Figure S1. Change in daily proteinuria in patients treated with immunosuppressants, stratified by timepoint. Change in daily proteinuria is expressed as ratio of means (response ratio) between different timepoints and baseline measurements. If a study reported several timepoint measurements, only the most common timepoints between the included studies were considered. Study arms with the same treatment within one study were included if they corresponded to different patient populations. Agrawal et al.: tacrolimus-responsive (first arm in the figure) and tacrolimus-resistant (second arm in the figure) patients; Mahmoud et al.: SRNS (first arm in the figure, Arm 2 in Table 1) patients and SDNS (second arm in the Figure, Arm 1 in Table 1) patients. ROM: ratio of means, 95%-CI: 95% confidence interval, N: number of patients in sample group, Tac: tacrolimus, CNI: calcineurin inhibitors; CsA: cyclosporine A; MMF: mycophenolate mofetil; CYC: cyclophosphamide, RTX: rituximab; ACEi/ARB - Treatment with either ACE alone, ARB alone, or a combination or both, Pred: prednisone, AH: antihypertensives, Asa: acetylsalicylate, chl: chloramphenicol; CCB: calcium channel blockers, AP: antiplatelets. Summary effect of the different follow-up timepoint subgroups is highlighted in grey.

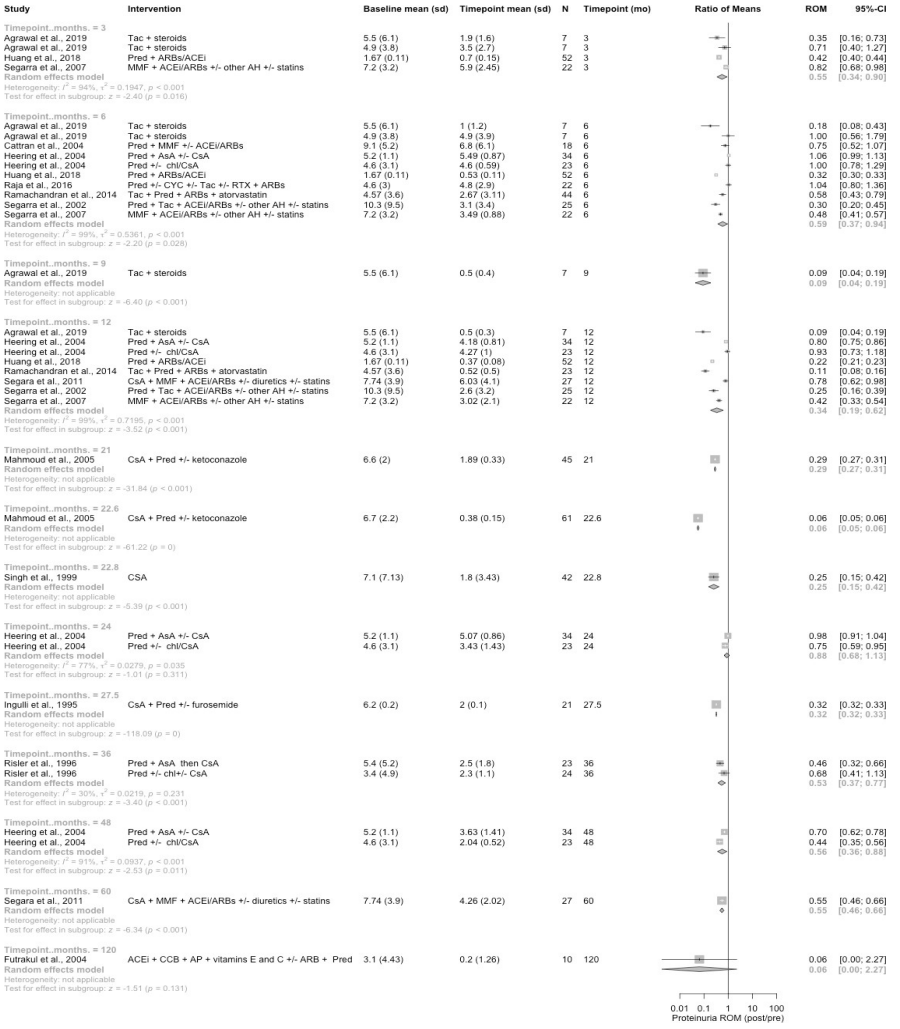

Figure S2. Change in UP/C ratio in patients treated with immunosuppressants. Change in UP/C ratio is expressed as ratio of means (response ratio) between last timepoint and baseline measurements. ROM: ratio of means, 95%-CI: 95% confidence interval, N: number of patients in sample group, Tac: tacrolimus; CsA: cyclosporine A; MMF: mycophenolate mofetil; CYC: cyclophosphamide; ACEi/ARB - Treatment with either ACE alone, ARB alone, or a combination or both, Pred: prednisone, MP: methylprednisolone, AH: antihypertensives, AZA: azathioprine, chl: chloramphenicol; CCB: calcium channel blockers. Summary effect of all studies, regardless of the type of IS therapy is highlighted in bold.

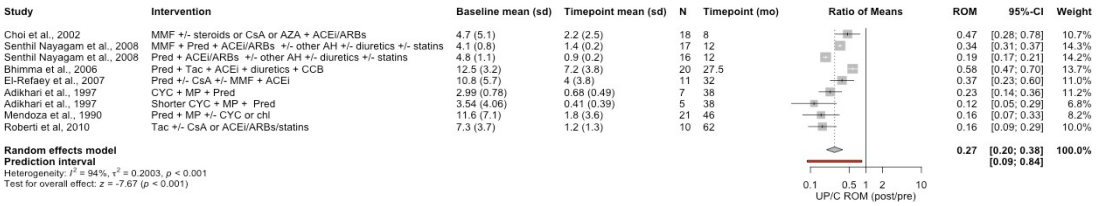

Figure S3. Change in eGFR in patients treated with immunosuppressants, stratified by timepoint. Change in eGFR is expressed as mean difference between different timepoints and baseline measurements. If a study reported several timepoint measurements, only the most common timepoints between the included studies were considered. Study arms with the same treatment within one study were included if they corresponded to different patient populations. Agrawal et al.: tacrolimus-responsive (first arm in the figure) and tacrolimus-resistant (second arm in the figure) patients; Gulati et al.: early-onset (first arm in the figure) patients and late-onset (second arm in the figure) of idiopathic FSGS. MD: mean difference, 95%-CI: 95% confidence interval, N: number of patients in sample group, Tac: tacrolimus, CNI: calcineurin inhibitors; CsA: cyclosporine A; MMF: mycophenolate mofetil; CYC: cyclophosphamide, RTX: rituximab; ACEi/ARB - Treatment with either ACE alone, ARB alone, or a combination or both, Pred: prednisone, MP: methylprednisolone, AH: antihypertensives, Asa: acetylsalicylate, chl: chloramphenicol; CCB: calcium channel blockers, AP: antiplatelets, AZA: azathioprine. Summary effect of all studies, regardless of the type of IS therapy is highlighted in bold. Summary effect of the different follow-up timepoint subgroups is highlighted in grey.

