively); Delucchi et al. 2007[6] and Valenzuela et al. 2008[7] were both conducted at the same single centre in Chile; Mosaad et al. 2012[10] was conducted in a single Egyptian centre; Cransberg et al. 2008[8] was conducted over four Dutch centres and one Belgium centre; and Staskewitz et al. 2001[13] study was conducted in 12 German centres. Garcia et al. 2002[9] did not report where or within how many centres their study was performed, however the authors are all based in Brazil, and therefore it is likely that this study was completed in Brazil.

Not surprisingly, the baseline characteristics of the non-RCTs varied, not only across the studies, but also within the studies. Mean age across the studies arms ranges from 7.2 years to 14 years. Only Hymes et al. 2011[15] and Delucchi et al. 2007[6] reported the proportion of pre/pubertal children (proportion of pubertal children 20% and 30-35% respectively). The sex distribution of participants varied widely (ranging from 17% to 76% male).

In respect of ethnicity, three studies had a high proportion of white participants (75%-100%),[5, 9, 13] one study reported between 19% and 25% black participants (dependent on treatment group),[4] one study reported that the cohorts race was 52 % white, 24 % African American, 16 % Hispanic and 8 % Asian, [15]. Finally, five studies did not report ethnicity.[6-8, 10, 11]

Six studies included a high proportion of living donors (56% -100%).[4, 5, 9-11, 15] The remaining studies reported lower proportions of living donors (6-56%).[6-8, 13] Mean HLA mismatches were reported in three studies with a mean range from 2.2 -2.89.[6, 8, 13]

Table 6 Baseline characteristics; non- randomised comparative studies

Study id	Induction therapy	Maintenance therapy	N[a]	Mean age, yrs (sd) [range]	Adolescents n/N, %	First transplant n/N, %	Male n/N, %	Donor type n/N, %				Race (%)	Mean HLA mismatches
								Living	DBD	DCD	Cadaveric		
Antoniadis et al. 1998[11]	Methyl-prednisolone	CSA+MMF+CCS	7	10 [4-12][b]	NR	NR	NR	7/7, 100%	NA	NA	NA	NR	NR
		CSA+AZA+CCS	7		NR	NR	NR	7/7, 100%	NA	NA	NA	NR	NR
Benfield et al. 1999[4 c]	OKT3	CSA+MMF+ CCS	20	10.7 (5.3)	NR	NR	20/36, 55%	25/36, 69%	NA	NA	11/36, 31%	9/36, 25% Black	NR
	CSA	CSA+MMF+CCS	16		NR	NR			NA	NA			NR
	OKT3	CSA+ AZA+CCS	14	9.4 (5.1)	NR	NR	19/31, 61%	24/31, 77%	NA	NA	7/31, 23%	6/31, 19% Black	NR
	CSA	CSA+ AZA+CCS	17		NR	NR			NA	NA			NR
Chavers et al 2009[5g]	ATG (5-7 days)	CsA+ MMF+CCS (CCS for 6 days only)	21	14 (3) [7.8-18.1]	NR	19/21, 90%	16/21, 76%	15/21, 71%	NA	NA	6/21, 29%	17/21, 81% White; 4/21, 19% non white	NR
	ATG (6-15 days)	CsA+ AZA+CCS	39	14 (3) [8.1-18]	NR	21/39, 54%	16/39, 41%	29/39, 74%	NA	NA	10/39, 26%	32/39, 82% White; 7/39, 18% non white	NR
Cransberg et al 2008[8]	BAS	CSA+ MMF+CCS	110	12.6 [2.7-18.1] [b, f]	NR	92/109, 84%	65/110, 59%	38/110, 35%		2/110, 2%	70/110, 64%	NR	2.2 (1.2) (n=101)
	No Induction	CSA+MMF+CCS	123	11.6 [3.4-18.0][b]	NR	95/121, 79%	71/123, 58 %	33/123, 27 %		1/123, 1%	89/123, 72%	NR	2.2 (1.2) (n=102)
Delucchi et al 2007[6]	BAS	TAC+MMF+CCS (CCS for 6 days only)	23	7.2 (3.8)	8/23, 35% pubertal	23/23, 100%	14/23, 60%	3/23, 13%	NA	NA	20/23, 87%	NR	2.5 (0.8)
	BAS	CSA+AZA+CCS	23	8.6 (3.8)	7/23, 30% pubertal	23/23, 100%	12/23, 65%	7/23, 27%	NA	NA	16/23, 73%	NR	2.8 (0.9)
Garcia et al. 2002[9]	BAS	TAC+AZA+CCS	12	11.3 (9.3)	NR	NR	6/12, 50%	8/12, 66.7%	NA	NA	4/12, 33.3%	11/12, 92% White 1/12, 8% Black	NR
		CSA+MMF+CCS	12	9.0 (6)	NR	NR	8/12, 66.7%	7/12, 58.3%	NA	NA	5/12, 41.7%	9/12, 75% White 3/12, 25% Black	NR

Hymes et al 2011[15]	BAS	SRL+MMF+CCS[h]	25	8 (5) [g]	5/25, 20% pubertal (Tanner stage 3-4)	24/25, 96%	16/25, 64%	14/25, 56%	NA	NA	11/25, 44%	13/25, 52% Caucasian 6/25, 24% African American 4/25, 16% Hispanics 2/25, 8% Asians	NR
	BAS	TAC+MMF+CCS	23	8 (5)	NR	NR	17/23, 74%	NR	NR	NR	NR	NR	NR
Mosaad et al 2012[10]	No induction	CsA+CCS	11	all participants < 25 kgs; assumed all participts were younger ≤18 [e]	NR	NR		11/11, 100%	NA	NA	NA	NR	Zero matches n=2
	No induction	CsA+AZA+CCS	27		NR	NR		27/27, 100%	NA	NA	NA	NR	One match, n=5
	BAS	MMF+TAC+CCS	5		NR	NR	18/63, 29%	5/5, 100%	NA	NA	NA	NR	Two matches, n=40 Three matches, n=6
	BAS	MMF+TAC	20		NR	NR		20/20, 100%	NA	NA	NA	NR	Four matches, n=1 Missing data, n=9
Staskewitz et al 2001[13]	Prednisone/ methylprednisolone	CSA+MMF+CCS	85[d]	11.5 (3.6)	NR	61/65, 94%	42/65, 65%	4/65, 6%	NA	NA	61/65, 94%	65/65, 100% Caucasian	2.69 (0.87)[i]
	NR	CSA+AZA+CCS	54	9.9 (4.7)	NR	53/54, 98%	32/54, 59%	5/54, 9%	NA	NA	49/54, 91%	54/54, 100% Caucasian	2.89 (0.96)[i]
Valenzuela et al 2008[7]	BAS	TAC+MMF+CCS	12	7.8 [2.8-12.2]	NR	12/12, 100%	2/12, 17%	3/12, 25%	NA	NA	9/12, 75%	NR	NR
	BAS	CsA+AZA+CCS (CCS for 6 days only)	11	6 [1.1-14.2]	NR	11/11, 100%	5/11, 42%	5/11, 45%	NA	NA	6/11, 55%	NR	NR

Key: ATG, anti-lymphocyte globulin ; AZA, azathioprine; BAS, basiliximab; CSA, ciclosporin; DBD, donation after brain death; DCD, donation after cardiac death; MMF, mycophenolate mofetil; NA, not applicable, NI; no induction; NR, not reported; PBO, placebo; CCS, steroids; TAC, tacrolimus; SRL, sirolimus; OKT3, Orthoclone OKT3; NR, not reported; NA, not available.

Notes: a, ITT population; b, only median and [range] reported; c, this was randomised trial of OKT3 vs CSA at the time of transplantation. Firsts 31 participants were given AZA and subsequent 36 participants were given MMF. In addition participants were randomly assigned to receive Sandimun or Neoral CSA preparations. Numbers of participants in the OKT3 group were reported from text (17 & 19) text, however numbers reported in a table differed (16 & 20; numbers from text were reported because they were relevant to outcomes reported in this section); d, Staskiewitz et al. 2001 reported results for 65 MMF and 54 AZA participants, however the following two publications (Jungraithmayr et al. 2003 and Jungraithmayr et al. 2007) reports on 85 MMF and 54 AZA participants; e, the proportin of ages was as follows: 5-7 years, n=20, 8-10 years, n=22, and >10 years, n=21; f, age reported in 109 participant; g, the overall study age range was 1-15 years; h; sirolimus switched to replace tacrolimus at 3 moths post transplantation; i, SD calculated from SEM.

1.3 Results of the included studies

Of the ten included studies, eight studies investigated maintenance treatments,[4-7, 9, 11, 13, 15] one study focused on induction treatments[8], and one study compared a combination of induction and maintenance regimes[10].

This section summarises the identified non-randomised comparative evidence in children and adolescents. In addition, a summary of randomised evidence in children (three RCTs identified in the HTA 09/119/01 appraisal "Immunosuppressive therapy for kidney transplantation in children and adolescents"), and a summary of randomised evidence in adults (results of meta-analyses [MA] at 1 year-follow up as determined in the parallel HTA 09/46/01 appraisal "Immunosuppressive therapy for kidney transplantation in adults") is presented next to the the non-randomised comparative evidence in children to allow comparision of the three types of evidence.

1.3.1 Induction therapy

Only one non-RCT was identified. Cransberg et al. 2008 compared BAS-based regimen (**BAS**+CSA+MMF+CCS) with no induction (CSA+ MMF+CCS).[8]

1.3.1.1 Basiliximab versus placebo and no induction

The table below (Table 7) shows the 1-year evidence from the one non-RCT induction study[8] against the child and adolescent RCT evidence (Offner at al. 2008[24]) and the adult RCT evidence (results of meta-analyses at one year follow-up).

Table 7 Summary of randomised and non-randomised evidence comparing basiliximab, and placebo and no induction

Outcome	Child RCTs BAS vs control 1 year	Adult RCTs BAS vs control (MA at 1 year follow-up)	Child Non-RCTs BAS vs control 1 year
	OR (95% CI)	OR (95% CI)	n/N (%)
Mortality	6.64 (0.34,130.33)[24]	0.95 (0.49, 1.87) I^2=0.7%[25-28] no deaths in either arm[29, 30]	3/110 vs 1/123; OR 3.42, 95%CI (0.35, 33.34)[8]
Graft Loss	0.92 (0.06,14.92)[24]	0.82 (0.56, 1.21) I^2=0% [25-28, 30] no deaths in either arm[29]	12/110 (11%) vs 10/123 (8%); OR 1.38, 95%CI (0.58, 3.33)[8]
BPAR	0.51 (0.24, 1.08)[24]	**0.53 (0.40, 0.70)** I^2=0% [25-28, 30]	23/110 (21%) vs 44/123 (36%); **OR 0.47, 95%CI (0.27, 0.85)**[8]
eGFR	Mean (SD): 79 (23) vs 82 (24); p=0.38 [24,a]	WMD (95% CI): 1.93 (-0.97, 4.83) I^2=23.9% [26-29,b]	Mean (SD): 64 (NR) vs 62 (NR); p=0.383 [8,c]

Key: BAS, basiliximab; BPAR, biopsy proven acute rejection; eGFR, estimated glomerular filtration rate; MA, meta-analysis; vs, versus; WMD, weighted mean difference.
Notes: a, result of t-test comapring means and SDs; b, various equations (creatine clearance, eGRF); c, eGFR estimated using Schwartz equation (ml/min/1.73m^2).
Evidence suggesting a statistically significant difference between treatments highlighted in bold. All OR were calculated by PenTAG. OR < 1 favours BAS; WMD >0 favours BAS.

Both the non-RCT evidence in children and adolescents and the RCT evidence in adults suggests lower odds of BPAR with BAS compared with control conditions; OR (95% CI) 0.47, (0.27, 0.85) and OR (95% CI) 0.53 (0.40, 0.70) I^2=0% respectively. No other significant results were identified.

1.3.2 Maintenance therapy

Eight non-RCTs comparing maintenance regimens were identified.[4-7, 9, 11, 13, 15]

1.3.2.1 Mycophenolate mofetil versus azathioprine

Three non-RCTs compared **MMF** and **AZA**. Staskewitz et al. 2001compared MMF+CSA+CCS (participants received Prednisone/ methylprednisolone induction in this arm) with AZA+CSA+CCS (no induction reported for the historical control arm).[13] Antoniadis et al. 1998 compared MMF+CSA+CCS with AZA+CSA+CCS.[11] Finally, Chavers et al. 2009 compared ATG+MMF+CSA+CCS with ATG+AZA+CSA+CCS.[5]

The table below (Table 7) shows the evidence from these non-RCT studies against the adult RCT evidence (results of meta-analyses at one year follow-up). No child and adolescent RCTs comparing MMF and AZA were identified.

One child and adolescent non-RCT suggests reduced odds of graft loss with MMF compared with AZA; OR 0.14, 95%CI (0.03, 0.68). [13] However two other non-RCTs in children and adolescents[5, 11] and the adult RCT evidence did not find any significant differences for graft loss between MMF and AZA. In addition, one study[5] found improved height standard deviation scores with MMF compared with AZA; -0.6 (1.1) vs 2.0 (1.5); p=0.001. No other significant results were identified.