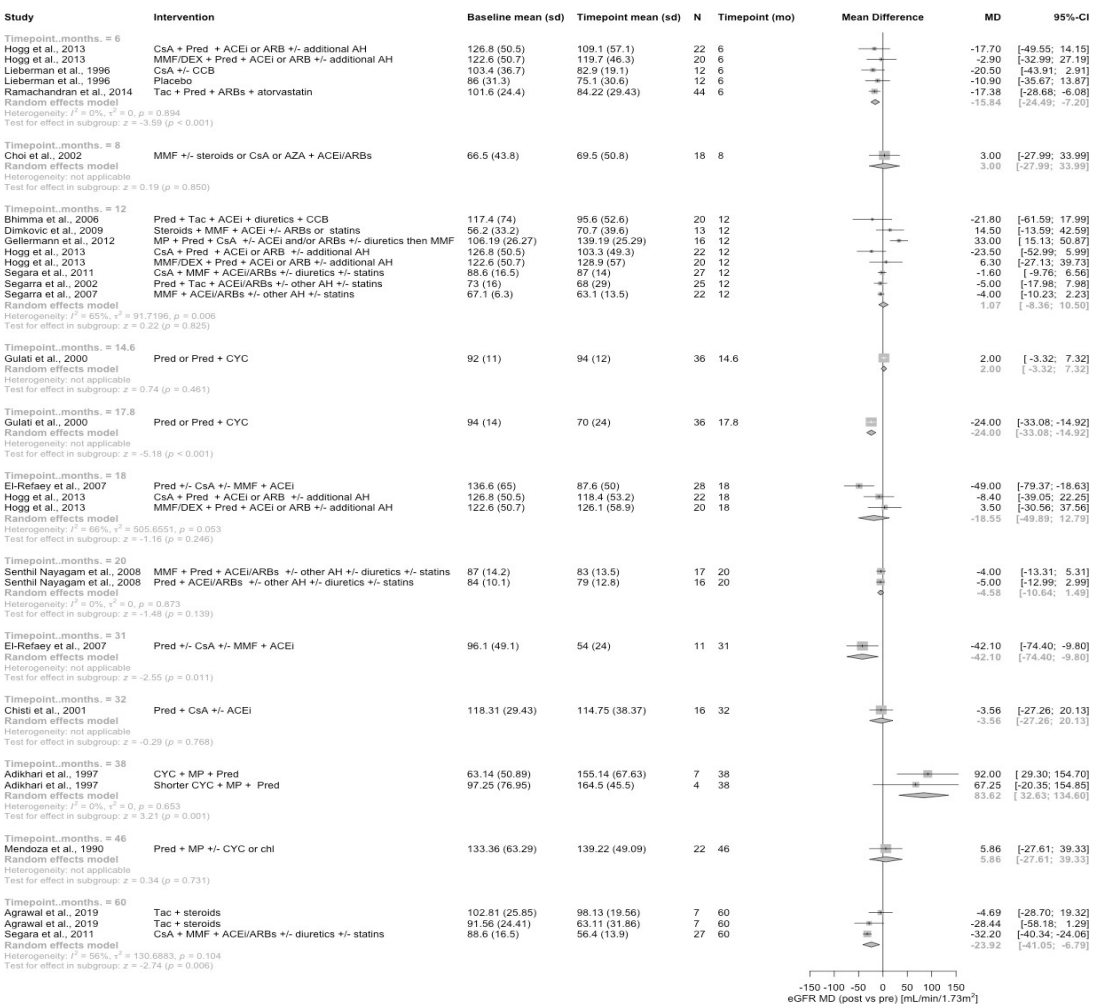

Figure S4. Correlation between the last reported follow-up timepoint and the eGFR mean difference from baseline to last reported follow-up timepoint.

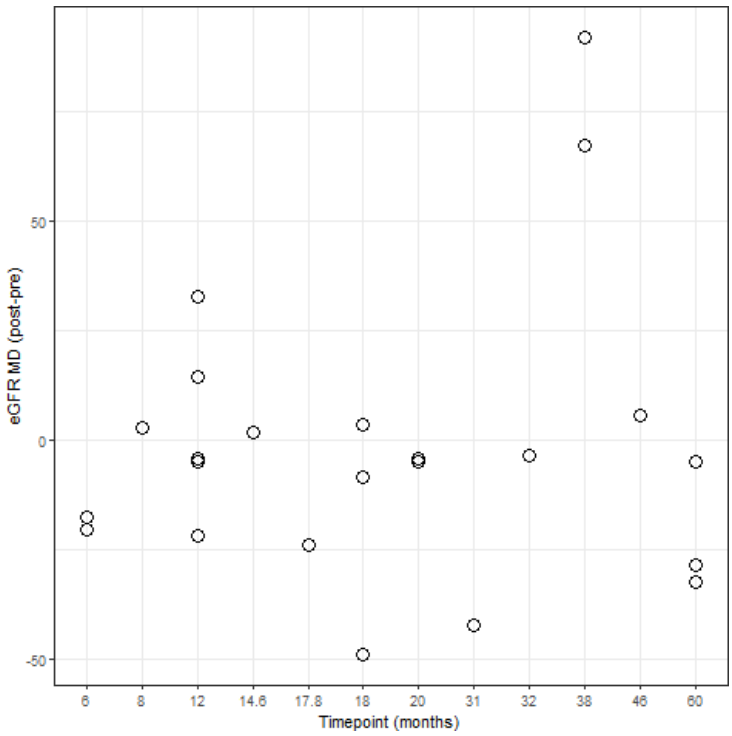

Table S1. Systematic literature review protocol for PubMed search

Search element		Search string
Population	**1**	((FSGS[TW] OR focal segmental glomerulosclerosis[TW] OR focal glomerular sclerosis[TW]) AND (primary[TW] OR idiopathic[TW])) OR ((glomerulosclerosis[TW] OR glomerulonephritis[TW] OR nephritis[TW]) AND (focal[TW] OR segmental[TW]))
Intervention/ Comparator	**2**	immunosuppress*[TW] OR immune suppress*[TW] OR immunot*[TW] OR corticosteroid*[TW] OR Steroids[mh:noexp] OR calcineurin Inhibitors[mh:noexp] OR prednisone[TW] OR prednisolone[TW] OR methylprednisolone[TW] OR dexamethasone[TW] OR cyclosporine[TW] OR tacrolimus[TW] OR inosine monophosphate dehydrogenase inhibitor[TW] OR IMPDH[TW] OR mycophenol*[TW] OR MMF[TW] OR azathioprine[TW] OR leflunomide[TW] OR cyclophosphamide[TW]
Clinical outcomes	**3**	proteinur*[TW] OR antiproteinuric effect[TW] OR nephrotic range[TW] OR protein excretion[TW] OR (urine protein to creatinine ratio)[TW] OR UP*C*[TW] OR uPCR[TW] OR creatinine[MeSH] OR Renal Insufficiency, Chronic[mh:noexp] OR ((chronic kidney disease[TW] OR CKD[TW]) AND (progress*[TW] OR stage[TW])) OR Kidney Failure, Chronic[mh:noexp] OR renal failure[TW] OR renal function[TW] OR kidney function[TW] OR kidney transplant*[TW] OR renal transplant*[TW] OR renal survival[TW] OR Renal Dialysis[MeSH] OR kidney dialysis[TW] OR Glomerular Filtration Rate[MeSH] OR eGFR[TW] OR estimated Glomerul* Filtration Rate[TW] OR slope of eGFR[TW] OR slope of estimated Glomerul* Filtration Rate[TW] OR renal plasma flow[TW] OR