Table 8 Summary of randomised and non-randomised evidence comparing mycophenolate mofetil and azathioprine

Outcome	Adult RCTs MMF vs AZA (MA at 1 year follow-up) OR (95% CI)	Child Non-RCTs MMF vs AZA 1 year n/N (%)
Mortality	1.19 (0.47, 3.02)[31-35]	1/21 (5%) vs 1/39 (3%), p=0.61; OR 1.9, 95%CI (0.11, 31.48) [5] 0/86, 0% vs 3/54, 6%. OR 0.08, 95%CI (0.004, 1.67) [13] 0/7 (0%) vs 0/7 (0%)[11]
Graft Loss	0.76 (0.38, 1.50) [31-35]	2/21 (10%) vs 3/39 (8%), p=0.86; OR 1.26, 95%CI (0.20, 8.00) [5] 2/86 (2%) vs 8/54 (15%); **OR 0.14, 95%CI (0.03, 0.68)** [13] 0/7 (0%) vs 0/7 (0%)[11]
BPAR	0.67 (0.37,1.22)[31, 33, 35, 36]	3/21 (14%) vs 9/39 (23%), p=0.17; OR 0.56, 95%CI (0.14, 2.23) [5] 6 months: 10/65 (15%) vs14/54 (26%), OR 0.52 95%CI (0.21, 1.29)[13] 6 months: 0/7 (0%) vs 3/7 (43%), OR 0.08 95%CI (0.003, 1.94)[11] 6 months: 4/17 (24%) vs 6/17 (35%), OR 0.56 95%CI (0.13, 2.47)[4]
eGFR	Mean (SD): 61.3 (15.8) vs 63.1 (16.8); WMD (95% CI): -0.11; 95%CI (-0.58 to 0.35), p=0.66[33,a]	Mean (SD) 87.7 (27.8) vs 83.0 (36.8); p≥0.05[13, b, c] Mean (SD): 73 (24) vs 76 (22); p=0.63[5, d,e] 6 months: Mean (SD): 62 (NR) vs 60 (NR)
Growth	NA	Height SDS (SD): -0.6 (1.1) vs 2.0 (1.5); **p=0.001**[5,f]

Key: MMF, mycophenolate mofetil, AZA, azathioprine, MA, meta-analysis; vs, versus; SDS, standard deviation score; WMD, weighted mean difference.

Notes: a, Cockcroft-Gault formula. (ml/min)[2]; b, creatine clearance (ml/min/1.73m^2); c, SD calculated from SEM it was assumed that all 65 MMf and 54 AZA childred provided measurements; d, eGFR estimated using Schwartz equation (ml/min/1.73m^2); e, T-test was calculated by PenTAG; f, reported Wilcoxon rank-sum test, assumed that SD was reported.

Evidence suggesting a statistically significant difference between treatments highlighted in bold. All OR were calculated by PenTAG. OR < 1 favours MMF; WMD >0 favours MMF.

1.3.2.2 Tacrolimus versus sirolimus

One non-RCT compared **TAC** and **SRL** regimens; Hymes et al. 2011 compared BAS+TAC+MMF+CCS with BAS+SRL+MMF+CCS.[15]

Table 9 shows both the child and adolescent non-RCT evidence and the adult RCT evidence (results of meta-analyses at one year follow-up). No child and adolescent RCTs comparing TAC and SRL were identified.

Table 9 Summary of randomised and non-randomised evidence comparing tacrolimus versus sirolimus

Outcome	Adult RCTs TAC vs SRL (MA at 1 year follow-up)	Child Non-RCTs TAC vs SRL 2 years
	OR (95% CI)	n/N (%)
Mortality	0.80 (0.13, 4.99) I^2=19.2%[37-40]	NR
Graft Loss	0.68 (0.18, 2.58) I^2=0.0%[37-40]	NR
BPAR	**0.32 (0.12, 0.87**) I^2=0.0%[37-40]	NR
eGFR	WMD (95% CI): -2.50 (-6.85, 1.85) I^2=0.0%[37, 39 , a]	Mean (SD): 69 (16) vs 77 (23); p=0.32[15,b]
Growth	NA	Height Z score (SD): -1.6 (1.4) vs -1.6 (1.0); p=0.94[15,c]

Key: TAC, tactrolimus; SRL, sirolimus; MA, meta-analysis; vs, versus; WMD, weighted mean difference.
Notes: a, Iothalamate clearance (ml/min/1.73m^2) and EPI formula (ml/min/1.73m^2); b, eGFR estimated using Schwartz equation (ml/min); c, assumed that SD was reported.
Evidence suggesting a statistically significant difference between treatments highlighted in bold. All OR were calculated by PenTAG. OR < 1 favours TAC; WMD >0 favours TAC.

The RCT evidence in adults suggests reduced BPAR with TAC compared with SRL; OR (95% CI) 0.32 (0.12, 0.87) I^2=0.0%, but BPAR was not reported in the child and adolescent non-RCT study. No other statistically significant results were identified.

1.3.2.3 Tacrolimus and azathioprine versus ciclosporin and mycophenolate mofetil

One non-RCT, Garcia et al. 2002 compared BAS+**TAC**+**AZA**+CCS with BAS+**CSA**+**MMF**+CCS.[9] The table below (Table 10) summarises the study results. No child and adolescent RCTs, and no adult RCTs comparing TAC+AZA and CSA+MMF were identified.

Table 10 Summary of randomised and non-randomised evidence comparing tacrolimus and azathioprine versus ciclosporin and mycophenolate mofetil

Outcome	Child Non-RCTs TAC + AZA vs CSA + MMF 3 months n/N (%)
Mortality	0/12 (0%) vs 0/12 (0%)[9]
Graft Loss	0/12 (0%) vs 1/12 (8%); OR 0.30, 95%CI (0.01, 8.30)[9]
BPAR	1/12 (8%) vs 2/17 (8%); OR 0.45, 95%CI (0.04, 5.78)[9]
eGFR	Mean (SD): 71 (23) vs 82 (19); p=0.21 [9,a ,b]

Key: MMF, mycophenolate mofetil; AZA, azathioprine; TAC, tacrolimus; CSA, ciclosporin; MA, meta-analysis; vs, versus.
Notes: a; creatinine clearance (mL/min); b, T-test was calculated by PenTAG.

No difference between TAC+AZA and CSA+MMF for mortality, graft los, BPAR, and graft function in the child/adolescent non-RCT evidence was identified.

1.3.2.4 Tacrolimus and mycophenolate mofetil versus ciclosporin and azathioprine

Two non-RCTs compared **TAC**+**MMF** and **AZA**+**CSA** regimens. Delucchi et al. 2007 and Valenzuela et al. 2008 compared BAS+TAC+MMF+CCS (CCS were given for 7 days) and BAS+AZA+CSA+CCS (CCS were given daily).[6, 7] Both non-RCTs were conducted at the same centre in Chile, share some co-authors, and reported similar study designs. Therefore it is possible that both papers are reporting the same study. The authors have been contacted to clarify this, but no reply has been received to date.

Table 11 shows the child and adolescent non-RCT evidence against the adult RCT evidence (results of meta-analyses at one year follow-up). No child and adolescent RCTs comparing TAC+MMF and CSA+AZA were identified.

Table 11 Summary of randomised and non-randomised evidence comparing tacrolimus and mycophenolate mofetil versus ciclosporin and azathioprine

Outcome	Adult RCTs TAC + MMF vs CsA + AZA (MA at 1 year follow-up) OR (95% CI)	Child Non-RCTs TAC + MMF vs CsA + AZA 1 year n/N (%)
Mortality	2.07 (0.37,11.49)[41]	1/19 (5%) vs 1/20 (5%), OR 1.06, 95%CI (0.06, 18.10)[6]
Graft Loss	1.75 (0.62, 4.96)[41]	NR[b]
BPAR	**0.35 (0.15, 0.82)**[41]	1/19 (5%) vs 2/20 (10%), OR 0.50, 95%CI (0.04, 5.99)[6] 6 months: 0/12 (0%) vs 0/11 (0%)[7]
eGFR	NR	Mean (SD): 88.0 (20.9) vs 82.7 (16.8); p=NS [6a] 6 months mean (SD): 76 (19.5) vs 97.9(17.8); **p<0.05**[7 a]
Growth	NA	Height Z score (SD): -1.8 (0.88) vs -2.3 (1.42) ; p=NS [6,c] 6 month height Z score (SD): -2.6 (0.97) vs -2.1 (1.47); p≥0.05[7 ,c]

Key: MMF, mycophenolate mofetil, AZA, azathioprine, TAC, tacrolimus; CSA, ciclosporin, MA, meta-analysis; NS, not significant; vs, versus.
Notes: a, creatinine clearance (no units given); b, Delucchi et al. 200 reported no difference between the two arms for graft survival.[6]; c, assumed that SD was reported.
Evidence suggesting a statistically significant difference between treatments highlighted in bold. All OR were calculated by PenTAG. OR < 1 favours TAC+MMF.

The RCT evidence in adults suggests less frequent BPAR with TAC+MMF compared with CSA+AZA; OR (95% CI) 0.35 (0.15, 0.82). No statistically significant differences between TAC+MMF and CSA+AZA for BPAR were observed in the two non-RCTs.[6, 7] One non-RCT in children and adolescents found improved graft function with CSA+AZA compared with TAC+MMF at 6 months follow-up.[7] No other statistically significant results were identified.

1.3.2.5 Tacrolimus versus ciclosporin

No non-RCTs compared **TAC** and **CSA**. For completness, a table allowing a comparison of the child and adolescent RCT[42] (identified in HTA 09/119/01) with the adult RCT evidence (results of meta-analyses at one year follow-up) is presented below (Table 12).

Table 12 Summary of randomised and non-randomised evidence comparing tacrolimus versus ciclosporin

Outcome	Child RCTs TAC vs CSA 1 year	Adult RCTs TAC vs CSA (MA at 1 year follow-up)
	OR (95% CI)	OR (95% CI)
Mortality	0.9 (0.18, 4.58) [42]	1.51 (0.75, 3.06) I^2=14.8%[35, 43-49]
Graft Loss	0.44 (0.18, 1.09) [42]	1.18, (0.72,1.93) I^2=0% [35, 44-49]
BPAR	6 months: **0.29 (0.15; 0.57**)	**0.50 (0.39, 0.64)** I^2=8.1%[35, 44-51]
eGFR	Mean (SD): 64.9 (20.7) vs 57.8 (21.9); **p=0.04**[42,a,b]	No MA was performed; conflicting results were reported by all four trials across all time points (one month to three years) [26-29,c]

Key: TAC, tacrolimus; CSA, ciclosporin, MA, meta-analysis; vs, versus.
Notes: a, eGFR estimated using Schwartz equation (ml/min/1.73m2). eGFR values reported in Trompeter et al. 2002[42] and the four year follow-up paper by Filler et al. 2005[52] differ, we used data reported in Filler et al. 2005[52] b, result of t-test comparing means and SDs;c, various equations (creatine clearance, eGRF).
Evidence suggesting a statistically significant difference between treatments highlighted in bold. All OR were calculated by PenTAG. OR < 1 favours TAC; WMD >0 favours TAC.

Higher rates of BPAR were found in CSA compared with TAC in the child/adolescent RCT[42] at six months follow-up; OR (95% CI) 0.29 (0.15; 0.57). Similarly, higher rates of BPAR were found in CSA compared with TAC in the adult RCT evidence; OR (95% CI) 0.50 (0.39, 0.64) I^2=8.1%. In addition, significantly higher graft function in the TAC arm compared with the AZA arm was reported in the child/adolescent RCT.[42] No other statistically significant results were identified.

1.3.3 Combination of induction and maintenance therapy; Basiliximab and tacrolimus and mycophenolate mofetil versus ciclosporin and azathioprine

One non-RCT, Mosaad et al. 2012 compared **BAS**+**TAC**+**MMF**+CCS with **CSA**+**AZA**+CCS.[10] Table 13 summarises the study results. No child and adolescent RCTs, and no adult RCTs comparing BAS+TAC+MMF+CCS with CSA+AZA+CCS were identified.

Table 13 Summary of non-randomised evidence basiliximab and tacrolimus and mycophenolate mofetil versus comparing ciclosporin and azathioprine

Outcome	Child Non-RCTs BAS + TAC + MMF vs CSA + AZA 1 year n/N (%)
Mortality	NR
Graft Loss	0/5 (0%) vs 1/27 (4%), OR 1.89, 95%CI (0.07, 48.53)[10]
BPAR	NR
eGFR	NR
Growth	20 years data: Children below -2SD: 3/5 (60%) vs 14/27 (52%)[10,a] Children above -2SD: 2/5 (40%)vs 7/27 (26%)[10,a]

Key: MMF, mycophenolate mofetil; AZA, azathioprine; TAC, tacrolimus; CSA, ciclosporin; vs, versus.
Notes: a, date were not reported for 7 children in CSA+AZA group.
Evidence suggesting a statistically significant difference between treatments highlighted in bold. All OR were calculated by PenTAG. OR < 1 favours BAS + TAC+MMF.

No difference between BAS + TAC + MMF and CSA+AZA for mortality, graft loss, BPAR, and graft function in the child/adolescent non-RCT evidence was identified.

1.4 Summary

In summary, we identified ten non-RCTS in children and adolescents of which six were newly identified in the rapid (systematic) review. All non-RCTs were small in size including between 14 and 233 children and adolescents; only two studies[8, 13] included more than 100 children and adolescents. The non-RCT evidence identified was very limited. The main findings are summarised below:

Basiliximab versus placebo and no induction

One new non-RCT[8] compared **BAS** with no induction; both the non-RCT evidence in children and adolescents and the RCT evidence in adults suggests less BPAR with BAS compared with control conditions. However, the child and adolescent RCT evidence [24] did not find any statistically significant differences between BAS and no induction for mortality, graft los, BPAR, and graft function. No other statistically significant results were identified.

Mycophenolate mofetil versus azathioprine

Three non-RCTs[5, 11, 13] compared **MMF** with **AZA**; one was newly identified.[5] One non-RCT in children and adolescents suggested reduced graft loss with MMF compared with AZA[13] However two other non-RCTs in children and adolescents,[5, 11] and the adult RCT evidence did not find any significant differences for graft loss between MMF and AZA. In addition, one non-RCT[5] found improved height standard deviation scores with MMF compared with AZA. No other statistically significant results were identified. No child and adolescent RCTs comparing MMF and AZA were identified.

Tacrolimus versus sirolimus

One new non-RCT compared TAC and SRL.15 The RCT evidence in adults suggests reduced occurrence of BPAR with TAC compared with SRL. No other statistically significant results were identified. No child and adolescent RCTs comparing TAC and SRL were identified.

Tacrolimus and azathioprine versus ciclosporin and mycophenolate mofetil

One non-RCT, Garcia et al. 2002 compared BAS+**TAC**+**AZA**+CCS with BAS+**CSA**+**MMF**+CCS.[9] No evidence in the non-RCTs of a difference between TAC+AZA and CSA+MMF for mortality, graft los, BPAR, and graft function in the child/adolescent. No child and adolescent RCTs, and no adult RCTs comparing TAC+AZA and CSA+MMF were identified.

Tacrolimus and mycophenolate mofetil versus ciclosporin and azathioprine

Two new non-RCTs comparing **TAC**+**MMF** and **AZA**+**CSA** regimens were identified.[6, 7] It is possible that both papers report the same study; we have contacted the authors to resolve this, but received no reply. The RCT evidence in adults suggests reduced BPAR with TAC+MMF compared with CSA+AZA. However, no statistically significant differences between TAC+MMF and CSA+AZA for BPAR were observed.[6, 7] In addition, one non-RCT in children and adolescents found improved graft function with CSA+AZA compared with TAC+MMF at six months follow-up. [7] No other statistically significant results were identified. No child and adolescent RCTs comparing TAC+MMF and CSA+AZA were identified.

Basiliximab and tacrolimus and mycophenolate mofetil versus ciclosporin and azathioprine

One non-RCT compared **BAS**+**TAC**+**MMF**+CCS with **CSA**+**AZA**+CCS.[10] No difference between BAS + TAC + MMF and CSA+AZA for mortality, graft los, BPAR, and graft function in the child/adolescent non-RCT evidence was identified. No child and adolescent RCTs, and no adult RCTs comparing BAS+TAC+MMF+CCS with CSA+AZA+CCS were identified.

1.5 Conclusions

There is limited evidence for the effectiveness of immunosuppressive agents in children and adolescents. Only three randomised controlled trials were included in the reported dated April 29th 2015 and only ten non-randomised comparative studies were included in the rapid review.

For induction thjerapy, one new non-RCT[8] supported the findings of the meta-analysis of adult RCTs reported in the parallel HTA in adults suggesting less BPAR with BAS compared with control conditions. However, the child and adolescent RCT evidence [24] did not find any statistically significant differences between BAS and no induction for BPAR.

For maintenance therapy (as already described in the report dated April 29th 2015), higher rates of BPAR were found in CSA compared with TAC in one child/adolescent RCT[42] (six months follow-up), and in the meta-analysis of adult RCTs (one year follow-up).

Despite finding six new non-RCTs in this rapid review, they were all small studies and of low quality (e.g. no evidence of similar basline charactersitics). The one-year outcomes of these newly identified non-RCTs did not alter the conclusions of the original Final Report (section 4 “ASSESSMENT OF CLINICAL EFFECTIVENESS”).

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3 APPENDICES

Appendix 1 Literature searching strategies

The following search strategy was used:

1. Kidney Transplantation/
2. (Kidney$ adj3 transplant$).ti,ab,kw.
3. (Renal adj3 transplant$).ti,ab,kw.
4. ((kidney or renal) adj3 (recipient$ or dono$ or donation$ or replac$)).ti,ab,kw.
5. ((graft$ or allograft$ or homograft$ or allogeneic) and (kidney$ or renal)).ti,ab,kw.
6. 1 or 2 or 3 or 4 or 5
7. (Basiliximab or Basiliximabum or Simulect or "interleukin 2 receptor antibody").ti,ab,kw.
8. ((rabbit$ adj3 Anti-thymocyte$1) or (rabbit$ adj3 Antithymocyte$1) or (rabbit$ adj3 thymocyte$1) or (rabbit$ adj3 polyclonal) or (rabbit$ and ATG) or RATG or thymoglobulin$2).ti,ab,kw.
9. (Tacrolimus or Fujimycin or Prograf or Advagraf or Adoport or Capexion or Modigraf or Perixis or Tacni or Vivadex or Protopic or Tsukubaenolide or "FK 506" or "FK-506" or "FK506" or "fr-900506").ti,ab,kw.
10. Tacrolimus/
11. (Belatacept or Nulojix or "lea29y" or "lea 29y" or "bms 224818").ti,ab,kw.
12. ("Mycophenolic acid" or MPA or Mycophenolate or Arzip or CellCep$1 or Myfenax or Myfortic or Mofetil).ti,ab,kw.
13. (Sirolimus or Rapamune or Rapamycin or "ay 22-989").ti,ab,kw.
14. Sirolimus/
15. (Everolimus or Zortress or Certican or Afinitor or Evertor or "SDZ RAD").ti,ab,kw.
16. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17. clinical trial.pt.
18. ("controlled trial$" or "clinical trial$").ti,ab,kw.
19. exp cohort studies/
20. cohort$.tw.
21. controlled clinical trial.pt.
22. epidemiologic methods/
23. exp case-control studies/
24. (case$ and control$).tw.
25. (case$ and series).tw.
26. 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27. exp Child/
28. (child$ or infant$1 or toddler$1 or youngster$1 or young people or young person$1 or young adult$ or early adult$ or kid or kids or youth or youths or underage or under age or teen$1 or teenage or teenager$ or minor or adolesce$ or offspring or juvenile$1 or school or pre-school or student$).ti,ab,kw.
29. 27 or 28
30. 6 and 16 and 26 and 29
31. limit 30 to yr="2002 -Current"
32. limit 31 to english language

Appendix 2 Data extraction forms

Available on request

Appendix 3 Excluded studies

Table 14 Excluded studies

No	Study	Reason
1	Acott PD, Lawen JG, Crocker JF. Third dose of basiliximab in pediatric renal transplantation. Transplantation Proceedings. 2004;36:2628-31.	Design
2	Akioka K, Takahara S, Ichikawa S, Yoshimura N, Akiyama T, Ohshima S. Factors predicting long-term graft survival after kidney transplantation: multicenter study in Japan. World Journal of Surgery. 2005;29:249-56.	Treatment
3	Alarcon-Zurita A, Munar MA, Losada P, Morey A, Martinez J, de la Prada FJ, et al. Steroids withdrawal after 3 months of successful renal transplantation using a tacrolimus- and mycophenolate-based immunosuppression. Transplantation Proceedings. 2002;34:118-9.	Population
4	Aoun B, Decramer S, Vitkevic R, Wannous H, Bandin F, Azema C, et al. Protocol biopsies in pediatric renal transplant recipients on cyclosporine versus tacrolimus-based immunosuppression. Pediatric Nephrology. 2013;28:493-8.	Mixed Population
5	Atkison P, Filler G. New trends in immunosuppression for pediatric renal transplant recipients. Current Opinion in Organ Transplantation. 2007;12:509-14.	Not-obtainable
6	Ault BH, Honaker MR, Gaber AO, Jones DP, Duhart Jr BT, Powell SL, et al. Short-term outcomes of Thymoglobulin induction in paediatric renal transplant recipients. Pediatric Nephrology. 2002;17:815-8.	Treatment
7	Baltzan MA, Sr., Shoker AS, Baltzan MA, Jr. Prevention of CAN graft loss in the medium term without HLA disparity reduction. Transplantation Proceedings. 2003;35:2400-2.	Population
8	Barletta GM, Kirk E, Gardner JJ, Rodriguez JF, Bursach SM, Bunchman TE. Rapid discontinuation of corticosteroids in pediatric renal transplantation. Pediatric Transplantation. 2009;13:571-8.	Design
9	Baron PW, Ojogho ON, Yorgin P, Sahney S, Cutler D, Ben-Youssef R, et al. Comparison of outcomes with low-dose anti-thymocyte globulin, basiliximab or no induction therapy in pediatric kidney transplant recipients: a retrospective study. Pediatric Transplantation. 2008;12:32-9.	Treatment
10	Beaunoyer M, Busque S, St-Louis G, Smeesters C, Paquet M, Lallier M, et al. Low-dose tacrolimus, trough-monitored mycophenolate mofetil, and planned steroid withdrawal for cadaveric kidney transplantation: a single center experience. Transplantation Proceedings. 2002;34:1694-5.	Population
11	Becker T, Neipp M, Reichart B, Pape L, Ehrich J, Klempnauer J, et al. Paediatric kidney transplantation in small children - A single centre experience. Transplant International. 2006;19:197-202.	Treatment
12	Becker-Cohen R, Nir A, Ben-Shalom E, Rinat C, Feinstein S, Farber B, et al. Improved left ventricular mass index in children after renal transplantation. Pediatric Nephrology. 2008;23:1545-50.	Treatment
13	Beil S, Kreuzer M, Pape L. Course of immunization titers after pediatric kidney transplantation and association with glomerular filtration rate and kidney function. Transplantation. 2012;94:e69-e71.	Treatment

No	Study	Reason
14	Benfield MR, McDonald RA, Bartosh S, Ho PL, Harmon W. Changing trends in pediatric transplantation: 2001 Annual Report of the North American Pediatric Renal Transplant Cooperative Study. Pediatric Transplantation. 2003;7:321-35.	No Data
15	Billing H, Burmeister G, Plotnicki L, Ahlenstiel T, Fichtner A, Sander A, et al. Longitudinal growth on an everolimus- versus an MMF-based steroid-free immunosuppressive regimen in paediatric renal transplant recipients. Transplant International. 2013;26:903-9.	Treatment
16	Birk PE, Stannard KM, Konrad HB, Blydt-Hansen TD, Ogborn MR, Cheang MS, et al. Surveillance biopsies are superior to functional studies for the diagnosis of acute and chronic renal allograft pathology in children. Pediatric Transplantation. 2004;8:29-38.	Treatment
17	Broniszczak D, Ismail H, Nachulewicz P, Szymczak M, Drewniak T, Markiewicz-Kijewska M, et al. Kidney transplantation in children with bladder augmentation or ileal conduit diversion. European Journal of Pediatric Surgery. 2010;20:5-10.	Design
18	Bruel A, Allain-Launay E, Humbert J, Ryckewaert A, Champion G, Moreau A, et al. Early protocol biopsies in pediatric renal transplantation: Interest for the adaptation of immunosuppression. Pediatric Transplantation. 2014;18:142-9.	Design
19	Bunnapradist S, Daswani A, Takemoto SK. Graft survival following living-donor renal transplantation: a comparison of tacrolimus and cyclosporine microemulsion with mycophenolate mofetil and steroids. Transplantation. 2003;76:10-5.	Mixed Population
20	Bunnapradist S, Neri L, Wong W, Lentine KL, Burroughs TE, Pinsky BW, et al. Incidence and risk factors for diarrhea following kidney transplantation and association with graft loss and mortality. American Journal of Kidney Diseases. 2008;51:478-86.	Design
21	Buyan N, Bilge I, Turkmen MA, Bayrakci U, Emre S, Fidan K, et al. Post-transplant glucose status in 61 pediatric renal transplant recipients: Preliminary results of five Turkish pediatric nephrology centers. Pediatric Transplantation. 2010;14:203-11.	Treatment
22	Cameron C, Vavilis G, Kowalski J, Tyden G, Berg UB, Krmar RT. An observational cohort study of the effect of hypertension on the loss of renal function in pediatric kidney recipients. American Journal of Hypertension. 2014;27:579-85.	Design
23	Carcas-Sansuan AJ, Espinosa-Roman L, Almeida-Paulo GN, Alonso-Melgar A, Garcia-Meseguer C, Fernandez-Camblor C, et al. Conversion from Prograf to Advagraf in stable paediatric renal transplant patients and 1-year follow-up. Pediatric Nephrology. 2014;29:117-23.	Population
24	Carmellini M, Collini A, Ruggieri G, Garosi G, Bernini M. Excellent long-term results in de novo renal transplant recipients treated with proliferation signal inhibitors and reduced calcineurin inhibitors exposure. Transplantation Proceedings. 2008;40:1858-61.	Population
25	Carroll RP, Macgregor L, Walker RG. The improvement in survival of expanded criteria donor kidneys with transplantation era. Clinical Transplantation. 2008;22:324-32.	Treatment
26	Casas RV, Lopez AV, Rey JLN, Moctezuma LEL, Aris AM, Montero MQ, et al. Mycophenolic Acid Reaches Therapeutic Levels Whereas Mycophenolate Mofetil Does Not. Transplantation Proceedings. 2006;38:2400-1.	Treatment