Glomerul* permeability[TW] OR ESKD[TW] OR ESKF[TW] OR ESRD[TW] OR ESRF[TW] OR RRT[TW] OR Renal Replacement Therapy[MeSH] OR acute kidney injury[TW] OR AKI[TW] OR edema[TW] OR aedema[TW] OR CHF[TW] OR chronic heart failure[TW] OR blood pressure[TW] OR cardiovascular[TW] OR hypertensi*[TW] OR adverse effect*[TW] OR adverse event*[TW] OR adverse reaction*[TW] OR adverse outcome*[TW] OR side effect*[TW] OR side event*[TW] OR side reaction*[TW] OR side outcome*[TW] OR undesirable effect*[TW] OR undesirable event*[TW] OR undesirable reaction*[TW] OR undesirable outcome*[TW] OR TEAE*[TW] OR SAE[TW] OR AEOI[TW] OR safety profile[TW] OR toxicit*[TW] OR Vital Signs[MeSH] OR disabilit*[TW] OR incapacit*[TW] OR symptomatic management*[TW] OR physical examination[TW] OR body weight[TW] OR clinical lab* analysis[TW] OR clinical lab* parameter[TW] OR Hyperkalemia[MeSH] OR albumin*[TW] OR potassium[TW] OR ACR[TW] OR UACR[TW] OR SCr[TW] OR Lipids[MeSH] OR lipid profile[TW] OR cholesterol[TW] OR triglycerides[TW] OR low density lipoprotein cholesterol[TW] OR LDL-C[TW] OR very low density lipoprotein cholesterol[TW] OR VLDL-C[TW] OR very low density lipoprotein triglycerides[TW] OR VLDL-TG[TW] OR high-density lipoprotein cholesterol[TW] OR HDL[TW] OR hyperlipidemia[TW] OR Hospitalisation*[TW] OR hospitalization*[TW] OR medical visit*[TW] OR hospital visit*[TW]
Final search	**4**	**1 AND 2 AND 3**
	5	**English language:** 4 AND (english[la])
	6	**Articles including abstract:** 5 AND (hasabstract[text])
	7	**Exclusion of non-human studies:** 6 NOT animals[MH:noexp]