No	Study	Reason
27	Cavanaugh TM, Schoenemen H, Goebel J. The impact of sirolimus on sex hormones in male adolescent kidney recipients. Pediatric Transplantation. 2012;16:280-5.	Population
28	Chacko B, Rajamanickam T, Neelakantan N, Tamilarasi V, John GT. Pediatric renal transplantation - A single center experience of 15 yr from India. Pediatric Transplantation. 2007;11:844-9.	Treatment
29	Chavers BM, Ellis D. Pediatric kidney transplantation. Current Opinion in Organ Transplantation. 2007;12:357-61.	Design
30	Cherala G, Munar MY, Naher A, Al-Uzri A. Tacrolimus pharmacokinetics in Hispanic children after kidney transplantation. Transplantation Proceedings. 2011;43:3708-12.	Population
31	Chu L, Jacobs BL, Schwen Z, Schneck FX. Hydronephrosis in pediatric kidney transplant: Clinical relevance to graft outcome. Journal of Pediatric Urology. 2013;9:217-22.	Design
32	Chu SH, Chiang YJ, Huang CC, Lee PH, Hu RH, Lai MK, et al. Use of simulect can reduce the incidence of acute rejection and demonstrates with superior 3-year patient and graft survival rates in renal transplantation. Transplantation Proceedings. 2004;36:2108-9.	Design
33	Clark G, Walsh G, Deshpande P, Koffman G. Improved efficacy of basiliximab over antilymphocyte globulin induction therapy in paediatric renal transplantation. Nephrology Dialysis Transplantation. 2002;17:1304-9.	Treatment
34	Colleen Hastings M, Wyatt RJ, Lau KK, Jones DP, Powell SL, Hays DW, et al. Five years' experience with thymoglobulin induction in a pediatric renal transplant population. Pediatric Transplantation. 2006;10:805-10.	Treatment
35	Comak E, Akman S, Ongut G, Colak D, Koyun M, Dogan CS, et al. Epstein-Barr virus infection in children with renal transplantation: 17 years experience at a single center. Renal Failure. 2014;36:760-6.	Design
36	Comoli P, Ginevri F. Monitoring and managing viral infections in pediatric renal transplant recipients. Pediatric Nephrology. 2012;27:705-17.	Design
37	Cotellessa M, Pastorino N, Cresta L, Minicucci L, Basile GC, Perfumo F, et al. Diabetes mellitus after kidney transplantation in pediatric recipients [5]. Pediatric Nephrology. 2003;18:1315-6.	Design
38	Cransberg K, Cornelissen EAM, Davin JC, Van Hoeck KJM, Lilien MR, Stijnen T, et al. Improved outcome of pediatric kidney transplantations in the Netherlands - Effect of the introduction of mycophenolate mofetil? Pediatric Transplantation. 2005;9:104-11.	Treatment
39	Cristelli MP, Tedesco-Silva H, Medina-Pestana JO, Franco MF. Safety profile comparing azathioprine and mycophenolate in kidney transplant recipients receiving tacrolimus and corticosteroids. Transplant Infectious Disease. 2013;15:369-78.	Population
40	Dagan A, Eisenstein B, Bar-Nathan N, Cleper R, Krause I, Smolkin V, et al. Tubular and glomerular function in children after renal transplantation. Pediatric Transplantation. 2005;9:440-4.	Design
41	De Paula Meneses R, Halusch Kotsifas C. Benefits of conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium in pediatric renal transplant patients with stable graft function. Pediatric Transplantation. 2009;13:188-93.	Design

No	Study	Reason
42	De Petris L, Faraggiana T, Rizzoni G. Renal mass dosing and graft function in children transplanted from pediatric donors. Pediatric Nephrology. 2002;17:433-7.	Treatment
43	Delucchi A, Valenzuela M, Lillo AM, Guerrero JL, Cano F, Azocar M, et al. Early steroid withdrawal in pediatric renal transplant: five years of follow-up. Pediatric Nephrology. 2011;26:2235-44.	Treatment
44	Dharnidharka VR, Gupta S, Al Khasawneh E, Haafiz A, Shuster JJ, Theriaque DW, et al. Immune biomarker panel monitoring utilizing IDO enzyme activity and CD4 ATP levels: Prediction of acute rejection vs. viral replication events. Pediatric Transplantation. 2011;15:321-8.	Design
45	Dharnidharka VR, Ho PL, Stablein DM, Harmon WE, Tejani AH. Mycophenolate, tacrolimus and posttransplant lymphoproliferative disorder: A report of the North American Pediatric Renal Transplant Cooperative Study. Pediatric Transplantation. 2002;6:396-9.	Design
46	Dharnidharka VR, Stevens G. Risk for post-transplant lymphoproliferative disorder after polyclonal antibody induction in kidney transplantation. Pediatric Transplantation. 2005;9:622-6.	Design
47	Dincel N, Bulut IK, Sezer TO, Mir S, Hoscoskun C. Clinical everolimus experience in pediatric renal transplant patients. Transplantation Proceedings. 2013;45:913-6.	Treatment
48	Duzova A, Aki T, Bakkaloglu A, Besbas N, Topaloglu R, Ozen S, et al. Triple Immunosuppression With Tacrolimus in Pediatric Renal Transplantation: Single-Center Experience. Transplantation Proceedings. 2008;40:132-4.	Treatment
49	Duzova A, Buyan N, Bakkaloglu M, Dalgic A, Soylemezoglu O, Besbas N, et al. Triple immunosuppression with or without basiliximab in pediatric renal transplantation: acute rejection rates at one year. Transplantation Proceedings. 2003;35:2878-80.	Treatment
50	Eid L, Tuchman S, Moudgil A. Late acute rejection: Incidence, risk factors, and effect on graft survival and function. Pediatric Transplantation. 2014;18:155-62.	Treatment
51	Einollahi B, Lessan-Pezeshki M, Nourbala MH, Simforoosh N, Pourfarziani V, Nemati E, et al. Posttransplant lymphoproliferative disorders in kidney transplant recipients: an Iranian multicenter experience. Iranian journal of kidney diseases. 2008;2:227-33.	Design
52	El-Faramawi M, Rohr N, Jespersen B. Steroid-free immunosuppression after renal transplantation - Long-term experience from a single centre. Nephrology Dialysis Transplantation. 2006;21:1966-73.	Treatment
53	El-Sabrout R, Delaney V, Qadir M, Butt F, Hanson P, Butt KM. Sirolimus in combination with tacrolimus or mycophenolate mofetil for minimizing acute rejection risk in renal transplant recipients--a single center experience. Transplantation Proceedings. 2003;35:89S-94S.	Population
54	El-Sabrout R, Weiss R, Butt F, Delaney V, Qadir M, Hanson P, et al. Rejection-free protocol using sirolimus-tacrolimus combination for pediatric renal transplant recipients. Transplantation Proceedings. 2002;34:1942-3.	Design
55	El-Sabrout R, Weiss R, Butt F, Rashid I, Delaney V, Qadir M, et al. Improved lipid profile and blood sugar control in pediatric renal transplant recipients using sirolimus-tacrolimus combination. Transplantation Proceedings. 2002;34:1946-7.	Treatment

No	Study	Reason
56	Ellis D, Shapiro R, Moritz M, Vats A, Basu A, Tan H, et al. Renal transplantation in children managed with lymphocyte depleting agents and low-dose maintenance tacrolimus monotherapy. Transplantation. 2007;83:1563-70.	Treatment
57	Ellis EN, Martz K, Talley L, Ilyas M, Pennington KL, Blaszak RT. Factors related to long-term renal transplant function in children. Pediatric Nephrology. 2008;23:1149-55.	Design
58	Elmagd MMA, Bakr MA, Metwally AHA, El Wahab AM. Clinicoepidemiologic study of posttransplant diabetes after living-donor renal transplant. Experimental and Clinical Transplantation. 2008;6:42-7.	Design
59	Elsheemy MS, Shouman AM, Shoukry AI, Soaida S, Salah DM, Yousef AM, et al. Surgical complications and graft function following live-donor extraperitoneal renal transplantation in children 20 kg or less. Journal of Pediatric Urology. 2014;10:737-43.	Design
60	Elster EA, Leeser DB, Morrissette C, Pepek JM, Quiko A, Hale DA, et al. Obesity following kidney transplantation and steroid avoidance immunosuppression. Clinical Transplantation. 2008;22:354-9.	Population
61	Englund MS, Tyden G, Wikstad I, Berg UB. Growth impairment at renal transplantation - A determinant of growth and final height. Pediatric Transplantation. 2003;7:192-9.	Treatment
62	Farge P, Ranchin B, Cochat P. Four-year follow-up of oral health surveillance in renal transplant children. Pediatric Nephrology. 2006;21:851-5.	Population
63	Feber J, Spatenka J, Seeman T, MatouSovic K, Zeman L, DuSek J, et al. Urinary tract infections in pediatric renal transplant recipients - A two center risk factors study. Pediatric Transplantation. 2009;13:881-6.	Design
64	Feltran LDS, Koch Nogueira PC, Ajzen SA, Verrastro CGY, Pacheco-Silva A. Does graft mass impact on pediatric kidney transplant outcomes? Pediatric Nephrology. 2014;29:297-304.	Design
65	Ferraresso M, Belingheri M, Ginevri F, Murer L, Dello Strologo L, Cardillo M, et al. Three-yr safety and efficacy of everolimus and low-dose cyclosporine in de novo pediatric kidney transplant patients. Pediatric Transplantation. 2014;18:350-6.	Design
66	Ferraris JR, Ghezzi L, Waisman G, Krmar RT. Potential cardiovascular risk factors in paediatric renal transplant recipients. Pediatric Nephrology. 2006;21:119-25.	Population
67	Ferraris JR, Ghezzi LF, Vallejo G, Piantanida JJ, Araujo JL, Sojo ET. Improved long-term allograft function in pediatric renal transplantation with mycophenolate mofetil. Pediatric Transplantation. 2005;9:178-82.	Mixed Population
68	Ferraris JR, Tambutti ML, Cardoni RL, Prigoshin N. Conversion from cyclosporine a to tacrolimus in pediatric kidney transplant recipients with chronic rejection: Changes in the immune responses. Transplantation. 2004;77:532-7.	Population
69	Ferraris JR, Tambutti ML, Prigoshin N, Grosman M, Cardoni RL. Conversion from mycophenolate mofetil to delayed formulation in pediatric renal transplantation: Higher mycophenolic acid predose level but no changes in the immune biomarkers. Pediatric Transplantation. 2009;13:731-6.	Population
70	Filler G, Foster J, Berard R, Mai I, Lepage N. Age-dependency of mycophenolate mofetil dosing in combination with tacrolimus after pediatric	Treatment

No	Study	Reason
	renal transplantation. Transplantation Proceedings. 2004;36:1327-31.	
71	Filler G. Is it premature to use calcineurin-inhibitor-free immunosuppression in pediatric renal transplantation? Commentary. Nature Clinical Practice Nephrology. 2007;3:16-7.	Design
72	First MR, Gerber DA, Hariharan S, Kaufman DB, Shapiro R. Posttransplant diabetes mellitus in kidney allograft recipients: incidence, risk factors, and management. Transplantation. 2002;73:379-86.	Treatment
73	Gallinat A, Paul A, Minor T, Treckmann JW, Molmenti EP, Witzke O, et al. Optimized outcomes for renal allografts with cold ischemic times of 20 h or greater. International Urology and Nephrology. 2012;44:1417-23.	Population
74	Ganschow R, Pape L, Sturm E, Bauer J, Melter M, Gerner P, et al. Growing experience with mTOR inhibitors in pediatric solid organ transplantation. Pediatric Transplantation. 2013;17:694-706.	Design
75	Garcia CD, Bittencourt VB, Alves AB, Garcia VD, Tumelero A, Antonello JS, et al. Conversion to Sirolimus in Pediatric Renal Transplantation Recipients. Transplantation Proceedings. 2006;38:1901-3.	Design
76	Garcia CD, Bittencourt VB, Pires F, Didone E, Guerra E, Vitola SP, et al. Renal transplantation in children younger than 6 years old. Transplantation Proceedings. 2007;39:373-5.	Treatment
77	Garcia CD, Bittencourt VB, Tumelero A, Antonello JS, Moura DM, Vitola SP, et al. 300 Pediatric Renal Transplantations: A Single-Center Experience. Transplantation Proceedings. 2006;38:3454-5.	Treatment
78	Garcia Meseguer C, Vila Lopez A, Luque De Pablos A, Vallo Boado A, Simon JM. Immunoprophylaxis with Simulect (basiliximab) in pediatric kidney transplant recipients: Results from routine clinical practice at 5 kidney transplant units. Transplantation Proceedings. 2003;35:1697-8.	Treatment
79	Garcia-Meseguer C, Roldan M, Melgosa M, Alonso A, Pena A, Espinosa L, et al. Efficacy and safety of basiliximab in pediatric renal transplantation. Transplantation Proceedings. 2002;34:102-3.	Design
80	Ghafari A, PourAli R, Sepehrvand N, Hatami S, Modarres V. Post-transplantation diabetes mellitus; frequency and related risk factors: a single center study. Saudi Journal of Kidney Diseases & Transplantation. 2010;21:842-5.	Design
81	Gheith O, Sabry A, El-Baset SA, Hassan N, Sheashaa H, Bahgat S, et al. Study of the effect of donor source on graft and patient survival in pediatric renal transplant recipients. Pediatric Nephrology. 2008;23:2075-9.	Treatment
82	Ghio L, Ferraresso M, Vigano SM, Ginevri F, Perfumo F, Gianoglio B, et al. Mycophenolate mofetil pharmacokinetic monitoring in pediatric kidney transplant recipients. Transplantation Proceedings. 2005;37:856-8.	No Data
83	Ghio L, Ferraresso M, Zacchello G, Murer L, Ginevri F, Belingheri M, et al. Longitudinal evaluation of mycophenolic acid pharmacokinetics in pediatric kidney transplant recipients. The role of post-transplant clinical and therapeutic variables. Clinical Transplantation. 2009;23:264-70.	Design
84	Giessing M, Muller D, Winkelmann B, Roigas J, Loening SA. Kidney Transplantation in Children and Adolescents. Transplantation Proceedings. 2007;39:2197-201.	Design

No	Study	Reason
85	Gonzalez D, Garcia CD, Azocar M, Waller S, Alonso A, Ariceta G, et al. Growth of kidney-transplanted pediatric patients treated with sirolimus. Pediatric Nephrology. 2011;26:961-6.	Population
86	Gonzalez-Jorge AL, Hernandez-Plata JA, Bracho-Blanchet E, Raya-Rivera AM, Romero-Navarro B, Reyes-Lopez A, et al. Should a complex uropathy be a contraindication for renal transplantation in children? Transplantation Proceedings. 2010;42:2365-8.	Design
87	Greenspan LC, Gitelman SE, Leung MA, Glidden DV, Mathias RS. Increased incidence in post-transplant diabetes mellitus in children: A case-control analysis. Pediatric Nephrology. 2002;17:1-5.	Design
88	Grenda R, Prokurat S, Ciechanowicz A, Piatosa B, Kalicinski P. Evaluation of the genetic background of standard-immunosuppressant-related toxicity in a cohort of 200 paediatric renal allograft recipients - A retrospective study. Annals of Transplantation. 2009;14:18-24.	Treatment
89	Grenda R. Minimizing steroid use in pediatric kidney recipients. Pediatric Transplantation. 2011;15:32-6.	Design
90	Groothoff JW, Cransberg K, Offringa M, Van De Kar NJ, Lilien MR, Davin JC, et al. Long-term follow-up of renal transplantation in children: A Dutch cohort study. Transplantation. 2004;78:453-60.	Design
91	Grushkin C, Mahan JD, Mange KC, Hexham JM, Ettenger R. De novo therapy with everolimus and reduced-exposure cyclosporine following pediatric kidney transplantation: A prospective, multicenter, 12-month study. Pediatric Transplantation. 2013;17:237-43.	Design
92	Gulati A, Sarwal MM. Pediatric renal transplantation: An overview and update. Current Opinion in Pediatrics. 2010;22:189-96.	Design
93	Gulati S, Kher V. Kidney transplantation in children. Journal International Medical Sciences Academy. 2009;22:15-8.	Design
94	Gulati S, Sharma RK, Gupta A, Bhandari M, Kumar A, Srivastava A. Outcome of pediatric renal transplants in a developing country. Pediatric Nephrology. 2004;19:96-100.	Treatment
95	Guleria S, Kamboj M, Sharma M, Chatterjee A, Dinda A, Chaudhary A, et al. Tacrolimus (Pan Graf) in Live Related Renal Transplantation: An Initial Experience of 101 Recipients in India. Transplantation Proceedings. 2007;39:747-9.	Treatment
96	Gulleroglu K, Baskin E, Bayrakci US, Aydogan M, Alehan F, Kantar A, et al. Neurocognitive functions in pediatric renal transplant patients. Transplantation Proceedings. 2013;45:3511-3.	Treatment
97	Haberal M, Karakayali H, Emiroglu R, Basaran O, Moray G, Bilgin N. Malignant tumors after renal transplantation. Artificial Organs. 2002;26:778-81.	Treatment
98	Hamiwka LA, Burns A, Bell L. Prednisone withdrawal in pediatric kidney transplant recipients on tacrolimus-based immunosuppression: Four-year data. Pediatric Transplantation. 2006;10:337-44.	Treatment
99	Hasegawa A, Oshima S, Takahashi K, Uchida K, Ito K, Sonoda T. Improvement of quality of life in tacrolimus-based pediatric renal transplant recipients and their caregivers, including donors. Transplantation Proceedings. 2005;37:1771-3.	Design

No	Study	Reason
100	Hasegawa A, Oshima S, Takahashi K, Uchida K, Ito K, Sonoda T. Successful treatment of 115 pediatric renal transplant recipients with tacrolimus-based immunosuppressive therapy: A 7-year multicenter study in Japan. Transplantation Proceedings. 2005;37:1769-70.	Design
101	Hasegawa A, Takahashi K, Ito K, Oshima S, Uchida K, Sonoda T. Optimal use of tacrolimus in living donor renal transplantation in children. Transplantation Proceedings. 2002;34:1939-41.	Design
102	Hasegawa A, Takahashi K, Ito K, Oshima S, Uchida K, Sonoda T. Optimal use of tacrolimus in living donor renal transplantation in children. Transplantation Proceedings. 2002;34:1939-41.	Duplicate
103	Haysom L, Rosenberg AR, Kainer G, Waliuzzaman ZM, Roberts J, Rawlinson WD, et al. BK viral infection in an Australian pediatric renal transplant population. Pediatric Transplantation. 2004;8:480-4.	Design
104	Hazza I, Al-Mardini R, Salaita G. Pediatric renal transplantation: Jordan's experience. Saudi Journal of Kidney Diseases & Transplantation. 2013;24:157-61.	Treatment
105	Herman J, Van Ranst M, Snoeck R, Beuselinck K, Lerut E, Van Damme-Lombaerts R. Polyomavirus infection in pediatric renal transplant recipients: Evaluation using a quantitative real-time PCR technique. Pediatric Transplantation. 2004;8:485-92.	Population
106	Hocker B, Feneberg R, Kopf S, Weber LT, Waldherr R, Wuhl E, et al. SRL-based immunosuppression vs. CNI minimization in pediatric renal transplant recipients with chronic CNI nephrotoxicity. Pediatric Transplantation. 2006;10:593-601.	Population
107	Hocker B, Fickenscher H, Delecluse HJ, Bohm S, Kusters U, Schnitzler P, et al. Epidemiology and morbidity of Epstein-Barr virus infection in pediatric renal transplant recipients: A multicenter, prospective study. Clinical Infectious Diseases. 2013;56:84-92.	Treatment
108	Hocker B, John U, Plank C, Wuhl E, Weber LT, Misselwitz J, et al. Successful withdrawal of steroids in pediatric renal transplant recipients receiving cyclosporine A and mycophenolate mofetil treatment: results after four years. Transplantation. 2004;78:228-34.	Population
109	Hocker B, Kovarik JM, Daniel V, Opelz G, Fehrenbach H, Holder M, et al. Pharmacokinetics and immunodynamics of basiliximab in pediatric renal transplant recipients on mycophenolate mofetil comedication. Transplantation. 2008;86:1234-40.	Design
110	Hocker B, Tonshoff B. Treatment strategies to minimize or prevent chronic allograft dysfunction in pediatric renal transplant recipients: an overview. Paediatric Drugs. 2009;11:381-96.	Design
111	Hocker B, Weber LT, Bunchman T, Rashford M, Tonshoff B. Mycophenolate mofetil suspension in pediatric renal transplantation: Three-year data from the tricontinental trial. Pediatric Transplantation. 2005;9:504-11.	Treatment
112	Hoyer PF, Ettenger R, Kovarik JM, Webb NJ, Lemire J, Mentser M, et al. Everolimus in pediatric de nova renal transplant patients. Transplantation. 2003;75:2082-5.	Treatment
113	Hurst FP, Jindal RM, Graham LJ, Falta EM, Elster EA, Stackhouse GB, et al. Incidence, predictors, costs, and outcome of renal cell carcinoma after kidney transplantation: USRDS experience. Transplantation. 2010;90:898-904.	Design

No	Study	Reason
114	Hymes L. BK virus nephropathy: a pediatric nephrologist's perspective. Transplantation Reviews. 2010;24:28-31.	No Data
115	Hymes LC, Greenbaum L, Amaral SG, Warshaw BL. Surveillance renal transplant biopsies and subclinical rejection at three months post-transplant in pediatric recipients. Pediatric Transplantation. 2007;11:536-9.	Design
116	Hymes LC, Warshaw BL, Hennigar RA, Amaral SG, Greenbaum LA. Prevalence of clinical rejection after surveillance biopsies in pediatric renal transplants: does early subclinical rejection predispose to subsequent rejection episodes? Pediatric Transplantation. 2009;13:823-6.	Design
117	Ibanez JP, Monteverde ML, Diaz MA, Goldberg J, Turconi AF. Sirolimus in chronic allograft nephropathy in pediatric recipients. Pediatric Transplantation. 2007;11:777-80.	Design
118	Imanishi Y, Matsui K, Ishida K, Ito S, Matsuura K, Deguchi T, et al. Pharmacokinetic properties of a once-daily formulation of tacrolimus in patients with renal transplantation. Arzneimittel-Forschung. 2011;61:191-6.	Mixed Population
119	Iorember FM, Patel HP, Ohana A, Hayes JR, Mahan JD, Baker PB, et al. Steroid avoidance using sirolimus and cyclosporine in pediatric renal transplantation: one year analysis. Pediatric Transplantation. 2010;14:93-9.	Mixed Population
120	Ireland R. Pediatrics: Sirolimus may stunt growth of kidney-transplanted children. Nature Reviews Nephrology. 2011;7:303.	Design
121	Jensen CJ, Shrivastava S, Taber DJ, Weimert NA, Shatat IF, Orak J, et al. A critical analysis of racial difference with mycophenolate mofetil (MMF) dosing, clinical outcomes and adverse effects in pediatric kidney transplant patients. Clinical Transplantation. 2011;25:534-40.	Treatment
122	Jensen S, Jackson EC, Riley L, Reddy S, Goebel J. Tacrolimus-based immunosuppression with steroid withdrawal in pediatric kidney transplantation - 4-Year experience at a moderate-volume center. Pediatric Transplantation. 2003;7:119-24.	Treatment
123	John U, Everding AS, Kuwertz-Broking E, Bulla M, Muller-Wiefel DE, Misselwitz J, et al. High prevalence of febrile urinary tract infections after paediatric renal transplantation. Nephrology Dialysis Transplantation. 2006;21:3269-74.	Treatment
124	Johny KV, Nampoory MRN, Hamid MH, Nair MP, Samhan M, Al-Moussawi M. Low-dose sirolimus in combination with mycophenolate in calcineurin inhibitor elimination: The Kuwaiti experience. Transplantation Proceedings. 2003;35:2750-1.	Design
125	Jungraithmayr T, Staskewitz A, Kirste G, Boswald M, Bulla M, Burghard R, et al. Prevalence of arterial hypertension and its morbidity in children and adolescents 3 years after renal transplantation with mycophenolate mofetil-based immunosuppression. Transplantation Proceedings. 2002;34:2215.	Abstract
126	Kamel MH, Mohan P, Conlon PJ, Little DM, O'Kelly P, Hickey DP. Rabbit antithymocyte globulin related decrease in platelet count reduced risk of pediatric renal transplant graft thrombosis. Pediatric Transplantation. 2006;10:816-21.	Treatment
127	Kamel MH, Mohan P, Little DM, Awan A, Hickey DP. Rabbit antithymocyte globulin as induction immunotherapy for pediatric deceased donor kidney transplantation. Journal of Urology. 2005;174:703-7.	Treatment

No	Study	Reason
128	Kandus A, Grego K, Arnol M, Kovac D, Lindic J, Buturovic J, et al. Effective immunoprophylaxis with basiliximab plus triple therapy in renal transplantation: five-year single-center experience. Transplantation Proceedings. 2006;38:2853-5.	Population
129	Kanzelmeyer NK, Ahlenstiel T, Kreuzer M, Becker JU, Pape L. Correlations with six-month protocol biopsy findings in pediatric transplant recipients on low- and regular-dose CNI regimens. Clinical Transplantation. 2013;27:319-23.	Treatment
130	Kasiske BL, Snyder JJ, Gilbertson DT, Wang C. Cancer after kidney transplantation in the United States. American Journal of Transplantation. 2004;4:905-13.	Design
131	Kavaz A, Ozcakar ZB, Bulum B, Tuzuner A, Keven K, Sengul S, et al. Pediatric renal transplantation: A single center experience. Transplantation Proceedings. 2013;45:917-8.	Treatment
132	Kavucku S, Soylu A, Turkmen M, Kasap B, Gumustekin M, Gulay H. Two-hour post-dose cyclosporin A levels in adolescent renal transplant recipients in the late post-transplant period. Pediatric Nephrology. 2004;19:667-71.	Treatment
133	Keough-Ryan TM, Prasad GV, Hewlett T, Shapiro RJ, Canadian Community Nephrology Study G. Similar outcomes for Canadian renal transplant recipients followed up in transplant centers and satellite clinics. Transplantation. 2010;90:591-6.	Population
134	Kerecuk L, Horsfield C, Taylor J. Improved long-term graft function in pediatric transplant renal recipients with chronic allograft nephropathy. Pediatric Transplantation. 2009;13:324-31.	Population
135	Khositseth S, Matas A, Cook ME, Gillingham KJ, Chavers BM. Thymoglobulin versus ATGAM induction therapy in pediatric kidney transplant recipients: A single-center report. Transplantation. 2005;79:958-63.	Treatment
136	Khosroshahi HT, Tubbs RS, Shoja MM, Ghafari A, Noshad H, Ardalan MR. Effect of With Low-Dose Anti-Thymocyte Globulin on Prevention of Acute Kidney Allograft Rejection. Transplantation Proceedings. 2008;40:137-9.	Design
137	Khwaja K, Humar A, Najarian JS. Kidney transplants for children under 1 year of age - A single-center experience. Pediatric Transplantation. 2003;7:163-7.	Population
138	Kim JJ, Balasubramanian R, Michaelides G, Wittenhagen P, Sebire NJ, Mamode N, et al. The clinical spectrum of de novo donor-specific antibodies in pediatric renal transplant recipients. American Journal of Transplantation. 2014;14:2350-8.	Design
139	Kim S, Webster AC, Craig JC. Current trends in immunosuppression following organ transplantation in children. Current Opinion in Organ Transplantation. 2013;18:537-42.	Not-obtainable
140	Kitada H, Okabe Y, Nishiki T, Miura Y, Kurihara K, Terasaka S, et al. One-year follow-up of treatment with once-daily tacrolimus in de novo renal transplant. Experimental and Clinical Transplantation. 2012;10:561-7.	Mixed Population
141	Kong JM, Ahn J, Park JB, Chung BH, Yang J, Kim JK, et al. ABO incompatible living donor kidney transplantation in Korea: highly uniform protocols and good medium-term outcome. Clinical Transplantation. 2013;27:875-81.	Population
142	Koshy SM, Guttmann A, Hebert D, Parkes RK, Logan AG. Incidence and risk factors for cardiovascular events and death in pediatric renal transplant patients: A single center long-term outcome study. Pediatric Transplantation.	Design