	8 **Type of studies:** 44 NOT (Case Reports[Publication Type]OR letter[Publication Type] OR comment[Publication Type] OR editorial[Publication Type] OR patient education handout[Publication Type] OR Personal Narrative[Publication Type])

Table S2. Systematic literature review protocol for EMBASE search

Search element		Search string
Population	**1**	((FSGS:ab,ti,de OR "focal segmental glomerulosclerosis":ab,ti,de OR "focal glomerular sclerosis":ab,ti,de) AND (primary:ab,ti,de OR idiopathic:ab,ti,de)) OR ((glomerulosclerosis:ab,ti,de OR glomerulonephritis:ab,ti,de OR nephritis:ab,ti,de) AND (focal:ab,ti,de OR segmental:ab,ti,de))
Intervention/ Comparator	**2**	immunosuppress$:ab,ti,de OR "immune suppress$":ab,ti,de OR immunot$:ab,ti,de OR corticosteroid$:ab,ti,de OR 'Steroids'/de OR 'calcineurin Inhibitors'/de OR prednisone:ab,ti,de OR prednisolone:ab,ti,de OR methylprednisolone:ab,ti,de OR dexamethasone:ab,ti,de OR cyclosporine:ab,ti,de OR tacrolimus:ab,ti,de OR "inosine monophosphate dehydrogenase inhibitor":ab,ti,de OR IMPDH:ab,ti,de OR mycophenol$:ab,ti,de OR MMF:ab,ti,de OR azathioprine:ab,ti,de OR leflunomide:ab,ti,de OR cyclophosphamide:ab,ti,de
Clinical outcomes	**3**	proteinur$:ab,ti,de OR "antiproteinuric effect":ab,ti,de OR "nephrotic range":ab,ti,de OR "protein excretion":ab,ti,de OR "urine protein to creatinine ratio":ab,ti,de OR "UP/C$":ab,ti,de OR uPCR:ab,ti,de OR 'creatinine'/exp OR (("chronic kidney disease":ab,ti,de OR CKD:ab,ti,de) AND (progress$:ab,ti,de OR stage:ab,ti,de)) OR 'Kidney Failure'/de OR "renal failure":ab,ti,de OR "renal function":ab,ti,de OR "kidney function":ab,ti,de OR "kidney transplant$":ab,ti,de OR "renal transplant$":ab,ti,de OR "renal survival":ab,ti,de OR 'Renal Dialysis'/exp OR "kidney dialysis":ab,ti,de OR 'Glomerular Filtration Rate'/exp OR eGFR:ab,ti,de OR "estimated Glomerul$ Filtration Rate":ab,ti,de OR "slope of eGFR":ab,ti,de OR "slope of estimated Glomerul$ Filtration Rate":ab,ti,de OR "renal plasma flow":ab,ti,de OR "Glomerul$ permeability":ab,ti,de OR ESKD:ab,ti,de OR ESKF:ab,ti,de OR ESRD:ab,ti,de OR ESRF:ab,ti,de OR RRT:ab,ti,de OR 'Renal Replacement Therapy'/exp OR "acute kidney injury":ab,ti,de OR AKI:ab,ti,de OR edema:ab,ti,de Or aedema:ab,ti,de OR CHF:ab,ti,de OR "chronic heart failure":ab,ti,de OR "blood pressure":ab,ti,de OR cardiovascular:ab,ti,de OR hypertensi$:ab,ti,de OR "adverse effect$":ab,ti,de OR "adverse event$":ab,ti,de OR "adverse reaction$":ab,ti,de OR "adverse outcome$":ab,ti,de OR "side effect$":ab,ti,de OR "side event$":ab,ti,de OR "side reaction$":ab,ti,de OR "side outcome$":ab,ti,de OR "undesirable effect$":ab,ti,de OR "undesirable event$":ab,ti,de OR "undesirable reaction$":ab,ti,de OR "undesirable outcome$":ab,ti,de OR TEAE$:ab,ti,de OR SAE:ab,ti,de OR AEOI:ab,ti,de OR "safety profile":ab,ti,de OR toxicit$:ab,ti,de OR "vital sign$":ab,ti,de OR disabilit$:ab,ti,de OR incapacit$:ab,ti,de OR "symptomatic management$":ab,ti,de OR "physical examination":ab,ti,de OR "body weight":ab,ti,de OR "clinical lab$ analysis":ab,ti,de OR "clinical lab$ parameter":ab,ti,de OR 'Hyperkalemia'/exp OR albumin$:ab,ti,de OR potassium:ab,ti,de OR ACR:ab,ti,de OR UACR:ab,ti,de OR SCR:ab,ti,de OR 'Lipids'/exp OR "lipid profile":ab,ti,de OR cholesterol:ab,ti,de OR triglycerides:ab,ti,de OR "low density lipoprotein cholesterol":ab,ti,de OR "LDL-C":ab,ti,de OR "very low density lipoprotein cholesterol":ab,ti,de OR "VLDL-C":ab,ti,de OR "very low density lipoprotein triglycerides":ab,ti,de OR "VLDL-TG":ab,ti,de OR "high-density lipoprotein cholesterol:ab,ti,de" OR HDL:ab,ti,de OR hyperlipidemia:ab,ti,de OR Hospitali?ation$:ab,ti,de OR "medical visit$":ab,ti,de OR "hospital visit$":ab,ti,de

Final search	**4**	**1 AND 2 AND 3**
	5	**English language:** 4 AND English:la
	6	**Articles including abstract:** 5 AND [abstracts]/lim
	7	**Exclusion of non-human studies:** 6 NOT [animals]/lim
	8	**Type of studies:** 7 NOT ([letter]/lim OR [note]/lim OR [editorial]/lim OR 'case report'/de)