No	Study	Reason
	2009;13:1027-33.	
143	Kovac D, Kotnik V, Kandus A. Basiliximab and mycophenolate mofetil in combination with low-dose cyclosporine and methylprednisolone effectively prevent acute rejection in kidney transplant recipients. Transplantation Proceedings. 2005;37:4230-4.	Mixed Population
144	Kovarik JM, Offner G, Broyer M, Niaudet P, Loirat C, Mentser M, et al. A rational dosing algorithm for basiliximab (Simulect) in pediatric renal transplantation based on pharmacokinetic-dynamic evaluations. Transplantation. 2002;74:966-71.	Treatment
145	Kranz B, Wingen AM, Vester U, Konig J, Hoyer PF. Long-term side effects of treatment with mTOR inhibitors in children after renal transplantation. Pediatric Nephrology. 2013;28:1293-8.	Population
146	Krischock L, Gullett A, Bockenhauer D, Rees L, Trompeter RS, Marks SD. Calcineurin-inhibitor free immunosuppression with mycophenolate mofetil and corticosteroids in paediatric renal transplantation improves renal allograft function without increasing acute rejection. Pediatric Transplantation. 2009;13:475-81.	Design
147	Krystufkova E, Sekerkova A, Striz I, Brabcova I, Girmanova E, Viklicky O. Regulatory T cells in kidney transplant recipients: the effect of induction immunosuppression therapy. Nephrology Dialysis Transplantation. 2012;27:2576-82.	Treatment
148	Laftavi MR, Hai F, Laftavi H, Feng L, Said M, Patel S, et al. Mycophenolic acid dose reductions result in poor long-term renal allograft survival: comparison between mycophenolate sodium and mycophenolate mofetil. Transplantation Proceedings. 2011;43:478-81.	Population
149	Larkins N, Matsell DG. Tacrolimus therapeutic drug monitoring and pediatric renal transplant graft outcomes. Pediatric Transplantation. 2014;18:803-9.	Treatment
150	Lau KK, Haddad MN, Berg GM, Perez RV, Butani L. Rapid steroid discontinuation for pediatric renal transplantation: A single center experience. Pediatric Transplantation. 2007;11:504-10.	Design
151	Lau KK, Tancredi DJ, Perez RV, Butani L. Unusual pattern of dyslipidemia in children receiving steroid minimization immunosuppression after renal transplantation. Clinical Journal of the American Society of Nephrology. 2010;5:1506-12.	Design
152	Laube GF, Falger J, Kemper MJ, Zingg-Schenk A, Neuhaus TJ. Selective late steroid withdrawal after renal transplantation. Pediatric Nephrology. 2007;22:1947-52.	Treatment
153	Leeser DB, Aull MJ, Afaneh C, Dadhania D, Charlton M, Walker JK, et al. Living donor kidney paired donation transplantation: Experience as a founding member center of the National Kidney Registry. Clinical Transplantation. 2012;26:E213-E22.	Design
154	Levy Y, Davidovits M, Cleper R, Shapiro R. New-onset post-transplantation food allergy in children--is it attributable only to the immunosuppressive protocol? Pediatric Transplantation. 2009;13:63-9.	Population
155	Li L, Chang A, Naesens M, Kambham N, Waskerwitz J, Martin J, et al. Steroid-free immunosuppression since 1999: 129 pediatric renal transplants with sustained graft and patient benefits. American Journal of Transplantation.	Treatment

No	Study	Reason
	2009;9:1362-72.	
156	Li L, Chaudhuri A, Chen A, Zhao X, Bezchinsky M, Concepcion W, et al. Efficacy and safety of thymoglobulin induction as an alternative approach for steroid-free maintenance immunosuppression in pediatric renal transplantation. Transplantation. 2010;90:1516-20.	Treatment
157	Li L, Weintraub L, Concepcion W, Martin JP, Miller K, Salvatierra O, et al. Potential influence of tacrolimus and steroid avoidance on early graft function in pediatric renal transplantation. Pediatric Transplantation. 2008;12:701-7.	Treatment
158	Li M, Nicholls KM, Becker GJ. Risk factors for late renal allograft dysfunction: Effects of baseline glomerular size. Journal of Nephrology. 2002;15:620-5.	Design
159	Lim W, Chadban S, Campbell S, Dent H, Russ G, McDonald S. Effect of interleukin-2 receptor antibody therapy on acute rejection risk and severity, long-term renal function, infection and malignancy-related mortality in renal transplant recipients. Transplant International. 2010;23:1207-15.	Treatment
160	Logan AJ, Morris-Stiff GJ, Bowrey DJ, Jurewicz WA. Upper gastrointestinal complications after renal transplantation: A 3-yr sequential study. Clinical Transplantation. 2002;16:163-7.	Treatment
161	Lucan M, Iacob G, Lucan C, Lapusan C, Munteanu A, Sirbu S. Ten years of cyclosporine use in renal transplantation: a single-center experience with 479 renal transplants. Transplantation Proceedings. 2004;36:177S-80S.	Mixed Population
162	Mali V, Robless P, Loh D, Yap HK, Krishnan P. Slower rate of compensatory hypertrophy in pediatric en bloc kidney transplantation in a pediatric recipient. Pediatric Transplantation. 2012;16:511-2.	Design
163	Martin-Pena A, Cordero E, Fijo J, Sanchez-Moreno A, Martin-Govantes J, Torrubia F, et al. Prospective study of infectious complications in a cohort of pediatric renal transplant recipients. Pediatric Transplantation. 2009;13:457-63.	Treatment
164	Martinez Urrutia MJ, Pereira PL, Avila Ramirez LF, Romera RL, Meseguer CG, Monereo EJ. Double renal transplantation - A strategy with donors under 3 years old. Journal of Pediatric Urology. 2006;2:340-3.	Population
165	Martinez-Mier G, Avila-Pardo SF, Mendez-Lopez MT, Budar-Fernandez LF. Long-term results after conversion from calcineurin inhibitors to sirolimus in renal transplant patients. Clinical Transplantation. 2010;24:467-73.	Population
166	Martinez-Mier G, Enriquez-De Los Santos H, Mendez-Lopez MT, Avila-Pardo SF, Budar-Fernandez LF, Gonzalez-Velazquez F. Rejection is a strong graft survival predictor in live donor pediatric renal transplantation using cyclosporine, mycophenolate mofetil, and steroids: 5-Year outcomes in a single Mexican center. Transplantation Proceedings. 2013;45:1442-4.	Treatment
167	Martinez-Mier G, Mendez-Lopez MT, Budar-Fernandez LF, Estrada-Oros J, Franco-Abaroa R, George-Micelli E, et al. Pediatric renal transplantation with mycophenolate mofetil immunosuppression in a single center from Mexico. Pediatric Transplantation. 2007;11:134-8.	Design
168	Matas AJ. Minimization of steroids in kidney transplantation. Transplant International. 2009;22:38-48.	Design
169	Mehls O, Wilton P, Lilien M, Berg U, Broyer M, Rizzoni G, et al. Does growth hormone treatment affect the risk of post-transplant renal cancer? Pediatric	Design

No	Study	Reason
	Nephrology. 2002;17:984-9.	
170	Melgosa Hijosa M, Garcia Meseguer C, Pena Garcia P, Alonso Melgar A, Espinosa Roman L, Pena Carrion A, et al. Preemptive treatment with oral ganciclovir for pediatric renal transplantation. Clinical Nephrology. 2004;61:246-52.	Design
171	Min SI, Ha J, Kang HG, Ahn S, Park T, Park DD, et al. Conversion of twice-daily tacrolimus to once-daily tacrolimus formulation in stable pediatric kidney transplant recipients: Pharmacokinetics and efficacy. American Journal of Transplantation. 2013;13:2191-7.	Population
172	Miners AH, Yao G, Raftery J, Taylor RS. Economic evaluations of calcineurin inhibitors in renal transplantation: a literature review. Pharmacoeconomics. 2007;25:935-47.	Design
173	Mishra S, Ganpule A, Muthu V, Sabnis R, Desai M. Evaluating graft function in pediatric recipients for living donor renal transplantation: Is laparoscopic donor nephrectomy safe? Indian Journal of Urology. 2009;25:195-8.	Design
174	Mital D, Podlasek W, Jensik SC. Sirolimus-based steroid-free maintenance immunosuppression. Transplantation Proceedings. 2002;34:1709-10.	Treatment
175	Montini G, Murer L, Ghio L, Pietrobon B, Ginevri F, Ferraresso M, et al. One-year results of basiliximab induction and tacrolimus associated with sequential steroid and MMF treatment in pediatric kidney transplant recipient. Transplant International. 2005;18:36-42.	Design
176	Montini G, Ujka F, Varagnolo C, Ghio L, Ginevri F, Murer L, et al. The pharmacokinetics and immunosuppressive response of tacrolimus in paediatric renal transplant recipients. Pediatric Nephrology. 2006;21:719-24.	Design
177	Morales JM, Hartmann A, Walker R, Arns W, Senatorski G, Grinyo JM, et al. Similar lipid profile but improved long-term outcomes with sirolimus after cyclosporine withdrawal compared to sirolimus with continuous cyclosporine. Transplantation Proceedings. 2009;41:2339-44.	Design
178	Morita K, Iwami D, Hotta K, Shimoda N, Miura M, Watarai Y, et al. Pediatric kidney transplantation is safe and available for patients with urological anomalies as well as those with primary renal diseases. Pediatric Transplantation. 2009;13:200-5.	Treatment
179	Moudgil A, Martz K, Stablein DM, Puliyanda DP. Variables affecting estimated glomerular filtration rate after renal transplantation in children: A NAPRTCS data analysis. Pediatric Transplantation. 2010;14:288-94.	Design
180	Muorah MR, Brogan PA, Sebire NJ, Trompeter RS, Marks SD. Dense B cell infiltrates in paediatric renal transplant biopsies are predictive of allograft loss. Pediatric Transplantation. 2009;13:217-22.	Treatment
181	Naesens M, Lerut E, Sarwal M, Van Damme B, Vanrenterghem Y, Kuypers DR. Balancing efficacy and toxicity of kidney transplant immunosuppression. Transplantation Proceedings. 2009;41:3393-5.	Design
182	Nafar M, Roshan A, Pour-Reza-Gholi F, Samadian F, Ahmadpoor P, Samavat S, et al. Prevalence and risk factors of recurrent cytomegalovirus infection in kidney transplant recipients. Iranian journal of Kidney Diseases. 2014;8:231-5.	Treatment
183	Nahas WC, Antonopoulos IM, Piovesan AC, Pereira LM, Kanashiro H, David-Neto E, et al. Comparison of renal transplantation outcomes in children with and without bladder dysfunction. A customized approach equals the difference.	Design

No	Study	Reason
	Journal of Urology. 2008;179:712-6.	
184	Nampoory MR, Abdulhalim M, Johny KV, Al-Jawad Donia FA, Nair MP, Said T, et al. Bolus anti-thymocyte globulin induction in renal transplant recipients: a comparison with conventional ATG or anti-interleukin-2 receptor antibody induction. Transplantation Proceedings. 2002;34:2916-9.	Population
185	Nehus E, Goebel J, Abraham E. Outcomes of steroid-avoidance protocols in pediatric kidney transplant recipients. American Journal of Transplantation. 2012;12:3441-8.	Treatment
186	Neu AM, Ho PL, Fine RN, Furth SL, Fivush BA. Tacrolimus vs. cyclosporine A as primary immunosuppression in pediatric renal transplantation: A NAPRTCS study. Pediatric Transplantation. 2003;7:217-22.	Treatment
187	Niaudet P, Charbit M, Loirat C, Lapeyraque AL, Tsimaratos M, Cailliez M, et al. Enteric-coated mycophenolate sodium in de novo pediatric renal transplant patients. Pediatric Nephrology. 2009;24:395-402.	Design
188	Offner G, Broyer M, Niaudet P, Loirat C, Mentser M, Lemire J, et al. A multicenter, open-label, pharmacokinetic/pharmacodynamic safety, and tolerability study of basiliximab (Simulect) in pediatric de novo renal transplant recipients. Transplantation. 2002;74:961-6.	Treatment
189	Ojogho O, Sahney S, Cutler D, Baron PW, Abdelhalim FM, Hasan SM, et al. Mycophenolate mofetil without antibody induction in cadaver vs. living donor pediatric renal transplantation. Pediatric Transplantation. 2003;7:137-41.	Treatment
190	Ojogho O, Sahney S, Cutler D, Baron PW, Abdelhalim FM, James S, et al. Mycophenolate mofetil in pediatric renal transplantation: non-induction vs. induction with basiliximab. Pediatric Transplantation. 2005;9:80-3.	Treatment
191	Ojogho ON, Sahney S, Cutler D, Baron PW, Abdelhalim FM, Hasan SM, et al. Mycophenolate mofetil without antibody induction in pediatric renal transplantation. Transplantation Proceedings. 2002;34:1953-4.	Treatment
192	Okamoto M, Omori Y, Kadotani Y, Ushigome H, Nakamura K, Akioka K, et al. Tacrolimus-based immunosuppression in renal transplantation: 78 experiences in a single Japanese center. Transplantation Proceedings. 2002;34:1666.	Treatment
193	Ortiz J, Palma-Vargas J, Wright F, Bingaman A, Agha I, Rosenblatt S, et al. Campath Induction for Kidney Transplantation: Report of 297 Cases. Transplantation. 2008;85:1550-6.	Treatment
194	Osorio JM, Bravo J, Perez A, Ferreyra C, Osuna A. Magnesemia in renal transplant recipients: relation with immunosuppression and posttransplant diabetes. Transplantation Proceedings. 2010;42:2910-3.	Treatment
195	Otte JB. Historical review and perspectives in pediatric transplantation. Current Opinion in Organ Transplantation. 2006;11:508-15.	Design
196	Otukesh H, Hoseini R, Rahimzadeh N. Treatment update of sensitized pediatric kidney transplant recipients: A review. Experimental and Clinical Transplantation. 2012;10:523-30.	Design
197	Otukesh H, Sharifian M, Basiri A, Simfroosh N, Hoseini R, Sedigh N, et al. Mycophenolate mofetil in pediatric renal transplantation. Transplantation Proceedings. 2005;37:3012-5.	Mixed Population
198	Pape L, Ehrich JHH, Offner G. Long-term follow-up of pediatric transplant recipients: Mycophenolic acid trough levels are not a good indicator for long-	Population

No	Study	Reason
	term graft function. Clinical Transplantation. 2004;18:576-9.	
199	Pape L, Ganschow R, Ahlenstiel T. Everolimus in pediatric transplantation. Current Opinion in Organ Transplantation. 2012;17:515-9.	Not-obtainable
200	Pape L, Henne T, Strehlau J, Latta K, Ehrich JH, Offner G. Long-term stable glomerular filtration rate achieved with tacrolimus in pediatric renal transplantation. Transplantation Proceedings. 2002;34:2211-2.	Treatment
201	Pape L, Lehner F, Blume C, Ahlenstiel T. Pediatric kidney transplantation followed by de novo therapy with everolimus, low-dose cyclosporine a, and steroid elimination: 3-year data. Transplantation. 2011;92:658-62.	Design
202	Pape L, Offner G, Kreuzer M, Froede K, Drube J, Kanzelmeyer N, et al. De novo therapy with everolimus, low-dose ciclosporine A, basiliximab and steroid elimination in pediatric kidney transplantation. American Journal of Transplantation. 2010;10:2349-54.	Design
203	Pasti K, Szabo AJ, Prokai A, Meszaros K, Peko N, Solyom R, et al. Continuous glucose monitoring system (CGMS) in kidney-transplanted children. Pediatric Transplantation. 2013;17:454-60.	Population
204	Patel N, Taber DJ, Weimert NA, Fleming JN, Egidi FM, McGillicuddy J, et al. Potential differences in kidney allograft outcomes between ethnicities when converting to sirolimus base immunosuppression. Transplantation Proceedings. 2009;41:4131-7.	Population
205	Pham PT, Pham PC. The impact of mycophenolate mofetil versus azathioprine as adjunctive therapy to cyclosporine on the rates of renal allograft loss due to glomerular disease recurrence. Nephrology Dialysis Transplantation. 2012;27:2965-71.	No Data
206	Plank C, Benz K, Amann K, Nusken KD, Dittrich K, Rascher W, et al. Stable graft function after reduction of calcineurin inhibitor dosage in paediatric kidney transplant patients. Nephrology Dialysis Transplantation. 2006;21:2930-7.	Treatment
207	Pourmand G, Saraji A, Salem S, Mehrsai A, Nikoobakht MR, Taherimahmoudi M, et al. Could prophylactic monoclonal antibody improve kidney graft survival? Transplantation Proceedings. 2009;41:2794-6.	Treatment
208	Powell HR, Kara T, Jones CL. Early experience with conversion to sirolimus in a pediatric renal transplant population. Pediatric Nephrology. 2007;22:1773-7.	Design
209	Puliyanda DP, Stablein DM, Dharnidharka VR. Younger age and antibody induction increase the risk for infection in pediatric renal transplantation: A NAPRTCS report. American Journal of Transplantation. 2007;7:662-6.	Design
210	Qvist E, Their M, Krogerus L, Holmberg C, Jalanko H. Early treatment of acute rejections gives favorable long-term function after renal transplantation in small children. Pediatric Transplantation. 2007;11:895-900.	Design
211	Raheem OA, Kamel MH, Daly PJ, Mohan P, Little DM, Awan A, et al. Mycophenolate mofetil in pediatric renal transplantation: a single center experience. Pediatric Transplantation. 2011;15:240-4.	Treatment
212	Rahimzadeh N, Otukesh H, Hoseini R, Riahifard A. Pretransplant Epstein-Barr virus serostatus and incidence of posttransplant lymphoproliferative disorder in pediatric renal transplants. Experimental and Clinical Transplantation. 2013;11:299-302.	Design

No	Study	Reason
213	Ramalho AL, Custodio FB, Tokuda BM, Caldas HC, Fernandes IM, Abbud-Filho M, et al. Clinical and histopathologic comparative analysis between kidney transplant recipients from expanded-criteria donors and standard-criteria donors. Transplantation Proceedings. 2013;45:3234-8.	Population
214	Rehman S, Wen X, Casey MJ, Santos AH, Andreoni K. Effect of different tacrolimus levels on early outcomes after kidney transplantation. Annals of Transplantation. 2014;19:68-75.	Population
215	Renoult E, Clermont MJ, Phan V, Buteau C, Alfieri C, Tapiero B. Prevention of CMV disease in pediatric kidney transplant recipients: Evaluation of pp67 NASBA-based pre-emptive ganciclovir therapy combined with CMV hyperimmune globulin prophylaxis in high-risk patients. Pediatric Transplantation. 2008;12:420-5.	Design
216	Reyes H, Hernandez AM, Valverde S, Cataneo A, Mendoza A, Barrera I, et al. Efficacy and safety of conversion of mycophenolate mofetil to enteric-coated mycophenolate sodium in Mexican renal transplant children. Pediatric Transplantation. 2010;14:746-52.	Population
217	Rizvi SAH, Naqi ZM, Lanewala AA, Naqvi SAA. Challenges in pediatric renal transplantation in developing countries. Current Opinion in Organ Transplantation. 2009;14:533-9.	Design
218	Rizvi SAH, Naqvi SAA, Hussain Z, Hashmi A, Akhtar F, Zafar MN, et al. Living-related pediatric renal transplants: A single-center experience from a developing country. Pediatric Transplantation. 2002;6:101-10.	Treatment
219	Roberti I, Vyas S, Pancoska C. Donor-specific antibodies by flow single antigen beads in pediatric living donor kidney transplants: Single center experience. Pediatric Transplantation. 2007;11:901-5.	Design
220	Robinson LG, Hilinski J, Graham F, Hymes L, Beck-Sague CM, Hsia J, et al. Predictors of cytomegalovirus disease among pediatric transplant recipients within one year of renal transplantation. Pediatric Transplantation. 2002;6:111-8.	Treatment
221	Rocha A, Rocha L, Malheiro J, Azevedo P, Tavares T, Faria MS, et al. Predictive factors of graft-censored failure in pediatric kidney transplantation. Transplantation Proceedings. 2014;46:1723-6.	Treatment
222	Ruiz E, Cateriano JE, Lobos P, de Badiola FIP, Boer M, Moldes J, et al. Kidney transplantation in small children with live related donors: 20 years of experience. Journal of Pediatric Urology. 2006;2:373-9.	Treatment
223	Ruzics EP, Abe M, Escobedo W, Gull P, Weil M. One hundred percent three-year graft and patient survival: kidney transplantation at Saint Joseph Hospital of Orange. Clinical Transplants. 2010:169-78.	Population
224	Salamzadeh J, Foroutan N, Jamshidi HR, Rasekh HR, Ghatari AR, Foroutan A, et al. Costs of treatment after renal transplantation: Is it worth to pay more? Iranian Journal of Pharmaceutical Research. 2014;13:271-8.	Design
225	Salesi M, Rostami Z, Foroushani AR, Mehrazmay AR, Mohammadi J, Einollahi B, et al. Chronic graft loss and death in patients with post-transplant malignancy in living kidney transplantation: A competing risk analysis. Nephro-Urology Monthly. 2014;6.	Design
226	Samhan M, Fathi T, Al-Kandari N, Buresley S, Nampoory MRN, Nair P, et al. Renal Transplantation in Children. Transplantation Proceedings. 2007;39:911-3.	Treatment

No	Study	Reason
227	Sampaio MS, Cho YW, Shah T, Bunnapradist S, Hutchinson IV. Association of immunosuppressive maintenance regimens with posttransplant lymphoproliferative disorder in kidney transplant recipients. Transplantation. 2012;93:73-81.	Population
228	Sampaio MS, Poommipanit N, Kuo HT, Reddy PN, Cho YW, Shah T, et al. Induction therapy in pediatric kidney transplant recipients discharged with a triple drug immunosuppressive regimen. Pediatric Transplantation. 2010;14:770-8.	Treatment
229	Sarwal M, Pascual J. Immunosuppression minimization in pediatric transplantation. American Journal of Transplantation. 2007;7:2227-35.	Design
230	Schachter AD, Meyers KE, Spaneas LD, Palmer JA, Salmanullah M, Baluarte J, et al. Short sirolimus half-life in pediatric renal transplant recipients on a calcineurin inhibitor-free protocol. Pediatric Transplantation. 2004;8:171-7.	Population
231	Schwartz JJ, Ishitani MB, Weckwerth J, Morgenstern B, Milliner D, Stegall MD. Decreased incidence of acute rejection in adolescent kidney transplant recipients using antithymocyte induction and triple immunosuppression. Transplantation. 2007;84:715-21.	Design
232	Seikaly MG. Recurrence of primary disease in children after renal for transplantation: An evidence-based update. Pediatric Transplantation. 2004;8:113-9.	Design
233	Seikku P, Krogerus L, Jalanko H, Holmberg C. Better renal function with enhanced immunosuppression and protocol biopsies after kidney transplantation in children. Pediatric Transplantation. 2005;9:754-62.	Design
234	Shah DS, Shrestha S, Kafle MP. Renal transplantation in Nepal: beginning of a new era! Nephrology. 2013;18:369-75.	Treatment
235	Shah MH, Bokhari MZ, Bokhari MT, Farooq A, Yousaf SM. Safety and efficacy of basiliximab for the prevention of acute rejection in kidney transplant recipients. Transplantation Proceedings. 2003;35:2737-8.	Population
236	Shang W, Feng G, Gao S, Wang Z, Pang X, Li J, et al. Reduced ATG-F dosage for induction in pediatric renal transplantation: A single-center experience. Pediatric Transplantation. 2014;18:240-5.	Design
237	Sharifan M, Arad B, Simfroosh N, Basiri A, Otukesh H, Esfandia N. Effects of interleukin 2 receptor blockers on patient and graft survival in renal-transplanted children. Nephro-Urology Monthly. 2014;6.	Treatment
238	Shenoy M, Roberts D, Plant ND, Lewis MA, Webb NJA. Antithymocyte treatment of steroid-resistant acute rejection in renal transplantation. Pediatric Nephrology. 2011;26:815-8.	Treatment
239	Shilbayeh S, Hazza I. Pediatric renal transplantation in the jordanian population: The clinical outcome measures during long-term follow-up period. Pediatrics and Neonatology. 2012;53:24-33.	Treatment
240	Shipkova M, Armstrong VW, Weber L, Niedmann PD, Wieland E, Haley J, et al. Pharmacokinetics and protein adduct formation of the pharmacologically active acyl glucuronide metabolite of mycophenolic acid in pediatric renal transplant recipients. Therapeutic Drug Monitoring. 2002;24:390-9.	Design
241	Shrestha A, Shrestha A, Basarab-Horwath C, McKane W, Shrestha B, Raftery A. Quality of life following live donor renal transplantation: a single centre experience. Annals of Transplantation. 2010;15:5-10.	Population

No	Study	Reason
242	Sindhi R. Sirolimus in pediatric transplant recipients. Transplantation Proceedings. 2003;35:113S-4S.	Population
243	Sinha A, Hari P, Guleria S, Gulati A, Dinda AK, Mehra NK, et al. Outcome of pediatric renal transplantation in north India. Pediatric Transplantation. 2010;14:836-43.	Treatment
244	Sinha R, Marks SD. Comparison of parameters of chronic kidney disease following paediatric preemptive versus non-preemptive renal transplantation. Pediatric Transplantation. 2010;14:583-8.	Treatment
245	Sinha R, Saad A, Marks SD. Prevalence and complications of chronic kidney disease in paediatric renal transplantation: A K/DOQI perspective. Nephrology Dialysis Transplantation. 2010;25:1313-20.	Treatment
246	Sitek JC, Tangeraas T, Bjerre A, Helsing P. The prevalence of skin disorders in Norwegian paediatric renal transplant recipients. Acta Dermato-Venereologica. 2014;94:421-4.	Population
247	Smedbraten YV, Sagedal S, Leivestad T, Mjoen G, Osnes K, Rollag H, et al. The impact of early cytomegalovirus infection after kidney transplantation on long-term graft and patient survival. Clinical Transplantation. 2014;28:120-6.	Treatment
248	Smith JM, Martz K, McDonald RA, Harmon WE. Solid tumors following kidney transplantation in children. Pediatric Transplantation. 2013;17:726-30.	Design
249	Sodemann U, Bistrup C, Marckmann P. Cancer rates after kidney transplantation. Danish Medical Bulletin. 2011;58.	Design
250	Soliman AR, Fathy A, Khashab S, Shaheen N. The burden of anti-HCV genotye-4 positivity in renal transplant recipients: 8 years follow-up. International Urology & Nephrology. 2013;45:1453-61.	Design
251	Sparta G, Kemper MJ, Neuhaus TJ. Hyperuricemia and gout following pediatric renal transplantation. Pediatric Nephrology. 2006;21:1884-8.	Treatment
252	Spivey CA, Chisholm-Burns MA, Damadzadeh B, Billheimer D. Determining the effect of immunosuppressant adherence on graft failure risk among renal transplant recipients. Clinical Transplantation. 2014;28:96-104.	Population
253	Sumboonnanonda A, Lumpaopong A, Kingwatanakul P, Tangnararatchakit K, Jiravuttipong A. Pediatric kidney transplantation in Thailand: experience in a developing country. Transplantation Proceedings. 2008;40:2271-3.	Treatment
254	Sundberg AK, Smith LD, Somerville KT, Cox R, Sherbotie JR. Conversion from cyclosporine to tacrolimus is preferred by pediatric renal transplant recipients: a focus on opinions and outcomes. Transplantation Proceedings. 2002;34:1951-2.	Design
255	Sung J, Barry JM, Jenkins R, Rozansky D, Iragorri S, Conlin M, et al. Alemtuzumab induction with tacrolimus monotherapy in 25 pediatric renal transplant recipients. Pediatric Transplantation. 2013;17:718-25.	Treatment
256	Supe-Markovina K, Melquist JJ, Connolly D, DiCarlo HN, Waltzer WC, Fine RN, et al. Alemtuzumab with corticosteroid minimization for pediatric deceased donor renal transplantation: a seven-yr experience. Pediatric Transplantation. 2014;18:363-8.	Treatment
257	Suszynski TM, Rizzari MD, Gillingham KJ, Rheault MN, Kraszkiewicz W, Matas AJ, et al. Antihypertensive pharmacotherapy and long-term outcomes in pediatric kidney transplantation. Clinical Transplantation. 2013;27:472-80.	Design