Table S3. Systematic literature review protocol for Cochrane search

Search element		Search string
Population	**1**	((FSGS:ti,ab,kw OR focal segmental glomerulosclerosis:ti,ab,kw OR focal glomerular sclerosis:ti,ab,kw) AND (primary:ti,ab,kw OR idiopathic:ti,ab,kw)) OR ((glomerulosclerosis:ti,ab,kw OR glomerulonephritis:ti,ab,kw OR nephritis:ti,ab,kw) AND (focal:ti,ab,kw OR segmental:ti,ab,kw))
Intervention/ Comparator	**2**	immunosuppress*:ti,ab,kw OR immune suppress*:ti,ab,kw OR immunot*:ti,ab,kw OR corticosteroid*:ti,ab,kw OR [mh ^"Steroids"] OR [mh ^"calcineurin Inhibitors"] OR prednisone:ti,ab,kw OR prednisolone:ti,ab,kw OR methylprednisolone:ti,ab,kw OR dexamethasone:ti,ab,kw OR cyclosporine:ti,ab,kw OR tacrolimus:ti,ab,kw OR inosine monophosphate dehydrogenase inhibitor:ti,ab,kw OR IMPDH:ti,ab,kw OR mycophenol*:ti,ab,kw OR MMF:ti,ab,kw OR azathioprine:ti,ab,kw OR leflunomide:ti,ab,kw OR cyclophosphamide:ti,ab,kw
Clinical outcomes	**3**	proteinur*:ti,ab,kw OR antiproteinuric effect:ti,ab,kw OR nephrotic range:ti,ab,kw OR protein excretion:ti,ab,kw OR (urine protein to creatinine ratio):ti,ab,kw OR UP*C*:ti,ab,kw OR uPCR:ti,ab,kw OR [mh "creatinine"] OR [mh ^"Renal Insufficiency, Chronic"] OR ((chronic kidney disease:ti,ab,kw OR CKD:ti,ab,kw) AND (progress*:ti,ab,kw OR stage:ti,ab,kw)) OR [mh ^"Kidney Failure, Chronic"] OR renal failure:ti,ab,kw OR renal function:ti,ab,kw OR kidney function:ti,ab,kw OR kidney transplant*:ti,ab,kw OR renal transplant*:ti,ab,kw OR renal survival:ti,ab,kw OR [mh "Renal Dialysis"] OR kidney dialysis:ti,ab,kw OR [mh "Glomerular Filtration Rate"] OR eGFR:ti,ab,kw OR estimated Glomerul* Filtration Rate:ti,ab,kw OR slope of eGFR:ti,ab,kw OR slope of estimated Glomerul* Filtration Rate:ti,ab,kw OR renal plasma flow:ti,ab,kw OR Glomerul* permeability:ti,ab,kw OR ESKD:ti,ab,kw OR ESKF:ti,ab,kw OR ESRD:ti,ab,kw OR ESRF:ti,ab,kw OR RRT:ti,ab,kw OR [mh "Renal Replacement Therapy"] OR acute kidney injury:ti,ab,kw OR AKI:ti,ab,kw OR edema:ti,ab,kw OR aedema:ti,ab,kw OR CHF:ti,ab,kw OR chronic heart failure:ti,ab,kw OR blood pressure:ti,ab,kw OR cardiovascular:ti,ab,kw OR hypertensi*:ti,ab,kw OR adverse effect*:ti,ab,kw OR adverse event*:ti,ab,kw OR adverse reaction*:ti,ab,kw OR adverse outcome*:ti,ab,kw OR side effect*:ti,ab,kw OR side event*:ti,ab,kw OR side reaction*:ti,ab,kw OR side outcome*:ti,ab,kw OR undesirable effect*:ti,ab,kw OR undesirable event*:ti,ab,kw OR undesirable reaction*:ti,ab,kw OR undesirable outcome*:ti,ab,kw OR TEAE*:ti,ab,kw OR SAE:ti,ab,kw OR AEOI:ti,ab,kw OR safety profile:ti,ab,kw OR toxicit*:ti,ab,kw OR [mh "Vital Signs"] OR disabilit*:ti,ab,kw OR incapacit*:ti,ab,kw OR symptomatic management*:ti,ab,kw OR physical examination:ti,ab,kw OR body weight:ti,ab,kw OR clinical lab* analysis:ti,ab,kw OR clinical lab* parameter:ti,ab,kw OR [mh "Hyperkalemia"] OR albumin*:ti,ab,kw OR potassium:ti,ab,kw OR ACR:ti,ab,kw OR UACR:ti,ab,kw OR SCr:ti,ab,kw OR [mh "Lipids"] OR lipid profile:ti,ab,kw OR cholesterol:ti,ab,kw OR triglycerides:ti,ab,kw OR low density lipoprotein cholesterol:ti,ab,kw OR LDL-C:ti,ab,kw OR very low density lipoprotein cholesterol:ti,ab,kw OR VLDL-C:ti,ab,kw OR very low density lipoprotein triglycerides:ti,ab,kw OR VLDL-TG:ti,ab,kw OR high-density lipoprotein cholesterol:ti,ab,kw OR HDL:ti,ab,kw OR hyperlipidemia:ti,ab,kw OR