No	Study	Reason
258	Sutherland S, Li L, Concepcion W, Salvatierra O, Sarwal MM. Steroid-free immunosuppression in pediatric renal transplantation: Rationale outcomes following conversion to steroid based therapy. Transplantation. 2009;87:1744-8.	Treatment
259	Sy SK, Heuberger J, Shilbayeh S, Conrado DJ, Derendorf H. A Markov chain model to evaluate the effect of CYP3A5 and ABCB1 polymorphisms on adverse events associated with tacrolimus in pediatric renal transplantation. AAPS Journal. 2013;15:1189-99.	Design
260	Taheri M, Pourmand G, Mehrsai AR, Mansoori D. Omission of azathioprine and mycophenolate mofetil in immunosuppressive regimen in kidney transplantation. Transplantation Proceedings. 2003;35:2752-3.	Treatment
261	Tan HP, Kaczorowski D, Basu A, McCauley J, Marcos A, Donaldson J, et al. Steroid-free tacrolimus monotherapy after pretransplantation thymoglobulin or campath and laparoscopy in living donor renal transplantation. Transplantation Proceedings. 2005;37:4235-40.	Population
262	Tang W, Bose B, McDonald SP, Hawley CM, Badve SV, Boudville N, et al. The outcomes of patients with ESRD and ANCA-associated Vasculitis in Australia and New Zealand. Clinical Journal of the American Society of Nephrology. 2013;8:773-80.	Design
263	Tayfur AC, Besbas N, Bilginer Y, Ozaltin F, Duzova A, Bakkaloglu M, et al. Follow-up of patients with juvenile nephronophthisis after renal transplantation: A single center experience. Transplantation Proceedings. 2011;43:847-9.	Treatment
264	Tirelli S, Ferraresso M, Ghio L, Meregalli E, Martina V, Belingheri M, et al. The effect of CYP3A5 polymorphisms on the pharmacokinetics of tacrolimus in adolescent kidney transplant recipients. Medical Science Monitor. 2008;14:CR251-CR4.	Treatment
265	Tonshoff B, Hocker B, Weber LT. Steroid withdrawal in pediatric and adult renal transplant recipients. Pediatric Nephrology. 2005;20:409-17.	Design
266	Tromp WF, Cransberg K, Van Der Lee JH, Bouts AH, Collard L, Van Damme-Lombaerts R, et al. Fewer pre-emptive renal transplantations and more rejections in immigrant children compared to native Dutch and Belgian children. Nephrology Dialysis Transplantation. 2012;27:2588-93.	Treatment
267	Tsai MK, Hu RH, Lee CJ, Lee PH. Efficacy of low-dose mycophenolate mofetil therapy for Taiwanese renal transplantation patients receiving primary cyclosporine immunosuppression. Journal of the Formosan Medical Association. 2002;101:616-21.	Population
268	Turconi A, Rilo LR, Goldberg J, de Boccardo G, Garsd A, Otero A. Open-label, multicenter study on the safety, tolerability, and efficacy of Simulect in pediatric renal transplant recipients receiving triple therapy with cyclosporin, mycophenolate, and corticosteroids. Transplantation Proceedings. 2005;37:672-4.	Design
269	Turunen AJ, Lindgren L, Salmela KT, Kyllonen LE, Makisalo H, Siitonen SM, et al. Association of graft neutrophil sequestration with delayed graft function in clinical renal transplantation. Transplantation. 2004;77:1821-6.	Population
270	Ulinski T, Cochat P. Longitudinal growth in children following kidney transplantation: From conservative to pharmacological strategies. Pediatric Nephrology. 2006;21:903-9.	Design
271	Urschel S, Altamirano-Diaz LA, West LJ. Immunosuppression Armamentarium in 2010: Mechanistic and Clinical Considerations. Pediatric Clinics of North	Not-obtainable

No	Study	Reason
	America. 2010;57:433-57.	
272	Ushigome H, Okamoto M, Kadotani Y, Nakamura K, Akioka K, Ohmori Y, et al. Pediatric living-related renal transplantation under tacrolimus as the primary immunosuppressive agent. Transplantation Proceedings. 2003;35:165-6.	Treatment
273	Uslu Gokceoglu A, Akman S, Koyun M, Comak E, Dogan CS, Akbas H, et al. Hyperuricemia in pediatric renal transplant recipients. Experimental & Clinical Transplantation: Official Journal of the Middle East Society for Organ Transplantation. 2013;11:489-93.	Treatment
274	Valera B, Gentil MA, Cabello V, Fijo J, Cordero E, Cisneros JM. Epidemiology of Urinary Infections in Renal Transplant Recipients. Transplantation Proceedings. 2006;38:2414-5.	Treatment
275	Van Damme-Lombaerts R, Webb NA, Hoyer PF, Mahan J, Lemire J, Ettenger R, et al. Single-dose pharmacokinetics and tolerability of everolimus in stable pediatric renal transplant patients. Pediatric Transplantation. 2002;6:147-52.	Design
276	Velez C, Zuluaga G, Ocampo C, Aristizabal A, Serna LM, Serrano Gayubo AK, et al. Clinical description and evolution of renal transplant pediatric patients treated with alemtuzumab. Transplantation Proceedings. 2011;43:3350-4.	Treatment
277	Vester U, Kranz B, Testa G, Paul A, Broelsch CE, Hoyer PF. Medical and surgical aspects of pediatric renal transplantation using living donors. Transplantation Proceedings. 2004;36:1308-10.	Treatment
278	Vester U, Kranz B, Wehr S, Boger R, Hoyer PF, Group RBS. Everolimus (Certican) in combination with neoral in pediatric renal transplant recipients: interim analysis after 3 months. Transplantation Proceedings. 2002;34:2209-10.	Treatment
279	Vester U, Schaefer A, Kranz B, Wingen AM, Nadalin S, Paul A, et al. Development of growth and body mass index after pediatric renal transplantation. Pediatric Transplantation. 2005;9:445-9.	Design
280	Vidal E, Edefonti A, Puteo F, Chimenz R, Gianoglio B, Lavoratti G, et al. Encapsulating peritoneal sclerosis in paediatric peritoneal dialysis patients: The experience of the Italian Registry of Pediatric Chronic Dialysis. Nephrology Dialysis Transplantation. 2013;28:1603-9.	Population
281	Vilalta R, Vila A, Nieto J, Espanol T, Caragol I, Callis L. Experience with basiliximab in pediatric renal transplantation. Transplantation Proceedings. 2002;34:100-1.	Design
282	Vo AA, Toyoda M, Peng A, Bunnapradist S, Lukovsky M, Jordan SC. Effect of induction therapy protocols on transplant outcomes in crossmatch positive renal allograft recipients desensitized with IVIG. American Journal of Transplantation. 2006;6:2384-90.	Treatment
283	Vyas S, Roberti I. Lymphocyte ATP immune cell function assay in pediatric renal transplants: is it useful? Transplantation Proceedings. 2011;43:3675-8.	Treatment
284	Wafa EW, Shokeir AA, Akl A, Hassan N, Fouda MA, El Dahshan K, et al. Effect of donor and recipient variables on the long-term live-donor renal allograft survival in children. Arab Journal of Urology. 2011;9:85-91.	Treatment
285	Watson AR. Rejection, recurrence, or non-adherence? Lancet. 2002;359:1997.	Design
286	Wayman MR, Oniscu GC, Forsythe JL, Whitworth CE. Two-year outcome in renal allograft recipients comparing neoral-led with tacrolimus-led therapy.	Population

No	Study	Reason
	Transplantation Proceedings. 2002;34:1663-5.	
287	Weber LT, Armstrong VW, Shipkova M, Feneberg R, Wiesel M, Mehls O, et al. Cyclosporin A absorption profiles in pediatric renal transplant recipients predict the risk of acute rejection. Therapeutic Drug Monitoring. 2004;26:415-24.	Design
288	Weber LT, Hoecker B, Armstrong VW, Oellerich M, Tonshoff B. Long-term pharmacokinetics of mycophenolic acid in pediatric renal transplant recipients over 3 years posttransplant. Therapeutic Drug Monitoring. 2008;30:570-5.	Design
289	Weintraub L, Li L, Kambham N, Alexander S, Concepcion W, Miller K, et al. Patient selection critical for calcineurin inhibitor withdrawal in pediatric kidney transplantation. Pediatric Transplantation. 2008;12:541-9.	Design
290	Willoughby LM, Schnitzler MA, Brennan DC, Pinsky BW, Dzebisashvili N, Buchanan PM, et al. Early outcomes of thymoglobulin and basiliximab induction in kidney transplantation: application of statistical approaches to reduce bias in observational comparisons. Transplantation. 2009;87:1520-9.	Population
291	Wisanuyotin S, Jiravuttipong A. Pediatric renal transplantation: A single-center experience in Northeast Thailand. Journal of the Medical Association of Thailand. 2009;92:1635-9.	Design
292	Wisgerhof HC, Wolterbeek R, Haasnoot GW, Claas FHJ, de Fijter JW, Willemze R, et al. The risk of cancer is not increased in patients with multiple kidney transplantations. Transplant Immunology. 2012;27:189-94.	Design
293	Wittenhagen P, Thiesson HC, Baudier F, Pedersen EB, Neland M. Long-term experience of steroid-free pediatric renal transplantation: Effects on graft function, body mass index, and longitudinal growth. Pediatric Transplantation. 2014;18:35-41.	Population
294	Wolters HH, Vowinkel T, Brockmann J, Palmes D, Heidenreich S, Dietl KH. Living donor renal transplantation - Experience with 50 patients in 5 years. Transplantation Proceedings. 2002;34:2216.	Treatment
295	Yang S, Wu Z, Wu W, Lin W, Xu T, Cai J, et al. Characteristics of long-term immunosuppressive therapy in Chinese pediatric renal transplant patients: a single-center experience. Transplantation Proceedings. 2009;41:4169-71.	Treatment
296	Yu X, Zhang B, Xing C, Sun B, Liu M, Zhang W, et al. Different effect of cyclosporine and tacrolimus on renal expression of P-glycoprotein in human kidney transplantation. Transplantation Proceedings. 2008;40:3455-9.	Population

Table 15 Summary table of non-randomised comparative studies excluded due to mixed population

Author	Design	N	Compares	Reason for Exclusion
Aoun et al 2013[53]	Non-randomized controlled trial	26 vs 10	BAS+**CSA**+MMF+CCS vs BAS+**TAC**+MMF+CCS	Age range <19 years: Mean age 14.1 (1.9), range [1-19]
Bunnapradist et al. 2003[54]	Retrospective clinical study	2393 vs 4686	**CSA**+MMF +CSS **TAC**+MMF +CCS	Primarily adult study: ~10 % aged 0-20 years ~72 % 21/55 years ~18 % >55 years Results combined for age
Ferrais et al 2005[55]	Historically controlled study	29 vs 29	CSA+**MMF**+CCS vs CSA+**AZA**+CCS	No age range specified. Mean(SD) age: 13.0(0.9) vs 12.0(0.2)
Imanishi et al 2011[56]	Non-randomized controlled trial	13 vs 10	BAS+**TAC PR**+MMF+CCS BAS+**TAC**+MMF +CCS	Primarily adult study: Mean age (SD) [range]: 38.2 (11.2) [17-62] vs 49.8 (14.8) [32-68]
Iorember et al 2010[57]	Historically controlled study	22 vs 22	**ATG**+**SRL**+CSA+CCS vs **BAS**+**MMF**+CSA+CCS[a]	Inclusion criteria states children <21 years; Mean (SD) 13.4 (NR) vs 13.28 (NR)
Kitada et al 2012[58]	Retrospective clinical study	23 vs 27	BAS+**TAC PR**+MMF+CCS BAS+**TAC**+MMF+CCS	Primarily adult study: Mean age (SD) [range]: 41.6 (NR) [11-62] vs 36.0 (NR) [8-62]
Kovac et al 2005[59]	Retrospective clinical study		**AZA**+CSA+CCS **BAS+MMF**+CSA+CCS	Primarily adult study: Mean age (SD) [range]: 41 (13) [13-65] vs 44 (10) [32-64]
Lucan et al. 2004[60]	Historically controlled study	154 vs 199 vs 114	**CSA+AZA**+CCS **CSA+ MMF**+CCS **TAC + MMF +** CCS	Pediatric participants represented 12 % of total cohort, mean age range from 2-69 %
Otukesh et al 2005[61]	Non-randomized controlled trial	100 vs 116	**MMF** + CSA + CCS[b] vs **AZA** + CSA + CCS	No age information, just stated participants were paediatric renal transplant recipients

Key: ATG, anti-lymphocyte globulin; AZA, azathioprine; BAS, basiliximab; MMF, mycophenolate mofetil; CCS, steroids; TAC, tacrolimus; CSA, ciclosporine; SRL, sirolimus; TAC, taclorimus; TAC PR, prolong release TAC.

Notes: b, MMF group, subdivided into those receiving MMF immediately after transplant (group 1), those receiving MMF following diagnosis of chronic rejection (group 2) and finally those convering to MMF several years after transplantation in the absence of chornic rejhection (group 3), only data from group 1 was considered.