		Hospitalisation*:ti,ab,kw OR hospitalization*:ti,ab,kw OR medical visit*:ti,ab,kw OR hospital visit*:ti,ab,kw
Final search	**4**	**1 AND 2 AND 3**
	5	**English language:** 4 AND (english[la])
	6	**Articles including abstract:** 5 AND (hasabstract[text])
	7	**Exclusion of non-human studies:** 6 NOT animals[MH:noexp]
	8	**Type of studies:** 7 NOT (Case Reports[Publication Type]OR letter[Publication Type] OR comment[Publication Type] OR editorial[Publication Type] OR patient education handout[Publication Type] OR Personal Narrative[Publication Type])

Table S4. Bias assessment for RCTs included in the SLR.

Reference	Selection bias (systematic differences between the comparison groups)				Performance bias (systematic differences between groups in the care provided, apart from the intervention under investigation)				Attrition bias (systematic differences between the comparison groups with respect to loss of participants)				Detection bias (bias in how outcomes are ascertained, diagnosed or verified)		
	An appropriate method of randomization was used to allocate participants to treatment groups	There was adequate concealment of allocation	The groups were comparable at baseline, including all major confounding and prognostic factors	Based on your answers to the above, in your opinion was selection bias present?	The comparison groups received the same care apart from the intervention(s) studied	Participants receiving care were kept 'blind' to treatment allocation	Individuals administering care were kept 'blind' to treatment allocation	Based on your answers to the above, in your opinion was performance bias present?	All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow-up)	a) How many participants did not complete treatment in each group? b) The groups were comparable for treatment completion	a) For how many participants in each group were no outcome data available? b) The groups were comparable with respect to the availability of outcome data	Based on your answers to the above, in your opinion was attrition bias present?	Investigators were kept 'blind' to participants' exposure to the intervention	Investigators were kept 'blind' to other important confounding and prognostic factors	Based on your answers to the above, in your opinion was detection bias present?
Canetta *et al.*, 2013	Unclear	No	Yes	Yes	Yes	No	No	Yes	Yes	a) MMF-DEX=6, CsA=15 b) Yes	a) MMF-DEX=6, CsA=15 b) Yes	No	No	No	Yes
Cattran *et al.*, 1999	Yes	No	Yes	No	Yes	Yes	No	No	Yes	a) CsA=2 ; Placebo=0 b) Yes	a) CsA=2; Placebo=0 b) Yes	No	No	No	Yes
Gipson *et al.*, 2011	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	a) Unclear b) Yes	a) Unclear b) Yes	No	No	No	Yes
Heering et al., 2004	No	Unclear	Yes	Yes	Yes	Unclear	Unclear	Unknown risk	Yes	a) Group=0, Group=1 b) Yes	a) Group=0, Group=1 b) Yes	No	Unclear	Unclear	Unknown risk
Lieberman *et al.*, 1996	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	a) CsA=4, Placebo=3 b) Yes	a) CsA=4, Placebo=3 b) Yes	No	No	No	Yes

Ren *et al*., 2013	Unclear	No	Yes	Yes	Yes	No	No	Yes	Yes	a) CYC=3, Tac=3 b) Yes	a) CYC=3, Tac=3 b) Yes	No	No	No	Yes
Senthil Nayagam et al., 2008	Yes	No	Yes	No	Yes	No	No	Yes	Yes	a) Group A=1, Group B=0 b) Yes	a) Group A=0, Group B=0 b) Yes	No	No	No	Yes
Tarshish *et al.*, 1996	No	Unclear	Yes	Yes	Yes	Unclear	Unclear	Unknown risk	Yes	a) Experimental=3, Control=2 b) Yes	a) Unclear b) Yes	No	Unclear	Unclear	Yes